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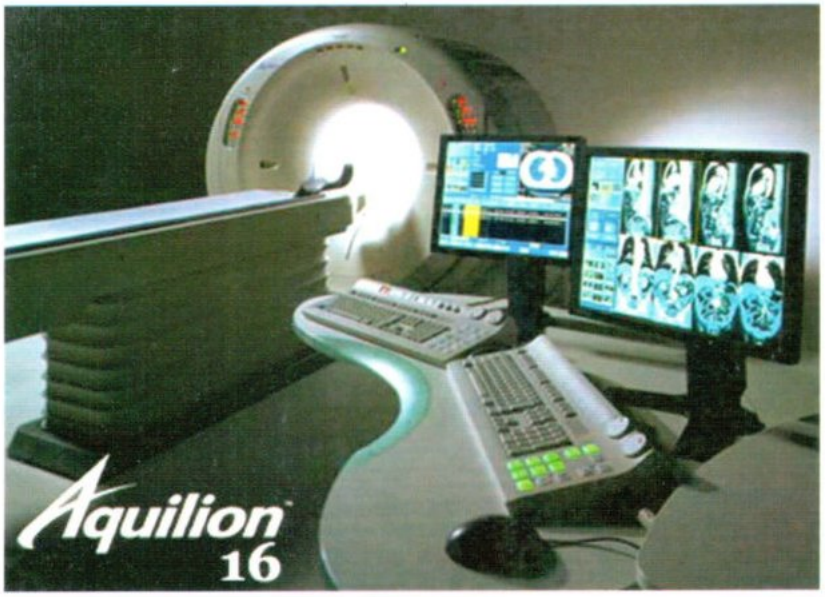

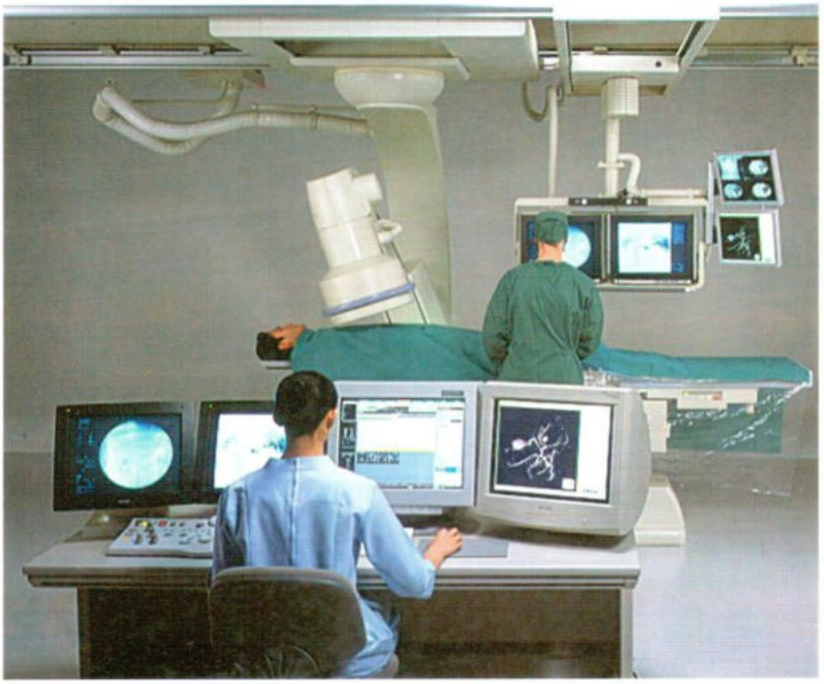

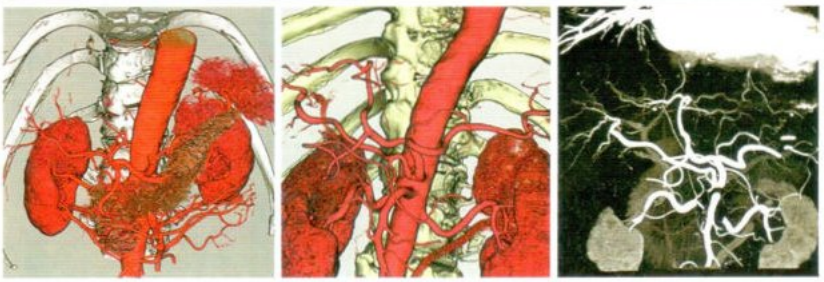

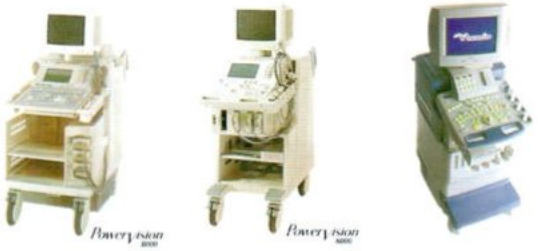

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CONTENTS

RANDOMIZED CONTROLLED TRIAL ACCELERATED HYPERFRACTIONATION RADIOTHERAPY CONCURRENT WITH CISPLATINUM VERSUS CONVENTIONAL RADIOTHERAPY FOR TREATING LOCALLY ADVANCED NASOPHARYNGEAL UNDIFFERENTIATED CARCINOMA

Maesadjie TJOKRONAGORO MD, PhD

ABSTRACT

Background : Nasopharyngeal carcinoma (NPC) is the most frequent head and neck cancer, and a serious health problem in most radiotherapy centers in Indonesia. Patients usually come when they are in locally advanced stage, with poor prognosis.

Problem encountered in the bulky primary tumor and lymph node metastasis in the neck of the locally advanced stage III and IV, non distant metastasis, which is the majority of cases particularly in the hospitals in Indonesia. The result of the treatment with radiotherapy is unsatisfactory. For this reason, attention is being paid to the combined use of modified radiation therapy and chemotherapy for solving this problem. Chemotherapy would probably increase the chances of local tumor control, either by : (1) reducing cell burden in tumors undergoing radiotherapy, (2) rendering tumor cells more suspectible to radiation damage, or (3) spatially cooperating radiotherapy through its systemic action on micro metastastic disease.

Objective : To investigate the efficacy of concurrent therapy Cisplatinum + accelerated hyperfractionation radiotherapy (C+AHR) for treatment of un differentiated type (WHO type III) carcinoma of the nasopharynx in locally advanced stage, compared to the treatment of conventional radiotherapy (CRT).

Material and method : Randomized control trial is designed in two arms,: investigated arms consist of 55 cases of Nasopahryngeal carcinoma stage III and IV without distance metastasis, undifferentiated carcinoma histology, treated concurrently with Cisplatinum + accelerated hyperfractionation,, radiotherapy (C+AHR), a two fraction dose per day, and the dose per fraction is 125 cGy, with the interval between fraction 4-6 hours to total dose equal with 70 Gy. Control arm consists of 55 cases NPC, treated with only conventional radiotherapy (CRT) of 70 Gy. Observation after treatment includes (1) Response of the primary tumor, (2) response of the lymph node metastasis in the neck, (3) relapse of the primary tumor and lymph node metastasis, (4) Duration of free disease interval.

Result : (1) Response of the primary tumor : in the arm treated with Cisplatinum

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+radiotherapy accelerated hyperfractionation , complete response in the primary tumor is 52/55 (94.5%), compared to conventional Radiotherapy, wich is only 33/55 (58. 9 %). The differences of statistical analysis are significant ($p < 0.001$). (2) Response of the Lymph node metastasis : C + AHR : 47/55 (8.5%), CRT: 39/55 (69.6%) $p = 0.131$ (3) Relapse rate of the primary tumor : C+AHR : 10/55 (18.2%), CRT : 27/55 (48.2%) $p = 0.007$. (4) Relapse rate of lymph node metastasis in the neck : C+AHR : 13 / 55 (23. 6%), CRT 16 / 55 (28. 6%) $p = 0.554$ (5) Duration of relapse : C+ AHR : mean duration of local free relapse 17 .2 months, and CRT : 9.11 months. F probability 0.003. This mean C+ AHR is able to inhibit the development of local relapse.

Conclusion : Radiotherapy accelerated hyperfractionation, conncurrent with Cisplatinum for treament of local advanced Undifferentiated Carcinoma of the nasopharynx produce better result compared to the conventional fractionation of external radiotherapy, in terms of local response, relapse rate and disease free interval.

BACKGROUND

The failure of treating local advanced Nasopharyngeal carcinoma with conventional radiation therapy is widely published. The efficacy of radiotherapy as a single modality treatment in patients with local or regional advanced cancers is limited by a number of factors : (1) High number of clonogenic cells, (2) Intrinsic cellular radioresistance, (3) Repair proficiency from radiation damage, (4) Hypoxia, and (5) accelerated cell proliferation. Tumor cells may resist undergoing cell death after radiation, efficiently repair DNA damage, may be able to resume or even accelerate proliferation in the period between radiation fractions, or posses radioresistence associated with hypoxia within the tumor mass. In addition, occult tumor cells may exist outside the irradiated field and thus lead to distant metastasis. For this reason , increased attention is being paid to the combined use of radiotherapy and chemotherapy. Chemotherapeutic agent increases the chances of local tumor control, either by : (1) Reducing cell burden in tumors undergoing radiotherapy or by (2) Rendering tumor cells more suspectible to radiation damage. (3) They may also spatially cooperate with radiotherapy through their systemic action on micro metastasic disease.[1]

Several approaches have been used in combining radiotherapy and chemotherapy. They include alternating chemotherapy and radiotherapy, which is given before radiation (neo adjuvant chemotherapy) or after radiation adjuvant chemotherapy), administration of drug during the course of radiation (Concurrent or simultaneous chemotherapy)

The rationale of accelerated hyperfractionation is based on the fact that malignant cells after single hit of one radiation fraction of 2 Gy, small part of cell going to cell death because of severe double strand break damage of DNA, but another surviving fraction still becomes sub lethal because of the moderate damage of DNA, such as single strand break DNA, base damage, sugar damage, DNA-DNA Cross link or DNA Protein cross link. These sub lethal cells, within 4 to 6 hours, are going to repair from sublethal damage, and after 6 hours, complete repair has been done, and the cells become potent malignant cells. These lead to repopulation after the completion of radiotherapy and residual disease after radiotherapy.[2] The second fraction of radiation therapy is given within 4 to 6 hours after the first fraction, the process of repairing DNA will be inhibited, and

lead to cell death. This procedure of radiotherapy is called accelerated hyperfrac-tionation.[4]

The administration of cisplatinum which also inhibits and destroys DNA by 4 types of cross links, will enchance cell killing of malignant cells in accelerated hyperfractionation combined simultaneously with cisplatinum.

The objective of this research is to investigate the efficacy of concurrent thepapy Cisplatinum + Radiotherapy accelerated hyperfrac-tionation for the treatment of locally advanced stage nasopharyngeal carcinoma compared to the treatment with conventional radiotherapy.

OBJECTIVE

The objective of this research is to investigate the efficacy of concurrent therapy cisplatinum + radiotherapy accelerated hyperfractionation for the treatment of locally advanced stages nasopharyngeal carcinoma compared to the treatment with conventional radiotherapy.

MATERIAL AND METHOD

All cases were nasopharyngeal carcinoma Stage III and IV without distant metastasis (T3 N0-3 M0, T4, N0-M0), Undifferentiated carcinoma histology, admitted to DR. Sardjito Hospital during 1993-1998, which were selected using exclusion and inclusion criteria One hundred and eleven cases were collected, and randomized, into two groups. The first group consisted of 55 cases treated with radiotherapy accelerated hyperfractionation simultaneously with cisplatinum, and the second group consisted of 56 cases treated with conventional radiotherapy.

INCLUSION CRITERIA

(1) Minimum age was 10 years old and maximum 80 years old. and average was 45. (2) Perfomance status measured uses Karnofski Index, minimum 70 (3) Normal haemopoetic system (normal WBC, haemoglobin and platelet count) (4) TNM stage III (T3N0M0, T1-2-3 N1M0) and stage IV without distant metastasis (T4N0M0, T1-2-3N2-3M0, T1-2-3N1-2-3 M0). (5) Undifferentiated carcinoma is the histology of the nasophrayngeal cancer. This histologic type is the most frequent (95%) of all Nasopahryngeal cases admitted to RSUP. DR. Sardjito Hospital in Yogyakarta (6) Normal function of the visceral organs, normal liver function test, normal kidney function and normal heart detected by electrocardiograph.

EXCLUSION CRITERIA

(1) Distant metastasis including lung metastasis was detected by chest x ray, and liver metastasis was detected by abdominal ultrasonography and laboratory test. Bone metastasis was detected by bone scintigraphy. Brain metastasis was detected by head CT Scan (2) Having previous radiotherapy or chemotherapy, or locoregional recurrences after previous treatment (3) Diabetes mellitus (4) Heart diseases including coronary heart disease, malignant hypertension, defect of valve caused by reheumatic heart disease, congenital heart diseases.

CRITERIA OF RESPONSE

The criteria of response include : (1) local response (2) regional response (3) Local relapse (4) regional relapse (5) duration of relapse

The determination of Local response of the primary tumor by clinical examination, rhinoscopy anterior / posterior, done by two ENT surgeons, and the disagreement were measured by Kappa index. Head CT scan with axial and coronal plane, observed by two radiologists. The disagreement was measured by Kappa Index.

Determination of regional remission was done by properly palpating and measuring the size of lymph node metastasis of the neck by two Radiation Oncologists. The disagreement was measured by Kappa index.

The disappearance of primary tumor after treatment had to be proven histologically. A re-biopsy of the primary tumor was done 3 months after the completion of treatment. The specimen of biopsy was then scored into 7 categories: Score 1: Malignant cell intact, no change at all. Score 2: There was a change of the differentiation of malignant cells. Score 3 : There were changes from undifferentiated into moderate differentiation. Score 4 ; There were changes from undifferentiated into good differentiation. Score 5: Malignant cells underwent subtotal necrosis with differentiation. Score 6 : Malignant cells underwent total necrosis. Score 7 : Malignant cells completely dissappeared

RESEARCH DESIGN

Research design was a randomized control trial with two arms. One arm was the investigated arm, treated with radiotherapy accelerated hyperfractionation combined simultaneously with Cisplatinum. The other arm was the control arm, treated with conventional radiotherapy. Statistical analyses of Chi square Pearson method were used to analyse the significance, multi variate analysis was used to investigate the variables, the distribution of which was not homogeneous. The research design as seen in figure I

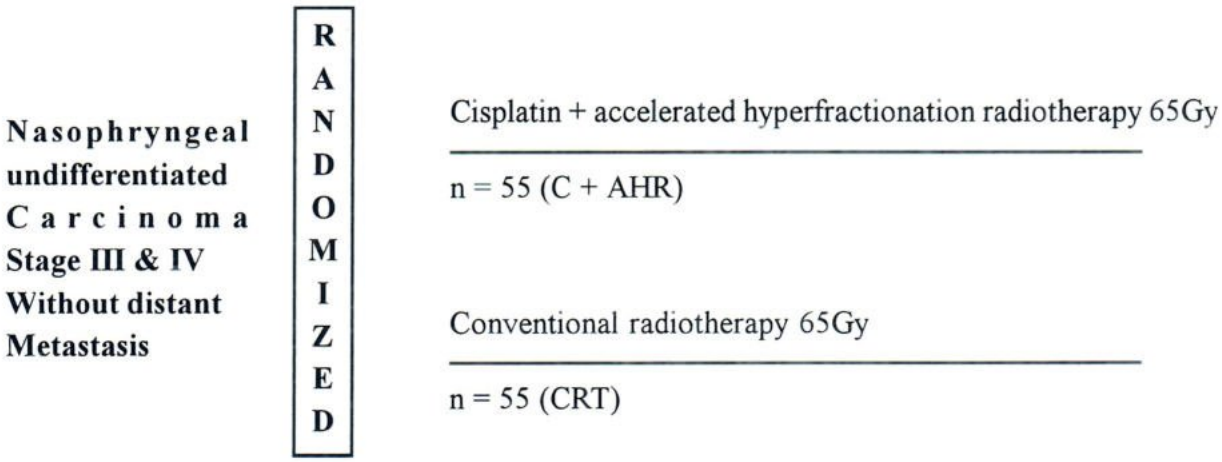


Fig. 1. A schematic diagram of a randomized control trial. First arm consisted of 55 cases, treated with Cisplatin 100 mg + Radiotherapy accelerated hyperfractionation which equal to 65 Gy. Control or second arm consisted of 55 cases, treated with conventional radiotherapy 65 Gy.

TREATMENT PROCEDURE

ACCELERATED HYPERFRACTIONATION RADIOTHERAPY

The external radiation therapy using two fractions a day with fraction size 1,25 Gy. The interval between fraction minimal 4 hours and maximal 6 hours. The total dose would be equal to 65 Gy. After 40 Gy, shielding to spinal cord was done. After 50 Gy, a rest of a week was given to relief severe mucositis

CISPLATINUM

Cisplatinum were given prior to accelerated hyperfractionation radiotherapy. A total dose of 100 mg Cisplatinum were given in divided doses, 20 mg per day for 5 days in 500 cc Dextrose. Prior the administration of cisplatinum, a hydration with Dextrose 5% 1500cc and diuresis with mannitol 20 % 500cc were given, in order to eliminate the nephrotoxicity of cisplatium. For anti-vomiting, ondansetron 8 mg were given prior the administration of Cisplatinum, oral or intravenous.

CONVENTIONAL RADIOTERAPY

The conventional radiotherapy using single fraction a day, with fraction size 2 Gy per fraction. Total dose 65 Gy. after 40 Gy a shield of spinal cord were done. After 50 Gy, a rest of one week were given to relief mucositis.

RESULT

RESPONSE OF PRIMARY TUMOR

The response of the primary tumor in the group treated with combination of Cisplatinum and radiotherapy accelerated hyperfractionation seemed to be much more superior than the result of conventional radiotherapy. In the group treated with Combination of Cisplatinum + Radiotherapy accelerated hyperfractionation complete remission was achieved in 52 cases (94,5 %), only 3 cases had partial remission (5,5 %) and no one had no change (nc) or progressive diseases (pd). In the control arm, of conventional radiotherapy complete remission occurred in only 33 cases (58,9%), 22 cases had partial remission (39,5 %) and 1 case (1,8 %) did not change (nc). The statistical differences were very significant ($p < 0,001$) as shown in table 1.

Stastical analyses of Chi square table Pearson Method revealed a very significant difference in the result of this two types of treatment. The treatment with cipslatin + radiotherapy accelerated hyperfractionation was more superior than the conventional radiotherapy, with $p < 0,001$ (table 1)

Table 1. Response of the Primary tumor of the nasopharyngeal carcinoma undifferentiated type, fisrt arm consists of 55 cases treated with 100 mg cisplatinum + accelerated hyperfractionation radiotherapy (CISPL + AHR). And second arm consist of 56 cases treated with Conventional radiotherapy (CRT)

Type of treatment	Complete Remission (CR)		Partial Remission (PR)		No Change (NC)		Progressive Disease (PD)		Total	
	N	%	n	%	n	%	n	%	n	%
CISPL + RAH	52	94.5	3	5.5	0	0	0	0	55	49.5
Conventional Radiotherapy	33	58.9	22	39.5	1	1.8	0	0	56	50.5
	85	76.6	25	22.5	1	0.9	0	0	111	100
										P < 0. 001

RESPONSE OF LYMPH NODE METASTASIS

The reponse in the lymph node metastastic tumor in the neck region was not as good as the result of the primary tumor. This was probably influenced by many factors: (1) The difference in the nature of the tumor, (2) the environment where the tumor grows, (3) the vascularization systems of the lymph node influencing the distribution of chemotherapy cisplatinum, and (4) the hypoxic cells inside the tumor.

Even there were differences between the results of the two treatments, the results of concurrent chemo radiation cisplatin + radiotherapy accelerated hyperfractionation were better than conventional radiotherapy, but the statistical analyses with Chi square Pearson method was p = 0, 131 , or the difference was not significant (table 2).

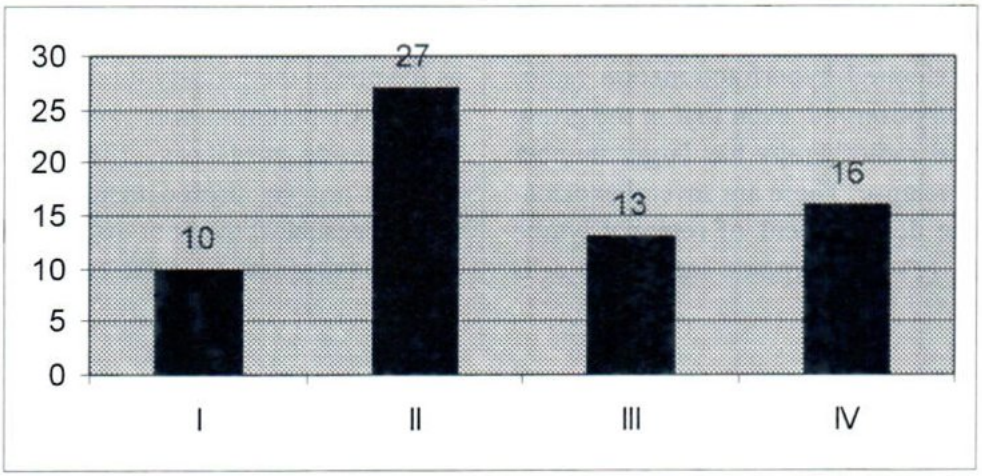
The explanation of this phenomenon could be several points: (1) The differences of vascularization in the lymph node metastasis were not as rich as those of vascularization in the primary tumor of the nasopharynx, this lead to hypoxia of the majority of the malignant cells in the lymph node that made intrinsic cellular resistence within the cells. (2) In the big lymph node metastasis in the neck, (N 3) there was a high number of clonogenic cells (3) The ability of malignant cells to repair proficiency from radiation damage

Table 2. Response of the lymph node metastastis of nasopharyngeal undifferrentiated carcinoma in the neck region. The first arm treated with Concurrent Cisplatin 100 mg in 5 days + accelerated hyperfractionation radiotherapy. The second arm treated with conventional radiotherapy.

Type of treatment	Complete Remission		Partial Remission		No Change		Progressive Disease		Total	
	N	%	n	%	n	%	n	%	n	%
CISPLATIN + RAH	47	85.5	7	12.7	1	1.8	0	0	55	49.5
Conventional Radiotherapy	39	69.6	14	25.0	3	5.4	0	0	56	50.5
	86	77.5	21	18.9	4	3.6	0	0	111	100
	P = 0. 131									

LOCO REGIONAL RELAPSE
LOCAL RELAPSE

After the completion of the treatment in both arms, observation was periodically made every month until 2 years after the treatment, to observe : (1) The locoregional relapse (2) The duration of the development of locoregional relapse. The result of this observation can be seen in figure 2



I : Primary tumor relapse group cisplatinum + AHR
II : Primary tumor relapse conventional radiotherapy
III : Regional lymph node metastasis relapse group cisplatinum + AHR
IV : Regional lymph node relapse conventional radiotherapy

Fig. 2. Local relapse in the primary tumor in group of Cisplatin + AHR (I) compared to Conventional Radiotherapy (II). Regional relapse in the Lymph node in Group of Cisplatin + RTAH (III) compared to Conventional Radiotherapy (IV).

Statistical analysis was done by Chi Square Pearson method resulted in $p = 0.007$ ($p < 0.05$). There is significant difference in local relapse treated by concurrent Cisplatin + Radiotherapy accelerated hyperfractionation with much less relapse compared to conventional Radiotherapy (table 3)

Table 3. Local relapse in the primary tumor of Nasopharyngeal undifferentiated carcinoma local advanced Stage III and IV without distant metastasis treated with concurrent cisplatin + accelerated hyperfractionation radiotherapy compared to conventional Radiotherapy

Type of treatments	Relapse +		Relapse --		
	n	%	n	%	P
Cisplatin + accelerated hyperfractionation radiotherapy	10	18.2	45	81.8	0.007
Conventional Radiotherapy	27	48.2	29	51.8	

REGIONAL RELAPSE

The regional relapse in the lymph node metastasis of undifferentiated nasopharyngeal carcinoma, after the treatment with concurrent cisplatin + accelerated hyperfractionation radiotherapy was still observed, even that in the group of Conventional radiotherapy has larger number of lymph node relapse. There are several explanations about the development of regional lymph node relapse.: (1) The hypoxic malignant cells resistance to radiation, then lead to residual disease and create regional relapse (2) The vascularization in the lymph node tumor was not as good as the one in the primary tumor, then the distribution of Cisplatinum was not optimal inside the Lymph node metastasis . (3) The repair mechanism is not so altered inside the lymph node tumor because of the poor distribution of Cisplatin due to inadequate vascularization

Table 4. Lymph node metastasis tumor relapse after the treatment with Cisplatin + Radiotherapy accelerated hyperfractionation and Conventional Radiotherapy.

Type of treatments	Relapse +		Relapse --		P
	n	%	n	%	
Cisplatinum + radiotherapy accelerated hyperfractionation	13	23.6	42	76.4	0.554
Conventional Radiotherapy	16	28.6	40	71.4	

Statistical analysis reveals p = 0,554 (p< 0,05), the differences in regional lymph node relapse after the treatment are not significant in both treatments.

DURATION OF FREE DISEASE

DURATION OF LOCAL RELAPSE.

Local relapse in the arm consisting of 55 cases treated with Cisplatinum + Radiotherapy accelerated hyperfractionation, was only 10 cases (18.18%), and the mean duration of relapse (disease free) was 17.2 month

Among local relapses in the control arm consisting of 56 cases treated with conventional Radiotherapy, 27 cases have local relapse (48.21%). Mean duration of local relapse (disease free) was 9.11 months. Statistical analyses of F Probability 0,003. This means the addition of Cisplatinum and radiotherapy accelerated hyperfractionation is able to delay the development of local relapse.

DISCUSSION

Undifferentiated carcinoma of the nasopharynx is the most frequent head and neck cancer in Indonesia .Treatment in early stage T1 and T2 with small tumor using conventional radiotherapy, the result is satisfactory. But in locally advanced disease with large tumor in T3 or T4, the result is poor. Innovation in the treatment of this local advanced stage nasopharyngeal undifferentiated carcinoma should be created to obtain better result, by analyzing factors causing the failure of radiotherapy treatments. The factors are : (1) Large tumor have clonogenic cells, (2) Intrinsic cellular resistence (3) Repair proficiency from radiation damage (4) Hypoxia (5) Accelerated cell proliferation (6) Repair mechanism in the malignant cells. These factors are taken into account in designing innovation in radiotherapy. The most suitable method to overcome this problem is Cisplatinum concurrent with accelerated hyperfractionation radiotherapy. To make sure that the result is better, compared to conventional radiotherapy. The result in group treatment of cisplatin + accelerated hyperfractionation radiotherapy is significantly better compared to conventional radiotherapy (p < 0,001). The local relapse rate is significantly better compared to the conventional radiotherapy (p = 0,007)

CONCLUSION

Local advanced stages of nasopharyngeal undifferentiated carcinoma, if treated with concurrent cisplatin + accelerated hyperfractionation radiotherapy, the result of treatment compared to the result of Conventional Radiotherapy alone : The complete response of the primary tumor of the Nasopahrynx are much better than the conventional radiotherapy

The complete response in the lymph node metastastic tumor in the neck are better in the treatment of Cisplatin + accelerated hyperfractionation radiotherapy, compared to the conventional radiotherapy alone, but statistically not significant.

Relapse rate in the primary tumor of nasopharynx is significantly much less in the treatment group of cisplatin + accelerated hyperfractionation radiotherapy compared to the conventional radiotherapy. The relapse rate in the lymph node metastasic tumor of the neck, the differences between the two treatment modalities were not statistically significant

The duration of development of local relapse in the primary tumor of nasopahrynx (disease free survival period) is significantly longer in the group treated with cisplatin + accelerated hyperfractionation radiotherapy compared to the conventional radiotherapy alone.

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RENAL ONCOCYTOMA: ULTRASOUND AND COMPUTED TOMOGRAPHY APPEARANCES

M. Puvaneswary, M.B.B.S., F.R.C.R.
K. Thong, M.B.B.S.

INTRODUCTION

Renal oncocytoma is a relatively rare tumour that has an excellent prognosis and generally treated adequately by local resection or heminephrectomy. Pre-operative radiologic differentiation from renal cell carcinoma is important as renal cell carcinoma requires radical nephrectomy. A case of renal oncocytoma is presented with a review of the radiological features and current literatures.

CASE REPORT

A 73 years old woman presented with one week history of a constant dull ache in the right loin. There was no history of haematuria. She has a history of hypertension, glaucoma and a past history of hysterectomy and recurrent palpitation. On physical examination tenderness in the right flank to deep palpation was evident but no abnormal masses were felt. Blood urea and creatinine levels were normal. Urinalysis showed 10-40 wbc/dL and less than 10 rbc/dL. The haemoglobin was 13.1 gm/dL, haematocrit 0.41, platelet count $349x10^3$/L and the wbc count was $11.4x10^3$/L. Plain abdominal radiography was normal. Abdominal sonography revealed a 3cm well circumscribed hypoechoic mass with an irregular hyperechoic centre arising from the posterolateral surface of the lower pole of the right kidney and several sonolucent cysts within the liver.

Abdominal computed tomography (CT) confirmed the presence of a 3cm solid mass in the lower pole of the right kidney. The mass demonstrated an inhomogenous enhancement, an irregular contour and an indistinct interface with adjoining renal parenchyma. There was no evidence of tumour extension into the renal vein or perinephric space. There was no evidence of intratumoural calcification or retroperitoneal lymphadenopathy. No masses were seen in the left kidney and the liver demonstrated several low attenuation cysts and a diagnosis of renal cell carcinoma with liver secondaries was made. A right radical nephrectomy was performed. On sectioning a well encapsulated 3cm mass with homogenous tan tissue with cystic areas containing haemorrhage as well as yellow tissue in the centre was present. Microscopically the tumour consisted of sheets of cells with abundant eosinophilic cytoplasm, regular nuclei with pleomorphism but no mitotic activity was found. A central scar was present within the tumour. The histologic features were typical for renal oncocytoma. In retrospect the irregular hyperechoic centre within the mass on ultrasound examination represented the central scar within the tumour mass.

The patient made an uneventful post -operative recovery. At the time of surgery some bruising in the right abdominal muscle was noted and it was thought that this small haematoma may have actually been the cause of her initial pain.

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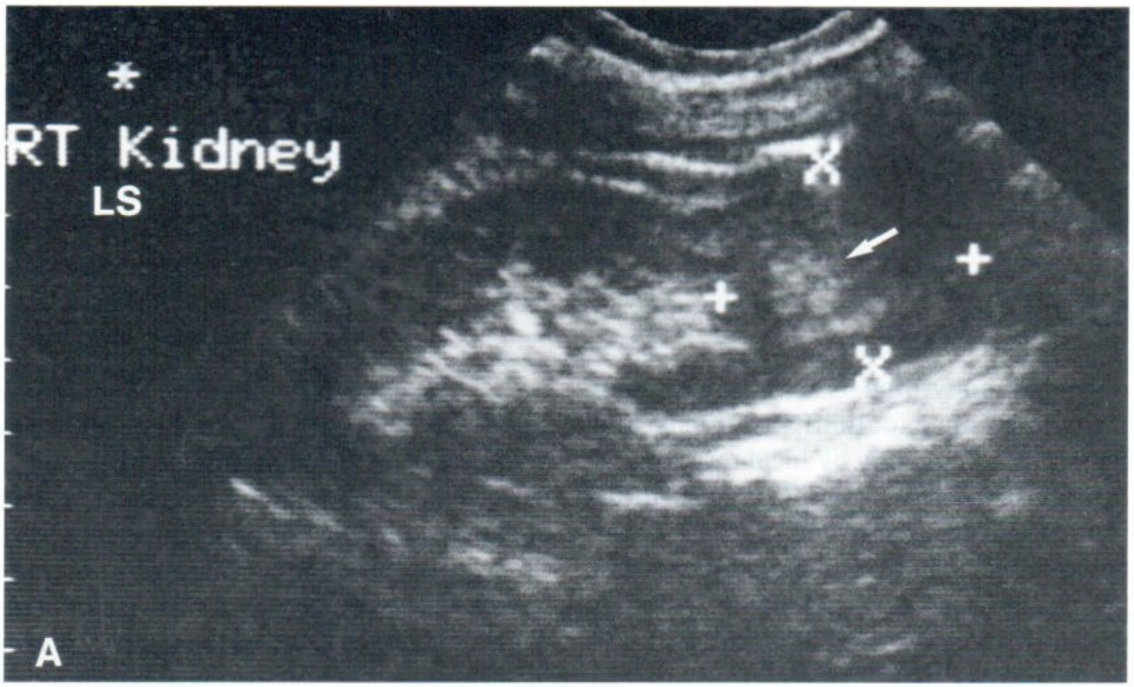

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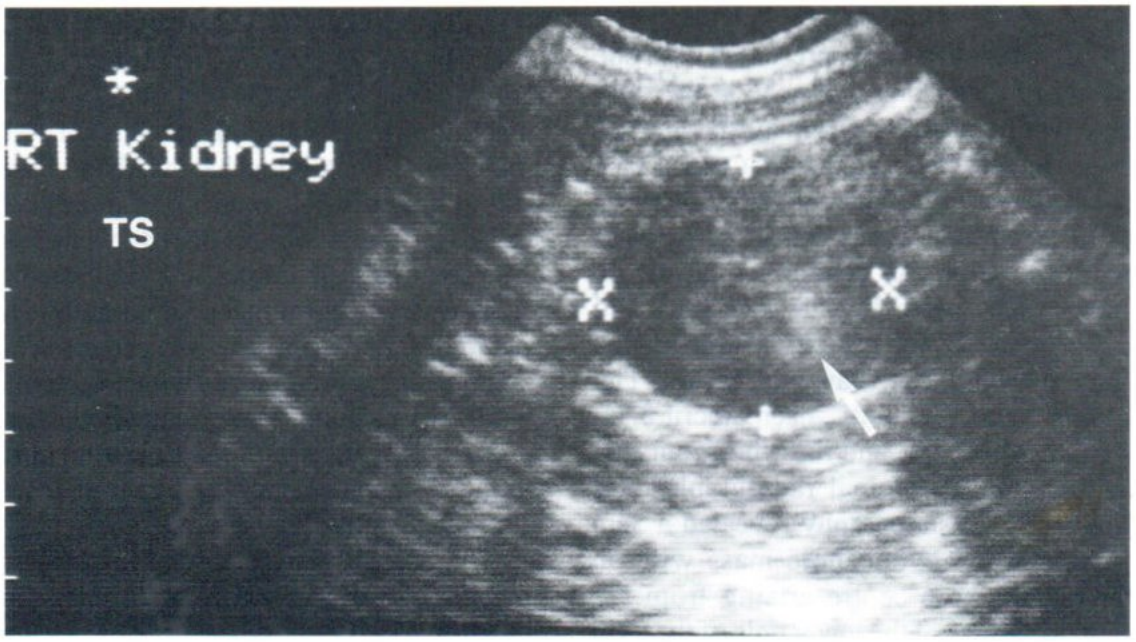

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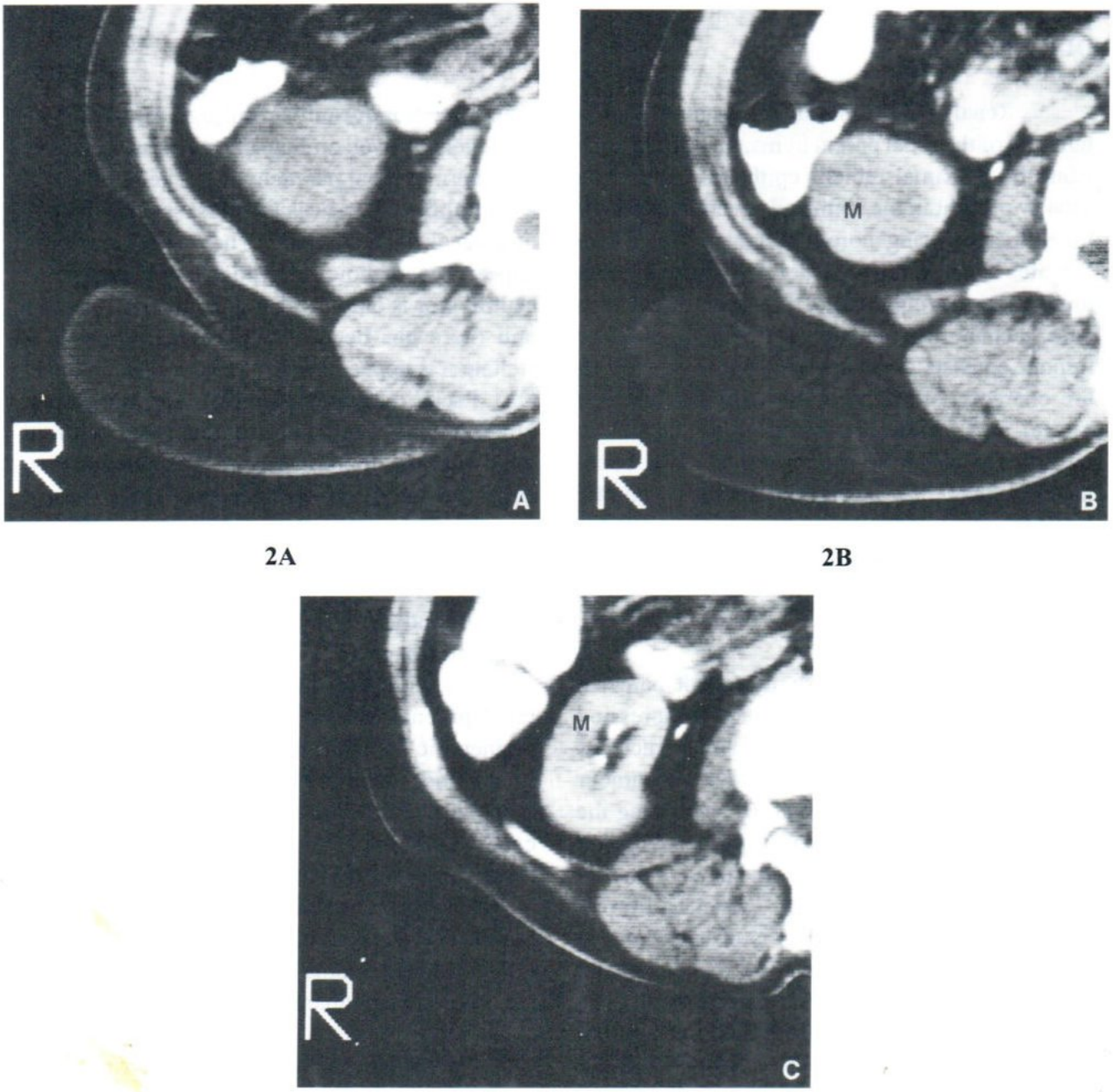
Fig. 1 Longitudinal (A) and transverse (B) ultrasound of the right kidney. A 3cm well circumscribed hypoechoic mass with irregular hyperechoic central scar (arrow) arising from the posterolateral surface of the lower pole of the right kidney.



2A 2B

2C

Fig. 2 (A) Pre contrast scan. Tumour in the lower pole of right kidney is inhomogenous in appearance, (B&C) Post contrast scan. Tumour (M) demonstrates inhomogenous enhancement, irregular contour and indistinct interfaces with adjoining renal parenchyma.

DISCUSSION

Renal oncocytoma are uncommon, benign tumours of the renal parenchyma, thought to arise from the proximal tubular epithelial cells.[1] The usually present in the sixth and seventh decade of lift with males being more commonly affected than females with a ratio of 3:1.[2] Although most tumours are asymptomatic, they can present with pain, haematuria or palpable abdominal mass. The tumour consists exclusively of oncocytes which are characteristic large cells with small round nuclei and abundant granular eosinophilic cytoplasm on light microscopy. Mild focal pleomorphism may be present there is no mitotic activity on electron microscopy. The striking features are the large numbers of mitochondria with few other organelles and absence of fat vacuo les.

Oncocytomas are usually well demarcated lesions with a pseudocapsule due to compression by adjacent parenchyma. They have characteristic tan-brown to mahogany red colour[3] and tumour size varies from 1-14 cm with 6-7 cm being the average size at diagnosis.[2] Central necrosis and haemorrhage are typically absent but were present in the larger tumour (> 8 cm).[4] A central fibrotic scar may be present and this is possibly due to previous haemorrhage, necrosis and infarction with subsequent organization and healing. The scar is usually stellate in appearance but occasionally circular scars have been encountered.[5] Calcification occurs rarely.[6] Oncocytomas may occur in other organs such as salivary glands, thyroid, parathyroid, pituitary gland and adrenal. Renal oncocytomas are usually single. But can be multicentric, bilateral or associated with renal cell carcinoma.[4,7] The main differential, diagnosis is renal cell carcinoma but unlike renal carcinoma, oncocytomas are not associated with vascular invasion, local recurrence or distant metastasis. Excretary urography can confirm the presence of a discrete non-invasive solid mass but is non -specific. Sonographic findings are that of a homogenous, well circumscribed mass, isoechoic with normal renal parenchyma.[4] The presence of a central fibrotic scar is the most specific feature of a renal oncocytoma.[4,5] The central scar may appear hyperechoic or hypoechoic however the central scar is only present in a minority of cases and there has been a single case report of a stellate scar appearance in a renal cell carcinoma.[9] On CT scan, oncocyoma typically appear as a solid homogenous, well-marginated mass without calcification and have homogenous contrast enhancement. A low density central scar if present may be demonstrated with fine sections.[9,10] In contradistinction, renal cell carcinoma often have calcification, generally demonstrate inhomogenous contrast enhancement due to the presence of haemorrhage and necrosis and have lobulated contours with indistinct interfaces with normal renal parenchyma. Invasion of the renal vein, perinephric invasion of the fat and metastasis to lymph nodes tend to occur. However no pathognomonic features are present as small renal cell carcinoma may demonstrate homogenous enhancement, differentiating it from oncocytoma by CT findings alone is impossible. As haemorrhage may occur in large oncocytoma, on CT scans oncocytoma may demonstrate inhomogenous contrast enhancement.

On scintigraphy both renal cell carcinoma and oncocytoma are photon-deficient on static scans and therefore indistinguishable from each other. Typical angiographic features of oncocytomas include "spoke wheel" configuration of vassels and a homogenous nephrographic blush, sharp, marginated and absence of vascular pooling or venous shunting. Renal cell carcinoma however have displayed the "spoke wheel" pattern and homogenous blush.[11] However the majority of oncocytoma have hypovascular or avascular appearance on angiography.

Percutaneous biopsy of renal masses is not particularly useful in differentiating from renal cell carcinoma since oncocytes may be present focally within renal cell carcinoma.[11] However if oncocytoma is suspected pre-operatively, a local resection should be performed. If the tumour have the typical tan-brown appearance and well circumscribed on macroscopy, a frozen section should be performed. If this confirms an oncocytoma, no further surgery is required. However, if on subsequent electron microscopy renal cell carcinoma is diagnosed a secondary nephrectomy can be performed.

SUMMARY

In summary there appears to be no pathognomonic findings of oncocytoma. Typical sonography, CT and angiographic findings may suggest the diagnosis pre-operatively. If at surgery, a uniform tan-brown, well encapsulated tumour is present, and a frozen section confirms oncocytoma, a local resection or partial nephrectomy should be performed. If subsequent histology reveals renal cell carcinoma a secondary nephrectomy is performed.

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ACCURACY OF THE MRA FOR THE DETECTION OF INTRACRANIAL ANEURYSM AS COMPARED TO THE CATHETER ANGIOGRAM

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ABSTRACT

Purpose: To assess the role of MRA for detection of intracranial aneurysm as compared to catheter angiogram by using standard method of post processing (MIP) in blinded-reader study.

Material and Method: Two hundred vessels were examined with catheter angiogram and 3DTOF MRA in 50 patients with SAH (38 aneurysms ,1 DAVF and 13 patients with no aneurysm at DSA). MRA were interpreted by neuroradiologist blinded to the DSA results for presence, location, size and morphology of the aneurysm.

Results: Mean sensitivity for detection of aneurysm was 92.1% specificity 100%,positive predictive value 100%and negative predictive value 81.3%. 38 aneurysms were found; A-com 14, P-com 8, MCA 7, Basilar 4, ICA 3, SCA 1, vertebral 1, 1 DAVF and 13 no aneurysm. True positive 35, true negative 13,false positive 0 and false negative 3.

Conclusion : MRA with standard post processing can result in high sensitivity and specific studies for the diagnosis of intracranial aneurysm that are of sufficient size to be considered for surgical treatment. The positive predictive value is also very high but the negative predictive value is not high enough. Therefore, in negative study of MRA, cather angiogram is still recommended.

Key word : MRA, SAH, Aneurysm. **SAH** = Subarachnoid Haemorrhage, **SCA** = Superior Cerebellar Artery
3DTOF = 3 dimentional Time of Flight, **DAVF** = Dural AV Fistular, **MIP** = Maximum Intensity Projection

Cerebral aneurysms are found in 1 to14% of population[1] in USA, suggesting that more than 0.6 million people of Thai people have this serious lesion. Aneurysms, most commonly are discovered when they rupture and acute subarachnoid hemorrhage (SAH) ensues. Aneurysms are treatable lesions, with extremely high morbidity and mortality if left untreated.[1] Intracranial aneurysms represent a major public health problem in a population with increasing longevity, with considerable cost in terms of diagnostic work up, hospitalization, treatment, morbidity and mortality.[2] It has been long considered desirable 2 to have a noninvasive test to replace the invasive catheter angiogram, a procedure with documented morbidity and mortality.[3] Moreover at least in selected population such as 1st degree relative of a family member with aneurysm, it may be

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desirable to have a noninvasive screening examination for intracranial aneurysm because of the known very low morbidity (<5%) and mortality (0%) rates when an unruptured aneurysm is operated on.[7-9]

An improved Magnetic resonance angiogram (MRA) method might permit the early detection of intracranial aneurysm in patients and family members with a higher potential incidence of aneurysm and allow surgery before rupture of the aneurysm. An improved MRA post processing technique could directly reduce costs involved in diagnosis and follow up of the aneurysm by catheter angiogram, a higher cost, invasive procedure with known morbidity and mortality, a further source of high medical costs. To our knowledge, few blinded reader studies have been published on MRA for intracranial aneurysm proved by catheter angiogram, and most used the standard Maximum intensity projection (MIP) of post processing. In these studies,[12-15] the sensitivity of MRA for detection of aneurysms has ranged from 55.6 to 75% overall. These studies also showed a reduction in sensitivity for detection of smaller aneurysm. Two of these studies showed an increase in sensitivity in detection of aneurysm when conventional MRI was combined with MRA, a difference due mainly to the depiction of very large aneurysm known to be characterized by slow flow that often results in low signal intensity (SI) on MRA due to saturation effects. One shows very high sensitivity with advanced post processing The purpose of this study was to assess the accuracy of MRA in blinded-reader study for detection and characterization of angiographic proved aneurysm by using standard method of post processing. We hypothesized that the use of this technique would permit a high sensitivity and specificity for detection of intracranial aneurysm and would allow accurate characterization of aneurysm and morphology, an important indicator of prior rupture.

MATERIALS AND METHODS

SUBJECTS

All patients referred to our MR imaging suite for intracranial MRA during the previous 12 months (June 2000-2001) served as the initial data base for the study. Inclusion criterion was obtainment of both intracranial three dimensional time of flight (3DTOF) MRA and selective catheter angiograms. Subject was skewed toward those with a highly likelyhood of having vascular disease presenting with SAH. Exclusion criteria were the following : inability to recover the MRA data form optical disc for post processing, inability to recover catheter angiogram, failure to include the circle of Willis with the volume of MRA, severe motion.

50 patients who ranged in age form 21 to 77 years met the inclusion cliterion and were included in the final study. A total 200 vessels were examined with MRA and catheter angiogram. 38 aneurysms were studied and categorized by location and size as depicted on DSA and MRA. Of these 38 aneurysms, 3 were 1.0-2.4 cm and 35 were 0.4- 0.9 cm. 14 aneurysms originated from Anterior communicating artery (A-com), 8 from Posterior communicating artery (P-com), 7 from middle cerebral artery (MCA), 3 from internal carotid artery (ICA) and 6 from the vertebrobasilar system.

MRA TECHNIQUE

We used three dimensional time of flight technique without injection of exogenous contrast agent for MRA. In all cases, we used a four-slabs excitation divided into 24x4 sections, 8 mm in thickness, TR 27 msec, TE 7.2 msec and flip angle 20 degree. The acquisition matrix is 200x512.

Key Word : SAH = Subarachnoid Haemorrhage, **MIP** = Maximum Intensity Projection, **SI** = Signal Intensity.

MRA POST PROCESSING TECHNIQUE

A standard post processing protocol performed off- line 30 minutes was followed in all cases. 3 operated selected manually drawn, rectangular volumes of interest were determined from the collapsed volume image of the axial image for post processing, so that selective segmentation of the data could be obtained in the projection image. For each case, one standard volume of interest was selected to included the vertebrobasilar artery (VBA) system and one standard volume of interest was selected to encompass each ICA, MCA bifurcation region, (each carotid segmentation was designed to include A-com artery,) A series of 12 projection images at every 15 degree around the cephalocaudal axis were generated from each of the 3 volumes of interest. The segmented projections derived from the 3 standard volumes of interest were post processed by using the standard MIP. All images were then obtained on hard copy films for review with a format that presented rotations of projection images of ICA,MCA and VBA

MRA AND CATHETER ANGIOGRAPHIC INTERPRETATION.

MRA and catheter angiogram were evaluated separately and blindly by neuroradiologist whose experience in DSA for more than 10 years and MRA at least 2 years. The presence and ollowing characteristics of aneurysms (location, size and morphology) were asked

RESULTS

PRESENCE OF ANEURYSM

The data of blinded reader are shown in tables 1-3. overall sensitivity is 92.1% and specificity is 100 %, positive predictive value 100 % and negative predictive value is 81.3%.

SIZE OF ANEURYSM

Table 3 illustrates the relationship between size estimates from MRA as compared with the true luminal diameter as depicted on DSA, for all correctly identified aneurysm on MRA. The data indicated that in an average of 75% of correctly identified aneurysm on MRA, the correct size was noted. 16% of identified aneurysm, the MRA estimate of aneurysm size was too large and in an average of 11% of correctly identified aneurysm the estimate size was too small.

MORPHOLOGY OF ANEURYSM LUMEN

All aneurysm of this study was noted to have irregular contour (the indicating of ruptured aneurysm). This is due to characteristic selection of patients in our study (all patients presented with SAH)

Key Word : **A-com** = Anterior Commucating artery,
MCA = Middle Cerebral Artery,
ICA = Internal Carotid Artery,
VBA = Vertebrobasilar Artery,
P-com = Posterior Commucating artery,
3DTOF = 3 dimensinal Time of Flight,
SAH = Subarachnoid Haemorrhage.

Table 1 Sensitivity for detection of aneurysm with MRA

No .of aneurysms detected(n=38)	Sensitivity(%)
35	92.1

Table 2 Detection of at least one aneurysm in 37 patients known to have 38 aneurysms

Sensitivity(%)	Specificity(%)	Positive predictive value(%)	Negative predictive value(%)
92.1	100	100	81.2

Table 3 Size estimates of correctly identified aneurysms on MRA

Size Estimate	% (n=35)
Correct	75 (26)
Overestimate	14 (5)
Underestimate	11 (4)

DISCUSSION

Although MRA is a relatively new technique in the array of diagnostic tools to define cerebrovascular disease, it has already become accepted in some clinical setting of suspected neurological disease as an effective method of delineating vascular anomalies. This is particular true in the evaluation of suspected extracranial carotid atherosclerotic diseases.[19-25] However, it is also generally acknowledged that MRA still suffers from very important limitations in the depiction of intracranial vascular anomalies,[26] despite its attractiveness as a noninvasive modality. In our study, we attempted to investigate the accuracy of MRA for the detection and characterization of intracranial aneurysm by using standard post processing technique shown to have several advantages.

Our literature search revealed only few blinded-reader studies of MRA for intracranial aneurysm have been published in the radiology literatures to date, and all have noted relatively low sensitivity for these highly morbid yet treatable lesions. Ross et al[12] studies 21 aneurysms in 19 patients by using 3DTOFMRA and MIP method. 17 of the aneurysms were greater than 5 mms in diameter. Overall sensitivity of MRA was 67%and when combined with imaging the sensitivity was 86%. Huston et al[3] used 3DTOFMRA and MIP method in a combined-reader study, in which 2of 3 positive readings were needed to indicate positive, in 16 patients with 27 aneurysms. 22of 27 aneurysms were larger than 3 mm. Overall sensitivity was 55.6 % which rose to 87.5% if considering only aneurysm 5 mms in diameter or larger. Korogi et al[14] reported on 61 patients with 78 aneurysms in a 3DTOFMRA study with MIP method, 60 aneurysms were 5 mms or smaller. They also included 65 control subjects. Overall sensitivity for detection of aneurysm was 63 % which dropped to 56% for those aneurysms 2-5 mms in size. Scott W Atlas et al[15] used 3DTOF and advanced post processing method in 44 patients with 63 aneurysms and 15 patients with no aneurysms. Overall sensitivity is 75% and rose to 95% when considered only aneurysm larger than 3 mms

To date, most potential improvement for intracranial MRA of aneurysm has been the subject of post processing. In this still relative early stage of clinical evaluation of MRA for clinical efficacy, most investigators have used MIP post processing, so that the MIP has been de facto standard method. This situation has probably evolved because of the computational simplicity of the MIP.

Important problems with the MIP method were noted by Anderson et al.[10]

In the diagnostic work-up of intracranial aneurysms, there are specific characteristics of the lesion and surrounding vessels that the radiologist must demonstrate with any angiographic technique. An MRA protocol should be directed toward achieving these objectives for the study to be of clinical value, particularly if it is intended to be used as a replacement for catheter angiogram. Aside from the essential detection of the aneurysm in question, one must be documented of other aneurysms, since approximately one fourth of patients with one aneurysm have multiple aneurysms. This fact under scored the need for the four vessels study routinely obtained in the angiographic suite. Once an aneurysm is discovered, specific characteristic must be delineated, including the vessel of origin, definition of the aneurysmal neck, and the relationship of the aneurysm to nearby small vessels. The morphologic characteristic of the aneurysm must be displayed since this is the key feature of the aneurysm, that allow one to deduce which of the aneurysms had in fact ruptured. Additionally, the definition of the luminal size of the circle of Willis vessels must be fairly accurate for normal versus spasm which is so highly influential on the outcome of the patients. Our results indicate that with the MIP post processing technique a high degree of sensitivity for clinical diagnosis of intracranial aneurysm can be achieved by using MRA (table 2).

The data are promising if one analyzes the data with perspective that MRA could be used as screening test for the presence of these lesions, so that the identification of at least one aneurysm would necessitate a conventional angiogram. We acknowledge that the ultimate role of screening patients for the intracranial aneurysm is largely uncertain and the subject of several recent investigator. We do note that, not withstanding the relatively high sensitivity, specificity and positive predictive value with our method for most aneurysms, there remain a fairly substantial number of false negative studies, making MRA still unacceptable as the final diagnostic study for such a serious and treatable disease.

This study showed fair success in the characterization of aneurysm size and morphology. On approximately 3 in 4 aneurysms were correctly categorized according to size. Size is an important predictor of aneurysm rupture, since the proportion of aneurysm that rupture increases according to size.[30] Interestingly, about equal frequency of the over estimates and under estimate of the aneurysm size were found similar to the study of scott WA et al[15] In conclusion, intracranial MRA by using MIP post processing can result in highly sensitivity and specificity for the diagnosis of intracranial aneurysm that are of sufficient size to prompt serious consideration of surgical treatment. The positive predictive value is also very high but the negative predictive value is not high enough. It still be necessary to perform catheter angiogram in negative study of MRA for detection of aneurysm. Moreover this method of MRA is also relative accurate for size determination. Although the data are promising, a better understanding of natural history of intacranial aneurysms, as well as risk-benefit and cost-benefit assessment, will determine to a great extent the ultimate clinical role of MRA as a screening tool.

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PARADUODENAL HERNIA ; CASE REPORT

Siriporn POOLSIRI MD. [1],Watcharin CHUNSAM MD.[2]

Internal hernia is a clinical problem of abnormal internal rotation and fixation of the intestine. Paraduodenal hernias are the commonest of internal hernia. The symptom and sign are recurrent, intermitent intestinal obstruction and non specific chronic abdominal pain. Because the clinical diagnosis of internal hernia is often difficult, imaging studies such as upper gastrointestinal study and small bowel follow through play an important role in establishing the diagnosis. In this case, we reported a case of left paraduodenal hernia which the patient suffered from recurrent non specific chronic abdominal pain.

CASE REPORT

A 6 year - old Thai girl, presented several times with the chief complaint of chronic intermitent colicky abdominal epigastric pain, on and off over the past few years and having noticed that the symptom was aggrevated at night. Sometime, she presented with nausea and vomiting. Everytime, she was admitted and treated with bed rest, antispasmodic drug or treated as peptic ulcer or gastitis, which she was reported to have clinical improvement.

Plain abdomen, abdominal sonogram and the first upper GI study were read as normal study. Several months later, she presented again with the same complaint. Upper GI with small bowel follow through study was done and showed the loops of small bowel crowded together in the hernial sac and widely separated from other segment of terminal small bowel that remained in the peritonium cavity. Paraduodenal hernia was concluded (figure 1-5). Exploratory laparotomy was performed and found nearly total herniation of small bowel in a retroperitoneal space through a defect on the left mesocolon, and a left paraduodenal (mesocolic) hernia was diagnosed. The patient made an uneventful recovery after the hernia was surgically repaired.

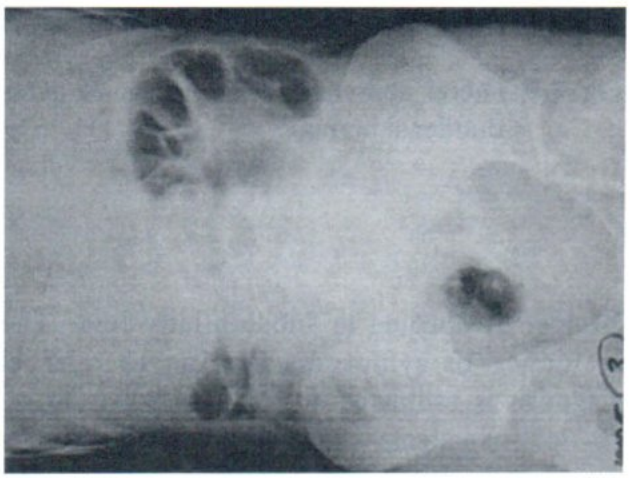

Fig. 1 A. Plain abdomen, supine

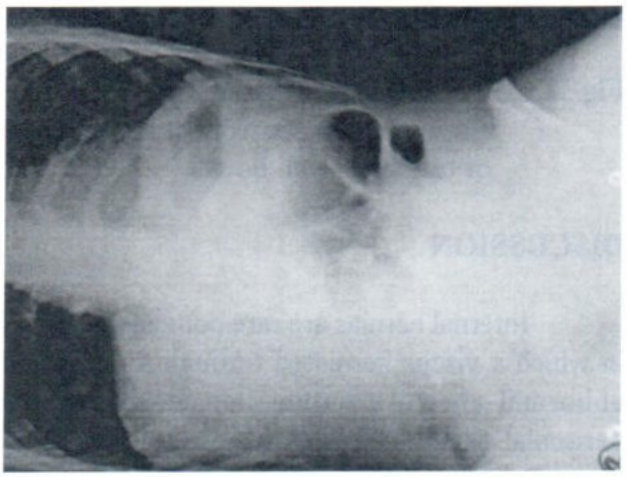

Fig.2 B. Plain abdomen, upright non specific small bowel dilatation.

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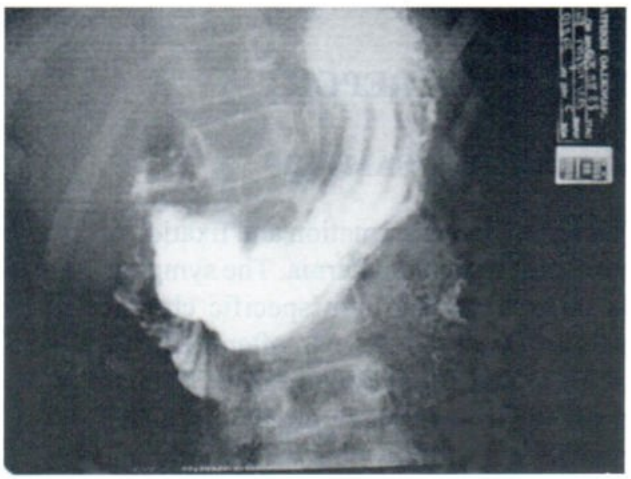

Fig 2 small bowel follow through study.
2.A normal stomach and duodenum.

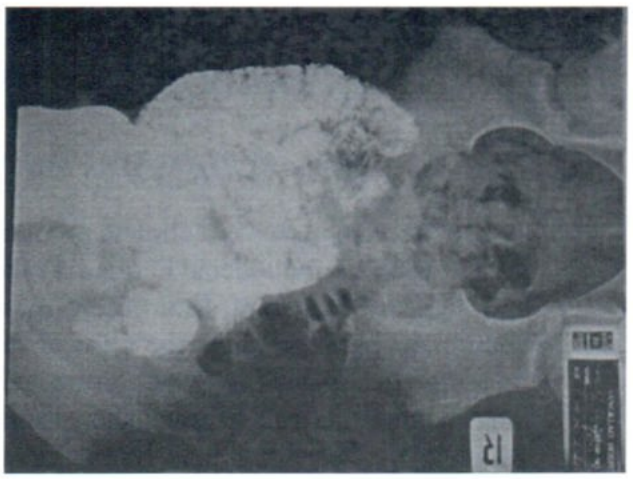

Fig. 2.B 15 min after intake minimal dilated bowel loops in the left upper quadrant of abdomen.

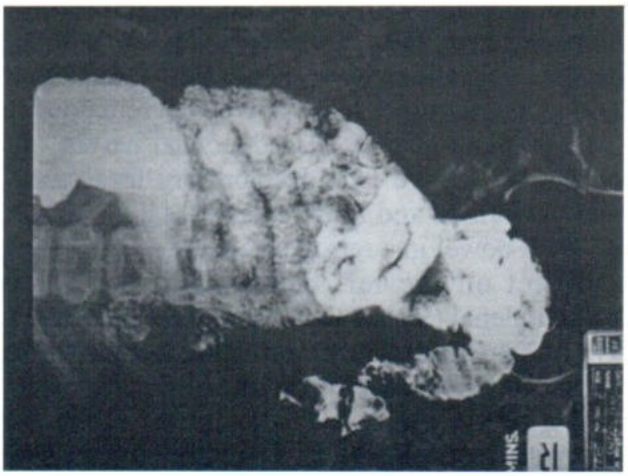

Fig. 2.C 30 min widely separated of small bowel loops in hernia sac from other segments of terminal small bowel.

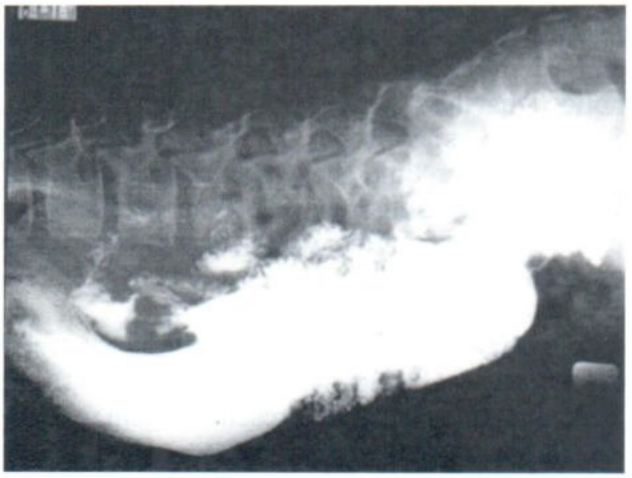

Fig. 2.D lateral abdomen, showing sac of para-duodenal hernia

DISCUSSION

Internal hernias are rare congenital lesions in which a viscus herniated through a normal or abnormal aperture within the confine of the peritonial cavity. The true incidence of rotation abnormalities of the mid gut is difficult to be determined. The autopsy prevalence is high as 0.5 to 1% of the total population but the incidence of clinical symptoms is substantially less. The incidence of symptoms leading to clinical diagnosis is estimated at 1 in 6,000 live births. 50- 75% of patients with malrotation who become symptomatic do so within the first month of life, and approximately 90% occur in children younger than 1 year of age. The remainder are seen later in life.

ETIOLOGY

1. Congenital. Some result from anormalous internal rotation causing various defects in the developing peritoneum and mesenteries with lack of fixation of the mesentery of right and left colon and of the duodenum, results in the formation of the potential hernial pouches that containing the herniated viscera become enlarged, and a portion of the developing bowel elongates within them.
2. Following trauma.
3. Post surgical procedure.

Internal hernias can contain a few loops of bowel or almost the entire small bowel. More than half of all internal hernias are paraduodenal, resulting from failure of the mesentery to fuse with the parietal peritonium at the ligament of Treitz (mesentericoparietal hernia). Depending on the position of the duodenum and the orientation of the opening of the paraduodenal fossa, either left or right paraduodenal hernias can result. The left paraduodenal hernia is about 3 to 4 times more frequent than the right.

CLINICAL FINDINGS

The presentation of patients with paraduodenal hernias, varies from mild intermittent gastrointestinal complaints to acute intestinal obstruction with volvulus and infarction from entrapment bowel, recurrent and intermittent bowel obstruction, which may lead to constant abdominal pain, vomiting and sometimes constipation. The symptoms are often considered to be psychological.

INVESTIGATION

A paraduodenal hernia is best demonstrated by an upper gastrointestinal series during the period of acute symptoms. Examination during an asymptomatic interval can fail to show the hernia or merely demonstrate a non specific dilatation with stasis and edematous mucosal folds.

Even at surgery a paraduodenal hernia may not be evident, either because of the spontaneous resolution of the hernia or because of an inadvertent operative reduction due to traction on small bowel loops. In addition, the extent of potential space in a peritoneal fossa seen at exploratory laparotomy is generally not appreciated from the relatively small size of the orifice of the fossa.

The small intestine generally fills the lower half of the abdomen, extending laterally into each flank, where it is bounded by the colon, and downward into the true pelvis. The jejunum chiefly occupies the left side of the abdomen, and the ileum the right. Dilated loops of the jejunum or ileum extending beyond the midline are strong presumptive sign of the presence of an internal hernia, torsion or adhesions. In both types of paraduodenal hernia, the principal radiographic finding is that of displaced, bunched loops of small bowel that appear to be confined in a sac. In partial obstruction, dilatation of bowel loops and delay in transit time can be noted. In the more common left paraduodenal hernia, small bowel loops pass into the paraduodenal fossa posteriorly and into the left mesocolon, producing dilated loops of bowel clustered in the left upper quadrant of the abdomen lateral to the fourth portion of the duodenum. Paraduodenal hernias occurring on the right side are associated with incomplete intestinal rotation. The junction of the duodenum and the jejunum has a low, right paramedian position. The duodenum is dilated with the jejunal loops situated on the right side of the abdomen, extending into the right transverse mesocolon. In both types of paraduodenal hernias, transverse colon tend to be depressed inferiorly by the mass.

Repeated episodes of paradiodenal herniation can increase the size of the defect and lead to adhesions between the trapped bowel and hernia sac. This process can result in obsruction or circulatory compromise. Therefore, even a small paraduodenal hernia is potentially dangerous and is usually considered to be an operable condition.

TREATMENT

Neonates and infants with rotational abnormalities require operative management, laparotomy. The management of the older asymptomatic patient with malrotation is controversial.

In this case, the patient presents with suggestive symptom even though the initial investigation including ultrasonogram of the whole abdomen, and the first upper GI study are negative, resulting in the delay of the surgical treatment. The second gastrointestinal follow through study was done during acute symptom which resultted in the demonstration of the paraduodenal hernia. The finding led to curative treatment with exploratory laparotomy.

CONCLUSION

Paraduodenal hernias are rare. Most of them are congenital, but the rest are incidences of after trauma or post surgical procedure. They usually present during early childhood and often were delayed due to non specific abdominal symptoms. During asymptomatic period, definitive diagnosis may be possible. With recurrent and intermittent intestinal obstruction, upper gastrointestinal series study is recommened during acute symptom.

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SPONTANEOUS INTRACRANIAL HYPOTENSION : A CASE REPORT

Chewarat WIROJTANANUGOON, MD, Wiyada BHOOPAT, MD

Spontaneous intracranial hypotension (SIH) is uncommon and can be misdiagnosed as Chiari I malformation, carcinomatous meningitis, idiopathic hypertrophic pachymeningitis, or subdural hematoma. If this is not recognized, it could lead to improper management. Many have been reported in the literature abroad, but to our knowledge, not in Thailand. Therefore we would like to present our case of SIH along with the overseas literature reviews.

CASE REPORT

A 42-year-old man presented with 1-month history of headache, predominantly at the occiput and a flashing pain along the right arm when he turned his neck. Previously, he had been healthy and had had no history of operation, trauma or lumbar puncture. Physical examination revealed no abnormality. Plain films of the cervical spine showed no abnormality.

MRI of the spine and brain was performed. Cranial sagittal and axial MR images revealed bilateral subdural effusions, generalized descent of midline structures that crowded the posterior fossa with tonsilar herniation, flattening of the pons against the clivus and elongated shape of the midbrain (Figure1-3). Postgadolinium enhanced images showed diffuse symmetrical pachymeningeal enhancement which is often referred to as pachymeningitis (Figure4). On MRI of the whole spine, there was only mild anterior epidural enhancement at the level of C2, but no spinal hygroma (subdural or epidural fluid collection) was observed.

The MRI findings are compatible with spontaneous intracranial hypotension. Additional information that the headache was relieved by lying down and that onset occurred after trying to move a heavy cabinet was obtained.

Conservative treatment was performed (high fluid intake and bed rest) and followed by clinical improvement.

Repeated cranial MR images obtained 4 months later demonstrated complete resolution of the disease. (Figure 5-6)

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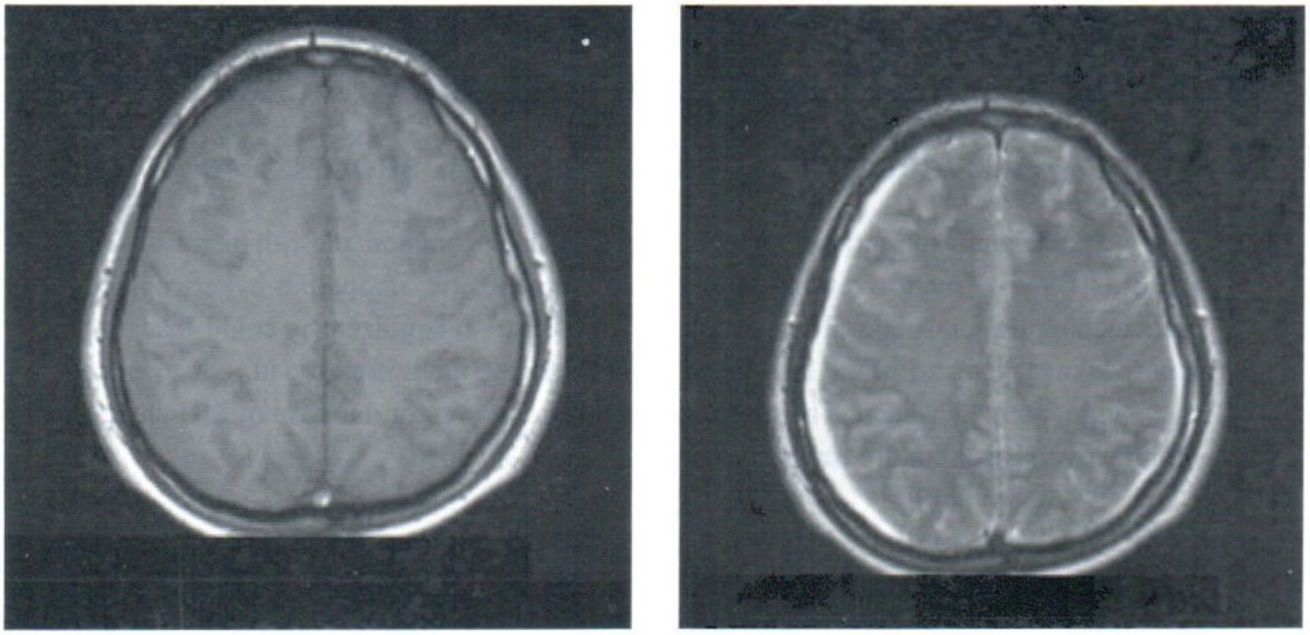
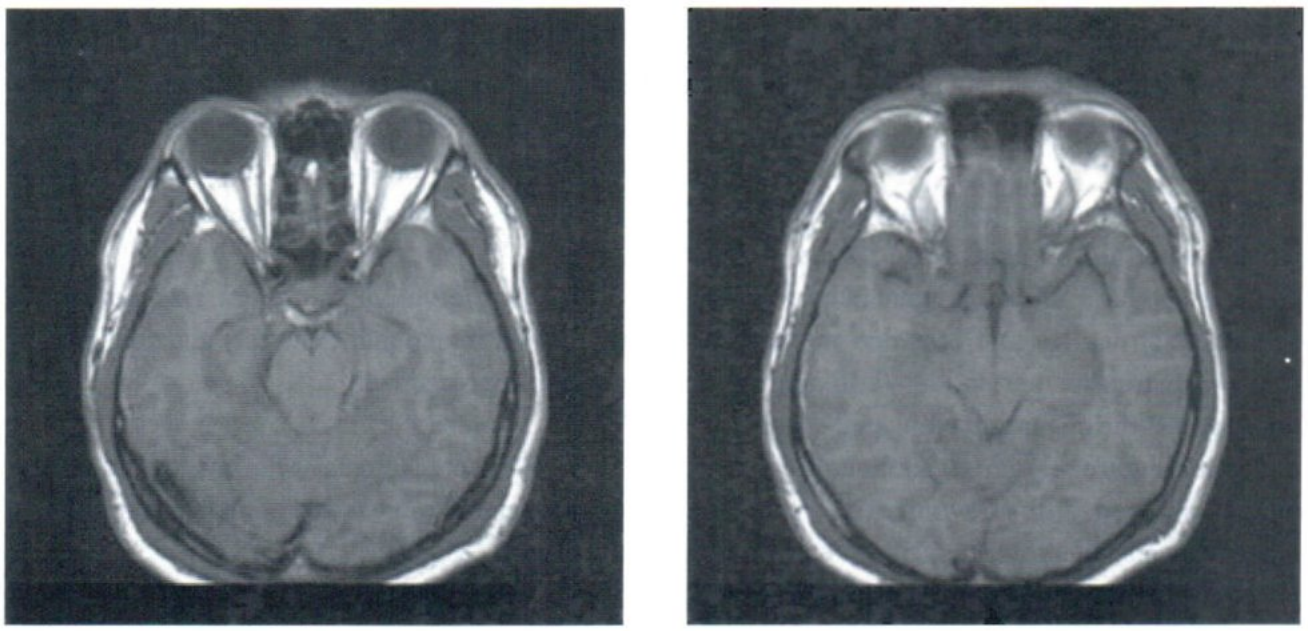


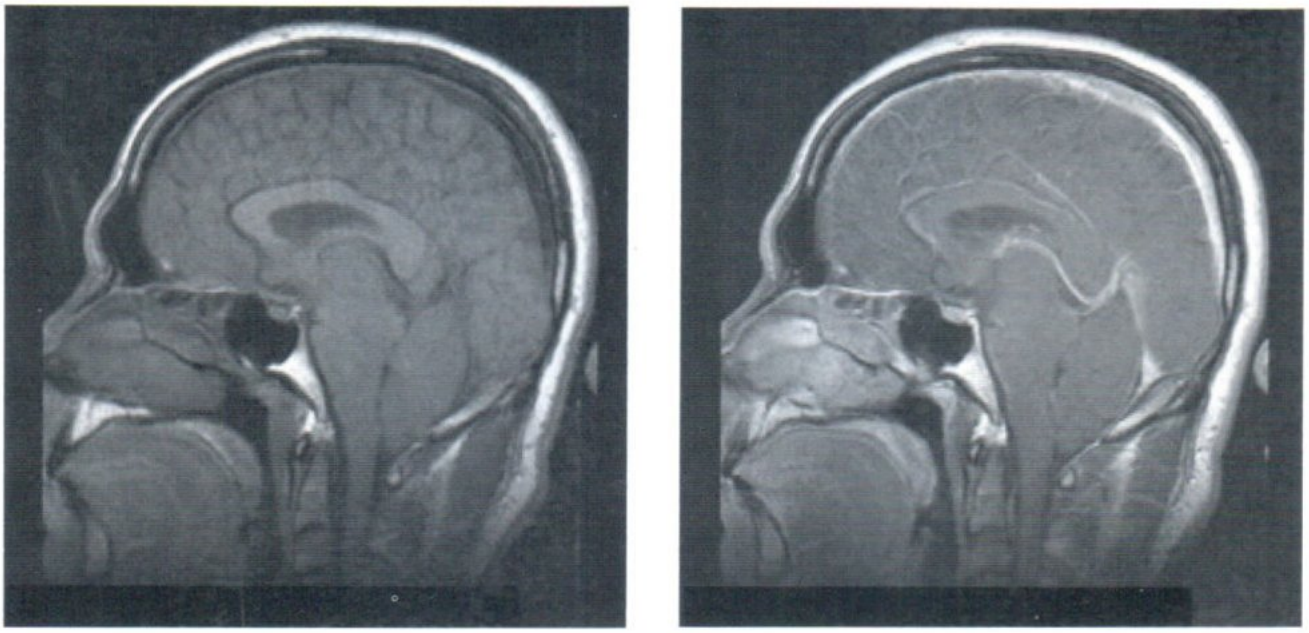
1A 1B

Fig. 1. Axial SE T1WI (A) and FSE T2WI (B) show bilateral subdural effusion.



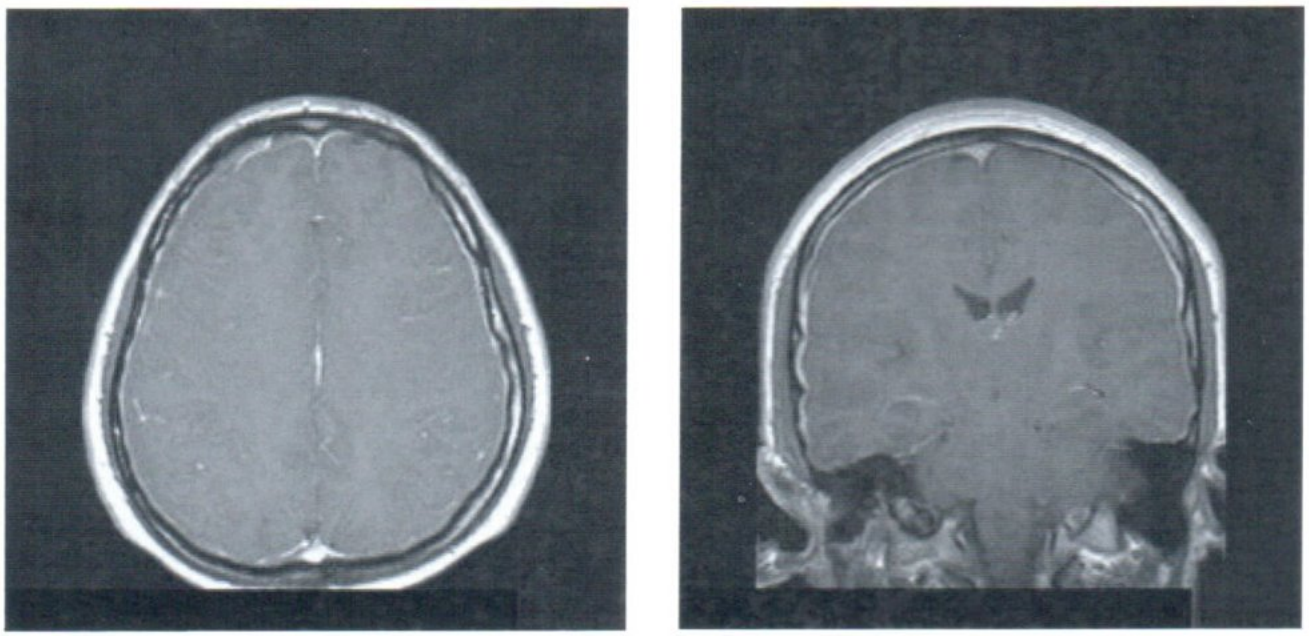
2A 2B

Fig. 2. Axial SE T1-weighted images at the level of midbrain show elongated shape of the midbrain in AP dimension with effacement of basal cisterns due to descent of the midline structure.



3A 3B

Fig. 3. Pregadolium-enhanced (A), and postgadolinium-enhanced (B) sagittal SE T1WI show flattening of the pons against the clivus and tonsilar herniation. Venous dilatation is also noted on the postcontrast image.



4A 4B

Fig. 4. Postgadolium-enhanced axial (A) and coronal (B) SE T1WI show diffuse symmetrical pachymeningeal enhancement.

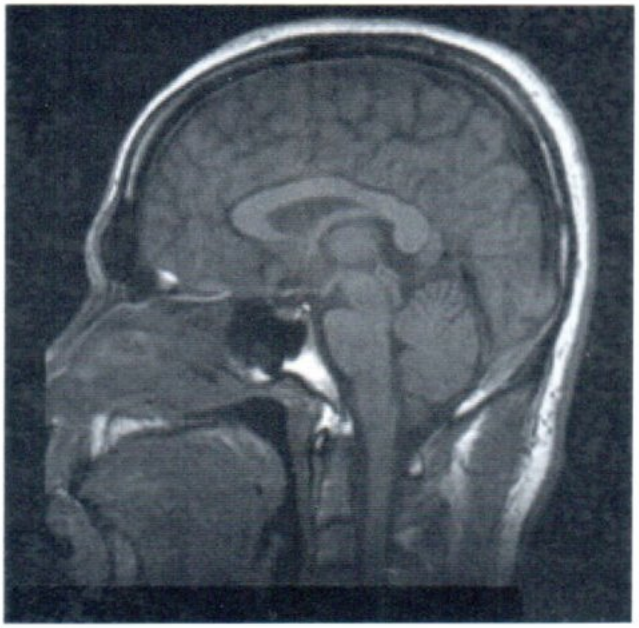
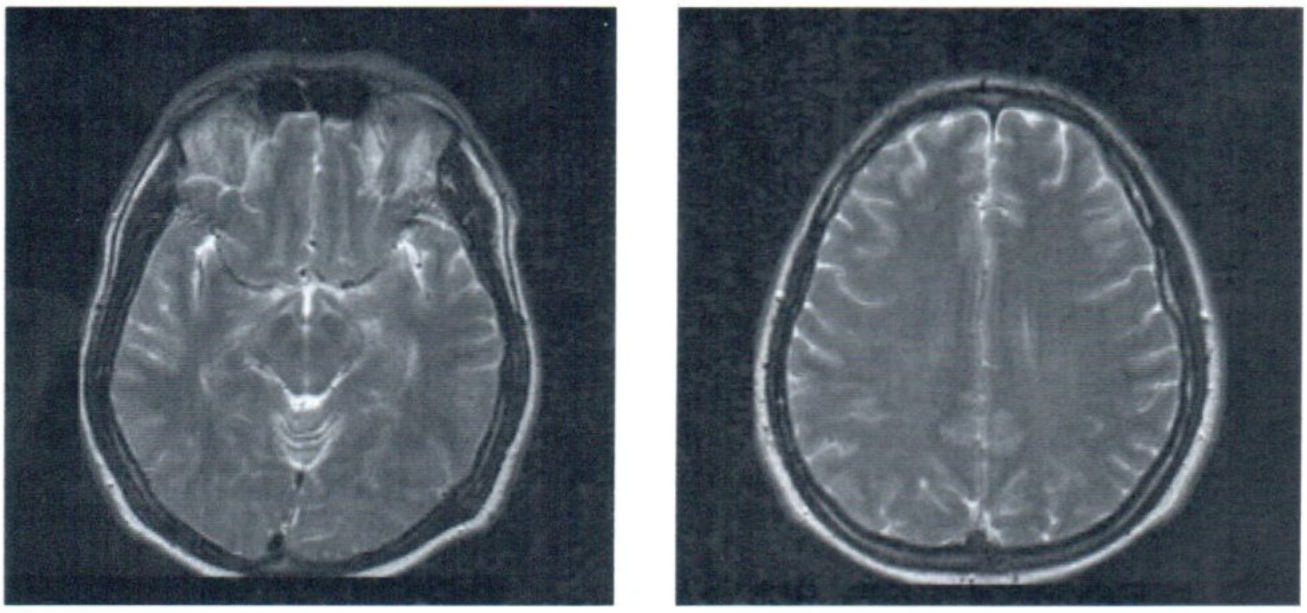


Fig. 5. Sagittal SE T1WI after conservative treatment demonstrates disappearance of flattening of the pons against the clivus and inferior displacement of the brain.



3A **3B**

Fig. 6. Axial FSE T2WI after conservative treatment 4 months later, shows normal appearance of the midbrain and basal cistern (A) and complete disappearance of the bilateral subdural collections (B).

DISCUSSION AND REVIEW OF LITERATURE

Spontaneous intracranial hypotension was first described by Schaltenbrand in 1938. Three mechanisms were suggested by Schaltenbrand: occult dural tear, overabsorption of CSF, and decreased CSF production. The similarity of SIH to the post-LP headache syndrome supports the notion that a CSF leak may be the cause.

In 1968, Teng and Papatheodorou summarized findings in 31 cases and found a female preponderance of 3.4:1 with the majority of patients in the third or fourth decade of life.

Epidemiological studies have not been reported, but the prevalence of SIH in Olmsted County, Minnesota, in 1995 was approximately one in 50,000 patients (unpublished data).[18]

The leak is typically at the level of the spine, particularly the thoracic spine and cervicothoracic spine, rarely at the skull base. CT myelography and radionuclide cisternography are the most useful radiographic studies to diagnose and localize the spinal CSF leak.

The cause of CSF leakage reported in the literature are a cervical bone spur,[14] disc herniation,[2] meningeal diverticula, tear in the nerve root sleeves, or Tarlov's cyst. However it often remains undetermined. In a substantial minority of patients, there is a history of trivial or minor trauma (as in our case)or evidence of connective tissue disease (eg. Marfan's syndrome, Ehlers-Danlos syndrome, NF, ADPCK, etc)[4,5]

The common clinical features of SIH are orthostatic headaches, neck or interscapular pain, nausea, emesis, horizontal diplopia, change in hearing, blurring of vision, facial numbness and upper limb radicular symptoms.[3,6,15,16]

The headache associated with SIH is probably caused by dilatation of cerebral veins and meningeal vasculature because there is a reciprocal relationship between CSF volume and intracranial blood volume (The Monroe-Kelly rule)[9]; it may be a consequence of the low CSF pressure producing displacement of pain-sensitive structure (particularly traction of the intracranial dura); or both factors may be involved.[1]

The average human brain weights approximately 1400g in air. When floating freely in CSF, the human brain has an effective weight of approximately 50 g. The brain depends greatly on the antigravity effect of CSF to maintain its delicate structure. Robbed of this buoyancy, the brain may sag, collapsing in on itself.[15]

The headache may be gradual or acute in onset and may be generalized or localized to the frontal or occipital regions.[10]

Visual disturbances are related to occur in 23% of patients and may be attributed to distortion of the optic chiasm or compression or vascular congestion of the intracranial portions of the optic nerves.

Auditory or vestibular symptoms include hypoacusis, hyperacusis, tinnitus, nausea, vomiting and dizziness. These are reported to occur in approximately 20% of cases and probably result from a change in intralabyrinthine pressure transmitted through the cochlear aqueduct.[1]

The diagnosis of intracranial hypotension is confirmed by a low (< 6cm H2O) or low-normal opening pressure on LP. Results of examination of CSF may be normal or show mildly raised

protein levels, increased cell count, or xanthochromia; these may be caused by meningeal hyperemia resulting from the low CSF pressure, accompanied by diapedesis of cells into the subarachnoid space or from disruption of the normal hydrostatic and osmotic pressure across the venous sinuses and arachnoid villi, accompanied by protein accumulation.[1,12]

On cranial MR imaging, subdural effusions are seen in approximately 10% of cases and are probably the result of the rupture of bridging veins caused by the decrease in CSF volume and downward displacement of the brain. Subdural effusions or hematomas in SIH have been shown not to be under pressure. Diffuse thickening of the meninges and choroid plexus, and meningeal enhancement may result from dilated meningeal vessels and small vessel rupture.[7]

In a few cases, meningeal biopsy samples have either shown nonspecific inflammation or no abnormality, supporting the hypothesis that dural enhancement is caused by venous enlargement.

The spinal manifestations associated with SIH-spinal dural enhancement, spinal epidural venous engorgement, subdural or epidural collections (spinal hygroma)- have been reported by several authors.[8,17]

Conservative treatment, with bed rest and high fluid intake, often suffices. Symptoms, however, can take several months to resolve. A short course of steroid medication or orally administered caffeine may be considered.[2]

If conservative measures fail to resolve symptoms, then extradural saline infusions or and epidural blood patch can be effective at stopping the leak, even if the source of the CSF fistula has not been demonstrated.[11] The epidural blood reportedly can travel up to nine spinal segments from its site of placement. Epidural blood produces an organized clot that could effectively tamponade any dural CSF leak. The rapid relief from headache seen immediately after the infusion of the blood must occur by some other mechanism, such as an increase in subarachnoid pressure. Placement of epidural blood patch can be repeated at the same level or applied directly at the site of CSF fistula.[11]

The indications for surgical treatment of spontaneous spinal CSF leakage have not been firmly established. The most straightforward indication may be the presence of persistent symptoms in spite of the placement of multiple epidural blood patches in a patient in whom a discrete leaking meningeal diverticulum has been radiographically demonstrated. In addition, surgery may be considered as the primary treatment in all patients who have such meningeal diverticula, particularly when the patients are young and the diverticula are large. Spinal meningeal diverticula may grow and cause other neurological symptoms.[18]

In our case, history of postural related headache was initially missed. If we did not recognize this condition, it would have been misdiagnosed as bilateral chronic subdural hematomas, and proper management would have been delayed. Lumbar puncture was not done in this case, because the MR findings, symptom of postural headache and absence of history of LP were sufficient to diagnose SIH. The patient has been asymptomatic for 7 months up to now after conservative treatment. So further investigation for the site of CSF leakage (myelography or radionuclide cisternography) and epidural blood patching were not performed.

CONCLUSION

The imaging and clinical manifestation of

SIH have become well known, many patients have been diagnosed who otherwise would have been misdiagnosed with migraine, headache of unknown origin, aseptic meningitis, or subdural hematomas. Attention to the myriad manifestations of CSF hypovolemia both intracranially and extracranially will prevent such errors of diagnosis and facilitate prompt treatment of CSF fistula.

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MAMMOGRAPHY OF THE IRRADIATED BREASTS

Tatsanee TANGPRASERT,M.D.

Purpose : To evaluate the mammographic findings and role of detection of local recurrence in breast cancer patients, who underwent breast conserving surgery and radiation therapy.

Materials and methods : From 1988 to 1998, 78 women with early breast cancer (stage I,II) were treated with lumpectomy and axillary nodes resection, followed by radiation treatment. Mammographic imagings were taken yearly after complete treatment. Needle biopsy was done for suspected local recurrence on mammography.

Results : Duration of follow-up ranged from 3 years to 10 years. Seventy-three of 78 patients (93.6%) had evidence of parenchymal changes on serial annual mammography. Twenty-eight of 73 (38.4%) had diffuse dense parenchymal changes. Twenty-four of 73 patients (32.9%) had focal fibrotic changes, and 21 of 73 patients (28.8%) had evidence of parenchymal distortion with mass like lesion. Skin thickening was found in 54 of 78 patients (69.2%). Calcification was the least change, found in only 2 of 78 patients (2.6%). Nine of 78 patients (11.5%) had mammographic signs of local recurrence. Seven of 9 had suspected local recurrence by needle biopsy. Four of seven had proven of local recurrence on mastectomy, and 3 of 7 (42.8 %) had false positive on mastectomy.

Conclusion : Annual mammography in post breast conserving treatment showed beneficial results for detection of recurrent cancer with acceptable false positive rate.

INTRODUCTION

Many randomized trials had published the comparable results between breast conserving treatment and mastectomy.[1,2,3,4] There was no statistically significant difference in the overall survival or disease-free survival. However, some reported a higher risk of local recurrence in breast conserving group than mastectomy group.[2]

In Thailand, breast cancer was the second most common cancer in women following cancer of the uterine cervix. Before the last decade, most of the early stages cancer (stage I and II) were treated by mastectomy. Because of the excellent cosmetic result of breast conserving treatment, which assured woman self-esteem, this treatment protocol became more recognized and more popular as an alternative choice of treatment. However, the goals of cancer treatment were to obtain the cure rate and prolong disease-free survival. So, early detection of curable local recurrence was the most important challenge.

The purpose of this study were to evaluate the mammographic changes of post conserving treated breasts and the role of such changes in the detection of the local recurrences

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in the earliest stage as possible.

METERIALS AND METHODS

From 1988 to 1998, 78 women with pathological diagnosis of early stage of invasive ductal carcinoma were treated with breast conserving treatment.

Inclusion criterias:

1. Stage I and II invasive ductal carcinoma.
2. Primary tumor less than 5 cm in diameter.
3. No evidence of distant metastasis.

Exclusion criterias :

1. Multifoci carcinomas.
2. Presence of extensive intraductal carcinoma components.
3. Pendulous and fatty breasts.
4. Poor compliance for regular follow-up.

Treatment protocol :

Surgical procedure consisted of lumpectomy with axillary nodes dissection. Free surgical margin was required. Radiation therapy was started within 2-3 weeks after surgery. The radiation dose of 4500 - 5400 cGy with 5 - 5½ weeks was delivered to the afftected breasts, using Linac 6 MV Therapy, both medial and lateral tangential fields techinque.

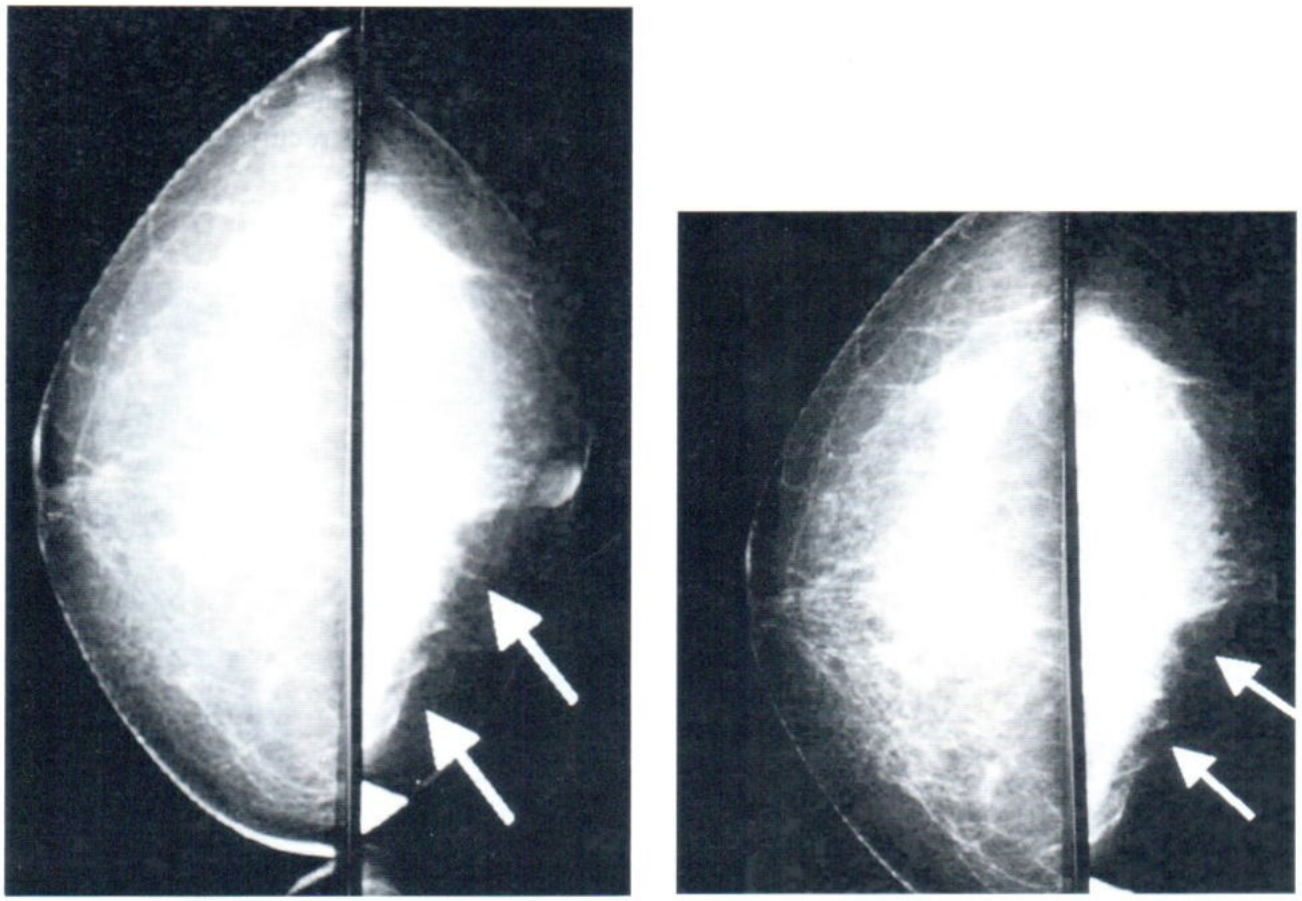
The surgical scars were boosted with additional 1000 cGy in 5 fractions with Electron beam.

Annual mammography was done after 12 months of radiation. Routine imaging consisted of cephalocaudad and lateromedial oblique views. Spot and magnification views were obtained in cases of interval changes. Needle biopsy was done in patients who had mammographic changes which suspected of local recurrence.

RESULTS

From 1988 to 1998, 78 women with pathological diagnosis of stage I and II invasive ductal carcinomas were included in the study. Age of the patients ranged from 26 years to 63 years, median age was 35 years. Primary tumor size ranged from 1 cm to 4 cm in diameter. The majority of patients had tumor less than 4 cm diameter, about 75 of 78 patients (96.2 %). Only 3 patients had 4 cm tumor masses. Duration of follow-up ranged from 3 to 10 years.

Parenchymal changes were the most common changes on mammography, accounted about 73 of 78 patients (93.6%). Twenty-eight of them showed diffuse dense parenchyma on mammography. Twenty-four of 73 patients (32.9%) had focal fibrotic changes, and 21 of 73 patients (28.8%) had parenchymal distortion with mass like lesions. Skin thickening was found in 54 of 78 patients (69.2%). Calcification was the least change, and was found in only 2 of 78 patients (2.6%). Most of the patients had more than one mammographic changes.

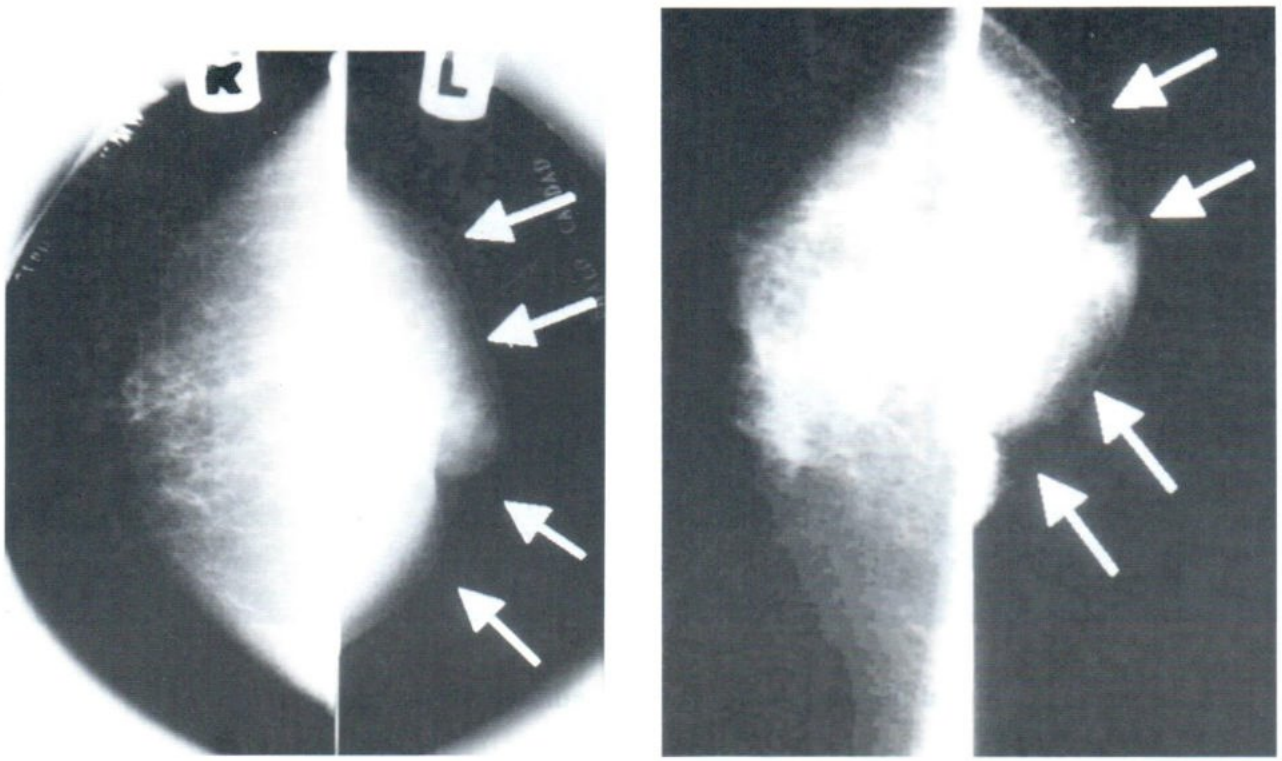


Focal fibrotic changes of the radiated breast (arrows)

Table showed mammographic findings.

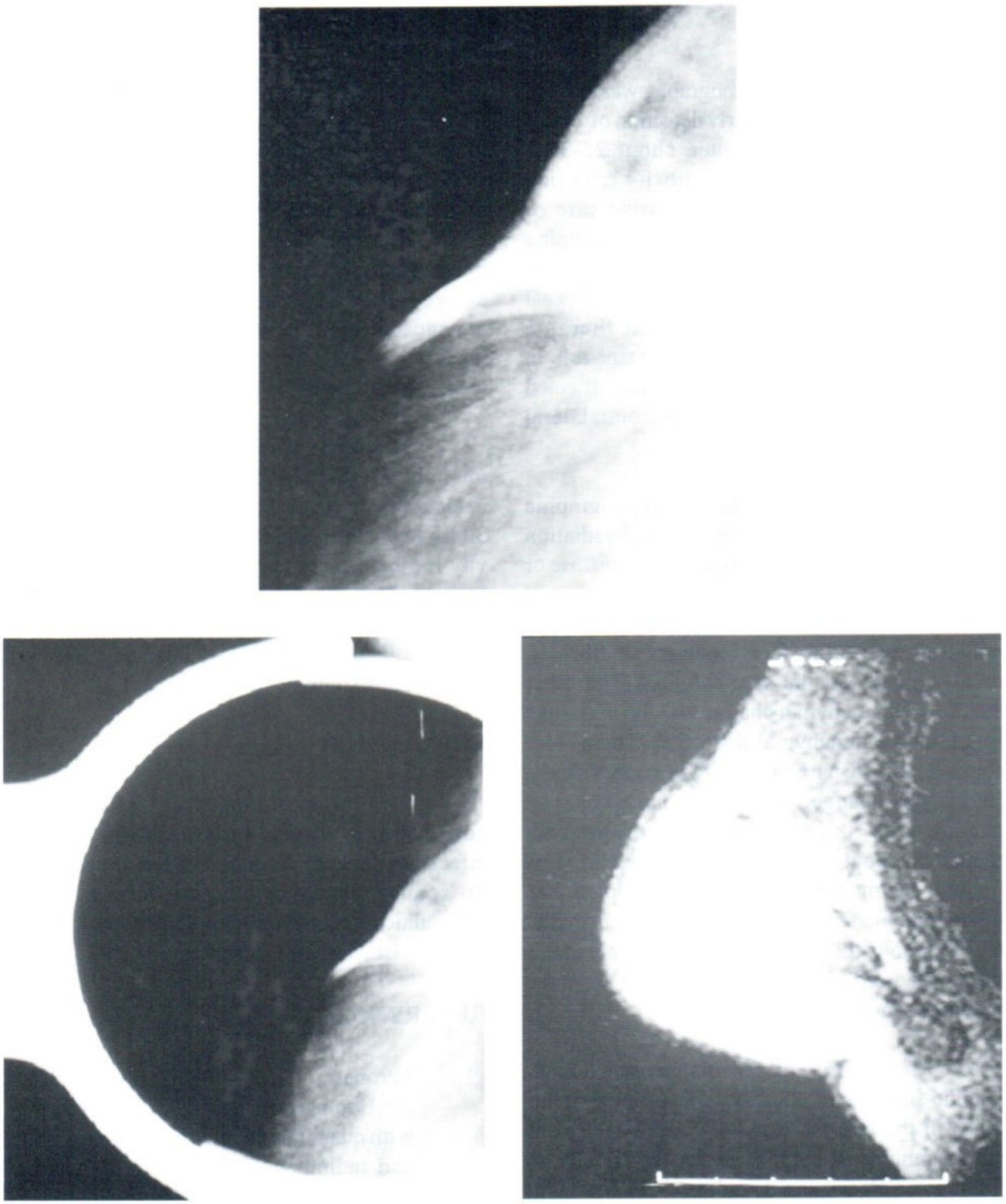
	Mammography findings	Number	Percentage
1.	Paenchymal changes	73	93.6%
	- diffuse dense	28	38.4%
	- focal fibrosis	24	32.9%
	- mass like with parenchymal distortion	21	28.8%
2.	Skin thickening	54	69.2%
3.	Calcification	2	2.6%
4.	No significant change	2	6.8%
	Total	78 patients	

Nine of 78 patients had mammographic signs of suspected local recurrence, (criterias included new appearance of mass-like lesion with parenchymal distortion with or without palpable mass on physical examination). Seven of them had suspected malignant cells on needle biopsy. All patients underwent mastectomy. Four of seven patients had proven recurrent invasive carcinoma in mastectomy specimens. The rest of 3 patients had false positive of recurrent carcinoma in mastectomy specimens.



Diffuse dense parenchymal changes of radisted breast

Case reported of false positive mammography : A 52 year woman was diagnosed as invasive ductal carcinoma, primary tumor about 3 cm in diameter. She underwent breast conserving surgery (pathological reported of free surgical margin, with negative involvement of all 16 dissected axillary nodes). She was treated with a complete course of radiation therapy within 10 days after surgery. The third of her annual follow-up mammography, a new mass-like lesion, without microcalcification was found at the surgical scar. MR imaging with gadolinium-DTPA showed an enhanced lesion, suggestive of recurrent tumor. Fine-needle biopsy showed suspected malignant cells. Mastectomy was performed within 7 days. Pathological report showed a cluster of microabscesses with fibrosis of the suspected lesion, no evidence of malignant cells on surgical specimen (Picture shown below).



Mass-like lesion

DISCUSSION

In this decade, mammography was proven to be the gold standard for early detection of breast cancer. It showed to produce about 25-30% reduction in breast cancer mortality for screening program.[5,6,7] However, false negative rate of cancer detection in mammography for screening program remained high, up to 15-20 %.[8,9,10,11] For breast cancer patients who underwent breast conserving surgery and radiation therapy, mammography also played an important role in the detection of local recurrence in the afftected breast and possible cancer in the contralateral breast.

In this study, the main mammographic changes after conserving surgery and radiation was parenchymal tissue changes (either diffuse or focal). The diffuse parenchymal changes of increasing in breast density was secondary to radiation, while the focal changes of fibrosis, usually located at the surgical sites. The other feature of parenchymal change was the mass-like lesion with parenchymal distortion. There were about 21 of 78 patients (28.8%) in this study, having this change. The second most common change was skin thickening, which were accounted about 54 of 78 patients (69.3%). This finding was more common in Thai women than western women, which may due to rather smaller breasts among them. Calcification was rare in this study, occurred in only 2 patients, and appeared as dense benign calcifications.

The majority of patients whose mammographic findings mimic the signs of local recurrence in the affected breasts, (mass-like lesions with parenchymal distortion) showed stability of findings on closed serial studies. Only 9 patients demonstrated progression of changes, and the interventional cytology were performed. Seven of 9 patients had the findings of suspected malignant cells on fine-needle biopsy. Only 4 of the 9 patients were proven of recurrent cancer in the mastectomy specimens. Two patients had false positive in the mastectomy specimens and evidence of fat necrosis and massive fibrosis noted at the surgical sites. Because of more concerned about false positive mastectomy, additional MR imaging was performed in the last patient (shown above). The MR imaging also showed an enhanced lesion at the surgical site. But the mastectomy specimen was shown to have a cluster of microabscesses.

The false positive result of MR imaging might be due to its limited specificity for cancer detection with reports of specificity ranged from 30 to 90 %, even it demonstrated a high sensitivity for the detection of abnormal breast lesions, both malignancy and some benign lesions, such as atypical hyperplasia and sclerosing adenosis.[12,13,14,15] No case of false negative was noted in this study.

CONCLUSION

Annual mammography after breast conserving surgery and radiation showed effeciency in early detection of local recurrence. To reduce the false positive rate, a closed communication between surgeon, radiologist and pathologist was recommended.

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BRONCHIAL ARTERY EMBOLIZATION FOR HEMOPTYSIS : EXPERIENCEIN SRINAGARIND HOSPITAL, KHON KAEN UNIVERSITY

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ABSTRACT

Purpose: The purpose of this retrospective study was to report our experience with bronchial angiography and bronchial embolization.

Materials and Methods: A retrospectively reviewed medical record and imagings of 32 patients presented with moderated to severe hemoptysis who underwent to bronchial angiography and embolization at Srinagarind hospital Khon Kaen University from 1999 to 2002.

Results: The majority of the etiologies of hemoptysis in our series were tuberculous bronchiectasis (14 patients), pulmonary tuberculosis (9 patients) and nontuberculous bronchiectasis (6 patients). The findings of angiography included hypervascularity in 100% (32 of 32), bronchial artery hypertrophy and tortuousity in 59.3% (19 of 32), parenchymatous staining in 75.0% (24 of 32), pseudoaneurysm formation in 9.3% (3 of 32), bronchial to pulmonary artery communication in 6.2% (2 of 32) and extravasation of contrast medium into bronchial lumen in 3.3% (1 of 32). We achieved an overall success rate of 87.5% (28 of 32), in immediately control of hemoptysis and technical success rate of 98.87% (31 of 32). Recurrent rate of hemoptysis was 9.4% (3 of 32) within 1 month and 9.4% (3 of 32) in more than 1 month.

The complications of bronchial embolization in our series included subintimal dissection in one patient and chest pain during the embolization procedure in two patients.

Conclusion: Bronchial embolization is an effective and safe procedure to control hemoptysis, particularly in emergency control of hemoptysis which caused by benign diseases. Bronchial embolization may help to avoid surgery in patients who are not good surgical candidates.

INTRODUCTION

Bronchial artery embolization is a well-accepted and widely utilized technique in the management of massive hemopotysis,[1] which is defined as having blood loss of 300-600 ml over 24 hrs.[2,3] Bronchial artery embolization has been established for the treatment of massive hemop-

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tysis as an effective alternative to surgical resection in emergency treatment of massive hemoptysis which carries a mortality rate of 50-85%.[2] The cause of death is usually asphyxia. Many of the patients with severe hemoptysis are poor surgical candidates with poor respiratory reserve from extensive disease. Over the last few years, an increasing number of the patients with moderate hemoptysis have been referred to our department or emergency bronchial angiography and embolization. Our hospital is a referral tertiary center of the northeast Thailand, we therefore get the majority of bronchial embolization cases in the northeastern part of Thailand. The purpose of this retrospective study was to report our experience with bronchial angiography and bronchial embolization.

MATERIALS AND METHODS

Over a 4-years period, from 1999 to 2002, a total number of 32 patients presented with moderate to severe hemoptysis were consulted for bronchial angiography and embolization. Thirty-two patients had bronchial digital substraction angiography and embolization were performed via the femoral route. In all cases a 5Fcatheter sheath was inserted to facilitate multiple catheter changes if necessary. We used pre-shaped 4F-5F angiographic catheters. The commonest initial shape chosen was the Side-wider. Other catheters employed were the Cobra, the simple curve catheter. The guidewire used in all cases was 0.035 inch Terumo guidewire. The embolic material used was Gelfoam^{R} particles. The medical records and medical imagings of the patients who underwent bronchial angiography and embolization at the department of radiology, Khon Kaen University between 1999 and 2002 were reviewed.

RESULTS:

A total number of bronchial angiography and embolization was 32 cases. Etiology of the hemoptysis was shown in Table 1, with the majority of cases being due to tuberculous bronchiectasis. The age range of the patients was from 9-67 years (mean 58 years). There were 18 men and 14 women. Our oldest case was infected bronchiectasis with old pulmonary TB, while our youngest case was a patient with status post modified BT shunt operation of DORV with VSD.

Bronchial angiography was performed in all patients. The findings of angiography included hypervascularity (Fig. 1) in 32 patients (100%), bronchial artery hypertrophy and tortuousity (Fig. 2) in 19 patients (59.3%), parenchymatous staining (Fig. 3) in 24 patients (75.0%), pseudoaneurysm formation (Fig. 4) in 3 patients (9.3%), bronchial to pulmonary artery communication (Fig. 5) in 2 patients (6.2%) and extravasation of contrast medium into bronchial lumen in 1 patient (3.3%). In our series, no nonbronchial systemic arterial or pulmonary arterial supply hemoptysis lung was demonstrated.

Bronchial artery embolization was performed in all patients (Fig. 6). The procedure was performed using selective technique. Bronchial embolization was technical successful in 31 of 32 patients (98.87%). The case of technical unsuccessful was due to subintimal dissection of the bronchial artery origin during embolization procedure. Bronchial embolization was successful controlling hemoptysis immediately in 28 of 32 patients (87.5%). Four patients had failure in controlling hemoptysis immediately. One of these patients, with severe pulmonary TB and destroyed both lungs which the angiography showed pseudoaneurysm formation, died 3 days after the attempted procedure due to sepsis. One of these patients, with infected bronchiectasis required surgery (subintimal dissection at the bronchial artery during embolization procedure, technical failure) One patient with status post BT shunt operation of DORV with VSD, required surgery to control hemoptysis 3 days after bronchial

BT shunt = Blalock taussig shunt

embolization and another patient, with malignant mesothelioma, fail to control hemoptysis before chemotherapy. Three patients had recurrent hemoptysis within 1 mouth after bronchial embolization. One of these patients, nontuberculous bronchiectasis, died of hemoptysis at his home 3 weeks after undergoing embolization. One patient with bronchiectasis underwent successful repeated embolization and another patient with tuberculous bronchiectasis required surgery.

Three patients had recurrent hemoptysis more than 1 month after undergoing bronchial embolization. Hemoptysis in one of these patients (old pulmonary tuberculosis) was mild degree off and on hemoptysis and resolved with antibiotic therapy. Two patients (tuberculous bronchiectasis) underwent successful repeated embolization 1.5 and 2 years after the first embolization.

The complications of bronchial embolization in our series included subintimal dissection in one patient and chest pain during the embolization procedure in two patients.

From the total bronchial embolization of 32 of patients, one patient had technical failure, three patients were failed in controlling hemoptysis immediately, four patients had recurrent hemoptysis within 1 mouth and three patients had recurrent hemoptysis more than 1 month as describe above. The remaining 20 patients with single session embolization and 3 patients with repeated embolization had follow up period ranging from 3 months to 3 years without evidence of recurrent hemoptysis.

Table 1. Etiology of hemoptysis

Etiology	No of cases
Tuberculous bronchiectasis	14
Pulmonary TB	9
Infected bronchiectasis (nontuberculous bronchiectasis)	6
Status post BT shunt of a case with DORV and VSD	1
Acquired heart disease (Rheumatic heart disease)	1
Malignant mesothelioma	1
Total	32

Table 2. Comparison of control hemoptysis in patients undergoing bronchial embolization. (modified from Kalen L, et al. Bronchial Artery Embolization: experience with 54 patients. Chest 2002; 121:789-95.)

Study	Technical Succes	1 mouth Control	Control > 1 mouth
Remy et al	41/49(84)	NA	35/49(71)
Uflacker et al	49/75(65)	NA	39/75(52)
Rabkin et al	278/306(91)	230/306(78)	242/306(79)
Hayakawa et al	50/63(79)	NA	36/63(57)
Cremaschi et al	205/209(98)	NA	172/209(82)
Ramakantan et al	102/140(73)	72/140(51)	94/140(67)
Mal et al	43/56(77)	36/56(64)	39/56(70)
Swenson et al	51/54(94)	46/54(85)	43/54(80)
Present study	31/32(98)	28/32(87)	25/32(78)

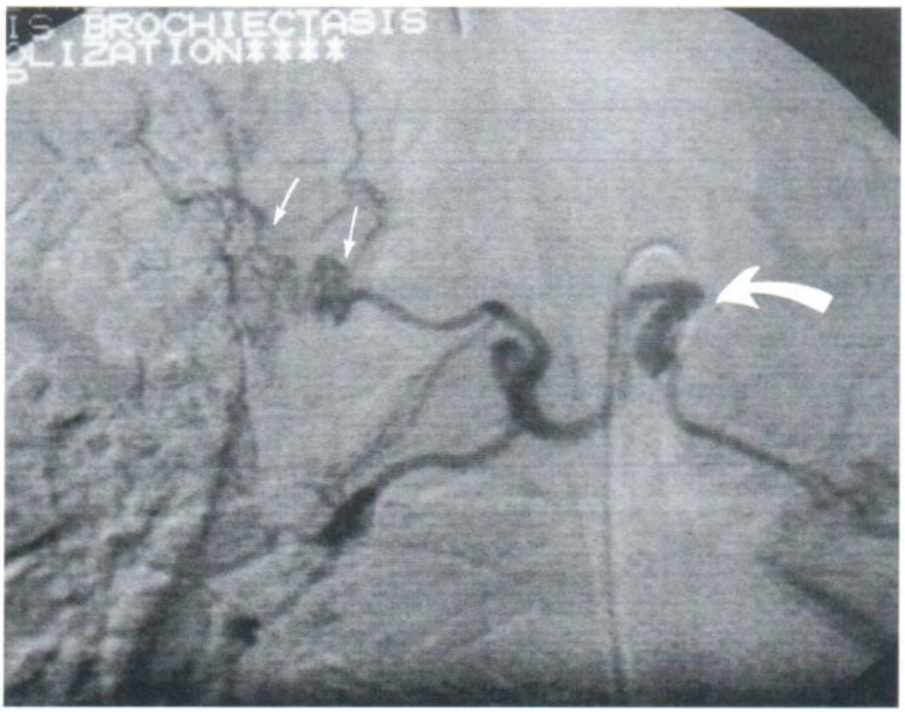


Fig. 1 Bronchial angiogram reveals common trunk of right and left bronchial arteries and hypervascularity in the right lung. Small arrows showed hypervascularity. Curve arrow showed common trunk.

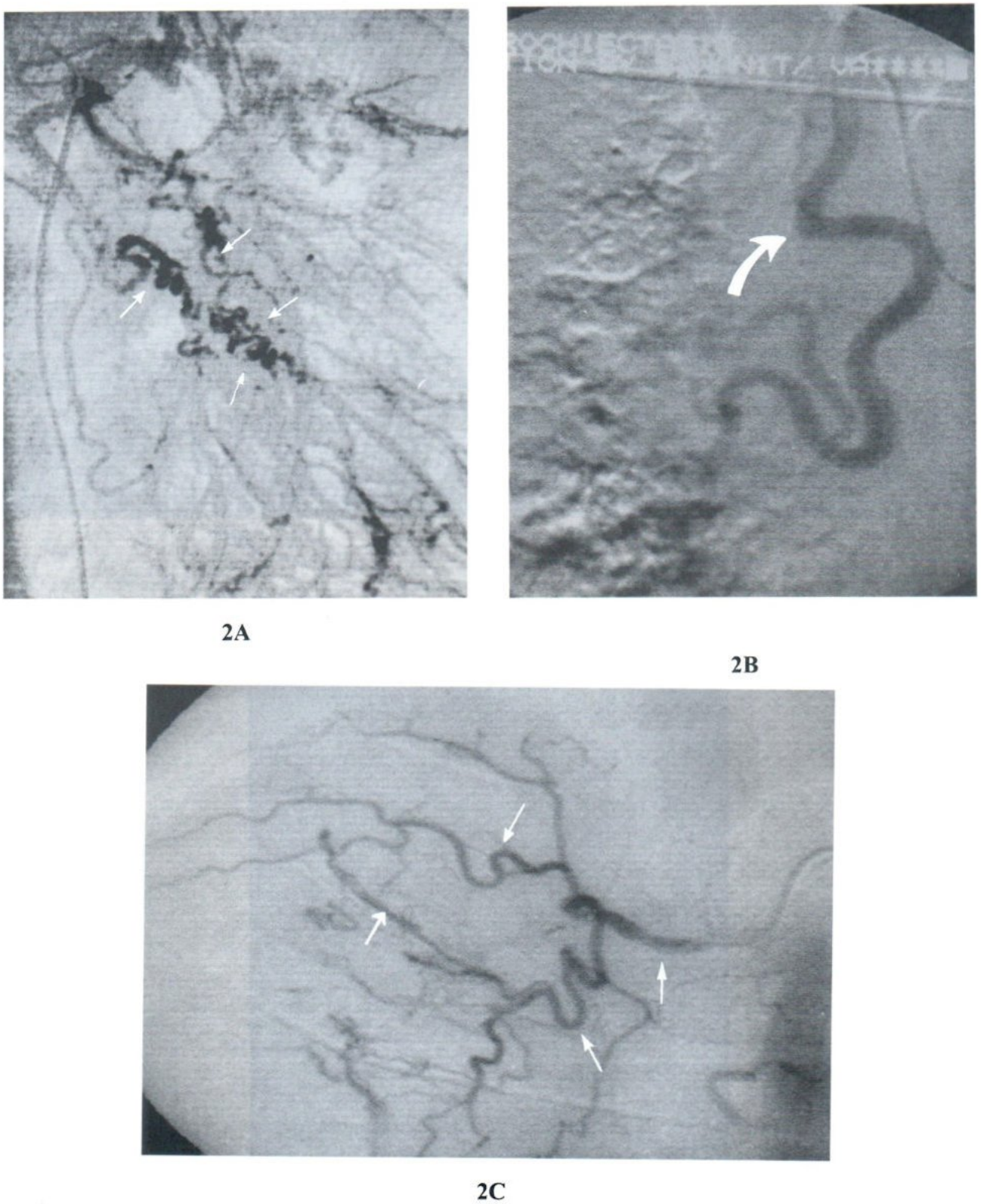
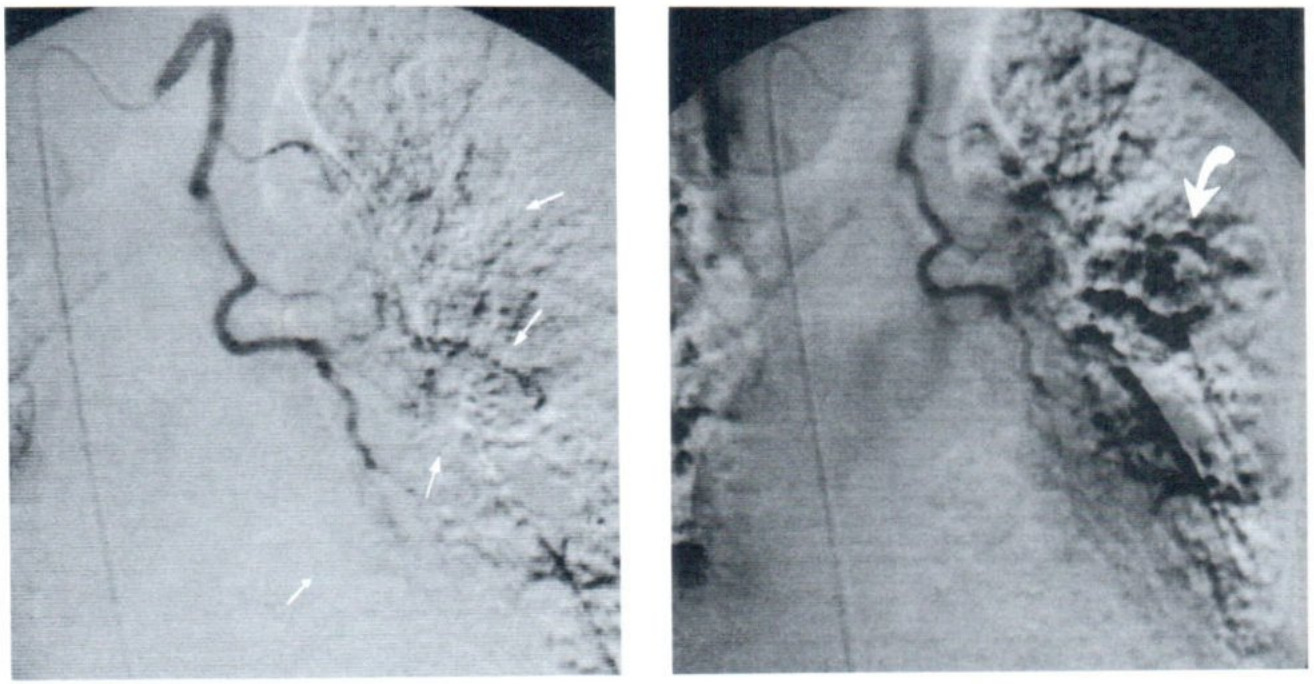


Fig. 2 Bronchial angiogram reveals hypertrophy and tortuousity of the bronchial arteries (A-C), small arrows showed hypervascularity. Curve arrow showed common trunk.



3A 3B

Fig. 3 Bronchial angiogram reveals parenchymatous staining of the contrast medium in the left lung (A and B)

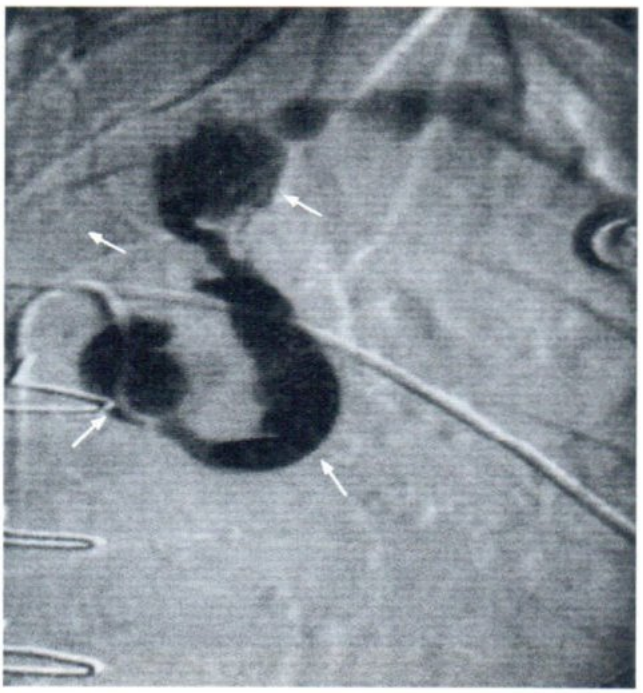
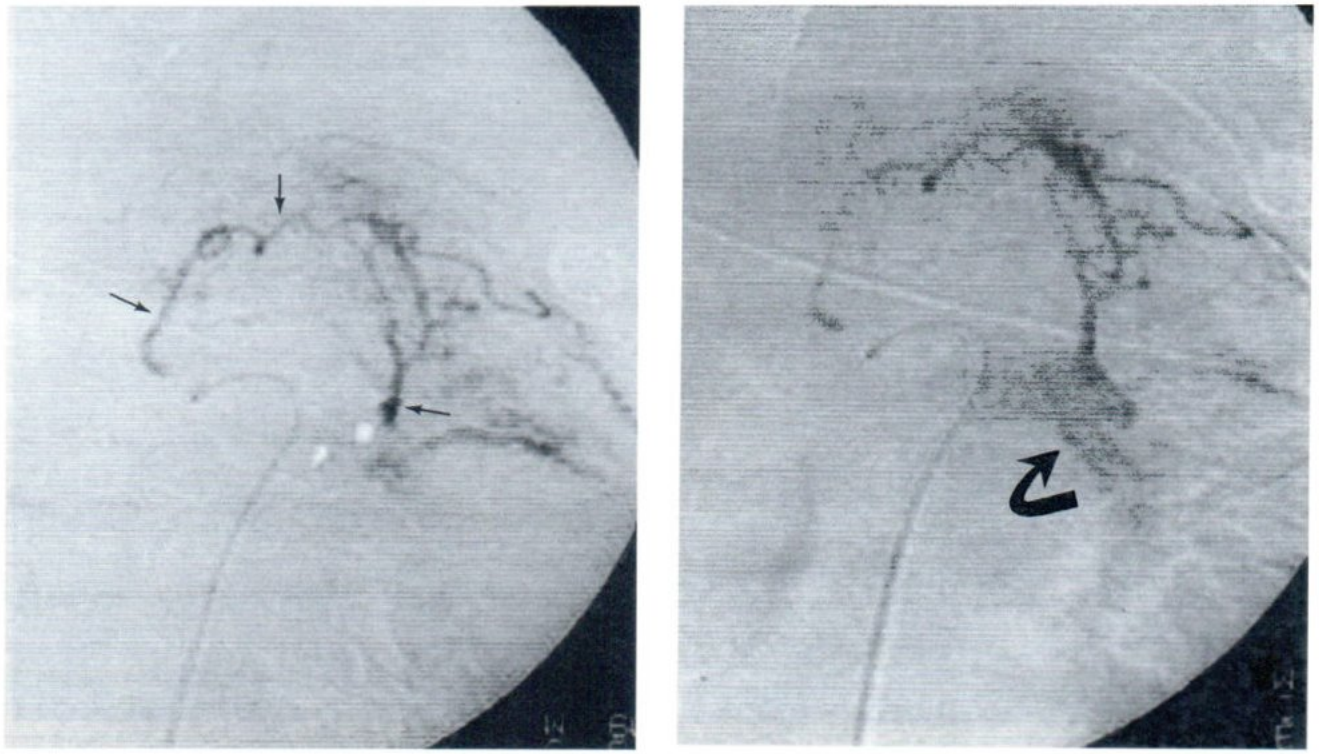
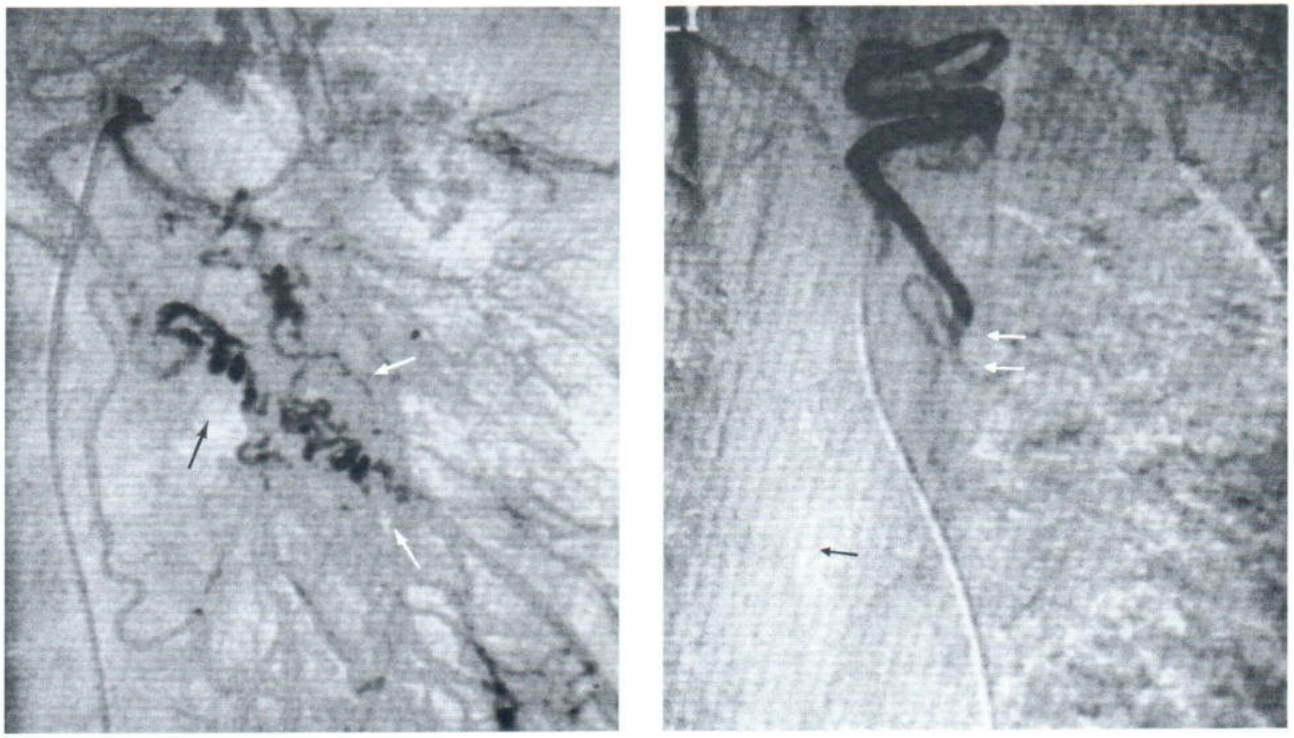


Fig. 4 Bronchial angiogram reveals pseudoaneurysm of the left bronchial artery. (small arrows)



5A 5B

Fig. 5 Bronchial angiogram of the left bronchial artery shows communication between bronchial and pulmonary arteries (A-B). Small arrows showed bronchial arteries. Curved arrow showed pulmonary artery.



6A 6B

Fig. 6 Left bronchial angiogram of a patient with massive hemoptysis shows marked hypertrophy and tortuousity of left bronchial artery branches pre-embolization (A) and post-embolization (B)

DISCUSSION

Over the last 3 years we achieved a technical success rate of 98.87% (31 of 32) and overall success rate of 87.5% (28 of 32) in immediately control of hemoptysis. Recurrent rate of hemoptysis was 9.4% (3 of 32) within 1 mouth and 9.4% (3 of 32) in more than 1 mouths. The majority of etiology of hemoptysis in our series were tuberculous bronchiectasis, pulmonary tuberculosis and nontuberculous bronchiectasis. The findings of angiography included hypervascularity in 100% (32 of 32), bronchial artery hypertrophy and tortuousity in 59.3% (19 of 32), parenchymatous staining in 75.0% (24 of 32), pseudoaneurysm formation in 9.3% (3 of 32), bronchial to pulmonary artery communication in 6.2% (2 of 32) and extravasation of contrast medium into bronchial lumen in 3.3% (1 of 32).

Selective bronchial artery catheterization and angiography in humans was originally performed by Viamonte in 1964.[4,5] Remy et al reported the first successful bronchial artery embolization in a patient with hemoptysis.[6] This was followed by many reports of bronchial embolization for control hemoptysis.[6-19] Subsequently, bronchial embolization was widely used,[1] because patients could be treated without operative procedures. With the advent of digital subtraction angiography and non ionic contrast medium, bronchial embolization become easier, faster and safer.[1]

Bronchial angiography and embolization were well tolerated by our patients. Over the last 3 years we achieved an overall success rate of

90.6%(29 of 32 patients) in immediately control of hemoptysis. Our results are similar to those of several previous reports (Table 1). The angiographic findings also are similar to those previous reports.[6-18]

In our series, recurrent hemoptysis occured within 1 mouth in 3 of 32 patients (9.3%). Others have noted recurrent hemoptysis within 1 mouth in 10 to 30 % of patients.[6-18] Only one of four patients had repeated bronchial angiography and embolization. Bronchial collateral artery developed in this patient and bronchial collateral artery was embolized resulting in the successful control of hemoptysis. In the previous reports, bronchial and nonbronchial collateral artery developed in recurrent hemoptysis patients within 1 mouth. Although, there were some researchers analyzed outcomes by the type of embolic material that was used but there have not been any studied to determine optimal embolic material that should be used in order to prevent recanalization. The embolic material used in bronchial embolization that were reported included the followings: gelatin sponge (Gelfoam^{R}),[7,10,11,14,19] polyvinyl alcohol,[3, 7, 10- 15] microspheres,[10] coils,[7,9,11,13,14,19] Spongel,[6] polyurethane or velour plus albumin macroaggregates plus sclerosing agents,[17] gelatin sponge plus bucrylate,[10] gelatin sponge plus coils,[7,19] polyvinyl alcohol plus coils,[7,14] and polyvinyl alcohol plus gelatin sponge.[7,11,14] Polyvinyl alcohol, microspheres, and coils provide permanent occlusion, while gelatin sponge particles are considered to be temporary occlusion. In our series, we used Gelfoam^{R} as embolic material. Someone have suggested that coils should not be used for bronchial embolization because coils may cause proximal occlusion and do not allow for repeat embolization if necessary.

The complication rate for bronchial embolization has decreased gradually over the years and probably related to the toxicity of ionic contrast medium used at that time. The majority of reported case of serious complication, such as a transverse myelitis and bronchial or aortic necrosis, occurred during the early years of bronchial angiography.[1] A few cases have been reported since the availability of non ionic contrast medium. Distal non-target organ infarction, such as small bowel and limbs, has rarely been reported. More commonly, less-serious side effects are encountered such as chest pain and dysphagia. These symptoms may be due to reflect occlusion of intercostal and esophageal vessels, respectively, and are usually transient.

The complications amoung our patients included subintimal dissection in one patient and chest pain during the embolization procedure in two patients. No serious complication was found in our patients. To prevent such neurologic complication, superselective bronchial embolization was utilized. This refer to embolization of more terminal branches beyond the origin of spinal arteries. Although, co-axial catheter (microcatheter) was not used in our patients, but co-axial catheter may be required for superselective catheterization in some case where a selective catheter position can not be achieved for embolization with a conventional catheter.

In summary, bronchial artery embolization is an effective and safe procedure to control hemoptysis, particularly in immediately control hemoptysis and caused by benign diseases as the patients in our series. Bronchial embolization may help to avoid surgery in patients who are not good surgical candidates.

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ROLE OF BONE SCINTIGRAPHY IN THE DIAGNOSIS OF PLANTAR FASCIITIS: A CASE REPORT AND LITERATURE REVIEW

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ABSTRACT

Bone scintigraphy is usually requested as a part of the investigation of foot pain, but its contribution to the diagnosis and management of plantar fasciitis has not been widely used. Pertinent published data are limited. This article demonstrates an example case presenting with chronic foot pain and shows the advantages of bone scintigraphy in the diagnosis of plantar fasciitis. Comparison of the information derived from bone scintigraphy and other imaging modalities is reviewed. Roles of bone scintigraphy in the management of patients with heel pain and in particular plantar fasciitis are also discussed.

Key words: calcaneus; plantar fasciitis; scintigraphy.

INTRODUCTION

One of the most common heel pain in clinical practice especially in the individuals older than 35 years, plantar fasciitis is usually diagnosed on the clinical basis of having heel pain and localized heel tenderness.[1] Although in some cases, it may occur in seronegative spondyloarthropathy,[2] typically plantar fasciitis results from repetitive trauma, leading to microscopic tears of the plantar fascia near its attachment to the calcaneus. These tears followed by the attempted repair lead to chronic inflammatory response evidenced by localized fibrosis or granulomatous changes in histological study.[3] The processes cause pain and tenderness at the medial aspect of its posterior attachment to the calcaneal tuberosity.[4]

Predisposing factors in developing plantar fasciitis include abnormal arch of foot, both flat foot and high arch of foot, overweight and prolonged period of standing or walking. These abnormal biomechanical and overload pressures on the foot enhance the inflammation of the plantar fascia.[3] Pain in plantar fasciitis typically starts as a dull, intermittent pain in the heel and may progress to sharp and constant pain. It is usually worse in the morning or after sitting, and then decreases as the patient begins to walk around. In addition, the pain usually increases after standing or walking for long periods of time and at the beginning of a sporting activity.

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Most cases of plantar fasciitis can be diagnosed on the clinical grounds of typical site of pain and tenderness as mentioned earlier. However, some have equivocal symptoms and signs, and thus raise the possibility of other causes of heel pain, which may require different treatment. It is these cases that need further investigations to disclose the real underlying pathology. The majority of cases of plantar fasciitis respond favorably to non-operative treatment such as activity modification, orthoses and corticosteroid injection.[4] In some intractable cases, however, plantar fasciotomy usually gives an excellent result.[5]

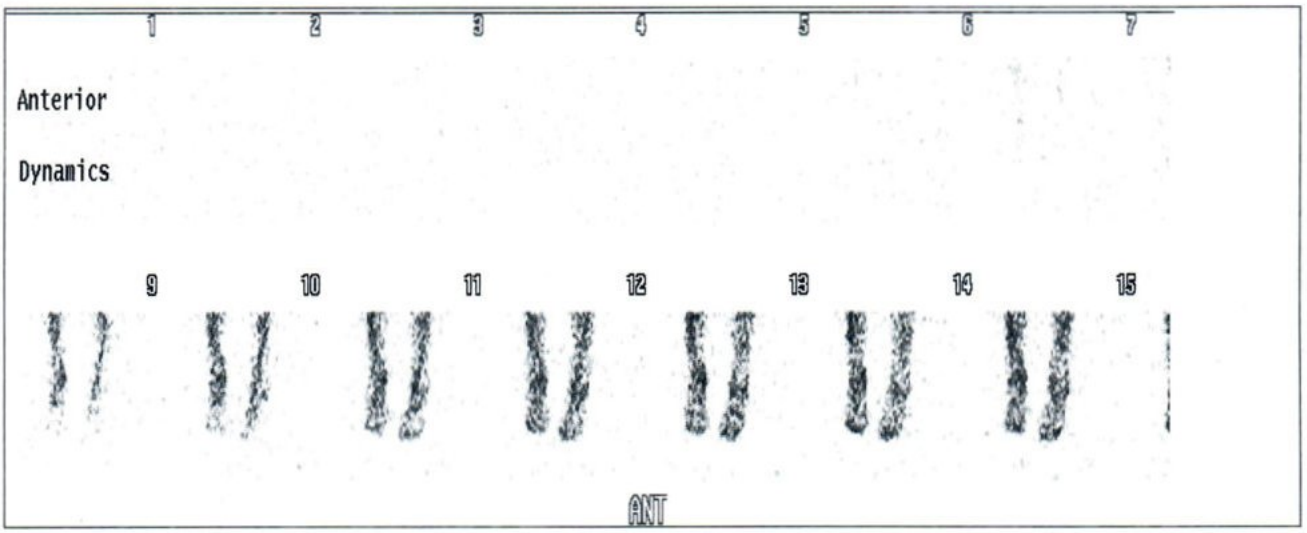
HISTORY

A 51-year old female was referred for bone scintigraphy for evaluation of her right foot. She had got intermittent pain at the right first metatarsophalangeal joint and right heel for three months. She had a history of continual exercise, but refused a history of prior trauma to the feet. On physical examination, the right first metatarsophalangeal joint appeared normal but a point of tenderness could be localized at the medial aspect of the plantar surface of her right heel. Plain radiograph of the right heel revealed a calcaneal spur at the plantar aspect. Plantar fasciitis is suspected.

Three-phase bone scintigraphy was performed by intravenous injection of 800 MBq of ^{99m}Technetium methylene diphosphonate (^{99m}Tc MDP) to elucidate the possible causes of heel pain and other possible related pathologies at the metatarsophalangeal region. The blood flow and blood pool images revealed slightly increased vascularity to the medial aspect of the posterior part of the right foot (Fig. 1a and 1b). In three-hour delayed image, a focal area of increased radiotracer uptake was apparent at the plantar aspect of the posterior part of the right calcaneus medially, consistent with plantar fasciitis. Moreover, a focal increased radiotracer uptake is also noted at the right first metatarsophalangeal joint, likely from osteoarthritis (Fig. 1c).

Table 1. Common causes of heel pain

Calcaneal stress fracture
Archilles tendenitis
Plantar fasciitis
Retrocalcaneal bursitis
Calcaneal osteochondritis dissecans
Tarsal coalition
Osteomyelitis
Reflex sympathetic dystrophy



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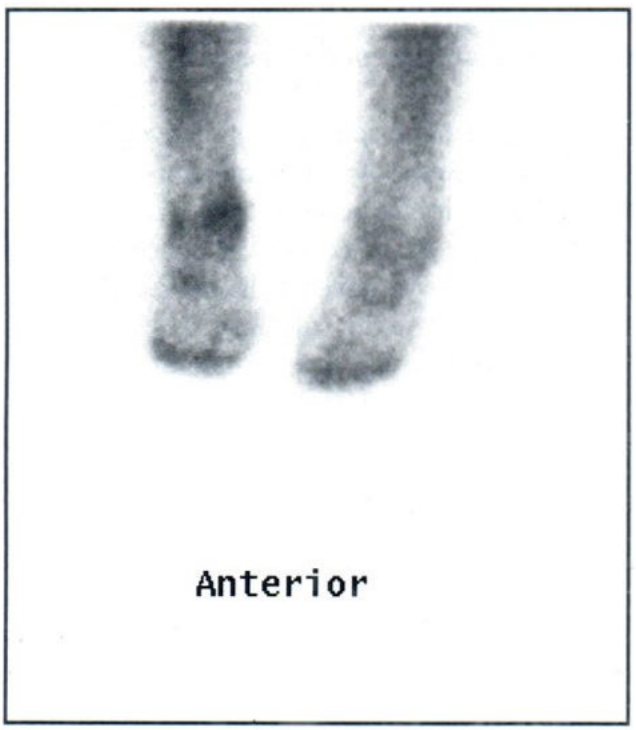

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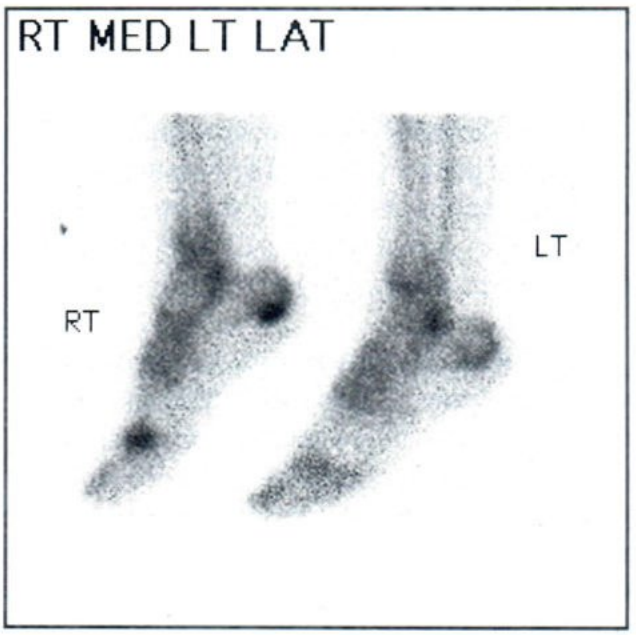

C.

Fig. 1. Three-phase bone scintigraphic findings of the feet (a: blood flow images, b: blood pool image, c: delayed static image)

DISCUSSION

The sites of tendon, ligament and articular capsule insertion to bone are called entheses.[6] Entheses act like the periosteum of bone at the region attached to bone. The disease process at the entheses can cause periosteal reaction, therefore creating osteoblastic activity at the region to the subjacent bone.[7]

Various imaging modalities can help diagnose the equivocal cases of plantar fasciitis. Plain radiographs are of limited value as a diagnostic imaging method for plantar fasciitis, although may be helpful in identifying stress fracture or articular cartilage loss for other possibilities contributing heel pain. Radiograph on the lateral projection of the foot may show the characteristic pattern of fascial swelling with displacement of the overlying fat line.[8] In chronic case, fascial calcification may be visualized. The presence of plantar calcaneal spur seems to be an incidental finding rather than the true contribution to pain. About only a half of patients with heel pain was reported to have a spur.[9]

Plantar fasciitis is also considered when ultrasonographic findings show that the plantar fascial thickness is greater than or equal to 4.5 mm, or there is more than one- mm difference in plantar fascial thickness between symptomatic and asymptomatic heels, with reduced echogenicity or loss of definition of fascial border distal to the antero-inferior aspect of the calcaneus.[10,11] Kane et al.[11] studied 23 patients with a clinical diagnosis of plantar fasciitis in 28 symptomatic heels, and found these sonographic findings in 24 of 28 (85.7%) heels. In addition, they also compared the clinical response after corticosteroid injection into the plantar fascia between ultrasound-guided method and palpation-guided method to the point of tenderness, and found no significant difference in the response rate in terms of decreasing pain, tenderness and plantar fascial thickness. Nonetheless, the apparent weakness of ultrasonography is that it essentially provides an anatomical detail without little or no information on physiological change.

Magnetic resonance imaging has been increasingly used in the diagnosis of plantar fasciitis, since it can provide useful information on changes in water content within the bone and soft tissue with high-resolution anatomical details, thus accurately identifying areas of inflammation. The thickness of the plantar fascia could be determined and an increased signal on T1-weighted images was found to suggestive of plantar fasciitis. 9 However, its relatively high cost seems to be a major limitation for evaluation of patients with clinically suspected plantar fasciitis.

Since bone scintigraphy can provide the objective evidence of an inflammatory process at the entheses, it can be used to diagnose plantar fasciitis in the cases of clinical uncertainty. An increase in bone turnover at the region of plantar fascial insertion to the calcaneus, resulting from the inflammatory process, causes abnormal radiotracer accumulation. Focally increased radioactivity in the delayed images restricted to the sites of tendon or ligament insertions, associated with increased blood flow and blood pool in the early images, is typical of enthesopathy.[12]

Plantar fasciitis is a common enthesopathy causing heel pain. Surprisingly, the clinical benefit of bone scintigraphy for this issue seems to be underused. In 1980, Sewell et al.[13] reported the diagnostic value of bone scintigraphy in painful heel syndrome in identifying the site of inflammation at the calcaneus in the patients with plantar fasciitis. However, validation of its performance in the diagnosis of plantar fasciitis has been rarely reported in the literature. Typically, the scintigraphic findings of this condition

include increased blood flow and blood pool to the medial aspect of the affected heel and focally intense radioactivity on the plantar surface of the calcaneus at the site of insertion of the plantar fascia.[10,14] This pattern is specific for plantar fasciitis, and helps to differentiate it from a retrocalcaneal bursitis and Achilles tendinitis, which would show increased radioactivity extending posteriorly or superiorly, respectively, beyond the margin of the calcaneus.[14] Our demonstrated case also had the characteristic findings of plantar fasciitis. Overuse injury leading to degenerative process was probably, in part, a shared predisposing factor for developing both plantar fasciitis and osteoarthritis of the metatarsophalangeal joint.

Intenzo et al.[15] studied 15 patients with chronic heel pain without a known traumatic event or excessive exercise, and found that three-phases bone scintigraphy correctly diagnosed plantar fasciitis in 10 patients, and ruled out plantar fasciitis in the remaining five patients. They found that typically plantar fasciitis showed a linear or elongated appearance of increased tracer activity along the medial ventral surface of the calcaneus, while on static images there was a more focal region of increased uptake localized within the inferior calcaneal surface anteriorly. Of five patients without plantar fasciitis, two had normal scintigraphic findings and their pain eventually subsided without treatment. Other two cases had calcaneal stress fracture and the other case had a calcaneal spur that required no treatment. These findings demonstrated the role of bone scintigraphy not only in the diagnosis of plantar fasciitis, but also in the differentiation of the causes of heel pain. Various causes of heel pain are shown in Table 1.[16-18]

In comparing bone scintigraphy with other imaging modalities, Tudor et al.[19] more recently compared bone scintigraphy and plain radiograph in the evaluation of 33 patients with clinically diagnosed chronic plantar fasciitis refractory to treatment. Increased 99mTc MDP uptake at the medial calcaneal spur was found in 28 cases, while the calcaneal spur was shown in 21 cases. Furthermore, almost all patients (95%) with the spur had abnormal radiotracer uptake, while only 75% of patients with abnormal uptake had the spur, indicating that bone scintigraphy could help to diagnose plantar fasciitis in about a quarter of patients without the spur or with atypical symptoms and signs. On the contrary, it may not provide additional diagnostic information in the group of patients having the spur.

Although a number of studies reporting the performance of ultrasonography in the diagnosis of plantar fasciitis,[20-22] there is rarely study comparing its performance with the bone scintigraphy. Only the study of Kane et al.[11] that showed significant correlation between ultrasonographic and bone scintigraphic findings in the diagnosis of plantar fasciitis is noted. Unlike ultrasonography, bone scintigraphy, even giving a low radiation dose to the patients, can provide significant information in patients presenting with heel pain in terms of early focal metabolic alteration without apparently anatomical change,[23] which could not be derived from ultrasonography. This value is crucial in making differential diagnoses of heel pain patients, particularly, who have previously been diagnosed as plantar fasciitis, but are refractory to conventional treatment, since other bone or soft tissue pathologies causing pain such as stress fracture may be discovered.[24]

Role of bone scintigraphy in the management of plantar fasciitis was demonstrated by Dasgupta and Bowles.[25] They studied 15 patients with a clinical diagnosis of plantar faciitis and found that 12 of them (80%) had abnormal focal uptake of ^{99}mTc MDP at the subcalcaneal region on the medial and posterior part. Additionally, corticosteroid injection into this abnormal uptake area, instead of the site of maximal tenderness,

provided the positive response, evident by improvement of the symptoms evaluated at 4-week postinjection, in all 12 cases. It was surprising that the site of abnormal uptake was usually at the region of more medial and more posterior than the site of maximal tenderness at the plantar aspect of the heel. Since the technique could enhance the accuracy and efficacy of cortcosteroid treatment, they therefore recommended bone scintigraphy as a guide for the site of corticosteroid injection in the patients who had failed more than one steroid injection before. This could reduce the need for repeated injection, since it had been reported to cause plantar fascia rupture.[26]

CONCLUSION

Bone scintigraphy can provide a useful information for evaluation of appropriately selected patients with plantar fasciitis, since it can help to confirm the diagnosis in atypical cases or those intractable to conservative treatment. Furthermore, it may be used to guide the site for corticosteroid injection in cases without satisfactory response to prior steroid treatment.

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DOSE CALCULATION USING 4 HOUR I-131 UPTAKE FOR RETREATMENT RADIOIODINE THERAPY OF PATIENTS WITH GRAVES' DISEASE

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ABSTRACT

Objective: The purpose of this study is to evaluate the feasibility of using the 4 hour ^{131}I uptake value in the calculation of treatment dose of radioiodine for the patients previously treated by ^{131}I for hyperthyroidism but still having persistent symptoms. This would permit uptake measurement and therapy within the same day,thus reducing the cost and inconvenience to the patient.

Subject: One hundred and sixty Graves'disease patients who were previously treated with ^{131}I but remain hyperthyroid are included in this study.

Method: The patients were randomly devided into 2 groups. First group was used to develop a regression relationship between 4 hr. and 24 hr ^{131}I uptake. The second group was used to calculate the predicted therapeutic dose of ^{131}I, which was calculated from 4 hr. ^{131}I uptake.

Result: Correlation between 4 hr. and 24 hr. ^{131}I uptake is high (r= 0.71).These data allow us to develop a linear regression equation ;24 hr. ^{131}I uptake = 36.764 + 0.518 (4 hr. ^{131}I uptake). The predicted therapeutic doses calculation using 4 hr. ^{131}I uptake, correlate well with the calculated doses, base on the actual 24 hr. ^{131}I uptake (r = 0.92).

Conclusion: There is a high correlation in the predicted dose derived by calculation using 4 hr ^{131}I uptake and the actual doses calculated by using 24 hr. ^{131}I uptake. Therefore, the 4 hr. ^{131}I uptake value can be used to calculate the treatment doses of radioiodine for the previously treated patients who still have persistent hyperthyroidism

Key words: radionuclide therapy, ^{131}I ,hyperthyroidism, Graves'disease, Thyroid uptake

INTRODUCTION

Radioiodine therapy of hyperthyroidism was first used in 1942 by physicians at Massachusetts General Hospital.[1] Currently radioiodine therapy is the most common method for

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treatment of Graves' disease.The cumulative experiences of this therapy has been confirmed for its efficacy,safety and cost-effectiveness.[2,3]

Traditionally, 24-hour radioactive iodine uptake (RAIU) has been used to calculate therapeutic doses of ^{131}I for Graves'disease. However ,this method requires that the patient has to come for measurement thyroid uptake for at least two consecutive days. Recently a few studies have shown that early uptake (3 to 6 hour) of ^{131}I or ^{123}I can be used to accurately predict 24-hour uptake in hyperthyroid patients using a logarithmic regression equation.[4-6]

About 10 – 30 % of patients did not respond to first therapeutics doses of ^{131}I.[7] The purpose of this study is to evaluate whether the 4-hour ^{131}I uptake value can be used to calculate treatment doses of radioiodine for the previous irradiated thyroid gland of persistent hyperthyroid patients.

MATERIALS & METHODS

One hundred sixty Graves'disease patients (127 females and 33 males; mean age 38.9 years; range 16 – 72 years) who were previously treated with ^{131}I but remain hyperthyroid are included in this study. The diagnosis of persistent hyperthyroidism were confirmed by clinical symptoms, physical examination and persisted high level of serum thyroid hormones. The patients were then randomly divided into 2 equal groups. The first group was used to develop a regression relationship between 4 hour and 24 hour ^{131}I uptake. The second group was used to calculate the predicted therapeutic dose of ^{131}I which can be calculated given an oral each from 4 hr. ^{131}I uptake.

All patients (n = 160) were given an oral dose of ^{131}I approximately 20 μci each orally. Radioactive iodine uptake was then performed at 4 hour and 24 hour using a single probe counting system consisting of sodium iodine crystal and single chanel analyzer (Quadra 605, Macintosh Corp.) This study protocol was approved by Ethics committee of the Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

RESULTS

The results of the study of 80 Graves' disease patients with persistent hyperthyroid in the first group are shown in table 1.

Table 1. 4 hour and 24 hour radioactive iodine-131 uptake of persistent Graves'disease patients in the first group (n=80)

	4 hr I-131 uptake (%)	24 hr I-131 uptake (%)
Minimum	19	30
Maximum	97	95
Mean	54.33	64.93
SD	18.23	13.30

The data from 80 patients in the first group allowed us to develop a regression relationship between the 4 hour and 24 hour ^{131}I uptake. Early uptake (EUp) at 4 hour was plotted againts late uptake (LUp) at 24 hour (Fig 1). Linear regression analysis was used to predicted 24 hour from 4 hour ^{131}I uptake. The regression equation for the persistent hyperthyroid patient is as follow ; **LUp = 36.764 + 0.518 (EUp)**. This formula was then used to calculate predicted 24 hour uptake base on measured 4 hour uptake in the second group of patients. Predicted 24 hour uptake correlated well with the actual measured 24 hour uptake in these patients (r = 0.73) (Fig. 2).

These predicted 24 hour uptake were then used to calculate the therapeutic doses to be given to the patients. The therapeutic doses were calculated using the following formula;

^{131}I Therapeutic dose (mCi) =

$$\frac{100\ \mu ci/gm \times gland\ weight\ (gm)}{\%\ 35\ hour\ I\text{-}131\ uptake \times 100}$$

These predicted doses calculated from predicted 24 hour uptake (PUp) correlated well with the actual doses calculated from the measured 24 hour uptake ($r = 0.92$) (Fig. 3). In approximately 80% of the patients, the therapeutic doses calculation using the predicted 24 hour uptake (PUp) were within plus or minus 1 mCi of the dose calculated from the measured 24 hour uptake.

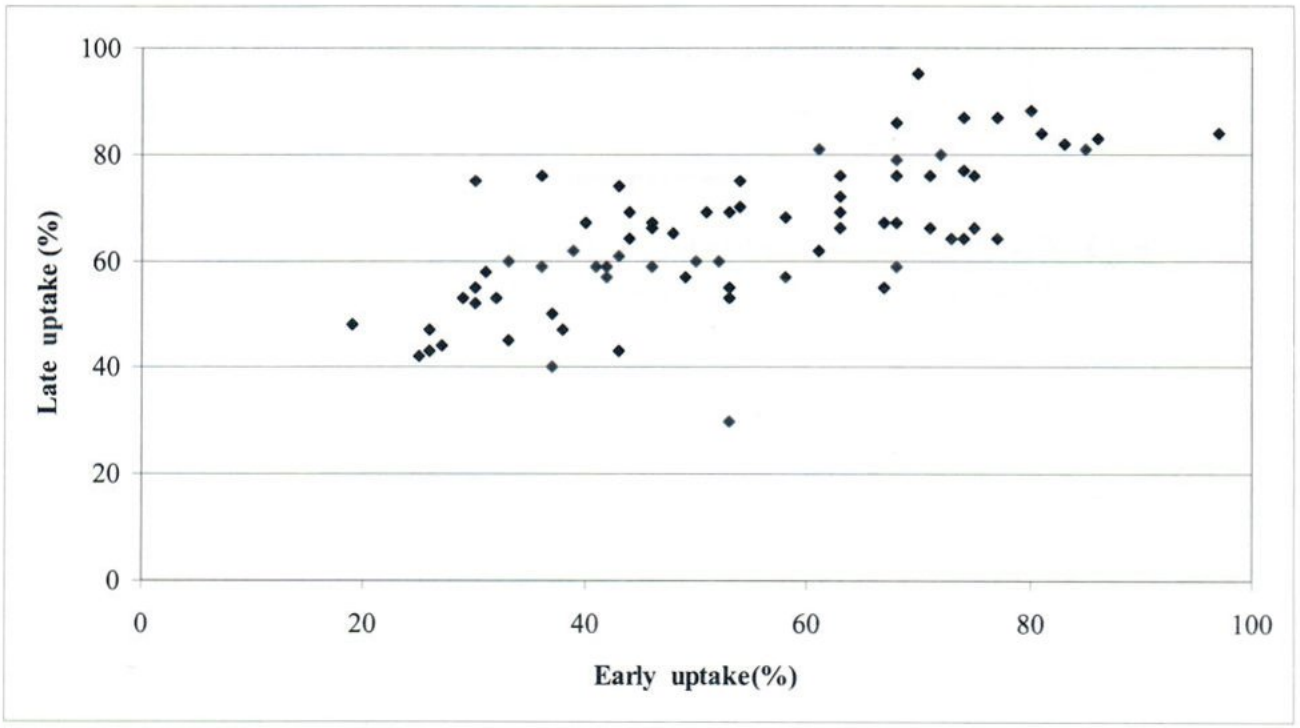

Fig.1 Regression analysis correlation 4 hour ^{131}I uptake (early uptake) versus 24 hour ^{131}I uptake (late uptake) of patients in Group 1. ($r = 0.71$)

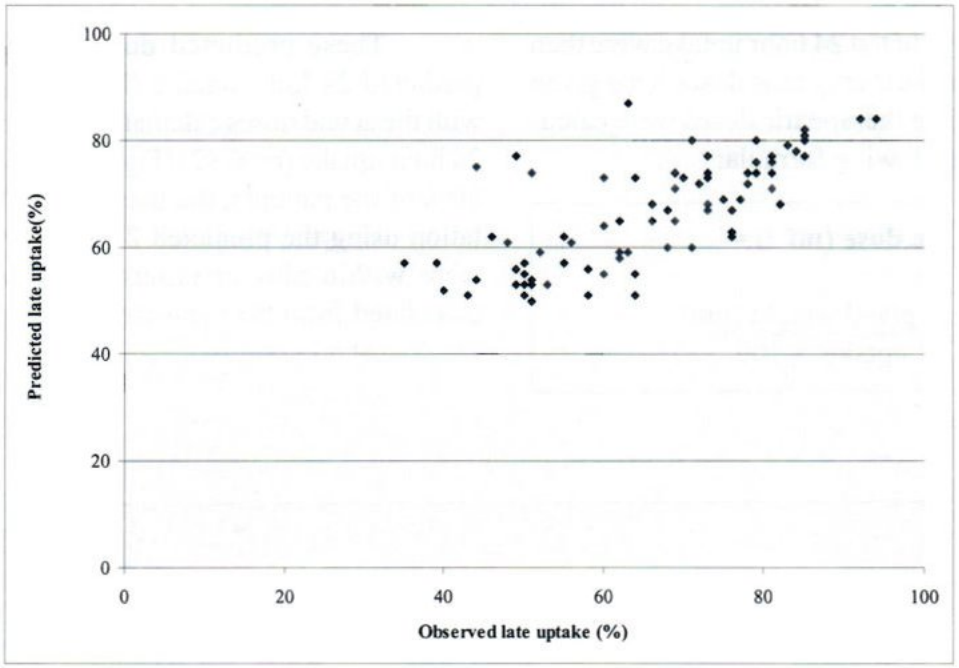

Fig.2 Correlation of measured 24 hour ^{131}I uptake (observed late uptake) versus predicted 24 hour ^{131}I uptake (predicted late uptake) of patients in Group 2. (r = 0.73)

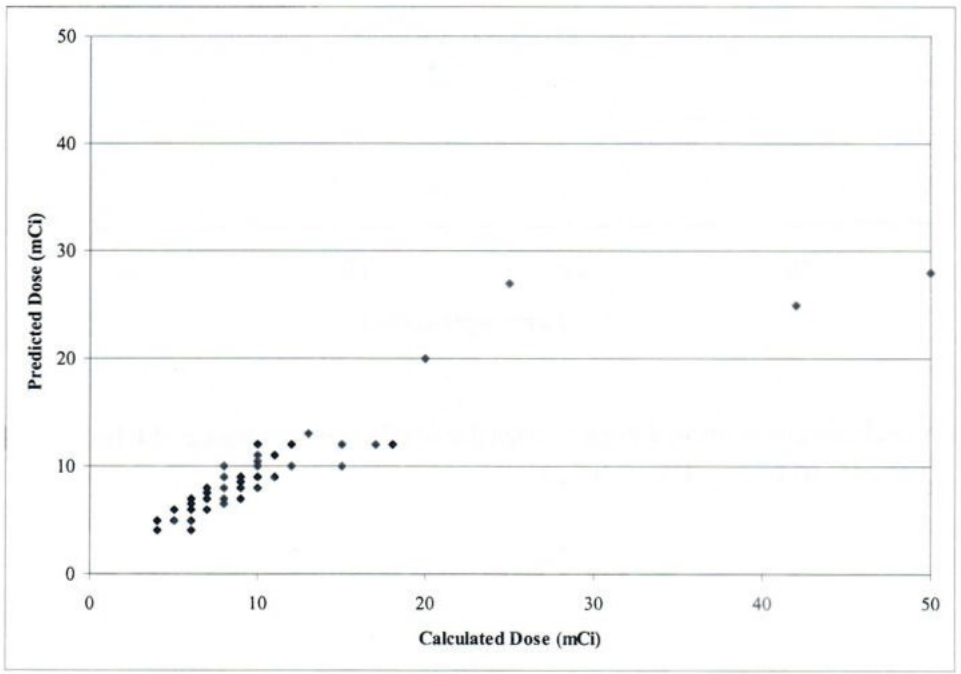

Fig. 3. Correlation of doses calculation using measured 24 hour ^{131}I uptake (actual calculated dose) versus doses calculation using the predicted 24 hour ^{131}I uptake (predicted dose) of patients in Group 2. (r = 0.91)

DISSCUSSION

The effectiveness of ^{131}I treatment depends on multiple factors including, iodine uptake, effective half-life of the iodine in the gland, distribution of radioactivity within tissue and radio-sensitivity of follicular cells.Five approaches for therapeutic doses calculation for patients with Graves'disease have been employed;[8]

1. small doses repeated as necessary.
2. a large ablative dose.
3. a " sliding scale" based on thyroid size.
4. a standard formula for administered dose based on estimated thyroid size.
5. precise dosimetry for the administered dose.

The most common method in dose determination employs a formula based on estimated thyroid size and 24-hour radioactive iodine (RAI) uptake as used in this study.

Hayes et al.[4] studied a group of 27 hyperthyroid patients with Graves' disease using a logarithmic regression equation which was developed to predict 24 hour ^{131} I uptake (PUp) from the 4 hour ^{131} I uptake (EUp). They obtained a high correlation between predicted and measured 24 hour uptake with ^{131}I (r =0.94). Hennessy JV et al.[5] also studied a group of 51 hyperthyroid patients with Graves'disease using ^{123} I uptake and reported that the PUp correlated well with measured 24 hour ^{131}I uptake (r = 0.73) and the correlation of calculated doses obtaining from the predicted and measured 24 hour ^{131}I uptake were highly significant (r = 0.91).

According to our former study of a group of 167 Graves'disease patients before ^{131}I treatment we found high correlation (r = 0.79) between 24 hour ^{131}I uptake(LUp) and 4 hour ^{131}I uptake (EUp). These data allowed us to develop a linear regression equation ; LUp = 39.06 + 0.52 (EUp). Then,we obtained a high correlation between predicted and measured 24 hour ^{131}I uptake (r = 0.94).[9]

Following our former study, in this study, we would like to know whether the use of 4 hour ^{131}I uptake for calculation of therapeutic doses for Graves'disease patients who were not respond to previous ^{131}I treatment is different from the thyroid glands that had not been irradiated .

From this study the correlation between predicted 24 hour ^{131}I uptake and measured 24 hour ^{131}I uptake is 0.73 and the correlation between therapeutic doses base on predicted 24 hour ^{131}I uptake and measured 24 hour ^{131}I uptake is 0.92. About 80% of patients, the therapeutic doses calculation using the predicted 24 hour uptake were within plus or minus 1 mCi of the dose calculated using the measured 24 hour uptake.

The results of our study indicated that the regression equation of previous irradiated thyroid gland is slightly different from unirradiated gland .However ,the predicted 24 hour ^{131}I uptake can be used to estimate ^{131}I treatment dose for previous irradiated thyroid gland as well as unirradiated thyroid gland. The advantage of this method is that the uptake and ^{131}I therapy can be performed within the same day, therefore it is convenience for the patient, less time consuming, and reduced the travelling cost of the patients. However, the efficacy of therapeutic doses calculation using the predicted 24 hour ^{131}I uptake needs further studies.

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APPLICATION OF RADIOIMMUNOASSAY DETERMINATION OF ERYTHROPOIETIN IN MONITORING OF THALASSEMIC PATIENTS

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ABSTRACT

Erythropoietin (EPO) is a glycoprotein produced primarily by the kidney in response to hypoxia and anemia. A number of kits are available for measuring EPO, using different immunoassay techniques. Analysis of serum EPO measurement variation between methods showed evidence of significant negative bias with ELISA when compared with RIA methods. Therefore, the RIA method seems better method for determination of EPO. In this article, the author reviewed the previous studies on using EPO determination in monitoring of the thalassemic patients.

Key words: EPO, RIA, thalassemia

WHAT IS ERYTHROPOIETIN ?[1-13]

Erythropoietin (EPO) is a glycoprotein produced primarily by the kidney in response to hypoxia and anemia.[1] It is the principal factor initiating and regulating red cell production.[2] EPO is responsible for the regulation of red blood cell production. Secondary amounts of this hormone are synthesized in liver hepatocytes of healthy adults. In premature as well as full term infants, the liver is the primary site of EPO production. The kidney becomes the primary site of EPO synthesis shortly after birth. EPO production is stimulated by reduced oxygen content in the renal arterial circulation. Circulating EPO binds to EPO receptors on the surface of erythroid progenitors resulting in replication and maturation to functional erythrocytes by an incompletely understood mechanism. Recent knowledge gained regarding the relationship between erythropoietin, iron, and erythropoiesis in the patients with anemia has implications for patient management.[1-3]

Clinical conditions that give rise to tissue hypoxia including anemia, lung disease, or cyanotic heart disease, lead to increased levels of serum EPO. In anemia, serum EPO levels do not rise above normal until hemoglobin levels fall below 110 g/L. As may be expected in patients with renal insufficiency, serum EPO levels remain inappropriately low despite the anemia. However, inappropriately low serum EPO levels may also be seen in anemic patients with cancer, as well as those with rheumatoid arthritis, HIV infection, ulcerative colitis, sickle cell anemia, and the anemia of prematurity. The mechanism of the inappropriate EPO response varies.[3-4]

Treatment with recombinant erythropoietin (rHuEPO) has been shown to be useful in disease states such as anaemia of chronic renal failure[5] inflammatory bowel disease,[6] multiple myeloma[7] and acquired immunodeficiency syndrome.[8] Other uses include treatment of anaemia of orthostatic hypotension[9] and anaemia

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of prematurity.[10] Monitoring serum EPO concentrations enables detection of toxicity and ensures adequate therapeutic concentrations are achieved.[11]

The availability of rHuEPO since the mid 1980s has led to the development of sensitive and specific immunoassay methods for measuring EPO and it has become easier to determine the role of abnormal circulating serum EPO concentrations in a variety of clinical states.[12]

DETERMINATION OF ERYTHROPOIETIN BY RADIOIMMUNOASSAY

A number of kits are available for measuring EPO, using different immunoassay techniques. Most are based on ELISA or RIA. Some of these kits are EPO-Trac RIA (Incstar Corporation, Stillwater, MN, USA), EPO RIA (Ramco Laboratories Inc. Houston, Texas, USA) and DSL RIA (Diagnostic Systems Laboratories Inc. Webster, Texas, USA), which are competitive binding disequilibrium radioimmunoassay (RIA) methods which use recombinant human EPO for both tracer (^{125}I) and standards. The other kits are EPO EIA (bioM?rieux, Marcy-I'Etiole, France), IBL ELISA (Immunobiological Labs.Hamburg, Germany) and Medac ELISA (Medac, Hamburg, Germany) are assays based on a sandwich technique using two monoclonal antibodies.[13]

According to a recent study of evaluated these kit,[13] analysis of serum EPO measurement variation between methods showed evidence of significant negative bias with ELISA when compared with RIA methods. Therefore, the RIA method seems better method for determination of EPO.

SOME STUDIES ON THE ERYTHROPOIETIN MONITORING IN THALASSEMIC PATIENTS[14-22]

In Thailand, thalassemia syndromes, which are a group of disorders resulted from inherited abnormality of globin chain production, is another hematologic disease presented with anemia. This diseases is interest about the serum EPO levels.[14] Presently, the radioimmunoassays for serum erythropoietin seem valuable tools for clinical research, but their roles in routine clinical practice remain undefined.[15-16] Because hyperstimulated ineffective erythropoiesis due to inappropriate transfusion regimen in the therapy of thalassaemia major may lead to complications, hence, serum EPO may be a useful test in follow up of these patients.

Presently, the only one classical tool for monitoring of erythropoiesis in the thalassemic patients is determination of reticulocyte count. Serum EPO is of interest for many research group focused on its possibility as alternative tool in monitoring of these patients. Of interest, recent study of Paritpokee et al, showed the high level of serum EPO in the beta thalassemia /Hb E patients despite polytransfusion.[17] However, it does not agree with those of Dore et al (1993)[18] and Nisli et al (1997),[19] which suggest that even a low transfusional regimen may cause a decrease in serum concentration of EPO, independent of the level of total Hb.

Paritpokee et al's observation in this regard agrees with those reported by Chen et al (1998),[20] who found a significant inverse correlation between serum EPO levels and Hct in polytransfused beta thalassemia major patients, but not with Dore et al (1993)[18] and Nisli et al (1997)[19] who found a significant inverse correlation between serum EPO levels and Hct only in the patients who had only a few or no transfusions. The conflicting data on the studies of EPO level in thalassemic patients may be due to the method of serum EPO evaluation, the few number of subjects and the time of drawing the sample at pre or post transfusion.

Nevertheless, an increase in circulating hematopoietic progenitor cells with an elevated serum EPO level in polytransfused beta thalassemia major was well described by Chen et al (1992).[21] This observation can suggest that physiologic suppression of erythropoiesis is not successful in thalassemic patients, who were oftenly transfused. Nevertheless, in 1999 Chaisiripoomkere et al reported that serum EPO levels increased in all thalassemia patients despite repeated transfusion.[22] The similar findings in our polytransfused beta thalassemia /Hb E pediatric patients can be demonstrated.

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EXPECTED VALUE OF SERUM FERRITIN BY RADIOIMMUNOASSAY: A STUDY IN 80 THAI HEALTHY MALES

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ABSTRACT

Serum ferritin determination is a useful test for determination of iron deficiency. The radioimmunoassay test is a widely used method to determine serum ferritin. Due to the fact that each laboratory should set its own reference value, therefore, we performed this study. Here, we reported the expected range of serum ferritin among 80 healthy Thai subjects. The average level of ferritin was 24.50 $\pm$ 9.57 ng/ml. The expected range for our subjects are 22.39 – 26.61 ng/ml.

Key words: ferritin, RIA, expected value

INTRODUCTION[1-3]

Ferritin is a large protein shell (MW 450,000) comprised of 24 subunits, covering an iron core containing up to 4000 atoms of iron. Ferritin acts as the soluble storage form of iron in tissue (hemosiderin is relatively insoluble). It may serve other functions as well although these are controversial. It is found in most cells of the body, especially macrophages, hepatocytes and erythrocytes. Synthesis occurs in the liver and the rate correlates directly with the cellular iron content.

There are iron- and cytokine-responsive elements in ferritin mRNA. Increased iron or cytokines (such as IL-1, IL-6) promotes ferritin translation, resulting in increased iron storage. This is one of the causes of iron "sequestration" that occurs in animals with chronic or inflammatory disease and will reduce serum iron values.[2] The function of serum ferritin is not known, but the concentration correlates well with the amount of stored iron in normal (and most diseased) subjects. Serum ferritin concentrations are quite stable with lower diurnal rhythm effect, in contrast to serum iron.

Concerning measurement: of ferritin, sensitive methods are needed, since serum levels are very low. Immunologic assays requiring species-specific reagents, such as RIA and ELISA, have been employed.[1] Here, we reported the expected value of serum ferritin by RIA method among healthy Thai adult males.

MATERIALS AND METHOD

SUBJECTS

This study was designed as a descriptive study. Eighty healthy Thai male subjects were

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assessed. All subjects were Thai adults and lived in rural area. Fasting blood sample from each subject was collected using vacuum tube 5 milliliters as clotted blood. Physicians also performed physical examination on all subjects. Those subjects who had abnormal results from examination were also excluded. The protocol of this study was approved by the Ethical Committee of Faculty of Medicine, Chulalongkorn University.

LABORATORY ANALYSIS

Each collected specimen was analyzed for serum ferritin by RIA method (CIS Biointernational) at the Nuclear Medicine Unit, Department of Radiology, Faculty of Medicine, Chulalongkorn University.

STATISTICAL ANALYSIS

A. Setting of the reference values

The reference values in this study are primarily assumed as the expected value. The mean, standard deviation (SD), range of subjects were calculated. The expected values in this study were accepted at mean $\pm$ 95% confidence interval.

RESULT

A total of 80 subjects were analyzed. The average level of ferritin was 24.50 $\pm$ 9.57 ng/ml. The mean, standard deviation (SD), range of subjects were calculated and presented in Table 1. The expected range for our subjects are 22.39 – 26.61 ng/ml.

Table 1. Statistical data of ferritin determination.

Mean (ng/ml)	SD (ng/ml)	Maximum (ng/ml)	Minimum (ng/ml)
24.50	9.57	41.70	5.11

DISCUSSION

Ferritin is a protien in the body that binds to iron. Most of the iron stored in the body is attached to ferritin. Ferritin is found in the liver, spleen, and bone marrow. Only a small amount is found in the blood. The amount of ferritin in the blood may help to indicate the amount of iron stored in the body. This test is most commonly done on a blood sample taken from a vein. Less commonly, the amount of iron in the body can be evaluated during a bone marrow analysis.[1,3]

In the present day, determination for ferritin is accepted for determination of iron deficiency. However, most of present references are according to the textbook or the old reference from the Western.[4–5] Due to the fact that ferritin levels are altered by many factors, especially for geographic and demographic distribution, therefore, each laboratory setting should set the reference values according to demographic distribution. The references values for ferritin among Thai males

in this study can be applicable. Although the oriental life-style is different from the western way, but because of the globalization, some western life styles such as eating behaviors are introduced to Thailand. Results in this study can well reflex this fact.

Here we derived the expected value for the Thai males as 22.39 – 26.61 ng/ml. Comparing our references to the previous reports.[4-5] the similar trend can be observed. However, our references is lower than those of the Thai children[6] (Expected range for serum ferritin level for the healthy control from this study was 67.895 to 96.692 ng/ml). This finding can showed the fact that the serum ferritin in adult is usually lower than the children.

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FAILURE TO VISUALISE A MULTICYSTIC KIDNEY WITH TECHNETIUM 99m-DTPA DOSE NOT PRECLUDE RECOVERABLE FUNCTION.

Dr. M. A. Taher, Director,

ABSTRACT

We present a patient with multicystic left kidney as diagnosed by ultrasonography. A 99m Tc-DTPA scan showed absent uptake by the left kidney. However, post-operative scan after partial nephrectomy was normal. In this case, absence of 99m Tc-DTPA uptake by the kidney does not necessarily mean that renal function is irreversible lost in patient with multiple cysts.. In general, the renal uptake of 99m Tc-diethylenetriamine pentaacetic acid (DTPA) is a measure of glomerular filtration rate (GFR) and absent uptake is equivalent to non-function. In this report, we describe a patient who had non-visualised left kidney on 99m-Tc DTPA scan due to obstruction by multiple cysts, but normal renal function returned after surgical removal of the cysts.

CASE REPORT

A 48 years old male presented with loin tenderness. On examination, the left kidney was found to be enlarged. Abdominal sonogram revealed multiple cysts in the left kidney pressing the left ureter. Other investigations including biochemical tests were all normal except the 99m Tc-DTPA scan which showed absent uptake in the left kidney only. As the right kidney was normal in sonogram and 99m Tc-DTPA scintiscan, surgery on left kidney was planned. Partial nephrectomy was done to remove the cysts. A repeat scintiscan was done when the patient began to recover, it clearly showed bilateral renal activity.

DISCUSSION

This patient demonstrated recoverable kidney function as documented by reversal of absent renal uptake of 99m Tc-DTPA when the cysts were removed. Of interest, Taylor et al, have described absence of 99m Tc-DMSA (dimercaptosuccinic acid) uptake in a patient with acute tubular necrosis from ischemia, but normal renal function returned after hemodialysis.[1] Sherman and Blaufox[2] reported reversal of absent renal uptake of I-131 orthoiodohippurate in obstructive uropathy when the obstruction was relieved. Quinn and Elder[3] presented a patient with very poor uptake of 99m Tc-DMSA on two occasions despite a 99m Tc-DTPA scan demonstrating only mild renal impairment. Our patient shows recoverable kidney function following removal of

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multiple cysts and highlights the importance of ultrasonography in renal disease.

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THYROID DISEASES FOLLOWING GRIEF: REPORT OF THREE CASES

Dr. M. A. Taher, Director,

ABSTRACT

Hypothyroidism and hypopituitarism following post-partum hemorrhage (PPH) is a well-established phenomenon in Sheehan's syndrome. A case of hypothyroidism following death of husband and two cases of thyrotoxicosis following death of a child and father are reported here considering their rarity.

CASE-1

A 26 years old Muslim female was examined in Sept. 1991 in Nuclear Medicine Centre, Dinajpur who was quite normal before the death of her husband. She had no history of goiter, obstetric problem, goitrogens or radiation therapy. The patient complained loss of memory, constipation, anorexia and somnolence. Her pulse rate was 50/minute, skin was dry and coarse. Radioiodine uptake was low (24h. 4%), T_3=0.99n mol/L, T_4=14.67n mol/L, TSH>100/u IU/ml. The patient improved after thyroxine therapy (150 micrograms/day orally).

CASE-2

A muslim widow aged 40 years complained of increased perspirations, trembling, insomnia, weight loss, occasional loose motions and anorexia. Her thyroid hormone levels were elevated, thyrotropin (TSH) was low (Table-1) and she took carbimazole (neomercazole) 45 mg/day for 1 month (March 1997) with little benefit. She was treated with iodine-131 on 10th August 1997 (1.5 milliCuries), had follow-up visits on 27 October and 28 December 1997 which showed her status as euthyroid. Unfortunately her father died on 13 October, 2000 and she had a recurrence of thyrotoxicosis as documented by clinical examinations and hormone levels (Table-1). She had a second dose of iodine-131 therapy (1.6 milliCuries) on 29 November, 2000 and is being followed-up.

Table 1 Hormone levels of case-2

Date	T3	T4	TSH
22-3-97	11.92 nmol/L	648.9 nmol/L	<0.2 mIU/L
24-7-97	4.44 "	267.2 "	0.59 "
31-10-2000	20.0 "	400.0 "	0.05 "

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CASE-3

A hindu lady of age 35 years presented on 2nd June 1999 with bilateral exophthalmos, excessive sweating, loose motions and insomnia. Her jaundiced neonate child died on 6th June 1999. She was confirmed to suffer from diffuse toxic goitre (Table 2), had carbimazole therapy with little benefit and was improved by iodine-131 therapy on divided doses (Table 3). She is being followed-up.

Table 2 Hormone levels of case-3

Date	T3	T4	TSH
31-1-2000	12.2 nmol/L	285 nmol/L	0.15 mIU/L
14-6-2000	13.05 "	400 "	0.75 "
4-12-2000	7.9 "	197 "	0.35 "

Normal ranges: T3 = 0.8-3.16 nmol/L
T4 = 64.5-152 "
TSH = 0.3-6 mIU/L

Table 3 Iodine-131 therapy of case-3

Date	Dose I-131 in milli-Curies
9-6-1999	0.5
15-3-2000	1.0
20-8-2000	1.5
7-1-2001	0.5

DISCUSSION

Treatment of hypothyroidism is straight-forward-oral thyroxine usually single daily dose. However, thyrotoxicosis is quite difficult to manage especially if we try to avoid hypothyroidism, small doses of indine-131 therapy may help in these situations as we have shown in our series reported earlier.[1]

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CASE REPORT: A HEALTHY DAUGHTER BORN TO A CRETIN.

Dr. Md. Abu Taher, Director,

Thyroxine replacement therapy can cure congenital hypothyroidism (cretinism) if instituted early in life. We like to report a case of healthy daughter born to a congenitally hypothyroid woman considering its rarity.

CASE REPORT

A girl aged 11 months was put on thyroxine therapy in 1971 by the renowned pediatrician Prof. Dr. M. R. Khan who diagnosed her to be congenitally hypothyroid. The initial dose was 12.5 microgram (mcg) daily and gradually it was increased to 150 mcg/day in adult life. She was highly educated (Master of Science) and was married on 18 August/2000 and got pregnant in 2001 when her thyroxine dose was increased further upto 200 mcg/day. She gave birth to a healthy daughter on 03 January/2002 by Caesarean section due to transverse lie. Cord blood hormones were assayed: T_3=0.76 nmol/L (normal range 0.8-3.16), T_4=113 nmol/L (normal range 64-175), TSH=6 mIU/L (normal range 0.4-5). However, she was euthyroid clinically on 13.03.2002.

DISCUSSION

Permanent primary congenital hypothyroidism affects about one newborn in 3500. Eighty to ninety percent of the cases are due to developmental defects of the thyroid gland (thyroid dysgenesis), such as arrested migration of the embryonic thyroid (ectopic thyroid) or a complete absence of thyroid tissue (athyreosis). Most cases of thyroid dysgenesis are sporadic and result from as yet unknown mechanisms. The remaining 10-20% have functional defects in one of the steps involved in thyroid-hormone biosynthesis (thyroid dyshormonogenesis)-defects transmitted by an autosomal recessive mode of ingeritance.[1] The pathogenesis of thyroid dysgenesis is not known.[2] Healthy baby born to a hypothyroid mother is a rare phenomenon, however, early treatment and regular monitoring of hormone levels may lead to an absolutely normal life. In 1989, a starting dose of 10-15 mcg./kg per day of thyroxine was proposed and has been widely used since.[3] The upper range of normal values for plasma free thyroxine in normal infants is much higher than that for older children or adults.[4] Premature fusion of the fontanelles, a recognised complication of perinatal hyperthyroidism (such as seen in children born to mothers with Graves' disease), had never been reported in infants with congenital hypothyroidism treated with 10-15 mcg/kg per day of levothyroxine.[1] During pregnancy and estrogen therapy the need for thyroxine is increased.[5] Screening of neonates for congenital hypothyroidism is being done in many conutries,[6] but screening of pregnant women for hypothyroidism is not yet universal.[7] Haddow et al and Utiger encouraged adequate iodine intake and it should be increased during pregnancy.[8,9]

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NON-OSSEOUS UPTAKES OF TC-99M PHOSPHONATE DURING THREE PHASE BONE SCAN.

Dr. M. A. Taher, Director,

ABSTRACT

Objective : The purpose of this study was to visualize non-osseous uptakes of bone scanning agent.

Methods : Amongst 51 patients (M21, F30) of age range 8-80 years having three phase bone scan at NNC, Rangpur during January 2000 to January 2002, we looked for non-osseous uptake.

Results : Twenty four patients had non-osseous uptakes of 99 metastable technetium methylenediphosphonate (99m Tc MDP), 19 in kidneys (14 in right, 4 in left kidney, one patient showing hold-up in both kidneys), 3 in breasts (2 in left, 1 in right breast), and two patients had lung uptakes. Renal, pulmonary and mammary uptakes of this series are not always due to malignant process, however, one patient had cisplatin nephrotoxicity.

Conclusion : Non-osseous uptake of bone-seeking radiopharmaceutical is quite common (24/51 i.e. about 48% in this series), however, most of these may be non-malignant.

Key words : Bone scan, Non-osseous Uptake.

INTRODUCTION

Staging of tumours is important both for the selection of appropriate treatment and to provide information about prognosis. Inadequate or inaccurate staging may lead to under-or over-treatment, resulting in failure to care or unnecessary toxicity respectively. The increased sensitivity of bone scanning provides a 6 to 18 months lead over X-rays in demonstrating conversion from focal to metastatic disease.[1] Breast uptake of bone scanning agents is non-specific, it has been reported in the normal breast as well as in benign or malignant disease of breast.[2,3] Holmes et al. showed that 95% of benign lesions including fibroadenomas, mammary dysplasia and cystic mastitis has bilateral uptake, while 25% of malignant lesions showed a similar pattern.[4]

METHODS

Three phase bone scans were performed using 5-20 milli-Curies (mCi) of 99m Tc phosphonate under a computerized gamma camera (Siemens Microdelta). Amongst 51 patients (M21, F30) of age range 8-80 years having three phase bone scans at NMC, Rangpur during January 2000 to January 2002, we looked

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for non-osseous uptakes in all phases i. e. during post-injection flow, blood pool and late static views.

RESULTS

Twenty four patients had non-osseous uptakes of 99 metastable technetium methylene-diphosponate (99m Tc MDP), 19 in kidneys (14 in right, 4 in left kidney, one patient showing hold-up in both kidneys), 3 in breasts (2 in left, 1 in right breast), and two patients had lung uptakes. Renal, pulmonary and mammary uptakes of this series are not always due to malignant process, however, one patient had cisplatin nephrotoxicity.

DISCUSSION

Bone-seeking radiopharmaceuticals had been used for skeletal survey as well as for non-osseous pathology, sometimes serendipitious (incidental) and also purposeful detection e. g. scintimammography. However, the non-specific nature of the findings should be kept in mind.

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