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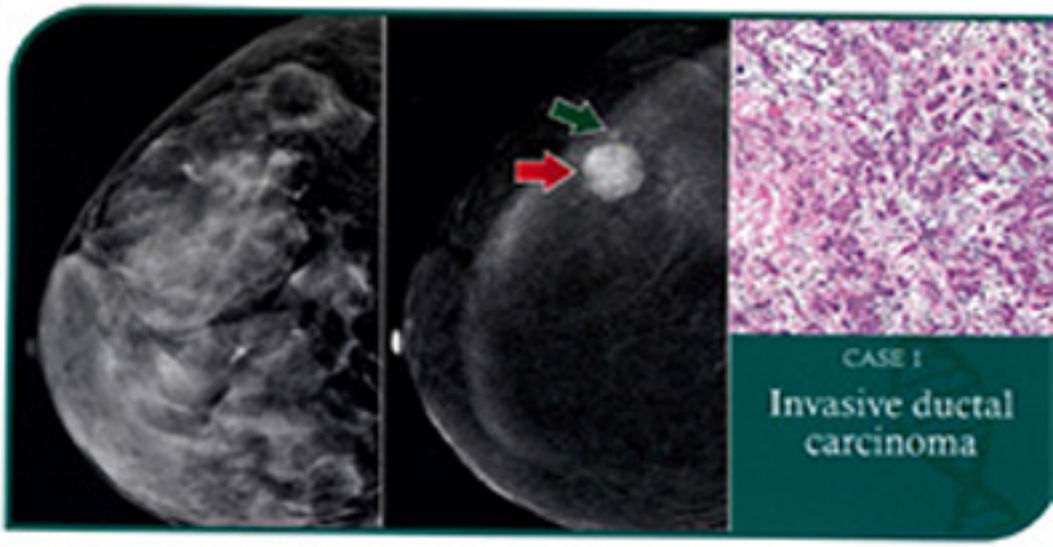
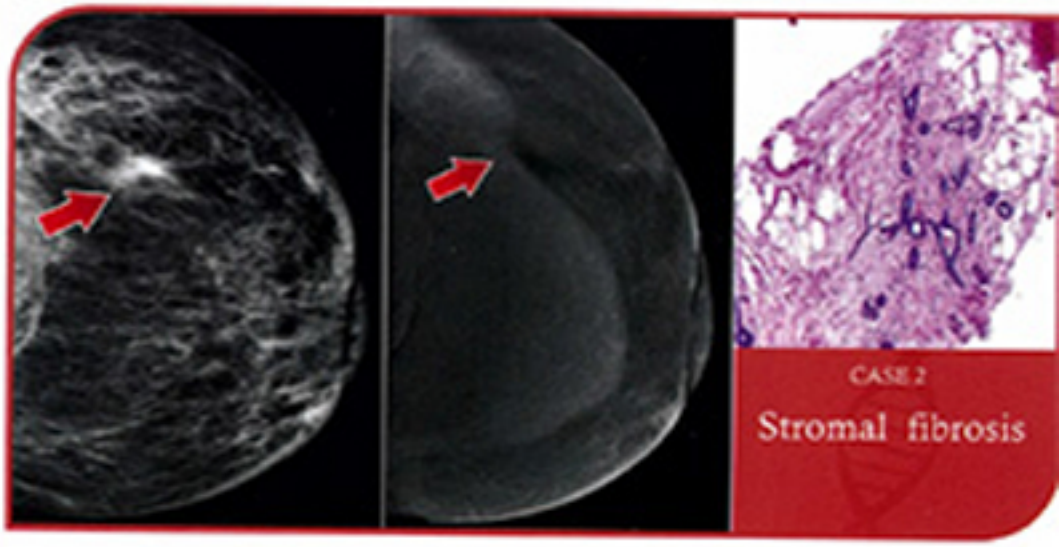
Highlights

Contrast Enhanced Spectral Mammography (CESM)





Description in detail is shown on page 71-74

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Editorial

Dear readers

It is with great pleasure that we bring you this eigth edition of the Bangkok Medical Journal. As always, we highlight some of the excellent work underway from doctors and nurses across the tertiary care sector working tirelessly to improve the quality and standard of care to patients.

In this edition, we bring your attention to the pioneering work of Dr.Wilaiporn Bhothisuwan and the extraordinary benefits of Contrast Enhanced Spectral Mammography (CESM). This innovative technique detects breast cancer, by determining the pattern of tissue contrast enhancement as well as detecting the extension of the disease. It improves diagnostic accuracy, giving anatomical, pathological and physiological imaging when compared with digital mammography and breast ultrasound. This technique not only saves the patient valuable time in the time, it takes to perform the tests and study the results. The case report and review article show the theory behind the process and a selection of real-life cases where this diagnostic tool was used to bring the patient a higher level of care. CESM should be the imaging modality of choice in detection and evaluation the extent of breast cancer, particularly in problem cases, or when conservative breast therapy is attempted. Dr Shanob Shoungshoti emphasized on his article on heterogeneity of unilateral multiple breast cancer: implications for biomarker testing those heterogeneity biomarkers may occur in multiple lesions in the same breast and more frequent differences at genetic levels. The topic fatal and near fatal ascending aortic dissection are serious complication with difficult surgery is the best way to safe life. The article on mydriatic is a pilot study to present a new method of mydriatic application before eye ground examination. The study shows to use mydriatic with less amount and less time than the conventional method but the result is the same.

We are also delighted to bring you the latest findings from Dr.Vajara Phiphobmongkolon Minimally Invasive Plate Osteosynthesis (MIPO) with Vertical Incisions for Midshaft Clavicular Fractures: a Surgical Technique and Results. This article reviews the advantages of MIPO vertical incisions as opposed to horizontal incisions, with better clinical outcomes and recovery rates of patients. We also highlight the diagnosis and treatment for the most common of shoulder traumas with an image review of a fracture of the anterior labrum with dislocation. We trust that you will find the journal elucidating, informative and inspiring, whether you are in Thailand or abroad, whether you are a nursing student, intern, medical doctor or professor. The Bangkok Medical Journal is committed to bring you valuable insights that can be shared, applied and replicated with your colleagues and wider teams. Our ultimate aim is to elevate the services offered to patients, with the improvement of patient care at the forefront of our dedicated services to improving health outcomes.

Chirotchana Suchato, MD
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Original Article

Prevalence of Carotid Artery Disease and Risk Factors in Asymptomatic Thai Population using Carotid Duplex Ultrasonography at the Check-up Clinic, Health Promotion Center at Bangkok Hospital

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Keywords: carotid artery disease, asymptomatic, carotid duplex ultrasonography, prevalence

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OBJECTIVE: To examine the prevalence of carotid artery disease and to determine risk factors for carotid duplex abnormalities among asymptomatic Thai subjects.

MATERIALS AND METHODS: The cross-sectional observation study was conducted in a sample of patients (Thai population) who took an annual health check-up at the Bangkok Medical Center (BMC) over a 10 month period from June 1, 2011 to March 31, 2012. A total of 2,105 subjects were enrolled and underwent a carotid duplex examination using the standard procedure. The results from the carotid duplex ultrasonography and risk factors that contribute to carotid artery abnormalities were recorded and analyzed using a multiple logistic regression method and a prevalence rate ratio.

RESULTS: The study enrolled 2,105 Thai participants aged 25-79 years old with a mean of age of 54 ± 10.4 years. The population was equally divided by gender, and 44% of subjects were current smokers and 25% of the patients were overweight. Approximately 30.5% of participants had hypertension (HT) and 9.3% had diabetes mellitus (DM). Abnormal carotid duplex examinations were found in 912 cases accounting for 45.7% of the participants.

Atheromatous plaque and thickening of the intimal media thickness was observed in 784 cases (37.2%) and 314 cases (14.9%) respectively. Internal carotid stenosis results were detected including 11 mild, 9 moderate and 2 severe stenotic cases; however, no carotid occlusion reported. Underlying HT and DM were related to abnormal duplex results. Factors including increasing age ($p < 0.001$), male gender (odds ratio (OR) 1.5, 95% confidence interval (CI) 1.2-2.0), and HT associated (OR 2.4, 95% CI 1.8-3.1) were associated with carotid atherosclerotic disease observed by the duplex examination.

CONCLUSION: The prevalence of atherosclerotic carotid arteries detected by duplex ultrasonography was approximately 45% among asymptomatic Thai population who took an annual health check at the BMC. Atheromatous plaque is the most common finding and significant (moderate to severe) internal carotid artery (ICA) stenosis was observed in 0.5% of participants. Factors including age, male gender, DM, and HT were associated with atherosclerotic carotid disease. High fasting plasma glucose (FPG) and low-density lipoprotein (LDL) were also related to abnormal carotid duplex results. The carotid duplex examination provided health information to the participants to help control risk factors and to raise awareness of cerebrovascular disease.

Carotid artery disease (CAD) is caused by an accumulation of cholesterol plaque or atherosclerosis resulting in the thickening of the arterial wall at the intima media layer. Atherosclerotic plaques lead to a reduction in the size of arterial diameters and ultimately stenosis. Large plagues can potentially disrupt arterial blood flow and eventually reduce blood supply to the cerebral hemispheres.[1] Carotid plaque is established as an important risk factor for cerebrovascular disease or stroke.[2]

A systemic review and meta-analysis from 40 studies conducted in subjects worldwide from 1966-2007 revealed that moderate stenosis and more (≥ 50%) were associated with gender and age. In subjects aged less than 70 years old, the prevalence of stenosis was 4.8% in men and 12.5% in women. In subjects aged 70 years and older, the prevalence was 2.2% and 6.9% in men and women respectively.[3]

In Thailand, a study of extracranial internal carotid artery (ICA) and intracranial artery stenosis in asymptomatic subjects aged 45 years and older revealed that the prevalence of moderate stenosis of the ICA was 1.5% and intracranial artery stenosis was 5%. In people of 60 years and older, HT and ischemic heart disease were associated with plague formation of the extracranial ICA.[4]

The US Preventive Service Task Force has addressed important risk factors for CAD including aging, male gender, HT, smoking, hyperlipidemia and heart disease. These established risk factors are also related to cardiovascular disease risk.[5] In addition, a study showed that Thai elders with ischemic stroke were 4 times more likely to have moderate to severe carotid arterial stenosis.[6] Moreover, people who had 60-99% ICA stenosis would have a likelihood of suffering large artery disease stroke, lacunar or cardioembolic stroke at a rate of 9.9%, 6% and 2.1%, respectively during 5 years.[7]

The intimal media thickness (IMT) can be used as a predictor for vascular disease. The carotid IMT has been linked to HT and stroke.[8] A study of cervical carotid IMT in 5,855 elderly patients, without a history of cardiovascular disease, revealed that for each 0.2mm of common carotid artery (CCA) IMT thickening the risk of ischemic stroke and myocardial infarction increased by 1.27 times and for each 0.55mm of ICA thickening the risk increased by 1.3 times.[9] In addition, HT and ischemic stroke were linked to CCA IMT thickening.[8]

Clinical manifestations of ICA diseases can be divided into two syndromes consisting of cerebral hemispheric infarct and ophthalmic ischemia. Brain parenchymal symptoms include motor weakness, abnormal movement, sensory disturbance, dysphasia, dysphagia, and visuospatial neglect. Ophthalmic symptoms include amaurosis fugax and visual impairment which can be temporary (retinal transient ischemic attack) or progressive to permanent visual loss with central retina occlusion.[7]

There are several screening and diagnostic tests including magnetic resonance angiography (MRA), computerized tomography (CT) or computerized tomography angiogram (CTA) and carotid angiography. However, the carotid duplex ultrasonography is a cost-effective tool for carotid artery disease diagnosis. The duplex examination is non-irradiating, time-saving and is accessible bedside. The carotid duplex test examines the carotid artery and vertebral artery systems which provide blood supply to both the anterior and posterior cerebral circulation. The examination can detect occlusion, stenosis, abnormal plagues in lumens of the carotid system and the IMT of arterial vessels. The IMT reflects abnormality of the arterial wall which in turn leads to subsequent stenosis or obstruction leading to inadequate blood supply to the brain.[10] In the present day, carotid duplex ultrasound is a convenient procedure with high resolution and accuracy.[11,12]

Patients with asymptomatic CAD including atheromatous plague, thickening of the IMT or stenosis are supposed to follow recommendations for stroke prevention to reduce the risk of disease progression. HT should be controlled to remain under 140/90mmHg.[13] LDL ought to be kept below 100mm/dL using statin medication[12] and cessation of smoking is compulsory to reduce risk. Since carotid artery disease is a risk factor of cardiovascular disease and stroke, patients with an existing or suspected carotid artery disease should adopt lifestyle changes appropriate to both developing ischemic heart disease and stroke. This includes maintaining a healthy body mass index (BMI) in the range of 18.5-24.9 and doing enough aerobic exercise.[13]

Treatment is considered for symptomatic carotid patients with moderate to severe stenosis (≥ 50% stenosis) and asymptomatic stenosis with a threshold of 60%. A carotid endarterectomy may be performed to directly remove atheromatous plague to re-canalize vessel diameters. Carotid stenting may be considered as an alternative option to insert a stent to widen the arterial lumen without major surgical procedures required. Treatment options are suitable for particular conditions.[14] A review of 11 studies comparing efficacy and safety between carotid endarterectomy and stenting, conducted in 4,796 patients, showed that carotid endarterectomy provided more efficacy in the short-term (a year). However, there was no significant difference between both procedures in middle-term efficacy (1 to 4 years). Conversely, carotid artery stenting provided lower rates of cranial nerve injury and myocardial infarction. Comparing endarterectomy with medication and medication alone in asymptomatic patients showed that combination therapy provided slightly more efficacy. There were less ipsilateral strokes and less intra-operative deaths than in patient's taking medication alone (at a ratio of 5:11).[15]

Most studies regarding CAD have been conducted in symptomatic patients; however asymptomatic cases are vitally

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important since they carry a risk factor for cardiovascular disease and stroke. A comprehensive carotid research among Thai populations has not been undertaken. Once carotid arterial disease is diagnosed and recognized, clinicians can effectively provide useful interventions to patients in order to reduce subsequent comorbidities.

Material and Methods

Research Method

The study design was a cross-sectional and observational study.

Population

The study was conducted in an asymptomatic Thai population who took an annual health check-up at the BMC during a 10 month period from June 1, 2011 to March 31, 2012. A total of 2,105 participants who had never previously experienced stroke were enrolled in the study. Patients from other ethnic groups, and patients with established CAD such as amaurosis fugax, transient ischemic attack or unknown cause drop attack and a history of stroke were excluded from the study.

Data collection

Enrolled participants were examined for CAD by experienced sonographers with two-dimenstional (2-D), colour-mode and pulse-wave doppler ultrasonography together with a standard procedure. The off-line results were completely interpreted following standard criteria.[16] Demographic data were collected including age, gender, exercise activity, smoking and drinking status. Comorbid diseases including DM and HT were also recorded. Body and biochemical profiles were measured, blood pressure, BMI, fasting plasma glucose (FPG) and lipid profile (total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL) and triglyceride (TG)). Carotid duplex examinations were categorised into normal and abnormal results. Abnormal results were classified according to the severity category following the consensus criteria for carotid stenosis into plaque of the Society of Radiologists, the thickening of the IMT, and stenosis (mild, moderate and severe) (Table1).

Data Analysis: SPSS (Statistical Package for Social Science) version 19.0

1. Demographic data including gender, age, carotid results and risk factors were presented by descriptive analysis of frequency, percentage, mean, and standard deviation.

2. Risk factors for contributing abnormal carotid artery were analyzed using a multiple logistic regression method and risk was also reported as a prevalence rate ratio.

Table 1: Degrees of Carotid Artery Stenosis.[16]

Severity	Description
Normal	- Normal velocities (< 125cm/s) - No plaque
IMT	- 0-15% subcategory - Mild intimal thickening - PSV < 125cm/s
Plaque	- 0-15% subcategory - Normal velocities - Minimal plaque
Mild	- 16-49% Stenosis - Normal velocities - Plaque ≥ 2mm thickness - PSV < 125cm/sec - Min spectral turbulence
Moderate	- 50-69% Stenosis - PSV > 125cm/s with spectral turbulence and plaque; ICA:CCA = 2.0-3.99
Severe	- > 70% Stenosis - PSV > 230cm/s with one of following: EDV>100cm/s or ICA:CCA > 4.0 with spectral turbulence
Occlusion	- 100% occlusion No flow by spectral, color, and if available by power Doppler - Plaque or thrombus present on B mode

IMT = Intimal media thickness, PSV = peak systolic velocity, ICA = internal carotid artery, CCA = common carotid artery, EDV = end diastolic velocity

Results

Demographic data

The majority of enrolled participants were between 40-59 years of age with the mean of 54.1 ± 10.4 SD and ages ranged between 25 and 89 years old. Male and female patients were approximately balanced proportionally (50.8% & 49.2%). Most participants had a normal BMI but 24.2% (around a fourth) fell into the overweight category (Table 2).

Over half of participants did not smoke while 44.6% were active smokers, and 6.3% of subjects were regular drinkers whereas most subjects (61.7%) did not consume alcohol. About 42.2% of subjects occasionally exercised and 45.8% performed regular exercise (Table 6). Approximately 30.5 % of subjects had HT and 9.3% of them were diabetic (Table 3).

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Carotid study results

A total of 2,105 participants underwent a carotid duplex examination, 912 cases were found to have an abnormal carotid artery accounting for a prevalence of 45.7%. Degrees of abnormal severity are classified in Table 4 below. Plaque was found in 784 cases (37.2% of participants) and the frequency of IMT thickness was 14.9% (314 cases). ICA stenosis was reported, including mild stenosis, in 11 cases, moderate in 9 cases and severe in 2 cases but there was no occlusion observed.

There was a significantly higher prevalence of abnormal carotid arteries in the elderly, in males, and in patients with higher BMI, who are smoking and drinking alcohol ($p < 0.05$). A history of HT and DM were also statically different in the prevalence of abnormal results (Table 3 and 5).

Body and biochemical profiles

Blood pressure ranged within normal levels for 18.3% of subjects. 19.1% of participants had pre-hypertension and 27.7% had grade-I HT. There was a significant difference in the prevalence of an abnormal carotid study among those with higher degrees of blood pressure. Thirty six percent of subjects were found to have a FPG of more than 100 mg/d and there was a higher prevalence of abnormal carotid studies in the higher FPG group (Table 4).

In the lipid profile study, those who had high levels of LDL, cholesterol and TG were 54.6%, 59.8% and 25.3% respectively. There was no association between TG, cholesterol, and HDL levels in males with carotid abnormality but lower HDL levels in women was statistically associated to abnormal carotid results ($p = 0.02$).

Risks for acquiring an abnormal carotid study (Table 6)

Using logistic regression analysis showed risks factors for acquiring abnormal results. Age was an independent factor and a dose-response trend was observed from the analysis. Patients aged under 40 were classified as a reference and increasing age was found to be a risk factor to identifying carotid abnormality ($p < 0.001$).

Male patients were 1.5 times more likely to have an abnormal carotid study (95% CI 1.2-2.0). HT associated with carotid abnormality (OR 2.4, 95% CI 1.8-3.1) whereas BMI, smoking, alcohol drinking and exercise status was not significantly linked to abnormal results.

For the biochemical profile, the relative risk of having FPG ≥ 100mg/dL and LDL ≥ 130mg/dL for acquiring an abnormal carotid examination were 1.3 (95% CI,1.0-1.6) and 1.4 (95% CI,1.0-2.0) respectively. Higher HDL level also showed a protective effect against abnormal carotid duplex, but it was not statistically significant (0.7-1.2, 95% CI).

Table 2: Patient characteristics.

Group Categories	Carotid duplex study n (%)		
	Normal	Abnormal	Total
Patients (n)	1,193	912	2,105
Age (year)			
≤ 29	9 (0.8)	1 (0.1)	10 (0.5)
30 - 39	117 (9.8)	10 (1.1)	127 (6.0)
40 - 49	472 (39.6)	138 (15.1)	610 (29.0)
50 - 59	413 (34.6)	332 (36.4)	745 (35.4)
60 - 69	154 (12.9)	281 (30.8)	435 (20.6)
≥ 70	28 (2.3)	150 (16.5)	178 (8.5)
Mean ± SD	50.18 ± 9.01	59.33 ± 9.87	54.14± 10.43
(min, max)	(25, 79)	(29, 89)	(25, 89)
Sex			
Male	550 (46.1)	519 (56.9)	1069 (50.8)
Female	643 (53.9)	393 (43.1)	1036 (49.2)
BMI			
Underweight (≤ 18.4)	41 (3.4)	27 (3.0)	68 (3.2)
Normal (18.5-24.9)	694 (58.2)	476 (52.2)	1170 (55.6)
Overweight (25-27.9)	278 (23.3)	231 (25.3)	509 (24.2)
Pre-obese (28-29.9)	93 (7.8)	93 (10.2)	186 (8.8)
Obese (≥ 30.0)	87 (7.3)	85 (9.3)	172 (8.2)
Mean ± SD	24.32 ± 3.98	24.95 ± 3.71	24.59 ± 3.88
(Min, Max)	(13.09, 52.22)	(13.93, 38.96)	(13.09, 52.22)

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Table 3: Correlation between underlying diseases and carotid results.

Underlying	Carotid n (%)		*p*
	Normal	Abnormal	
Hypertension (HT)			< 0.001
No	1023 (85.75)	590 (64.69)	
Yes	120 (10.06)	278 (30.48)	
Unknown	50 (4.19)	44 (4.82)	
DM			< 0.001
No	1103 (92.46)	783 (85.86)	
Yes	40 (3.35)	85 (9.32)	
Unknown	50 (4.19)	44 (4.82)	

Table 4: Classification of the severity of abnormal carotid artery. (n = 2,105)

Level	Abnormal carotid n (%)
Plaque	784 (37.2
IMT	314 (14.9)
Stenosis	
Mild	11 (0.5)
Moderate	90 (0.4)
Severe	2 (0.1)
Occlusion	-

IMT = Intimal media thickness

Table 5: Correlation between blood pressure (BP), Lab results and carotid duplex results.

Underlying	Carotid n (%)		*p*
	Normal	Abnormal	
Blood pressure (BP)			< 0.001
Optimal	491(41.16)	174 (19.08)	
Normal	255(21.37)	167 (18.31)	
High normal	216(18.11)	205 (22.48)	
Hypertension (HT)			< 0.001
Grade 1 (mild)	180 (15.09)	253 (27.74)	
Grade 2 (moderate)	36 (3.02)	81 (8.88)	
Grade 3 (severe)	11 (0.92)	28 (3.07)	
Unknown	4 (0.34)	4 (0.44)	
Fasting plasma glucose (FPG)			< 0.001
< 100 mg/dl	930 (77.95)	584 (64.04)	
≥ 100 mg/dl	262 (21.96)	328 (35.96)	
Unknown	1 (0.08)	0	
Low-density lipoprotein (LDL)			0.006
< 130 mg/dl	624 (52.31)	413 (45.29)	
≥ 130 mg/dl	568 (47.61)	498 (54.61)	
Unknown	1 (0.08)	1 (0.11)	
Cholesterol			0.112
< 200 mg/dl	529 (44.34)	367 (40.24)	
≥ 200 mg/dl	663 (55.57)	545 (59.76)	
Unknown	1 (0.08)	0 (0)	
High-density lipoprotein (HDL); Male			0.065
≤ 40 mg/dl	127 (23.09)	96 (18.5)	
> 40 mg/dl	423 (76.91)	423 (81.5)	
High-density lipoprotein (HDL); Female			0.024
≤ 50 mg/dl	115 (17.88)	93 (23.66)	
> 50 mg/dl	528 (82.12)	300 (76.34)	
Triglyceride (TG)			0.058
< 150 mg/dl	939 (78.71)	681 (74.67)	
≥ 150 mg/dl	253 (21.21)	231 (25.33)	
Unknown	1 (0.08)	0 (0)	

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Table 6: Factors related to the carotid duplex results analyzed by multiple logistic regressions.

Factor	Carotid n (%)		OR (95% CI)	*p*
	Normal	Abnormal		
Age (year)				
< 40	126 (10.6)	11 (1.2)	1	
40 - 49	472 (39.6)	138 (15.1)	2.7 (1.4-5.2)	0.003
50 - 59	413 (34.6)	332 (36.4)	6.9 (3.6-13.3)	<0.001
60 - 69	154 (12.9)	281 (30.8)	15.3 (7.8-30.0)	<0.001
> 70	28 (2.3)	150 (16.5)	42.1 (19.5-90.7)	<0.001
Sex				
Female	643 (62.1)	393 (37.9)	1	
Male	550 (51.5)	519 (48.5)	1.5 (1.2-2.0)	<0.001
BMI				
Normal (≤ 24.99)	735 (59.4)	503 (40.6)	1	
Overweight (25 - 27.99)	278 (54.6)	231 (45.4)	0.9 (0.7-1.1)	0.389
Pre obese (28 - 29.99)	93 (50.0)	93 (50.0)	1.1 (0.7-1.5)	0.696
Obese (> 30.00)	87 (50.6)	85 (49.4)	1.0 (0.6-1.5)	0.986
Smoke				
Non Smoking	952 (58.9)	663 (41.1)	1	
Smoking	93 (55.4)	75 (44.6)	1.2 (0.8-1.8)	0.325
Quit	93 (44.1)	118 (55.9)	1.0 (0.7-1.5)	0.875
Alcohol				
No Alcohol Drinking	733 (61.44)	563 (61.73)	1	
Occasional Drinking	361 (30.26)	240 (26.32)	0.9 (0.7-1.2)	0.690
Regular Drinking	50 (4.19)	57 (6.25)	1.3 (0.8-2.2)	0.260
Quit	2 (0.17)	3 (0.33)	0.6 (0.1-5.6)	0.677
Exercise				
Regular Exercise	314 (54.2)	265 (45.8)	1	
Occasional Exercise	624 (57.8)	456 (42.2)	1.2 (0.9-1.5)	0.134
No Exercise	204 (59.6)	138 (40.4)	1.0 (0.8-1.5)	0.706
Hypertension (HT)				
No	1023 (63.4)	590 (36.6)	1	
Yes	120 (30.2)	278 (69.8)	2.4 (1.8-3.1)	<0.001
Fasting Blood Sugar (FBS)				
< 100 mg/dl	930 (61.4)	584 (38.6)	1	
> 100 mg/dl	262 (44.4)	328 (55.6)	1.3 (1.0-1.6)	0.042
Low-density lipoprotein (LDL)				
< 130 mg/dl	624 (60.2)	413 (39.8)	413 (39.8)	1
≥ 130 mg/dl	568 (53.3)	498 (46.7)	498 (46.7)	1.4 (1.0-2.0)
Cholesterol				
< 200 mg/dl	529 (59.0)	367 (41.0)	367 (41.0)	1
≥ 200 mg/dl	663 (54.9)	545 (45.1)	545 (45.1)	1.2 (0.8-1.7)
High-density lipoprotein (HDL)				
≤ 40 (male): ≤ 50 mg/dl(female)	951 (56.8)	723 (43.2)	723 (43.2)	1
> 40 (male): > 50 mg/dl(female)	242 (56.2)	189 (43.8)	189 (43.8)	0.9 (0.7-1.2)
TG				
< 150 mg/dl	939 (58.0)	681 (42.0)	681 (42.0)	1
≥ 150 mg/dl	235 (52.3)	231 (47.7)	231 (47.7)	1.1 (0.9-1.4)

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Discussion

Carotid atherosclerotic disease is common in patients with ischemic stroke and transient ischemic attack accounting for 4-12% of cases. The prevalence of asymptomatic carotid stenosis in developed countries was 2-8% in people with risk factors and they were twice as likely to develop acute ischemic stroke.[17]

A study performed in Thailand showed that acute cerebral ischemia was caused by ICA stenosis in approximately 4-5% of cases.[6] Asymptomatic carotid stenosis is an important disease that may cause stroke or can be an indicator for other atherosclerosis. Carotid disease is a marker for comorbid poly-vascular diseases, for instance coronary artery disease and peripheral artery disease. The American College of Cardiology recommended carotid endarterectomy and alternative stenting in asymptomatic carotid stenosis of 80% either prior to or combined with coronary artery bypass surgery.[18]

The annual rate of ipsilateral stroke associated with asymptomatic carotid stenosis is 2-4% and risk can be reduced to <1% by medical therapy. Although guidelines in management of carotid stenosis are marginally different between countries, risk factors modification and antiplatelet are commonly recommended.[19] Carotid revascularizations in asymptomatic stenosis including endarterectomy and stenting are advised in several circumstances.[20]

This study is a hospital-based cross-sectional study and aims to identify concealed carotid disease in the general population. These results may not represent the prevalence in the community, however, the number of enrolled participants in this study is sizable and sufficient to characterize carotid issues experienced in Thai populations who have never previously experienced cerebrovascular disease. The study showed that the prevalence of asymptomatic carotid abnormalities examined by a carotid duplex scan was 45% and the abnormalities consist of stenosis 1%, plaques 37.2% and thickening of the IMT 14.9% of total participants. Interestingly, abnormal carotid examinations were identified in young people (49 year olds and younger), which suggests that active atherosclerotic disease can develop at a younger age. High BP, FPG, and LDL on the examination day, indicating poor control of risk factors, were linked to abnormal duplex findings.

The high prevalence of abnormal carotid duplex ultrasonography in asymptomatic Thai middle-age populations, with or without risks of stroke, reflects the high magnitude of extracranial atherosclerosis. The significance of risk factors including age, gender (male), DM, hypercholesterolemia and HT correlated with the carotid artery abnormalities.

A regular carotid duplex check-up would, at least, be helpful to identify people at risk and encourage people to be concerned with their cerebrovascular risks. In spite of the fact that subjects may not require surgical or endovascular stenting for stenosis, atherosclerotic pathology of the carotid artery including plaques and thickening of the IMT will alert them to their cerebrovascular risks and also other co-existing vascular disease. Information obtained from the carotid duplex examination has provided participants with information to help control risk factors and to improve their awareness of cerebrovascular disease. Combined with clinical data, the carotid duplex ultrasonography provides useful information, as a preventive program for stroke and poly-vascular disease, and in appropriate situations the duplex scan should be incorporated.

Conclusion

The abnormal carotid arteries that were detected by the carotid duplex examinations were prevalent (approximately 45%) among asymptomatic populations who took an annual health check at the BMC. Atherosclerotic plaque is the most common finding and significant (moderate to severe) ICA stenosis was found in 0.5% of participants. Factors including age, gender (male), DM, and HT are associated with atherosclerotic carotid disease. High plasma glucose and LDL are linked to abnormal carotid duplex scans. Early control of risk factors will reduce atherosclerotic carotid disease and delay the progression of carotid atherosclerosis.

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Occurrence of Venous Thromboembolism and Outcomes of Preventive Protocols at the Bangkok Hospital Medical Center: a Retrospective Review of Years 2012-2013

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OBJECTIVE: To determine the occurrence of venous thromboembolism (VTE) of patients at the Bangkok Hospital Medical Center (BMC). To collect data of VTE patients at the BMC about their characteristics, underlying diseases, presenting symptoms and outcomes of diseases. Evaluate the outcome of preventive methods of VTE when using the BMC protocol.

MATERIALS AND METHODS: The retrospective review was conducted from January 1, 2012 to December 31, 2013. The total number of patients diagnosed with VTE is 190 patients. The patients were divided into two groups; in the first group were patients who had been diagnosed in the year 2012, and were not using the preventive protocol, and the second group, were patients who had been diagnosed in the year 2013, and were using the preventive protocol. In both groups, data was collected about their characteristics, underlying diseases, presenting symptoms, and outcomes. Then we further divided patients from both groups into two categories by using BMC protocol criteria; high thrombosis risk and low thrombosis risk. Following this categorisation, we used the Statistical Package for the Social Sciences (SPSS) program to analyze the data collected. We compared populations across both years to verify if there was any difference in any aspect of the baseline characteristics. We evaluated the outcomes of patients who did not develop VTE as a result of using the preventive protocol by comparing high thrombosis risk patients to low thrombosis risk patients across both years to verify if there were any differences in the number of patients who did not receive the protocol (2012), and patients who received the protocol (2013).

RESULTS: There were 190 patients with VTE, 104 patients in 2012 (54.73%) and 86 patients in 2013 (45.27%). Their mean age was 63.52 ± 17.70 years. Ninety two patients (48.42%) are Thai nationals, while 98 patients (52.58%) are non-Thai nationals. There were 76 inpatient department (IPD) patients (40%) and 114 outpatient department (OPD) patients (60%). In IPD patients, there were 71 patients with a high thrombosis risk, 39 patients (37.50%) in 2012 and 32 patients (37.21%) in 2013. There are two statistically significant differences in the populations between both years, first the mean thrombosis risk score (which in 2013 had a higher thrombosis risk score (4.94 vs. 5.86)) and second, the number of patients that died from VTE (with more deaths occurring in year 2012 (10 vs. 1)). Patients who have a high thrombosis risk score in 2012 represent 37.50% of cases, and in 2013 these patients represented 37.21% of cases. The odd ratio (OR) is 1.013 (0.561 - 1.828), relative risk is 1.008 (0.696 - 1.459), relative risk reduction is 0.77 and numbers needed to treat (NNT) is 344.82.

CONCLUSION: From our study we showed a reduction of risk in a number of high thrombosis risk VTE patients when using the risk assessment protocol of BMC with the number need to treat of 344.82. Although it is not statistically significant, due to the limitations of the study, we have seen a trend towards using the protocol to decrease the number of high thrombosis risk VTE patients.

The incidence of venous thromboembolism (VTE, i.e., deep venous thrombosis (DVT) and/or pulmonary embolism (PE)) is now increasing in Thailand because of the recognition of the disease's burden and greater accessibility to diagnostic tools even in rural areas. The delay in the diagnosis of diseases will bring about many complications, such as post-thrombotic syndrome, and that means more morbidities and mortalities. There is literature to indicate that the incidence of VTE in Thailand or Asian countries is no less than in Western countries.[1-8] Many studies on VTE in multiple countries (including Asian populations) have shown that the benefits of VTE prevention far outweigh the treatment of diseases in every aspect, e.g. less suffering and premature mortality, more quality of life and fewer costs overall.[9-13] VTE will occur more often if patients already have risk factors, both modifiable and unmodifiable. According to guidelines from National Institute for Health and Clinical Excellence (NICE) if patients, either medical or surgical, have at least one risk factor or have significant reduction in mobility they are considered to be at an increased risk of VTE and they require further evaluation of risk of bleeding before they are administered preventive interventions. If the patient has at least one risk factor for bleeding, NICE guidelines suggest not giving any pharmacological prophylaxis, unless the risk of VTE outweighs risk of bleeding.[13]

At the Bangkok Medical Hospital Center (BMC) we adapted the NICE guidelines to make a protocol (Appendix 1) to assess the risk of thrombosis and risk of bleeding in our patients, and to guide the prophylaxis interventions. We already knew that some patients are at high risk for VTE without any additional risk factor such as cancer patients, critically ill patients in the Intensive Care Unit (ICU), known cases of thrombophilia and post-operative orthopedic surgery patients, so we used this protocol first in this group of patients, starting from 1 Jan 2013.

Material and Methods

The study was a retrospective study; we collected data from January 1, 2012 to December 31, 2013 by electronic medical records. The populations are the patients who were admitted to the cancer unit, ICU or orthopedic unit which are the units that apply the VTE risk assessment protocol. Both medical and surgical patients were included. In these groups we selected the patients who met all of our inclusion criteria, those who had been diagnosed with VTE at the BMC, who were 15 years old or older, and have official radiologist reports diagnosis of VTE. Our exclusion criteria are patients aged below 15 years old or with no official radiologist reports.

Once the exclusion criteria were applied, the remaining patients were divided into 2 groups. The first group of patients attended BMC in 2012 and the second group attended in 2013. We applied the protocol only to patients who were hospitalized; therefore we selected IPD patients only. We categorized IPD patients into either high or low thrombosis risk groups using the risk assessment screening for the BMC VTE protocol. We define high thrombosis risk as patients with a thrombosis score ≥ 4 (in medical patients) or score ≥ 3 (in surgical patients). We then used the SPSS program for data analysis. We compared populations from both years to see if there were any differences in baseline characteristics. We evaluated the outcomes when using the preventive protocol by comparing high thrombosis risk patients to low thrombosis risk patients from each year to see if there were any differences in the number of patients before applying the protocol, (in 2012), and after applying the protocol, (in 2013). Then we calculated the odd ratio, relative risk, relative risk reduction and the number needed to treat (NNT).

Results

The total population hospitalized in the cancer unit, ICU or orthopedic unit is 50,027 patients, of whom 26,036 were patients in 2012 and 23,991 were patients in 2013. There were 225 patients with VTE (in 2012 n = 125 (55.56%) and in 2013 n = 100 (44.46%)). Of these patients, 25 patients were excluded (10 patients with no official radiologist reports and 15 patients with missing demographic and clinical data). Of the remaining total of 190 patients, 104 patients were seen in 2012 (54.73%) and 86 patients were seen in 2013 (45.27%). Of these 190 patients, 95 were men and 95 were women. Their mean age was 63.52 ± 17.70 years. Ninety two patients (48.42%) are Thai nationals, while 98 patients (52.58%) are non-Thai nationals. The top three nationalities are British (13 patients), Qatar (11 patients) and Kuwait (11 patients). Details are shown in Figure 1. There were 76 IPD patients (40%) and 114 OPD patients (60%). Of the IPD patients, 71 patients (93.42%) have high thrombosis risk, 39 patients (37.50%) in 2012 and 32 patients (37.21%) in 2013. A summary of patients' characteristics are shown below in Table 1.

One hundred and fifty patients (78.95%) have underlying diseases. The most common underlying disease that increases the risk of VTE is cancer, found in 56 patients (29.47%). Of these, 19 patients (33.99%) have advanced stage cancer with metastasis. The primary cancers are lung cancer (9 patients (16.07%)), breast cancer (6 patients (10.71%)), colon cancer (6 patient (10.71%)), and rectal cancer (5 patients (8.93%)). Details of primary cancer sites are shown below in Figure 2.

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Table 1: Summary of clinical characteristics of enrolled patients (n=190).

Characteristic	n (%)
Patient	190 (100)
Male	95 (50)
Female	95 (50)
Age Mean	63.52 ± 17.7
Nationality	
Thai	92 (48.42)
Foreigner	98 (52.58)
Service	
outpatient department (OPD)	114 (60.00)
inpatient department (IPD)	76 (40.00)
Diagnosis	
Deep venous thrombosis (DVT)	142 (74.74)
Pulmonary embolism (PE)	12 (6.32)
DVT and PE	36 (18.94)
Presenting symptom	
Leg swelling	147 (77.37)
Dyspnea	28 (14.74)
Leg swelling and dyspnea	10 (5.26)
Asymptomatic	3 (1.58)
Arm swelling	2 (1.05)

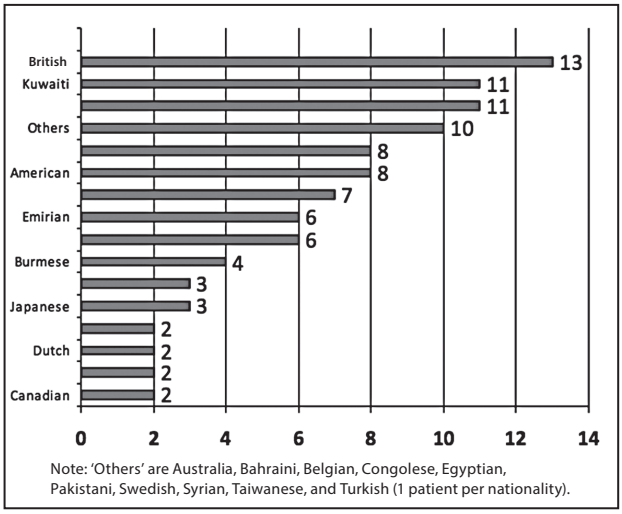

Figure 1: Nationalities of non-Thai population

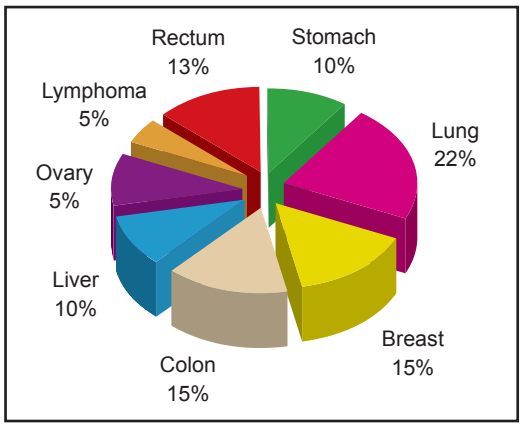

Figure 2: Primary cancer location

Other underlying conditions that increase the risk of VTE are stroke (after more than 1 month) 18 patients (9.47%), of whom 13 have been immobilized (72.22%). For each of the following diseases, protein C deficiency and protein S deficiency, there are 6 patients with deficiency (3.16%), 3 patients with antithrombin III deficiency (1.58%) and 1 patient with hyperhomo-cysteinemia (0.53%). A summary of details about underlying diseases is listed below in Table 2.

Their most common presenting symptoms are leg swelling (147 patients, 77.37%). The other symptoms are dyspnea (28 patients, 14.74%), leg swelling with dyspnea (10 patients, 5.26%) and arm swelling (2 patients, 1.05%). There are 3 asymptomatic patients (1.58%) with problems resulting from their cancer, and VTE was revealed in the imaging to define the cancer stage. There were 11 patients (5.79%) who died during our study, and every one of these patients had cancer as comorbidity. The causes of death are cancer (6 patients), massive pulmonary embolism (4 patients) and septic shock (1 patient). In 2012, 10 patients (9.61%) died and in 2013, 1 patient (1.16%) died. All of the deceased patients had a high thrombosis risk score. The VTE sites in our study include superficial femoral vein (115 patients (60.52%)), popliteal vein (99 patients (52.11%)), posterior tibial vein (75 patients (39.47%)), common femoral vein (73 patients (38.42%)), external iliac vein (38 patients (20.00%)), peroneal vein (35 patients (18.42%)) and subclavian vein (2 patients (1.05%)). Of the 2 patients with subclavian vein thrombosis, 1 patient has breast cancer, the other is a Kuwaiti female who has been taking oral contraceptive pills for a long time (> 5 years) without any other risk for thrombosis. The data on thrombosis sites are shown below in Figure 3.

For the statistical SPSS analysis, we used the independent t-test analysis and chi-square to find differences in characteristics between both years. The results found that there are two statistically significant differences in the populations between both years. The first is the mean thrombosis risk score, and the mean difference is -0.918 (-1.589 - -0.248, p = 0.008), (mean in 2013 > mean in 2012), the median score in 2012 is 5 and in 2013 it is 6. The second is the number of deceased patients, with more in 2012 than in 2013 (p = 0.013). The other non-significant values and summary details are listed below in Table 3. Patients who have a high thrombosis risk score in 2012 are 37.50% and in 2013 are 37.21%. The odd ratio is 1.013 (0.561 - 1.828), the relative risk is 1.008 (0.696 - 1.459), the relative risk reduction is 0.77 and number needed to treat is 344.82.

Table 2: Underlying diseases of enrolled patients.

Underlying diseases	n (%)
Hypertension	75 (39.47)
Cancer	56 (29.47)
Diabetes mellitus (DM)	35 (18.42)
Dyslipidemia	21 (11.05)
Stroke (> 1 month)	18 (9.47)
Old myocardial infarction	13 (6.84)
Atrial fibrillation	13 (6.84)
Asthma/COPD	12 (6.32)
Chronic kidney disease	10 (5.26)
Protein C deficiency	6 (3.16)
Protein S deficiency	6 (3.16)
Peripheral arterial disease	5 (2.63)
Varicose vein	4 (2.11)
Liver cirrhosis	3 (1.58)
Antithrombin III deficiency	3 (1.58)
Systolic heart failure	2 (1.05)
Polycythemia vera	1 (0.53)
Essential thrombocytosis	1 (0.53)
Hyperhomocysteinemia	1 (0.53)
Autoimmune hemolytic anemia	1 (0.53)
Chronic hepatitis C infection	1 (0.53)
Spinal cord injury	1 (0.53)
Hypertrophic cardiomyopathy	1 (0.53)

Table 3: Clinical characteristics compared between 2012 and 2013.

Characteristics	Year 2012 n (%)	Year 2013 n (%)	*p*
Patient (n)	104 (54.73)	86 (45.27)	
Sex			
Male	55 (52.88)	40 (46.51)	0.382
Female	49 (47.12)	46 (53.49)	
Mean age	62.83	64.35	0.557
Nationality			
Thai	48 (46.15)	44 (51.16)	0.492
Non-Thai	56 (53.85)	42 (48.84)	
Service			
OPD	63 (60.58)	51 (59.30)	0.858
IPD	41 (39.42)	35 (40.70)	
Diagnosis			
DVT	72 (69.23)	70 (81.40)	0.126
PE	9 (8.65)	3 (3.48)	
DVT and PE	23 (22.12)	13 (15.12)	
IPD			
High thrombosis risk	39 (37.50)	32 (37.21)	0.967
Low thrombosis risk	65 (62.50)	54 (62.79)	
Mean thrombosis risk score	4.94	5.86	0.008*
Mean bleeding risk score	3.79	3.82	0.941
Number of dead patients	10 (9.62)	1 (1.16)	0.013*

* = significant

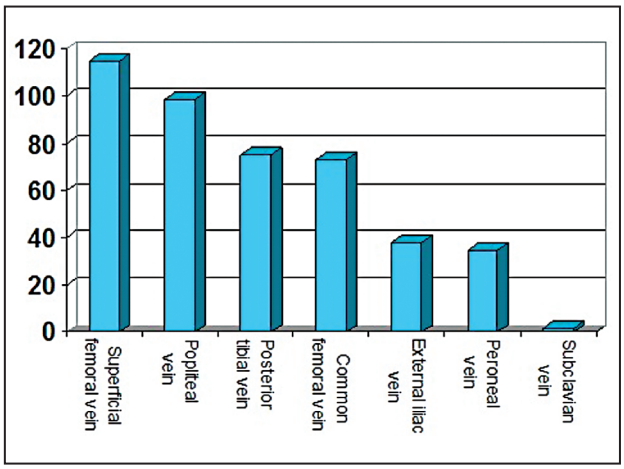

Figure 3: Site of thrombosis

Discussion

According to the Agency for Health Care Research and Quality, the prevention of VTE is the number one strategy to improve patients' safety in hospitals.[22] There is strong evidence from multiple randomized trials and analyses of appropriately employed prophylaxis of VTE that show it is cost effective and has a desirable benefit-to-risk ratio. In Thailand, however, due to many reasons, the VTE prevention strategy is not applied consistently or regularly. Our study of 190 VTE patients showed a trend in reducing the occurrence of VTE in patients, especially in high risk patients; although it's not statistically significant due to many limitations.

In our study the rate of occurrence of VTE was the same across men and women. With regards to nationality we found the rate of occurrence in Thai nationals is roughly the same as in non-Thai nationals. This concurs with the findings of previous studies that the incidence of VTE in Thailand is no less than in Western countries.[1-8] We used data, however, from a population with VTE, and not from a normal population, so we need to keep in mind that our findings are not necessarily a true rate occurrence of VTE across both Thai and non-Thai nationals. So this data shows that there is a tendency towards an incidence of VTE in Thai nationals that is not low after all, contrary to the old understanding we previously held.

About 60% of patients received OPD services, and the most common presenting symptom was leg swelling (78.5%). There are 3 patients (1.58%) with no symptoms but who do have radiological evidence of VTE. These asymptomatic patients (all cancer patients) incidentally found evidence of VTE from an examination to determine the staging of the cancer with computer tomography (CT). These symptomatic patients were treated for the incidental VTE with a standard treatment if there is no contraindication. Compared to the previous study[1] that found asymptomatic VTE to be about 80%, our study has less asymptomatic patients. This is due to differences in population characteristics, study methods and diagnostic tools for diagnosis.

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Hypertension is the underlying disease we found most often in our populations, cancer being the second. We know, however, that hypertension, diabetes mellitus, and dyslipidemia all increase the risk for VTE a little, about 1.1-1.3 times[14-17], so if we look into disease that significantly increases the risk of VTE the first is cancer, which increases the risk 2-3 times.[18-20] The most common primary site of cancer is the lung, followed by breast and colon, and 33.99% of cancer patients have advanced stage cancer. A review of previous literature shows that advanced cancer increases the risk of VTE more than early stage cancer.[18] The second most common significant disease that increases the risk of VTE is stroke (after more than 1 month) that confines about 72% of patients to bed. This correlates to previous analysis[21] that found VTE more often in paralyzed limbs of stroke patients compared to non-paralyzed limbs (60% and 7%). Inherited cases of thrombophilia in our study included antithrombin III deficiency, protein C deficiency, and protein S deficiency (15 cases (7.89%)). This is found in Thai (4 cases), French (1 case), American (3 cases), Swedish (1 case), Bangladesh (3 cases), Kuwaiti (2 cases), and Bahraini (1 case) patients. It can be inferred that most causes of VTE in Thai nationals are acquired, and not so many cases are due to inherited causes. Therefore, the key to preventing VTE is to reduce modifiable risks as much as possible.

From the analysis, we compared the number of high risk thrombosis patients in 2012 to patients in 2013 and we found the odd ratio for high thrombosis risk patients to low thrombosis risk patients is 1.013 and the relative risk is 1.008 with no statistical significance. But from the comparative characteristics data, between both years we found that patients seen in 2013 have a higher mean thrombosis risk score than patients seen in 2012 with statistical significance ($p < 0.05$). It's reflected that although patients in 2013 have a higher mean thrombosis risk score for VTE the occurrence is still lower in 2013. This is interesting data, as we infer that the protocol probably can reduce the number of VTE patients who have a high risk of thrombosis.

There are five limitations to our study. First, our study populations are patients who already have VTE, and are not drawn from the normal population, so there are some limitations to applying our data to real life practices. Second, the number of patients who have VTE is very low compared to the overall population, so when we use statistical analysis it hardly makes the results significant. We think the reason for this is that most patients are not yet aware of VTE, because most symptoms are not painful. Some patients may feel that VTE is not the main issue when they compare this to their underlying disease (for those who already have one, e.g. cancer.) The other reason may come from a lack of awareness of VTE in physicians because most of them just pay attention to the main diseases their patients have. Third, some patients were hospitalized first in other hospitals with no VTE prevention protocols. Then the patients are referred to BMC when their condition gets worse. Prevention in these cases may be too late, because patients may already have had VTE without symptoms and when the main diseases progress more, the symptoms of VTE appeared later. Fourth, this is a retrospective study; there were no randomization in the population and it cannot have a control confounding factor. Due to ethical considerations, it is not right to randomize patients to either use or not use preventive methods because there are many guidelines that recommend VTE prophylaxis in high risk patients.[13, 23-28] Fifth, the evidence of VTE using doppler ultrasound has its own limitations, such as in cases of major soft tissue swelling.

Conclusion

These days VTE is a disease that is occurring more frequently than in the past, due in part because today we are more aware of diseases and the technology for diagnosis is more easily accessible. VTE prevention has many benefits, and it is preferable to prevent the disease altogether than cure the disease after it occurs. From our study, we showed a relative reduction in VTE 0.77 when using risk assessment protocol and number needed to treat is 344.82. Although this number may not be statistically significant, due to our study's limitations, nonetheless we saw a trend towards a drop in the number of high thrombosis risk VTE patients when the prevention protocol was applied.

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Appendix 1: Risk assessment for VTE and Flow chart

ศูนย์การแพทย์โรงพยาบาลกรุงเทพ
BANGKOK HOSPITAL MEDICAL CENTER

Name: Room:
HN: Physician:
Visit Date: Department:
Birth Date: Age: Sex:
Allergies (แพ้ยา) :

Risk Assessment for Venous Thromboembolism (VTE)

I01-14-011422
Page : [A1]

Patient screening: ☐ **Surgical patient** ☐ **Medical patient**

1. Thrombosis Risk Assessment (Circle on the score of only applicable risk factor)

Risk Factors	Score	Risk Factors	Score
Patient Related Risk Factors			
Age ≥ 75 years	3	Familial history of thrombosis	3
Age 61 - 74 years	2	History of DVT/ Pulmonary embolism	3
Age 41 - 60 years	1	Known thrombophilia (such as Factor V (Leiden), Prothrombin 20210A,protein C deficiency, protein S deficiency, antithrombin deficiency, antiphospholipid syndrome)	3
Obesity (BMI > 25 kg/m^2)	1	Malignancy (present or previous)	2
Stroke (< 1 month)	4	History of inflammatory bowel disease	1
Acute spinal cord injury (< 1 month)	4	Pregnancy or postpartum (< 1 month)	1
Hip, pelvis or leg fracture (< 1 month)	4	History of unexplained or recurrent spontaneous abortion	1
Multiple trauma (< 1 month)	4	Oral contraceptives or hormone replacement therapy	1
Immobilizing plaster cast (< 1 months)	2	Acute myocardial infarction	1
History of prior major surgery (< 1 month)	1	Congestive heart failure (< 1 month)	1
Sepsis (< 1 month)	1	Central venous access	2
Serious lung disease including pneumonia (<1 month)	1	Varicose veins	1
Abnormal pulmonary function e.g. COPD	1	Swollen leg (current)	1
Patient Related Risk Factors			
Elective major lower extremity arthroplasty (such as hip or knee replacement)	4	Minor surgery planned	1
Arthroscopic surgery	2	Patient confined to bed (≥ 72 hours)	2
Major surgery (> 45 minutes)	2	Medical patient currently at bed rest	1
Laparoscopic surgery (> 45 minutes)	2	**Total Thrombosis Risk Factor Score**	

Thrombosis risk assessment: ☐ High risk (Score ≥ 3, in Surgical Patient or Score ≥ 4, in Medical Patient)
☐ Low risk (Score < 3, in Surgical Patient or Score < 4, in Medical Patient) [Skip 2.Bleeding Risk Assessment to Plan of the management for thromboprophylxis]

Screening by _____ RN Date _____ Time _____ hr.

2. Bleeding Risk Assessment (Circle on the score of only applicable risk factor)

Risk Factors	Score	Risk Factors	Score
Patient Related Risk Factors			
Active gastroduodenal ulcer	4.5	Severe renal failure (GFR< 30 ml/min)	2.5
Bleeding in 3 months before admission	4	Moderate renal failure (GFR 30 - 59 ml/min)	1
Platelet count < 50x10^{9}cells/L	4	Current cancer	2
Age ≥ 85 years	3.5	Central venous catheter	2
Age 40 - 84 years	1.5	Rheumatic diseases	2
Hepatic failure (INR > 1.5)	2.5	Male	1
ICU or critical care unit admission	2.5	**Total Bleeding Risk Score**	

Bleeding risk assessment: ☐ Score ≥ 7; High risk of bleeding (Mechanical thromboprophylaxis is indicated) ☐ Score < 7

3. Plan of the management for thromboprophylaxis:

☐ No thromboprophylaxis ☐ Pharmacological thromboprophylaxis (please order in the order sheet)
☐ Mechanical thromboprophylaxis (please order in the order sheet)
☐ Both pharmacological and mechanical thromboprophylaxis (please order in the order sheet)
☐ Consult: ○ Hematologist ○ Cardiologist ○ Neurologist ○ Nephrologist
☐ Other (if any)

Comment: _____

Physician Signature _____ **Medical License No.** _____ **Date** _____ **Time** _____ **hr.**
( )

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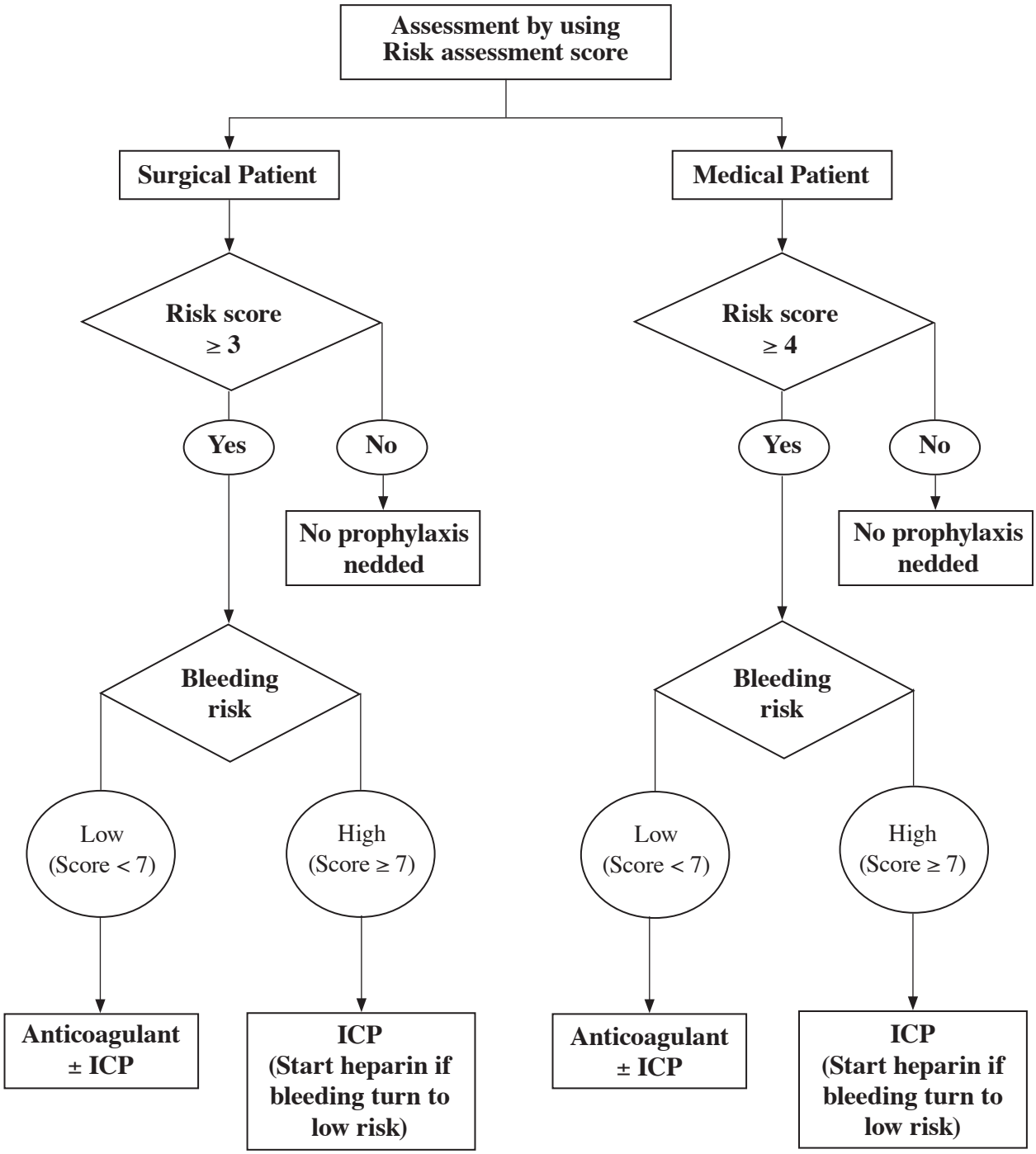
Appendix 2: Flow Chart



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Heterogeneity of Unilateral Multiple Breast Cancer: Implications for Biomarker Testing

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Keywords: breast cancer, unilateral multiple breast cancer, microsatellite, loss of heterozygosity, HER-2

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OBJECTIVE: This study was to re-examine the usefulness of biomarker assays in all multiple tumors in the same breast, and to evaluate the genetic heterogeneity of unilateral multiple breast carcinoma.

MATERIALS AND METHODS: All of the cases met the criteria for synchronous multicentric breast carcinomas. Tumors were either 5 cm apart or within the different breast quadrants, with no identifiable connection between lesions, and were diagnosed at the same time for an individual patient.

RESULTS: In the present study, 32 tumors from 15 patients with synchronous unilateral breast cancer were immunostained for estrogen receptor (ER), progesterone receptor (PR), and HER-2, and also underwent microsatellite analysis using 10 polymorphic markers. The ER and PR expression profile was similar in all tumors from the same patient. Discordant HER-2 immunoreactivity was found and confirmed by HER-2 FISH test in one case, and heterogeneity in the microsatellite pattern was observed in 6 patients.

CONCLUSION: With the routinely-used biomarkers (ER, PR, and HER-2), heterogeneity was minimal, however, with more frequent differences noted at the genetic levels.

Breast cancer is one of the most common malignancies in women worldwide. Even though most patients suffer a single lesion, approximately 5-10% of them have multiple tumors, either unilaterally or bilaterally.[1,2] Clonal determination of multiple breast cancers in the same patient has been evaluated by multiple techniques, and several lines of evidence have suggested that most cases of unilateral multiple breast cancer (synchronous or metachronous) are clonally-related, whereas the majority of bilateral breast cancers arise from different neoplastic clones.[1,3-10] With greater improvements in treating breast cancer in the past few decades, there has been an increasing awareness by both the clinician and the patient to request for biomarkers in order to determine treatment choices. This is particularly true for hormonal receptors (estrogen and progesterone) and for the HER-2 assessment. However, although currently it is recommended to perform these markers in every invasive breast cancer case, as well as in both tumors as in the case of bilateral breast cancer,[11] there is no specific recommendation as to whether these biomarkers should be obtained in one or all tumor(s) in patients with unilateral multiple breast cancer.

Based on the evidence that most unilateral multiple breast cancers are clonal-related; it is proposed that analyzing biomarkers on a single lesion is sufficient. This assumption has further been supported by a previous study by Middleton, et al. noting an identical immunohistochemical profile of synchronous unilateral multiple breast carcinomas, with regard to estrogen receptor (ER), progesterone

receptor (PR), and HER-2.[3] The purpose of this study was to re-examine the usefulness of biomarker assays in all multiple tumors in the same breast, and to evaluate the genetic heterogeneity of unilateral multiple breast carcinoma.

Material and Methods

Case Selection

A series of synchronous unilateral multiple breast cancers was assembled from the Pathology Files at Department of Pathology, Faculty of Medicine, Chulalongkorn University, Bangkok; Department of Pathology, Faculty of Medicine, Chiang Mai University, Chiang Mai; and the National Cancer Institute and the Institute of Pathology, Department of Medical Services, Ministry of Public Health, Bangkok. Formalin-fixed paraffin-embedded tissue was available on 32 tumors from 15 patients. All of the cases met the criteria for synchronous multicentric breast carcinomas.[2] Tumors were either 5 cm apart or within the different breast quadrants, with no identifiable connection between lesions, and were diagnosed at the same time for an individual patient. All tumors were classified and graded according to the recent World Health Organization Classification.[11]

Immunohistochemical Analysis

Immunohistochemical staining was performed on 4μ paraffin sections of all 32 tumors. The antibodies used were directed against ER (Neomarker, Fremont, USA; dilution 1:500), PR (Neomarker, dilution 1:500), and HER-2 (Dakocytomation, dilution 1:500). ER and PR stains were performed by automated immunostainer (Ventana Benchmark LT, Tucson, USA). The HER-2 staining was performed manually by the method described in the HercepTest (Dakocytomation). Immunoreactivity of ER and PR was recorded as positive if ≥1% of the tumor nuclei stained.[11] Immunoreactivity for HER-2 was considered to be positive if more than 10% of tumor cells showed intense circumferential membrane staining (3+).[12]

Fluorescence In Situ Hybridization (FISH) for HER-2 Gene Amplification

Multiple tumors in the same breast with discordant HER-2 immunoreactivity were subject to FISH assay for HER-2 gene amplification (Dakocytomation HER-2 FISH pharmDxTM Kit). HER-2 gene was considered to be amplified when the average HER-2 gene/chromosome 17 ratio was greater than 2.0.[12]

Microsatellite Analysis

Prior to DNA extraction by MasterPure™ Complete DNA & RNA purification kit (Epicentre, Madison, USA), manual microdissection was performed on paraffin sections to obtain tumor and normal tissue. The latter was derived from nipple skin or axillary lymph nodes of the corresponding case. Ten microsatellite polymorphic markers related to breast cancer on chromosome arms 1p (D1S228), 1q (D1S2878), 3p (D3S1300), 8p (D8S258), 8q (D8S137), 11q (D11S528 and D11S4175), 16q (D16S421 and D16S422) and 17q (D17S800) were used to assess the pattern of allelic loss.[1,13-15] Information regarding the cytogenetic localization of the markers was obtained from the Genome Data Base (http://www.ncbi.nlm.nih.gov). One strand of each primer pair was end-labelled, and the PCR reactions performed as described previously.[16-17] Microsatellite bands were visualized on a PhosphoImager, using ImageQuanNT™ software (Molecular Dynamics, Sunnyvale, CA). Loss of heterozygosity (LOH) was scored positive when a tumor sample demonstrated reduction of ≥ 66% signal intensity of a microsatellite allele, when compared to the matched normal DNA. Microsatellite instability (MSI), as defined by the presence of shifted or extra microsatellite allele(s) compared to normal, was also recorded.

Heterogeneity of Unilateral Multiple Tumors

The heterogeneity of tumors from the same breast were considered when they showed different immunohistochemical profiles (at least for one of the markers examined), a difference in FISH results, and/or a different pattern of allelic loss on at least one of the microsatellite markers.

Results

Pathological Findings

All tumors were classified as invasive carcinoma of no special type. The morphological features and histologic grades of tumors were comparable for an individual patient.

Immunohistochemical Analysis

For an individual patient, multiple tumors showed an identical immunohistochemical profile with respect to ER and PR (Table 1). The one exception was case 9 in which the multiple tumors had identical hormonal receptor immunostaining, but different HER-2 immunoreactivity, with one tumor showing 3+ HER-2 and the other showing a negative result (Figure 1).

HER-2 FISH Test

The two tumors in case 9 were evaluated by FISH for HER-2 gene amplification. The differences in HER-2 immunoreactivity between tumors correlated with amplification status of the gene by FISH assay. Amplification of the HER-2 gene was found in one (T2) but not the other (T1), with HER-2 gene/chromosome 17 ratios of 2.3 and 1.1, respectively (Figure 1).

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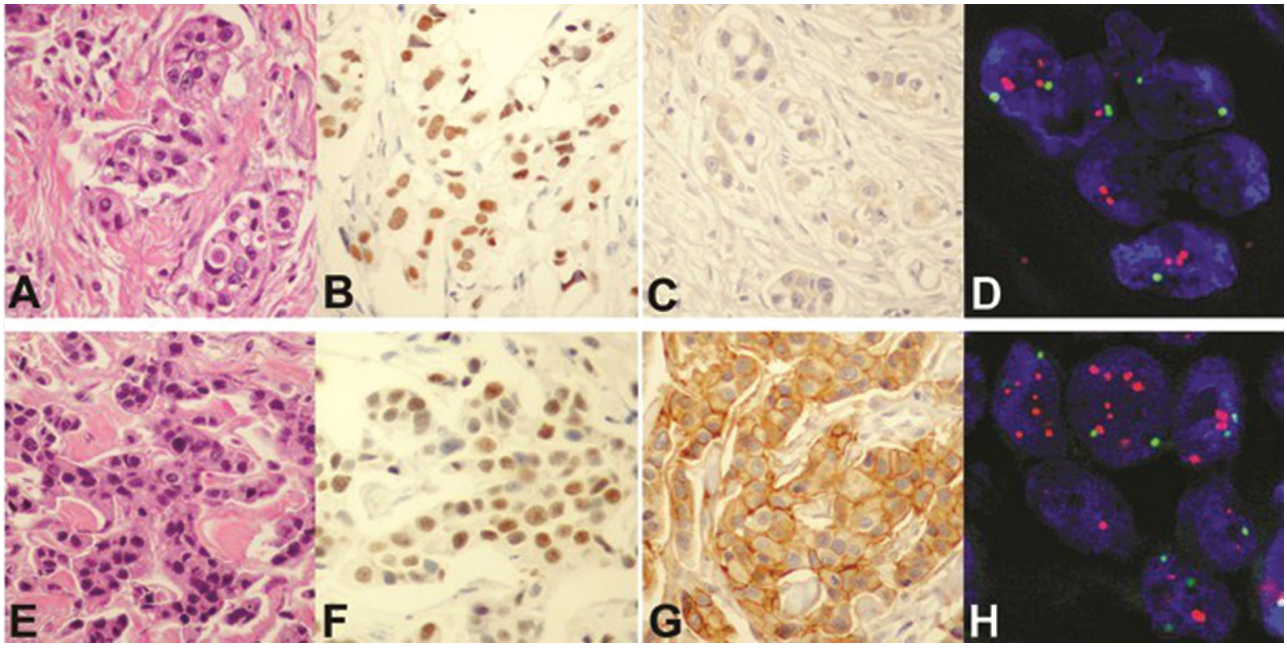

Figure 1: Morphological analysis of unilateral multiple breast cancers. Upper panel from T1 of case 9: Tumor cells (A, hematoxylin and eosin) are positive for estrogen receptor (B) and negative for HER-2 by immunostaining (C), and demonstrate no HER-2 gene amplification (D, FISH, red signals = HER-2 gene and green signals = centromere 17). Lower panel from T2 of the same case: Tumor cells (E, hematoxylin and eosin) are positive for estrogen receptor (F) and HER-2 by immunohistostaining (G), and show HER-2 gene amplification (H, FISH). Both tumors are immunonegative for progesterone receptor and p53 (not shown). (T=tumor)

Microsatellite Analysis

Thirteen cases (86.6%) showed LOH in at least one tumor and for at least one microsatellite locus examined (Table 1). Genetic heterogeneity was observed in 6 cases (cases 10-15) (40%). All of these cases had microsatellite marker(s) that showed allelic loss in one but not the other lesion(s). In case 15, loss of different alleles was observed at one locus (D1S2878). MSI was present in 2 cases (13.3%).

Heterogeneity of Unilateral Multiple Tumors

Based on the criteria outlined above, the heterogeneity of unilateral multiple breast carcinoma was present in 7 cases (46.7%), one (case 9) determined by HER-2 assessment and the remaining 6 cases (10-15) by microsatellite analysis. All tumors in the same breast showed identical immunostaining for ER and PR.

Discussion

Approximately 5-10% of breast cancer patients have multiple tumors, either unilaterally or bilaterally.[1,2] Although multiple lines of evidence have suggested that most unilateral multiple breast carcinomas are clonally-related and likely represent intra-mammary spread of a single lesion in synchronous cases and recurrences in metachronous cases,[3-5,7] this does not necessarily indicate that all cancers in the same breast are identical. Middleton et al noted previously an identical immunohistochemical profile of synchronous unilateral multiple breast carcinoma, with regard to ER and PR.[3] In contrast, this same study found no differences in HER-2 expression in unilateral multiple breast carcinomas, whereas we were able to establish one patient whose tumors showed different HER-2 status. Identification of the HER-2 gene amplification in one of her tumors played a significant role in the treatment of this particular patient, and the finding may have been missed had only one tumor been examined. In addition, we were able to demonstrate genetic heterogeneity between tumors in the same breast in 6/15 cases (40%) by assessment of the LOH pattern.

The frequency of MSI in breast carcinoma varies considerably, due largely to the lack of well-defined criteria for the assessment. MSI has been observed to be a frequent finding (33%) in advanced breast cancers.[18] Not all of our patients had advanced disease, however, so the lower frequency of MSI (13.3%) in our cases is not unexpected. Whether the presence of MSI has an impact upon the outcome of unilateral multiple breast cancer deserves additional study.

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Table 2. Immunohistochemical and microsatellite analyses of unilateral multiple breast cancer.

Case No		IHC			Microsatellite Analysis								
		ER	PR	HER2	D1S228	D1S2878	D3S1300	D8S258	D8S137	D11S528	D11S4175	D16S421	D16S422	D17S800
1	T1	+	+	-		U	L		U				U	U
	T2	+	+	-		U	NA NA		U				U	U
2	T1	+	+	-	U	U			NA NA		L		U	
	T2	+	+	-	U	U		NA NA	NA NA		NA NA		U	
3	T1	-	-	-					U	NA NA	M M			
	T2	-	-	-	M M				U	NA NA				
4	T1	-	-	+					U		NA NA		U	
	T2	-	-	+					U		NA NA		U	
5	T1	+	+	+	U	L				L			L	
	T2	+	+	+	U	L			NA NA	NA NA			L	
6	T1	+	-	-	U	U	L		L	U			U	
	T2	+	-	-	U	U	L		L	U			U	
7	T1	+	-	-	NA NA			NA NA	NA NA	L	U		L	
	T2	+	-	-				L	NA NA	L	U		L	
8	T1	-	-	+	NA NA	U		NA NA	NA NA		NA NA		U	L
	T2	-	-	+	NA NA	U	NA NA	NA NA	NA NA		NA NA		U	L
9	T1	+	-	-	L	U	U		NA NA	U	NA NA			
	T2	+	-	+	L	U	U		NA NA	U				
10	T1	+	-	-	U		U	NA NA	NA NA		NA NA	L	L	U
	T2	+	-	-	U		U		NA NA		NA NA		L	U
11	T1	+	+	-		U		U			U			L
	T2	+	+	-		U		U		L	U		L	L
12	T1	-	-	+	U	L			NA NA			U		
	T2	-	-	+	U	L			NA NA		NA NA	U	L	
13	T1	+	-	-			L		U					
	T2	+	-	-		L			U					
14	T1	-	-	-					NA NA	U	NA NA	U	U	
	T2	-	-	-					NA NA	U	NA NA	U	U	
	T3	-	-	-					NA NA	U	NA NA	U	U	
	T4	-	-	-	L				NA NA	U	NA NA	U	U	
15	T1	+	+	-		L		U	NA NA	NA NA	U	M M	L	
	T2	+	+	-		L	NA NA	U	NA NA	L	U	M M	NA NA	L

T= Tumor, IHC = Immunohistochemistry, ER = Estrogen receptor, PR = Progesterone receptor, HER = HER-2,
L = Allelic loss, M = Microsatellite instability, U = Uninformative, NA = Not amplified.
Each rectangle in microsatellite analysis (except ones with "U") represents one microsatellite allele.

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Conclusion

In conclusion, heterogeneity is commonly observed among tumors in unilateral multiple breast cancer. Even though the differences were minimal with respect to the routinely-used biomarkers (ER, PR, and HER2), more frequent differences were shown at the molecular level. Therefore, all of the present and future prognostic and therapeutic biomarkers should be evaluated in all masses in the same breast, in order to provide the full benefits of treatment modalities to patients with unilateral multiple breast cancer.

Acknowledgements

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Original Article

Preliminary Report of Minimally Invasive Plate Osteosynthesis with Vertical Incisions for Mid-shaft Clavicular Fractures: a Surgical Technique and its Results

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Keywords: fracture, osteosynthesis, mid-shaft clavicular fractures, minimally invasive plate osteosynthesis

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OBJECTIVE: One of the most common surgeries for mid-shaft clavicular fracture is an open reduction and internal fixation with plate and screws. When using a conventional technique of plate fixation, a long incision is used, compromising blood supply to the bone and soft tissues. This can result in delayed or nonunion, skin complications, painful scarring, infection and paraesthesia inferior to the clavicle. This study reports on a minimally invasive plate osteosynthesis with separated vertical incisions. The aim is to evaluate radiographic and clinical outcomes in mid-shaft clavicular fractures.

MATERIALS AND METHODS: From January 2011 to July 2013, eight cases were operated using the technique. Fracture reduction was arrived at by indirect manipulation with a postural reduction under fluoroscopic guidance. Vertical incisions were done proximally and distally. We evaluated the clinical and radiographic results immediately postoperation and at 2, 4, 8 weeks and thereafter every 4 weeks postoperative until union was achieved.

RESULTS: AO Type 15-B2.2 was the most common: all fractures healed within a mean period of 13.8 weeks (range 11-18 weeks). All patients showed good shoulder function, with a mean disabilities of the arm, shoulder and hand (DASH) score of 6.8 (range 4-15.3) at six months. There were no complications, except bending of an implant in one patient. However this patient achieved a bone union with good function. There was no numbness around the clavicle in this series. Average operative time was 128 minutes. Fluoroscopic exposure time was 29.5 seconds.

CONCLUSION: We propose vertical incisions as an approach for plate and screws application for this MIPO technique. This presented technique is good, not only with regards to appearance but also in avoiding any associated complications. We propose this technique as an option for minimally invasive plate osteosynthesis (MIPO) for mid-shaft clavicular fractures.

Conservative treatment of mid-shaft clavicular fracture has been a standard treatment in most cases.[1,2] However, there are many cases which need to be operated on to prevent complications of conservative treatment such as nonunion, malunion or malfunction of the shoulders.[3-7] In a systematic review of 2,144 acute mid-shaft clavicle fractures, Zlowodzki et al. found that comminuted displaced fractures had a higher rate of nonunion and longer term negative sequelae with nonsurgical management, and a relative risk reduction of 57% for nonunion when plate fixation was applied.[9]

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The most common surgery for mid-shaft clavicular fracture is open reduction and internal fixation (ORIF) with plate and screws.[3] Elastic intramedullary nailing is another common option,[5,8] however, migration of the implant, telescoping and shortening[8] are not infrequent in comminuted fractures when using this technique. The conventional technique for ORIF with plate and screws normally compromises blood supply to bone and soft tissues. This not only causes delayed union, nonunion and infection but the long horizontal skin incision can also cause skin complications such as painful surgical scarring on the prominent plate and paraesthesia of the supplied cutaneous nerve inferior to the clavicle.[3,9] Minimally invasive plate osteosynthesis (MIPO) technique for mid-shaft clavicular fractures[7,9] has become accepted and has overcome many of these complications. This is because the technique of short separated skin incisions provides good biological healing of fractures[10] and lowers the chance of injury to cutaneous nerve and results in less scarring on the prominent plate.

Comparing the type of incisions, horizontal or vertical incisions along the skin crease, some literature showed that postoperative numbness was lower in the vertical incision group.[9] Those who had undergone vertical incisions also reported a significantly reduced degree of numbness and significantly less awareness of the numbness with clothing and shoulder straps. Furthermore, a vertical incision may be substantially obscured by clothing when compared to a horizontal incision, resulting in a better cosmetic outcome.

We use MIPO technique with vertical separated incisions along the skin crease in the process of reduction and fracture stabilization to provide a good biological environment for healing and to minimize skin complications. We report the technique of minimally invasive plate osteosynthesis in mid-shaft fracture of clavicles with vertical incisions and evaluate the radiographic and clinical outcomes.

Materials and Methods

We performed percutaneous plating for displaced mid-shaft fractures of clavicles from January 2011 to July 2013. Institutional Review Board approval was obtained for a retrospective review of the medical and radiographic records of these patients.

The inclusion criteria were isolated, unilateral, displaced mid-shaft clavicular fractures with less than 25% cortical contact between the main fragments in patients aged between 18 and 65 years. The exclusion criteria were fractures of the medial or lateral third of the clavicle, former relevant injuries or previous surgical interventions of the upper extremity or additional pathological conditions affecting the limb function, pathological fractures, open fractures, fracture with associated neurovascular injury and cases with a contraindication for surgery.

Figure 1: 3.5 mm. Reconstruction LCP

Figure 2: Anatomical Superior Clavicle LCP

Surgical technique

A locking reconstruction plate or Superior Clavicle Anatomical Locking Plate (Synthes, Oberdorf, Switzerland) were chosen (Figure 1 and 2), long enough to place at least three screws on each side of the fracture fragment. Preoperative planning for plate length selection was routinely done (Figure 3). For the locking reconstruction plate, it was manually contoured preoperatively on a plastic clavicle model in order to accommodate a superior surface of the clavicle before processing for sterilization (Figure 4). General anesthesia was a standard procedure for every patient. The patient was set in a supine position on a fluoroscopic transparent operative table. A fluoroscope was positioned at the contralateral side of the injured arm, perpendicular to the longitudinal axis of the table. The C-arm of the fluoroscope was placed to obtain AP view (Figure 5), 30 to 40 degrees of cephalad tilting and 30 to 40 degrees of caudad tilting (Figure 6-9). This will provide images for the reduction and proper plate positioning before fixation. The pre-draping images were acquired for all three views before skin preparation for an adequate intraoperative assessment. Then sterile draping was administered to the whole upper limb capable of being moved freely during operation.

Anatomical landmarks, clavicle, fracture site, coracoid process, acromion and A-C joint were identified and marked (Figure 10). The selected plate was placed over the clavicle outside the skin and fluoroscopic images were taken to confirm the plate length and positioning (Figure 11). A 3 cm. vertical skin incision was made along the skin crease at the level of the second hole of the plate on the lateral fragment. A subcutaneous-supraperiosteal plane was created using a periosteal surfer along the

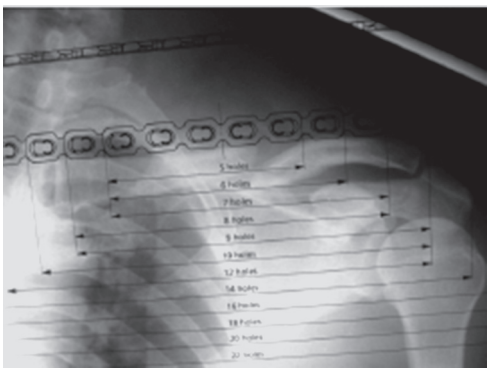
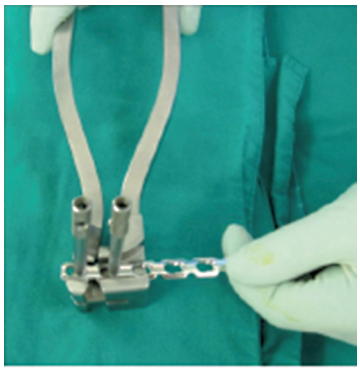


Figure 3: Preoperation template.



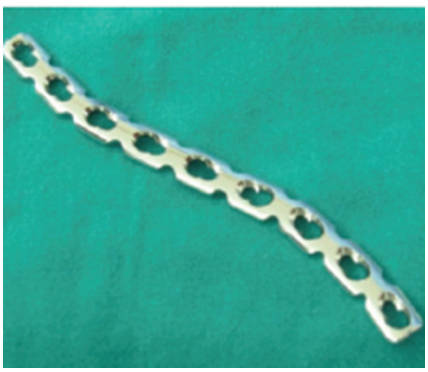


Figure 4: Preoperation contouring of 3.5 mm., reconstruction LCP.

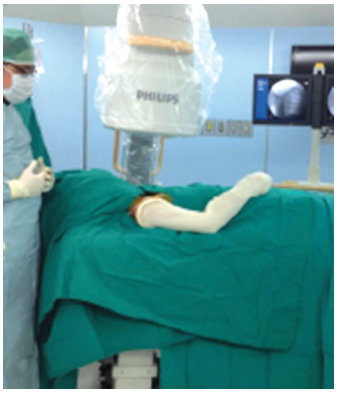


Figure 5: Intraoperative setting of patient position and C-arm.

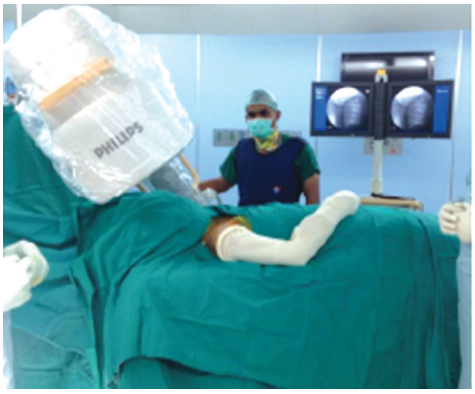


Figure 6: Caudad tilting of C-arm.

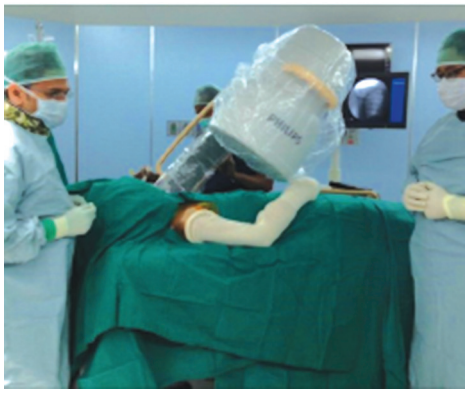


Figure 7: Cephalad tilting of C-arm.

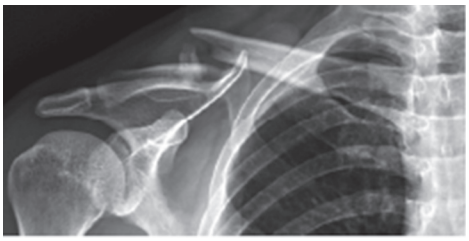


Figure 8: Preoperative x-ray.

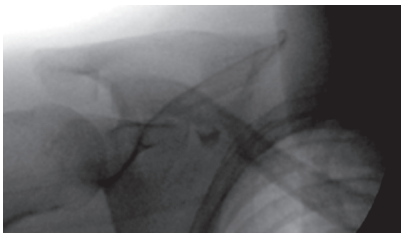


Figure 9: X-ray demonstration of Caudad tilting of C-arm.

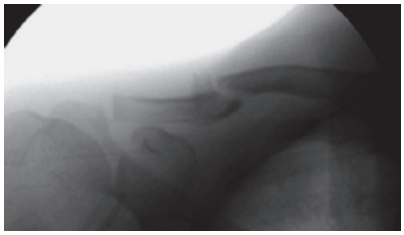


Figure 10: X-ray demonstration of Cephalad tilting of C-arm.

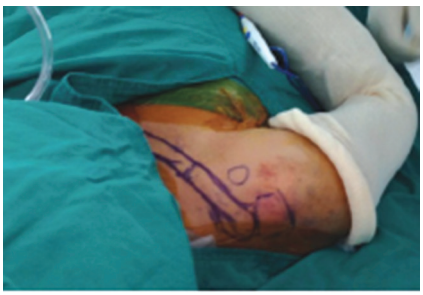


Figure 11: Marking of anatomical landmarks before making incisions.

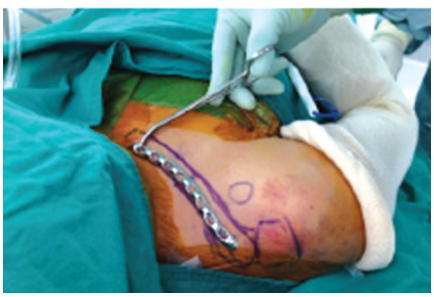


Figure 12: Plate length and position identification under C-arm guidance.

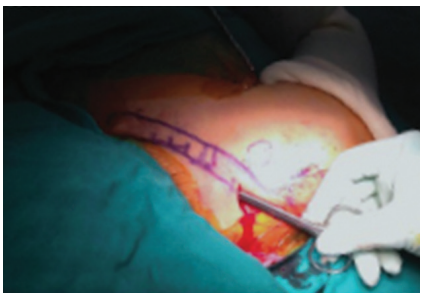


Figure 13: Vertical lateral skin incision and tunnelling technique.

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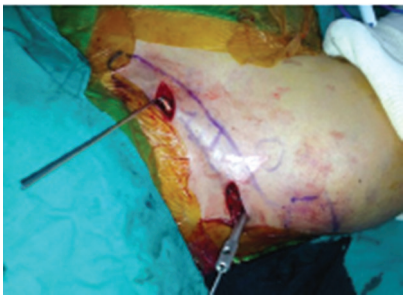

Figure 14: Insert the plate, reduce the fracture and temporary fix with K wires through the medial and lateral incision.

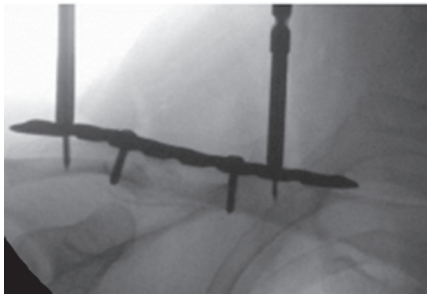

Figure 15: The 3.5 cortical screws were used to pull the main fragments to the bone, as a reduction template.

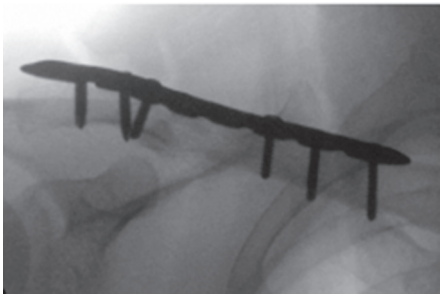

Figure 16: The amount of screws on each side is three screws.

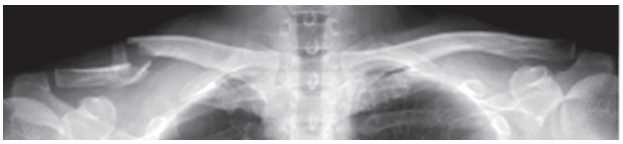

Figure 17: X-ray of both clavicles preoperatively.

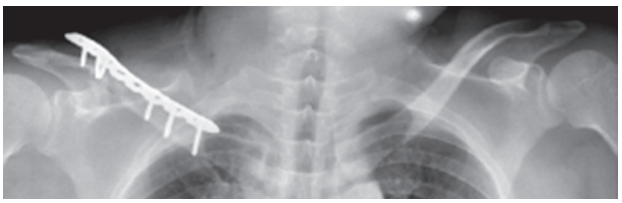

Figure 18: X-ray of both clavicles postoperatively, to compare the length of the normal and injured side.

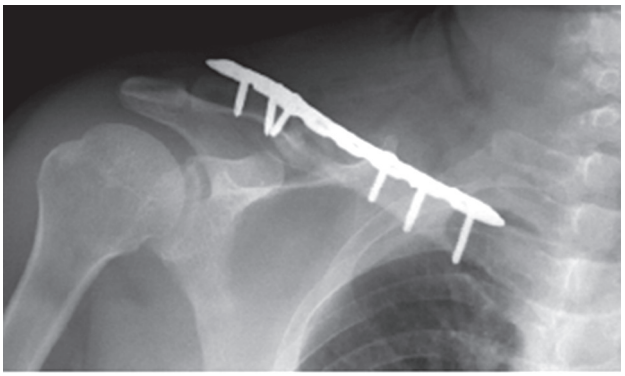

Figure 19: Postoperative x-ray in AP to monitor healing.

superior surface of the clavicle from the lateral to medial fragment; this is a tunnel for further plate insertions (Figure 12). The medial vertical skin incision along the skin crease then was opened. The plate was inserted from the lateral surgical incision to the medial side. The fracture was reduced indirectly by manipulation of the arm with fluoroscopic guidance. If necessary, a 3.5 mm. Schanz screw was fixed on each main fragment, as a joystick, to facilitate reduction of the fracture and a small external fixator was applied to maintain reduction.

When reduction was achieved with an acceptable alignment, with the correct length, angulation and rotation, the k wires were inserted for temporary stabilization through the most lateral and most medial hole of the plate (Figure 13). After the fluoroscopic images confirmed an acceptable alignment, the 3.5 mm cortical screws were inserted to pull the main fragments to the plate, using the plate as a reduction template (Figure 14). Then the 3.5 locking head screws were fixed to provide better stability. At least three screws on each side of the fragment would be fixed to ensure adequate stabilization (Figure 15). Before skin closure, three images were acquired to evaluate the bone-implant construction. No bone grafting was used in this series. Skin was closed with a subcutaneous absorbable suture following with a subcuticular skin closure to reduce any scarring complications (Figure 16).

Postoperative rehabilitation

Postoperatively, the patient's injured arm was supported in a sling to protect the load of the whole upper extremity and to increase comfort. An early range of motion of the shoulder was started with active assistance according to individual tolerance. As this was a subcutaneous suturing there was no need to remove stitches. Heavy lifting, pushing or pulling was not permitted until evidence of bone union was observed.

The follow-up period, with clinical evaluations and x-rays, was done at 2 weeks, 4 weeks, 8 weeks, 12 weeks and 24 weeks postoperatively.

Evaluation of results

Demographic data, fracture type, mechanism of injury, associated injury, fluoroscopic exposure time, time to union, skin numbness inferior to the clavicle and complications were recorded and assessed at the immediate post-operative period and during follow-up. For clinical evaluations we used the Disability of the Arm, Shoulder, and Hand (DASH) score[11,12] which was assessed at six months postoperatively. An x-ray of both clavicles (Figure 17-18) of cephalad and caudad views were taken to evaluate the degree of shortening and signs of radio-

graphic union, those defined as bridging of fracture with callus in three views. Clavicular shortening was measured[15] as the proportional difference in length between the affected and unaffected sides. Radiographs were reviewed by an independent examiner in order to verify the state of the bone union (Figure 19).

Results

There were eight patients who met the inclusion criteria and had sufficient hospital and radiographic records and were available for follow-up for at least six months after surgery. Patients included seven males, one female, with a mean age of 36.8 years (range, 20-55 years). Six out of the eight clavicles treated were right side clavicles. The most common type of fracture is AO 15 type B 2 (wedge fracture) in five patients. Six patients sustained an injury from motorcycle accidents. Four had a concomitant thoracic injury, most commonly, rib fractures. Intraoperatively, five clavicles were fixed with 3.5 mm anatomical locking plates while the other three were fixed with 3.5 mm. reconstruction locking compression plate (LCP). The average operative time was 128 minutes. Fluoroscopic exposure time was 29.5 seconds.

Postoperatively, there was no numbness of the skin inferior to the clavicle. All patients could start early range of motion exercises of the shoulder following the rehabilitation program without difficulty. The measurement of clavicular length was compared with the uninjured side. Five of the eight fractures were equal; there were three clavicles which were shorter (0.2-0.6mm). The average radiographic and clinical union was at 13.875 weeks. DASH scores were 6.7875. During history taking, no patient complained about the scar on the plate prominence and on physical examination, there were also no unsightly scars on the prominent plate (Figure 20).

There was one case which had a complication of a bent plate. This was a case which was fixed by 3.5 mm reconstruction LCP. However, the fracture healed and the patient did not complain about the angulation of the clavicle (Figure 21-22).

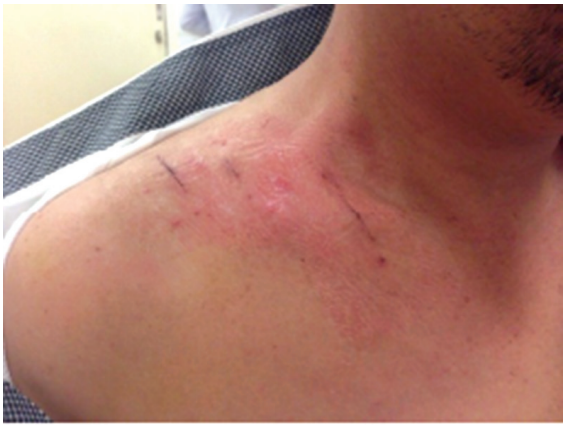

Figure 20: MIPO technique with vertical incisions.

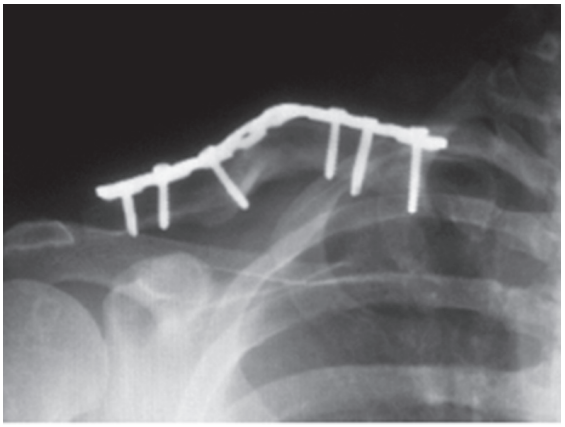

Figure 21: Reconstruction LCP is too weak to fix clavicle in some cases such as heavy arm and larger body.

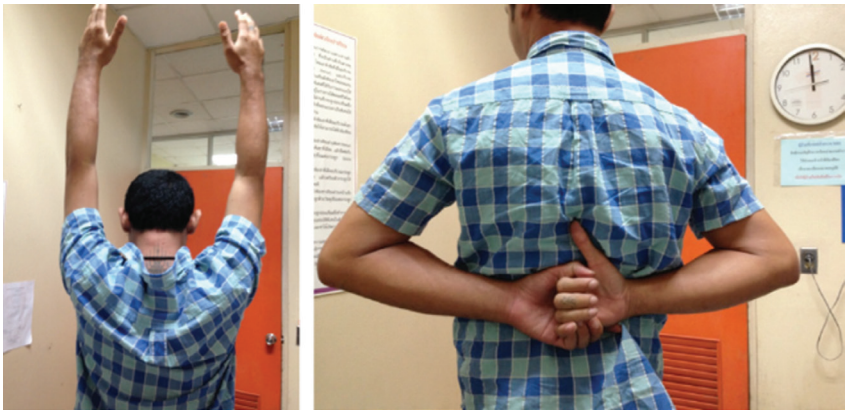

Figure 22: After early ROM exercise, most of the patients had good function.

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Case	Sex	Age	Side	Fracture type (AO)	Mechanism of injury	Associated injury	Fluoroscope Time (sec)	Union time (Wk.)	DASH Score	Clavicular shortening (mm.)	Plate type
1	M	45	R	B2.2	MCA		30	13	4	0.5	LCP Superior
2	F	49	R	B1.3	MCA	Fx Right 2nd-4th rib	39	11	3.3	0.2	LCP Superior
3	M	30	L	B2.2	Fall		24	12	15.3	0.6	LCP Superior
4	M	20	R	B2.1	MCA	Right Hemopneumothorax	24	15	13.3	0	LCP Superior
5	M	28	L	B3.3	MCA	Fx Rt. 3rd rib	39	18	1.7	0	LCP Reconstruction
6	M	55	R	B2.2	MCA		24	15	6.7	0	LCP Reconstruction
7	M	24	R	B2.2	MCA	Fx Rt. 4th-5th rib	28	12	9.2	0	LCP Reconstruction
8	M	44	R	B1.3	Fall		28	15	0.8	0	LCP Superior
Mean		36.875		B2.2 (Most)	MCA (Most)	Rib fractures (Most)	29.5	13.875	6.7875	0.16	

Discussion

The operative treatment for displaced mid-shaft fractures of the clavicle has been well accepted, and has resulted in good functional recovery as well as restoration of clavicular length.[3,9] Several authors have reported favorable results with open plating.[13] However, open plating may cause considerable complications such as nonunion, delayed union or infection.[3,14,15] To avoid these complications, biological and less invasive techniques are necessary.

Good radiologic results were achieved even though the fractures were comminuted. Sohn et al. reported a high union rate after MIPO for fractures of the clavicle; their study included simple as well as comminuted fractures.[16] The same was seen by Hyun-Joo Lee et al. with favorable outcomes reported in performing MIPO with nail assistance.[7]

Wang et al. reported a comparative study between vertical incision and horizontal incision open plating techniques and showed the result of less numbness around the clavicle in the vertical incision group.[11] Thus, we use the MIPO technique with vertical separated incisions along the skin crease to provide a good biological environment for healing and to minimize any skin complications.

In our series, it was very common for injuries to be motorcycle accident-related as this is a common transportation mode in the local area. Moreover, the pattern of injuries was high energy trauma which resulted in the most common type of fractures being multi-fragmentary ones. This kind of fracture should ideally be treated with a minimally invasive technique. MIPO of the clavicle is not a very common fracture treatment, nowadays. There are a very limited number of case series reported in literature.[7,8,16] We used to perform the MIPO by separated horizontal incisions but there were still some complications of the horizontal scar lying on the prominent implants. After we developed the new vertical incision technique along the skin crease, we have not detected any numbness or scarring and hardware complications. All patients could start an early rehabilitation program as planned. This was probably due to a minimal disturbance of the muscle and soft tissue attachment around the fracture and fixation zones. The DASH scores were quite satisfactory; this might be the cause of less unfavourable factors for healing. In comparison to other MIPO studies,[7,8,17] our results seem to be the same as their results.

The only case out of eight reported with any complication was related to a bent plate which was a reconstruction LCP. This plate was not designed to be used for clavicle fixation and was quite weak. Since the thicker anatomical LCP has become available for use, we have a tendency to use this new plate to fix the clavicle in all cases.

Conclusion

MIPO may be beneficial in treating the fracture shaft of the clavicle. Changing the incision style from horizontal to vertical may reduce skin complications. Using an anatomical plate specifically designed for this area is more appropriate than using a weaker reconstruction plate. However, this study was a preliminary report of this new technique and there are a limited number of cases. We need to collect more cases to report with better statistical evidence in the future.

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Comparison of Effectiveness of Pupil Dilatation Methods in Patients of Eye Ear Nose Throat Department at BNH Hospital

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Keywords: pupil dilatation, mydriatic drugs

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OBJECTIVE: This descriptive study aims to compare the effectiveness between two methods of pupil dilatation in patients of the Eye Ear Nose Throat (ENT) Department at the BNH Hospital.

MATERIALS AND METHODS: The specifically selected subjects are 222 ENT out-patients who received mydriatic agents for an eye examination from January 1, 2014 to February 28, 2014. The mydriatic drugs were administered to these patients using two different methods: 1) a mixture of tropicamide 0.75% and phenylephrine 2.5% given every 5 minutes for 4 times and 2) a mixture of tropicamide 0.75% and phenylephrine 2.5% given every 5 minutes for 2 times. A data collection sheet was designed to record personal information, pupil dilatation method and pupil size at 20, 30 and 45 minutes after drug instillation. The pupil size was measured using a Glasgow Coma Scale instrument. The measurement was done by trained nurses who knew the purpose of this study. The descriptive statistics, which included the number, percentage, mean and standard deviation, were used to present personal information and pupil size at 20, 30 and 45 minutes after drop instillation. The pupil sizes from the two methods were compared by using the non-parametric statistics: Friedman Test and Wilcoxon Signed Rank Test.

RESULTS: From the comparison at 20, 30 and 45 minutes after the first drop instillation, both methods showed that the difference of pupil size between the time points was statistically significant ($p > 0.001$). The comparison between the first and the second method illustrates that the difference of pupil size at each time point was not statistically significant ($p = 0.032, 0.800$ and 0.102, respectively) at the 99.9% confidence interval level. Thus, the second method should be used because it requires only two times of instillation (2 times less than the first method) and the pupil measurement at 20 minutes after the first drop instillation reduces waiting times for patients.

CONCLUSION: The study supports pupil dilatation by using a mixture of 0.75% Tropicamide plus 2.5% phenylephrine and improves the process by reducing the waiting times of patients. Patients receive a lower amount of the drug, decreasing from 4 times to 2 times, so the risk of side effects is reduced.

Pupil dilatation is an essential technique for ophthalmologists to diagnose eye diseases or to perform eye surgery more easily. Commonly-used mydriatic agents include: single drugs, such as 10% phenylephrine, 1% Mydriacal, 1% Tropicamide, 1% Cyclogyl, Cyclopentolate, 1% Isopto atropine, and Atropine, and a combination of two mydriatic agents, such as 1% Mydriacyl plus 10% Phenylephrine and 0.75% Mydriacal plus 2.5% phenylephrine.[1] Previous studies reveal that each mydriatic drug varies in the effectiveness of pupil dilatation. Besides the drug type, the

effectiveness depends on the technique of drop instillation used. Some research suggests alternate applications of single drugs every 5 minutes for 2-5 times.[1-4] However, choosing the most appropriate drug type and instillation technique requires careful consideration. Alternate applications of single drugs can lead to confusion and mistakes especially drop instillation with alternate sequence of mydriatic agents. The use of more drugs in a mixture causes more mistakes in the nursing practice. Almost all published studies show a significant difference of pupil dilatation in every method used in the research. Analysis and synthesis of research in evidence-based practice is the key that all ophthalmologists use when making a clinical decision. Mostly, ophthalmologists draw different conclusions, leading to different treatment plans.[5] This explains why ophthalmologist choose different ophthalmologic agents, both drug type and method, in their treatment plan.

Several studies support the use of drug combination, which shows higher effectiveness than single drugs. Anderson, et al.[3] investigated pupil dilation between two methods, 1% Tropicamide plus 2.5% phenylephrine and 1% Tropicamide plus 1% cyclopentolate. Each subject randomly received one drop of a mixture in each eye. Only one mixture was applied to both eyes of a subject and pupils were measured at 5, 10, 15, 20, 40 and 60 minutes to compare the effectiveness. It was found that the first method showed statistically more effectiveness of pupil dilatation of 7 mm than the second method ($p = 0.0062$).

Majid, et al.[4] conducted research into pupil dilatation with two regimens of mydriatic agents, 1) 0.75% Tropicamide plus 2.5% phenylephrine and 2) 1% Tropicamide plus 10% phenylephrine. One drop of each combination was delivered 10 minutes apart for 2 times and the pupil size was measured every 5 minutes until the size reached 7 mm. to compare the effectiveness of pupil dilatation. It was found that the first method significantly showed higher effectiveness than the second method ($p = 0.004$). However, the research results were inconsistent with those of Forman's study.[6] There was no significantly statistical difference of pupil size between the two methods (mean of the 1st method = 7.4 mm., mean of the 2nd method = 7.6 mm.). Phamonvaechavan, et al.[7] compared pupil dilatation between two methods of instilling a mixture of 0.75% Tropicamide and 2.5% phenylephrine. In the first method, drop instillation was given at 0 minute (the first time) and 5 minutes (the second time). For the second method, drop instillation was given at 0 minute (the first time) and 30 minutes (the second time). It was found that the difference of the effectiveness of pupil dilatation between the two methods was not statistically significant. It is assumed that if the number of instillation is reduced from 4 times to 2 times and the pupil sizes of both methods do not differ, this will reduce the number of steps and waiting times. Therefore, the teams designed the present study to compare the effectiveness of pupil dilatation between two methods.

Method and Material

This descriptive research was conducted in the Eye Ear Nose Throat Department at the BNH Hospital. The subjects were 222 patients in the ENT out-patient department, specifically chosen from 1 January to 28 February 2014. These patients were administered a mixture of 0.75% Tropicamide plus 2.5% phenylephrine with two methods as follows:

Method 1 (research from 1 to 31 January 2014):
The procedure started with instilling one drop of the drug combination, instilling another drop at 5 minutes (2nd time), instilling another drop at 10 minutes (3rd time), and instilling another drop at 15 minutes (4th time). Then, the pupil size was measured at 20 minutes (1st time), 30 minutes (2nd time), and 45 minutes (3rd time) to compare the difference in pupil size at each time point.

Method 2 (research from 1 to 28 February 2014):
The procedure started with instilling one drop of the drug combination, instilling another drop at 5 minutes (2nd time), resting at 10 minutes and 15 minutes. Then, the pupil size was measured at 20 minutes (1st time), 30 minutes (2nd time), and 45 minutes (3rd time) to compare the difference in pupil size at each time point.

	Method 1	Method 2
Start	1st Eye drop	1st Eye drop
5 min	2nd Eye drop	2nd Eye drop
10 min	3rd Eye drop	Rest
15 min	4th Eye drop	Rest
20 min	1st measure	1st measure
30 min	2nd measure	2nd measure
45 min	3rd measure	3rd measure

The research instruments include a data collection sheet designed by the researcher to record personal information, eye drop instillation and measurement of pupil size at 20, 30 and 45 minutes, and an instrument for measuring pupil size in the Glasgow Coma Scale. The measurement was done by nurses in the ENT out-patient department of the BNH Hospital.

Data analysis

The data were analyzed by using descriptive statistics, which include the number, percentage, mean and standard deviation, to present personal information and pupil size at 20, 30 and 45 minutes after drop instillation. The pupil sizes from the two methods were compared by using the non-parametric statistics: Friedman Test and Wilcoxon

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Table 1: The number and percentage of out-patients in the ENT department at the BNH Hospital from 1 January 2014 to 28 February 2014.

	n (%)
Patient	222 (100)
January	105 (47.3)
February	117 (52.7)
Sex	
Female	116 (52.3)
Men	106 (47.7)
Age (year)	
Youngest	15
Oldest	97
Mean age	52.96

Table 2: The pupil size of patients receiving mydriatic agents with the 1st and the 2nd method at 20, 30 and 45 minutes.

Time	Method	Lowest	Highest	Mean (SD)
20 min	1	5	8	5.49 (0.71)
	2	4	7	5.38 (0.71)
30 min	1	5	8	7.00 (0.62)
	2	5	8	7.04 (0.56)
45 min	1	7	8	7.94 (0.23)
	2	7	8	7.91 (0.23)

Table 3: Comparison of pupil size between the 1st and the 2nd method at 20, 30 and 45 minutes using the Friedman Test.

	Time	Mean	*p*
Method 1	20 min	5.49	0.000
	30 min	7.00	
	45 min	7.94	
Method 2	20 min	5.38	0.000
	30 min	7.04	
	45 min	7.91	

Table 4: Comparison of pupil dilatation between the 1st and the 2nd method at 20, 30 and 45 minutes using the Wilcoxon Signed Rank Test.

Time	Method 2	Method 1	*p*
20 min	5.38	5.49	0.032
30 min	7.04	7.00	0.800
45 min	7.91	7.94	0.102

Signed Rank Test. As the collected data violated the assumption of normality, parametric statistics (one-way analysis of variance) cannot be used.

Result

There were 222 ENT out-patients who received Mydriatic drugs for an eye examination at the BNH Hospital from 1 January 2014 to 28 February 2014. There were 105 patients (47.3%) in January and 117 patients (52.7%) in February. Most of the patients were female (n = 116, 52.3%). There were 106 male patients (47.7%). The mean age of the patients was 52.96 years. The youngest and oldest patient was 15 and 97 years old, respectively (See Table 1). The average pupil sizes after drop instillation by using the first method at 20, 30 and 45 minutes were 5.49 mm. (SD = 0.71), 7.00 mm. (SD = 0.56), and 7.91 (SD = 0.23), respectively. The means of pupil size increased gradually. For the second method, the average pupil sizes after drop instillation at 20, 30 and 45 minutes were 5.38 mm. (SD = 0.71), 7.04 mm. (SD = 0.56), and 7.91 (SD = 0.23), respectively. The means of pupil size also increased gradually (See Table 2).

Based on the comparison of pupil size in the first method at different time points, the differences of pupil size between time points were statistically significant at $p < 0.001$. For the second method, the pupil sizes at three time points also differed significantly at $p < 0.001$ (See Table 3). From the comparison of pupil size at 20 minutes after the first drop instillation, both methods showed the difference of pupil size with no statistical significance ($p = 0.032$). At 30 minutes, the difference of pupil size between two methods was not statistically significant ($p = 0.800$). Also, at 45 minutes after the first drop instillation, both methods showed the difference of pupil size with no statistical significance ($p = 0.102$) (See Table 4).

Discussion

This research compared the effectiveness of pupil dilatation between two methods used in the ENT out-patients at the BNH Hospital. It was found that the pupil size increased at 20, 30 and 45 minutes with statistical significance at $p < 0.001$. This is consistent with the action of 0.75% Tropicamide plus 2.5% phenylephrine combination, which starts 15 minutes after instillation and lasts for three hours.[7] The comparison of pupil size between the 1st and the 2nd method showed that at 20, 30 and 45 minutes the pupil size differed with no statistical significance at the 99.9% confidence interval level % ($p = 0.032$, $p = 0.800$ and $p = 0.102$, respectively). The results from this study suggest the use of the second method, as it requires only two times of instillation; the first drop and the second drop, given 5 minutes apart. In addition, the pupil measurement is done at 20 minutes after the first drop instillation.

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These studies show the following benefits:

1. Shorter preparation time of eye examination.
2. Patients receive fewer amounts of drugs, decreasing from 4 times to 2 times, so the risk of side effects is reduced.
3. Decrease in steps of drug administration, from 4 times to 2 times. Thus, the nurses can spend more time with other patients.
4. The error of drug administration is reduced.

Conclusion

With evidence-based medicine, extending the knowledge from previous research leads to the development of a process for pupil dilatation. The study supports pupil dilatation by using a mixture of 0.75% Tropicamide plus 2.5% phenylephrine and improves the process by reducing the waiting times of patients. Patients receive fewer amounts of drugs, decreasing from 4 times to 2 times, so the risk of side effects is reduced.

Acknowledgements

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Recommendations

Future research should investigate factors increasing the rate of pupil dilatation to reduce the waiting time of 20 minutes after the first drop instillation.

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Dental Implant for Teeth Replacement in Esthetic Zone

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Abstract

The replacement of multiple missing teeth in the anterior maxilla counts among the greatest challenges in dentistry. Implant-supported prosthesis has become the treatment of choice for a number of reasons. Most significant among these is its natural appearance and expected longevity. Although the results are easy to predict, the replacement of several missing anterior teeth can be difficult since it must meet functional requirements and satisfy patients' demands in this highly esthetically visual area.

Missing teeth: Treatment options

Generally there are three treatment options for replacing missing anterior teeth: removable partial dentures, fixed bridge, and dental implant. To varying degrees, all three options restore chewing function, and provide more normal speaking ability. They also prevent existing teeth from shifting and improve the look of an incomplete smile. The advantages and disadvantages of each of these solutions have been widely discussed in the literature; each treatment option may suit one differently, depending on individual patient's needs and expectations.

Teeth-supported removable partial denture (removable partial denture)

A well-made removable partial denture is still considered a viable alternative treatment for several patients with multiple missing anterior teeth, especially those with a significant residual alveolar ridge deficiency, medically compromised, and limited financial resources (Figure I).[1] Its unnatural feeling and discomfort are the main disadvantages of the removable partial denture.[2]

Teeth-supported fixed partial denture (fixed bridge)

A fixed bridge is a highly predictable and acceptable treatment option for replacing multiple missing anterior teeth. The predictability of its result is highly dependent on adequate in number and sufficiently healthy of the adjacent (abutment) teeth to support the artificial teeth in the missing area, as well as the patient's parafunctional activity.[2] In order to fabricate a fixed bridge, the abutment teeth are well prepared to reduce their size by removing all the enamel, making room for the prosthetic restoration. Then, a prosthetic (pontic) tooth can be suspended between abutment teeth in this way to provide a functional and esthetic replacement for the missing teeth. However, the limitation with this form of treatment is the permanent loss of tooth structure from the irreversible preparation of abutment teeth (Figure IIA-B). This condemns the patient to the risk of trauma to their nerves. In addition, replacement of fixed bridges often leads to further treatment as the abutment or supporting teeth have been further compromised over time by progressing dental disease such as dental caries or periodontal disease.

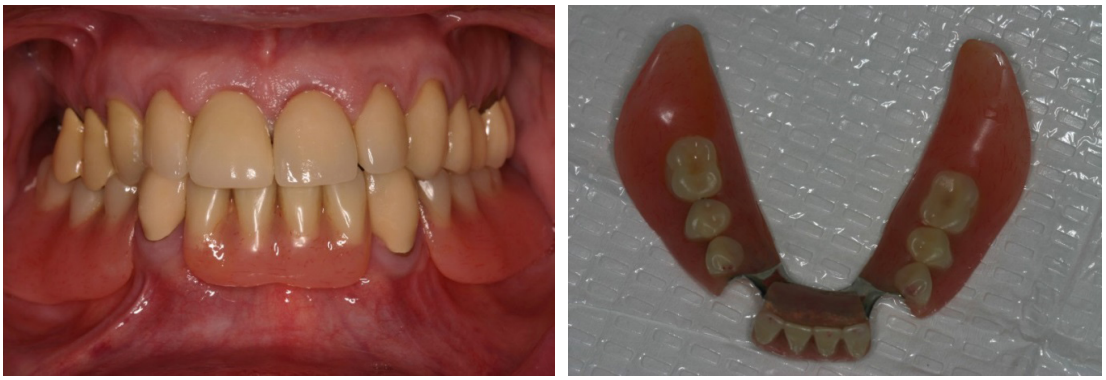

Figure I: Replacing multiple missing lower anterior and posterior teeth by removable partial denture

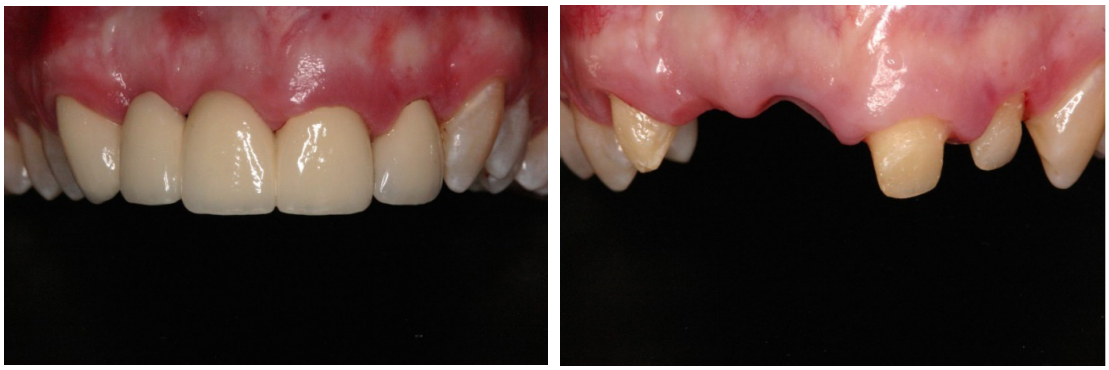

Figure IIA: Replacing right central and lateral incisors by fixed bridge

Figure IIB: Several adjacent (abutment) teeth; right canine, left central and lateral incisors, need to be prepared for supporting prosthetic (pontic) missing teeth

Implant-supported fixed partial denture (dental implant)

Nowadays, dental implants are appealing and are more widely accepted by several patients who have lost multiple teeth, since they offer better alternative options to patients, especially those who are not able to tolerate functionally poor removable dentures.[3] Dental implants are also preferable for patients who have compromised structural condition and remaining teeth, which would not make good abutments. Still, dental implants are not an alternative treatment for everyone, since patients may require surgery to build up the area needed for the implant, so it is necessary that patients should be in good health in general. There is also evidence showing that heavy tobacco and cigarette smoking may also compromise long term outcomes.[3] Patients should be ready to commit to a daily oral care routine and to regular dental visits. The success of dental implants depends on patient knowledge and expectations as well as the care, skill, and judgment of dental clinicians.

Dental implant in highly esthetic areas

The critical goal for esthetic dentistry is to harmonize with the frame of the smile, face and more importantly the individual. Achieving the best results involves comprehensive understanding of the objective and subjective criteria related to hard and soft tissue esthetics since both teeth and gums act together to provide a visual harmony and balance.[1]

In addition to the dental implants in visible areas, the successful result more specifically depends on the harmony of the crown-implant complex in terms of color and form with the soft tissue surrounding and the neighboring teeth. The predictability of its outcome is very different, and relies on the quality and quantity of the bone and soft tissue. As we know that following teeth extraction, the alveolar bone that supports the teeth tends to remodel over time (resorption), both in width and vertical height of the ridge. This resorption often compromises gingival tissue levels, as the body scallop for the facial to interproximal starts to flatten out, making it very difficult to achieve an excellent gingival scallop if implants are placed. In the so-called esthetic area of the mouth, where loss of ridge and gingival volume can be visibly apparent, this can lead to an esthetic imperfection as well as a higher likelihood to develop food impaction under adjacent teeth (Figure III).[4] Proper treatment planning must address hard and soft tissues deficiencies and combine this with precision in implant placement. Advances in bone grafting have made the outcome more predictable.

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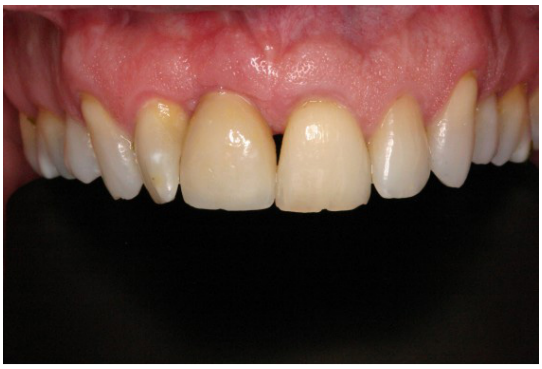

Figure III: Bone deficiency prior to implant placement on maxillary right central incisor creates compromised soft tissue level and interdental papilla imperfection (black triangle space) between implant and adjacent teeth.

The esthetic outcome of implant restorations are influenced by many variables including:

A. Patient's expectation and smile line: Patients' esthetic expectations must be evaluated together with the smile posture. Previous photographs may assist in determining the natural position of the lip when smiling. A high smile line poses considerable challenges because the restoration and gingival tissues are thoroughly displayed. The low smile line is a less critical situation due to the gingival display will be hidden behind the upper lip (Figure IV-V).

B. Implant position: The implants need to be evaluated in three dimensions: apicocoronal, faciolingual, and mesiodistal prior to the surgery since these positions will significantly influence the performing gingival architecture. Placing the implant close to adjacent root creates a great risk of the bone resorption.[4] The surgical and radiographic guide along with a computerized tomography scan is essential to evaluate the required precision in implant placement, and to determine the proper diameter size and length of implants.

C. The bony anatomy of the implant site: For successful esthetic restoration, the bony housing must have a three dimensional foundation that permits placement of an implant in a relatively ideal position. The bone graft procedure is necessary if the bony anatomy is inadequate. The most crucial dimension remains the apicocoronal dimension. The patient must understand that the missing hard and soft tissue architecture will need to be rebuilt so that optimum esthetics can be achieved.

D. Implant Restoration: Successful dental restorations on implant in the esthetic area are usually the result of close interdisciplinary cooperation between dental clinicians and technicians. The restorations need to be painstakingly fabricated in the laboratory to mimic the natural translucent appearance. In addition, several issues such as porcelain natural shade layering techniques, precision of margins, accuracy of framework, proper dental anatomy, and optimal occlusion are also a principal focus (Figure VI).[5]

E. Gingival Biotype: The healthy appearance of the gingiva is a crucial issue. Characteristics of the gingival soft tissue biotype will play a prominent role in the final planning for the implant.[4] A thick gingival biotype is more favorable since the thin biotype has a delicate soft tissue curtain, and reduced quantity and quality of keratinized mucosa. Therefore, the thin biotype will require the implant to be placed more palatal and deeper to allow a proper emergence profile and mask any metal show through.

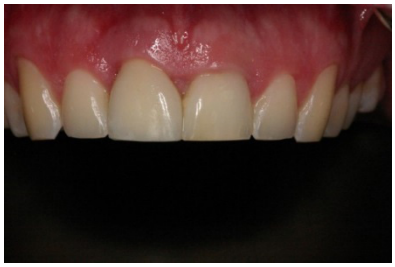

Figure IV: Receded gingival soft tissue level after placing the implant on maxillary right central incisor

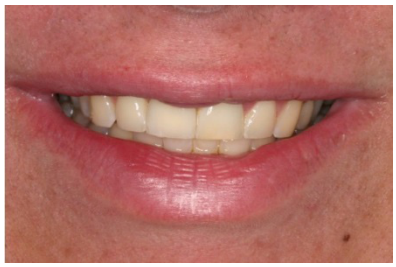

Figure V: The gingival display is hidden behind the upper lip in patient with low smile line creating a satisfactory appearance

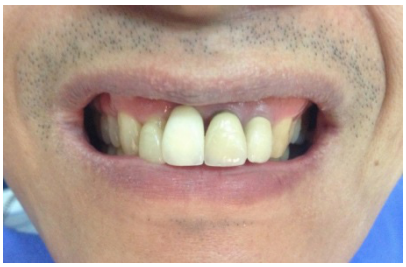

Figure VI: Placing the implant too far apically and the mismatched porcelain natural shade of the implant restoration creates a compromised esthetic outcome on the maxillary right central incisor

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Case Reports

These following cases require close cooperation among the orthodontist, oral surgeon, periodontist, and prosthodontist. They illustrate how multiple missing teeth can be replaced with dental implants.

Case Report # 1

A 19-year-old healthy female had several missing teeth congenitally, on the maxillary left and right lateral incisors, and two mandibular central incisors (Figure 1A-B). Orthodontic treatment was complete, and the patient was using a removable retainer with denture teeth attached for the prosthetic replacement of the teeth. The patient was unhappy with the appliance and wanted a permanently fixed solution. The oral examination revealed the edentulous alveolar ridge had a fair amount of bony and gingival architecture. A decision was made for dental implant treatment(Figure 1C-D). Several months follow up revealing interdental papilla levels were increased gradually and improved natural appearance (Figure 1E).

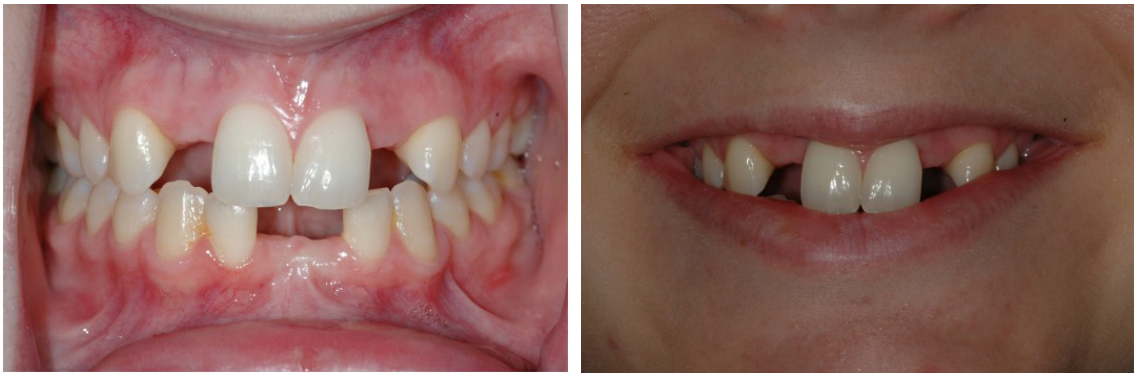

Figure 1A-B: After Orthodontic treatment, patient still has spaces of missing teeth area of maxillary left and right lateral incisors, and two mandibular incisors.

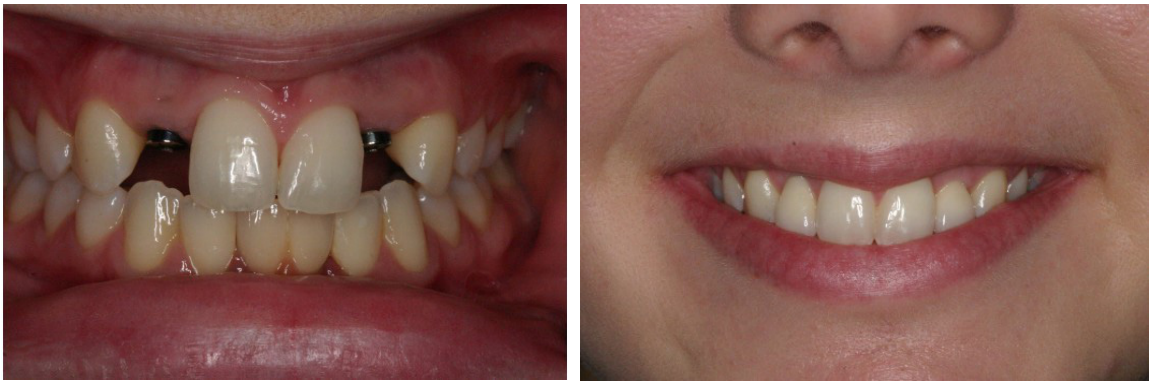

Figure 1C-D: Four implants were placed in the missing area.

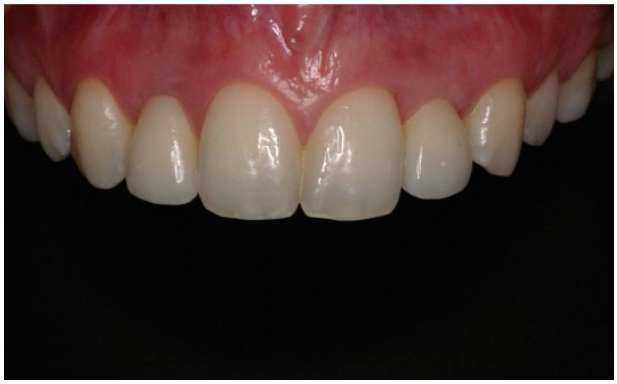

Figure 1E: The gingival tissue has a satisfactory natural appearance after several months follow up

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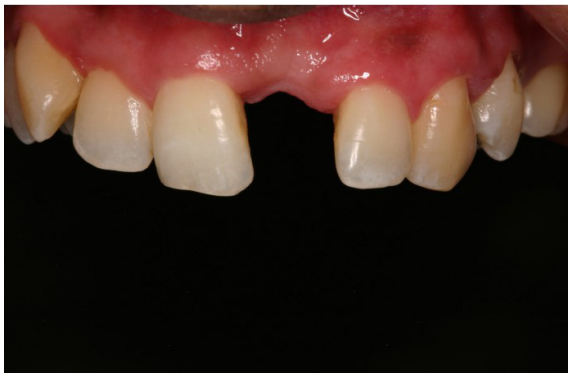
Case Report # 2

A 27-year-old healthy male, lost the maxillary left incisor in an accident 10 years ago. The bony anatomy is inadequate both in width and height due to the resorption after the tooth was extracted (Figure 2A-B).

The bone graft procedure was performed prior to the implant placement (Figure 2C). The final result is esthetically acceptable (Figure 2D).



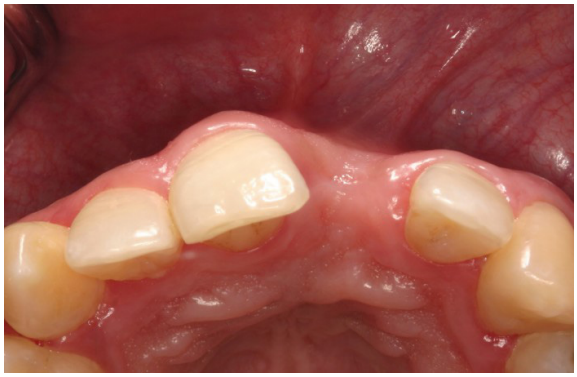


Figure 2A-B: Inadequate bone width and height for ideal implant position in all three dimensions

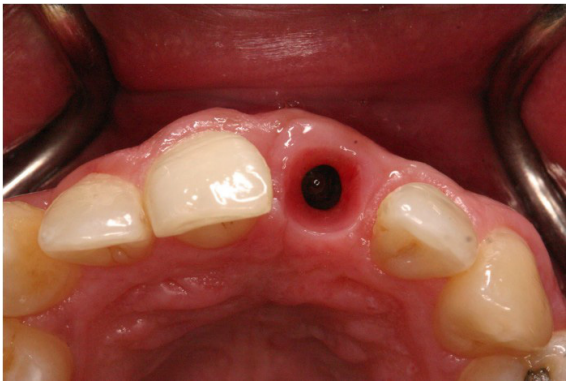


Figure 2C: Optimum implant positioning after the proper bony structure by bone grafting procedure

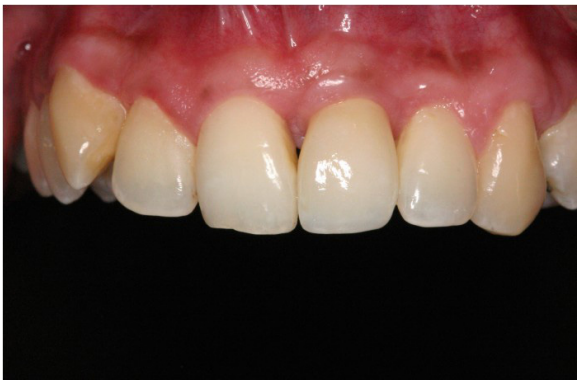


Figure 2D: Satisfied soft tissue profile and restoration on the implant

Case Report # 3

A 48-year-old healthy male lost several maxillary teeth from an infection (Figure 3A). The periodontal treatment and maintenance was performed before the patient went through the dental implantation procedure. Following the bone graft, two implants were placed in the precise positioning of the lateral incisor and premolar to support the multiple unit fixed implant prosthesis according to the surgical guide (Figure 3B-D). The patient was very satisfied with the esthetic and functional result (Figure 3E).

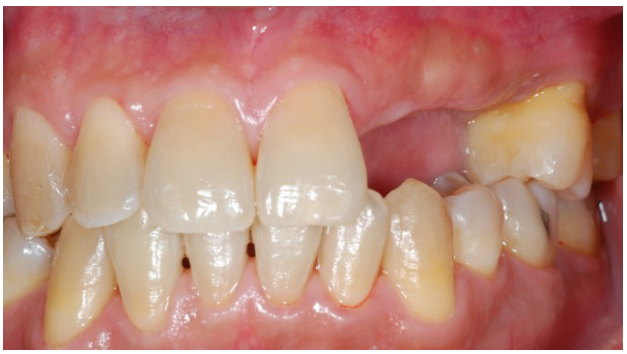
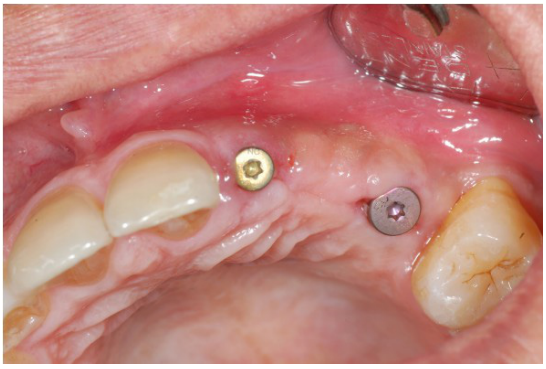


Figure 3A: Multiple missing teeth on maxillary left anterior to posterior teeth



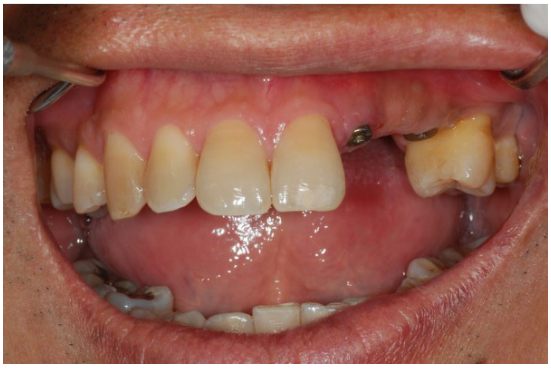


Figure 3B-C: Two implants were precisely placed at the lateral incisor and premolar sites to support a multiple unit fixed implant prosthesis

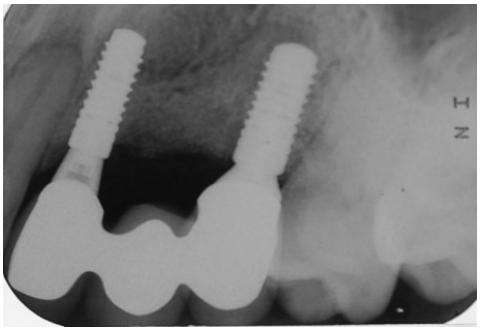


Figure 3D: Radiographic examination revealing precisely parallel placement of implants

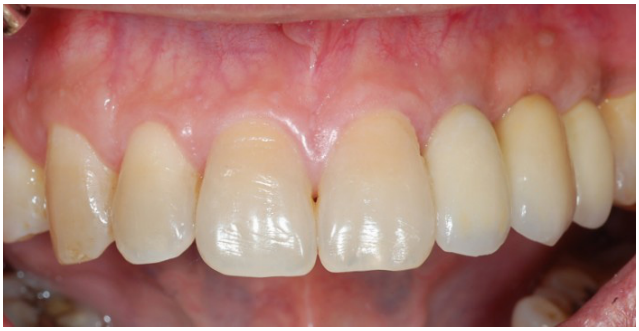


Figure 3E: Clinically-acceptable function and esthetic result

Conclusion

The decision of replacing missing anterior teeth must be performed by the dentist and patient after a proper discussion has been had. Common choices would include: fixed bridge, removable partial denture, and dental implants. Each has its advantages and disadvantages. The dental implant itself has several advantages, from its natural appearance, preservation of unrestored adjacent teeth, arresting the resorption of edentulous spaces and optimal support. However, it requires a longer treatment time, a delicate provisional restoration, precise surgical placement and it has a higher cost. Despite these disadvantages, however, a dental implant can be successfully executed when all the factors are addressed: then a dental implant can be considered the treatment of choice for replacing missing teeth.

In the esthetic area, it is critical that the treating dentists and patients are clear about what can be realistically expected and what changes may need to be made in the plan dependent upon the outcome of each phase of treatment. This allows the patient and clinician to proceed with a clear understanding of the potential complications and financial costs. Multidisciplinary treatment and team planning are necessary for the success of implant replacement in esthetically visual areas.

Acknowledgements

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Neuromyelitis Optica (NMO)

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Abstract *NMO is a is a rare entity which involves the central nervous system acting as an inflammatory process by attacking the optic nerve (ON) and longitudinally extensive transverse myelitis (LETM). The specificity of this disease is antibody aquaporin-4 (AQP4). Repeated relapses of the disease can lead to severe disability and blindness. MRI is none specific but at the cervical spinal cord shows the long extensive contrast enhancement. The specific diagnosis is NMO IgG.*

Keywords: neuromyelitis optica, NMO-IgG, aquaporin-4 antibody, APQ-4, multiple sclerosis, MS, oligoclonal band, azatrioprine

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Neuromyelitis optica (NMO), or Devic's disease, is a rare inflammatory and demyelinating autoimmune disorder of the central nervous system (CNS) characterized by recurrent attacks of optic neuritis (ON) and longitudinally extensive transverse myelitis (LETM) which is distinct from multiple sclerosis (Table 1).[1] The first case was reported by Eugene Devic in 1894, but the discovery of a highly specific serum autoantibody (NMO-IgG) was only recently found in 2004, with a high specificity of 91% and sensitivity of 73%.[1,2] This antibody is known to target aquaporin-4 (AQP4), an astrocyte water channel that is widely distributed, and this antibody is known as a pathogenesis of this disease. Patients often have relapses, which leads to severe disability and blindness.[3] Magnetic resonance imaging (MRI) of the brain and spine can show typical findings of this disease. Early diagnosis is key to successful management for prevention of disability. The most appropriate treatment approach in NMO is immuno-suppression: this is effective against antibody-mediated diseases such as azathioprine, and mycophenolate mofetil.

This is a report of a middle-aged Thai female, presenting as a classic case of NMO.

Case Report

A 48-year-old woman presented with a rapidly progressive left hemiparesis and numbness at left chest wall, back and left arm. There were no ocular symptoms or bowel and bladder symptoms. She had not experienced an accident or other preceding illness, including no rash and no arthritis.

Neurological examination showed grade IV/V left hemiparesis and loss of sensation at the left C2-6 dermatome distribution. She has generalized hyperreflexia with the presence of finger reflexes on both sides, but with a normal jaw jerk reflex. The tone was increased in both legs and Barbinski's sign was present on both sides. Her cranial nerve, including optic nerve and visual function, bowel and bladder were normal.

Magnetic resonance imaging (MRI) of the brain was normal (Figure 1). MRI of cervical spine showed heterogeneous patchy enhancement and swelling of the cervical spinal cord at C2-C6 levels, with a suspected long segment of cervical transverse myelitis (Figure 2).

Table 1: Definition and characteristic of Multiple Sclerosis (MS) and Neuromyelitis Optica (NMO).[1]

Details	Multiple Sclerosis	Neuromyelitis Optica
Definition	- Central nervous system symptoms and signs that indicate the involvement of the white-matter tracts - Evidence of dissemination in space and time on the basis of clinical or MRI findings - No better explanation	- Transverse myelitis and optic neuritis - At least two of the following: brain MRI, non-diagnostic for multiple sclerosis, spinal cord lesion extending over three or more vertebral segments, or seropositive for NMO-IgG
Clinical onset and course	- 85% remitting-relapsing - 15% primary-progressive - Not monophasic	- Onset always with relapse - 80-90% relapsing course - 10-20% monophasic course
Median age of onset (years)	29	39
Sex (F:M)	2:1	9:1
Secondary progressive course	Common	Rare
MRI: brain	- Periventricular white-matter lesions	- Usually normal or non-specific white-matter lesions, 10% unique hypothalamic, corpus callosal, periventricular, or brainstem lesions
MRI: spinal cord	- Short-segment peripheral lesions	- Longitudinally extensive (> 3 vertebral segments) central lesions
CSF white-blood-cell number and differential count	- Mild pleocytosis Mononuclear cells	- Occasional prominent pleocytosis - Polymorphonuclear cells and mononuclear cells
CSF oligodonal bands	85%	15-30%

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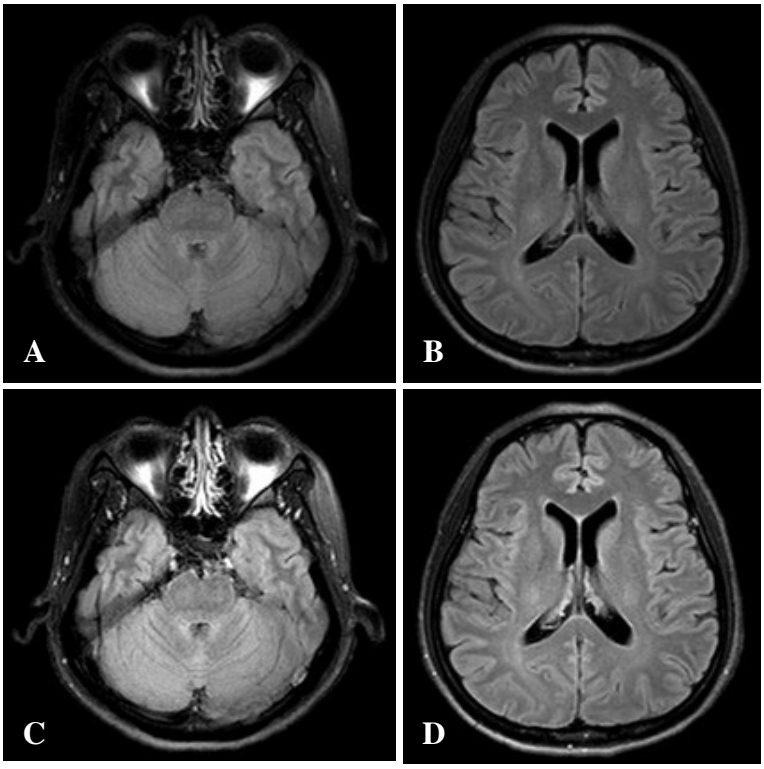

Figure 1: MRI brain T2 flair technique shows normal brain parenchyma (A,B) and post gadolinium injection reveals no enhancement (C,D).

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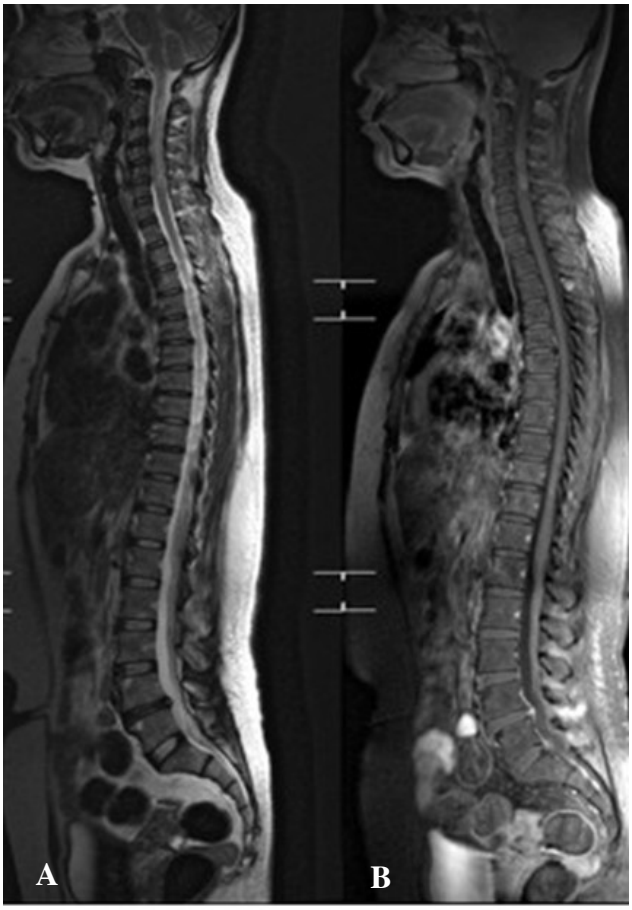

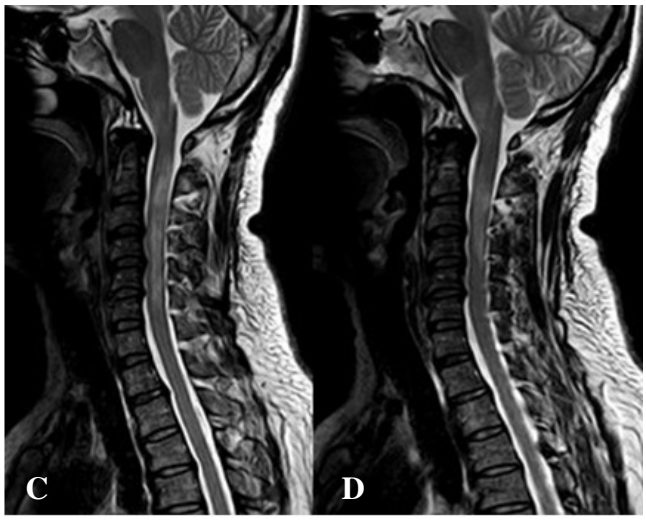

Figure 2: A, B: MRI whole spine neutral position: the sagittal T2- weight MR image shows a long segment of hyperintensity at cervical cord at level 2-6 with cord swelling.
C, D: MR image saggital T2-weight with gadolinium injection: Heterogeneous patchy enhancement and swelling of the cervical spinal cord at C2-C 6 levels, suspected transverse myelitis.

The complete blood count (CBC) results were as follows: Hemoglobin (Hb) 13.8 g/dL, white blood cell (WBC) 8,130 cell/mm^3 (neurotrophil 63.9%, lymphocyte 26.8%, monocytes 3.9%), platelet 314,000 /mm^3. Anti-nuclear factor (ANF) was 1:80, ESR was 14 mm/hr, and Anti-Ro and Anti-La were negative. A CSF oligoclonal band was negative. NMO-IgG antibody was positive.

Discussion

This case demonstrated a typical clinical finding and MRI specific example of NMO. Her clinical symptoms are typical of acute cervical myelitis that rapidly progresses like a natural history of NMO. Her MRI showed a long segment of intra-axial hyper intensity on T2W with heterogeneous patchy enhancement and swelling of the affected spinal cord, which is also a typical finding of NMO. The positive NMO IgG result confirms the diagnosis. NMO affects young adults with a median onset age of 39 years. Woman are much more commonly affected. NMO is more common in Asian populations than western populations (Japanese 20-30%, Hong Kong 36% of all demyelination diseases, similar to Thailand levels, according to a study by Siriraj Hospital, Bangkok).[4] The difference between MS and NMO is summarized in Table 1.[1]

Clinical presentation of NMO

- Optic neuritis: severe unilateral more commonly that bilateral.
- Myetitis: severe symmetrical paraplegia, and sensory loss below the lesion.
- Other: chronic vertigo, chronic hiccups, nausea, vomiting.

Patients with NMO tend to have a high chance of relapse 60% and 90% at 1 year and 3 years respectively. A criterion for diagnosis of NMO is shown in Table 2.[5,6]

Table 2: Revised neuromyelitis optica diagnosis criteria (2006).[4,5]

Diagnosis requires fulfillment of absolute criteria and least two of three supportive criteria	
Absolute criteria:	Supportive criteria:
1. Optic neuritis	1. Negative brain MRI at disease onset
2. Acute myelitis	2. Spinal cord MRI with contiguous T2-weighted signal abnormality extending over three or more vertebral segments
	3. NMO-IgG seropositivity

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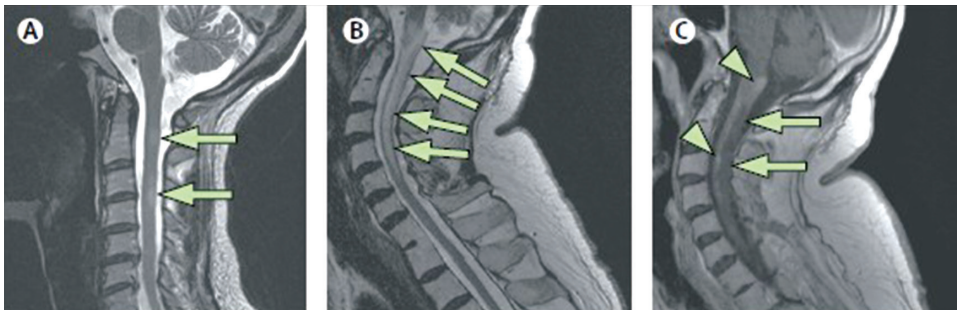

Figure 3: Spinal cord MRI in multiple sclerosis and neuromyelitis optica
A: Sagittal T2-weighted MRI of the cervical spinal cord shows typical dorsal, short-segment signal abnormalities (arrows) characteristic of multiple sclerosis.
B: Sagittal T2-weighted cervical spinal cord MRI from a patient with acute myelitis and neuromyelitis optica shows a typical longitudinally extensive, expansile, centrally located cord lesion that extends into the brainstem (arrows).
C: On T1-weighted sagittal MRI sequences, such acute lesions might be hypointense (arrows), which might indicate necrosis and cavitation, while showing enhancement with intravenous gadolinium administration (arrowheads), indicative of active inflammation.
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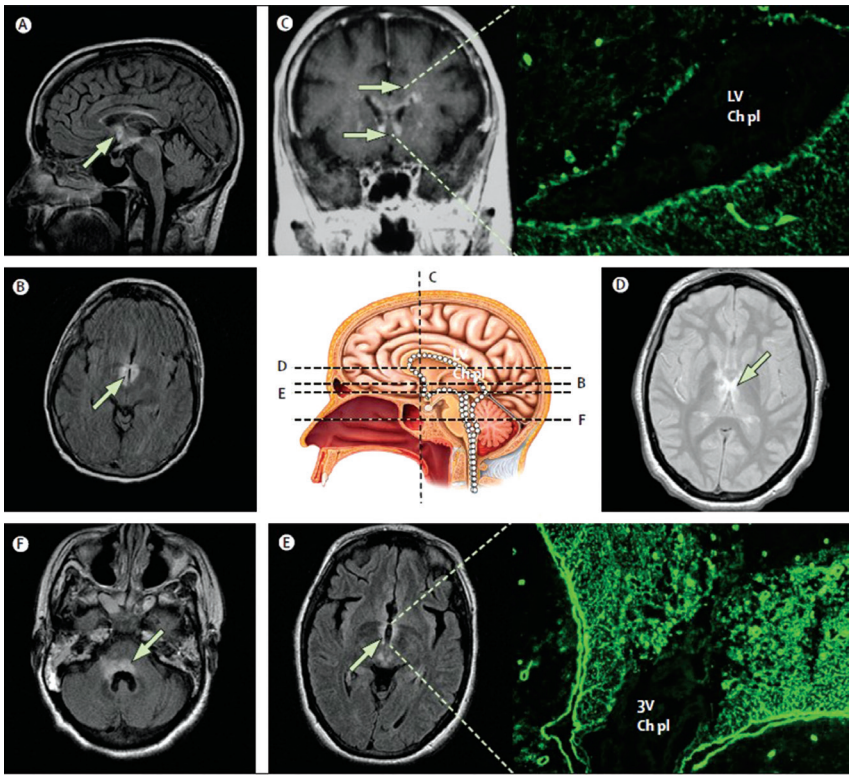

Figure 4: Brain lesions typical of neuromyelitis optica localised at the sites where aquaporin 4 expressions are normally highest. Representative MRI of three patients who are seropositive for NMO-IgG. The images show lesions in the periependymal regions of the brain; these sites are enriched with aquaporin 4 (white dots on centre picture of midline sagittal section). In the centre picture the dashed black lines show the anatomical level of MRI in the diagram; arrows show abnormality on fluid-attenuated inversion recovery (FLAIR), T2-weighted signal or after being given gadolinium. Patient 2 (image C; coronal, post-contrast T1-weighted image) has subependymal enhancement along the frontal horns bilaterally and in the adjacent white matter. The immunofluorescence photomicrograph linked to image C shows the binding pattern of the serum IgG from a patient with neuromyelitis optica in a mouse brain (400x). Intense immunoreactivity of basolateral ependymal cell membranes lining the lateral ventricle (LV) and extending into the subependymal astrocytic mesh coincides with aquaporin 4 immunoreactivity; the choroid plexus (Ch pl) is unstained. Patient 3 has contiguous signal abnormality throughout the periventricular tissues; diencephalon (image D; axial T2-weighted), third ventricle (image E; axial, FLAIR), and 4th ventricle (image F; axial FLAIR). Immunofluorescence photomicrograph linked to image E shows the binding pattern of the serum IgG from a patient with neuromyelitis optica in a mouse brain (400x), with intense staining of periventricular tissues (3rd ventricle, 3V); choroid plexus (Ch pl) is unstained image C is courtesy of Allen Aksamit, Mayo Clinic College of Medicine.
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Typical presentations of spinal cord MRI abnormalities in NMO include a longitudinally extensive intra-axial lesion, characteristically spanning over 3 or more contiguous vertebral segments, as shown in Figure 3.[1] In contrast to MS, the brain MRI of patients with NMO is usually normal or shows non-specific white matter lesions. Nevertheless, in some NMO cases, typical abnormalities of the brain at the hypothalamus, corpus callosum, periventricular area (area postrema), or brainstem can be seen (Figure 4).[1]

CSF analysis

Prominent CSF pleocytosis with a high proportion of neutrophil can be seen. CSF oligoclonal band is present in only 15% of cases, which is much lower than in MS (80% of cases). ANA can be detected in 53% and antibodies to extractable nuclear antigen (primarily anti-Ro, anti-La) in 17%.[7]

Treatment

Intravenous corticosteroid therapy is commonly used as an initial treatment. Patients who do not respond may undergo plasmapheresis. Maintenance immunosuppressive therapy is generally used to reduce the relapse of NMO, of which, azathioprine (2.5-3mg/kg/day), mycophenolate mofetil, rituximab ,mitoxantrone and prednisolone may be used.[8]

Conclusion

NMO is a severe, disability disease that primarily affects middle-aged working females. Early and correct diagnosis is of the highest importance. The NMO-IgG test is very specific and useful in diagnosis and is now available in Thailand.

Early immunosuppressive therapy is recommended.

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Case Report

Various Techniques on Distinct Cases of Tracheal Stenosis

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Abstract

Narrowing of the airway caused by several factors is a serious condition manifesting different signs and symptoms. Immediate attention is needed and treatment must be performed as this is a life-threatening condition. In the past decade, there have been massive advancements in the management of airway stenosis. Some of these are stent placement, tracheal reconstruction and tumor debulking. This article focuses on six different cases with distinct strategies in conducting treatment.

Airway stenosis is the partial or complete narrowing of the central airway passages. This may involve the subglottic, trachea-esophageal, broncho-esophageal or tracheo-broncho-esophageal area. The disease may be caused by focal inflammation or trauma (prolonged tracheostomy or intubation), systemic inflammation, infectious disease (Tuberculosis), or malignancy (primary or metastatic). It is a potentially life-threatening condition with varying signs and symptoms. Patients frequently do not recognize any symptom until at least 50% of the luminal diameter is compromised because of the distensible character of the esophagus. This explains the late presentation and or prognosis associated with the disease.[1] Management requires immediate attention, thorough physical examination, diagnostic tests computed tomography (CT) scan, accurate diagnosis and ultimate definitive treatment. Though there are many types, causes and management of tracheal stenosis, this article focuses on six cases of adult airway stenosis and the team's unique approach to each case.

We performed this study to analyze the different techniques used in handling six patients with different pathology/causes of airway stenosis. Between September 2012 and November 2013, we identified six patients diagnosed with central airway narrowing. All cases had symptomatic airway stenosis. We analyzed each case study, considered the pathology of the disease, treatment, prognosis, and improvement in quality of life.

Case Report #1

A 46-year-old male patient diagnosed with stage III lung cancer. He was referred to our medical facility nine months after a right upper lobectomy and subsequent external irradiation and chemotherapy. The cytopathology report from the lobectomy revealed large cell undifferentiated carcinoma, suggestive of Adenocarcinoma with 90% tumor necrosis, with a dimension of 7.0×6.0×4.2cm.

The physical examination revealed coughing for two months, progressive difficulty and shortness of breathing for two weeks, orthopnea, rhonchi upon auscultation of the lung and pain when in the right lateral position. No cardiac problems were noted. Neck, chest and abdominal CT scan presented a demon-strable consolidative mass with heterogeneous enhancement, central necroses, haemorrhage and lobulated contour; measuring about 82×48mm in the right lung apex, prevertebral and paratracheal

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regions. This mass extends to the pleurae, periphery, adjacent upper thoracic vertebrae, upper trachea & upper esophagus. The mass causes pressure that affects the upper trachea and upper esophagus which results in an upper tracheal stenosis/obstruction (more than 80-90%) (Figure 1A).

The patient was advised to undergo a bronchoscopic evaluation and insertion of a small endotracheal tube to establish patent airway. The direct visualisation of the location of the tumor was crucial (external or endobronchial in nature) in order to consider electrocautery in extraction of the mass or to establish if a stent placement were possible. A team of oncologists, anaesthesiologists, and a cardio-vascular surgeon were consulted regarding this scenario. The patient and relatives were made aware of the high risk of this procedure and possible complications, including complete airway obstruction, haemorrhage, infection, and mortality. The prognosis and better quality of life and alternatives were discussed. The patient and relatives acknowledged these but decided to delay the treatment.

Two months after the initial consultation, after progression of symptoms, the patient decided to undergo the bronchoscopy and stent placement. Flexible bronchoscopy showed endobronchial mass nearly completely obstructing the main airway. A rigid bronchoscope was used for stent placement. A polyflex airway stent was successfully inserted and the patient did not manifest any complications (Figure 1B). In the succeeding months, the patient underwent brachytherapy for treatment. Three months post stent placement, the patient came back complaining of dysphagia. A PET/CT scan presented a continued increase in size of the mass at the superior mediastinum which extended to the right upper paramediastinal region and partially encased trachea, now measuring about 6.9×5.2cm at the sternal notch level. The tracheal stent is in place from the sternal notch to the carinal level. The mass affects the proximal superior vena cava. The superior extension of this mass which extended beyond the apical lung, involved scalene muscle and involves compression to the right brachial plexus which also increased in size from 1.5cm to 2.3cm. He was then admitted to undergo a fiberoptic bronchoscopy and electrocautery to remove the tumor on both ends of the stent and to suction the mucus plug (Figure 2).

Post procedure, he was improving symptomatically with the infusion of antibiotics and palliative radiation therapy to the affected part of the tumor mass. The patient continued receiving treatment until he passed away eight months after the stent placement.

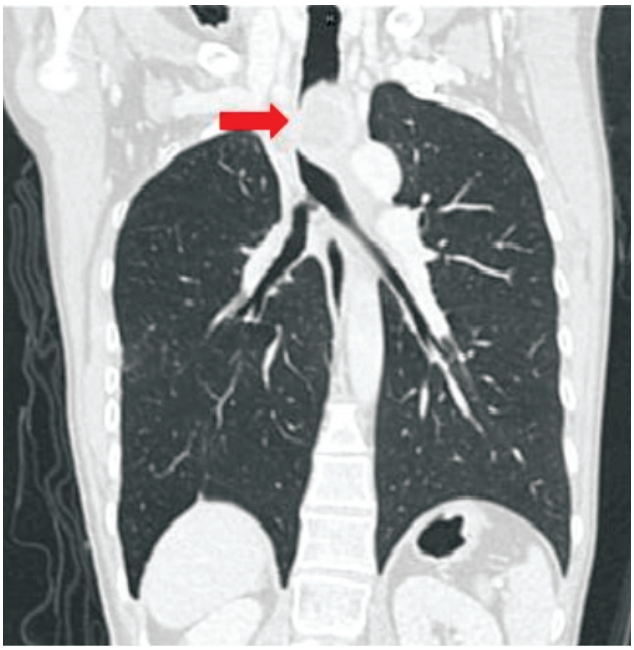

Figure 1A: CT scan demonstrating consolidative mass

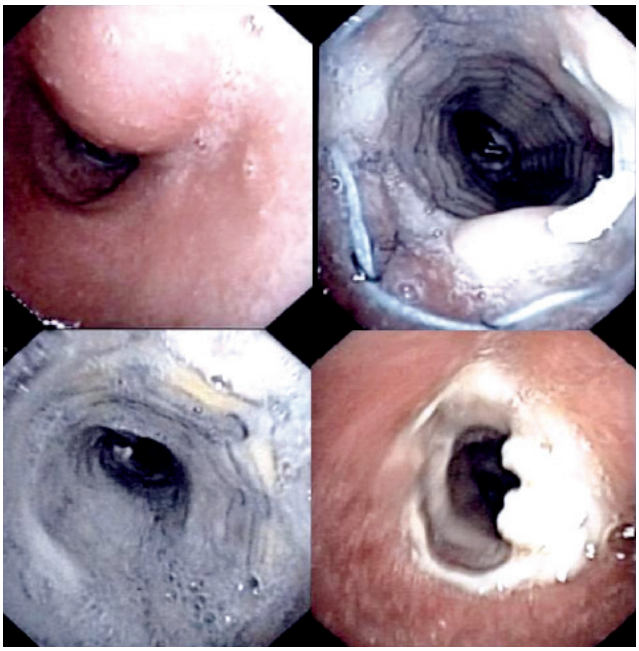

Figure 1B: Shows (clockwise from upper right) part of the mass, the stent placement, mucous plug and tumor regrowth

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Case Report # 2

The patient is a 46-year-old male who presented with progressive dyspnea for four months, hoarseness of voice and stridor for two months, fever, and cough with greenish secretions for two weeks. He was previously a smoker for 20 years but had stopped six months prior to consultation. The physical examination revealed stridor upon auscultation.

A chest CT scan revealed a thickened tracheal wall, more on the posterior wall about 5cm in length from about lower T1 to lower T4 level, causing narrowing trachea (Figure 2A-B). Multiple pulmonary nodules were noted (at least seven in the right and five in the left lung). Metastasis was suggested and the largest nodule near the right hilum may be a primary carcinoma. Laboratory markers were significant for carcinoembryonic antigen (CEA): 5.49ng/mL, Hemoglobin: 11.4g/dL and WBC: 13.54*10^3/mm3. The patient was then intubated with the use of a microlaryngeal tube no. 5 as the endotracheal tube no. 8 was unable to pass through. The plan was that once stable, the patient would undergo a FOB for tracheal examination, visualization, biopsy, and electro-cautery followed by stent placement with the use of a rigid bronchoscope. The risk of hypoxia was significant and recognized. Two days prior to the scheduled procedure, the patient exhibited hemoptysis. Bedside FOB was done to investigate and the cause of bleeding was stopped by electrocautery. The following day the patient exhibited bradycardia because of the sedative effects of anesthesia but this was controlled and managed properly. Then he underwent FOB which revealed tracheal stenosis due to the thickened endotracheal wall. Stent placement was done using a rigid bronchoscopy. A polyflex airway stent was successfully inserted. Specimens were sent to the laboratory for cytology and revealed that the tracheal tissue is positive for adenoid cystic carcinoma (Figure 2C).

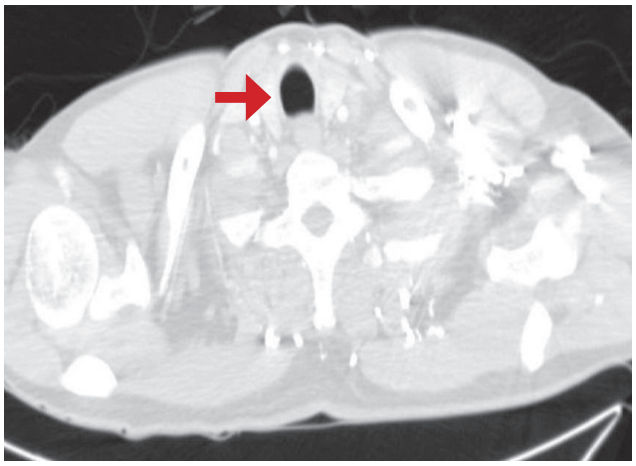

Figure 2A: This shows the normal upper trachea

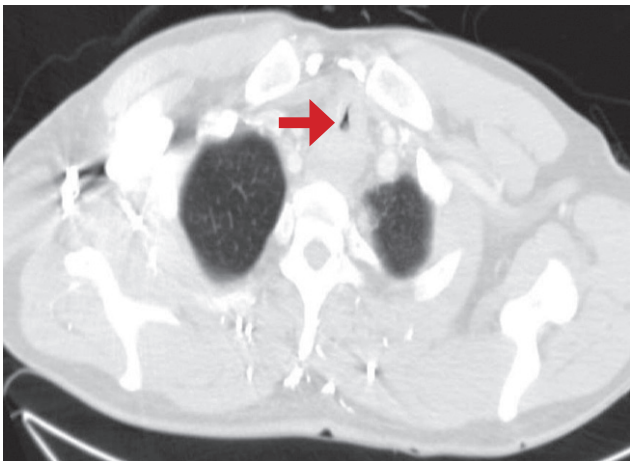

Figure 2B: Stenosis at the mid portion of trachea

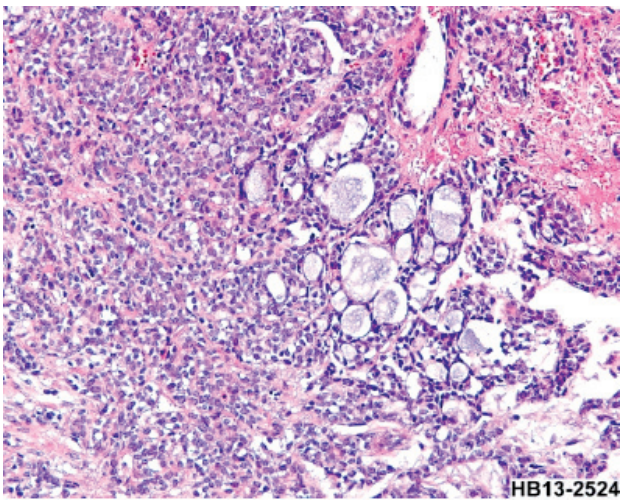

Figure 2C: Adenoid cystic carcinoma as described in case # 2

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Case Report # 3

This is a case of a 69-year-old male patient diagnosed with esophageal cancer with metastatic brain tumor status post craniotomy for removal of tumor. He was referred for co-management of a tracheal invasion. He was a known smoker for 10 years. He first complained of difficulty of breathing six months prior to consultation. The physical assessment revealed cough with whitish secretions, secretory sounds upon auscultation, dysphagia, abdominal discomfort, and episodes of fever. The neck and chest CT scan revealed a mass that invades the posterolateral aspect of upper intrathoracic trachea, causing an intra-luminal narrowing (6mm in anterior-posterior (AP) dimension) which also invades the posterior part of the right lobe of thyroid gland. A new lobulated contour subpleural nodule was also seen at the posterobasal segment of the right lower lobe, size = 2.1cm. A few millimeters of subpleural nodules were seen in the posterior segment of the right upper lobe, the apicoposterior segment of the left upper lobe, the superior segment of the left lower lobe, and the anterior basal segment of the left lower lobe. (Figure 3) Since the patient had been battling with metastatic brain cancer, palliative treatment of a stent placement was offered. Upon admission, the patient underwent a chest CT scan and the results revealed diffuse centrilobular nodules with interlobular septal interstitial thickening, multiple significant mediastinal lymphadenopathy and segmental esophageal mass (primary carcinoma); measuring about 6cm in length at the level of the cervico-thoracic junction. He was then scheduled for the operation and with the cooperation of the cardio vascular technologist (CVT), anaesthesiologist, and the operating (OR) team, the stent placement was done successfully. A fiberoptic bronchoscope was first used to suction secretions and help clear the airway then fluoroscopy to assess the location, and measure the size of the oesophageal mass. Electrocautery was performed to stop any source of bleeding followed by the insertion of the rigid brocho-scope for stent placement. Post procedure, the patient was intubated and was admitted to the intensive care unit (ICU) for continuous monitoring. No hemoptysis, vomiting, or untoward complications were noted.

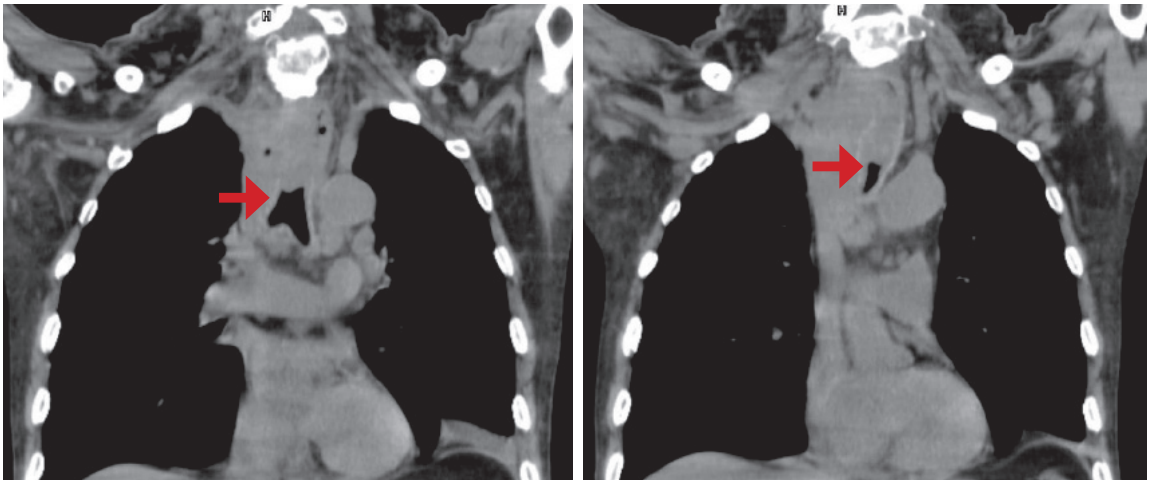

Figure 3: CT scan revealing a mass that invades the upper intrathoracic trachea

Case Report # 4

A 27-year-old woman, who is a foreign health care worker exposed to patients diagnosed of pulmonary tuberculosis, presented a productive cough with purulent sputum and right lateral chest pain in late 2012. Her acid fast bacilli (AFB) was positive and she was then diagnosed with pulmonary tuberculosis and underwent treatment for six months with the following course of drugs: Isoniazid, Rifampicin, Pyrazinamide and Ethambutol for two months then Isoniazid and Rifampicin for four months. Ten months later she presented stridor, wheezing, shortness of breath and dyspnea. The AFB was negative, the chest CT scan revealed atelectasis at the anterior and superior segments of the right upper lobe probably due to mucous impaction or aspergillosis in the bronchi and bronchioles. Bronchoscopy revealed narrowing in the near mid trachea (Figure 4A).

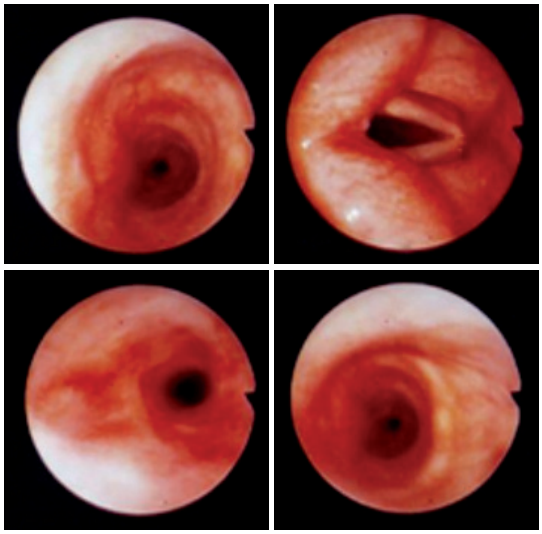

Figure 4A: Bronchoscopic findings showed narrowing in the near mid trachea

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She was then diagnosed with tracheal stenosis. She was prescribed Prednisone 5mg tab and a Flixotide inhaler. Two months following her diagnosis, she visited our medical facility for a 2nd opinion. She was provided with two treatment options. The first was a tracheal reconstruction and the second was stent placement with the use of a silicone stent. Benefits and risks such as infection, bleeding, tracheoesophageal fistula, laryngeal nerve injury, dehiscence of suture line of trachea, restenosis and mortality were discussed. The patient decided to undergo a tracheal reconstruction. Neck and chest CT scans revealed tracheal narrowing; 25mm long segmental circumferential thickened wall (6mm thick) at middle portion of trachea (sternal notch level). The narrowest portion has right to left diameter of 3mm as the narrowest portion, with an Anterior-Posterior diameter of 6mm. The right lung presented atelectasis of the upper lobe with minimal calcification (Figures 4B-C).

The patient underwent fiberoptic bronchoscopy first for direct visualisation before proceeding with the surgery. Tracheal resection and reconstruction under general anaesthesia were done. The stenotic parts of the trachea (proximal and distal end) were dissected and removed (Figure 4D). Post-surgery, she was admitted for observation. No untoward complications were noted and she was maintained on a neck flexion position. The cytopathology report from the tracheal tissue revealed that the trachea was lined by respiratory type mucosa with extensive squamous metaplasia. There are acute and chronic inflammatory infiltrates. The stroma shows fibrosis. There are no granulomas or viral inclusions. No evidence of dysplasia or malignancy noted (Figure 4E). The patient recovered well following the tracheal reconstruction surgery.

Figure 4B: Three-dimensional benign tracheal stenosis

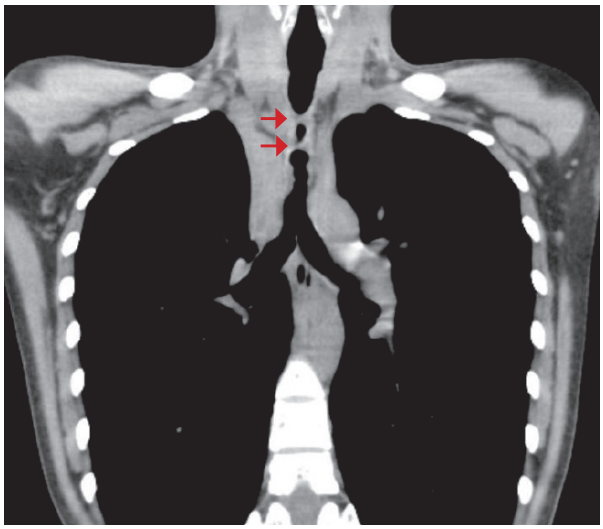
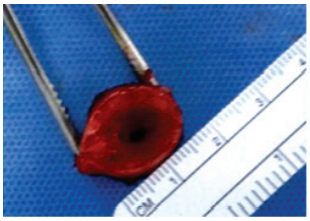
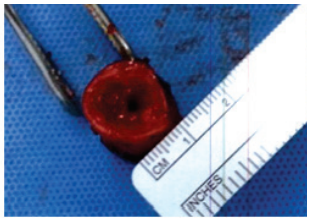


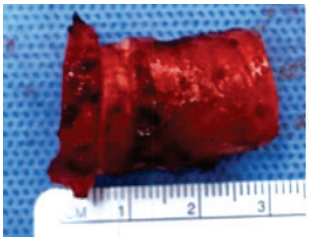
Figure 4C: Three-dimensional benign tracheal stenosis



Proximal End



Distal End



Part of Tracheal Stenosis

Figure 4D: The dissected stenotic part of trachea

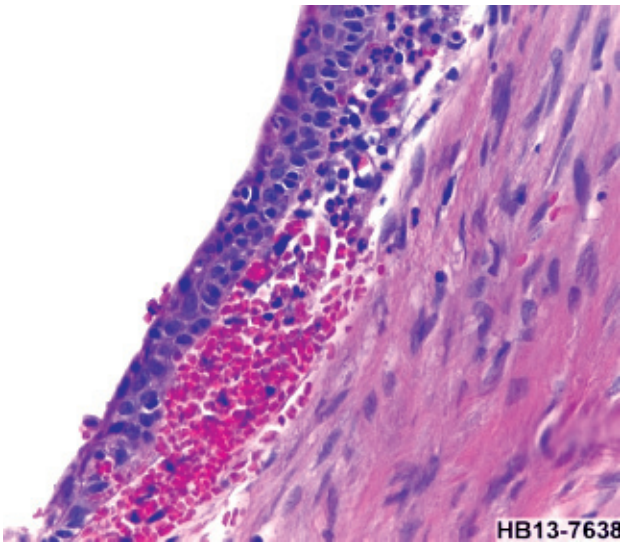


Figure 4E: Squamous metaplasia with acute inflammation

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Case Report # 5

The patient is a 41-year-old female from the Middle East, who presented dyspnea for two years. She has an underlying condition of bronchial asthma, for which she was taking Fluticasone Diskus 500mcg two times a day and Salbutamol Metered Dose Inhaler (MDI) for relief. For the preceding two years she has had frequent hospital admissions due to acute exacerbation of asthma. The chest CT scan revealed the presence of a lobulated well-defined soft tissue density. Endotracheal lesions were seen related to the anterior and right anterolateral walls of the distal trachea just above the level of the carina. It measures about 16×16×19mm along its maximum anteroposterior, transverse and craniocaudad dimensions respectively. A bronchoscopy with biopsy was advised for further evaluation. One month following the recommendation from her local physician, she sought medical consultation in our facility. The lung function test revealed severe obstruction without response to the bronchodilator.

A fiberoptic bronchoscopy was done and revealed a mid-endotracheal mass (Figure 5). The cytopathology from the biopsy presented the bronchial wall with chronic inflammatory cell infiltration without tumor cell or granuloma. Removal of the endotracheal mass and subsequent stent placement was advised for management. Benefits and risks such as tracheoesophageal fistula, hypoxia, bleeding and infection were discussed. The endotracheal mass was extracted via the combination of a rigid brochoscope and fiberoptic bronchosope with snare and electrocautery. She did not manifest untoward complications. The cytology report from the mass reveals unremarkable covering respiratory epithelial cells. The subepithelial element shows dense infiltration by mostly small lymphoid cells admixed with some plasmacytoid ones, plasma cells, and larger cells. Scattering secondary follicles were noted. There was no granuloma or necrosis.

The tumor panel concluded that the specimens must be sent to the laboratory for the following tests immunohistochemical stains for CD3, CD20, CD5, CD23, CD10, BCL6, BCL2, Ki-67, kappa, lambda, CD43, and cyclin D1 in order to determine if whether this is a lymphoma or a pseudo lymphoma.

Case Report # 6

This is a case of a 37-year-old female who was referred to our medical facility due to chronic cough for 6 weeks and weight loss (1.5 kgs) that seem unresponsive to antibiotic treatment. She took Amoxicillin 250 mg 3 times for 5 days but did not respond well to the prescription. None of the laboratory test result showed significant elevation or abnormality. Chest x-ray even revealed a negative chest study. To further investigate, FOB was suggested to directly visualize the airways. After giving consent and observing standard pre- procedure protocols, she underwent FOB under IV sedation. An endotracheal tumor was observed and was subsequently extracted by performing biopsy then snare electrocautery (Figure 6). Post procedure, she did not manifest bleeding or untoward signs and symptoms. Three days after, the results came back negative for malignancy and fungal infection but positive for mycobacterium tuberculosis. She was then diagnosed with Tracheal Tuberculosis. She was given the following oral antituberculosis regimen: Isoniazid 100 mg tablet 3 tablets once daily, Rifampicin 600 mg tablet 1 tablet once daily, Ethambutol 400 mg tablet 2 tablets once daily and Pyrazinamide 0.5 gram tablet 3 tablets once daily. Initially, while on treatment, she complained of diarrhea. A stool exam was done and revealed negative results. At two weeks on treatment, she reported that she experiences less coughing, better appetite but still has occasional weakness. She was asked to follow up for after two weeks to check her liver function test.

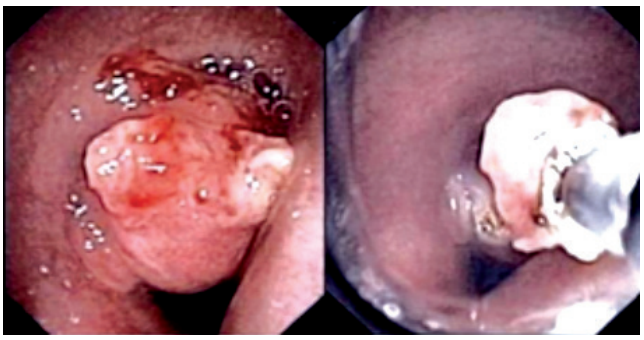

Figure 5: The first photo shows the mid endotracheal mass as described in case #5 and how it was removed using bronchoscopy and snare electrocautery.

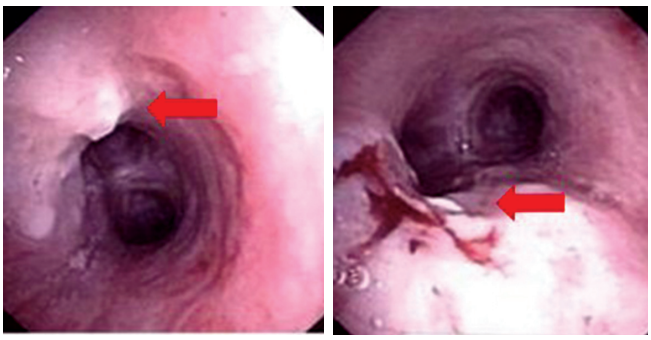

Figure 6: The first photo shows the endotracheal tumor while the second image shows the tumor was successfully extracted with minimal bleeding.

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Discussion

1. Tracheal stenosis caused by Malignancy

Both malignant and benign diseases may cause focal narrowing of the tracheobronchial tree. Within the trachea, malignancy predominates.[2] In July 2013, the World Health Organization (WHO) reported that chronic diseases cause increasing numbers of mortality worldwide. Lung cancers (along with trachea and bronchus cancers) caused 1.5 million (2.7%) deaths in 2011, a remarkable increase from 1.2 million (2.2%) deaths in 2000. The vast majority of these types of cancers are diagnosed at a critical later stage when the disease has metastasized to other organs and or lymph nodes. Primary tracheal malignancies include squamous cell carcinoma and adenoid cystic carcinoma, among others. Non-small cell lung cancer and small cell lung cancer are obvious causes of obstruction due either to extrinsic airway compression, intrinsic airway tumor, or a combination of both.[2] A recent study in 2008 presented that in one series of 264 patients with malignant esophago-respiratory fistulas (ERF), 243 (92%) had esophageal cancer, 19 (7%) had lung cancer, and 2 (1%) had mediastinal tumor.[3]

Signs and symptoms vary depending on the location of the narrowing and nature of the disease. Patients complain of dyspnea, shortness of breath and dysphagia which is progressive, most of the time constant and unresponsive to bronchodilators. Wheezing maybe present and stridor can be heard especially for severe tracheal obstruction. The onset and progression of these signs and symptoms generally depend on the pathology and extent of the disease. In a study of 207 malignant trachea-esophageal fistulas (TEFs), signs and symptoms include cough in 116 (56%), aspiration in 77 (37%), fever in 52 (25%), dysphagia in 39 (19%), pneumonia in 11 (5%), hemoptysis in 10 (5%), and chest pain in 10 (5%).[4] Surgical resection remains the gold standard for treatment of airway stenosis. However, most cancer patients are not medically fit and may have been diagnosed only in the later stages of malignancy. Palliative measures are offered to relieve worsening symptoms. Treatment includes chemo, radiation, brachytherapy, tumor ablation, endoscopic techniques, and stent placements. These options if successfully done may improve breathing, the swallowing mechanism and quality of life.

The latest standard therapy for cancer patients with airway stenosis is endoscopic or radiologic placement of endotracheal-covered self-expanding metallic stents (SEMS).[5] A covered expandable endotracheal stent can relieve symptoms in more than 80% of patients with malignant stenosis.[6,7] If performed early following diagnosis, this treatment may positively change quality of life and improve survival. Endotracheal stents can be inserted with the patient under general anesthesia via rigid or flexible bronchoscope with moderate sedation. The mean survival period of patients with ERF was 2.8 months in one study, but in patients with esophageal stents it was 3.4 months. With only supportive therapy, it was 1.3 months.[3] Overall median survival times after diagnosis of ERF is only 8 weeks.[8] Patients generally tolerate stent placement but close monitoring is needed so to assess complications ahead of time and manage appropriately. Potential issues include recurrence of obstruction, growth of granulation tissue, stent occlusion and migration, bleeding and infection. A recent study by Homann, et al. reported[1] late complications in 71 of 133 stented patients (53.4%) with a quarter of patients experiencing several complications. Recurrent dysphagia connected to tumor ingrowth (22%), overgrowth (15%), stent migration (9%), and food bolus obstruction (21%) were the most common complications, followed by the development of esophago-airway fistulas (9%). Successfully re-treated patients had a markedly longer life expectancy compared to those who did not come back for further management. In an additional retrospective review of 97 patients with SEMS placement, dysphagia improved in 86% and trache-osophageal fistula symptoms in 90% of the patients.[9]

2. Benign cause

A variable degree of stenosis has been reported in up to 90% of patients with tuberculosis.[10]

The application of surgical resection to airway narrowing caused by benign disease requires meticulous cooperation with the anesthesiologist, pulmonologist, nursing staff and thoracic surgeon who have been well trained in the reconstruction of complicated tracheo-bronchial abnormalities. Surgery can be done for benign stenosis that affects less than half of the trachea. The type of surgery performed depends on the site of stenosis. Preoperative requirements include history, physical examination, radiographic imaging such as chest x-rays, CT scans and bronchoscopy results. The direct visualization provided by the bronchoscope will show the anatomy of the airway at the same time the affected parts of the stenosis. It is important to note the distance from the stenosis to anatomic landmarks in addition to the length of the stenotic segment and the status of the mucosa. Operation of the airway needs constant communication between the pulmonologist, surgeon and anesthesiologist. The steps of tracheal resection and reconstruction are the following: 1.) localize the diseased segment, 2.) mobilize the trachea, 3.) transect the trachea, 4.) resect the affected area, 5.) and reconstruct.[11] Anastomotic complications are uncommon post operatively but may lead to serious complications. In one study conducted by Wright, et al. of 853 patients, 95% had a good result and 4% had an airway maintained by tracheostomy or T-tube. Tracheal resection with reanastomosis is seen as a procedure of choice given its high success rate (71%-95%) and minimal morbidity.[12] It is usually successful and patients often fully recover from the operation.

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Conclusion

Central airway stenosis is a life-threatening condition with severe pulmonary complications that may be caused by several factors. Patients diagnosed with airway narrowing often present with comorbidities that require medical attention. There are a number of factors considered in order to choose the appropriate treatment for the patient. These are nature of the disease, urgency for treatment, alternative procedures, current health status and improvement to the patient's quality of life.

Treatment is individualized and the management of this condition requires technical expertise of thoracic surgeons, pulmonologists and anesthesiologists. If caught early, and treatment has been determined and planned following diagnosis, improvement to the quality of life and potentially survival rates, may be achieved.

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Case Report

Straight Back Syndrome; A Misleading Condition in Cardiology, Demonstrated with Magnetic Resonance Imaging

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Keywords: straight back syndrome (SBS), MRI, misleading condition

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Abstract

Straight back syndrome (SBS) is a deformed thoracic spine disease sometimes considered as a pseudo-heart disease because its pathology can prominently affect the normal function of the heart system. SBS patients often present with signs and symptoms that are similar to some cardiac diseases that hide those of the thoracic spine.[1,2] Consequently, SBS has become the one of the most common misleading conditions in cardiology. Investigations for SBS are frequently performed in patients with an abnormal systolic murmur with no evidence of any cardiac-related cause. This article will detail the importance of the straight back syndrome in diagnostic cardiology and demonstrate a case with Magnetic Resonance Imaging.

Straight back syndrome (SBS) is a congenital disease of the thoracic spine and was described in 1960 by Dr Rawlings as a new cause of pseudo-heart disease as mentioned above. The pathology of SBS is defined as the loss of normal kyphosis of the thoracic spine that causes an abnormal straightness of the upper back. The thoracic spine in SBS is more straight than normal but is not stiff and can function in flexing and extending normally.[2,3] The etiology of the SBS is the congenital malformation of the osseous without intrinsic bone disease.[4] It always occurs in young slim patients, however, the actual level of incidence is unknown.[5] It has been reported that SBS mimics some cardiac diseases that produce an abnormal cardiac murmur such as atrial septal defect, pulmonic stenosis or mitral valve prolapsed.[6] This issue is the important clue to raise the awareness of SBS and to take into account that a differential diagnosis is necessary in some murmur-producing cardiac diseases.

The importance of straight back syndrome in cardiology

The hallmark of the Straight Back Syndrome is the loss of normal kyphosis of the thoracic spine.[5] Normal kyphosis refers to the normal apical-dorsal sagittal contour of the thoracic and sacral spine. Although the straight thoracic spine in SBS has normal spine function it behaves like a hard wall and causes a fixed narrowing of the thoracic cavity in the antero-posterior (A-P) direction. The A-P dimension of the thoracic cage in SBS is significantly shorter than normal. The fixed narrowing of the thoracic cavity in the SBS produces a fixed compression to the heart and great vessels that makes the heart and great vessels displace more to the left side of the thoracic cavity and appear enlarged. The SBS-affected patient often presents with an abnormal systolic murmur that is postulated to be due to the running of a large volume of blood flow through the fixed dilated lumen of the great vessel or may be due to the regurgitation flow that runs across the prolapsed atrio-ventricular valve back to the upstream chamber. The prolapsed atrioventricular valve in SBS may be caused by the displacement of the cardiac valve leaflets due to the fixed compression of the wall of the sternum in the anterior and from the straight thoracic spine in the posterior or this may be a coincidence. The mitral valve prolapse (MVP) is the most common associated cardiac condition reported about 64% of SBS cases.[7] Contrary to this, the occurrence of SBS is not

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found to increase in MVP cases. On the other hand, SBS and MVP can occur in the same patient without association.[8] The true congenital heart disease such as bicuspid aortic valve is also observed in the SBS patient but it is rare.[2] SBS affects not only the cardiovascular system but also the respiratory system by causing compression to the trachea.[7] For SBS patients, specific treatment is not required although it can become complicated with mitral valve prolapse.[9]

Straight back syndrome diagnosis

The key elements to diagnose SBS are the loss of normal kyphosis of thoracic spine that causes the narrowing of the thoracic cage in antero-posterior dimension without the other causes of bone deformity such as pectus excavatum. The pectus excavatum that produces an abnormal narrowing of the thoracic cage in the antero-posterior dimension must be ruled out before diagnosing SBS. There are proposals to establish diagnostic imaging criteria for SBS as follows:[3,6,10] the measured distance from the mid anterior surface of the T8 spine to the posterior aspect of the sternum is less than 13 cm in male and less than 11 cm in female;[10] the measured distance from the mid anterior surface of the T8 spine to the vertical line that connects between the top of anterior border of the T4 spine to the anterior surface of the inferior part of the T12 spine less than 1.2 cm;[6] or the ratio of the distance from the mid anterior border of the T8 spine to the sternum to the length of the thoracic cage in right-left direction at the level of the dome of the right diaphragm less than 1/3.[6] These criteria can be applied to the results of any imaging tools that provide the images needed for SBS diagnosis.

Conventional x-ray is the most convenient diagnostic tool for SBS diagnosis as it displays the thoracic cavity and the thoracic spine in the true coronal and true sagittal view. Multi-Detector Computed Tomography and Magnetic Resonance Imaging (MRI) may be used as optional techniques. Other investigations such as electrocardiography, echocardiography may be used as supporting tools for SBS assessment. The manifestation of twelve lead ECG in cases of SBS is usually in a normal pattern or may show an incomplete right bundle branch block.[6] Although twelve-lead ECG and echocardiography do not produce the typical manifestations of SBS they can be used to verify and confirm diagnosis.[5]

The differential diagnosis of straight back syndrome

SBS must be differentiated from any causes of the abnormal narrowing of the thoracic cage such as pectus excavatum. Pectus excavatum means hollowed chest and it produces a sunken appearance of the chest.[11] Although pectus excavatum produces an abnormal narrowing of the thoracic cage in the anterior-posterior direction as does SBS, Pectus excavatum can be differentiated from the SBS by the presence of the sunken sternum which is the hallmark of the pectus excavatum.[11] Both SBS and pectus exacavatum affect the heart function in similar ways by causing the narrowing of the thoracic cavity in A-P dimension. On the other hand, other murmur-producing cardiac diseases are also a differential diagnosis of SBS.

MVP is the most common associated disease that has been reported. It may be caused by SBS or may be a coincidence. The differential diagnosis between MVP including other cardiac diseases and SBS must be undertaken. The key characteristics of SBS are pancake appearance with cardiomegaly; leftward heart; prominent main pulmonary artery; the AP-dimension of the thoracic cage less than 13 cm in male and less than 11 cm in female; right bundle branch block in V1 and small terminal r wave in a VR lead; and a negative echocardiography study. The characteristics of classic MVP are: the thickening of the mitral leaflet >5 mm and leaflet displacement >2 mm. The ECG sign in a classic MVP is normal or may show ST-segment and T wave abnormalities especially in lead II, III and a VF.[8] If the classic signs of the mitral abnormality are found on the echocardiography or on the MRI in certain SBS cases, it should be considered that the MVP is just a coincidence.

Case Report

A 25-year-old male patient, with no underlying cardiac disease, came to the hospital for an annual health check-up. An abnormal cardiac systolic ejection murmur grade II at the second left parasternal border was found during the physical examination. Chest x-rays, twelve leads ECG and echocardiography examinations were performed. The twelve leads ECG showed left axis deviation, incomplete right bundle branch block, and the trans-thoracic echocardiography showed no significant abnormalities. A cardiac MRI was requested to rule out congenital heart disease.

A cardiac MRI examination began with the scout scan using the Gradient echo MRI sequence in transverse plane with whole heart coverage that shows the mildly flat chest wall with a significant narrowing of the thoracic cavity in the A-P direction from the posterior surface of the sternum to the anterior surface of the thoracic spine. The multi-slice gradient echo CINE MRI was performed on the axial and horizontal planes with whole cardiac chambers coverage. The A-P dimension of each thoracic spine opposite to the entire length of sternum is measured on the axial plane and showed a maximal length of 6.43 cm. The septal leaflet of the tricuspid valve showed a mild prolapse. The gradient echo CINE MRI with short axis view of the ventricles was performed to obtain both ventricular volume and ventricular systolic function. CINE MRI on short axis view of the ventricle was performed to calculate the cardiac ventricular function using Simpson's method. This showed a result of a normal sized left ventricle with good systolic function and mild global hypokinesia of the right ventricle. A mitral in-flow

study using gradient (Q) flow mapping technique showed an E/A ratio > 2.5 with a deceleration time of 193ms that indicates impaired left ventricular diastolic function grade II. As the result of the mitral inflow study, the tricuspid inflow study also showed the E/A ratio > 2.5 that may be due to the abnormal relaxation of the right ventricle. A normal value of peak flow velocity of the aortic and pulmonic valve flow was seen. There was no abnormal thickening of atrioventricular valve. A mild septal tricuspid valve prolapse was seen on the gradient echo CINE images on the horizontal plane. The Magnetic Resonance Angiography of the aorta-pulmonary artery with contrast injection demonstrated no patent ductus arteriosus, no partial and total anomalous pulmonary venous return. A delayed contrast enhancement MRI study was also performed and the result showed no peri-myocardial contrast enhancement. This indicated no prior myocardial infarction, fibrosis and active inflammation or myocardial infiltration.

Due to the abnormal narrowing of the antero-posterior diameter of thoracic cage with pathology findings of mild tricuspid valve prolapse, SBS was suspected. The CINE MRI on the sagittal plane of the thoracic spine and the CINE MRI on the coronal plane with entire A-P dimension coverage were performed. The patient was sent to undergo a Computed Tomography (CT) scan for thoraco-lumbar spine to confirm the exact location of the T4, T8 and T12 spine. The CT image shows the abnormal downward angulation of the sternum that causes the location displacement of pairing between sternum and the thoracic spine. The widest length of the thoracic cavity of the right-left direction just at the highest point of the right dome of diaphragm was measured on MRI images including the anterior–posterior diameter from the mid anterior aspect of the eighth thoracic spine to the posterior aspect of the sternum (that is opposite to the eighth thoracic spine) were measured and found to be 5.26cm. Also, the ratio of the length of the thoracic cavity in the right to left direction to the anterior–posterior diameter of thoracic was calculated and gave a result of (5.26 cm/25.8 cm = 0.20) < 0.33. This case was diagnosed as a straight back syndrome using the criteria mentioned above.

Discussion

Assessing SBS using MRI

Generally speaking, SBS is frequently diagnosed by conventional x-Rays of the chest and thoracic spine. Assessing SBS may be performed using MRI images if an MRI has been requested to rule out congenital heart disease that causes cardiac systolic murmur. An MRI has no angle limitation and has a large field of view, therefore an MRI can be used effectively to assess SBS using either Spin echo MRI or Gradient echo MRI pulse sequences. An MRI can provide a series of reference images of the thoracic spine on coronal and true sagittal views for diagnostic parameter measurements. To diagnose SBS by imaging, it is necessary to examine images of the spine on a sagittal view (this includes distal C spine, T, L, and proximal S spine) to localize the diagnostic reference point for measurement. To image the whole thoracic cavity that covers the whole length of the thoracic spine, including the width in A-P direction and the maximum length of the thoracic cavity in right-left direction, is the very least needed for SBS diagnosis and this can be obtained by MRI.

A **"short-cut method"** to diagnose SBS using MRI is proposed in this article. With this method, the image on the sagittal plane (with coverage of the whole length of sternum with a slice thickness of 8 mm using spin echo or gradient echo CINE MRI) is required. Then, the distance between the anterior surface of the thoracic spine to the posterior surface of the sternum is measured for each thoracic spine located between the angle of Louis and xyphoid. Normally, the heart contour occupies the space in the thoracic cavity at the level between the angle of Louis and xyphoid. According to the theory proposed by Datey and Davies, SBS can be positively identified if: the measured distance in every slice is less than 12 cm in male and 11 cm in female or the maximum length is less than 1.2 cm from the posterior surface of the thoracic spine to the vertical line connecting from the top of the anterior surface of the superior thoracic spine (that is opposite to the suprasternal notch and the antero-inferior surface of the thoracic spine that is opposite the xyphoid). Using this short-cut method for diagnosis, it is not essential to exactly localize the T4, T8 and T12 spine. It is enough to perform an MRI of the thoracic cage in the sagittal plane (covering the whole sternum and the whole thoracic spine) to diagnose the SBS. These two short-cut methods can be used together for consistency and to confirm the result. In addition, an MRI with a gradient echo CINE pulse sequence can provide information on the intra-cardiac disease that is associated with or caused by SBS. This includes the prolapsed mitral and tricuspid valve including cardiac function assessment. However, the MRI takes longer to scan compared with x-rays and CT scans of the thoracic spine.

Conclusion

Straight Back Syndrome causes a narrowing of the thoracic cavity in an anterior–posterior direction through loss of normal kyphosis of the thoracic spine. Although straight back syndrome is not a life-threatening disease, it should not be overlooked. It should be taken into account when the patient presents with an abnormal cardiac systolic murmur with no definite finding of cardiac cause. MRI can be considered as the one-stop-shop diagnostic tool for straight back syndrome because MRI can provide intra-cardiac views and great vessel information including the thoracic spine alignment and the diameter of the thoracic cavity in the right-left and anterior-posterior direction in a single procedure. Both spin echo black blood and gradient echo CINE MRI on sagittal view

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images can be used to measure the diagnostic parameters. The advantages of MRI include: providing high resolution images, a large field of view, and no angle limitation, and no radiation exposure. With MRI, congenital heart disease and other structural heart diseases can be ruled out and straight back syndrome can be diagnosed with much more confidence. In the case demonstrated in this article, the downward angulation of the sternum is observed on the MRI image when compared to the CT for the thoraco-lumbar spine. It causes the mal-position of the thoracic spine, the T4, T5 spine are not opposite to the angle of Louis and the T8, T9 spines are not opposite to the xyphoid. Hence it can be difficult to localize the reference T4, T8, T12 spine. Using the short-cut methods as described above proved to be a convenient way to diagnose SBS using MRI.

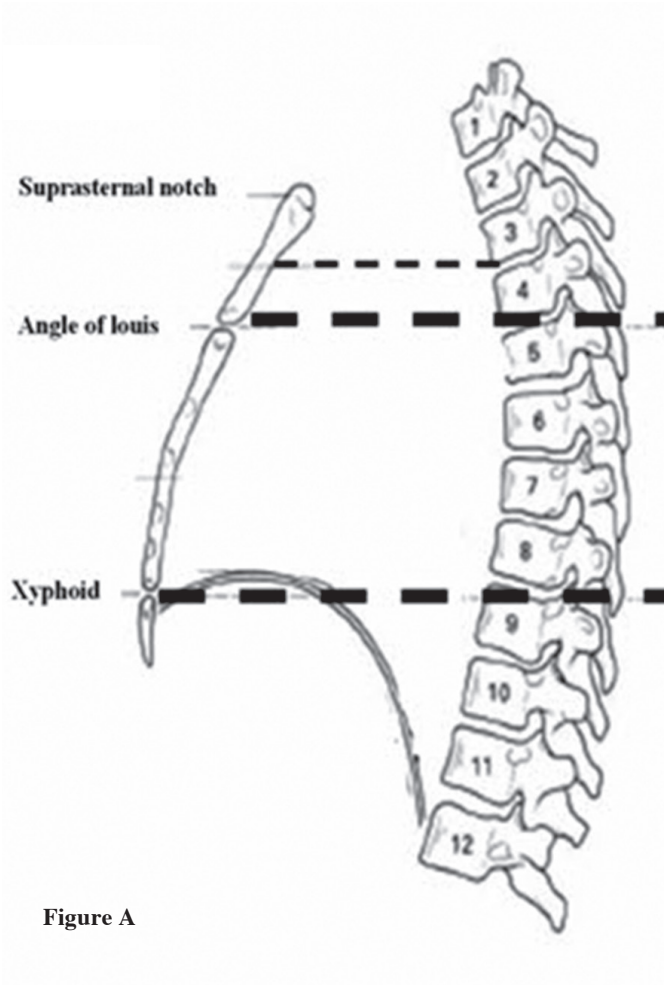

Figure A

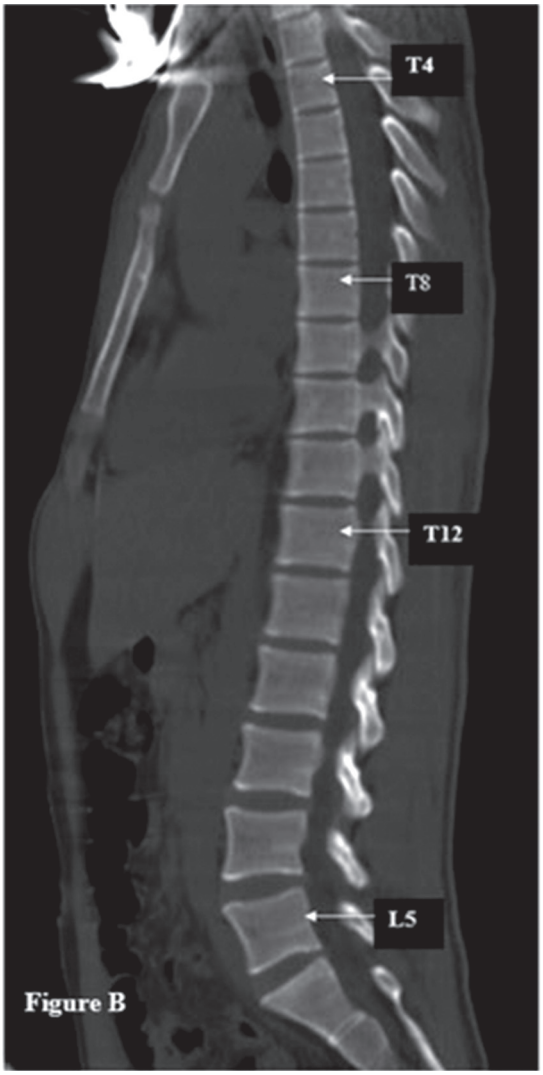

Figure B

Figure A: Normal anatomy of thoracic spine and sternum. The picture shows the reference point of the thoracic spine and sternum; the suprasternal notch is situated opposite the 3rd and 4th thoracic vertebrae, the angle of Louis (manibriosternal joint) is opposite to T4 and T5 spines, the body of the sternum (the area between the angle of Louis and the Xyphoid) is placed opposite T5-T8.

Figure B: The Computerized Tomography image on the sagittal view of the thoraco-lumbar spine of the SBS-affected patient shows the position displacement of the spine because of the loss of the normal kyphosis of the thoracic spine in SBS. The thoracic sternum is angled downwardly in the SBS hence the suprasternal notch is not situated opposite the 3rd and 4th thoracic vertebrae, the angle of Louis (manibriosternal joint) is not opposite to T4 and T5 spines, the body of the sternum (the area between the angle of Louis and the Xyphoid) is not placed opposite T5-T8.

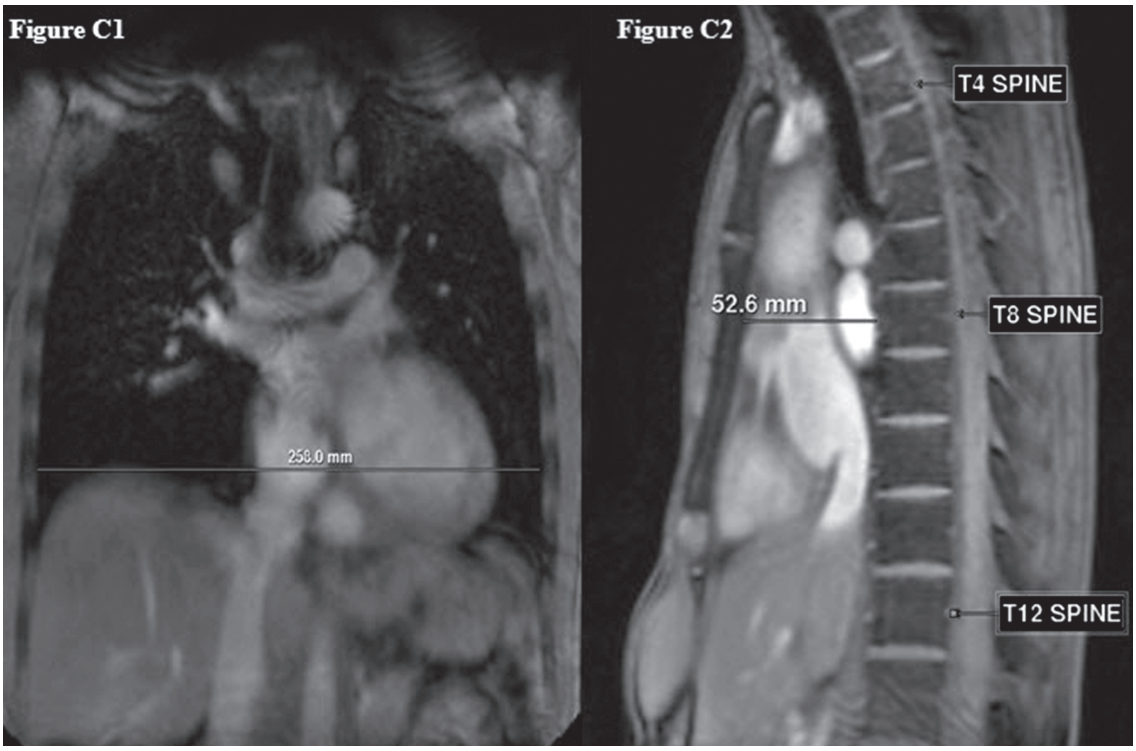

Figure C: Shows the diagnostic criteria of SBS 2; the ratio of the distance from the mid anterior border of the T8 to the sternum (C2) to the length of the thoracic cage in the right-left direction at the level of the dome of the right diaphragm (C1) less than 1/3 according to Davies's and Leon's proposal respectively.

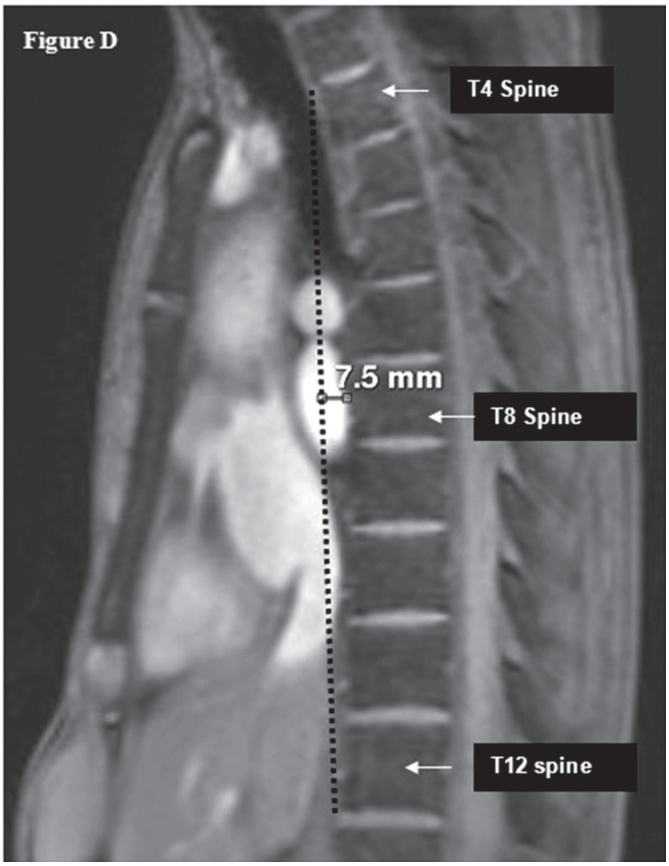

Figure D: Shows the diagnostic criteria of the SBS; the measured distance from the mid anterior surface of the T8 spine to the vertical line that connects between the top of the anterior border of the T4 spine to the anterior surface of the inferior part of the T12 spine (less than 1.2 cm).

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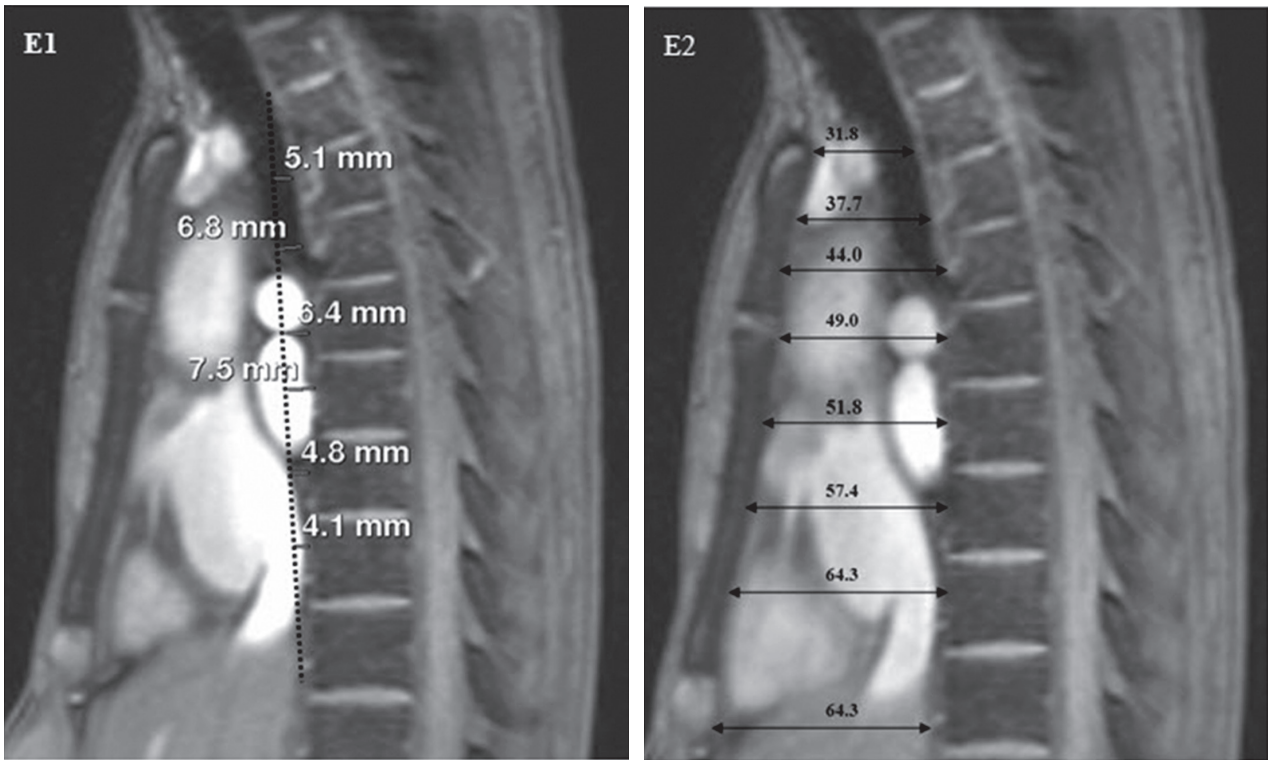

Figure E1-E2: Shows the short-cut method to diagnose SBS using MRI by measuring the distance (D2) between the anterior surface of the thoracic spine to the vertical line that connects between the posterior surface of the superior of the thoracic spine (that is opposite to the suprasternal notch and the posterior surface of the thoracic spine that is opposite to the Xyphoid) in every image slice on the sagittal view of the thoracic spine (E1). If the distance is less than 1.2 cm, SBS is diagnosed. The measurement of the A-P dimension of the thoracic cage on the sagittal view (by measuring the distance (D2) between the anterior surface of all the thoracic spine located within the length of the angle of Louis to the xyphoid to the posterior surface of sternum on the MRI image) on the sagittal view of the thoracic spine (E2) is necessary to make sure that the maximum distance value is measured. If the maximum value of the A-P dimension is less than 11 cm in female and 12 cm in male then SBS is diagnosed. The patient has D1 = 7.5 mm and D2 = 6.43 cm hence SBS diagnosis is confirmed.

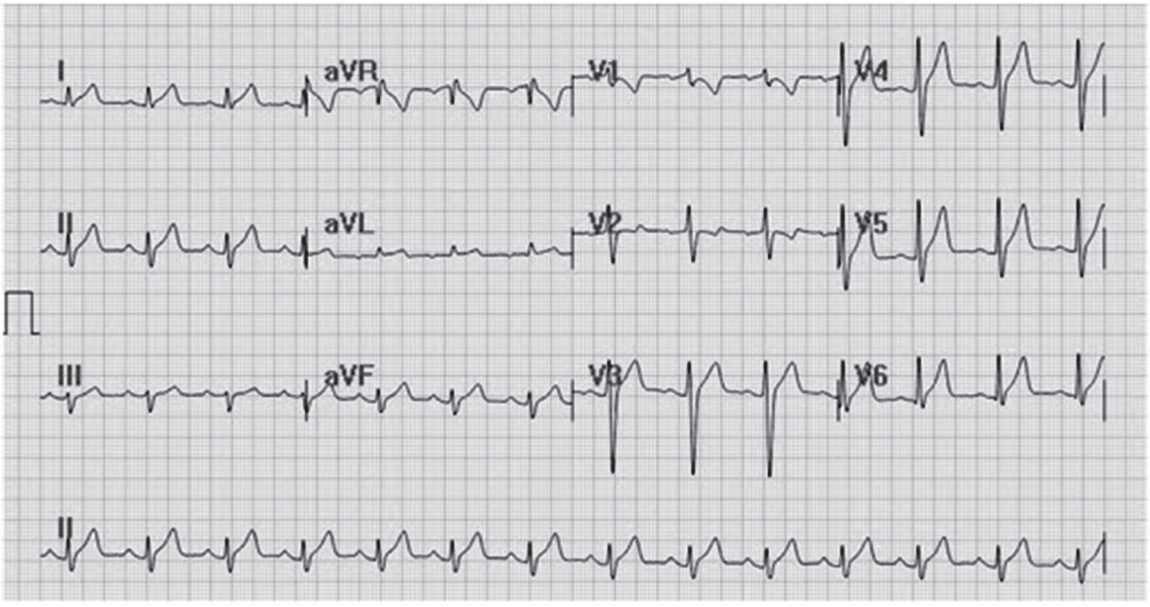

Figure F: Demonstrates the characters of the twelve lead ECG of the patient that shows left axis deviation and incomplete right bundle branch block.

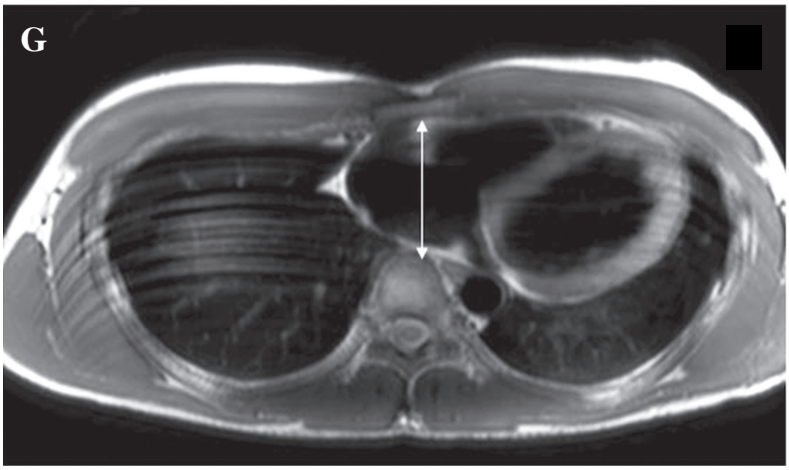

Figure G: Demonstrates the abnormal narrowing of the thoracic cage in the A-P dimension of the patient on the T1W bb image on the short axis plane.

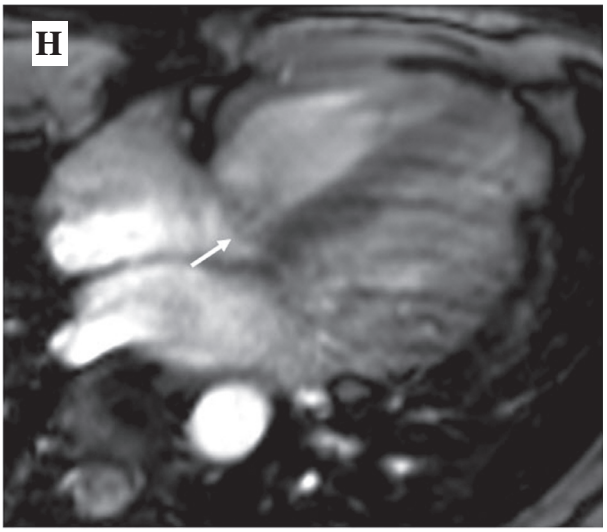

Figure H: Demonstrates the septal leaflet of the tricuspid valve prolapse of the patient (see arrow).

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Fatal and Near Fatal Acute Ascending Aortic Dissection: Two Case Reports with Different Cardiac Manifestations

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Abstract

Acute ascending AD remains a catastrophic disease that is liable to be missed or have a delayed diagnosis. With such diverse manifestations, the diagnosis in any atypical case is even more difficult and mortality rates are unacceptably high. We reported two cases of acute AD presenting with different manifestations. The first one was a typical Standford type A case, a 71-year-old hypertensive man presenting with chest pain and syncope. With the high risk predictors and delayed operation, he died from cardiac tamponade. In contrast, the second case was an atypical one, a young man who had no known risk factors for developing AD. He initially presented with upper back, leg pain (Standford type B) and later congestive heart failure from severe aortic regurgitation. He survived the complex aortic repair and valve replacement but the cause of AD remained unknown. We hope that these two reported cases will raise awareness of this lethal disease in clinical practice.

Acute ascending aortic dissection (AD) is a rare disease and carries a high fatality rate. Its mortality increased with time, 1-2% every hour after symptom onset. Occasionally, the diagnosis of acute AD could be missed or delayed since its presentation can mimic any arterial occlusive diseases including acute coronary syndrome, limb ischemia and stroke. To raise awareness of the medical community, we report on two acute ascending AD patients who presented with different cardiac manifestations.

Case Report # 1

A 71-year-old man, with a known history of hypertension, developed a persistent mid-chest discomfort for 12 hours. He felt dizzy while sitting up and was brought to Bhumibol Adulyadej hospital. Later, he fainted in the rest room and became hypotensive; his blood pressure (BP) was 68/43 mmHg. Since there was no palpable pulse, cardiopulmonary resuscitation was performed for seven minutes. After 2,000 ml of 0.9% NSS was given, his right and left arm BP was 90/50 and 120/60 mmHg respectively, the pulse rate was 94 per/min in sinus rhythm (SR). The echocardiogram showed moderate pericardial effusion, a hypertrophic left ventricle with normal systolic function and no wall motion abnormalities were noted. The chest film showed cardiomegaly, a dilated ascending aorta and wide mediastinum (Figure 1A). The initial electrocardiogram (ECG) showed sinus rhythm with occasional PAC and mild ST segment depression was noted in V5-6 (Figure 1B). To rule out aortic dissection, an emergent multi-slide computed axial tomogram (MDCT) was performed. It showed an acute ascending aortic dissection from the aortic root to the arch involving the brachiocephalic artery, right common carotids and right sub-clavian arteries (Figure 2). No flap was noted at the distal arch and descending aorta. The left subclavian artery, brachiocephalic artery were not involved. He became hypotensive again and improved after three liters of NSS intravenous infusion, BP was 120/66 mmHg, HR was 90 in SR. The right atrial pressure was 25 mmHg; the pulmonary capillary wedge pressure was 32 mmHg. The patient was just about to be transferred for aortic repair but he had bradycardia, hypotension and expired from cardiac tamponade. Pericardial taping obtained 300 ml of un-clotted blood. The total time from arrival to expiration was seven hours.

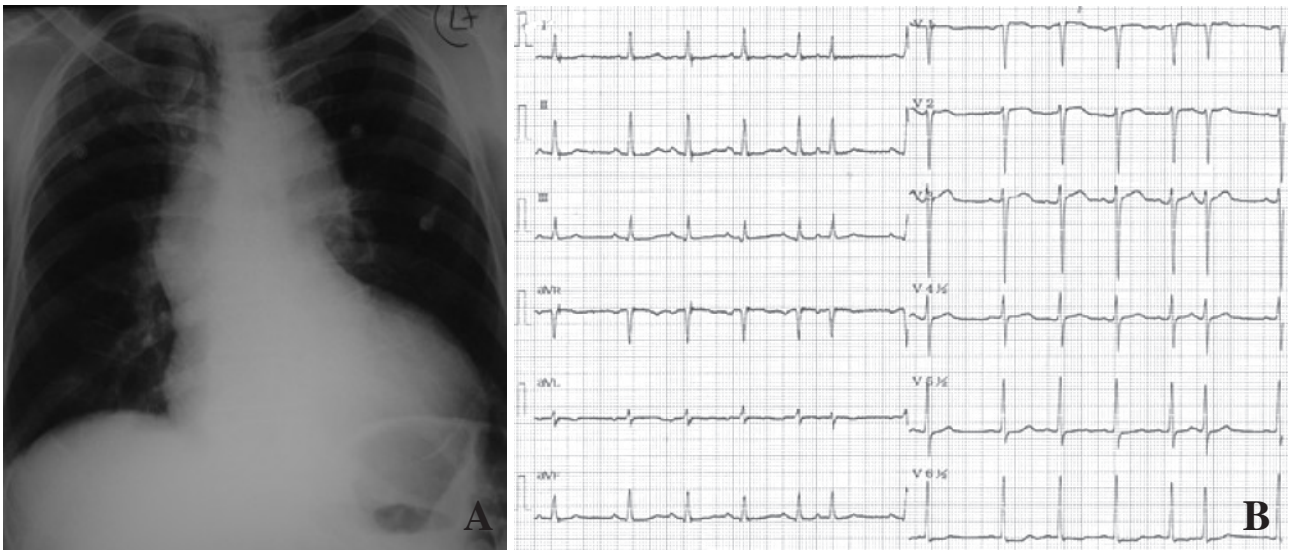

Figure 1A: Chest film showed widening mediastinum with cardiomegaly,
1B: ECG illustrated sinus rhythm with occasional PAC, mild ST depression in V5-6.

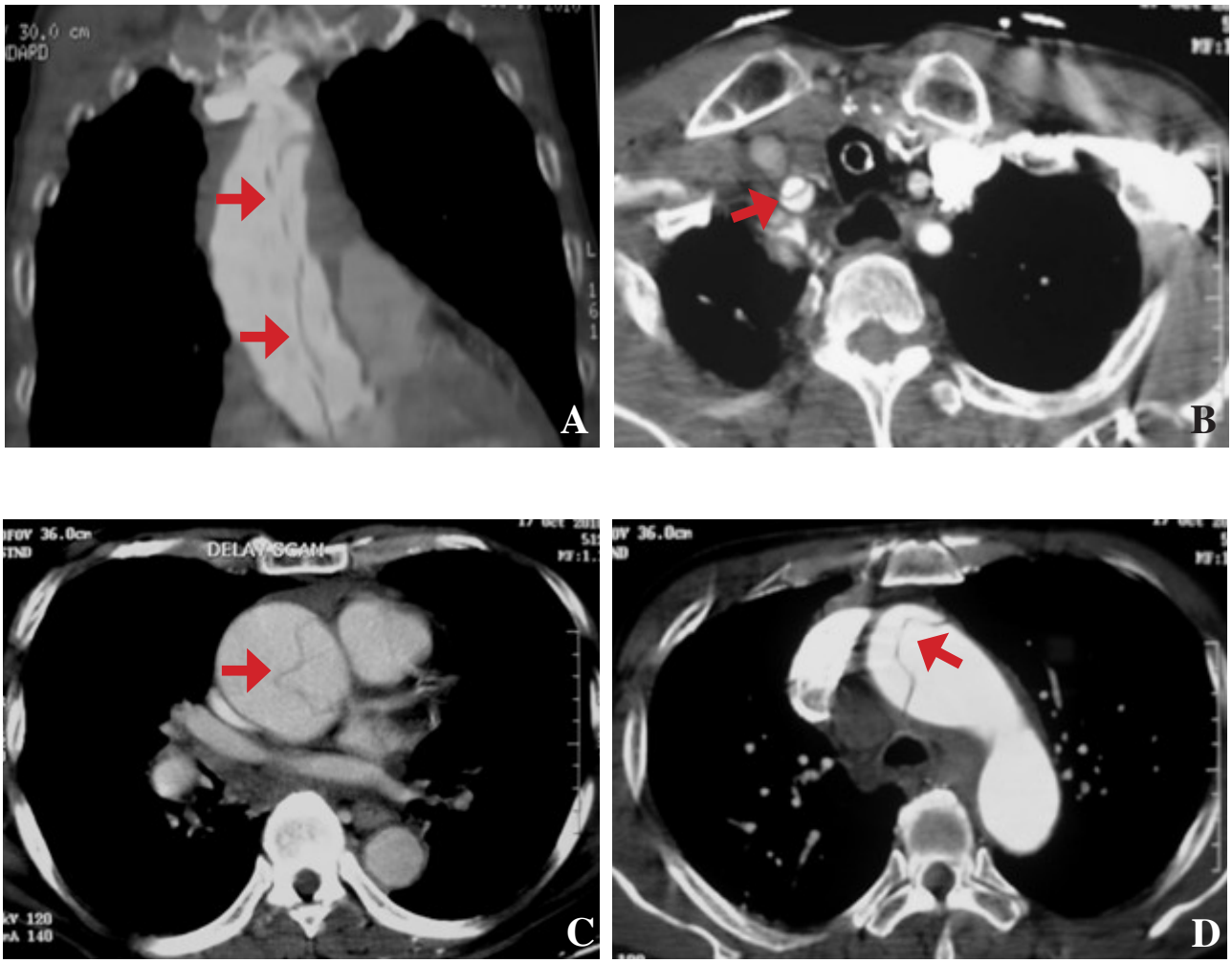

Figure 2: Computerized axial tomogram (CAT) showed an ascending aortic dissection, Standford type A (arrow 2A, C, D) extended to aortic arch involving brachiocephalic artery (arrow 2B), rt. common carotids and right sub-clavian arteries.

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Case Report # 2

A previously healthy 27-year-old man experienced pain in the upper back and shoulder region two weeks prior to admission. He had never had a physical check-up before but his systolic blood pressure was high; 170 mmHg when he was seen. After taking pain medication from the clinic, he felt better within a week but began to experience tightness and numbness of the right leg while walking. Three days prior to admission, he had progressive dyspnea and orthopnea and was brought to Chandrubeksa hospital (located in Nakorn Pathom, 100 km away from Bangkok). It was found that he had congestive heart failure from severe aortic valve leakage. His BP was elevated, ranging from 150/70 to 180/80 mmHg. The ECG showed sinus tachycardia with incomplete right bundle branch block (Figure 3B). The echocardiogram revealed three leaflet aortic valves with severe aortic regurgitation and fair left ventricular systolic function, LVEF of 0.50. The cardiac troponin T was elevated, 222ng/ml. The CAT scan showed Standford type A, acute aortic dissection, starting from the ascending aorta to the descending part so he was urgently referred to Bangkok Heart hospital. Atenolol and nitroglycerin were given to control the BP and the heart rate. On arrival, he was conscious with no palpable pulse in all extremities and only faint Doppler signal was seen at the left foot. The chest film showed an obvious widening superior mediastinum, diffuse interstitial infiltration of both lungs and minimal left pleural effusion (Figure 3A). The repeat 256 slide MDCT scan showed two entry sites at the proximal ascending aorta, just above the origin of the left main and right coronary arteries, and distal arch, with an extending flap to the aortic bifurcation and involved right common iliac artery (Figure 4A-E). After the risks and benefits of surgical intervention were explained and informed consent obtained, an emergent operation was performed for 10.7 hours. The time taken for a total aortic cross clamp and bypass was 293 and 348 minutes respectively. There were two ruptured sites, the first at the ascending aorta, 1 cm above the left coronary sinus and the second between the left subclavian and common carotid arteries. There was malcoaptation of the aortic valve causing severe regurgitation. The maximal diameter of the ascending aorta was 4 cm and no bloody pericardial effusion was found. The ascending aorta, aortic sinus and aortic valves were excised and replaced with no.25 St. Jude composite graft (Bentall procedure). Both coronary ostia were reattached to the ascending aorta. A total arch replacement (24/10/8/8 mm Galweave 4 branches plexus) and re-implantation of innominate, left common carotid, left subclavian arteries were performed, see Figure 5. The patient recovered well. Initially he had myonecrosis with a peak of creatinine phosphokinase (CPK) of 43,871 unit/L which compromised the kidney function (the serum creatinine rose from 1.3 to 4.33 mg/dl). With a forced diuresis and alkalinizing urine, the urine flow was fairly good and CPK was normalized.

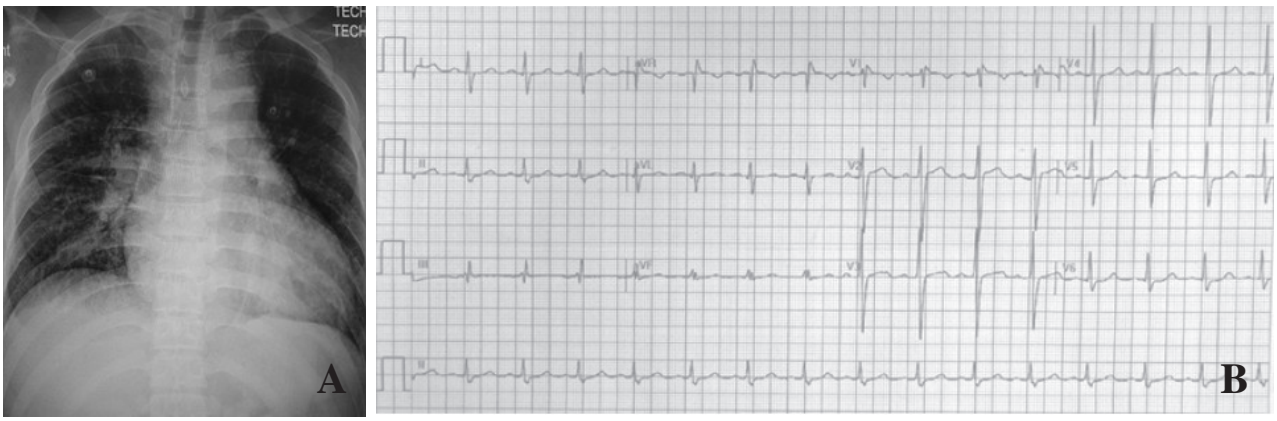

Figure 3A: Widening superior mediastinum with cardiomegaly was seen in chest film of case no.2,
3B: ECG showed sinus rhythm with incomplete right bundle branch block

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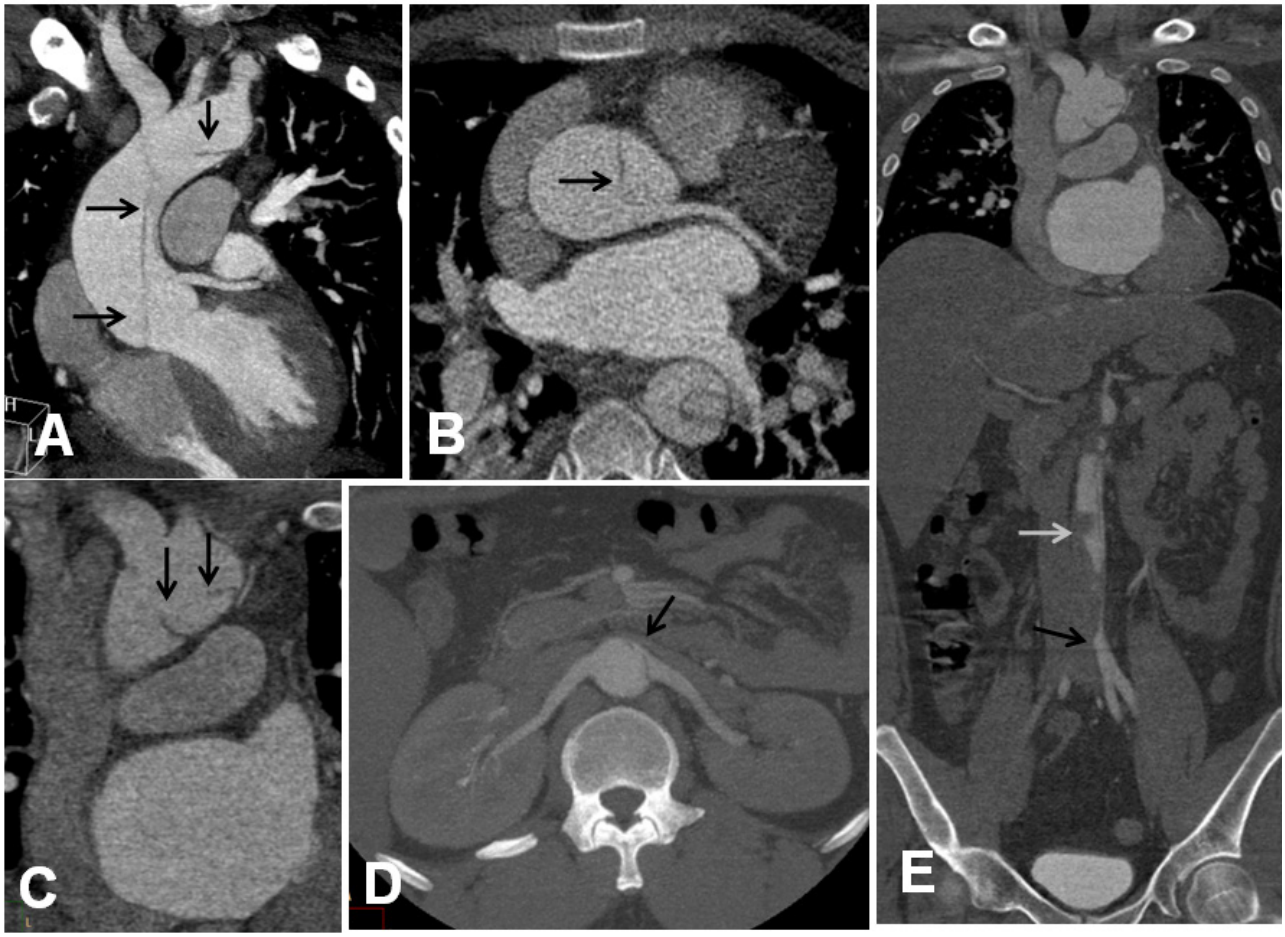

Figure 4A-E: Computerized axial tomogram (CAT) of case no.2 showed an ascending aortic dissection, Standford type A (arrow A), extending down to iliac artery. The proximal entry site was just above the left main origin (B, arrow). The distal entry site was between innominate and subclavian arteries (C, arrow). The dissection flap compromised the left renal (arrow D) and right common iliac arteries (E, black arrow). Intramural thrombus was also noted (white arrow, E).

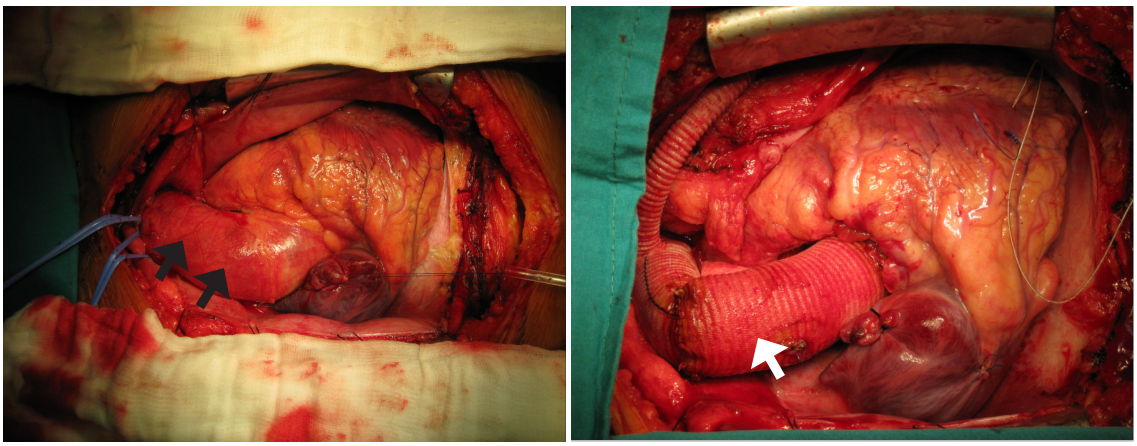

Figure 5: A dissected ascending aorta of case no. 2 was shown before (black arrow, A) and after resection with conduit graft replacement (white arrow, B).

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Discussion

Acute aortic syndrome, the highly fatal disease

Acute aortic syndrome refers to a group of lethal aortic diseases that share a common pathological background, acute aortic dissection (AD), intramural hematoma (IH) and symptomatic penetrating aortic ulcer (PAU).[1] Of these, acute AD is the most dangerous condition and carries the highest fatality rate. Its incidence ranges from 2.6 to 3.5 cases per 100,000 person-years.[1-4] The mortality rate of acute ascending AD (Stanford type A) patients increases with time after the onset of symptoms, by a factor of 1-2% per hour[5,6] while the 30-day mortality rate of uncomplicated descending AD (Stanford type B) cases is lower, at around 10%.[7] It is clear that acute ascending AD requires a rapid diagnosis and emergent surgical repair (1-7). In IH, the mortality is highest in the aortic sinus part (60%), followed by ascending aorta (50%), proximal arch (33%) and decreasing in distal arch (7%), descending thoracic aorta (13%) and abdominal aorta (0%).[8] Recently, we reported on a fatal penetrating aortic ulcer and aorto-iliac occlusion in a 56-year-old man who had a cardiac arrest and died from severe metabolic acid and multi-organ failure.[9]

Diverse clinical manifestation made the diagnosis of AD more difficult

The clinical manifestation of acute AD patients varies widely, depending on which arterial branches are involved. Therefore the presenting symptoms may be overlapping with any acute arterial occlusion such as acute coronary syndrome, and stroke.[1] Data from the international registry of acute AD (IRAD), based on 464 cases, indicated that most victims were men (65%) with a mean age of 63 years.[7] Other predisposing risk factors of developing AD were: hypertension (72%); history of atherosclerosis (32%); prior history of cardiac surgery (18%); Marfan syndrome (5%); and iatrogenic causes (4%, i.e. postvalvular, aortic surgery and vascular intervention).[1,7] The majority of acute AD cases presented with acute severe chest pain and only 4.5% of them experienced no pain.[1,10] Other presenting symptoms could be syncope, TIA, stroke[11], angina or myocardial infarction[12,13], and ischemic limbs with pulse deficit.[1] On rare occasions, an AD patient might come with supra-sternal bruising and neck swelling.[14]

Typical case presentation and high risk predictors

The first patient truly represented a typical case of Stanford type A, acute AD. This 71-year-old hypertensive man experienced chest pain which is common in proximal AD cases.[1] In addition, he had a syncopal attack and hypotension which were the risk predictors of death. In the IRAD registry, syncope was regarded as a poor prognostic indicator and was found in 13%. Syncopal cases trended to have proximal AD, more serious complications (i.e. cardiac tamponade, stroke and neurological deficit), and carried higher in-hospital mortality, 34%, vs 23% of cases who had no syncope.[15] In this particular case, moderate pericardial effusion was detected by echocardiogram suggested that the blood was dissecting down into the pericardial space, causing cardiac tamponade and shock. According to Mehta et al, tamponade, shock and hypotension are the strong independent predictors of in-hospital mortality with the odd ratio of 2.97 (95% CI 1.8-4.8), see Table 1.[16] In addition, the difference in systolic pressure between right and left arms (in this case 90 and 120 mmHg), as coded in the ACC/AHA guidelines of diagnosis and management of patients with thoracic aortic disease, is also indicated as a high-risk examination feature.[17] In cardiac tamponade cases, pericardiocentesis is still a matter for debate issue since it can make the patient's symptoms worse.[18] Owing to the late presentation (12 hours), all high-risk predictors and the delayed diagnosis, the patient died before referral.

Atypical proximal AD case with congestive heart failure

In contrast, the second case was of a quite young man who had no known predisposing factors of developing AD. Generally speaking, the younger AD cases (age < 40 years) are more likely to have Marfan syndrome, bicuspid aortic valve or prior aortic surgery[1] and none of these were found in this case. He smoked 1-4 cigarettes/day, had a small intake of beer or whisky but denied using cocaine or other drugs. It is possible that he might have asymptomatic hypertension as it is present in both sides of his family. He denied any history of blunt chest injury or vascular surgery in the past. On physical examination, there was no evidence of Marfan syndrome or other connective tissue disease and overt congestive heart failure from aortic regurgitation murmur was appreciated. The echo-cardiogram confirmed severe aortic valve leakage with three leaflets and no other valvular pathology was detected.

Unlike the first case, he did not have chest pain but had back and right ankle pain for two weeks. In type B, AD, back and/or abdominal pain were quite common.[1,7] It is possible that the dissecting blood first entered the wall at the distal arch, moving down to the abdominal aorta and occluded the right common iliac artery, see figure 4E. Operative findings confirmed two ruptured sites, one at the distal arch and another at the aortic root just above the left coronary sinus. As the blood entered the proximal entry site, it dissected into the aortic valve, causing severe regurgitation and congestive heart failure. A pulse deficit and murmur of aortic regurgitation were also the high risk features in this case.[13] The patient underwent complex surgical repair with no complication but the cause of AD remained unclear. Screening for family members was carried out as suggested in the current guidelines.[13]

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Conclusion

Acute ascending AD is one of the most catastrophic diseases that requires rapid diagnosis and surgical treatment. Missed or delayed diagnosis is quite possible and results in poor surgical outcomes or eventually death. We reported two cases of acute AD who presented with two different cardiac manifestations. The first one was typical Stanford type A AD who had syncopal attack from cardiac tamponade and died within 12 hours before surgery. The second case was a relatively young man, had no underlying disease, initially had Standford type B AD which later involved ascending aorta, causing severe aortic regurgitation and congestive heart failure. He survived complex surgical repair, aortic valve replacement and was discharged home. We hope that our reported cases will raise clinical attention for the early detection and treatment of this high fatality disease.

Table 1: Independent predictors of in-hospital death[12]

Variables	Overall Type A,%	Among survivors,%	Among death,%	Parameter Coefficient	*p*	Odd ratio for death (95%CI)
Age >70 yr	35.2	30.0	46.1	0.53	0.03	1.70 (1.05-2.77)
Female gender	34.5	30.7	42.7	0.32	0.20	1.38 (0.85-2.27)
Abrupt onset of pain	84.5	82.3	89.0	0.96	0.01	2.6 (1.22-5.54)
Abnormal ECG on presentation	69.6	65.2	79.5	0.57	0.03	1.77 (1.06-2.95)
Any pulse deficit on presentation	30.1	24.7	41.1	0.71	0.004	2.03 (1.25-3.29)
Kidney failure on presentation & before surgery	5.6	2.9	11.9	1.56	0.002	4.77 (1.80-12.6)
Hypotension/shock/tamponade	29.0	20.1	47.1	1.09	<0.0001	2.97 (1.83-4.81)

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Bilateral Idiopathic Granulomatous Mastitis: A Case Report

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Abstract

Idiopathic granulomatous mastitis is a rare, chronic inflammatory disease of the breast that frequently occurs in young women of childbearing age. The lesion usually presents as a unilateral firm breast mass with signs of inflammation but bilateral involvement has been reported. As the clinical presentation and radiological imaging of idiopathic granulomatous mastitis can mimic two common breast diseases, mastitis with abscess and breast cancer, a tissue biopsy is required for histopathological diagnosis. The etiology and ideal treatment remain unclear. Conservative treatment with immunosuppressive therapy has proven good efficacy. In this case report, we present a patient diagnosed with bilateral idiopathic granulomatous mastitis. We review and discuss the clinical presentation, imaging, diagnosis and management of this patient that eventually responds well to steroid therapy.

Idiopathic granulomatous mastitis is a relatively rare chronic inflammatory breast disease often mistaken for more common breast disorders, breast abscess or infectious mastitis, and can mimic inflammatory breast cancer.[1,2] Since it was first described in 1972 by Kessler and Wolloch[3], there have been only 541 cases reported worldwide as shown in a 2011 review article.[4] Most patients are women of reproductive age, most commonly aged 22 - 42.[5] It frequently occurs two to six years after pregnancy.[6] The lesion typically presents as a unilateral firm breast mass and can occur in any quadrants of the breast except in the subareolar area, sometimes with inflammation of overlying skin, abscesses and fistulae.[7-10] It usually poses a complex diagnostic and therapeutic dilemma because of the unknown etiology. A tissue biopsy is necessary to confirm the definite diagnosis. It is characterized by noncaseous granulomas and microabscesses confined to breast lobules with the absence of any infection during histopathological evaluation.[11,12]

Definitive treatment of idiopathic granulomatous mastitis remains controversial.[13] The available options of treatment include expectant management, antibiotics, steroids, other immunosuppressive drugs and surgical excision with varying degrees of response and recurrence.[2,8,14,15] Long-term follow-up is generally suggested in any treatments due to high rate of recurrence.[16,17]

In this report we present a patient with bilateral inflammatory breast mass finally diagnosed as idiopathic granulomatous mastitis. We review and discuss the history, clinical presentation, imaging, diagnosis and course of treatments for this disease in this patient who eventually was treated successfully with steroid therapy.

Case Report

A 44-year-old premenopausal Thai female, gravida 1 para 1, presented with a painful palpable right breast mass for four days, with associated inflammation of the overlying skin. She delivered her only son when she was 38 years old and had breastfed for 3 years. Her menarche was at the age of 13 and from then her menstrual cycles had come regularly. She had no history of drug or food allergy. Also, no history of smoking and previous use of

oral contraceptives or any hormone was detected. Her past medical and surgical histories were unremarkable, without any breast disease, surgery or recent breast trauma. Her family history was negative for both breast cancer and autoimmune disease along with no recent tuberculosis exposure. Systemic review was normal as well.

On physical examination, there was a 12×10cm firm mass with an ill-defined margin in the lower inner quadrant of her right breast with tenderness and localized erythematous skin. Axillary lymph nodes were not palpable. She did not have nipple discharge. Her temperature and other vital signs were normal.

Breast ultrasound revealed a focal area of swollen breast lobules consistent with inflammatory reaction in the lower inner portion of the right breast with moderate skin thickening (Figure 1). Mastitis in the right breast was suspected; therefore she was admitted to the hospital for parenteral antibiotics and nonsteroidal anti-inflammatory drugs (NSAIDs). Three days later, the patient's condition had improved and inflammatory symptoms had decreased, however, there was no change in the size of the mass. To confirm the definite diagnosis of the mass, a tissue biopsy was done by core needle method. Tissue was sent for histology, gram stain, acid-fast bacilli (AFB) stain, periodic acid-schiff (PAS) stain, aerobic and anaerobic cultures. All stains and cultures were negative. The histopathological evaluation showed poorly-formed noncaseating granulomas with many multinucleated histiocytes along with epitheloid cells, lymphocytes, aggregates of neutrophils and some eosinophils, which were compatible with idiopathic granulomatous mastitis (Figure 2). Microabscess formation was noted. Her chest imaging was also normal. A few days later she developed a fistula with pus-like discharge at the core biopsy wound. Although she was given oral antibiotics, there was no improvement. As the pain increased at her right breast mass with an area of induration and erythema, she subsequently underwent surgical incision and drainage. About 20 ml of purulent discharge drained from the lesion. Both discharge and inflamed tissue were sent for routine stains and cultures but all results returned negative. She received postoperative parenteral antibiotics and wound dressing changes (twice daily) for one week. As a result, the surgical wound improved with good granulation tissue and minimal pus discharge and all inflammatory symptoms disappeared. After being discharged, she took oral antibiotics and visited the breast clinic once a day for wound cleansing and dressing changes.

Two months later, the wound was completely healed and the size of the right breast mass had reduced slightly to 9.5 cm at its widest diameter. However, she developed a new painful 8.5×6 cm firm mass in the lower inner quadrant of the left breast with an ill-defined margin and signs of inflammation of the overlying skin like the previous one in her right breast (Figure 3). There was increased breast tissue density in the lower inner area of the left breast visible on the mammography. The ultrasound showed an ill-defined heterogeneous hypoechoic lesion at 8-9 o'clock of the left breast and surrounding tissue edema with skin thickening (Figure 4 and 5). The differential diagnoses were mastitis with early abscess formation, granuloma and inflammatory breast cancer. Initial treatment with NSAIDs had a good response. The inflammation had decreased and the left breast mass became about half the size. A core needle tissue biopsy was then performed for definitive diagnosis and the pathological report confirmed the diagnosis of idiopathic

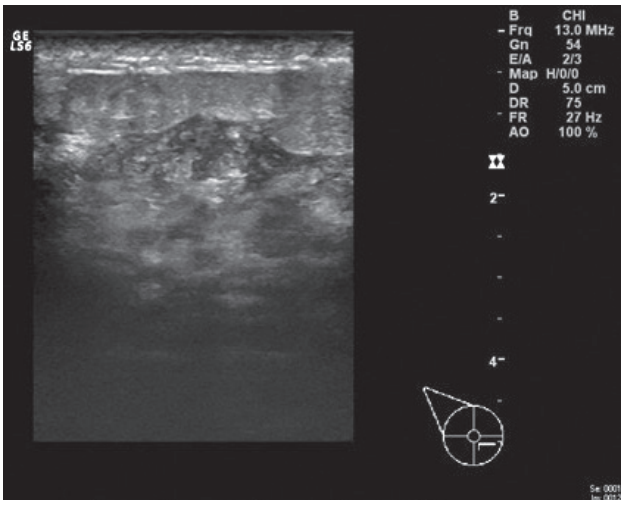

Figure 1: Ultrasonography of the patient's right breast lesion. Focal inflammation with moderate skin thickening in the lower inner quadrant.

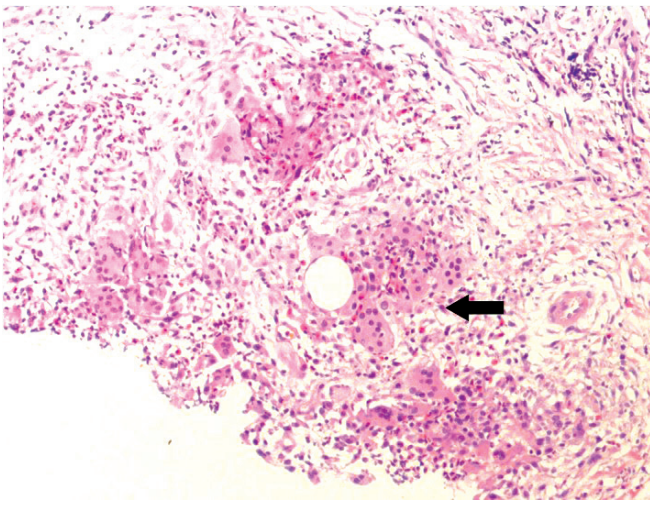

Figure 2: Histology slide of the patient's right breast mass. Poorly-formed granulomas with multinucleated giant cells (Black arrow).

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granulomatous mastitis. A week later, there was a fistula with minimal pus-like discharge at nipple areolar complex of the left breast near the mass area, while the core biopsy wound was well healed. A rheumatologist was consulted for evaluation and management of this case by using steroids. Several autoimmune serological tests were conducted, including anti-nuclear antibody (ANA), C-reactive protein, anti-double-stranded DNA antibody (anti-dsDNA), anti-Smith antibody (anti-Sm), anti-nuclear ribonucleoprotein antibody (anti-nRNP), anti-neutrophil cytoplasmic antibody (ANCA) and erythrocyte sedimentation rate (ESR) were ordered to rule out other autoimmune disorders and all tests provided negative results. The patient started on 20 mg of prednisolone daily and some improvement of symptoms was seen. The amount of discharge from one of the fistulas decreased and the size of both masses reduced significantly in just one week after starting this treatment. Three weeks later her symptoms had been completely resolved. The fistula closed and there was no palpable mass in both breasts. The patient maintained an initial dose of prednisolone for two months, then reduced this to 15 mg daily for four weeks and then to 5 mg daily over the next four weeks together with the addition of azathioprine at 50 mg daily.

After five months of treatment with steroids, prednisolone was tapered off completely. At the last follow-up visit, two months after stopping the steroid treatment, the patient was asymptomatic and no local recurrence was noted (Figure 6).

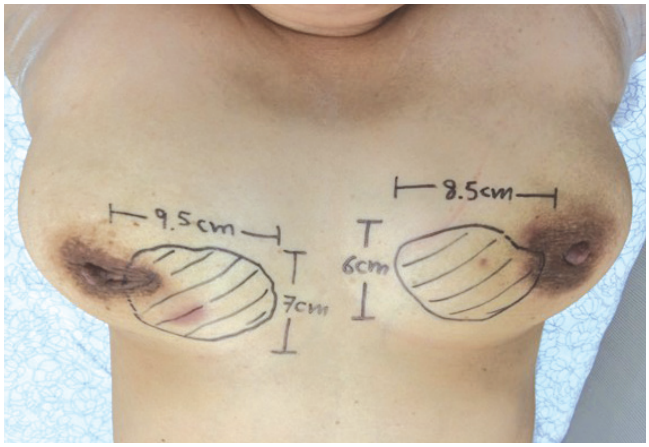

Figure 3: Clinical manifestation of bilateral breast masses of this patient diagnosed with bilateral idiopathic granulomatous mastitis.

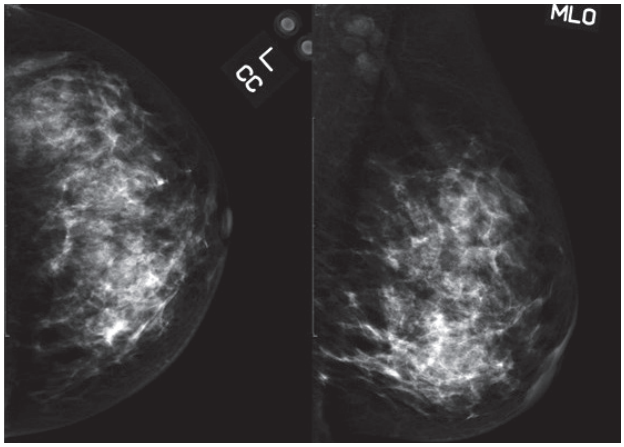

Figure 4: Mammography of the patient's left breast lesion. Increased breast density in the lower inner quadrant.

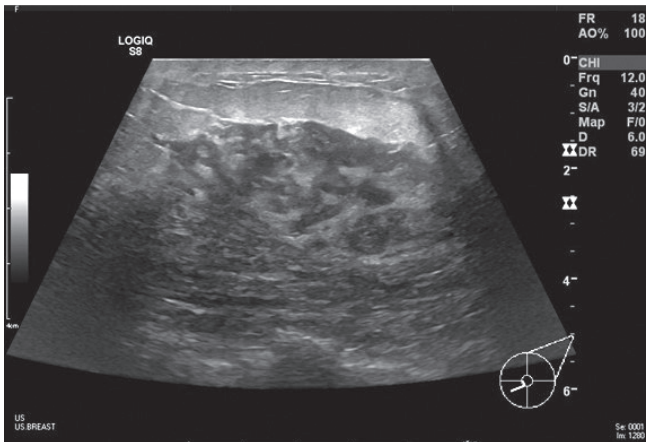

Figure 5: Ultrasonography of the patient's left breast lesion. An ill-defined hypoechoic lesion in the lower inner quadrant.

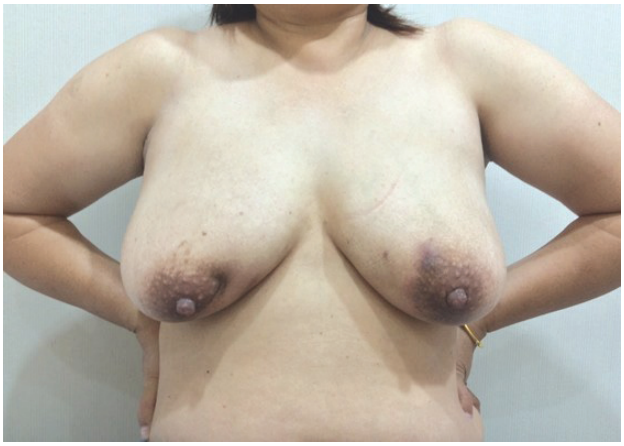

Figure 6: The patient's breasts at the last follow up visit after 5-months of steroid therapy.

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Discussion

Idiopathic granulomatous mastitis is a rarely seen, noncancerous, chronic inflammatory breast disease of unclear etiology and is diagnosed by exclusion.[17] It's commonly mistaken as common acute breast infection, infective mastitis or breast abscess and can clinically and radiologically imitate the symptoms of breast cancer, particularly if the regional lymph nodes are palpable.[1,2,18] Misdiagnosis as carcinoma may result in unnecessary wide local excision or mastectomy.[13,19] So a high index of suspicion is necessary. If symptoms of breast infection are not quickly improved or if there are repeated relapses after regular treatment, this disease should be included in the differential diagnosis.[20,21]

Idiopathic granulomatous mastitis is seen more commonly in young women of childbearing age and the usual age range is 22 to 42 years. However patients as young as 11 and as old as 83 years of age have been reported.[5,8] Women with a history of pregnancy and breast lactation within the preceding five years are the most frequently affected.[6] One third of the patients had previously used oral contraceptives.[11,22] It is exceptionally rare in men and during pregnancy.[23,24] Clinical presentation is usually unilateral, variable size, firm and ill-defined breast mass however bilateral lesions have also been reported in one fourth of cases.[25] The mass can occur in any of the four quadrants of the breast except for the subareolar region.[12,19] It is often associated with local tenderness, skin inflammation and nipple retraction like our patient with inflammatory mass in this report. In more chronic presentations, skin ulcerations, nipple inversion, fistulae and abscesses may eventually develop.[3,10,13] Peau d'orange-like change of the overlying skin is rarely seen.[7] While in some cases, no skin or nipple changes have been reported.[26]

The term granulomatous mastitis was first introduced by Veyssiere in 1967.[27] Idiopathic granulomatous mastitis is defined as granulomatous mastitis without any evidence of infection and no specific causes. The exact etiology of this disease is currently unknown.[19] Kessler and Wolloch who first described this disease in 1972 supported an autoimmune process corresponding to the histology.[3] An association has been suggested with recent pregnancy and breastfeeding has led to the foreign body reaction to extravasated secretions from the breast lobules.[28] Asso-ciations with blunt trauma, oral contraceptives, alpha-1-antitrypsin deficiency and hyperprolactinemia with galactorrhea (from pituitary prolactinoma or drug-induced galactorrhea) have also been reported.[29,30]

Mammographic features of this disease can be variable from normal findings in dense breast patients to masses with benign or malignant appearance and, most commonly focal asymmetrically increased density that mimic breast cancer. Sonographic imaging is also varied and relate to histologic patterns. The most common finding on breast ultrasonography is an irregular or ill-defined hypoechoic mass. Although breast MRI is better at detecting cancer than mammography and ultrasound it cannot differentiate between a granulomatous process and other inflammatory disorders.[12,31]

Histopathological evaluation remains the gold standard for the diagnosis of idiopathic granulomatous mastitis.[7,12] This is because the clinical signs and radiologic findings of idiopathic granulomatous mastitis are indistinguishable from carcinoma of the breast especially inflammatory type.[3,7,8,29,32] The differential diagnoses include carcinoma of the breast, other granulomatous breast infections such as tuberculous and mycotic infections especially when the fistulae to the skin occur, autoimmune diseases (sarcoidosis, Wegener's granulomatosis), foreign body reaction and granulomatous reaction in cancer must be ruled out before diagnosing idiopathic granulomatous mastitis.[19,25,32] A tissue sample is needed to avoid mis-diagnosing as breast cancer. The definitive diagnosis can be only made by tissue histopathological confirmation, so core needle tissue biopsy is preferred over fine needle aspiration cytology because a core biopsy is more accurate as it shows the tissue architecture.[19] The micro-scopic features such as lobular non-caseating granulomas with epitheloid histiocytes, multinucleated giant cells and predominantly composed of inflammatory cells, mainly lymphocytes background, plasma cells and less frequent neutrophils with micro-abscess formation and no specific etiologic microorganism or agent favor diagnosis of this disease.[7,12]

The variable clinical course of idiopathic granulomatous mastitis is troublesome for both clinicians and patients particularly in recurrent cases. Because of the unclear etiology of the disease, an ideal treatment method has not been established. Treatment depends on the severity of the disease and may include expectant management, anti-biotics, steroids, other immunosuppressive drugs or surgical excision.[9] The different rates of recurrence reported for each treatment method have been shown.[2,4] Initial treatment should be non-operative and conservative treatment that is usually recommended in patients with mild symptoms or uncomplicated disease. Some studies reported that in close observation groups, spontaneous resolution seen in approximately half of cases without any treatment with a mean interval of complete resolution of 14.5 months (range 2 - 24 months).[8]

In most patients with idiopathic granulomatous mastitis the initial clinical presentation leads to the use of antibiotics. Antibiotics may be useful in the treatment of other granulomatous breast infection. But in true cases of idiopathic granulomatous mastitis, even an association with local infection with Corynebacterium species has recently been proposed[33], antibiotics have no role in the management. This is because the condition of patients usually worsens or remains unresponsive to antibiotics and can lead to different antibiotic combinations.[20,34]

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For patients with more severe symptoms, steroids are administered. Although a low-dose is preferred, steroids should be started at a dose of 1 mg/kg per day and continually higher doses administered until the lesions completely resolve, then taper the steroids slowly according to clinical response.[21] Responses often present within weeks of treatment as seen in our patient. Treatment with steroids requires several months (usually up to six months) to achieve a complete response.[5,21] Complete resolution of the disease is seen in 80% of those who received steroids.[35] However about half of cases relapse after decreasing or stopping the dose of steroids.[15,21] Long-term steroid use can produce many unpleasant and often permanent side effects, therefore rheumatologists should be asked to help in the management of these patients.[27] The use of other immunosuppressive agents such as methotrexate or azathioprine as steroid-sparing drugs can be effective in treating patients refractory to steroid therapy, tapering steroid use and thus preventing many further complications after a long term treatment with steroids alone.[4,15,27] Some studies reported that a good therapeutic response can be seen in patients treated with methotrexate alone or in combination with steroids, with a more favorable side effect profile for treating idiopathic granulomatous mastitis.[14] Colchicine and anti-inflammatory drugs (NSAIDs) have also been used and have proven efficacy.[36,37]

Finally surgical therapy as surgical excision and/or mastectomy should be considered in recurrent cases and cases unresponsive to conservative or medical treatment.[13,38] Wide excision with negative margin is recommended due to a higher rate of recurrence after only a limited excision.[12,36] For surgical treatment, recurrence rates of 5-50% have been reported and may be higher than steroid treatment in some studies.[38] Furthermore, the high rate of postoperative wound complications and fistula formation have been reported.[8] In other reports, surgical excisions were performed after medical treatment because preoperative steroid treatment provided significant regression of the inflammatory lesion and then allowed more conservative surgery.[39]

Conclusion

Idiopathic granulomatous mastitis is a rare, benign inflammatory breast disease that typically occurs in women of reproductive age. It is commonly mistaken for two common disorders, inflammatory breast cancer and infectious mastitis with abscess, so the definitive diagnosis is made using tissue histopathology. Only a high index of suspicion will prevent the morbidity of misdiagnosis or delayed diagnosis and inappropriate therapy. Treatment depends on the severity of symptoms and available treatment options include close follow-up, medical and surgical therapy. In the future if we know the clear etiology of this disease, a new potential treatment with low recurrence may yet be discovered.

Conflict of interests: The authors have declared no conflicts of interests.
Ethical approval: A written informed consent was obtained from the patient for publication of this case report.

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Contrast Enhanced Spectral Mammography (CESM)

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Keywords: contrast enhanced spectral mammography (CESM), breast lesions, breast ultrasound, pathological and physiological imaging

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Abstract

CESM is a technique to detect abnormal contrast enhancement by dynamic iodinated contrast medium study via intravenous injection using digital mammographic unit on the basis of subtraction of low and high energies. The dynamic images are displayed to evaluate the depletion. The breast cancer will depict the contrast. The result is more sensitive and specific than CE-MRI. The other advantages to CE-MRI are lower cost of equipment, examination, contrast medium, shorter time of study and claustrophobia to MRI. It is recommended for the detection, extension of breast cancer or problem cases.

Contrast enhanced spectral mammography (CESM) is a technique to detect breast lesions, by determining the pattern of tissue contrast enhancement as well as detecting the extension of the disease. The images are derived from subtraction of dual exposures of low and high x-rays energies after intravenous infection of non-ionic iodinated contrast medium in order to show the enhancement of the lesions. The result is similar to a contrast-enhanced MR of the breast.[1] It improves diagnostic accuracy, giving anatomical, pathological and physiological imaging when compared with digital mammography and breast ultrasound.

Technique

-Equipment

The digital mammographic unit is designed for low energy simultaneous dual exposures for a routine digital mammogram and within a second, a high energy exposure for imaging the contrast enhancement of the breast lesion. The two images are automatically and digitally subtracted, leaving only the different patterns of enhanced pathological tissue on the image.

-Procedure

After an evaluation of the patient's renal function, a rapid intravenous injection is administered at the antecubital vein of non-ionic iodinated contrast medium (300-370mg/ml) in the amount of 1.5ml/kg of body weight, but not exceeding 100 ml. Two minutes or more after the initial injection, the image is taken with the routine positioning for mammography. The simultaneous dual exposures of low and high energy are performed mostly in CC and MLO (or ML) views. The total imaging study time is about 4-6 minutes. Additional views or wash-out patterns may be added. The total x-ray dose per view delivered to the patient averages between 1.30-3.13 mGy[1] depending on the breast tissue composition and the thickness of the whole breast.

Case Report # 1

A 45-year-old female with a history of breast cancer in her sister, with no presenting symptoms, came in for a routine mammography screening.

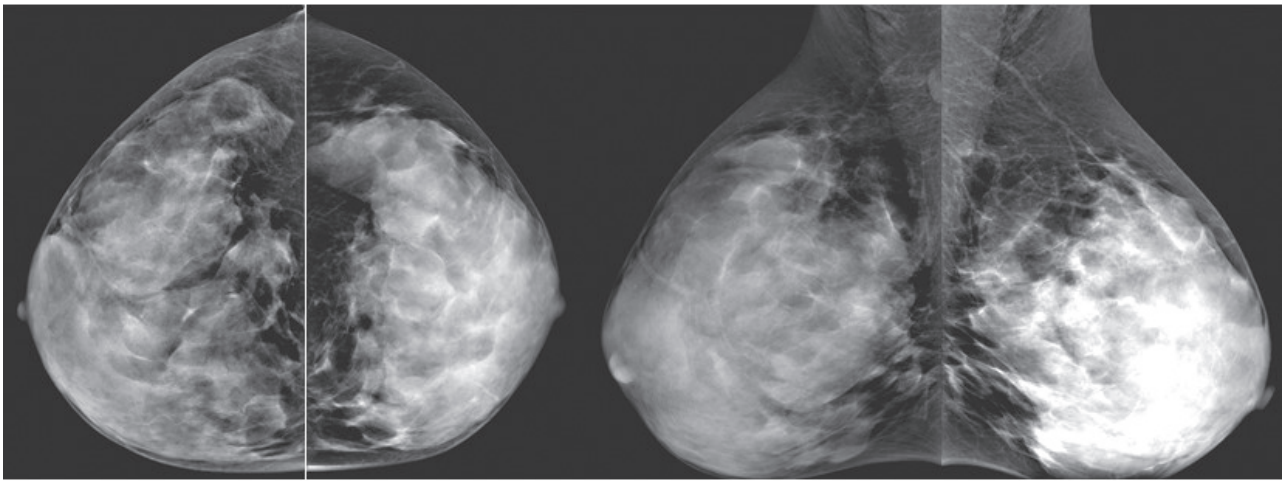

Figure 1A: Digital mammograms in CC and MLO views reveal extremely dense fibroglandular tissue, no detectable convincing lesion.

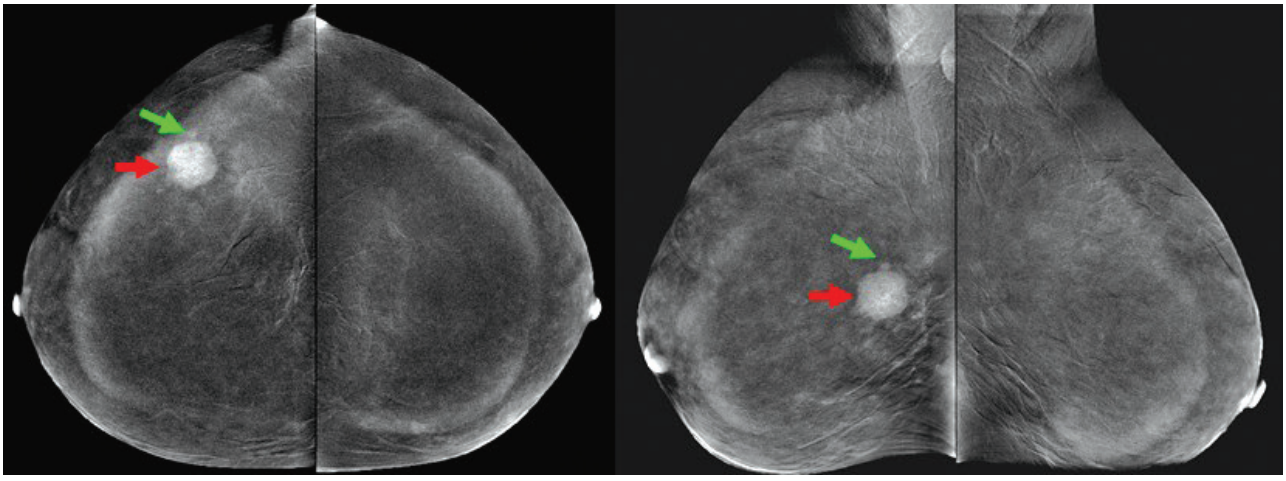

Figure 1B: CESM reveals extensive, inhomogeneous enhancement of a larger microlobulated round mass (red arrow) in outer part of right breast and another nearby tiny foci of enhancement (green arrow). Multiple tiny foci in right breast are not excluded.

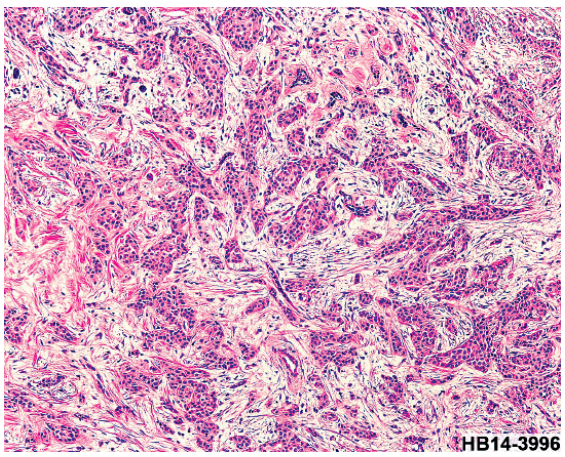

Figure 1C: Core needle biopsy (CNB) reveals invasive ductal carcinoma.

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Case Report # 2

A 60-year-old female had a left total mastectomy; axillary node clearance and TRAM flap operation about two years ago. She presented with pain and palpable abnormality in her post-operative breast.

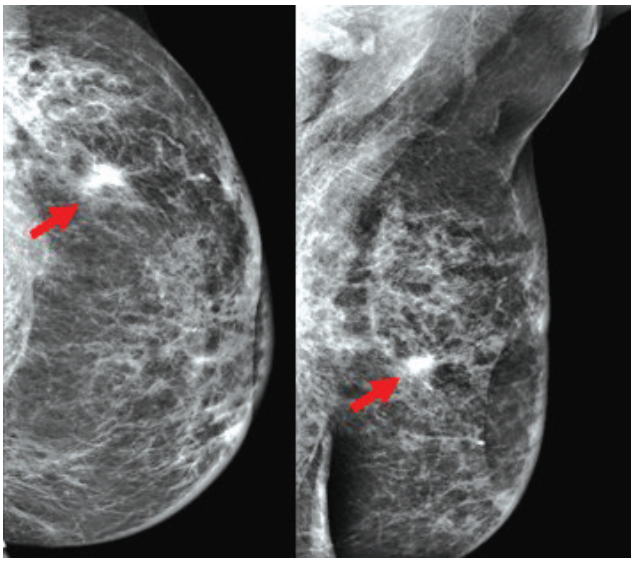

Figure 2A: Digital mammogram in left CC and MLO reveals an irregular shaped hyperdensity mass with spiculation, highly suspected of local recurrence (arrow).

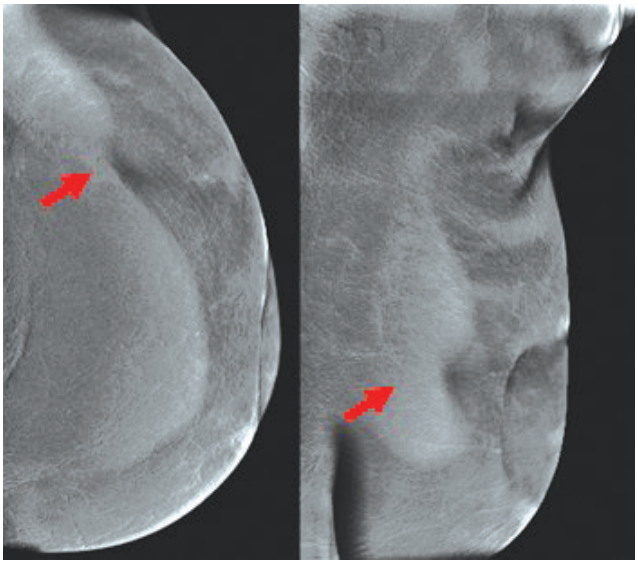

Figure 2B: CESM reveals no abnormal enhancement, particularly in the suspected area (arrow).

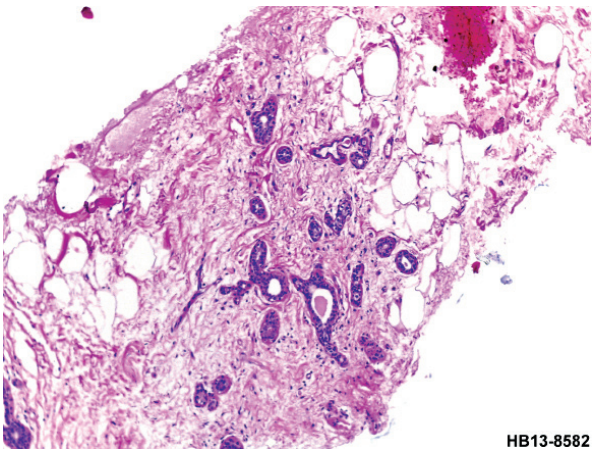

Figure 2C: CNB reveals only a stromal fibrosis. No malignancy is observed.

Discussion

Within the same breast compression, the low energy exposure gives a low dose; high resolution mammogram followed a second later by high energy exposure. This provides a contrast medium enhancement of abnormal breast lesions. These two images are taken immediately after exposure; meanwhile the automatic direct digital subtraction of the two images is presented immediately on the monitor. The enhancement pattern of the contrast enhanced spectral mammography (CESM) follows the rules of contrast enhanced MRI (CE-MRI). Comparing with CE-MRI, the CESM is expected to show better resolution of a mammography over the MRI resolution (including the presence of microcalcifications and its details, with no motion because both images are obtained in one breast compression of a couple of seconds. The equipment needed for this examination is much cheaper, using the well-known and cheaper iodinated contrast medium. The procedure is fast, not complicated, and similar to routine mammography that includes two views to study both breasts. The procedure takes less time, around four minutes for a capable technician. The CESM examination is not a claustrophobic experience; there are

no limitations for overweight patients, or patients with a cardiac pace-maker, a vascular stent, a metallic prosthesis, or old magnetic devices and clips.

We present a clear case of a malignancy not shown by mammography, but positively identified with CESM (Figure 1). We also present a highly suspected malignancy by mammography which proves negative in CESM (Figure 2). Breast mass is not commonly demonstrable in mammographic examinations of extremely dense breasts. Tomosynthesis cannot add enough information or comparable information for decision of treatment, unlike the CESM results. The extent of the disease is shown in our first case, as there are at least two cancers in one breast, and this result prevented the possibility of conservative breast surgery initially planned for this small mass. The local extension around the cancer can be seen with no difficulty. If there is no enhancement like in the second case, although digital mammography is highly suspicious, the presence of malignancy can mostly be excluded. The enhancement patterns resemble CE-MRI, believed to be the same principle of tumour vascularization and perfusion abnormality of abnormal cells. However, as in CE-MRI, there are the same overlapping patterns of benign and malignant enhancements. Fallenberg EM, et al.[2] shows CESM has a better detection rate and size estimation rate than digital mammography. The studies from Chen-Pin Chou, et al.[3] and Maha Helal, et al.[4] show CESM has a higher sensitivity and specificity than breast MRI (Table 1).

Table 1: Comparison of the sensitivity, specificity and accuracy of CESM with breast CE-MRI.

Authors		CESM (%)	MRI breast (%)	Accuracy
1. Chen-Pin Chou, et al. VSBR31-04, RSNA 2013	Sensitivity	97	63	-
	Specificity	91	63	
2. Maha Helal, et al. VSBR31-03, RSNA 2013	Sensitivity	93.7	66.6	80.6
	Specificity	93.7	86.6	90.3

MRI is beneficial in the differentiation of local recurrence of post treatment scarring after breast conserving therapy, evaluation of residual tumor post treatment, with unknown primary site of malignancy. Recently, the FDA approved the use of MRI in dense breast examinations, which should be replaced by CESM.

Dromain C, et al.[5] concluded that CESM improved diagnostic accuracy compared with the use of digital mammography and breast ultrasound. We agree with Dromain, et al. and one of our indications of CESM is to detect which one/ones of the numerous lesions in the breast require tissue study &/or surgery.

However the radiation dose for CESM is higher than digital mammography, ranging from 0.7-3.6 mGy[1], per view, almost the same or slightly lower than breast tomosynthesis. There also are untoward side effects of iodinated contrast medium, though this is uncommon in healthy women. Thus we suggest CESM should be performed when there is indication, not as a routine study.

Conclusion

CESM provides higher diagnostic accuracy, providing anatomical, pathological and physiological imaging superior to digital mammography and breast ultrasound. It shares the same principles with CE-MRI, in the enhancement pattern due to the similar uptake of contrast medium or enhancement. Therefore, the indication should be the same. However, CESM had been proved to be more sensitive and more specific than MRI. The image resolution is better than MRI. Microcalcifications are easily detected. There are no limitations as with MRI in regards to the ferromagnetic effect and machine design. It is much more cost-effective than CE-MRI due to the lower cost of equipment, contrast medium and less study time than using routine mammography views. The average time taken in the mammography room is around 4-6 minutes in a routine study. Thus, the patient flow is far better. Furthermore, tele-imaging is also possible.

CESM should be the imaging modality of choice in the detection and extension of breast cancer, particularly in problem cases, or when conservative breast therapy is attempted.

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Post-Traumatic High-Flow Priapism Treated with Gelatin Sponge Embolization: A Case Report

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Abstract

A 41-year-old male presented with a one week of ongoing priapism subsequent to an injury in a traffic accident (blunt perineal trauma). A selective arteriography of the right internal pudendal artery demonstrated an arterio-corporal fistula. A 2.8 French (2.8 Fr.) Renegade Microcatheter (Boston Scientific) was advanced proximal to the fistula over a 0.014 flexible guidewire. The fistula was then embolized with a gelatin sponge (gelfoam). Post embolization showed the closure of the fistula and significant detumescence. At 12 weeks later: there was no recurrence of priapism and the patient reported normal erectile function. Transarterial embolization appears to be a safe and effective treatment for managing patients with high-flow priapism.

Priapism is a relatively rare condition characterized by the persistent erection in the absence of sexual arousal. There are two main subtypes.[1] The more common ischemic or low-flow, is characterized by the impaired outflow from the corpora cavernosae, and non-ischemic, or high-flow is most often caused by trauma, characterized by the formation of an arteriovenous fistula, with increased flow of blood to the corpora cavernosae. With high-flow priapism, typically, the penis is neither fully rigid nor painful. Treatment of high-flow priapism in not an emergency case, as oxygen supply to the corpora cavernosae is maintained; hence, patients are at a low risk of permanent complications. The pathophysiology resembles that of compartment syndrome, with blood bypassing the capillary system completely and flowing directly into the lacunar spaces leading to persistent penile tumescence.[1,2] Conservative therapy, such as penile cooling, compression of the penile artery and application of vasoconstriction, is almost always without long-term benefits. Surgical intervention in high-flow priapism usually consists of the ligation of a cavernous artery or its branch and is reported to have the highest permanent erectile dysfunction rate, thus it is usually the last treatment option.[1-,3] Transarterial embolization using a small caliber coaxial catheter offers the ability to selectively occlude the fistula without damage to adjacent healthy tissue.[3-8]

We report a case of a post-traumatic high-flow priapism that underwent successful gelfoam embolization.

Case Report

A 41-year-old patient was referred to us from another hospital. He presented with priapism caused by previous perineal trauma. An urologist from the previous hospital consulted us for arteriography. The cavernous blood gas analysis was in keeping with arterial blood. The initial management involved pressure dressing for one week, but release of pressure caused immediate recurrence of priapism, typical of high-flow category.

Prior to the angiogram, a Foley catheter is placed. The patient was subsequently subjected to angiography under local anesthesia, the right femoral artery was punctured, and a 4 Fr. Cobra catheter was introduced through a 5 Fr. sheath. (The 5 Fr. Cobra catheter was out of stock at the time of the procedure).

The pelvic angiogram was performed in the antero-posterior projection and both obliques are obtained with the catheter at the aortic bifurcation to exclude correctable inflow disease of the common and internal iliac arteries. Selective internal pudendal arteriography is performed. The left internal pudendal artery angiogram showed no abnormality (Figure 1).

A Waltman loop is used to select the ipsilateral internal pudendal artery. The right internal pudendal angiogram shows extremely dense bulbar stain with shunting into the corpora. (Figure 2-3.)

A Curved-tip Microcatheter was advanced coaxially proximal to the fistula over a 0.014 flexible guide wire, but this was not successful. Several attempts were not successful. This was caused by the dislodgement of the Waltman loop: possibly due to the very sharp angle of the aortic bifurcation and the small size of the coaxial catheter. (4 Fr. Cobra) So, a new schedule for the angiogram was set, and the approach via the left femoral artery was undertaken.

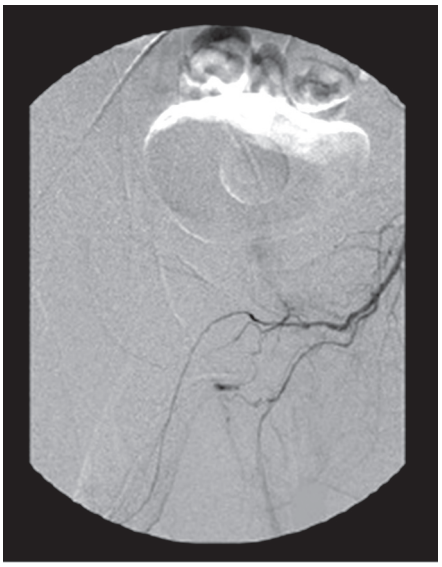

Figure 1: Selective angiogram of the left internal pudendal artery in right anterior oblique view appears unremarkable.

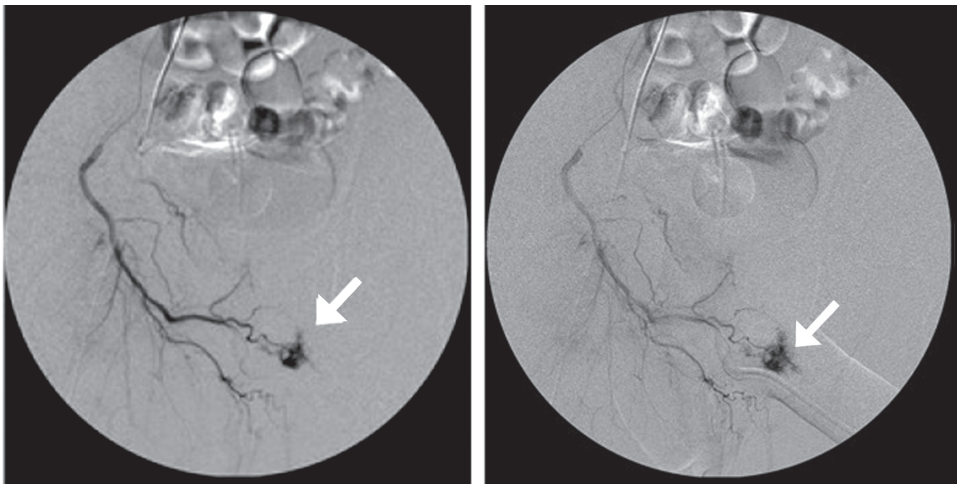

Figure 2-3: Selective angiogram of the right internal pudendal artery in left anterior oblique view shows blood pooling in the cavernosum secondary to arterio-corporal fistula. (see arrow).

Two days later, the patient still had priapism, so an angiogram was performed via the left femoral artery approach. A 5 Fr. Cobra catheter was used for the right internal pudendal angiogram. A Curved-tip Microcatheter was used for super selective examination. The defect was occluded using gelfoam. Improvement was reached with the closure of the fistula at the angiography check showed significant detumescence. He was kept in the hospital for 48 hours under observation after the procedure, and no complication occurred (Figure 4, Figure 5-6).

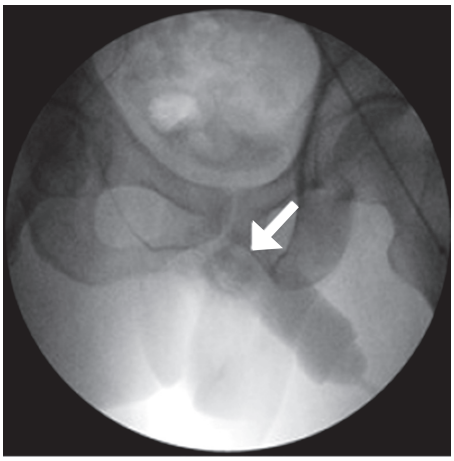

Figure 4: During gelatin sponge embolization. The gelatin sponge is impacted in the corpus cavernosum (see arrow).

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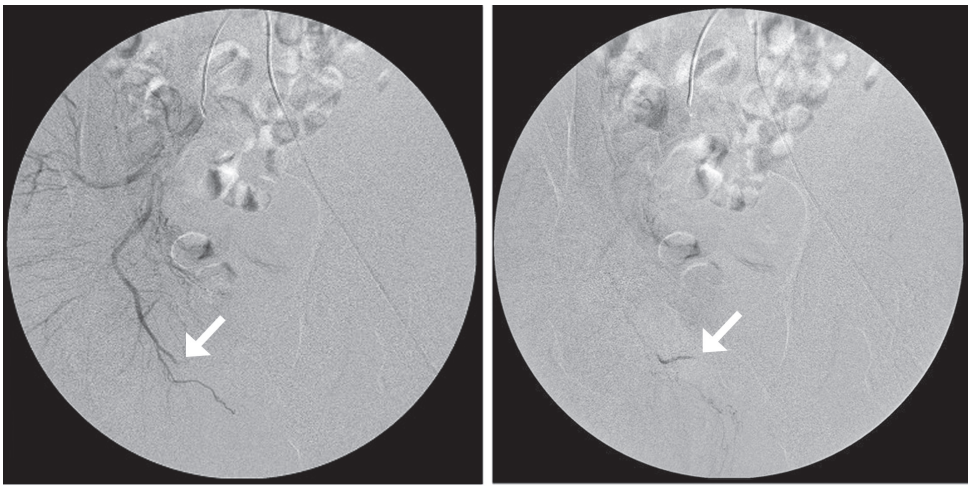

Figure 5-6: The selective angiogram of the right internal pudendal artery shows a complete occlusion of the arteriocorporal fistula (see arrow).

Discussion

Priapism is a prolonged unwanted erection in the absence of sexual stimulation, and is classified as either low-flow or high-flow. The most common low-flow priapism is due to veno-occlusion: these are painful rigid erections and need emergency treatment with penile drainage to prevent permanent damage. High-flow priapism is less common, and is usually caused by blunt trauma, resulting in a traumatic fistula into the corpus cavernosum. As this is a painless erection,[1] management of high-flow priapism includes conservative methods, selective embolization and surgery. Conservative methods include observation, mechanical compression, penile cooling, puncture of corpora cavernosa with blood aspiration, and intracarvernosal pharmacotherapy. However both conservative treatment and surgery are associated with a high risk of erectile dysfunction.[1-3,9,14] Selective arterial embolization is firmly established as the treatment of choice in high-flow priapism. The gold standard of super selective arterial embolization therapy is to temporarily interrupt the arterial blood flow feeding the fistula for enough time to allow the injury site to heal without permanently jeopardizing penile erectile function. Embolization can be done using either resorbable (blood clot and gelfoam) or non-resorbable (coil or microballoons) materials.[3,5,9,10,13,14] The majority of priapism cases reported in medical literature have been done using resorbable material.[3] Overall success rates with embolization are high, with very few complications. (Table 1)

Conclusion

Selective arterial embolization is a minimally invasive procedure; fistulae can be sealed without damage to surrounding healthy tissue or nerves, there is less morbidity, shorter hospitalization times and the recovery period is much faster.[3,4,6-8]

Table 1: Review of high-flow priapism treated with percutaneous embolization.

Study No.	Year/Ref	Patients (n)	Age (years)	Embolization Material	Detumescence	Mean FU (months)	Erection	Complication
1	1998[5]	1	6	Microcoil	yes	-	Present	nil
2	1998[6]	1	10	Microcoil	yes	-	Present	nil
3	2007[3]	27	6-67	Clot/ Gel Foam	yes	13.0 + 15.3	Present (n =21)	Erectile dysfunction in 6 pts and recurrence of priapism in 2 pts
4	2008[7]	8	22-59	Gel Foam/ Microcoils	yes	18.3 + 18.8	Absent (n =6) Present (n =6)	Erectile dysfunction and recurrence of priapism in 2 pts treated with gel foam
5	2008[10]	3	4-14	Gel Foam	yes	3.0 + 2.0	Absent (n =2)	nil
6	2002[11]	6	6-37	Gel Foam/ Microcoils	yes	11.8 + 6.7	Present Present	recurrence of priapism in 2 pts treated with gel foam

FU = follow-up, pts = patients

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Rescue Treatment for Migraine Headache in Emergency Department Part 2: Role of Antiepileptic, Magnesium, Corticosteroids, and Discharge Care

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Keywords: migraine, headache, treatment, rescue, emergency, antiepileptic, magnesium, corticosteroids, discharge care

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Abstract

Migraine is a common chronic neurological disorder, associated with a high disease-related disability and may lead migraineurs to the Emergency Department (ED). The efficacy of valproate, magnesium sulfate, corticosteroids as the rescue treatment for migraine headaches in ED has been reviewed. Nearly half of patients with migraine headaches discharged from the ED had received neither a specific diagnosis nor appropriate patient education. Hence, discharge planning and a migraine education program at the ED was also highlighted in this article.

Migraine is is one of the most common chronic neurological disorders. It is associated with a high disease-related disability and a significant impact on public health economies.[1-3] Global Burden of Disease studies reported that migraine headache is the third most prevalent disorder in the world. They also ranked migraine as the eighth most burdensome disease, and the seventh highest cause of disability in the world (responsible for 2.9% of all years of life lost due to disability).[4,5] The one year prevalence of migraine in the United States (US) was 11.7% (17.1% in women and 5.6% in men) of the adult population and highest in those aged 30 to 39 years for both men and women.[6] A report from the National Surveillance Studies shows the overall prevalence of migraine or severe headache in adults during the last 3 months was 16.6%. The highest prevalence occurred in females aged 18-44 and the lowest prevalence occurred in males 75 or older.[7] Headaches account for approximately 2.2% of all emergency department (ED) visits.[8] Management of acute migraine in ED is still suboptimal.[9] Migraine-specific medications such as triptans or ergotamine have been used only in few migraineurs who visited ED.[10] Over half of patients used simple analgesics to treat their headache attacks but this is often inadequate.[11] Opioids are commonly prescribed as the first line drug in US and Canadian EDs.[12,13] Rate of opioids prescription for migraine and headaches varied in EDs, ranged from 16% to 72%, which was not only ineffective for migraine headache but also increased risks of abuse, addiction, and contributed to poor clinical outcomes.[14-16]

US Headache Consortium provided the goals for acute migraine treatment as follows 1.) Treat attacks rapidly and consistently without recurrence. 2.) Restore patient's ability to function. 3.) Minimize the use of back-up and rescue medications. 4.) Optimize self-care and reduce subsequent use of resources. 5.) Be cost effective for overall management. 6.) Have minimal or no adverse events.[17]

Specific intravenous (IV) medications for rescue treatment in migraine that are commonly used in ED setting includes dopamine antagonists, nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, valproate, magnesium, and corticosteroids. We reviewed the efficacy of using dopamine antagonists, NSAIDs, and opioid in the Part 1 entitled The role of dopamine antagonists, NSAIDs, and opioids for rescue migraine treatment in ED (only medications that are available in Thailand)[18] that had been published in

The Bangkok Medical Journal 2014, Volume 7. This is Part 2 and details the efficacy of the other intravenous medications (valproate, magnesium, and corticosteroids) that had been used for rescue treatment of migraine headaches. We also highlighted the importance of appropriate discharge care for migraineurs at the emergence department.

Antiepileptic

Valproate, an antiepileptic medication, had established efficacy for prophylaxis of migraine with and without aura and was also approved by US Food and Drug Administration.[19,20] Intravenous valproate is useful as abortive treatment for acute moderate to severe migraine and even in refractory cases in ED and had been shown to be well tolerated, safe, and with rapid onset of action in several trials.[21-28] Valproate increases gammaaminobutyric acid (GABA) levels, an inhibitory neurotransmitter, by affecting the GABA-ergic enzymatic pathway.[29] This resulted in reduced firing rate of serotonergic cells in the dorsal raphe nucleus, and reduced central activation in the trigeminal nucleus caudalis.[23] Valproate had also been shown to act on the peripheral nerves by reducing neurogenic inflammation through GABA-A receptor antagonism.[30]

A randomized, double-blind study compared the efficacy of 1000 mg IV valproate, 10 mg IV metoclopramide, and 30 mg IV ketorolac for acute migraine treatment in ED. Valproate improved pain score by a mean of 2.8 points (95% CI: 2.3, 3.3) on 0 to 10 scale; those receiving metoclopramide improved by 4.7 points (95% CI: 4.2, 5.2); and those receiving IV ketorolac improved by 3.9 points (95% CI: 3.3, 4.5). IV valproate was less efficacious than IV metoclopramide or IV ketorolac in patients whom presented in ED with acute migraine attack.[31] In a randomized open-label study, valproate 400 mg IV was compared to sumatriptan-metoclopramide (metoclopramide 10 mg IM followed 10 minutes later by 6 mg SQ sumatriptan) in patients with prolonged migraine without aura (more than 4 hours but less than 72 hours). Pain relief at 1 hour (severe or moderate pain to mild pain or none) was observed in 53.3% in the valproate arm and 23.3% in the metoclopramide plus sumatriptan arm ($p = 0.033$), whereas pain relief at 2 hours was reported 60% and 30% respectively ($p = 0$ .037). Dizziness was reported in only one patient in the valproate group.[32]

In a prospective, randomized, double-blind trial in ED that compared 500 mg of IV sodium valproate to 10 mg IV prochlorperazine, the mean change of pain reduction on visual analog scale (VAS) at 1 hour was greater for prochlorperazine (-64.5 vs. -9.0 mm; $p < 0.001$). Median changes over a 60-minute period in VAS for nausea were also significantly different, favoring prochlorperazine over sodium valproate (-35.5 vs. -2 mm; $p < 0.001$). In post hoc analysis, valproate failed to demonstrate significant improvement in pain or nausea over time. In contrast, prochlorperazine showed significant improvement in pain by 30 minutes ($p <0$ .001) and nausea by 15 minutes ($p = 0.002$). Moreover, 79% of patients receiving valproate required rescue treatment compared with 25% of patients receiving prochlorperazine ($p =0$ .001). Sedative side effect was not statistically different between the 2 treatments ($p = 0.603$).[33] Valproate has a favorable side effect profile with lack of sedation, no cardiovascular side effects, no negative interactions with triptans or ergot alkaloids, and no dependence effect. Urine pregnancy test is recommended before use in a woman of child-bearing age. It is contraindicated in pregnancy, hepatic disease, and urea cycle defect.

In summary: IV sodium valproate was substantially less efficacious than IV prochlorperazine, IV metoclopramide, and IV ketorolac.[31,33] IV valproate should not be used as the first-line monotherapy for rescue migraine treatment in ED.[31] Canadian headache society recommended against the use of sodium valproate for the acute treatment of migraine pain in ED (weak recommendation, low quality of evidence).[34]

Magnesium

Magnesium is the second most abundant caution in the intracellular fluids in the human body. It is essential in biochemical and physiological processes especially for neurochemical transmission and muscular excitability.[35] Magnesium may play an important role in both neuronal (cerebral cortex, brainstem) and vascular (the trigeminovascular system) components in migraine pathophysiology and there is a possible relationship between intracellular magnesium levels and the threshold of migraine attacks.[36-38] Magnesium acts on N-methyl-D-Aspartate (NMDA) glutamate receptors to maintain calcium homeostasis, to modulate the release of substance P, and regulate the production of nitric oxide.[39,40] Low magnesium levels can result in opening of calcium channels, increased intracellular calcium, glutamate release, and increased extracellular potassium, which may in turn trigger cortical spreading depression.[38,41-44] In patients with acute migraine headache, 42% reported low intracellular magnesium levels but the total Mg level was normal in most cases.[45] Ionized magnesium levels were low in 45% of women with menstrual migraine attacks, however in menstruating women without migraine only 14% had low ionized magnesium levels.[46]

A case control comparison study in patients presented with a moderate or severe headache of any type reported 80% pain-free within 15 minutes post-infusion with 1 g IV magnesium sulfate ($MgSO_4$) ($p < 0.001$). Migraine-associated symptoms including nausea, photophobia and phonophobia were also completely eliminated. Low ionized magnesium was found in 37.5% of non-responders compared with 89% in those that had sustained pain-free

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at 24 hours. Almost all patients experienced flushing during magnesium infusion.[47] A randomized, single-blind, placebo-controlled trial compared 1 g IV $MgSO_4$ with IV placebo/normal saline (NS) in patients with moderate or severe migraine attacks. Pain-free and symptom-free after treatment with IV $MgSO_4$ was reported in 87% of the patients and 0% for placebo ($p < 0.0001$). Accompanying symptoms disappeared in all patients after IV $MgSO_4$ compared with 20% for placebo ($p < 0.0001$). Mild side effects such as flushing and burning sensation in face/neck were experienced by 86.6% of the patients and asymptomatic slight drop in systolic blood pressure (5 to 10 mmHg) by 13%.[48]

Magnesium sulfate 2 grams IV was compared with placebo/NS IV as an adjunctive medication in randomized double-blind, placebo-controlled study. All patients received 20 mg IV of metoclopramide (repeated up to 60 mg). Pain reduction (measured by VAS) was not different between two groups (magnesium -55 vs. placebo -71), but the proportion that returned to normal function was greater for placebo group (magnesium 8% vs. placebo 17%; $p < 0.05$).[49] The efficacy of magnesium in acute treatment of pain and associated symptoms in patients with migraine with and without aura was performed in randomized, placebo-controlled, double-blind fashion. Magnesium sulphate 1 g IV was compared with placebo/NS IV: in the migraine with aura group, statistically significant improvement of pain, nausea, photophobia and phonophobia compared with controls were reported (50% vs. 13.3%; $p <0 .05$). In the migraine without aura group, there was no statistically significant difference in pain relief and nausea improvement but there was significantly lower intensity of photophobia and phonophobia. Greater response in all symptoms in the migraine with aura group than in the migraine without aura group was observed.[50]

A randomized, placebo-controlled, double-blind study compared the effectiveness of $MgSO_4$ 2 g IV with metoclopramide 10 mg IV and with placebo/NS IV for acute migraine treatment in ED. Mean pain reduction was similar for metoclopramide vs. magnesium vs. placebo (mean VAS -38 vs. -33 vs. -24), but a smaller percentage in the metoclopramide and magnesium groups required rescue medications vs. the placebo group (38% vs. 44% vs. 65%; $p = 0.04$). The recurrent rate in 24 h was not statistically significant between the groups. However, the placebo group required rescue medication more than the others. Dystonia was reported in 3% of metoclopramide group, and flushing was reported in 8% of magnesium group.[51] A prospective study compared $MgSO_4$ 2 g IV with prochlorperazine 10 mg IV in ED patients with acute headache. VAS was obtained at 30 minutes after infusion, mean pain reduction was greater for prochlorperazine than for magnesium (47 mm vs. 24 mm, t = 0.208, $p = 0.045$). Prochlorperazine provided greater headache relief than magnesium (90% vs. 56%; $p = 0.038$). Dysphoria was reported in 1 patient (5%) with prochlorperazine, and IV burning pain in 4 patients (25%) with magnesium.[52] Magnesium has a minimal side effect profile. The common adverse effects were flushing, loose stool, and temporary blood pressure lowering. Magnesium is safe to use in children and pregnant women who have acute migraine attack.

In summary: IV magnesium sulfate can be an effective agent in migraine treatment, either alone or in combination with other medications, especially in patients who have aura.[53] Photophobia, phonophobia, and nausea can be reduced with IV magnesium in all migraineurs.[50] However, a recent meta-analysis failed to demonstrate the statistically significant pain relief of intravenous magnesium over placebo, metoclopramide or prochlorperazine for the treatment of acute migraine in adult patients. This meta-analyses also showed no benefit in terms of the need for rescue medication and patients were more likely to report significant adverse events when treated with magnesium.[54]

Corticosteroids

Intravenous or oral corticosteroids are typically used as rescue therapy for migraine headaches.[55] Corticosteroids have been used in the management of status migrainosus, bridging therapy during the detoxification in patients with medication overuse headache, and treatment of immunosuppressant-induced headache in organ transplant recipients.[17,56,57] The role of corticosteroids in acute migraine is limited. Evidence from meta-analysis of randomized controlled trials (RCTs) suggested that parenteral dexamethasone, a potent anti-inflammatory corticosteroid with almost no mineralocorticoid effect, did not significantly reduce pain scores before discharge from ED; however it could reduce the rate of headache recurrence within 72 hours of initial abortive therapy.[58] Recurrence of headache after ED treatment is one of the major concerns in migraine management. The rate of moderate or severe recurrent headache was reported up to 70% of all patients within 24-48 hours after ED discharge.[10,59,60] Neurogenic inflammation had been proposed as a one of the important mechanisms in migraine generation and relapse.[61-63] Corticosteroids can suppress the sterile neurogenic inflammation and reduce trigeminal sensitization in underlying pathophysiology of migraine.[64,65] Steroids are frequently used in ED to reduce the likelihood of headache recurrence and ED revisit.[66]

Pooled data meta-analysis and systematic review from 8 high-quality RCTs with a total of 905 patients suggested a significant benefit of corticosteroids compared with placebo in addition to standard abortive therapy for acute migraine management in ED (RR = 0.71; 95% CI: 0.59, 0.86). The estimated number needed to treat (NNT) to prevent one moderate or severe recurrent headaches were 10 (95% CI: 6, 22). Adverse events of steroids are benign

and not significant except for dizziness (RR = 2.78; 95% CI: 1.02, 7.61). Subgroup comparison between those who received parenteral versus oral dexamethasone treatment showed no significant difference between patients who received oral steroids and parenteral steroids treatment for the primary outcome of moderate or severe migraine headaches (RR = 0.82; 95% CI: 0.53, 1.27; p = 0.37). A trend of dose-dependent effect of dexamethasone was observed, dosage of greater than 15 mg showed higher efficacy than those less than 15 mg. However, this is not statistically significant.[67]

Side effects of single dose corticosteroids were relatively mild and not significant except for dizziness. However dexamethasone should be used with caution in the elderly, in patients who have diabetes, congestive heart failure, and a history of gastrointestinal ulcer or perforation.

In summary: the data of using corticosteroids for acute migraine headache treatment was limited. However, meta-analysis showed the benefit of added-on intravenous or oral dexamethasone to standard headache abortive therapies in terms of reducing the rate of headache recurrence at 24-48 hours after ED discharge. Side effects were mild and not significant except for dizziness.

Discharge care

Discharge planning and management of migraine in the ED seems to be ineffective due to underdiagnosis, inappropriate prescription of acute and prophylactic medications, or lack of patient education.[9-12] Forty two percent of patients were discharged from the ED without a proper and specific diagnosis[68] and only 20% of patient was headache-free on discharge from ED.[10] In patients who left ED with residual headache, 60% experienced persistent headache.[60] Up to 73% of all patients reported that the headache returned within 24-48 hours after ED discharge.[59] Moreover, at the time of discharge, 24% of patients received no prescriptions and 33% received no follow-up appointments.[68,69]

Effective migraine management requires accurate diagnosis, initiation of appropriate acute and prophylactic medications, patient education, and follow up plan. Migraine educational programs can help decrease headache frequency, reduce migraine-related disability scores, improve quality of life, and improve in cognitive and emotional aspects.[70,71] Active intervention programs including intensive patient education (involving the topics of migraine biogenesis, acute treatment of migraine, and prevention of migraine) can decrease migraine frequency, migraine disability, increase quality of life, and reduce their utilization of headache resources.[72]

Screening for psychiatric conditions is considered in all headache patients because of the high prevalence of psychiatric comorbidity in migraine populations, especially depression and anxiety.[73-77] A prospective cohort study in the Women's Health Study reported in the association between migraine and depression. The adjusted relative risks of incident depression were 1.53 (95% CI: 1.35, 1.74) for migraine with aura, 1.40 (95% CI: 1.25, 1.56) for migraine without aura, and 1.56 (95% CI: 1.37, 1.77) for persons who had past history of migraine compared to no history of headache.[78] Severity of depression was also associated with an increased risk of transformation from episodic to chronic migraine.[79] Migraine and psychiatric comorbidity are in bidirectional association, treatment of the psychiatric comorbidity will improve migraine and vice versa.[80,81]

Conclusion

The ideal rescue therapy for migraine in ED is to administer medicines which provide rapid, complete relief of headache and associated migraine symptoms, restore functional ability, with minimum adverse effects and without recurrence of headache after ED discharge.[82,83] Dopamine antagonists (chlorpromazine and metoclopramide) and parenteral NSAIDs (ketorolac) are recommended as the first line rescue medications for migraine in emergency setting.[34,84] Adequate hydration will promote rapid recovery. Healing environments such as a quiet room with suitable light should be provided to migraineurs with photophobia and phonophobia. Discharge planning, patient education and early detection of psychiatric comorbidity play crucial roles for enhancing treatment outcomes and for preventing transformation from episodic to chronic migraine.

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Fracture Anterior Labrum with Dislocation

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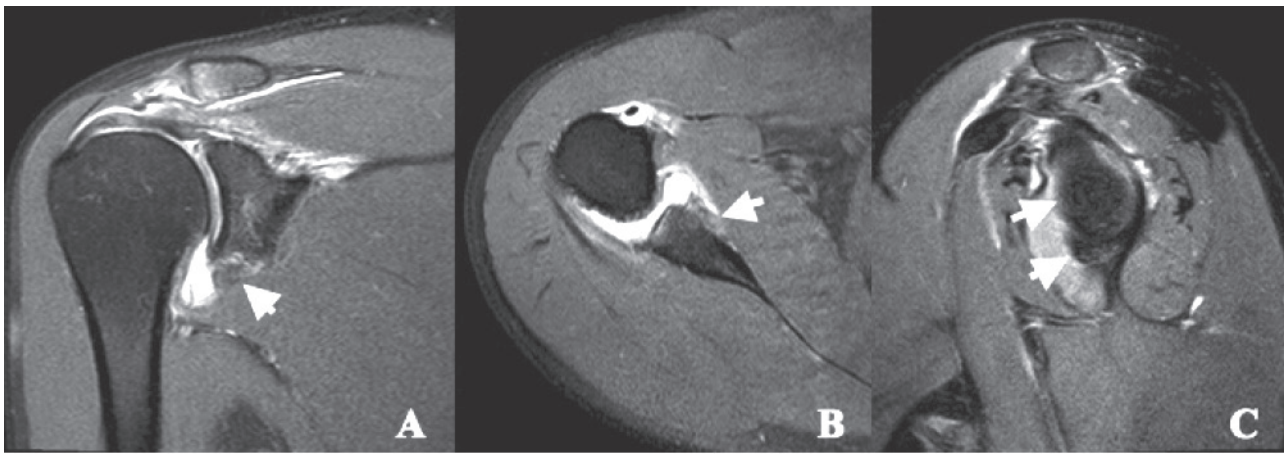

A: Inferomedial displacement of inferior labroligamentous complex

B: Displacement of the labroligamentous complex anterior to genoid neck

C: Labral defect from anterior middle to anterior inferior portion

Shoulder injuries are one of the most common problems faced by competitive athletes. A shoulder dislocation is a serious complication, and more than 95% of all shoulder injuries are anterior dislocations. Furthermore, the recurrent dislocation and subluxation are common complications after a traumatic shoulder dislocation. Conservative treatment is not sufficient to prevent future complications. An aggressive investigation and early surgical correction is called for as the best approach to achieve promising future results.[1]

A 28-year old man fell and sustained a blunt injury to the right shoulder. He had primary treatment at a local hospital, and one and a half months passed before he came to the Bangkok Academy of Sports and Exercise Medicine (BASEM) department at Bangkok Hospital. The magnetic resonance image (MRI) for arthrography rendered an excellent depiction of a localized labral injury. It was decided that an arthroscopic repair would be performed at the site of this major injury, with a shorter tear in-operation. The MRI arthrogram (see Figure A-C) revealed a tear of the anterior middle to anterior inferior labrum, inferomedial displacement of the inferior labroligamentous complex anterior to the glenoid neck and an osseous defect at the posterior portion of the humeral head. The findings were compatible with anterior labroligamentous periosteal sleeve avulsion (ALPSA) and Hillsach deformity. The athroscopy of the right shoulder revealed a right glenohumeral subluxation anteroinferior subluxation, a Bankart and an ALPSA lesion. The arthoroscope via an anterior glenoid approach was used to perform a Bankart and ALPSA repair.

The glenohumeral joint has a rather wide range of movement, wider than any joint in the body. It is the most common dislocated joint due to its small and shallow glenoid fossa.[2,3] The ALPSA is a main factor of shoulder instability.[4]

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Implementing a disease-specific Electronic Medical Record System at Bangkok Medical Center: Lessons Learned

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Diabetic Mellitus (DM) is a lifelong chronic disease that has a major impact on health care costs. Taking care of diabetic patients relies heavily on adequate and accurate informatics. In order for care providers to view a patient history and to be able to project the trend of future treatments, the health information system must be concise and include a function for easy access to patient records to efficiently locate all the related data. At the Bangkok Medical Center (BMC), the existing Hospital Information System (HIS) is mainly used to manage administrative functions, such as making appointments, registering patients, order entry, results reporting, and billing. The traditional paper clinical record from providers are still used and scanned as an image into the HIS. We found that the HIS is too generalized and broad, and does not meet the specific needs for diabetes management. The display of information is sub-optimal, not only because it's incomplete and often contains scanned images of illegibly written notes, but also because it presents a cluttered user interface (UI) that includes myriad windows with laboratory results, radiology reports and medication lists, making viewing of summarized data quite difficult.

Additionally, The American Diabetes Association's (ADA) standards of medical care in Diabetes 2014[1] suggested that optimal diabetes management requires an organized, systematic approach with the involvement of a coordinated team of dedicated health care professionals working in an environment where patient-centered high-quality care is a priority. Furthermore, the provision of care coordination as recommended by ADA and Joint Commission International (JCI), can only be achieved by leveraging information system technology.[2,3] We looked for a tool to compliment and extend our HIS to deliver diabetes-specific care.

We ultimately decided to innovate and develop a new disease-specific electronic medical record (EMR) system to support the management of diabetes patients. Hopefully, this project will encourage other specialists to use this disease-specific EMR instead of traditional clinical records stored on paper.

In summary, the expected goals of the project are as follows:

- To create a system of choice for endocrinologists and other physicians to use interactively, allowing them to focus on the medical history rather than resorting to paper for clinical notes and orders.
- To improve both function and workflow for effective management and care of DM Type 2 patients.
- To achieve and sustain the standard medical care recommended by JCI and ADA.
- To ensure effective communication between a multidisciplinary care team.
- To reduce the use of paper and enable a fully digital clinical record of care.

- To act as the source of reliable clinical data for data analysis for educational and medical research purposes.
- To be the first pilot project at BMC to study the utilization of disease-specific EMR.

The system called DM EMR was developed through a collaboration of in-house IT technicians who worked closely with endocrinologists and DM nurse specialists. The DM EMR was implemented in the Diabetes Center in 2011. The Diabetes Center latterly received a certification from JCI CCPC for DM Type 2 care management in the same year.

The pilot project

DM EMR project was proposed to the executive team and finally received approval to proceed in planned phases:

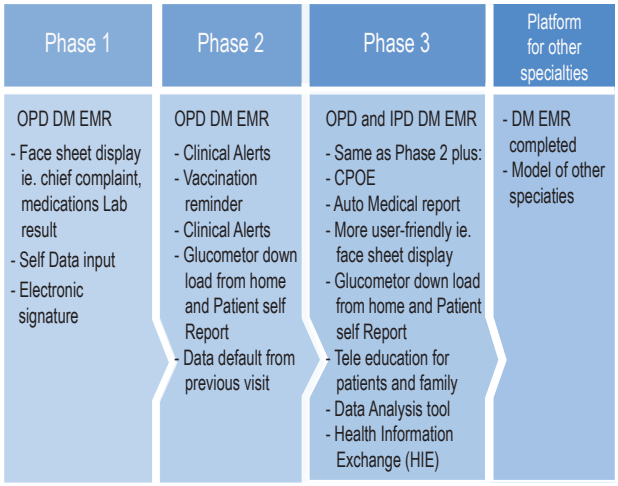

Figure 1: DM EMR Project Plan

Designing DM EMR

In order to serve as an IT tool in facilitating best clinical practice, the software development teams needed to track the office workflow and support the DM Type 2 management care recommendations. The starting point in designing an efficient EMR work process was to assess the clinical needs. As shown in Figure 2 and 3, IT technicians and clinical team members worked together to determine the user requirement. After in depth discussions, the project team decided to leave orders and prescribing functions in the HIS and to leverage these capabilities in developing the DM EMR as an additional independent module.

Initially the DM EMR will be used only for patients aged 15 to 80 years old with DM type 2 diagnosed and HbA1C ≥ 7. A requirement of the clinical team was to have the DM EMR automatically look for these required criteria in the DM type 2 pathways. Once the patient is selected to participate in the pathway, the patient data is transferred and integrated with the information from the HIS, including ICD 10, prescriptions and all lab values. The face sheet of the DM EMR includes: Chief Complaint, Medication List, Diagnosis List, Laboratory Results List, Vital Signs List, Cumulative Creatinine, Next Appointment List, and all the pathways the patient has been on. In addition to retrieving the HIS, DM EMR allows providers to manually enter medication lists as well as lab results from other hospitals.

Project Planing V4

Project Name : DM Pathway Phase 1

Subject: EMR DM Pahtway

No	Title	Duration	Oct 2011					Nov 2011					Dec 2011					Jan 2012					Feb 2012	
		week	Wk 1	Wk 2	Wk 3	Wk 4	Wk 5	Wk 1	Wk 2	Wk 3	Wk 4	Wk 5	Wk 1	Wk 2	Wk 3	Wk 4	Wk 5	Wk 1	Wk 2	Wk 3	Wk 4	Wk 5	Wk 1	Wk 2
		day (s)	3-7	10-14	17-21	24-28	31	1-4	7-11	14-18	21-25	28-30	1-2	5-9	12-16	19-23	26-30	2-6	9-13	16-20	23-27	30-31	2-6	9-30
1	Project Planing 7 Kick off	1																						
2	Requirement Phase 1	10			x																			
3	Design	11							x															
4	Code and System Test	55											x			x			x			x		
5	User accepant testing	5																						
6	Trainig	5																						
	Total	87																						

= On process
= On planning
x = Follow up

Figure 2: DM EMR Project Schedule

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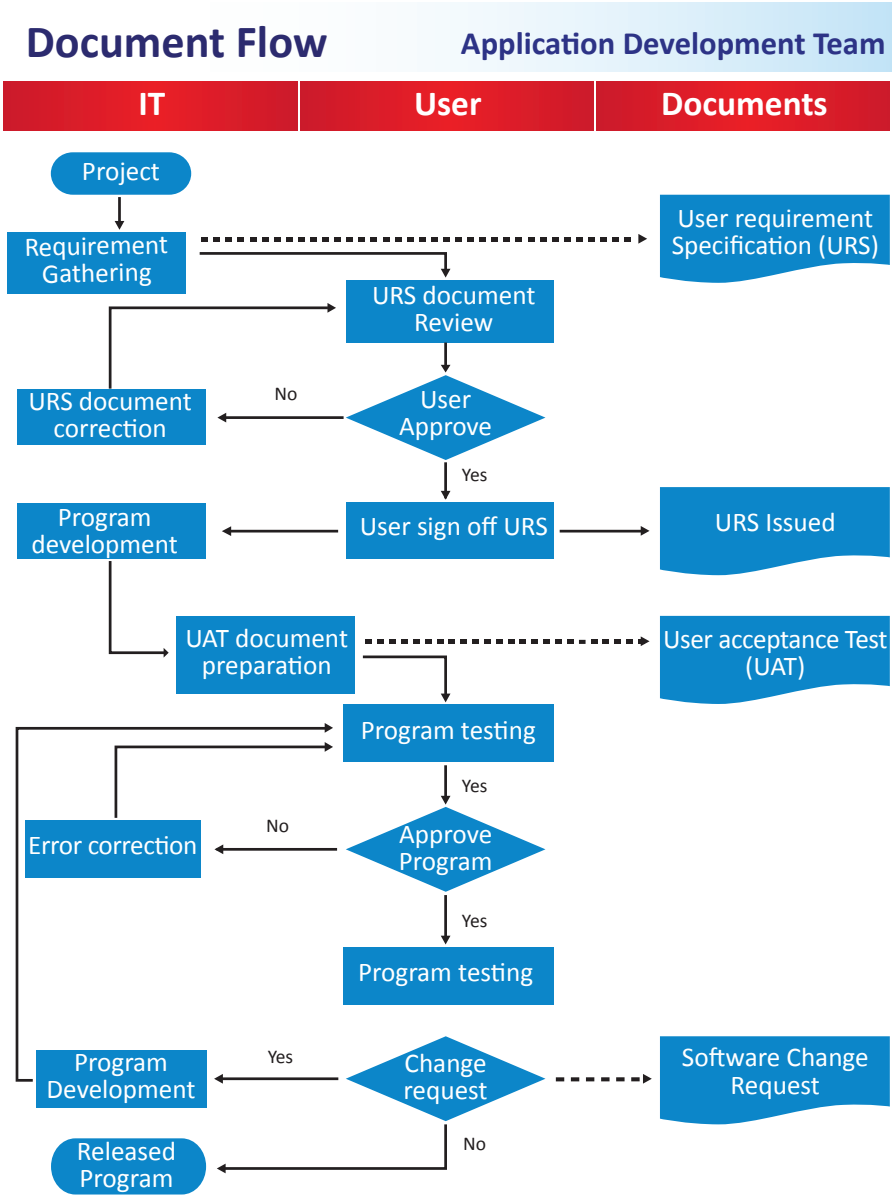

Figure 3: DM EMR designing process

One of the useful functions of EMR is automated alerts to improve the quality, safety, and consistency of the care process. The clinical team demanded automatic **"Clinical alerts"**, recommended by American Diabetes Association (ADA) and JCI standard care, as follows:

Clinical Alert	Remark
- HbA1C Examination needed	every 6 months
- LDL Cholesterol (direct) Examination needed	every 1 year
- Microalbumin (Urine) Examination needed	every 1 year
- Eye Examination needed	every 1 year
- Influenza Vaccination	every 1 year
- Foot examination needed	Low risk : every 1 year Moderate risk: every 4-6 months High risk: every 1-4 weeks

Reminders are required to assist the physicians in enabling evidence-based therapeutic decision-makingas well as increasing pathway compliance.

Condition	Warning
- HbA1C ≥ 9%	- Intensive therapy; 2 or more groups of medication required
- LDL ≥ 100 mg/dl	- Statin required
- Microalbumin urine > 30 mg/gm/	- Angiotensin-converting-enzyme inhibitor(ACEI) and/or Angiotensin II receptor blockers(ARB) required (Twice repeatedly)

Design performance requirement

Acceptance Criteria:
- Able to search for all patients in HIS with all complete data
- Able to transport the complete data as scheduled from HIS
- Able to alert all clinical teams for necessary diagnostic and treatment interventions
- Able to record all data as identical as First Visit Form and Follow-Up Form

Performance Requirements:
- DM EMR transporting the information from HIS every 5 minutes
- Unlimited access for users
- Timely response
- Easy to use
- If HIS system is down, the DM EMR system can operate independently of the HIS.

Document Scanning

Originally, the medical record was scanned and saved as an image for viewing. For the DM EMR, after physicians complete the clinical record form, it is sent to the Doc Scan system and saved in the HIS as show in Figure 4.

However, physicians cannot submit the clinical record to Doc Scan unless an ICD 10, diagnosis and all requirement sections and clinical alerts are completed. Unlike the existing HIS, the DM EMR record can be retrieved and edited later, with the time stamp and the signature of the person who modifies the record added to the saved record.

Figure 4: Documents flow

Evaluation after implementation

1. The benefits of the DM EMR

- Provides complete and comprehensive information: The patient face sheet gathers all relevant information in one place, i.e. lab results, which makes it easier to consider all aspects of a patient's condition and this results in an improved quality of care. Also an ICD 10 coded diagnosis is included for comorbid diseases.

- DM EMR enhanced documentation: After implementation, compared with the original paper clinical record and the statistics in completeness of clinical documents for DM Type 2 pathway first increased and eventually reached 100%. We have no more problems with being unable to read a physician's handwriting in the out-patient department (OPD). A comparison example of the clinical records is shown in Figure 5 and 6.

- Improving patient education and satisfaction: Most patients reacted positively to the DM EMR; it enables access to graphing and trending features. The patients were satisfied with a more responsive exchange of information with their physicians.

2. DM EMR Glitches

1. Technical problems

- The physicians have to work on two screens, requiring two sign-ons and additional effort.
- Data exchange problems: synchronization of data between two systems, the HIS and DM EMR is challenging and occasional glitches have resulted in laboratory missing values. Occasionally a laboratory value is missing in DM EMR.

2. IT technicians and Learning curve

- Over the period of the two years of the project, the high rate of IT staff turnover was a problem. It caused a lack of continuity in developing the software program and prolonged the development process. Hiring outsourced IT staff was a challenge.

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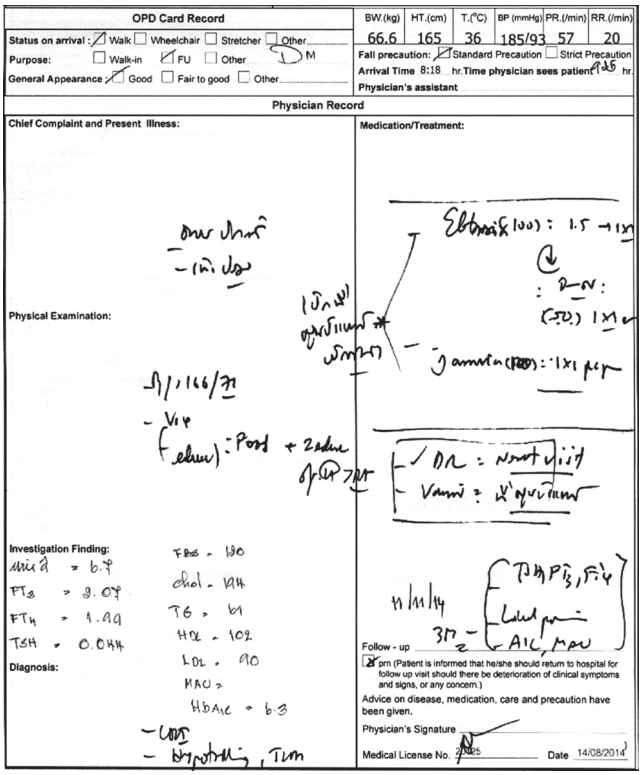

OPD Card Record

BW.(kg)	HT.(cm)	T.(°C)	BP (mmHg)	PR.(/min)	RR.(/min)
66.6	165	36	185/93	57	20

Status on arrival : ☑ Walk ☐ Wheelchair ☐ Stretcher ☐ Other
Purpose: ☐ Walk-in ☑ FU ☐ Other
General Appearance ☑ Good ☐ Fair to good ☐ Other
Fall precaution: ☑ Standard Precaution ☐ Strict Precaution
Arrival Time 8:18 hr. Time physician sees patient 9:45 hr.
Physician's assistant

Physician Record

Chief Complaint and Present Illness:

Medication/Treatment:

Physical Examination:

Investigation Finding:
Diagnosis:

Follow - up
☑ prn (Patient is informed that he/she should return to hospital for follow up visit should there be deterioration of clinical symptoms and signs, or any concern.)
Advice on disease, medication, care and precaution have been given.
Physician's Signature
Medical License No. 25 Date 14/08/2014

Figure 5: Original OPD Clinical Record

DM type2 pathway Follow Up Form

Page: [A 2]

Medication/Treatment:

1 . Actos 15 Mg Tab //	1 เม็ด	TAKE Once daily ac breakfast	60
2 . Zocor (10 Mg) Tablet	1 เม็ด	TAKE Once Daily pc dinner	60
3 . Januvia (100 mg) Tablet@	1 เม็ด	TAKE Once Daily pc breakfast	60
4 . Humalog MIX 25 Cartridge(300 Unit/3 mL)// ><	52 Amp	SC Once daily ac breakfast	3300
Note: 45 to be 52			
5 . Diamicron MR (60 mg) Tab.><//	1 เม็ด	TAKE Once daily ac breakfast	60
6 . Glucophage XR TABLET(1000 mg) @	1 tablet	TAKE Once Daily pc dinner	60

Management

Meet diabetic educator ,Meet pharmacist ,Meet dietitian , วัดความดันเอง

ให้เพิ่มยา คุมอาหาร

Clinical Alert

ตรวจตาล่าสุด (Last Ophthalmologist Examination)	เมื่อวันที่ (Date) : 13/08/2557	ผล (Result)	No DR	สถานที่ตรวจ (Place) :	BMC
ตรวจเท้าล่าสุด (Last Foot Examination)	เมื่อวันที่ (Date) : 13/08/2557	ผล (Result)	None	สถานที่ตรวจ (Place) :	BMC
การฉีดวัคซีนไข้หวัดใหญ่ล่าสุด (Last Vaccination)	เมื่อวันที่ (Date) : 13/11/2556	ชื่อยา(Name)	Vaxigrip	สถานที่ตรวจ (Place) :	BMC
Monofilament ล่าสุด (Last Monofilament)	เมื่อวันที่ (Date) : 11/06/2557	ผล (Result)	Normal	สถานที่ตรวจ (Place) :	BMC
HbA1C ล่าสุด (Last HbA1C)	เมื่อวันที่ (Date) : 13/08/2557	ผล (Result)	7.8 %	สถานที่ตรวจ (Place) :	BMC
LDL ล่าสุด (Last LDL)	เมื่อวันที่ (Date) : 13/08/2557	ผล (Result)	90 mg/dL	สถานที่ตรวจ (Place) :	BMC
MAU ล่าสุด (Last MAU)	เมื่อวันที่ (Date) : 02/10/2556	ผล (Result)	66.34 mg/gm.	สถานที่ตรวจ (Place) :	BMC

Plan

plan HBA1C cr eye

Follow-up : 08/10/2014 (2 Months)

☑ prn (Patient is informed that he/she should return to hospital for follow up visit should there be deteriodation of clinical symtoms and signs, or any concern).

Lab for next visit :

Creatinine,FBS,HbA1C,TSH

Figure 6: DM EMR OPD Clinical Record

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3. Time consuming

- Entering structured data is more time-consuming than charting free-text on the paper. Moreover, it requires physicians to map concepts into the new clinical record templates. Eventually, efficiency improved, but the process still took longer than writing in the original clinical record paper. It is yet another task to encourage the physicians to use EMR in their practice. The main strategy for overcoming this problem involves separating the EMR use from time spent communicating with patients. Modifying the software for easy data access and viewing, fewer clicks, and providing more check boxes would help reduce the time spent. Computer mastery and enhanced physicians' communication skills also helps.[4]

Lessons Learned

1. Project management team: The project should begin with forming a high-level implementation team plus key staff members throughout the unit, and assigning them to committees and design teams. The role and responsibility of each member should be defined. A project manager should also be officially appointed.

2. Implementation strategy: Stream lining implementation processes was not done properly in implementing the DM EMR. A project plan should address everything with project goals, committee role, timeframe, design of the EMR, workflow, staff training and post implementation support and evaluation. Also a more effective and productive communication between working teams is essential.

3. Software and design: Patient information in the DM EMR is easily accessible; however, the UI designed display menus formatting and lay outs are not yet fully realized. Some features require multiple clicks to access. The UI design and the system usability is a root cause of user dissatisfaction and needs careful consideration prior to re-implementing the entire system. The software design was supposed to sustain clinical workflows and work processes. Designing an easy-to-use EMR and providing convenience features such as spelling checks, dictation or tablet access can considerably simplify EMR use.

4. Clinical Process Analyst: The DM EMR development process should have been run smoother and faster, if we had had a clinical process analyst. This person is responsible for the coordination and performance of analysis, design, development, testing, validation and implementation of EMR. He or she works closely with the clinicians, physicians and ITS staff to ensure integration of technology into the patient care process. He or she provides ongoing support of the EMR system to the users from the beginning of design process to after implementation.

5. Top executive: The effective utilization of an electronic medical record will require a high investment.[5] Though we have always been fully supported and received commitment from CEOs, we require more communication. The strategic role of technology should be delivered from top down at the level of its administration to all working team members in order to run the project more smoothly. It is known that EMR is the heart of HIS and a substantial investment; however the return on value can be only be projected in the long-term. The advantages of building our own EMR were that we could address our requirements best with full control and flexibility.

Being the first hospital to use an EMR specifically for diabetes management in Thailand, and after more than two years of implementation, we achieved most of our goals. Besides, we have learned several lessons from the DM EMR development and implementation. The difficulties found after implementing the DM EMR were solved eventually by the dedicated working team. The Plan Do Check Act model has been used in helping reduce working times, and the program has been modified many times to resolve technical problems and respond to user requirements.

Finally the system is a success as a disease registry, and in providing data for research and quality improvement in the future. DM EMR is diabetes's oriented standard treatment; the physician can effectively deliver comprehensive and essential care to the patient. Recently, the JCI came for the re-certification of our hospital and they had very positive comments regarding our EMR project especially with regards to the safety part of patient care, and improvement in the legibility of records.

After we learned some hard lessons, our plans for a new DM EMR is make it more user-friendly, customizable, and for it to display information on one page to facilitate effective navigation, using fewer clicks. The provision of physician record templates would also help improving effectiveness.[3] A good sign is that most of our endocrinologists are now getting used to and are keen to use our DM EMR. We are now planning for phase 3, building IPD DM EMR as a tool for better diabetes care management in the Inpatient Department (IPD). This IPD EMR will extend the requirements of the OPD DM EMR, adding new features such as progress notes and Computerized Physician Order Entry (CPOE).

In the next phase of development, we would like more patient involvement, which we think will improve care and increase patient satisfaction[6]. Engaging our patients in the process is required to enable more interactive patient-centered care, allowing them for example to download their home monitoring glucose from home to the EMR for physician review. Other benefits include sharing tele-education with patients and their families. We also want to improve nursing satisfaction with the EMR as a tool for patient education. Beyond that, our patients can get their own summary reports every visit with their medications, blood sugars, weight loss and HbA1c's goals.

The leadership role as a project manager is to promote and to encourage the use of the EMR as a standard tool in hospital for better care for our patients. First, to create

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sufficient urgency, we are due for a recertifying survey of CCPC from the JCI at the end of this year. Also, we are seeking and applying for a new extension certification of the Inpatient Diabetes care for the next JCI's survey. This is an opportunity to lead and orchestrate the development process of both function and workflow for the EMR on the IPD service. To this extent, a clear vision will be passed to all working team members emphasizing that the EMR helps to prevent illegible handwriting of notes and orders. Also, in order to leverage the lessons learned from the current DM EMR to the 3rd phrase of the EMR, the IPD EMR will be re-engineered. A more powerful coalition will be extended to others such as IPD head nurses, critical care physicians and surgeons to demonstrate the good benefits of the EMR.

In the near future, a health information exchange project called B-Exchange will transfer clinical information between hospitals in Bangkok Dusit Medical Services Network. We hope that DM EMR can be implemented in other hospitals in the network, providing continuity of care and via B-Exchange. We are not declaring victory too soon, but we are ready for the challenges to come.

Acknowledgments

I would like to give a special thanks to Dr. Mike McCoy, BMC chief medical information officer, for being a supportive consultant for the DM EMR project and for his thoughtful reading of this article and critical comments. Thanks to IT Information Management Committee (IM) for supporting the project. Lastly, I also would like to thank the IT technical team of BMC and all the staff at the Diabetes, Thyroid and Endocrine Center for their devoted work.

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Contrast Enhanced Spectral Mammography (CESM) Indications

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Keywords: Contrast Enhanced Spectral Mammography, CESM, breast cancer

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Contrast enhanced spectral mammography (CESM), is a dual energy contrast enhanced digital subtraction mammography. This technique uses the same principle as MRI of the breast, but CESM uses digital mammography instead of magnetic resonance in MRI. It provides dual energy acquisitions through low and high energies in different filters. The subtraction is obtained by emitting a different energy after a complete non-ionic contrast media injection after 2 minutes with breast compression and preprogrammed software without motion artifact. The benefits include better resolution, and ability to evaluate microcalcifications, it is more cost-effective, easier to administer with a shorter time of examination.[1]

The proposed indications for CESM are as follows:

1. Inconclusive for presence of breast cancer by other modalities
2. Detection and evaluation of breast cancer
3. Screening patients with high risk symptoms
4. Histologically proved metastatic breast cancer with unknown primary origin
5. Evaluation of tumor post treatment
6. Detection of cancer recurrence after treatment including post-operative tissue reconstruction
7. Differential between scar tissue and local recurrent cancer after breast conserving therapy

I. Inconclusive for presence of breast cancer by other modalities

These situations predominantly include asymmetries, architectural distortions, numerous medium and/or large sized BIRADS 3 lesions and equivocal changes in the appearance of prior surgical or biopsy sites. Contrast enhanced magnetic resonance imaging (CE-MRI) is highly sensitive, but the specificity and negative predictive value are not sufficiently high to preclude biopsy when there are suspicious imaging findings, 67.4% and 85.4%, respectively by Bluemke et al.[2] However, in a recent study of 115 patients by Moy Let al,[3] the magnetic resonance image (MRI) was performed to evaluate equivocal mammographic findings, following a full diagnostic workup. The study found 100% sensitivity and 92% specificity of MRI. Presumably CESM should have more or less the same results.

Breast MRI, when combined with mammography and a clinical breast exam, has been shown to provide sensitivity of 99% for the preoperative assessment of the local extent of disease in patients with newly diagnosed breast cancer.[4] This is compared with sensitivities of 50% for clinical breast exam, 60% for mammography and 83% for ultrasound alone. Breast MRI can detect any additional unsuspected malignancy with in the ipsilateral breast, in 10% to 27% of patients.[5-8] When correlated with pathologic specimens,

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tumour size is more accurate with MRI than mammography.[9,10] Lehman et al. identified otherwise occult tumors in the contralateral breast in 6% of patients with newly diagnosed invasive lobular carcinoma and 3% in patients with invasive ductal carcinoma.[11]

We found the same findings in CESM, but the data collected in our study is not sufficient to show good statistics. According to our observations, microcalcifications are seen in CESM as normally seen white spots in low energy digital mammography and dark spots in high energy CESM. The CE-MRI cannot show these microcalcifications, which may be the only finding in ductal carcinoma in situ (DCIS). MRI requires an additional mammography to detect microcalcifications, but in one CESM examination, the low energy digital mammography is already provided. We demonstrate 3 different patterns of ultrasound (US) findings where the CESM of each finding is not the same: this is very beneficial in obtaining a more accurate diagnosis.

1. Examples of three patients whose ultrasound (US) shows microlobulate or irregular shaped cystic mass, with internal solid component, the CESM reveals three different findings, indicating different pathologies. The images and final pathological results are presented as follows:

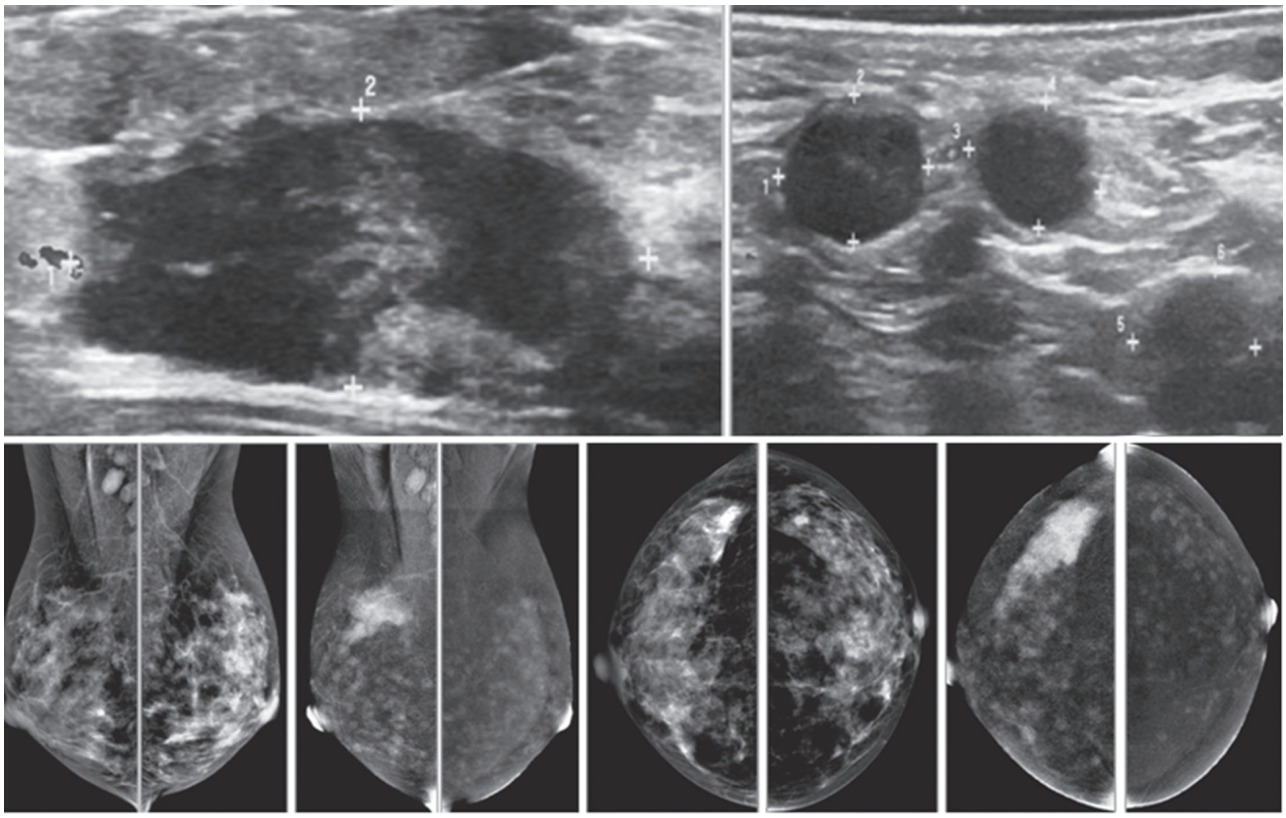

Figure 1A: Female 48-years of age, ultrasound (US) shows a microlobulate, irregular shaped cystic mass, with internal solid component. Multiple enlarged axillaries denote a denopathy with round shape, almost echo-free, no fatty hila are seen. Mammography shows focal density in craniocaudal (CC) view, not well defined in mediolateral oblique (MLO) view. CESM shows intense enhancement of that complex lesion, with its size much increased. Numerous enhanced small foci are noted in both breasts. US guided core needle biopsy (CNB) reveals invasive ductal carcinomas and these are confirmed in surgery.

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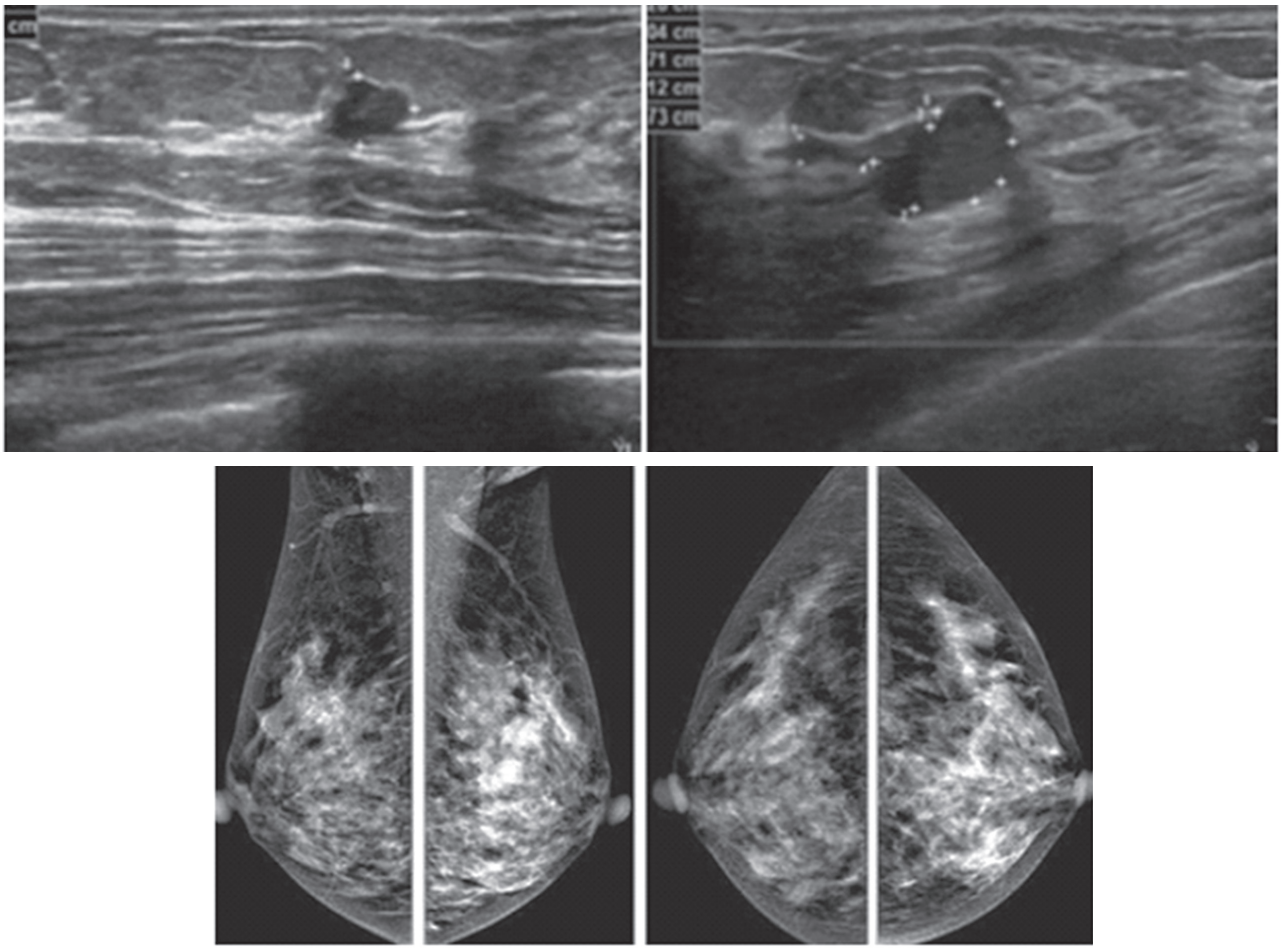

Figure 1B: Female 42-years of age, US shows a relatively large homogeneoushypoechoic solid mass in a cystic lesion with relationship to ducts, measuring 5.2×7.2mm in right upper outer quadrant (UOQ) and 7.3×11.2mm in left UOQ. Mammography shows a density suspected in left MLO at a second look. CESM reveals a moderate degree of uptake of contrast medium in left UOQ, measuring 11.6×11.9mm and an ill-defined focal minimal abnormal uptake in the right breast. CNB reveals fibrocystic changes of both lesions.

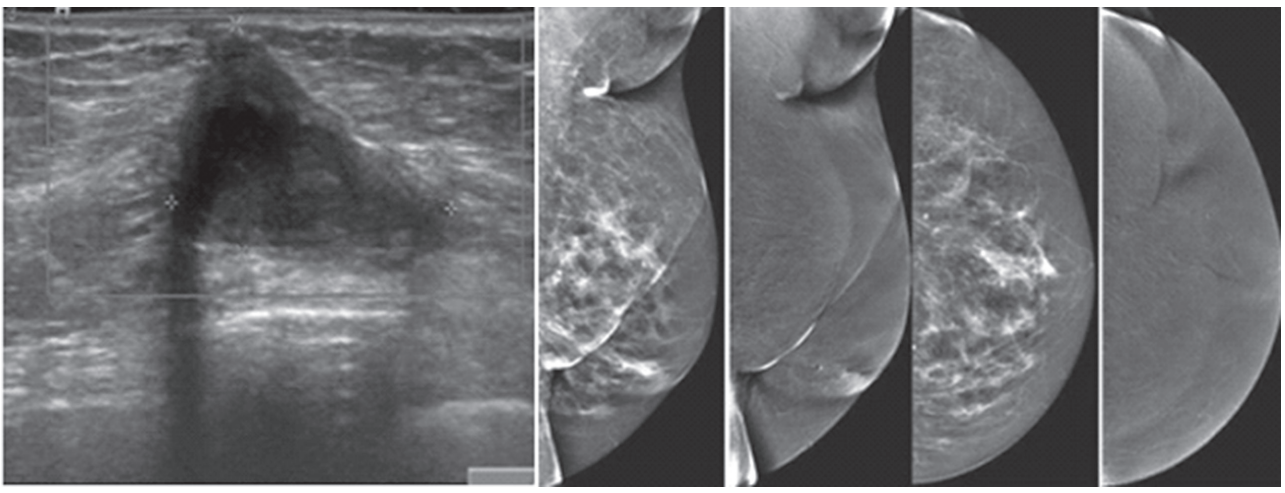

Figure 1C: Female 64-years of age, post op left breast conserving therapy (BCT). Mammography shows architectural distortion at surgical scar in left lower outer quadrant (LOQ). US reveal an enlarging cystic lesion with hypoechoic modularity on its wall and some echoic contents. CESM shows no enhancement of either breast. US guided aspiration yields old hemorrhagic fluid. At surgery, there are no residual malignant cells.

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2. Examples of three patients whose US shows heterogeneous hypoechoic solid masses with increased vascularity inside the lesions, the CESM reveals three different findings, indicating different pathologies. The images and final pathological results are presented as follows:

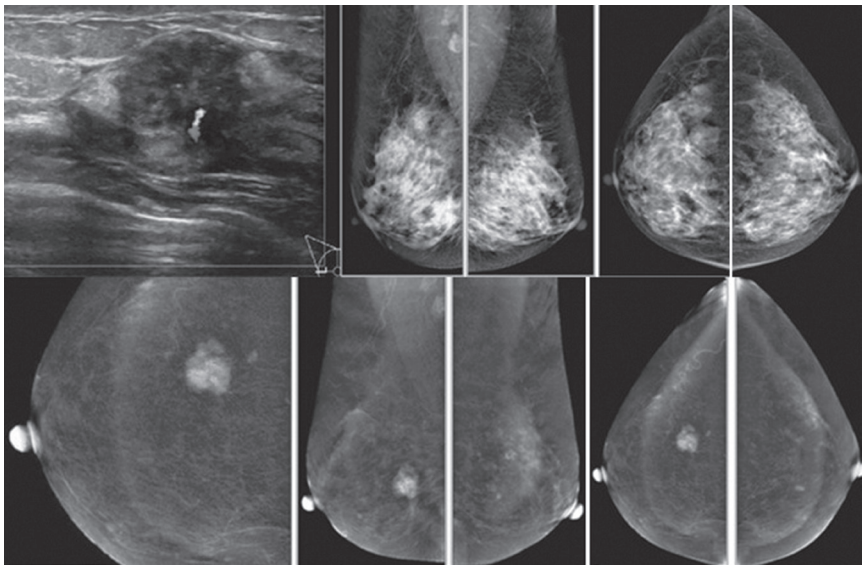

Figure 1D: Female 60-years of age, US shows a well-defined lobulated, minimally heterogeneous hypo-echogenic mass with increased vascularity in right LOQ of 2×1.2×2cm. Mammography shows coarse pleomorphic microcalcifications in the areas of the obscured masses. Axillary nodes are seen in the right MLO. CESM reveals an intensely heterogeneous and enhanced microlobulated mass in right LOQ, measuring 18×22mm, with multiple dark spots of non-enhanced microcalcifications inside the lesion. Multiple foci of mild and moderate enhancement are seen. Soft enhanced right axillary nodes are noted. CNB and surgical pathology reveal invasive ductal carcinoma.

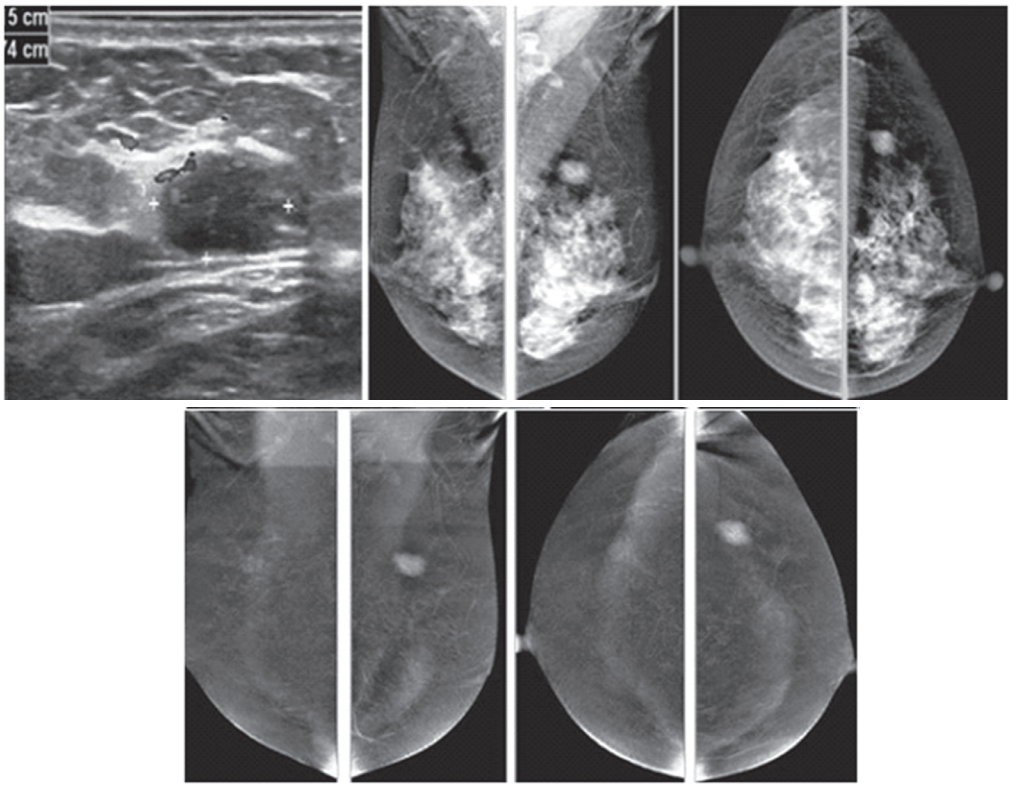

Figure 1E: Female 46-years of age, US shows a well-defined lobulated, minimally heterogeneous hypo-echogenic mass with increased vascularity in the left UOQ. Mammography shows a lobulated isodensity mass. CESM reveals a markedly homogenous enhanced lobulated mass. The outline is smooth and no spiculation is noted. CNB reveals a fibroadenoma.

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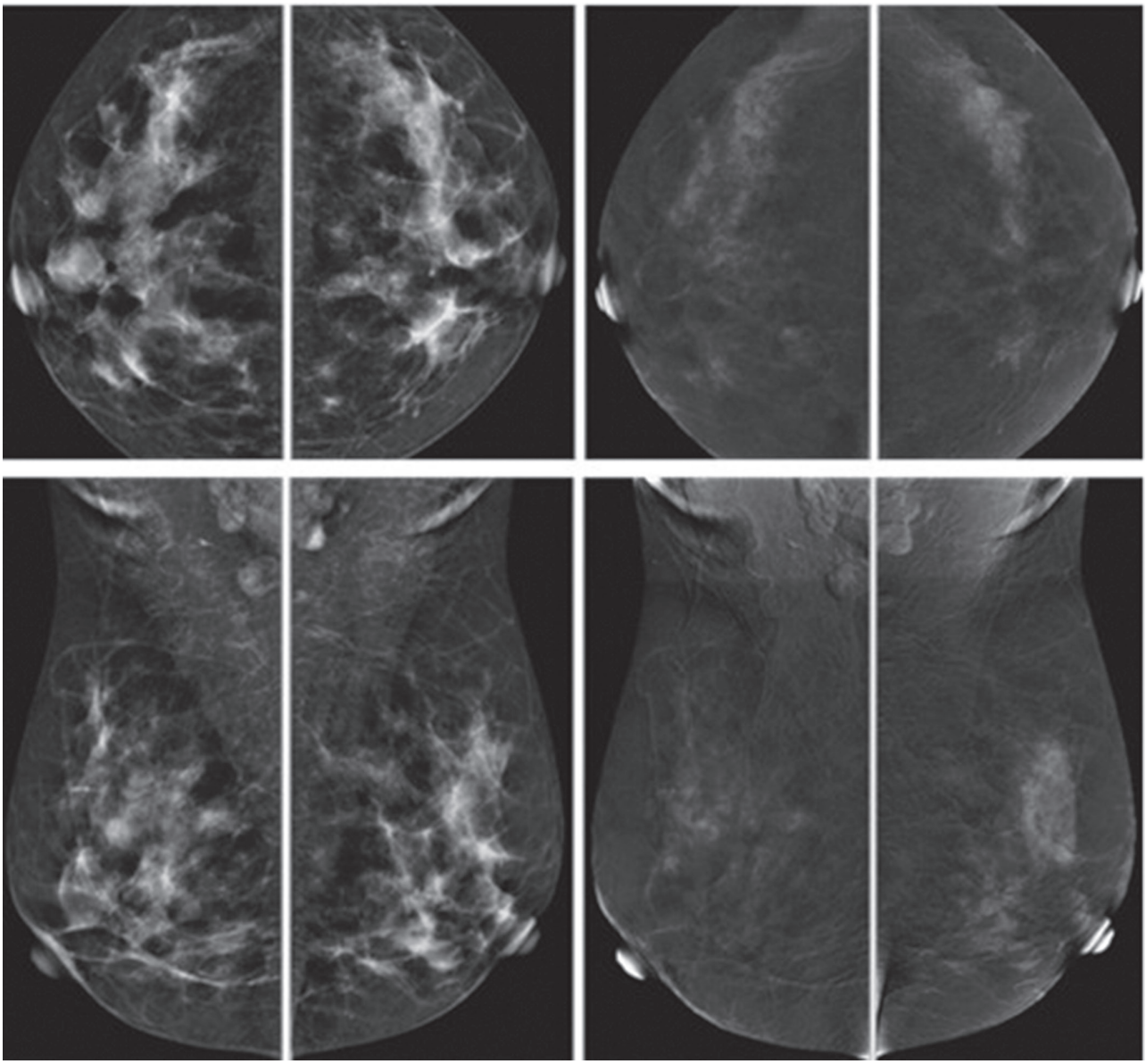

Figure 1F: Female 42-years of age, US shows a well-defined round to oval shaped, minimally heterogeneous hypo-echogenic mass with increased vascularity in the right subareolar area. Mammography shows a round isodense mass in the right SA in CC, partially obscured in MLO. CESM reveals no enhancement of this subareolar lesion a benign finding. CNB reveals fibrocystic changes.

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3. Examples of 2 patients whose US show slow hypoechoic lesions, increased depth to width ratio, acoustic shadowing and extensive spiculation. The CESM reveals two different findings, indicating different pathologies. The images and final pathological results are presented as follows:

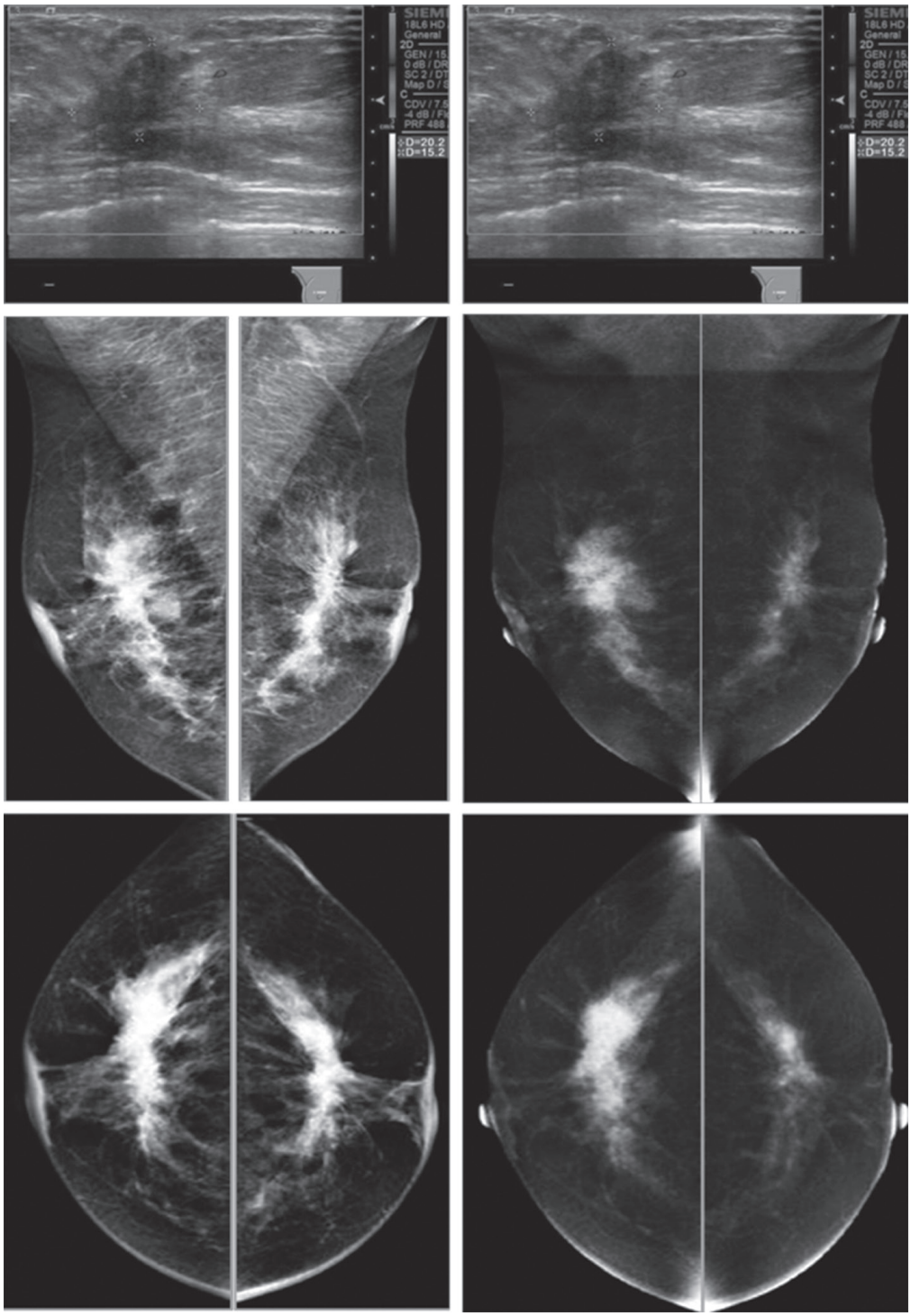

Figure 1G: Female 52-years of age, US of both SA areas show the same findings of a very low hypoechoic lesion with its depth more than width. Acoustic shadowing and extensive spiculation are seen. This may be seen in malignancy and benign lesions such as radial scar or sclerosingadenosis. However the former lesion is enhanced, while the 2 latter lesions show no significant enhancement. Mammography shows extensive breast asymmetry, irregular shaped lesion with extensive spiculation. CESM reveals very high uptake of contrast medium in almost the whole fibroglandular tissue in both breasts, with long spiculations to nipple and skin on a deep to posterior aspects, compatible with extensive involvement of malignancy. CNB reveals bilateral extensively invasive ductal carcinoma, grade II.

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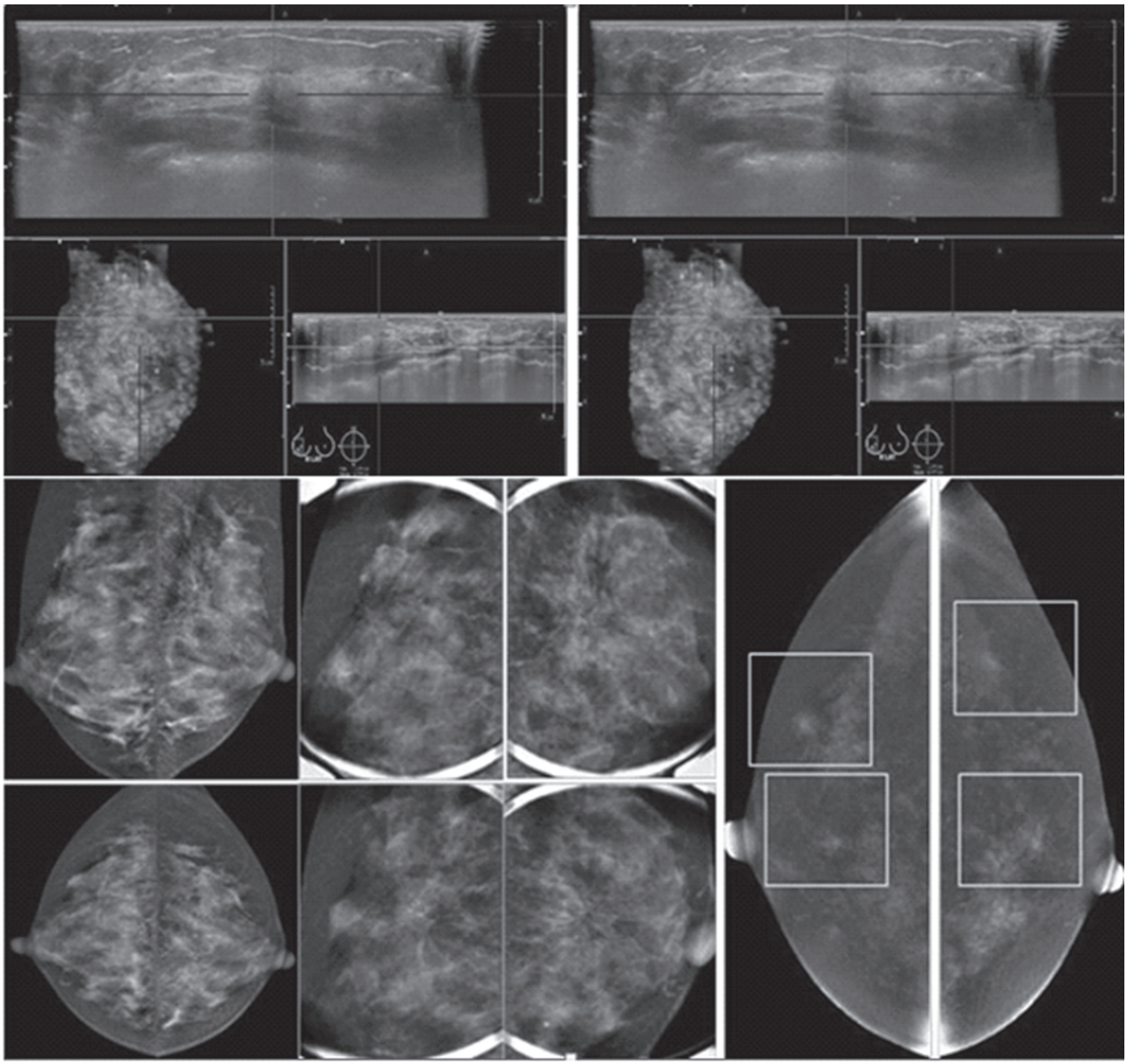

Figure 1H: Female 34-years of age, the automated breast volume scanner (ABVS) shows 2 poorly defined focal hypoechoic areas in left UIQ and right upper, associated with disruption of parenchyma and a lobulated hypoechoic mass in right UOQ: 7×9.9×12.6mm Mammography reveals architectural distortion in both areas, seen with no mass in a six category classification (SCC). CESM reveals multiple focal enhanced nodules of varying degrees, scattered in both breasts. Pathological study reveals a fibroadenoma with sclerosingadenosis.

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II. Detection and evaluation of breast cancer

In the detection and evaluation of the extent of breast cancer, apart from an evaluation of the extent of the cancer as mentioned earlier, DCE-MRI can identify occult contralateral cancer in 3-5% of cases[12,13] MRI has been considered limited in the evaluation of DCIS. However, more recent studies found MRI superior to mammography in detecting unsuspected DCIS.[14,15] The mammographic sensitivity for detecting invasive lobular carcinoma is around 34% to 81%, which is inversely related to mammographic density. Conversely, the reported sensitivity of MRI for invasive lobular carcinoma is 93% to 96%.[4,16] Dillon et al. reported that positive surgical margins occurred in approximately 50% of patients with invasive lobular carcinoma who did not undergo preoperative MRI and 25% in invasive ductal carcinoma.[17] MRI evaluates tumor size more accurately than mammography and ultrasound.[4,18] Again, considering the same basic principles as CE-MRI, the examples of CESM in the detection and evaluation of the extent of breast cancer are as follows:

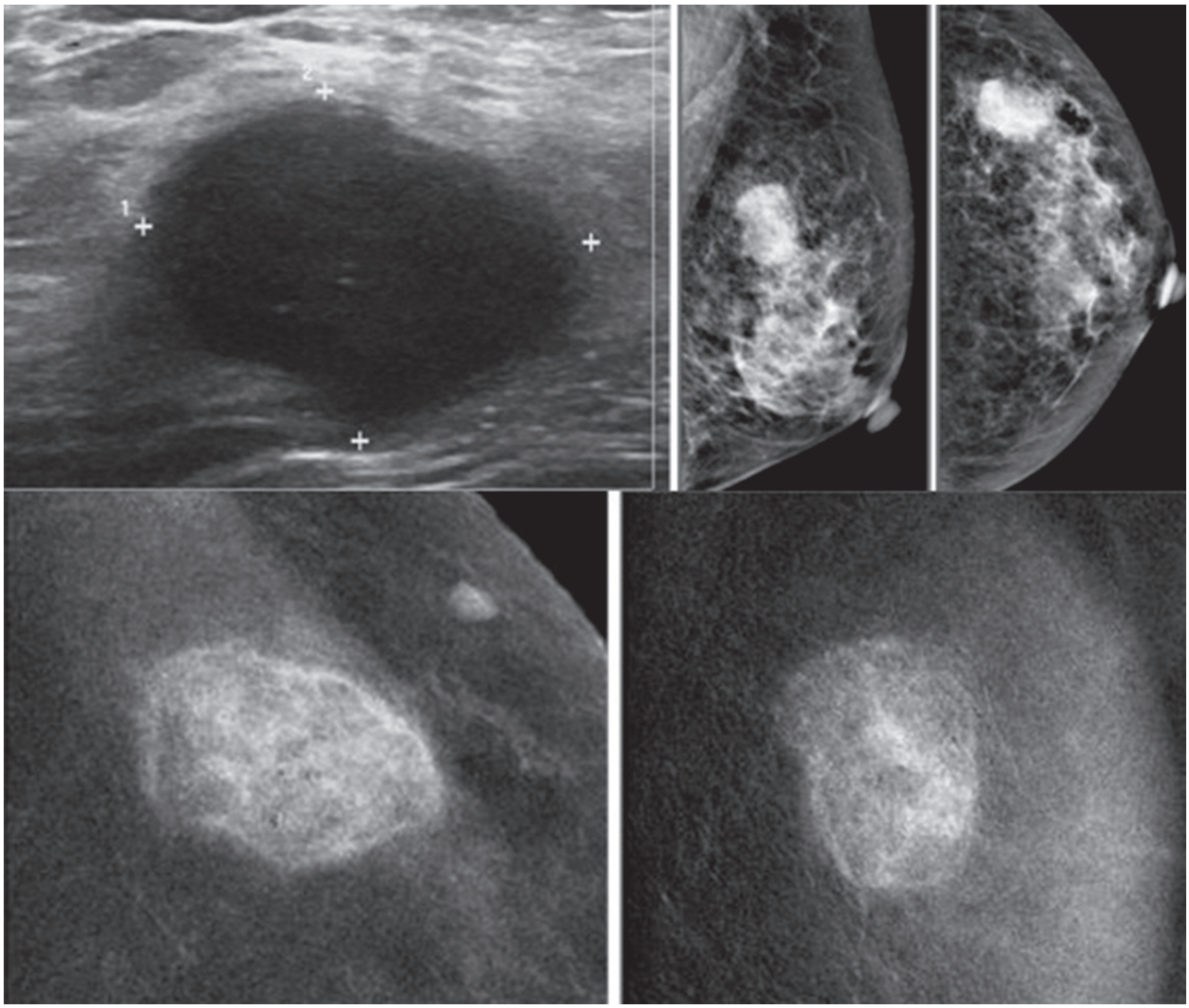

Figure 2A: Female 60-years of age, a mass is palpable in left UOQ Mammography shows a lobular shaped hyperdense mass and US shows an echo-free lobular mass with surrounding tissue reaction, combined type of posterior enhancement. CESM reveals an intensely heterogeneous enhancement of a microlobulate mass of 33×24×22mm in right UOQ, seen with multiple dark spots of non-enhanced microcalcifications inside the lesion, highly suggestive of malignancy. Another small markedly enhanced nodule is seen, which is not noticed initially by mammography and US. There is no abnormal enhancement of the entire right breast and axillary l.n. CESM defines the nature and existing of two cancers in the same breast.

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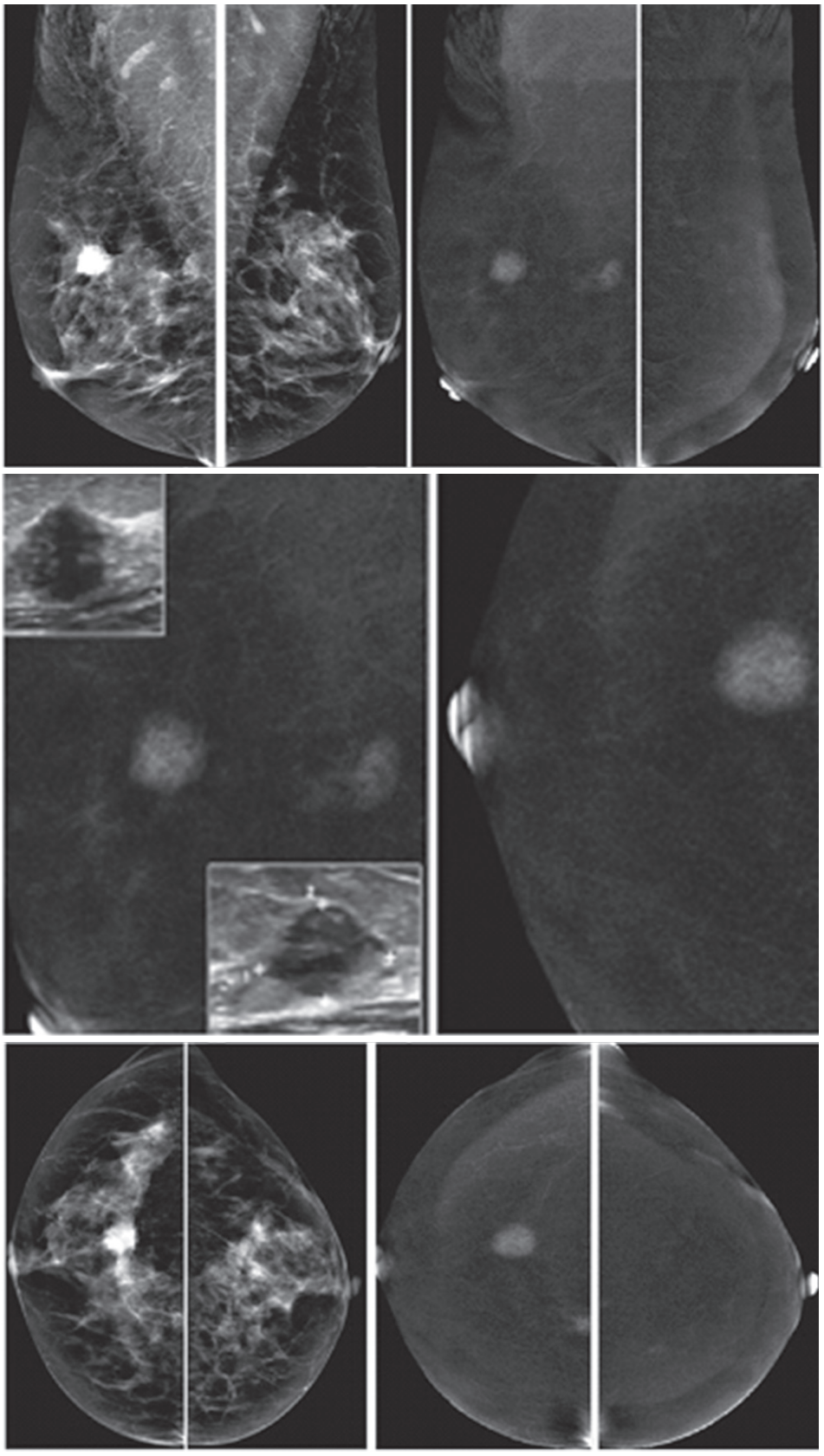

Figure 2B: Female 60-years of age, S/P left CBS, a round mass with microlobulation and spiculation is seen in right upper. Multiple equivocal nodes are seen in both axillae. CESM reveals aheterogeneous uptake of contrast medium in right upper of 16×17mm. An additional lesion is seen in right inner: 9×11mm. No abnormal uptake in left breast and axillary l.n. Second look US reveals two heterogeneous hypoechoic masses with microlobulated outlines. US guided CNB reveals invasive ductal carcinoma of both lesions. CESM detects the second primary multifocal cancers in contralateral breast.

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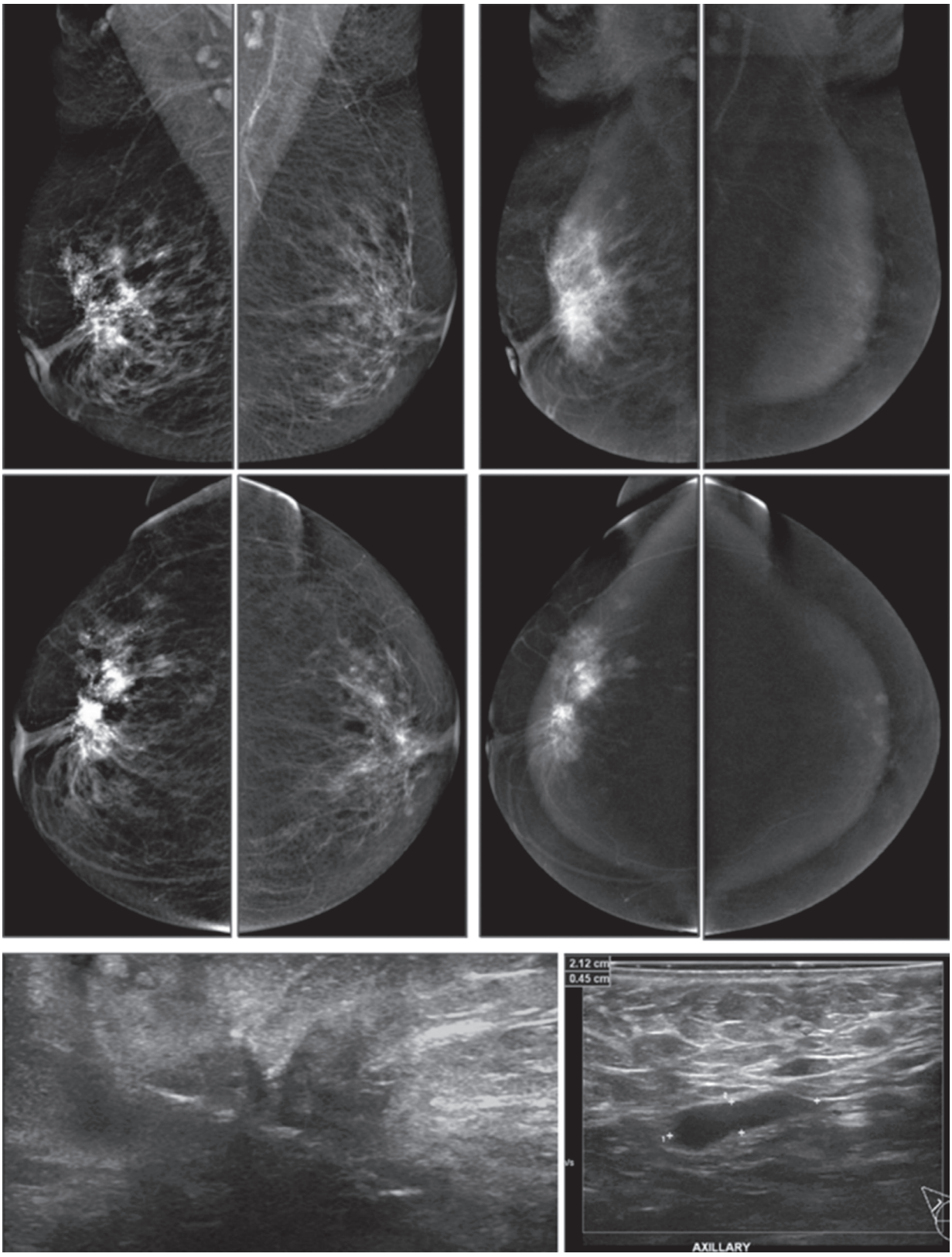

Figure 2C: Female 55-years of age, mammography shows a large irregular shaped focal asymmetry with spiculation in right breast. Ultrasound shows a large spiculated mass. The number of small axillary nodes has increased. CESM reveals an intensely heterogeneous enhancement of a large irregular-shaped mass with multiple dark spots of non-enhanced microcalcifications inside the lesion. Spiculations are seen around the lesion; extending anteriorly to skin and nipple and posteriorly to deep structures. Soft enhanced foci in both breasts and left axillary l.n. are noted, highly suggestive of malignancy. US guided CNB reveals invasive ductal carcinoma. CESM defines the nature, local extension and existence of this cancer, possible bilaterally.

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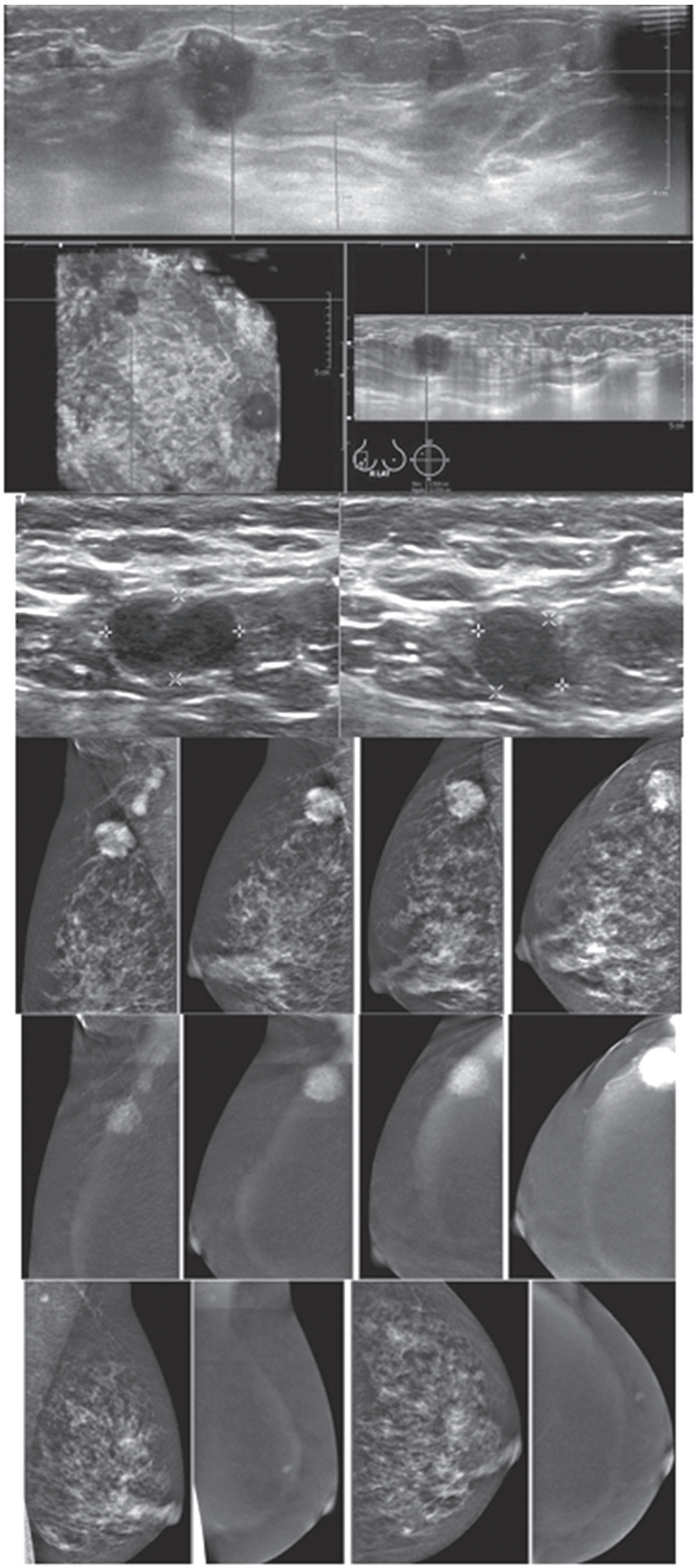

Figure 2D: Female 50-years of age, mammography and ABVS reveal a malignant appearing mass under 2 cm. in right UOQ, however, multiple enlarged adenopathy is noted. CESM shows the malignant nature of the mass as well as enhancement of multiple axillary adenopathy. Apart from that, another enhanced focus is seen in left breast. A tiny left axillary l.n. is minimally enhanced. Surgical pathology confirms invasive ductal carcinoma grade II with l.n. metastasis in 12 out of 18 removed nodes. CESM defines the nature of this small cancer, but with extensive adenopathy and possible additional small lesion in contralateral breast.

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III. Screening patients with high risk symptoms

When screening patients in high-risk groups, Breast MRI can detect small node-negative cancers in women at high risk for breast cancer and it is a useful screening tool when used as an adjunct to mammography in high-risk women. However, due to its limited specificity and high cost, MRI is not appropriate for screening the general population.[19,20] The American Cancer Society (ACS) has recommended annual screening breast MRI for very high-risk women, which includes:

- Women with breast cancer BRCA1 and BRCA2 gene mutations and their untested first-degree relatives
- Patients with prior chest radiation between the ages of 10 and 30
- Those with certain syndromes associated with propensity for breast cancer and other genetic mutations, including p53 and Cowden
- Patients with a lifetime risk for breast cancer of >20% to 25% as determined by risk models

For patients with these risk factors there is sufficient evidence to recommend annual CE-MRI in addition to annual mammography for screening for breast cancer. Insufficient evidence was found to recommend for, or against, screening MRI for women at intermediate risk, which included:

- Those with a lifetime risk for breast cancer of 15% to 20% definedby risk models
- Prior diagnosis of atypical ductal hyperplasia (ADH) or lobular carcinoma in situ
- Patients with dense breasts on mammography
- Patients with a personal history of breast cancer

The decision for screening these patients with CE-MRI should be made on a case-by-case basis. Screening with breast MRI is not recommended in women with <15% lifetime risk of breast cancer.

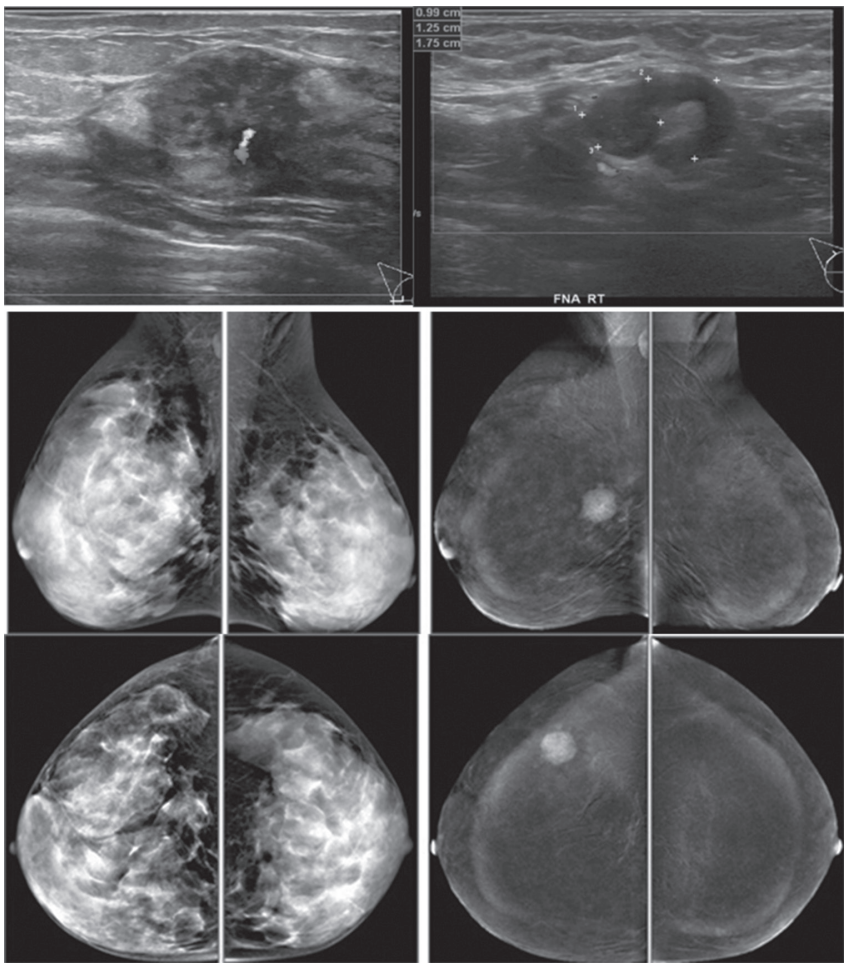

Figure 3: Female 45-years of age, screening in patient with family history of breast cancer. Mammography shows extremely dense breast, no lesion was detected initially. US reveals a round heterogeneously hypoechoic mass in right outer with abnormal vessel inside the lesion. A round axillary l.n. is seen with increased cortical thickness and focal bulging of the cortex, compatible with micrometastasis. CESM reveals an intensely, heterogenous enhanced round mass of 16x19x20.5mm., with partially seen enhanced axillary l.n. US guided CNB reveals invasive ductal carcinoma. CESM demonstrates a cancer with axillary adenopathy in a high risk patient, while the clinical examination and mammography is negative.

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IV. Histologically proved metastatic breast cancer with unknown primary origin

When examining the breasts of patients with histologically proved metastatic breast cancer with unknown primary origin, patients presenting with metastatic axillary adenocarcinoma with no evidence of breast cancer on physical exam or mammography represent less than 1% of all breast carcinoma cases. The identification of occult primary breast cancer by MRI is 62% to 86% of patients.[21,22] When the primary tumor found by MRI is less than 2 cm, the patient has a choice of breast conservation surgery as a treatment option with targeted hormonal and chemo-therapeutic treatments. However, identifying the primary breast tumor will not affect the prognosis when axillary node involvement is already present.

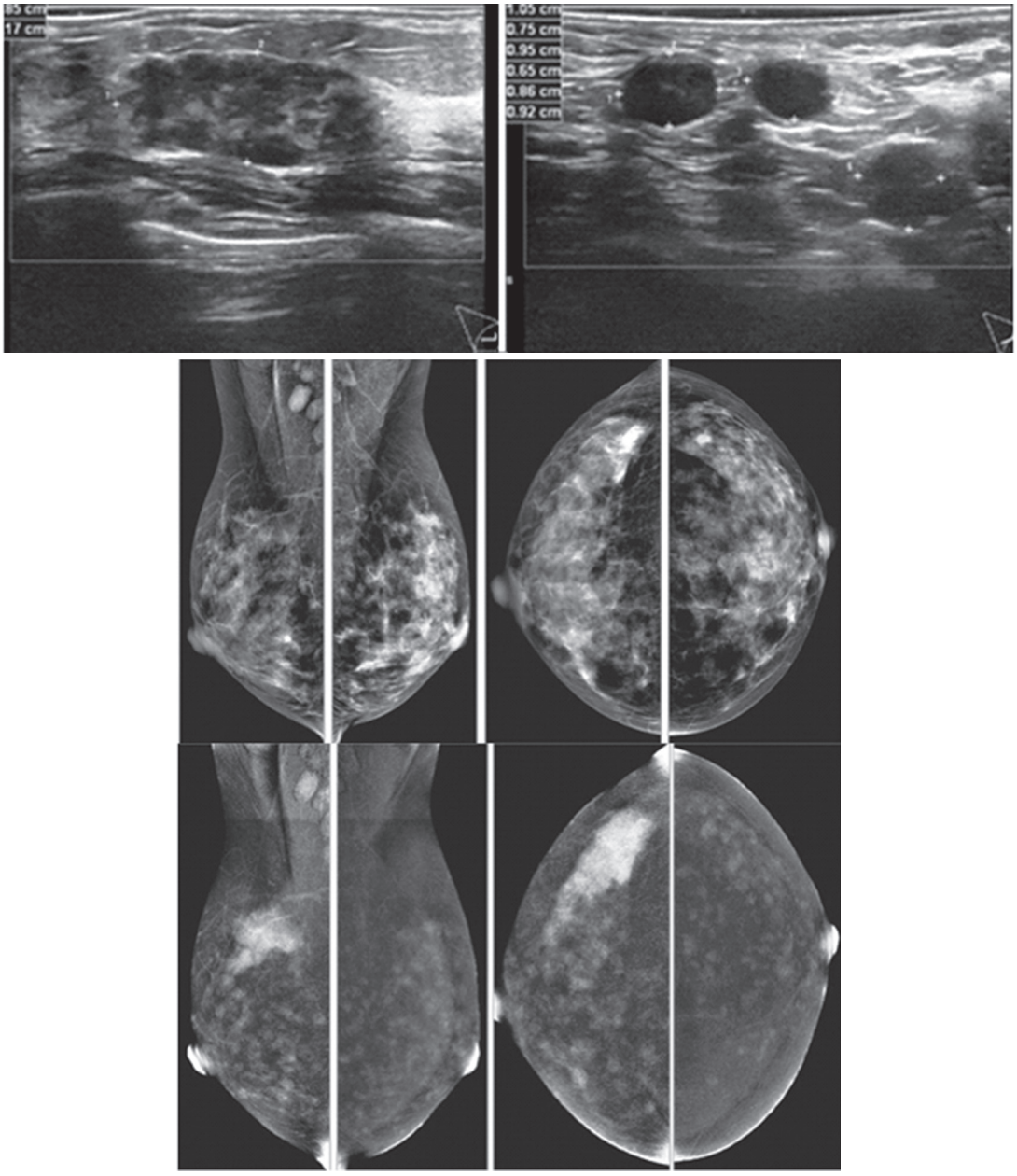

Figure 4: Female 48-years of age presents with palpable right axillary l.n. US confirms numerous axillary adenopathy and a well-defined mixed echoic mass in right UOQ. Mammography shows a focal density in right CC, obscured in the first look at right MLO. CESM reveals an intensely heterogenous enhancement of a large irregular shaped mass, seen with some dark spots of non-enhanced microcalcifications inside the lesion. Enormous moderately enhanced foci are seen in both breasts. The study was performed near the menstruation, thus repeat study should be performed to differentiate extensive bilateral cancer or physiological enhanced foci due to hormone effect. The partially seen enhanced right axillary nodes are extensive. CESM detects and confirms the unconvincing mammography abnormality, axillary adenopathy and possible extensive bilateral lesions or hormonal effect.

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V. Evaluation tumor post treatment

Residual disease post-lumpectomy, followed by radiation, is an acceptable choice in the treatment of stage I and II breast cancer and has been shown to provide the same survival rates as radical and modified radical mastectomies.[23] The rate of positive margins is around 40% of lumpectomies with increased chance of local recurrence. Breast MRI may reveal the presence of multifocal and multicentric disease as well as detect residual disease at the lumpectomy site, which is necessary information for judging whether re-excision or mastectomy is required. If microscopic residual disease at the surgical margins is present, surgical excision is still required, even though the MRI is negative. The sensitivity for detecting residual disease is around 61% to 86%.[24,25] Before 28 days after the operation, the granulation tissue may mimic residual tumour, causing false-positive study. Frei et al. stated that the false-positive results are decreased when MRI was performed between 35 to 42 days following surgery.[26]

In response to neoadjuvant chemotherapy, a breast MRI is helpful in demonstrating the tumor size, identifying residual tumor following the completion of neoadjuvant therapy. The accurate correlation with pathologic specimens is 71% to 90% for CE-MRI, 19% to 60% for clinical exam, 35% to 75% for ultrasound and 26% to 70% for mammography.[27-30] The MRI, however, tends to overestimate the size of residual disease because of the antiangiogenic effects of certain chemotherapeutic agents on the tumor, therefore the ability of DCE-MRI to evaluate lesion enhancement can be significantly lower. As was mentioned prior in the positive tumour margin, even though no residual disease is seen by MRI, surgical resection is still required due to the potential under-estimation of residual disease. So it is necessary to place a marker at the tumour site prior to treatment.

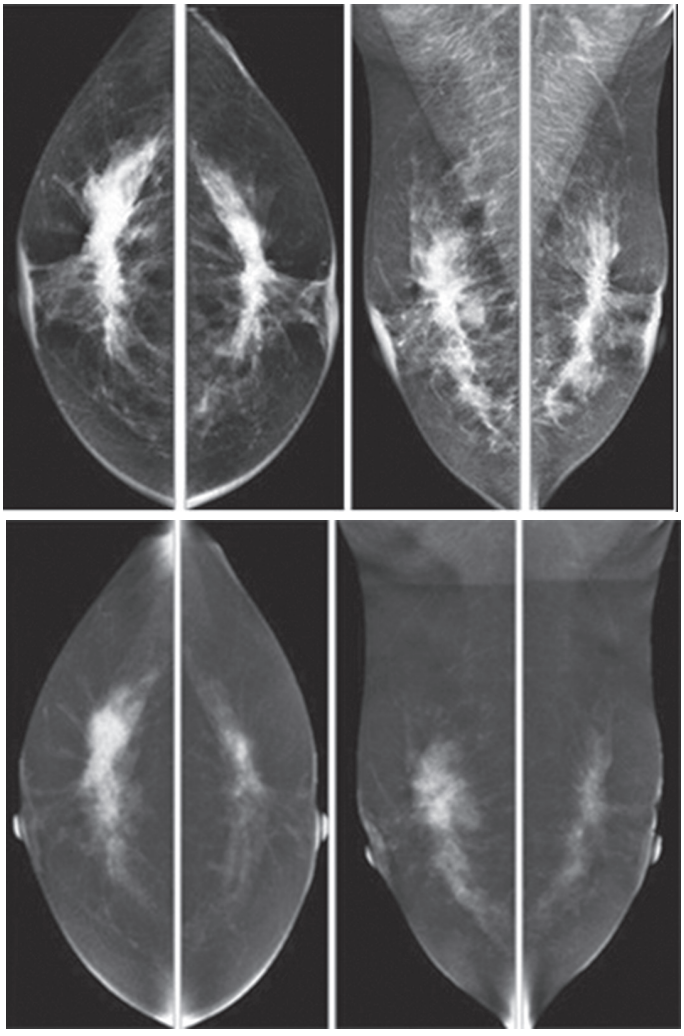

Figure 5: Female 52-years of age, CESM reveals very high uptake of contrast medium in almost the whole fibroglandular tissue in both breasts, with long spiculation to nipple, skin and deep to posterior aspects. CNB reveals bilateral extensive invasive ductal carcinoma; grade II, not suitable for surgery. Chemotherapy was given and CESM will be performed to evaluate the results of the treatment.

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VI. Detection of cancer recurrence after treatment including post-operative tissue reconstruction.

For the detection of cancer recurrence after treatment, including postoperative tissue reconstruction, in patients who have undergone mastectomy with a transverse rectus abdominismyocutaneous flap (TRAM), latissimusdorsi flap, or gluteal flap, the follow-up by mammography gives only limited information in detecting recurrence,[31] but it can be used as part of routine surveillance in patients with a history of breast cancer. CE-MRI is helpful in identifying local recurrent disease, especially at the chest wall[32] and differentiating the coincidental finding of benign lesion from cancer recurrence.

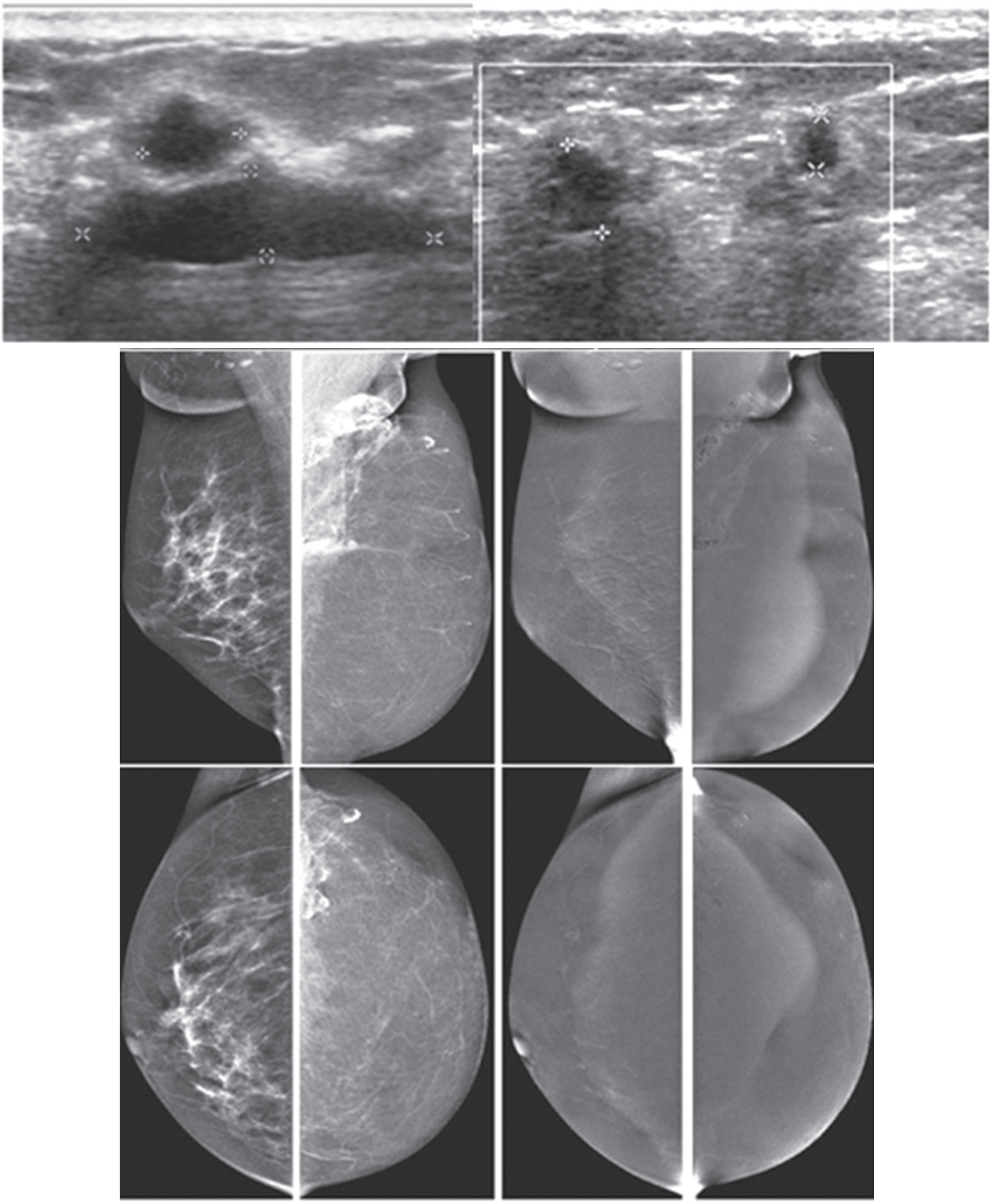

Figure 6A: Female 51-years of age, S/P left MRM with TRAM flap for left breast cancer. Mammography shows dystrophic calcified areas in far left UOQ US shows 9 lobulated echo-free lesions with wall thickening. There is no typical posterior enhancement that is usually seen in cystic lesions. CESM reveals no significant enhancement of both breasts, including at the dystrophic calcified area, compatible with oil cysts post TRAM flap, no evidence of recurrence. CESM post TRAM flap operation excludes local recurrent in multiple oil cysts with dystrophic calcifications.

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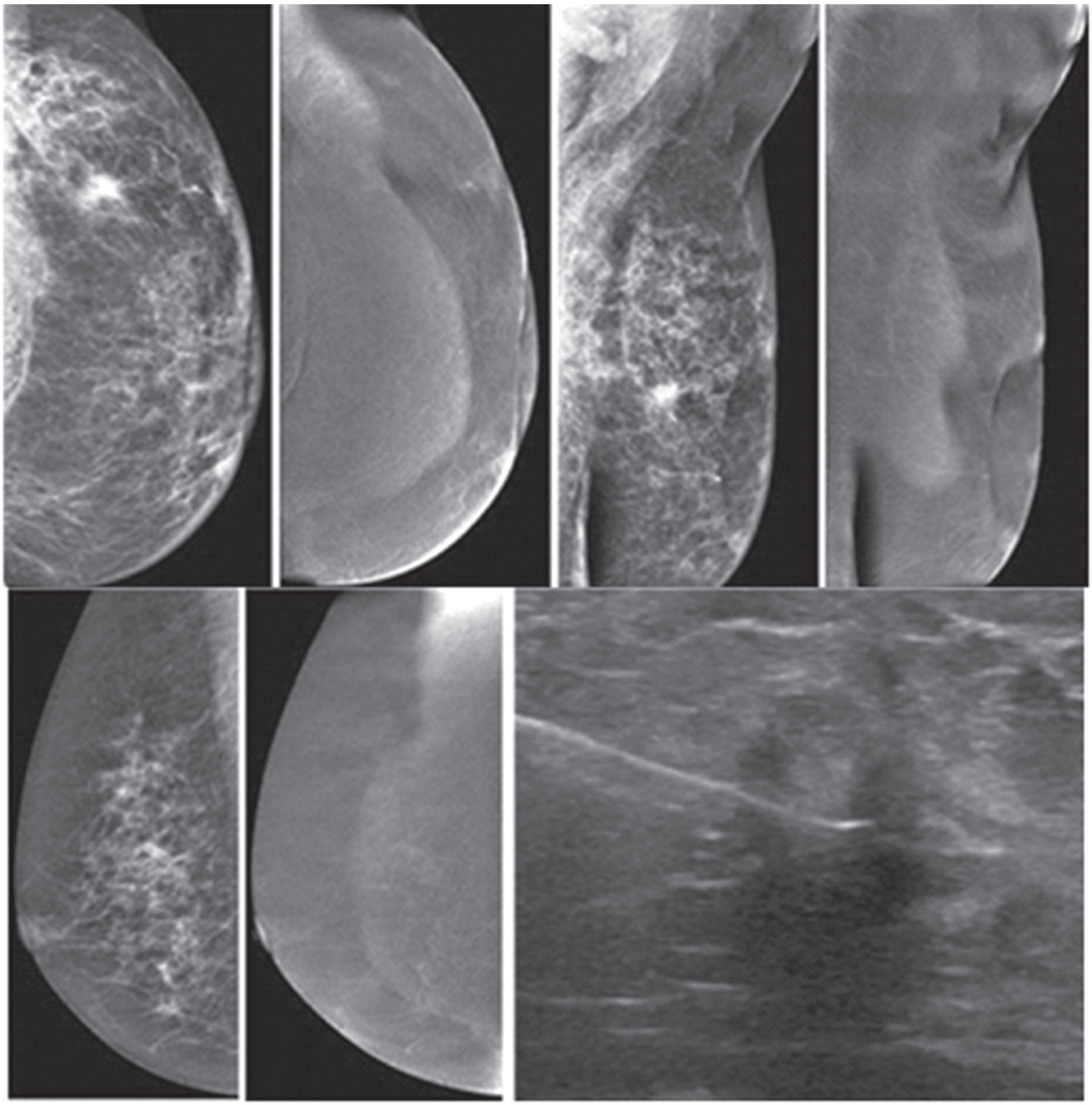

Figure 6B: Female 60-years of age, S/P left MRM with tram flap. Mammography shows a small spiculated mass in PO area, noted with other PO changes. CESM: No abnormal enhancement in both breasts, over all non- malignant lesions. U/S guided CNB of an irregular-shaped markedly hypoechoic mass reveals no residual cancer. CESM post TRAM flap operation excludes local recurrent in the PO spiculated mass.

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VII. Differential between scar tissue and local recurrent cancer after breast conserving therapy.

With the differentiation between scar tissue and local recurrent cancer after breast-conserving therapy, post-operative changes may mimic breast cancer recurrence at the lumpectomy site by conventional imaging. MRI is useful in differentiating recurrent disease from post-operative scarring; however it may enhance MRI for 1-2 years following surgery. A negative MRI may be helpful in excluding recurrent disease. This may be more difficult when the postoperative scar is still enhancing. In general, a scar tends to present as a thin rim or cloud of enhancement around the cavity, whereas a recurrent tumor tends to be more clumpy or mass-like.

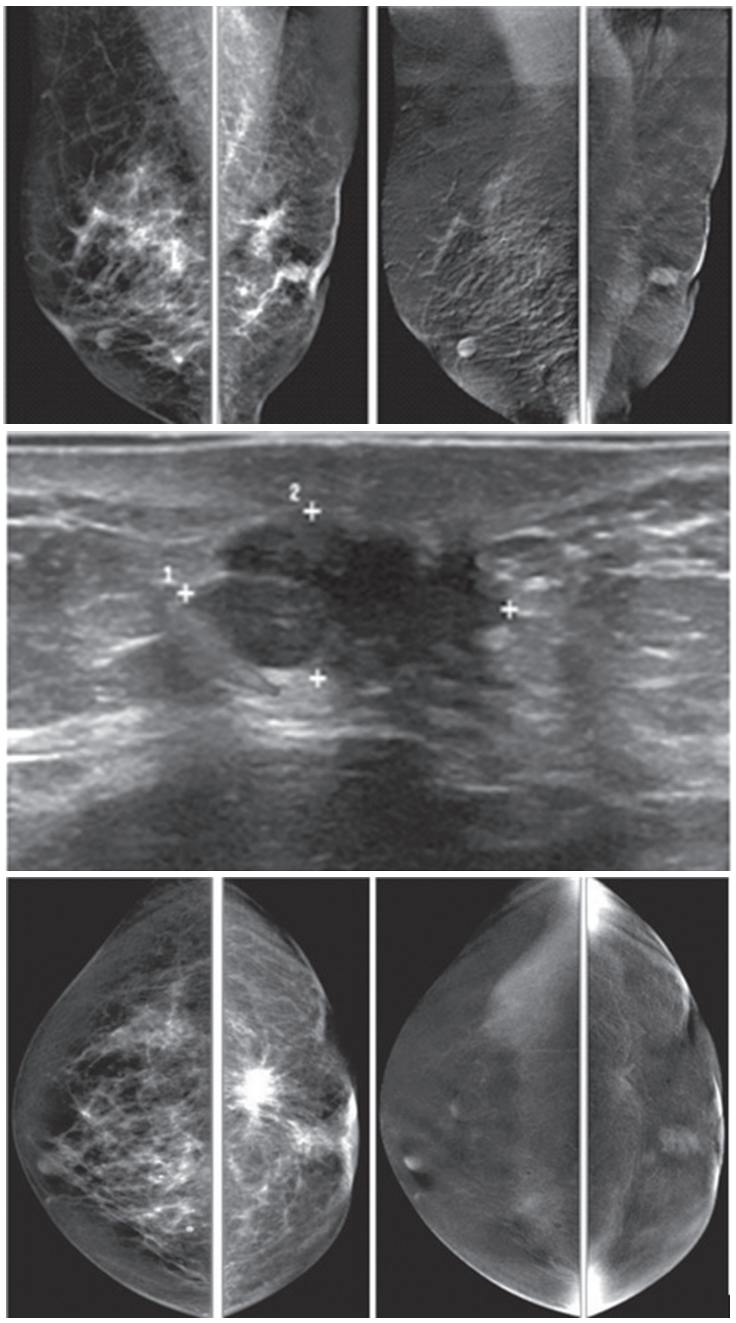

Figure 7A: Female 54-years of age, S/P lumpectomy in the left upper quadrant noted with palpable abnormality in PO area, not at the left subaredar SA. US shows an irregular mass-like lesion with spiculation in left central at post operation scar. A well-defined heterogeneous hypoechoic lobulated mass is noted in left SA: 8.1 x 16.2 mm CESM reveals the irregular mass-like lesion with spiculation in left central is not enhanced while the non-palpable nodule is densely enhanced in heterogeneous pattern. (The skin mole in right LOQ is seen with enhancement.) At surgery, the post-operative scar shows no malignancy, while the non-palpable SA mass is a recurrent invasive ductal carcinoma. CESM confirms no local recurrence, but another recurrent cancer is noted, slightly away from the PO scar.

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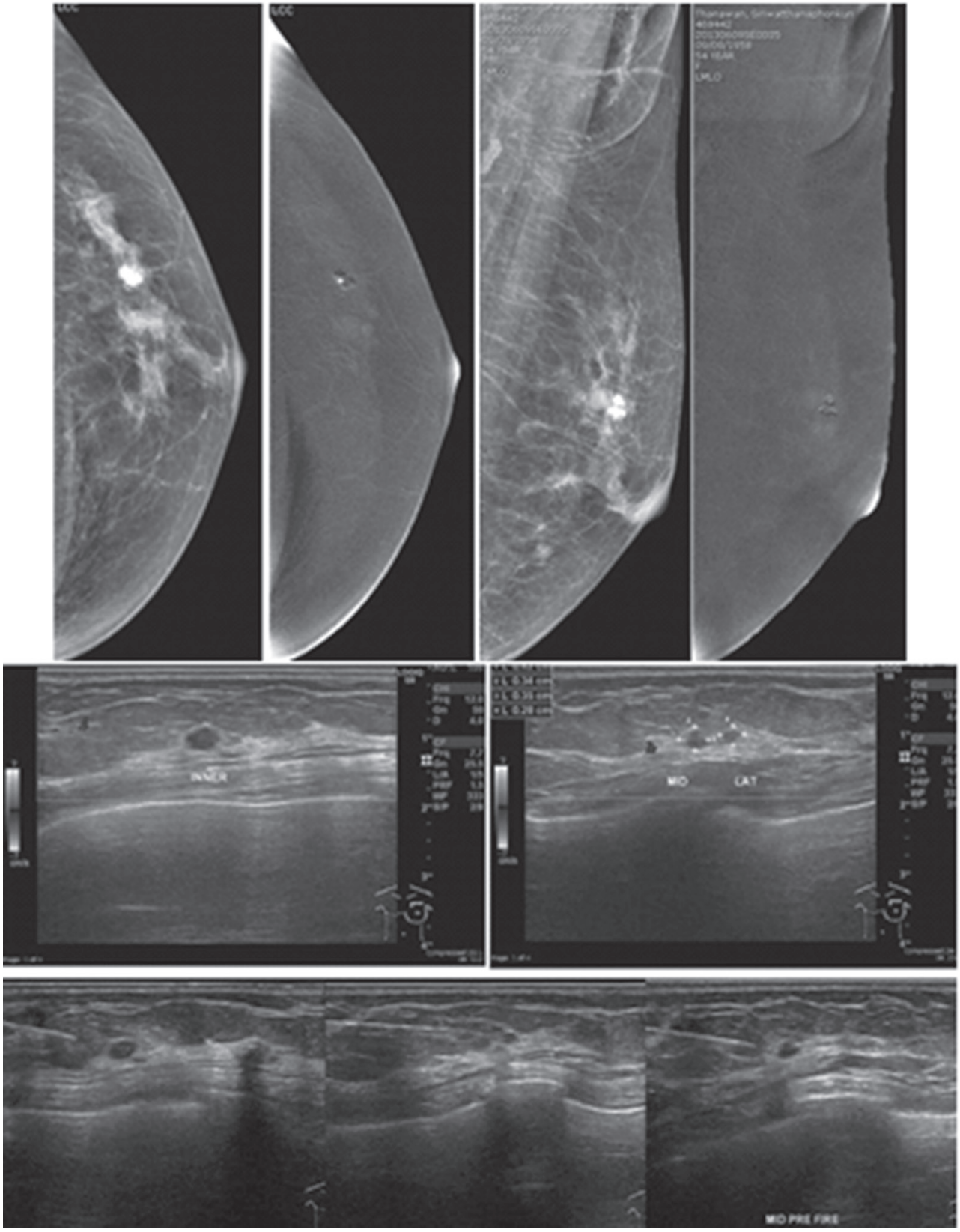

Figure 7B: Female 54-years of age, S/P left MRM for IDCA. Mammography reveals popcorn calcifications and a cluster of round microcalcifications in left UOQ. Breast US shows 3 microlobulated heterogeneous hypoechoic masses in left upper inner: 4.3×4.9×5mm, left upper middle: 3.1×4.3mm and left upper lateral: 3.1×4.5mm. CESM reveals very soft enhancement of these 3 tiny nodules. US guided CNB of these 3 lesions reveal IDCA, moderately differentiated in all specimens.

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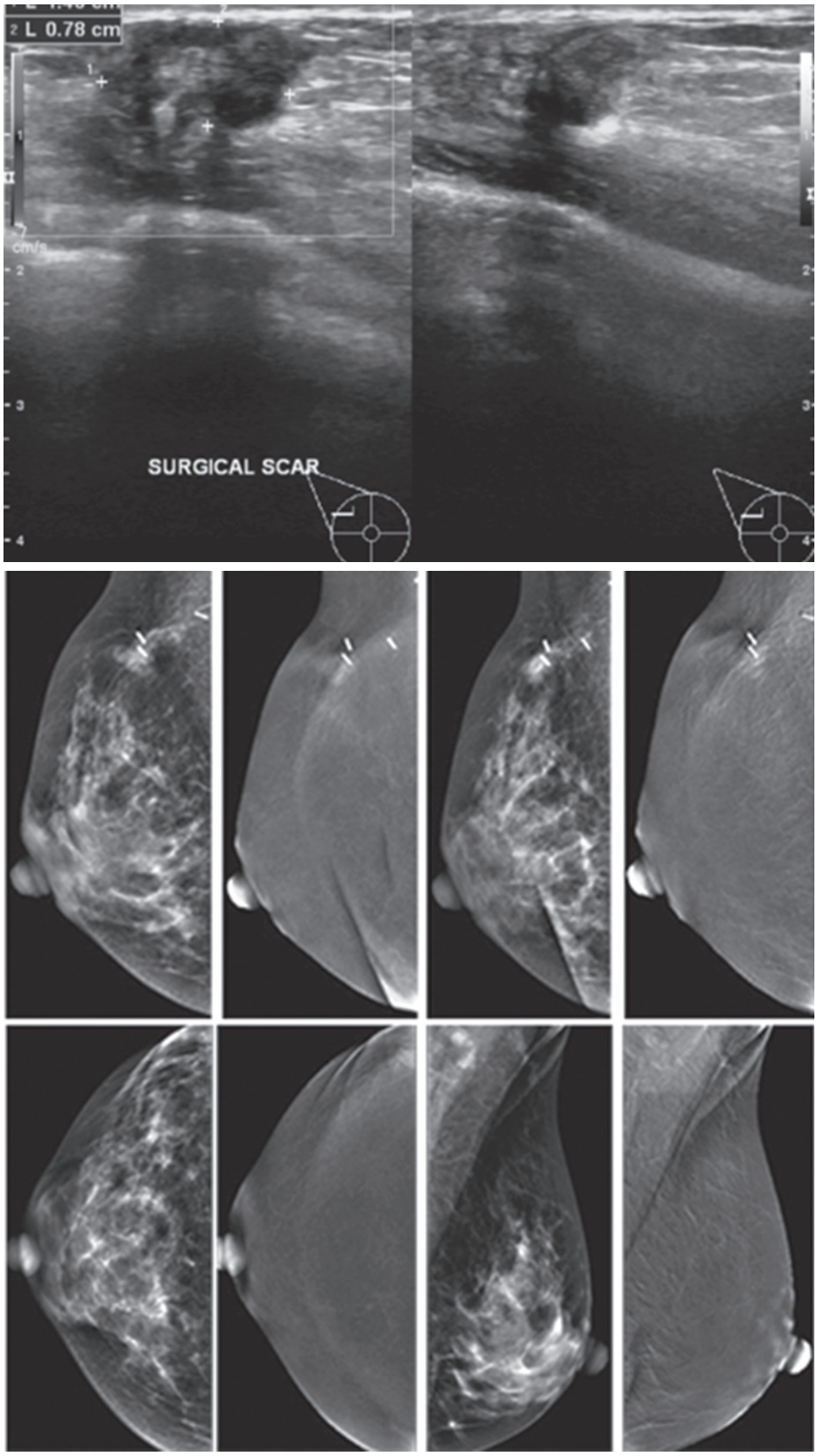

Figure 7C: Female 36-years of age, S/P right CBS for breast cancer came with palpable abnormality at PO area. US shows a heterogeneous hypoechoic mass, lobulated outline, near PO scar, 14.0x7.8 mm. with multiple heterogenous hypoechoic masses in both breasts, and recurrence cannot be excluded. CESM reveals soft enhancement at the PO area with palpable abnormality and surgical clips. There is no significant abnormal enhancement in the rest of both breasts. At surgery, there is no local recurrence. CESM confirms no local recurrence in equivocal mammography and US findings, as well as no evidence of malignancy elsewhere.

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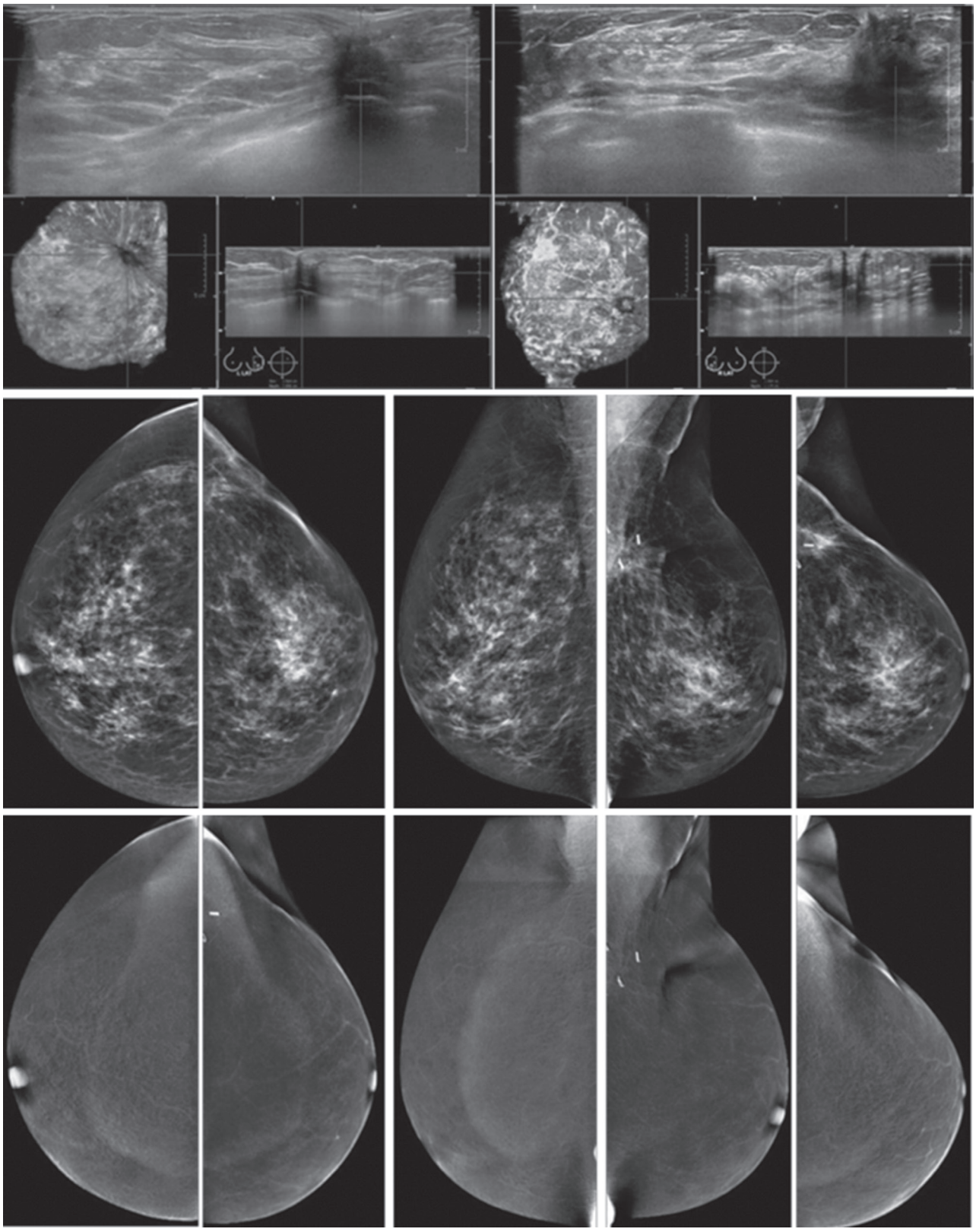

Figure 7D: Female 46-years of age, S/P left UOQ lumpectomy and left sentinel node biopsy for IDCA, grade II US shows an irregular mass--a lesion with spiculation in left central at post operation (PO) scar. Mammography shows architectural distortion at surgical scar with surgical clips in left UOQ.

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Benign-looking punctuated microcalcifications are noted in left outer; CESM reveals no enhancement at PO area in left UOQ and elsewhere in the breasts, compatible with no local recurrence or tumour elsewhere in the breasts. CESM confirms no local recurrence at PO scar with a tiny spiculated lesion and no evidence of malignancy elsewhere.

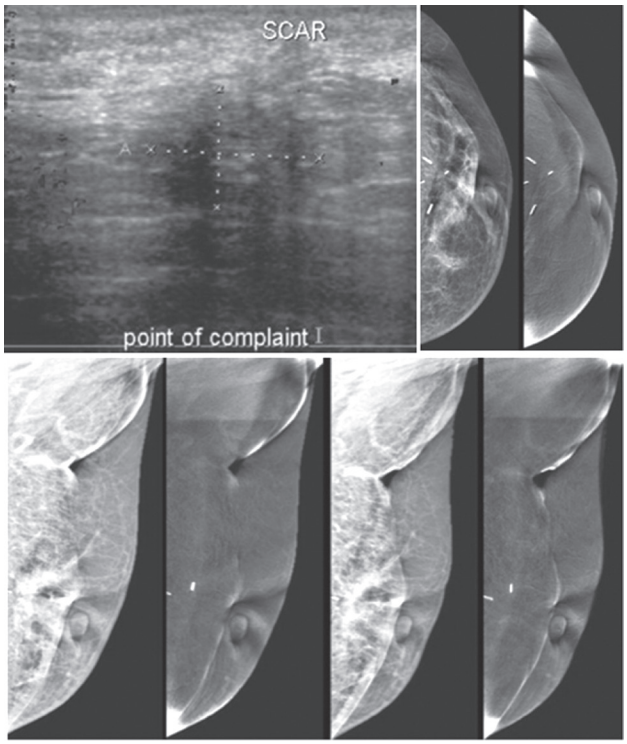

Figure 7E: Female 56-years of age, S/P left BCT for invasive ductal carcinoma, came with palpable abnormality in left axilla. US shows an ill-defined abnormal echoic area, no confined mass in left axillary area, at the palpable abnormality, measures 11×16mm. Mammography shows PO changes, no associated mass.

CESM shows no abnormal uptake of contrast medium, compatible with no malignancy, and CESM confirms no local recurrence at palpable abnormality around the PO scar and no evidence of malignancy elsewhere.

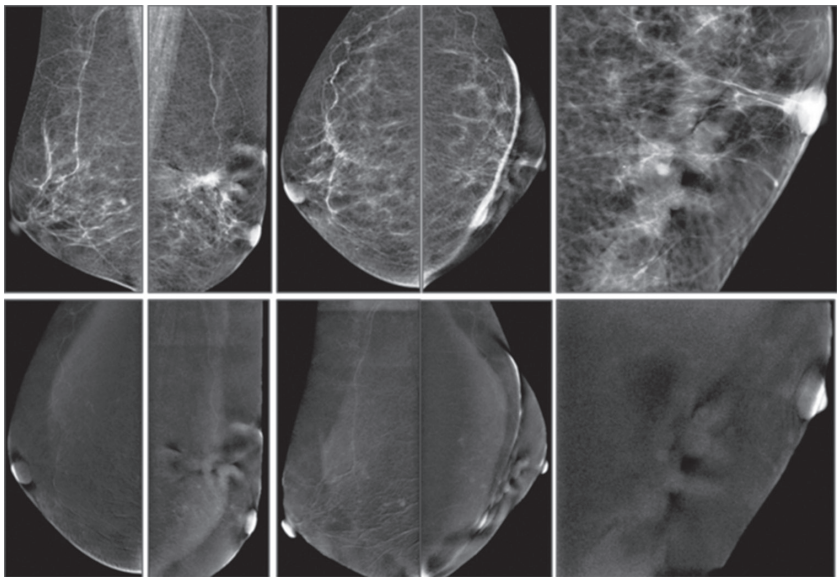

Figure 7F: Female 74-years of age, mammography shows a spiculated mass in PO area with severe deformity, skin thickening and thick strand extends to the nipple. CESM shows no enhancement of the mentioned areas. No local recurrence is detected. However, a few tiny soft enhanced foci are seen in both breasts, and this requires close follow-up. CESM confirms no local recurrence at PO scar and but cannot exclude tiny foci of malignancy, and this requires follow-up.

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Conclusion

The results obtained with CESM are immensely valuable, with better contrast resolution than CE-MRI. Extremely fine details of microcalcifications are obtained and very tiny spots of enhancement can be seen along the pathological ducts, not visualized in CE-MRI or breast ultrasound.

Our study of CESM examinations clearly shows its benefits over CE-MRI and it should be used when CE-MRI is required. With regards to radiation exposure and possible side effects of the already known iodinated contrast medium, we do not use CESM as a routine initial study, replacing mammography. Our routine breast imaging is still mammography, followed by breast ultrasound. If both prove inconclusive or if there is a possibility to reveal additional cancers in patients planned for breast conservative surgery and CE-MRI is requested, then CESM is recommended as a superior choice than CE-MRI alone. There are benefits for patients in shorter examination time and greater specificity in the identification of tumours and additional cancers that may remain undetected using conventional diagnostic imaging methods.

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Stroke and Cerebrovascular Disease

Oxford Textbook in Clinical Neurology

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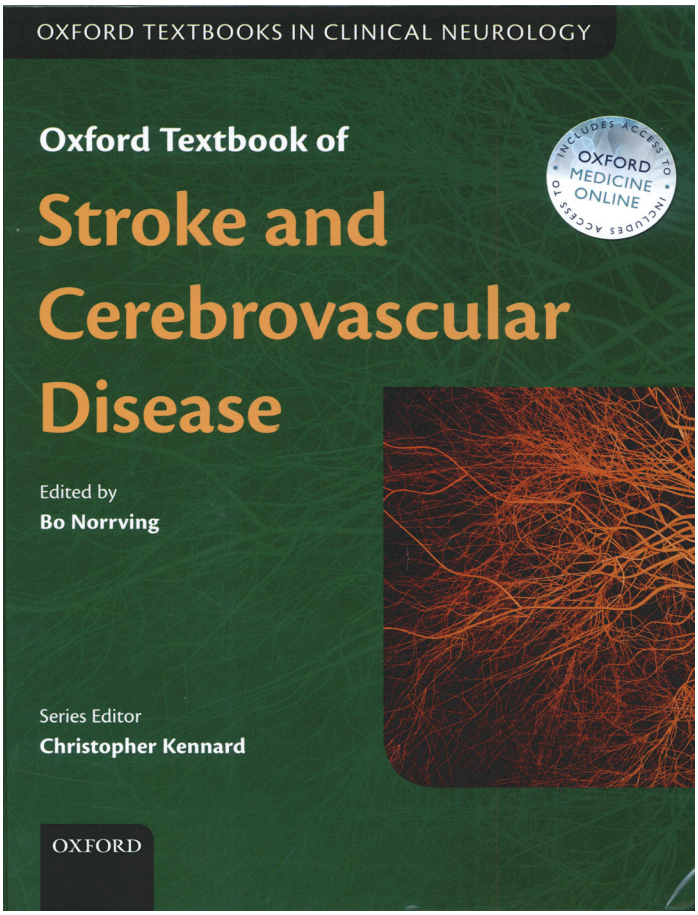

This is a recently-published text book that every neurologist or neuroscientist should have as a reference text to improve their understanding, and treatment, of stroke. This book includes a comprehensive review of the epidemiology of stroke, with a review of stroke trials and results worldwide. The book refers to the risk factors associated with stroke, and measures to prevent stroke from occurring. The latest information on how to manage acute and secondary stroke is given. The authors are well known international researchers and neurologists with extensive experience in the field of stroke management and cerebrovascular diseases. They provide a current, up to date and comprehensive overview of the disease, including clinical features and treatment. I highly recommend this publication to all neurologists, researchers, psychiatrists, specialists, and nurses. They will obtain valuable information from this book, which is an excellent reference to provide insight and advice to our stroke patients.