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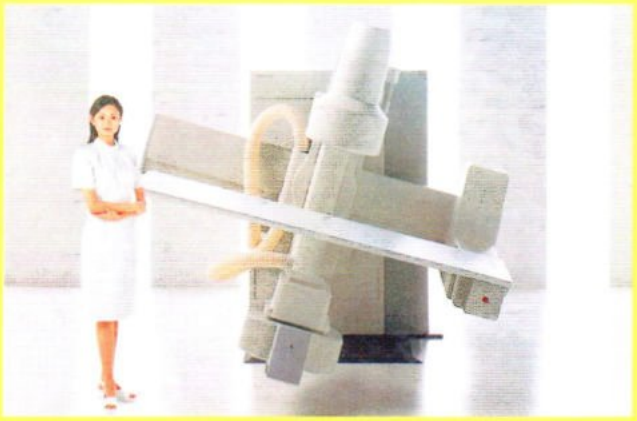

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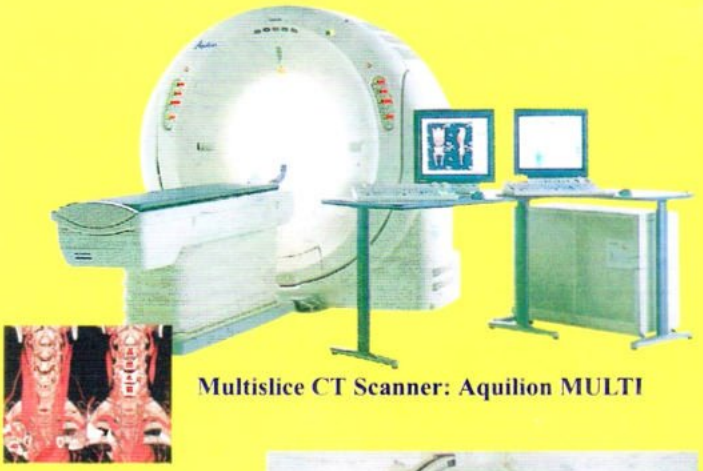

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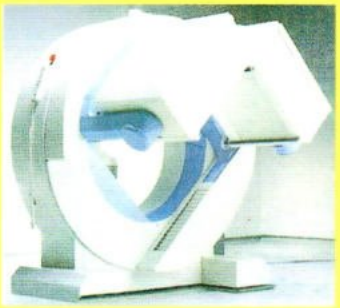

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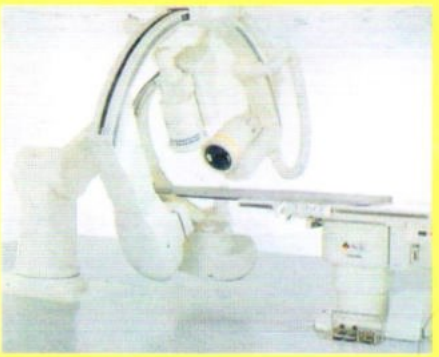

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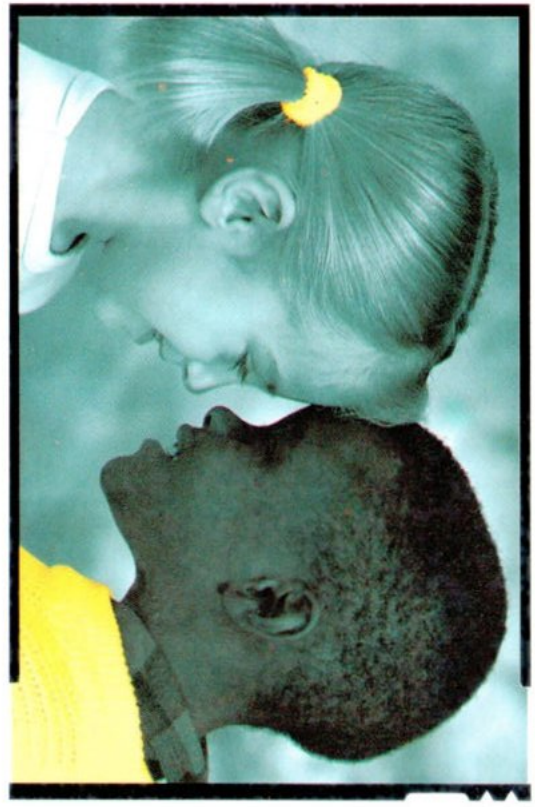

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CONTENTS

ULTRASONOGRAPHIC FINDINGS OF GALLBLADDER CARCINOMA

Prapasri EIAMTHONG, MD [1] Piyapong UNPUNYO,MD [2]

ABSTRACT

Sonographic findings of 20 patients with histologically proven primary gallbladder carcinoma during Jan. 1996- Feb. 1999 in Lampang Hospital were reviewed. The patients were 10 women and 10 men, with age ranging from 39 to 77 years(means 64 years). Clinical manifestations included RUQ pain, jaundice, dyspepsia, weight loss and fever.

Focal or diffuse thickening of the GB wall was the most frequent sonographic findings (50%), followed by mass replacing gallbladder fossa (25%) and polypoid intraluminal mass (15%). Mass at pancreatic head region and impacted gallstone were found at equal frequency, 5% each. Associated findings were gallstones (45%), CBD stones (10%), intrahepatic duct dilatation (40%), lymphadenopathy (20%) and ascites (10%).

The histologic diagnoses were adenocarcinoma (85%), adenosquamous carcinoma (10%) and papillary adenocarcinoma (5%).

The ultimate goal of this report is to increase the general awareness of radiologists to sonographic features of GB carcinoma.

The differential diagnosis and modes of tumor spreading will be discussed.

Abbreviation: RUQ = right upper quadrant, GB = gallbladder
GS = gallstone, CBD = common bile duct, US = Ultrasonography

INTRODUCTION

Gallbladder carcinoma has a low overall prevalence.[1] It is the fifth most common malignant tumor in the alimentary tract after colorectal, pancreatic, gastric and esophageal carcinoma.[2] Predisposing factors include porcelain GB, size of the gallstone, duration of harbored stones,[3] ethnic difference ; more common in Israel, Bolivia, Chile and in south western native Americans in the united States,[4] and anomalous junction of the pancreaticobiliary duct without congenital choledochal cyst.[5] It is preferently found in female with female-to male ratios in the range of 3-4: 1, older life, mostly in the 6th decade of life or later.[1,2,6-9] Prevalence of cholelithiasis is quite high in gallbladder carcinoma, ranging from 65-98%.[10-12] It has been noted that 1 to 3 percent

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Note: Most of this work was completed while the first author worked at Lampang Hospital.

of all patients with documented gallstones will eventually have development of gallbladder carcinoma.[13] The diagnosis of gallbladder carcinoma can be made using one of the following imaging modality, US, CT, MRI, that can provide accurate staging information.[4] The objective of this study is to evaluate sonographic features of gallbladder carcinoma.

MATERIAL AND METHOD

The patients of primary gallbladder carcinoma diagnosed at Lampang hospital, during January 1996 to February 1999 were retrospectively reviewed. Patient demographic data, clinical presentations, preoperative diagnosis, detailed sonographic features and histologic findings were analyzed.

RESULTS

There were 10 females and 10 males. The ages were between 39-77 years (mean age was 64 years). Female to male ratio was 1:1. Right upper quadrant pain was the most frequent chief complaint, followed by jaundice, dyspepsia/ weight loss, positive ultrasonographic Murphy"s sign and fever (Table 1). Regarding preoperative diagnosis, gallbladder carcinoma was correctly diagnosed in half of the patients. The remaining diagnoses included gallstone with obstructed CBD stones, acute cholecystitis with gallstone, acute acalculous cholecystitis, multiple gallstones, chronic cholecystitis with gallstone, empyema gallbladder with gallstone, emphysematous gallbladder with GS, Cholangiocarcinoma with invasion of GB, mass at pancreatic head and porta hepatis (table 2).

Ultrasonography was performed in all the patients, using 3.5 MHz. Transducer; SSD 1200 Aloka. Gallbladder carcinoma appeared as focal or diffuse thickening of gallbladder wall (Fig 1-3) in 10 patients. Mass replacing GB fossa (Fig 4,5) in 5 patients. Polypoid intraluminal mass (Fig 6,7) in 3 patients. Mass at pancreatic head region and porta hepatis (Fig 8) in 1 patient. Impacted gallstones (Fig 9) in 1 patient. The first two common associated findings were gallstones and Intrahepatic bile duct dilatation. Other associated findings were lymphadenopathy, CBD stoned and ascites. Sonographic findings in GB carcinoma and associated findings are summarized respectively in Table 3. and Table 4 .

Histologic diagnoses included adenocarcinoma in 17 patients (10 well differentiated, 5 poorly differentiated, 2 moderatedly differentiated), adenosquamous carcinoma in 2 patients, and papillary adenocarcinoma in 1 patient. Histologic diagnoses are summarized in table 5.

TABLE 1. Clinical manifestations of 20 studied patients

Clinical manifestations	No (%)
RUQ pain	11 (55%)
Jaundice	8 (40%)
Dyspepsia	5 (25%)
Weight loss	5 (25%)
Positive US Murphy 's sign	4 (20%)
Fever	3 (15%)

TABLE 2. Preoperative diagnosis of studied patients

Preoperative diagnosis	No (%)
Gallbladder carcinoma	10 (50%)
Gallstones with obstructed CBD stones	2 (10%)
Acute cholecystitis with GS	1 (5%)
Acute acalculous cholecystitis	1 (5%)
Multiple gallstones	1 (5%)
Chronic cholecystitis with GS	1 (5%)
Empyema GB with GS	1 (5%)
Emphysematous GB with GS	1 (5%)
Cholangiocarcinoma with invaded GB	1 (5%)
CA head of pancreas	1 (5%)
Total	20 (100%)

TABLE 3. Sonographic findings in studied patients with gallbladder carcinoma

Sonographic findings	No (%)
Focal or diffuse thickening of GB wall	10 (50%)
Mass replacing GB fossa	5 (25%)
Polypoid mass	3 (15%)
Mass at pancreatic head region/porta hepatis	1 (5%)
Impacted gallstones	1 (5%)
Total	20 (100%)

TABLE 4. Associated findings of 20 studied patients

Associated findings	No (%)
Gallstones	9 (45%)
Intrahepatic duct dilatation	8 (40%)
Lymphadenopathy	4 (20%)
CBD stones	2 (10%)
Ascites	2 (10%)

TABLE 5. Histologic diagnosis of studied patients

Histologic diagnosis	No (%)
Adenocarcinoma	17 (85%)
Well differentiated	10
Poorly differentiated	5
Moderate differentiated	2
Adenosquamous carcinoma	2 (10%)
Papillary adenocarcinoma	1 (5%)
Total	20 (100%)

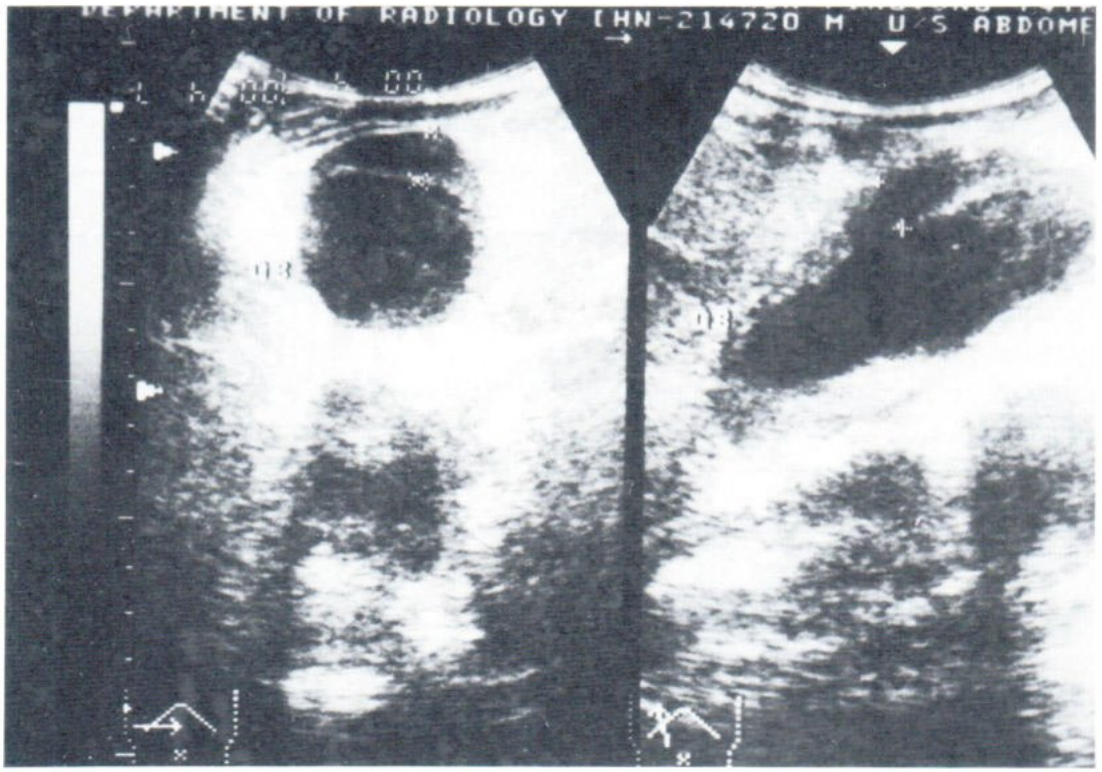

Fig. 1. Well differentiated adenocarcinoma in a 74-year-old man with RUQ pain for 3 days with fever. Transverse and longitudinal US images show non-uniform thickening of gallbladder wall without gallstone.

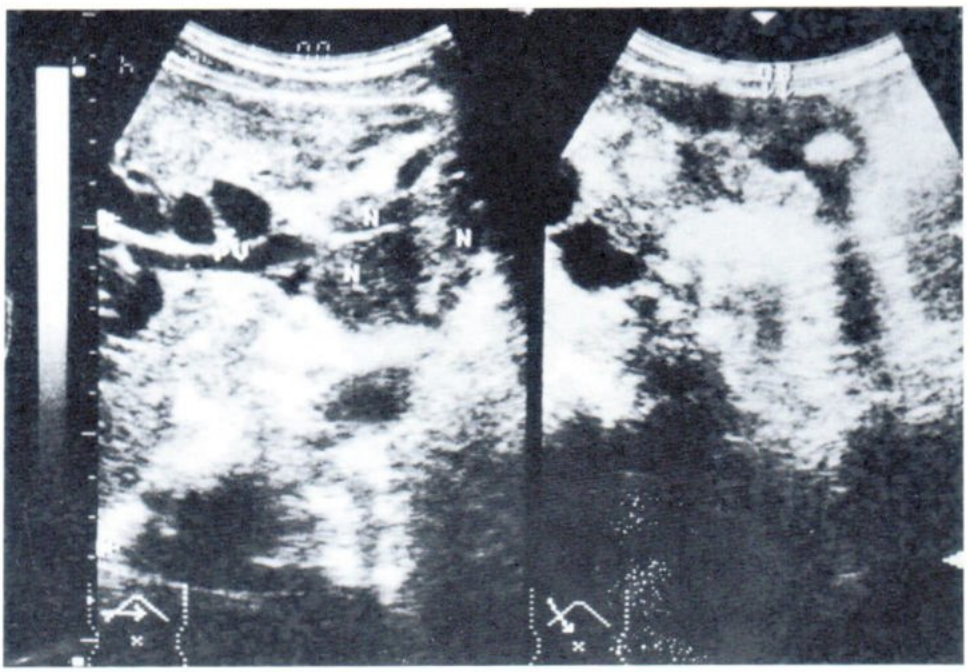

Fig. 2. Well differentiated adenocarcinoma in a 72-year-old man with dyspepsia and marked jaundice for 2 weeks. Transverse and longitudinal US images reveal enlarged porta hepatis/peripancreatic lymph nodes and diffuse GB wall thickening with gallstone.

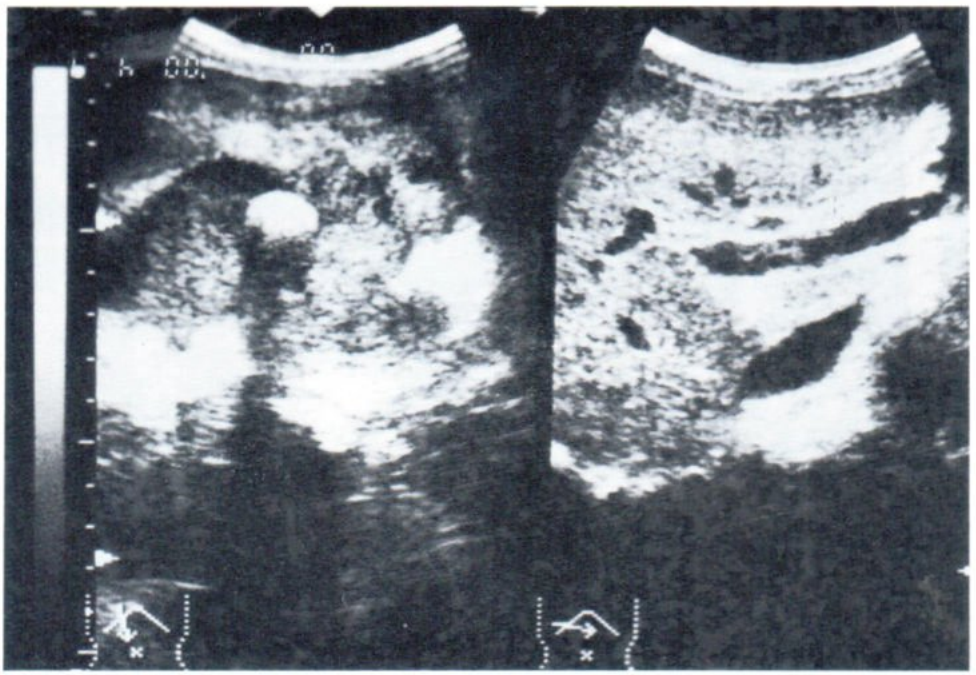

Fig. 3. A 64 -year-old man with RUQ pain and weight loss. (a) Longitudinal and transverse US images show thick irregularity of gallbladder wall with biliary sludge and gallstone without CBD dilatation.

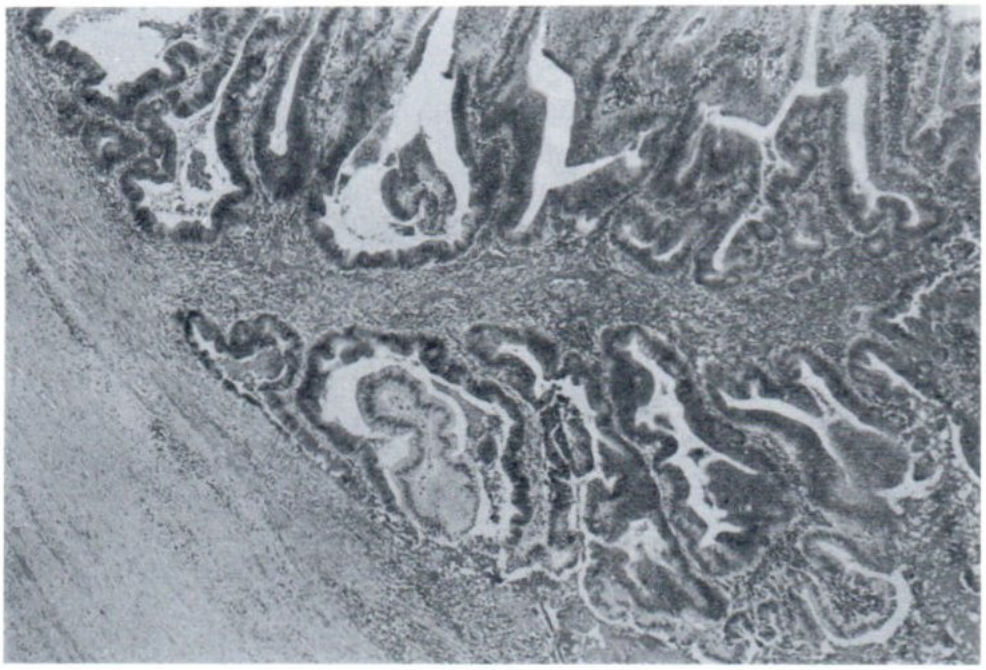

Fig. 3 b) Histology, original magnificationX100: hematoxylin-eosin stain of the tumor shows papillary adenocarcinoma ; the tumor limited to gallbladder wall.

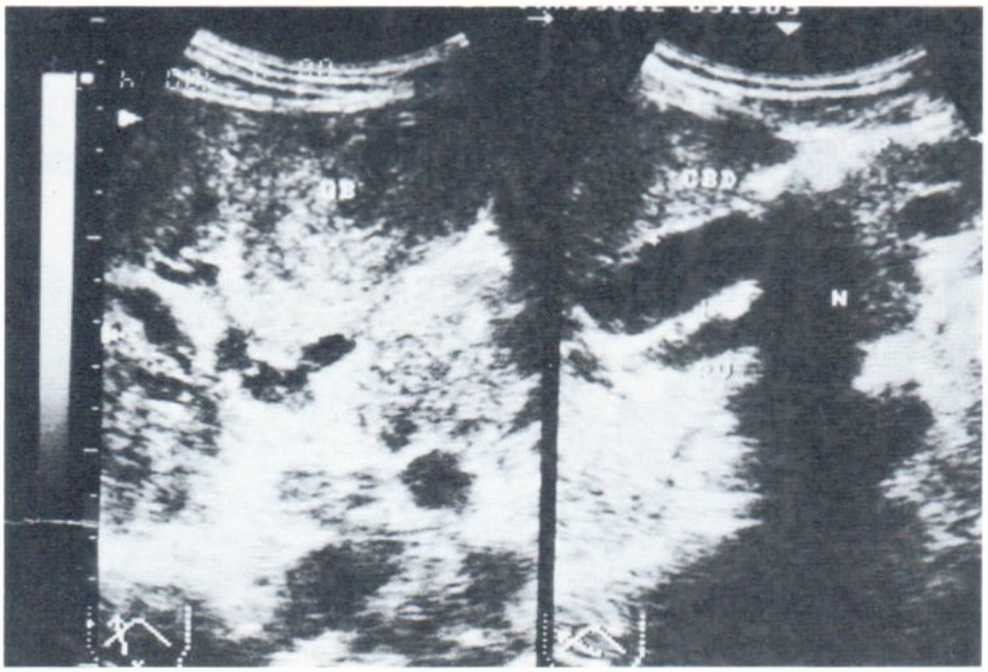

Fig. 4. A 48-year-old man with dyspepsia for 1 month and marked jaundice, 6 Kgs weight loss. (a) Longitudinal US image shows inhomogenous echogenic mass replacing GB fossa and CBD dilatation due to peripancreatic nodes.

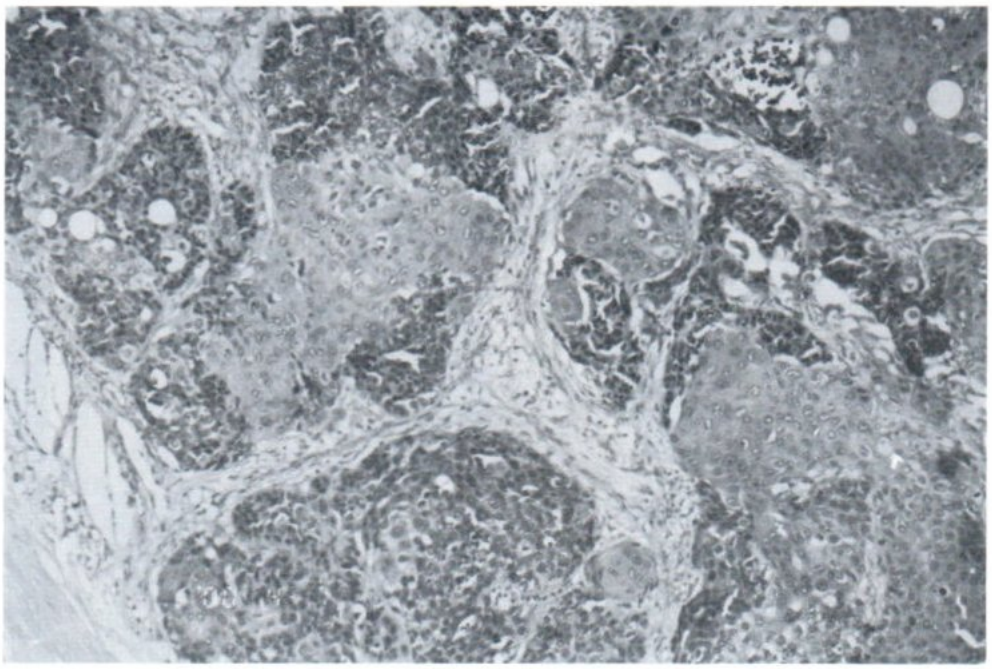

Fig. 4 (b) Histology, original magnificationX100: hematoxylin-eosin stain of the tumor shows invasive adenosquamous carcinoma.

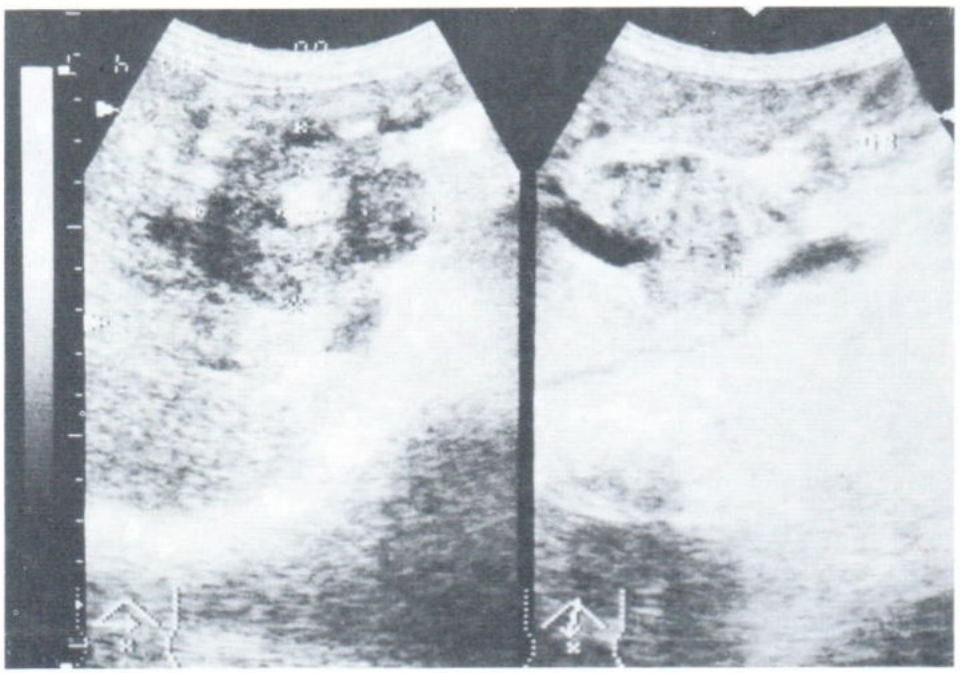

Fig. 5. Well differentiated adenocarcinoma in a 74-year-old woman with RUQ pain and weight loss. Transverse and longitudinal US images show inhomogenous mass filling the entire GB lumen with associated mass around the porta hepatis.

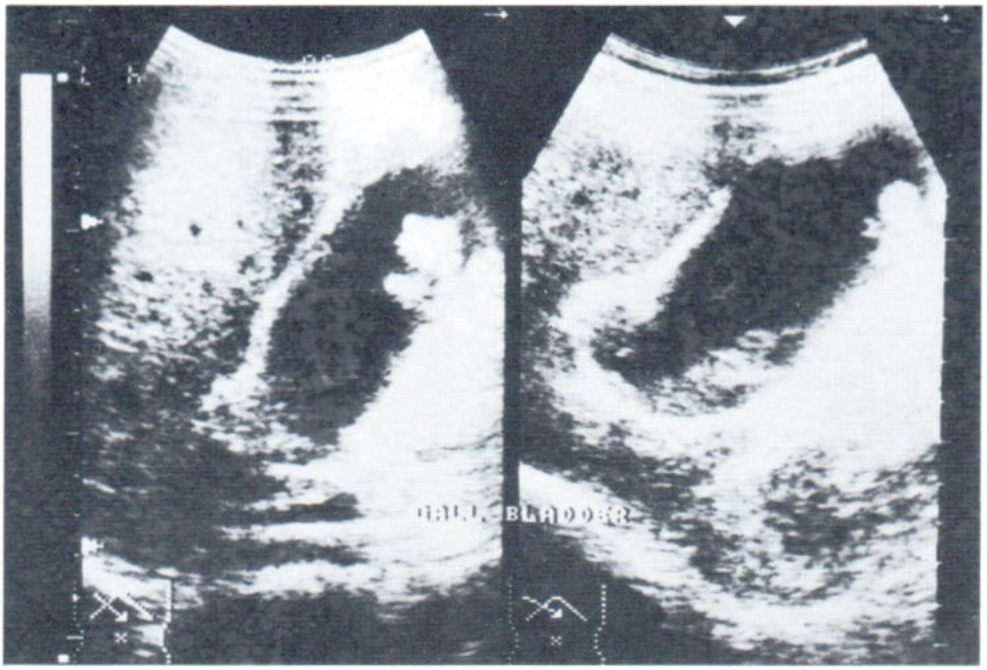

Fig. 6. A 39-year-old man with dyspepsia (a) longitudinal US image demonstrates non-movable polypoid echogenic mass extending from wall of GB near fundus.

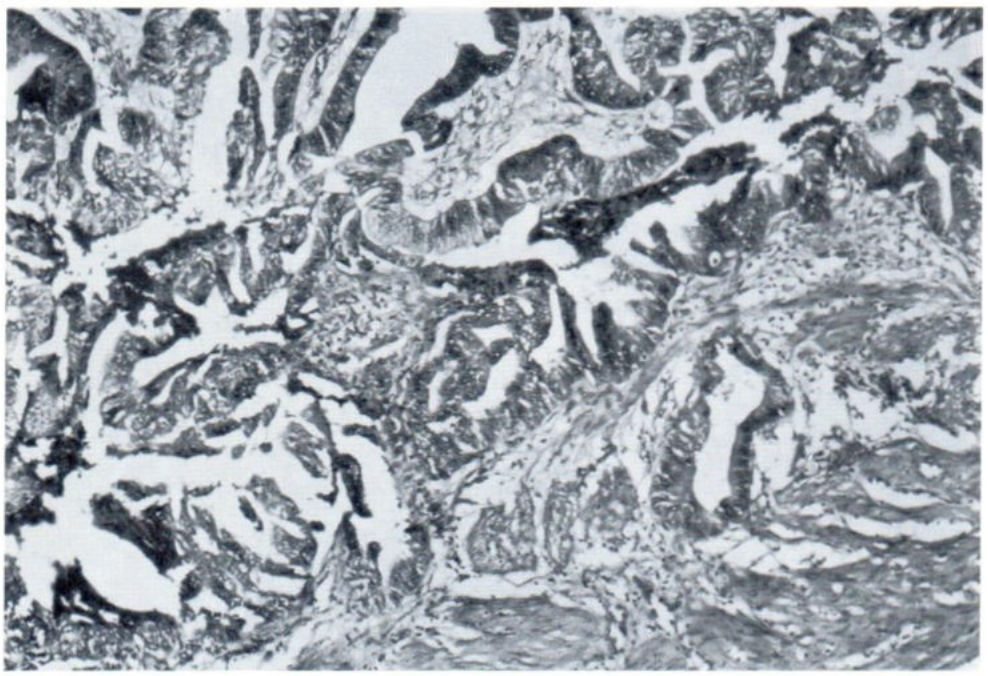

Fig. 6 (b) Histology, original magnificationX100: hematoxylin-eosin stain of the tumor shows well differentiated adenocarcinoma with transmural invasion.

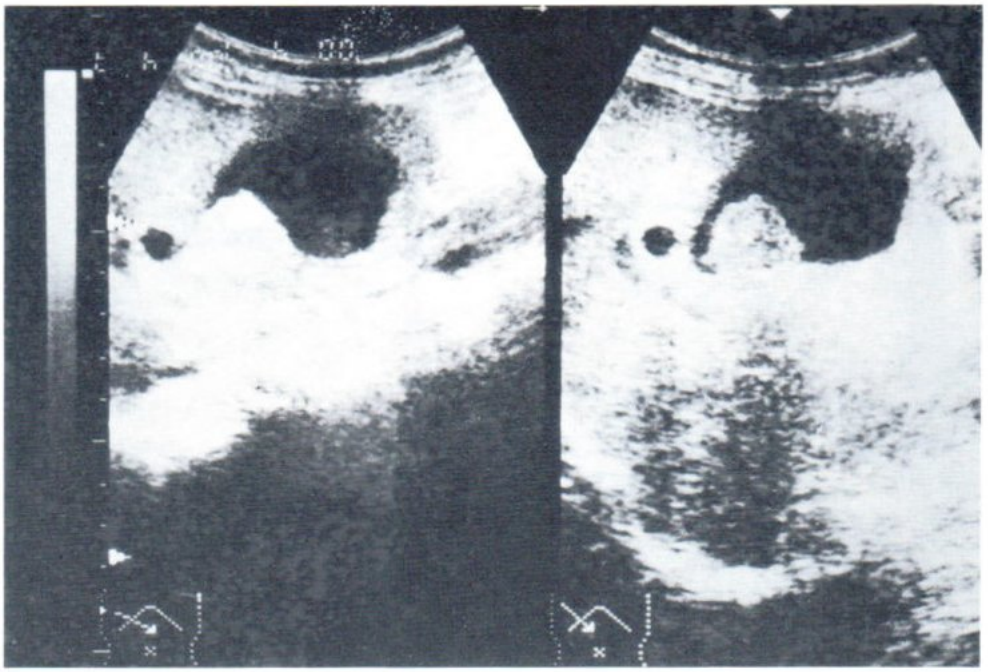

Fig. 7. Well differentiated adenocarcinoma in a 70-year-old woman with intermittent upper abdominal pain. Longitudinal US image reveals thickening of GB wall with a non-movable mass extending from GB neck.

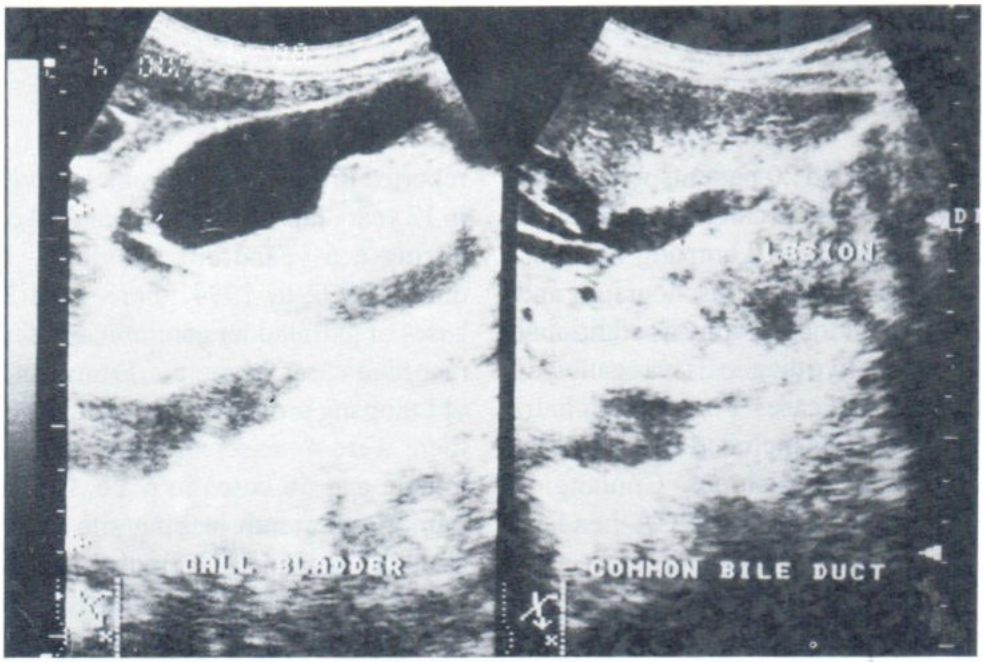

Fig. 8. Poorly differentiated adenocarcinoma in a 61-year-old woman with jaundice. Longitudinal US image shows dilated gallbladder with bile sludge and a large lobulated mass at pancreatic head region with CBD obstruction.

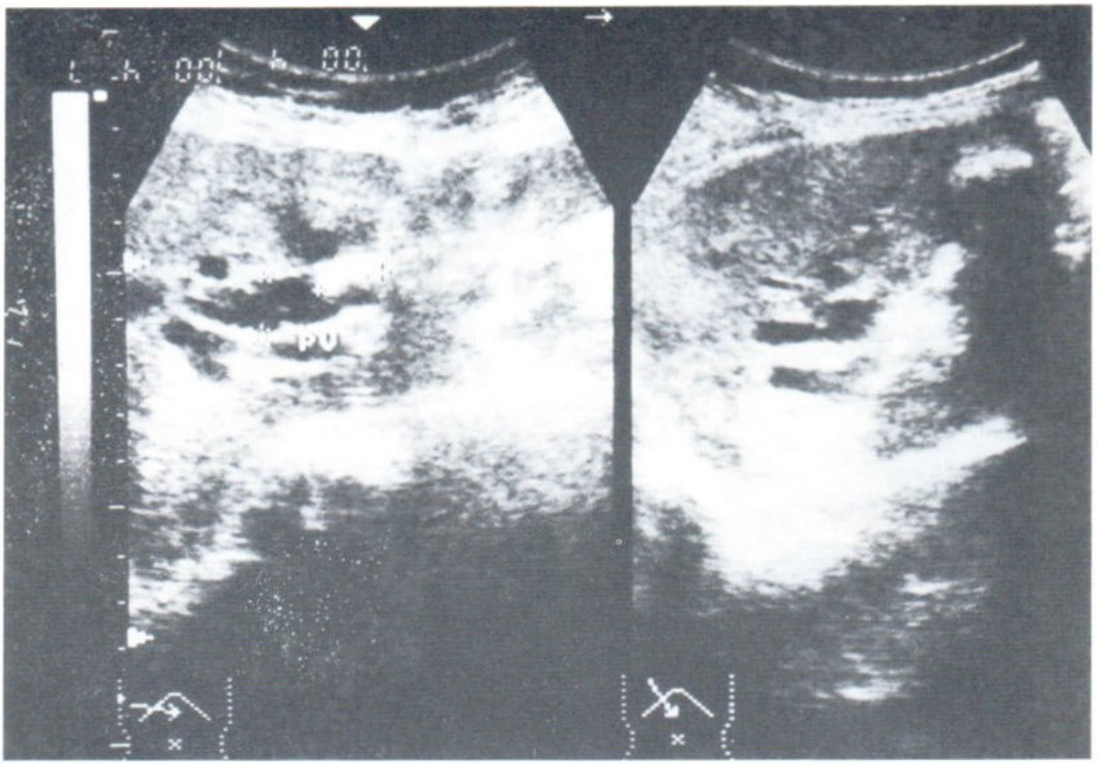

Fig. 9. Well differentiated adenocarcinoma in a 67-year-old woman with dyspepsia, jaundice and weight loss. (a)) Transverse and longitudinal US images show distal CBD stone causing CBD and intrahepatic duct dilatation as well as impacted gallstone; the detail of GB wall is not seen.

DISCUSSION

We have identified 20 patients with histologically proven gallbladder carcinoma during a period of three-year study at Lampang hospital. All 20 patients had abdominal ultrasonography and only two had computed tomography as additional investigation. Preoperative diagnosis was gallbladder carcinoma in 50% of cases. For the other half, the presumptive diagnosis included cholecystitis, obstructed CBD stone, gallstones, Cholangiocarcinoma with invaded GB and CA head of pancreas.

Gallbladder carcinoma is a rather rare malignant tumor of alimentary tract.This is supported by several previous studies i.e. 59 cases reported in a 17 year- U.S study,[14] 58 cases reported in a 14 year- Taiwanese review,[15] 44 cases in 12 year- Japanese study,[16] and 14 cases reported during a 6 year-Italian review.[17] In Thailand, during 1992 to 1994, there were 392 recorded cases of gallbladder carcinoma in female and 333 recorded cases in male.[18] From cancer incidence of Lampang province studies during 1988 to 1992, there were 42 cases of gallbladder carcinoma in female and 56 cases in male. Gallbladder carcinoma is the tenth leading site of new cancer in male in Lampang.[19] A finding of 20 new cases in a three year period of the present study support the significant incidence of this cancer in Lampang Province . This data raises at least three interesting questions. Firstly, why Thai male (in the north) has a high incidence of gallbladder carcinoma.

Secondly and thirdly, are there any predisposing factors of GB carcinoma in Lampang region and its surroundings, and what are they? Lampang Hospital is a regional center hospital located in the North of Thailand. It should be noted that Lampang province is one of a few province that have coal mines. Cooking behavior of people in the north is rather different from the other parts of Thailand. Whether or not this unique circumstance of Lampang is contributed to the high incidence of GB carcinoma remains to be studied. The equal sex distribution, in the present study is significantly different from report in the literatures. This is worthwhile to be further investigated.

Ultrasonographic and histologic findings of GB carcinoma in the present study were similar to those previously reported. However, there were some findings in this study that highly suggestive of gallbladder carcinoma. These were mass replacing GB fossa, fungate intraluminal mass with irregular border,[20] Irregularly thickened gallbladder wall, presence of lymphadenopathy and liver invasion. Findings of advanced stage were biliary dilatation, retroperitoneal lymphadenopathy, mass in porta hepatis and liver invasion. Thickening of gallbladder wall are found in many conditions such as acute, chronic,[21] emphysematous, empyematous,[22] xanthogranulomatous,[23] gangrenous cholecystitis,[24] adenomyomatosis of the gallbladder,[25] Cholesterosis, AIDS cholangiopathy.[26,27] Also other extrinsic causes such as congestive heart failure, renal failure, hypoalbuminemia,[28,29] ascites, viral hepatitis,[30] leukemic infiltration and metastasis to gallbladder.[31,32] Polypoid intraluminal mass should be differential diagnosed from cholesteral polyp as well as inflammatory polyp.[33] Other carcinomas that may mimic GB carcinoma are CA head of pancreas and cholangiocarcinoma.[34,35] Cholangiocarcinoma is more prevalence in North and Northeast of Thailand.

The most common route of tumor spreading is direct invasion into the liver. This can be explained that the hepatic surface of the gallbladder is drained by vessels communicated with adjacent hepatic veins.[36] Spread to lymph nodes around the common bile duct and other adjacent organs is also a common occurrence.[2] It should be noted that lymph node enlargement around the distal common bile duct and in the region of the head of the pancreas may be confused at sonography and CT in cases of pancreatic carcinoma.[37] Other structures that may be involved are lymph nodes in the region of the porta hepatis, hepatic and common bile ducts, pancreas, colon and duodenum.[9] Obstruction of the biliary tree results jaundice. 35-74% of patients with gallbladder carcinoma presented with jaundice at the time of admission.[37] Although jaundice is one of the earliest clinical presentations of the disease, it unfortunately signifies an advanced stage of the malignancy. In this study, 40% of patients presented with jaundice. Spread through the cystic duct and intraperitoneal seeding are encountered less often.[37] Endoscopic US is another new imaging modality, that can provide more accurate staging information, prognosis relates to depth of invasion.[38]

Prophylactic cholecystectomy is recommended for patients with anomalous pancreaticobiliary junction (APBJ) without congenital choledochal cyst, which carries a high risk of gallbladder carcinoma development. For early diagnosis of APBJ , gallbladder abnormality on ultrasonography or acute pancreatitis of unknown etiology should prompt further investigation with Endoscopic Resonance Cholangiopancreatography or less invasive imaging modalities such as endoscopic ultrasonography or MRCP (magnetic resonance cholangiopancreatography).[5]

Anomalous arrangement of the pancreaticobiliary duct is an anatomical maljunction of the bile duct and the pancreatic duct that is frequently associated with gallbladder carcinoma.

It has been postulated that pancreatic juice regurgitates into the biliary tree, and the mixture of refluxed pancreatic juice and stagnant bile juice acts as an irritant factor to the biliary tract epithelium, leading to chronic inflammation and metaplasia. Eventually these mucosal changes may progress to invasive carcinoma.[39]

CONCLUSION

Ultrasonography is a useful modality for the diagnosis of GB carcinoma ; providing critical diagnostic information which cannot be obtained by other conventional procedures. To make an early diagnosis of GB carcinoma is difficult but is essential to improve the survival of the patients with this cancer. Carcinoma tended to be missed when gallstone were present. Even in the presence of Gall stone or cholecystitis, any abnormal finding should make one suspicious of gallbladder cancer. A combination of diagnostic methods is important.

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TRANSABDOMINAL ULTRASOUND OF GASTRIC TUMOR

SUPAPORN PANICH M.D.

ABSTRACT

Ultrasound is often used as a primary procedure in the patient with a nonspecific abdominal complaint. Finding of atypical target pattern or pseudokidney sign anteriorly located in left upper abdomen to mid upper abdomen, adjacent to the visceral surface of left lobe of liver, suggested that the lesion may be originated from stomach. Although differentiation between benign or malignant patterns cannot be definitely made, recognition of ascites, intraabdominal lymphnode, invasion to adjacent structure or evidence of intraabdominal metastasis may be helpful for the indications of malignancy. Four cases of stomach tumor were preliminary diagnosed by ultrasound. The Upper Gastrointestinal study and gastroscopy were performed for definite diagnosis.

Many gastric diseases including gastric tumor usually present with nonspecific abdominal symptoms, such as dyspepsia or abdominal pain. Delayed diagnosis and treatment may lead to unsatisfactory result. In general, radiographic evaluation of the gastrointestinal tract using barium or gastroscopy have been the gold standard for the diagnosis of gastric diseases. However, the investigations mentioned above are not available in our out patient clinic or in some hospitals. The ultrasound is readily available to be used for examination as it is cheaper and being a noninvasive technique. So the ultrasonography is usually performed as a preliminary screening test prior to radiographic study or gastroscopy. Recognition of the sonographic patterns arising from the stomach is of practical important in patient care, since gastric mass may be encountered initially on sonography. Certained sonographic pattern arising from normal and abnormal stomach and ultrasonographic anatomy of stomach related to adjacent abdominal structures have been recognized to improved the accuracy of diagnosis.

CASE REPORT I

A 81 years old male patient came to the hospital with left upper abdominal pain for 3 days. Ultrasonographic finding revealed a hypoechoic mass with central echoic core located at anterior portion of left upper abdomen. The mass is just posterior to the left lobe of liver. The distance between peripheral hypoechoic wall to central echoic cavity was 2cm., represented thickened gastric wall, by which stomach malignancy was suggested. Gastroscopy found a gastric tumor. The tumor was ulcerative type, located at the fundus of stomach, extending upward to the esophagus. Unfortunately patient denied surgery.

CASE REPORT II

A 57 years old male patient complained of abdominal dyspepsia. Physical examination revealed ill defined mass at left upper abdomen. The ultrasonographic study showed multiple irregular target appearance mass, anteriorly located at left upper abdomen, just posterolateral to the visceral surface of left lobe of liver. Gastric

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cancer was first considered. The average gastric lesion wall thickness was about 2.2cm. The upper gastrointestinal study was done and revealed multiple malignant ulcers at the body of stomach. Gastroscopy also confirmed multiple ulcerative masses from fundus to body of stomach. The pathological report was poorly differentiated adenocarcinoma.

CASE REPORT III

A 67 years old man complained of progressive dyspepsia and weight loss. On physical examination and laboratory finding showed anemia and leukocytosis. Ultrasound of abdomen revealed mild hepatomegaly and marked splenomegaly. There is a large sonolucent mass at left upper abdomen, adjacent to the visceral surface of left lobe of liver. Stomach mass was suggested with a variable thickening gastric fold ranging from 0.7 to 1.5 cm. Most of the gastric wall thickness was about 7 mm. Additional paraaortic lymphadenopathies were detected. Intraabdominal Lymphoma with stomach involvement was first considered. Gastroscopy confirmed marked thickening and edematous folds of the whole stomach. The pathology of gastroscopic biopsy was malignant lymphoma, small lymphocytic type.

CASE REPORT IV

A 71 years old man, known case of stomach cancer, poorly differentiated adenocarcinoma, complained of progressive dyspepsia and dysphagia. Near total gastrectomy, Billroth II anastomosis and splenectomy was performed 7 months ago. Ultrasound screening showed a 5x5.6 cm. hypoechoic mass at the stomach location, adjacent to the visceral surface of left lobe liver. Another 3.2 cm. hypoechoic aortocaval lymphnode was also demonstrated. Recurrent stomach cancer was diagnosed. The upper gastrointestinal study confirmed a polypoid mass in the remnant stomach.

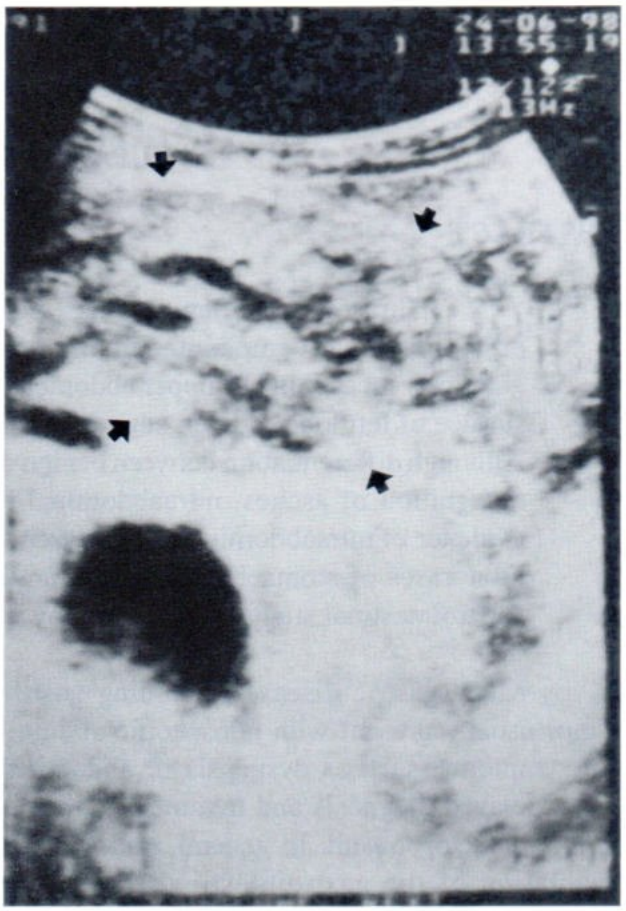


Fig. 1. Ultrasound done on an axial plane of left upper abdomen, revealed lobulated soft tissue mass (arrow), anteriorly located at left upper abdomen and just antero-left laterally to proximal abdominal aorta. Stomach mass was suggested.

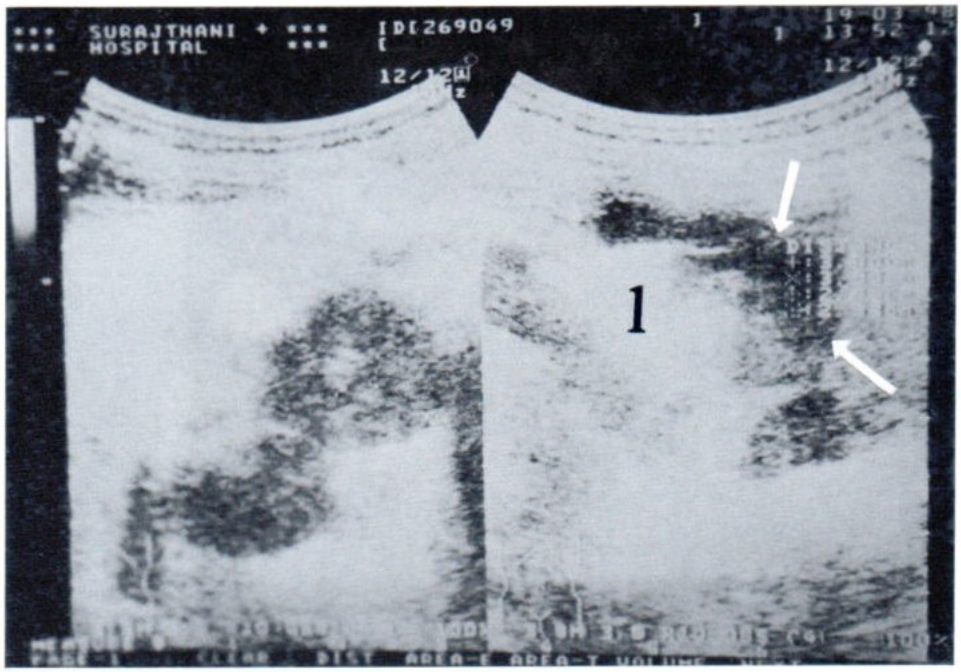
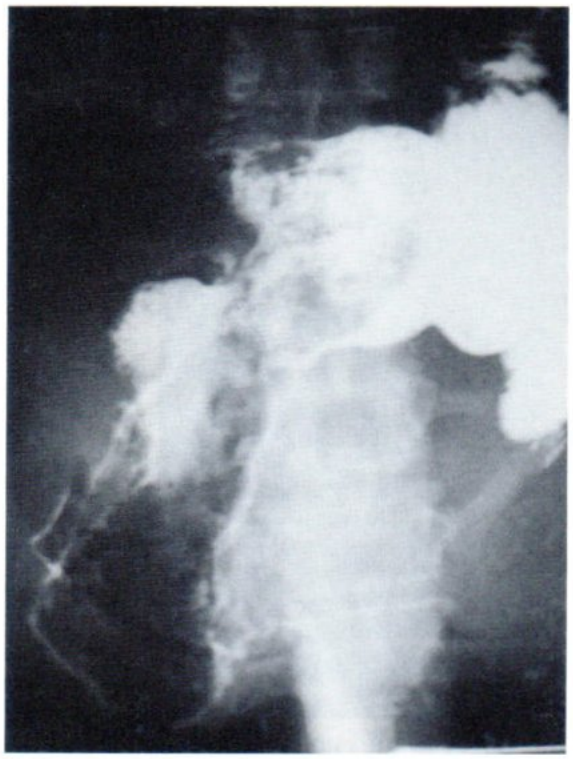


Fig. 2a and 2b Multiple atypical target appearance or pseudokidney-liked lesions at the stomach location. These lesions were included in Fleischer's characteristic of abnormal bowel mass pattern. The long arrow on Fig 2b demonstrated a focal thickened gastric wall. **l** referred to gastric lumen.



2C **2D**

Fig. 2c and 2 d Supine and prone projection of upper gastrointestinal study showed multiple malignant ulcerative masses at the body of stomach.

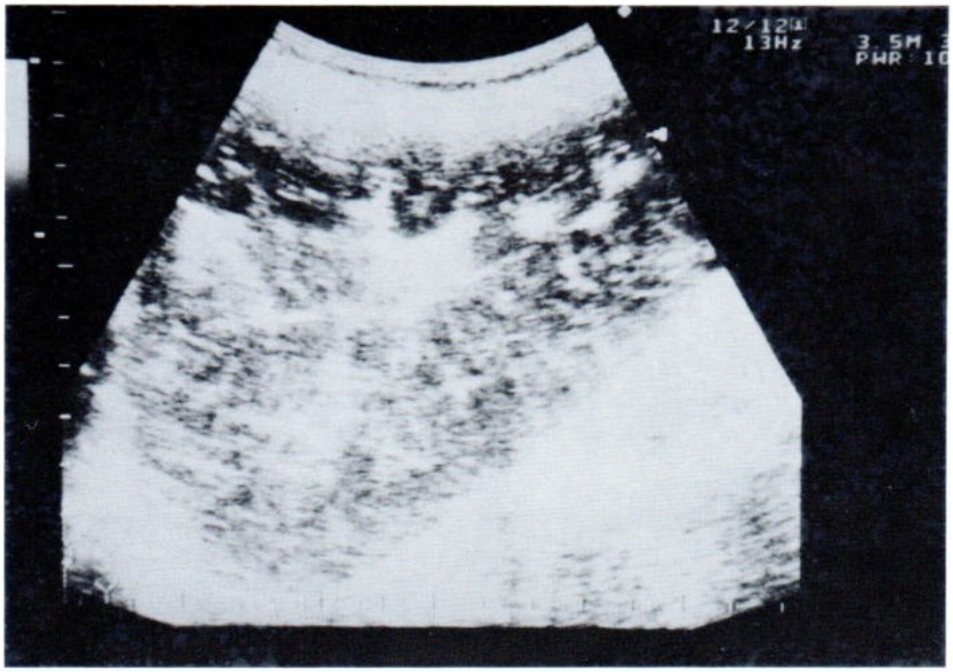


Fig. 3a. Ultrasound finding of gastric lymphoma, revealing sonolucent gastric masses with variable thickened gastric fold.

Fig. 3b. The stomach mass is anteriorly located in the left upper to mid upper abdomen, adjacent to the visceral surface of left lobe of liver. We can definitely separated the stomach mass from the left lobe of liver.

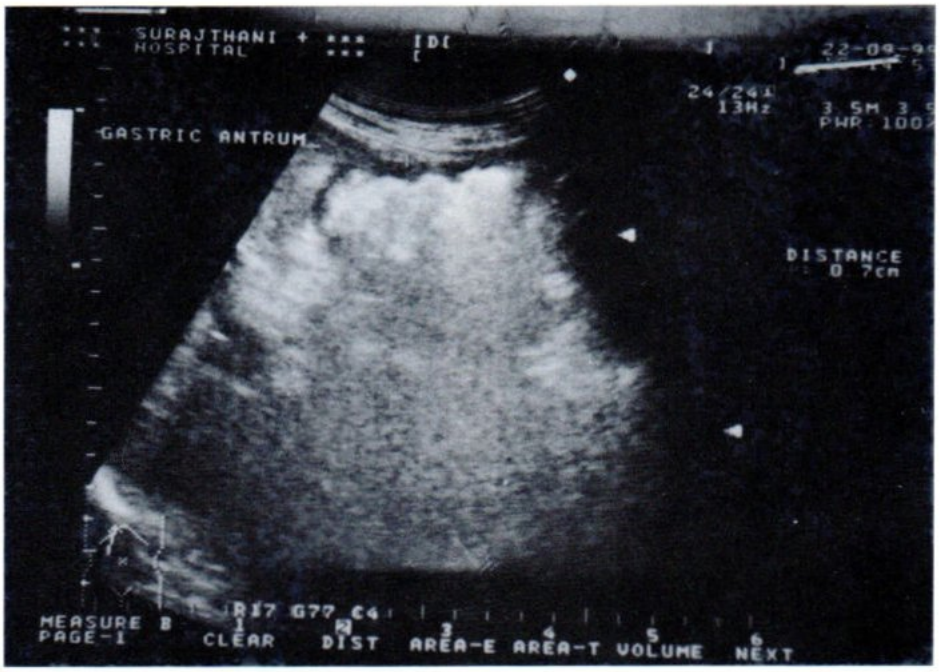


Fig. 3c. Sagittal plane of the stomach mass demonstrated diffuse thickened gastric wall about 7mm.

Fig. 3d. Excretory urogram of the same patient revealed air trapped between the enlarged folds from fundus to antrum of stomach (thick arrow).

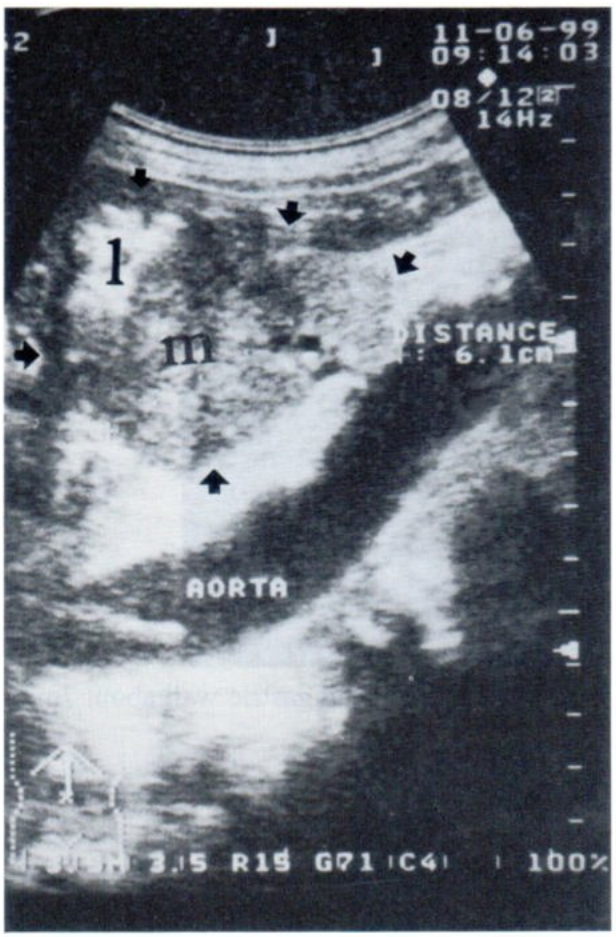


Fig. 4a. Ultrasound finding of recurrent gastric cancer, the sagittal plane of mid upper abdomen demonstrated asymmetrical target lesions, thickened posterior wall of gastric remnant (m) protuded into the gastric lumen.[1] Thin arrows demonstrated the whole gastric remnant, which was anteriorly located in mid upper abdomen.

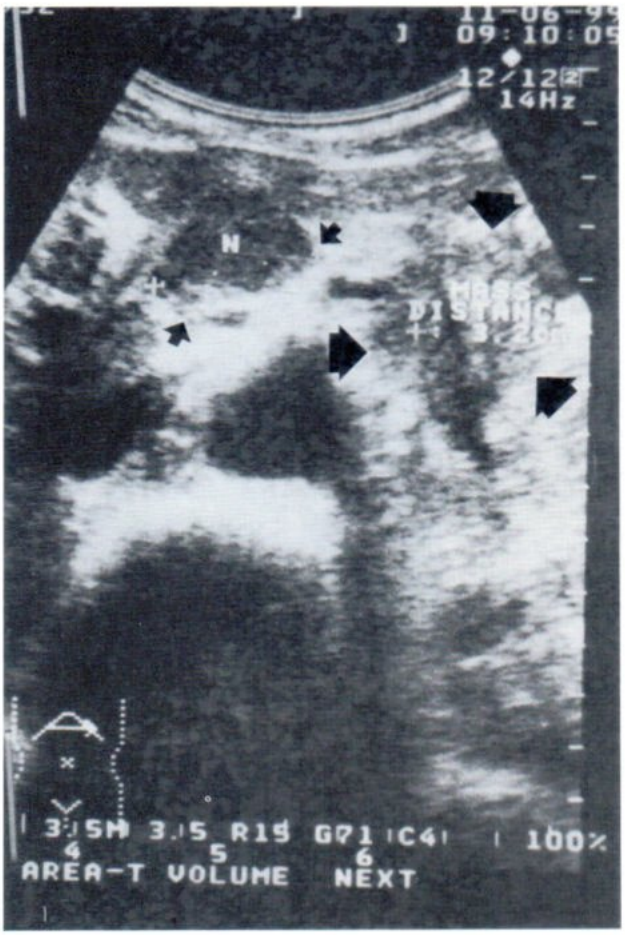
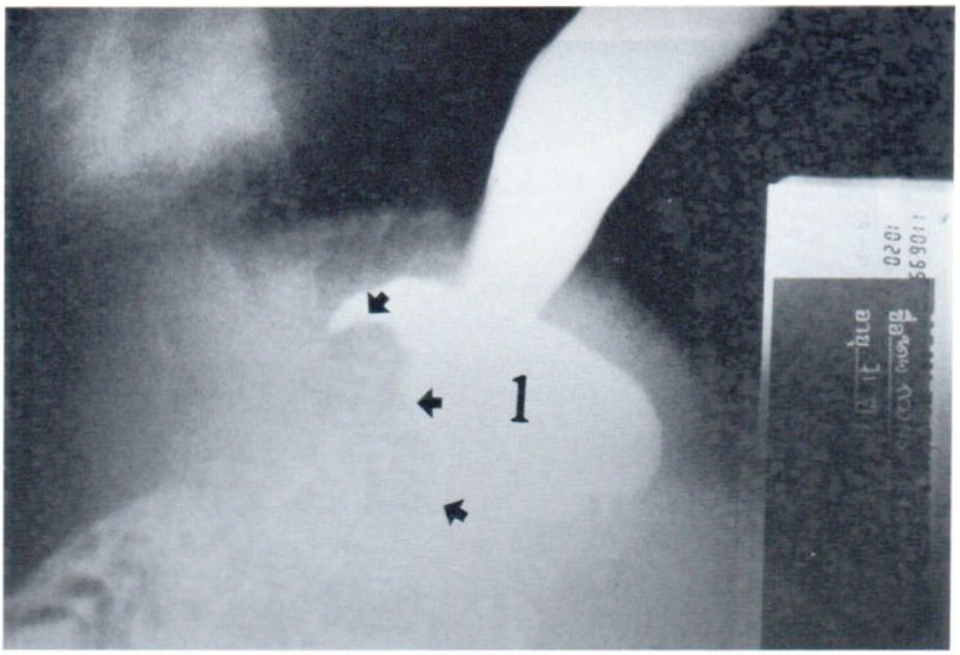


Fig. 4b. There is a 3.2cm. lymph node enlargement (thin arrows) adjacent to the right sided of gastric mass (thick arrows).



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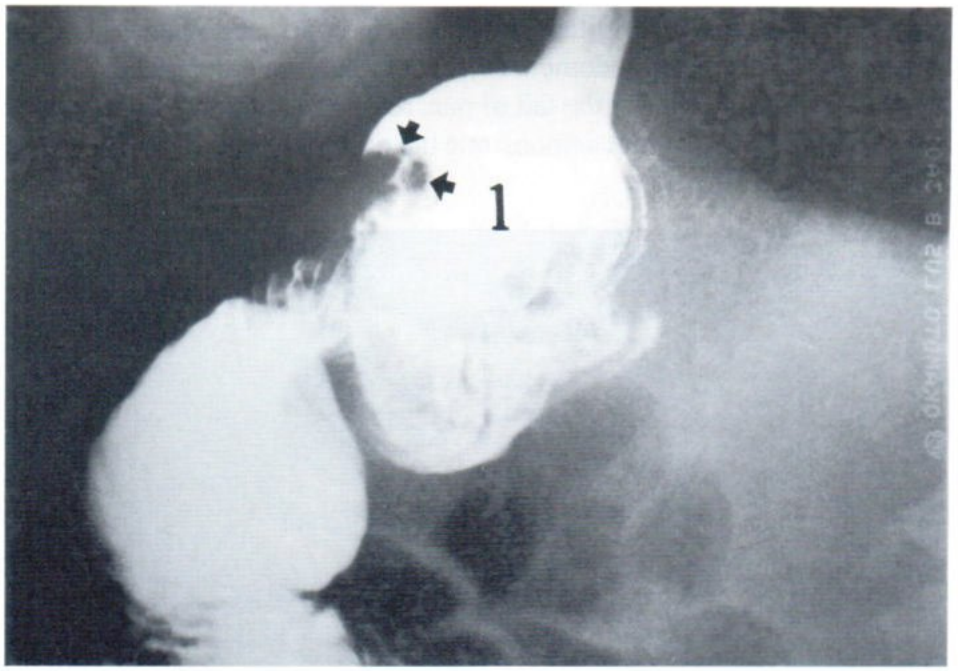

4D

Fig. 4c, 4d. Upper gastrointestinal study confirmed a polypoid mass (thin arrows) protuded into the posterior aspect of gastric remnant's lumen.[1]

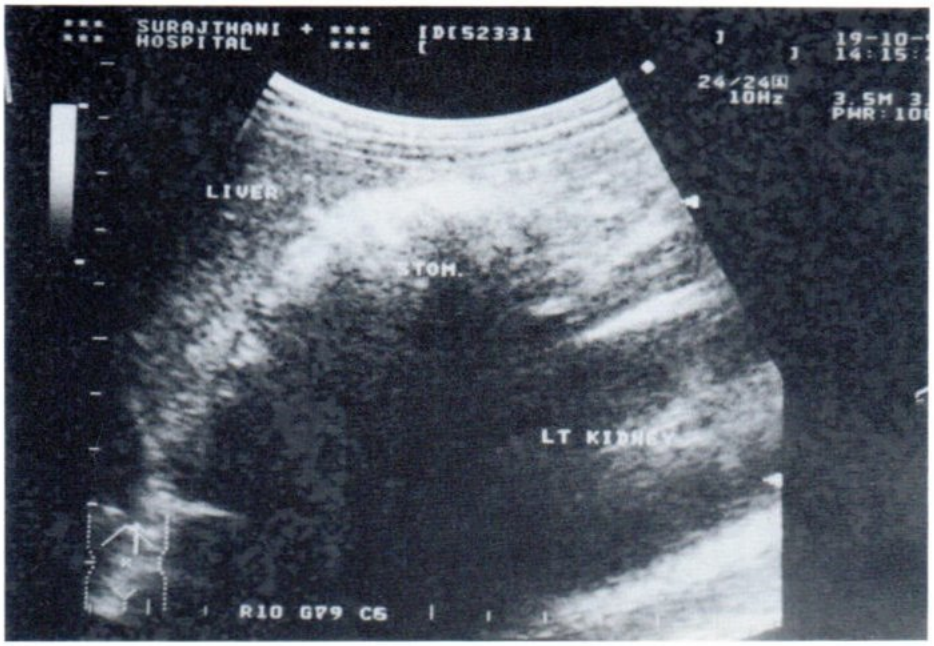

Fig. 5. Normal anatomy of gastric body by ultrasound
The examination was done in sagittal plane of left upper abdomen. The gastric body was located anteriorly in left upper abdomen, adjacent to the visceral surface of left lobe liver. The gastric body should be anterior to the tail of pancreas. The anterior wall of gastric body should be thin smooth outline. We cannot demonstrate the posterior wall of gastric body clearly, except in fluid filled stomach situation.

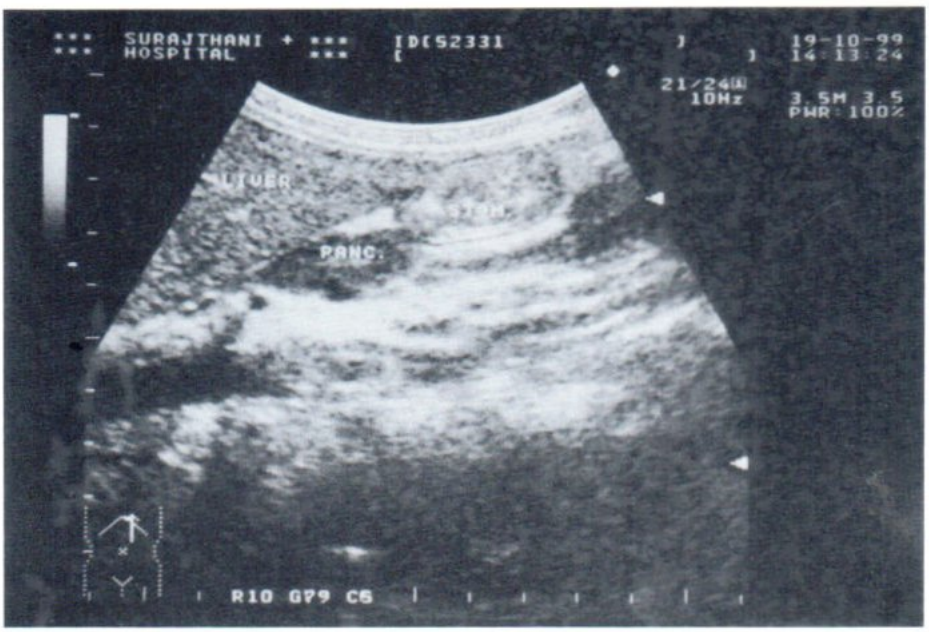

Fig. 6. Normal anatomy of gastric antrum by ultrasound
The gastric antrum was connected to the gastric body, anteriorly located from left upper abdomen to mid upper abdomen. The gastric antrum was anteriorly located to the pancreas body. Ultrasound can demonstrated well the whole gastric antrum as a thin round sonolucent ring structure (antrum wall) with symmetrical central echogenic core (antrum lumen).

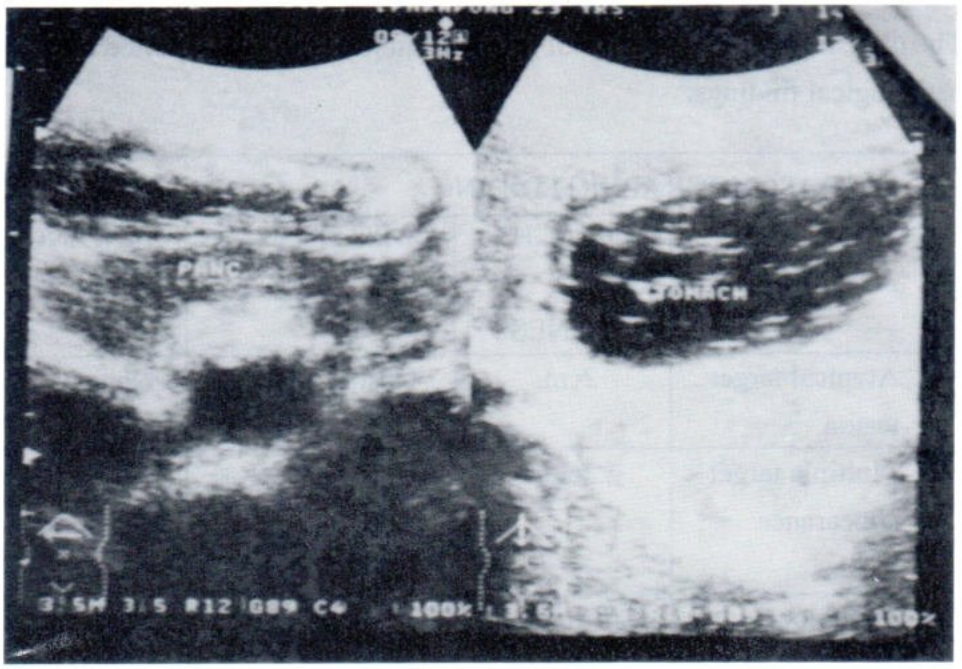

Fig. 7a,b Normal anatomy of stomach after intake of water 500ml.

Fig. 7a Axial plane in mid upper abdomen, revealed dilated stomach body and antrum. The stomach was anteriorly located to the pancreas. Smooth thin symmetrical 4 mm. Gastric wall was noted.

Fig. 7b Sagittal plane in mid upper abdomen, demonstrated dilated with fluid filled stomach.

TABLE I Sonographic measurement of normal bowel wall thickness[1]

BOWEL SEGMENT	NONDISTENDED			DISTENDED		
	No. patients	Range (mm.)	Average (mm.)	No. patients	Range (mm.)	Average (mm.)
STOMACH	12	2-6	5	6	2-4	4
SMALL BOWEL	4	2-3	3	7	2-3	3
LARGE BOWEL	3	4-9	6	4	2-4	3
TOTAL	19	2-9	5	17	2-4	3

TABLE II The ultrasonographic findings of gastric tumors of the four reported cases correlated with pathological findings.

CASE	ULTRASONOGRAPHIC FINDING			PATHOLOGICAL FINDING
	APPEARANCE	STOMACH WALL THICKNESS	LOCATION	
CASE I	Atypical target lesion	2cm.	Gastric fundus	None
CASE II	Multiple target appearance lesions	2.2cm.	Body of stomach	Poorly differentiated adenocarcinoma
CASE III	Variable thickened fold with dilated fluid filled stomach	7mm.	Whole stomach	Malignant lymphoma, small lymphocytic type.
CASE IV	Lobulated hypoechoic mass	-	Posterior wall of gastric remnant	Recurrent poorly differentiated adenocarcinoma

DISCUSSION

Fleischer proposed the ultrasonographic measurement of normal bowel wall thickness in non distended and distended status, as demonstrated in table I. The average difference in wall thickness between the distended and non -distended bowel segment was 2mm.. Especially the thickness of normal gastric body and antral wall, when nondistended measured upto 5mm..[1-2]

The ultrasonographic appearance of gastric and colonic tumor has been described since 1976,[3] as a round or an oval homogenous hypoechoic mass with a central collection of strong echo, doughnut shaped liked lesion: the so called "pseudokidney" or "target" pattern.[1-6] The abnormal configuration or atypical target pattern described by Fleischer must have the following characteristics: (a) A sonolucent halo greater than 5mm., represent the thickening of bowel wall. (b) Asymmetrically located central echogenic core, (c) A lack of demonstrable movement or change in configuration of the bowel on real time ultrasound scanning and (d) Irregular contour of the mass. Majority of the patients with bowel tumor will at least show two positive findings of these features.[5]

The ultrasonographic specific location of stomach was described in left upper abdomen, particular anterior location, adjacent to the visceral surface of left lobe of liver.[4,7-9] Whalen et al have demonstrated this anatomical relationship.[10] Wall reported the diagnostic accuracy of B scan ultra-

sonography in 11 patients with malignant gastric neoplasm, by using the criteria of atypical target lesion arising in the specific location of stomach as described by Whalen et al. as 73%.[8] In our report, all the 4 cases were initially diagnosed as gastric tumor by ultrasound, confirmed by upper gastrointestinal study using barium and gastroscopy (Fig. 1,2,4). However, we cannot definitely differentiated between benign and malignant lesion.

Most reports also indicated that many types of gastric lesion either benign or malignant conditions can result in atypical target pattern.[2-7] However, there is only Schoelmerich's study which reported patients with target sign relating to stomach was more likely to have malignancy disordered (72% positive predictive value) rather than those with target sign related to bowel (16% positive predictive value).[11] In our report, we regard the evidence of distant metastasis, ascites, abdominal lymphadenopathy or adjacent organ invasion to be helpful for evaluation. Additional irregular thickening of gastric wall with asymmetrical central echogenic gastric lumen referred to more malignant status as shown in case report I, II and IV. Whereas smooth symmetrical thickening of gastric wall and gastric lumen lesions, are more likely to be benign.[4,7]

Adenocarcinoma of stomach may appear in diffuse infiltrative or localized pattern. The target pattern was found in localized formed.[2-9,11] Whereas the finding of diffuse thickening of the wall of stomach may be seen in the infiltrative adenocarcinoma of stomach, as well as gastric lymphoma. Lymphoma cells infiltrated submucosal layer causing diffuse thickened gastric fold,[12] therefore the common finding of gastric lymphoma was a sonolucent mass with varying thickened gastric fold of the whole stomach (Fig. 3). In the case report III, additional intraabdominal lymphadenopathies and diffuse hepatosplenomegaly were helpful for the differentiation between gastric lymphoma and adenocarcinoma of stomach.

Chronic gastritis finding (Fig. 5) closely resembled diffuse form of gastric cancer or gastric lymphoma. However, the wall was not actually as thick as in tumor infiltration.[4,7] Gastric ulcer appeared as small echoes within focal thickening of the gastric wall, just liked ulcerated cancer. However, ulcerative gastric tumor had more irregular thickened gastric fold. Barium studies were often necessary.[7] In this study, case report I and case report II were ulcerative gastric tumor. However, only irregular thickened gastric wall were demonstrated. The ulceration ontop of the tumor cannot be seen.

Many reports also described stomach mass in gastric cardia or gastroesophageal junction which were usually difficult to delineate with ultrasound, because of the overlying rib cage.[4,7,8,11] The posterior wall of gastric body was not well demonstrated by ultrasound. Too small lesions or lesions infiltrating mucosa and muscularis layer only were usually difficult to be detected. Many recent reports proposed that dedicated transabdominal gastric ultrasound performed after ingestion of water and injection of a hypotonic agent may provided more detail and unique informations about both normal and abnormal gastric wall. The five layers of gastric wall and small lesion with only infiltrated mucosa or muscularis layer can be demonstrated by graded compression technique with high frequency transducer.[13-16] Ultrasound is good for demonstration of mass in the gastric antrum or anterior wall of body of stomach. These lesions should be located in the left upper quadrant close to the left costal margin, posterior or posterolateral to the left lobe of liver and can be separated from liver. The mass from gastric antrum should be anterior to the body of pancreas (Fig 6). Whereas the mass at the gastric body should be anterior to the tail of pancreas[4,7,8,11] (Fig7). Pancreatic tumor could also invade stomach and produce similar ultrasonographic

finding of an intramural gastric lesion, the same as a large intramural gastric tumor which is more difficult to be demonstrated. Spleen or splenic flexure colon lesions were also differentiated from gastric lesions by a more posterior location.[4,9,10]

CONCLUSION

Routine study of stomach with transabdominal ultrasound examination is very useful for evaluating patient with nonspecific abdominal dyspepsia. Although transabdominal ultrasound is not suitable as a screening test for early detection of gastric tumor. Transabdominal ultrasound cannot also definitely differentiate gastric lesions between a benign or a malignant one. However, by using the criteria as discussed previously, the ultrasound may suggest the gastric origin of a lesion and the evaluation of the patient may be expedited. Ultrasound can guide the proper use of the investigations and management.

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BILIARY ASCARIASIS

Dr.M.A. Taher, Director,

ABSTRACT

Roundworm is a common problem in Bangladesh, but biliary ascariasis is a rare phenomenon. Recently we found two cases of acute epigastric pain and roundworms were seen in the gallbladder on ultrasonographic examinations.

Key words : Ascariasis, acute abdomen, pregnancy, ultrasonography.

INTRODUCTION

Ascaris lumbricoides was first discovered by Ligneous in 1758. The detailed life-cycle of the ascaris, however, was not known until 1916. One guarter of the world's population is infected with ascariasis.[1] In a recent survey, the prevalence of Ascaris lumbricoides in 58.28 % among the school-children in Dhaka[2] and 41.12 % in Gangachara (Rangpur).[3] Clinical manifestations may result from the migration of larvae through the lungs and from the presence of adult worms in the small intestine, hepatobiliary system and pancreatic ducts. The adult worms may measure upto 45 cm in length.

CASE REPORT (1)

A medical student of 5th year MBBS (wife of a physician), primigravida, about 35 weeks of gestation, presented with acute epigastric pain on 19-5-98. She had loose motions on 17-5-98 and was taking oral rehydrations saline. Ultrasonography showed a male fetus of about 35 weeks (cephalic presentation) and serpiginious movenent of a live roundworm in the maternal gallbladder. However, abdominal pain subsided in a few hours. The patient gave a history of taking anthelmintic drug albendazole 400 mg single dose six months ago. She was improved by mebendazole and cephalexin this time.

CASE REPORT (2)

A man aged 45 years presented with acute upper abdominal pain which was subsided by hyoscine-N butylbromide and ranitidine, however, Ultrasonography revealed a dead roundworm inside the gallbladder. The patient told that he had taken mebendazole 400 mg one year ago. He was advised to take mebedazole again and repeat ultrasonography after 1 week.

DISCUSSION

Sonography is a rapid noninvasive way of imaging which shows the ascariasis in the biliary tree as a bull's eye on transverse section, as a long echogenic shadow in longitudinal section or as coils or amorphous fragments.[4-9] Pancreatic duct ascariasis has been described, although less commonly.[10-11] The worms may show characteristic sinuous movements, thus helping to confirm the diagnosis[12] as also in our present case. Peck reported a case of ultrasound imaging of intestinal ascaris.[13] Khan and Ali reported 19 cases of hepatobiliary ascariasis among 24697 persons (about 0.08%) during a ten years period in a mixed

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population from North-West Frontier province of Pakistan and Afghan refugees.[14] Khan of Bangladesh reported 4 cases of biliary ascariasis, all confirmed on surgery.[15]

Our case no. 1 is the first report of sonography of biliary ascariasis in pregnancy as far as the author knows from the available literature.

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RIGHT SIDED DIVERTICULITIS MIMICKING ACUTE APPENDICITIS: A CASE REPORT AND REVIEW OF ONE-YEAR BARIUM ENEMAS FOR LOCATION OF DIVERTICULOSIS

Linda PANTONGRAG-Brown, MD, Ekwan CHANSUE, MD

ABSTRACT

Right-sided diverticulitis is an uncommon cause of acute abdomen. We present a case of right-sided diverticulitis, whose presentation mimics acute appendicitis. We also review the prevalence of diverticulosis in our hospital, which shows that right-sided diverticulosis is very common, found in about 66% of diverticulosis cases. Because of high incidence of right-sided diverticulosis in our region, awareness of right-sided diverticulitis is important, since the treatment for this condition is mostly nonsurgical, which is opposite to acute appendicitis.

INTRODUCTION

Right-side diverticulitis is not a common cause of acute abdomen in the Western countries, because of low incidence of diverticulosis in this location.[1] In contrast, the incidence of right-sided diverticulosis in Asia is much higher than the West,[2-6] therefore, we should expect to encounter right-sided diverticulitis more often than those countries. We report a case of right-sided diverticulitis and review the prevalence of diverticulosis in our hospital in order to remind us of this condition.

CASE HISTORY

A 42-year-old woman presented with right lower quadrant (RLQ) pain for a few days and fever with chills for 1 day. She had a history of RLQ pain, on and off for a year. Physical examination revealed body temperature of 38.5 degree Celsius, RLQ tenderness and mild leukocytosis. Acute appendicitis was a presumptive diagnosis. However, history of chronic abdominal pain was unusual for appendicitis, therefore, barium enema was performed to confirm or rule out appendicitis. Barium enema revealed irritability and poor distension of the cecum. Multiple outpouchings, characteristic of diverticula, were noted along the cecum. Some diverticula showed slightly deformed sacs which suggested possible inflammation (Figure 1). The appendix was well distended and barium and air were filled to its tip, which helped to exclude appendicitis (Figure 2).

Based upon the barium enema and clinical findings, cecal diverticulitis was diagnosed. The patient was treated by antibiotics and supportive care and finally was discharged with full recovery.

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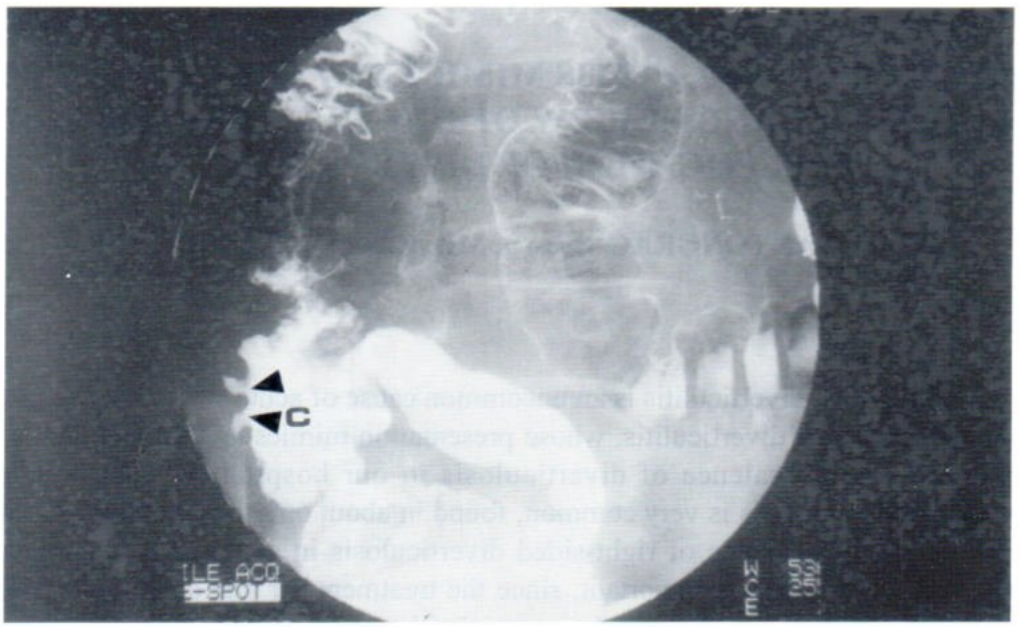

Fig. 1. Focus view of barium enema reveals poor distension of cecum (C) with deformed diverticula sacs (arrowheads), suggestive of inflammation.

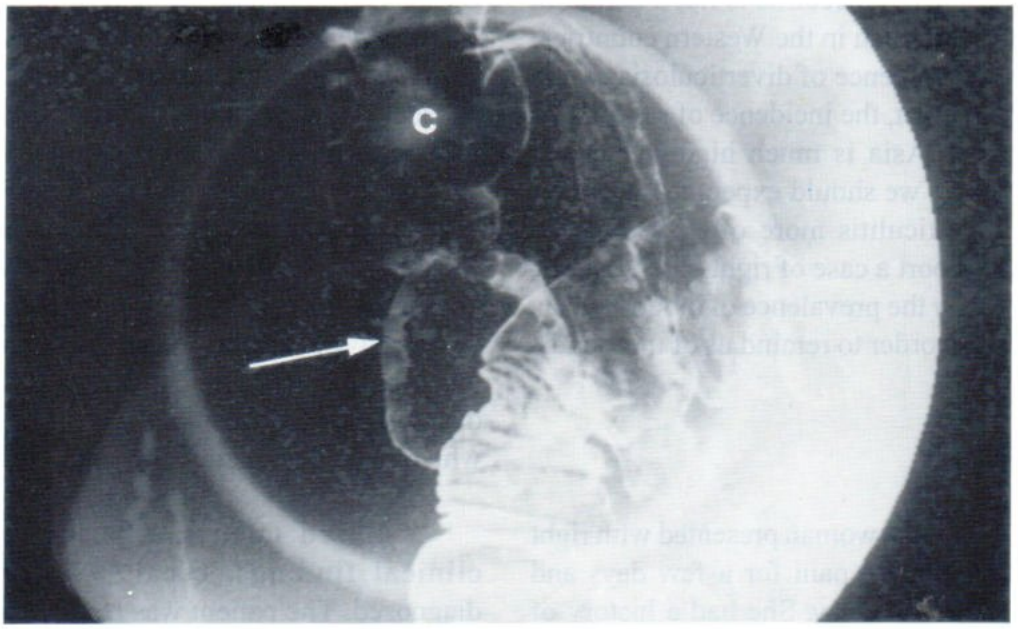

Fig. 2. Focus view of barium enema reveals the appendix (arrow) which is filled entirely with barium and air, therefore, excluding appendicitis.
C = cecum.

RETROSPECTIVE REVIEW OF BARIUM ENEMAS

According to out-patient medical records from the radiology department, barium enemas were performed in 388 patients during January to December 1997. Of these 388 patients, 228 patients had barium enemas available for review. Twenty-four patients were excluded from the study secondary to prior history of colonic surgery, colonic carcinoma, ulcerative colitis or suboptimal study. Of the remaining 204 patients, 149 patients (73%) showed no evidence of diverticulosis. The remaining 55 patients (27%) were positive for diverticulosis and were subjects for analysis.

Of these 55 patients, 31 were males and 24 were females, ages ranged from 25 to 81 years (mean, 61). The number of diverticula ranged from 1 to more than 20 (median, 4). Location of diverticula is shown on Table 1.

Table 1. Distribution of diverticulosis

Predominantly right-sided colon	36 patients (65.5%)
involve cecum	21 patients
not involve cecum	15 patients
Predominantly left-sided colon	13 patients (23.6%)
involve sigmoid	9 patients
not involve sigmoid	4 patients
Bilateral	5 patients (9.1%)
Transverse colon only	1 patients (1.8%)
Total	**55 patients (100.0%)**

Of the 55 patients, the majority of diverticula were predominantly involved right-sided colon (cecum, ascending colon, and hepatic flexure), accounting for 36/55 patients (65.5%). Of these 36 patients with right-sided diverticulosis, cecum involvement was very common, found in 21/36 patients (58.3%). The left-sided colon diverticulosis (sigmoid, descending colon, and splenic flexure) was found in 13/55 patients (23.6%). Of these 13 patients with left-sided diverticulosis, sigmoid colon was commonly involved (9/14 patients, 64.3%). Bilateral involvement was found in 5/55 patients (9.1%), whereas diverticulosis of transverse colon alone was found in only 1 patient (1.8%).

Comparing age distribution between the 2 dominant groups, the right-sided diverticulosis group ranged in age from 37-81 years old (mean, 61.5), and the left-sided diverticulosis ranged from 51-72 years old (mean, 63.1). There were 3 patients in right-sided diverticulosis group whose ages were under 50 years old (37, 39, and 43 years), whereas none was found in the left-sided diverticulosis group. Considering sex distribution, the right-sided diverticulosis group consisted of 22 males and 14 females (M:F = 1.6:1), whereas the left-sided diverticulosis group consisted of 6 males and 7 females (M:F = 0.9:1).

DISCUSSION

Diverticulosis is a common disorder in the Western countries, and is commonly involved the

left-sided colon, particularly sigmoid colon.[1] The pathophysiology is increased intraluminal pressure, which is highest within the sigmoid colon due to its smallest diameter. Moreover, fecal material at sigmoid colon is the hardest secondary to resorption of water content as stool travels through the colon, therefore pressure, needed to propel the stool, is also high. The less fiber food content, commonly consumed by the Westerners, is a contributing factor of high intraluminal pressure.

In contrast to the West, the Asian population tends to have right-sided diverticulosis. Our study, although small in number, is in concordant with prior studies,[2-6] of which right-sided diverticulosis is more common than the left side (66% vs 24%). The pathophysiology of right-sided diverticulosis is not clear. High intraluminal pressure alone cannot explain this phenomenon. Colonic muscle abnormality, motility dysfunction, as well as genetic factor, may contribute to the propensity of diverticulosis on the right side.[4,7-8]

Right-sided diverticulosis, similar to the left side, tends to occur in older age group. However, many reports revealed that right-sided diverticulosis were found in young people much more often than the left-sided diverticulosis.[3,7,9] Our study also shows 3 patients with right-sided diverticulosis whose ages were less than 50 years, while none was found in the left-sided diverticulosis group. Right-sided diverticulosis seems to occur more commonly in men and our review also confirms this finding[3,7,9] (M:F = 1.6:1).

Inflammation of right-sided diverticulosis, particularly at cecum, poses a clinical problem because it can mimic acute appendicitis, which is the most common surgical cause of acute RLQ pain. Awareness of the possibility of right-sided diverticulitis is, therefore, important since the treatment approach is different. Diverticulitis is usually treated by antibiotics, whereas appendicitis is by surgery.[10] If clinically doubtful, imaging study is recommended to differentiate these two diseases. The conservative imaging study is barium enema. Findings on BE of normal appendix is virtually exclude appendicitis. As shown in this case report, normal appendix and evidence of inflamed right-sided diverticula (deformed diverticula sacs) are well shown on BE, which makes diverticulitis the most likely diagnosis. However, the entire appendix is usually not filled on BE, posing a problem of "appendicitis is not excluded". More over, leakage of barium through the ruptured diverticula creates some concern to the clinician. Trend in the current literature suggests that CT scan is probably the best imaging modality for evaluation of RLQ pain.[11] Thin section helical CT can easily identify the appendix and diverticulosis. With optimal IV contrast enhancement, inflammation of either structure is also comfortably demonstrated by CT in most cases.[12-14]

In conclusion, we report a case of right-sided diverticulitis which clinically mimics acute appendicitis. As reviewed by this report, right-sided diverticulosis is common in our region, therefore, awareness of this condition is important so that appropriate treatment can be provided.

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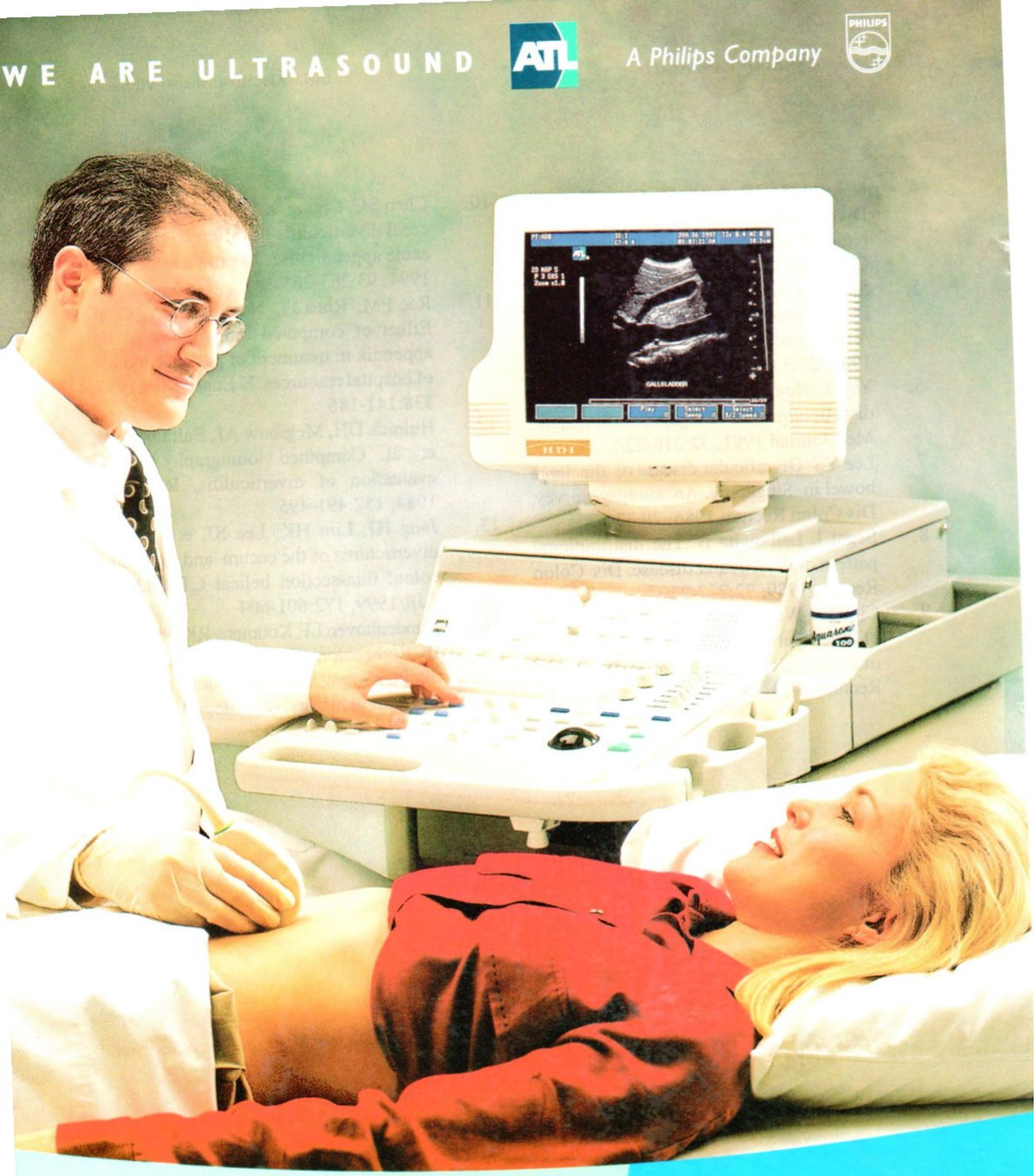

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CLINICAL EVALUATION OF TECHNETIUM-99M LABELLED HUMAN POLYCLONAL IMMUNOGLOBULIN G FOR MUSCULOSKELETAL INFECTION

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ABSTRACT

BACKGROUND: Three-phase bone scan is highly sensitive in detecting infection of the musculoskeleton. However, its low specificity necessitates the search for a more definite measure. This study was designed to determine the sensitivity and the specificity of ^{99m}Tc- labelled polyclonal human IgG (HIG) for the detection of infection of the musculoskeleton and to compare these to that of conventional three-phase bone scintigraphy.

METHODS: Thirty-four patients with suspected infection of the musculoskeleton underwent ^{99m}Tc-labelled polyclonal human IgG (HIG) scintigraphy 48 hours after 3-phase bone scintigraphy. Both scans were graded on a five-point scale by visual interpretation. The final diagnosis was established by means of bacteriologic culture, histopathologic analysis of surgical specimen or clinical follow-up (follow-up time of 28 ± 13 months). There were 44 sites evaluated. Receiver operating characteristic (ROC) curve analysis was generated for both modalities.

RESULTS: At their optimal threshold levels (score ≥ 3) of the HIG scan, the sensitivity, specificity, accuracy, likelihood ratios and area under the ROC curve were 84.61%, 96.77%, 93.18%, 26.23, and 0.967, respectively, while those of the 3-phase bone scan were 100%, 87.10%, 90.70%, 7.75, and 0.941, respectively. No adverse reaction was encountered.

INTRODUCTION

Infection of the musculoskeleton often presents a diagnostic and therapeutic problem, making the management of the disease difficult. This issue is troublesome in cases with post-traumatic, chronic infection, or those underwent surgical intervention. Its diagnosis may be aided by infection imaging.

Bone scintigraphy has been used for many years for the investigation of infection of the skeleton. Although the sensitivity of bone scan is close to 100% in chronic osteomyelitis, but specificity is low.[1] This justifies the use of additional techniques.

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^{67}Ga-citrate is more specific than bone scanning, but false-positives may occur in conditions such as healing fractures and noninfected prostheses.[2,3] Besides, it must be imported for each patient and be used within a certain period, otherwise it will decay away. Moreover, it is rather expensive in comparison to ^{99m}Tc, the most commonly used radionuclide in nuclear medicine.

Labelled-leukocytes do not accumulate at sites of increased bone-mineral turnover in the absence of infection and would seem to be an ideal radiotracer for infection. The sensitivity and specificity range from 66%-95% and from 35% -100%, respectively.[4,5,6,7] Furthermore, the labelling process is laborious, it requires a flow hood and other expensive equipment not readily available; and cells can become damaged during the labelling process if care is not taken.[8] There may be possibilities of contaminating and mis administering the blood.[9]

Radiolabelled monoclonal antigranulocyte antibodies and polyclonal human IgG have been recently introduced as radiotracers for infection imaging. Although no serious adverse reaction had been reported, when comparing radiolabelled polyclonal human IgG with monoclonal antigranulocyte antibodies, there is a problem of the mouse origin of the latter agent, thus possibly inducing HAMA with its risk for allergic reactions, altered biodistribution after repeated injection.[10] Like labelled leukocytes, radiolabelled monoclonal antigranulocyte antibodies have physiological uptake in bone marrow, making axial osteomyelitis almost impossible to diagnose with confidence.[11] Furthermore, marrow occasionally turns up in the distal extremities[12] so the addition of bone marrow imaging with ^{99m}Tc-sulfur colloid is required to improve specificity.[13]

Polyclonal human IgG is attractive in that it is available in kit form; the tedious labelling technique of leukocytes can be avoided; the chance of contamination is minimised; no expensive equipment is required; and there will be no HAMA (Human anti-mouse antibody) reaction. This study was designed to determine the sensitivity and the specificity of ^{99m}Tc- labelled polyclonal human IgG (HIG) for the detection of infection of the musculoskeleton and to compare these to that of conventional three-phase bone scintigraphy.

MATERIALS AND METHODS

PATIENTS

During October 1994-September 1996, 36 patients suspected of having musculoskeletal infection agreed to join this study were included. Informed consent were obtained from all patients. There were 16 patients with hip prosthesis and 19 patients without. Written informed consent was obtained from all patients. Two patients were loss to follow-up so we were left with 34 patients (21 females and 13 males), age ranged from 17-71 years (mean $\pm$ SD = 48 $\pm$ 19). In the patients with prosthesis, 4 patients had bilateral hip prostheses yielding 19 prostheses for assessment. The interval from replacement ranged from 1-216 months (mean $\pm$ SD = 45.11 $\pm$ 10.95). In those without prosthesis, there were 25 sites being suspected for infection. There were altogether 44 sites evaluated.

SCINITIGRAPHY

The protocol was approved by the hospital ethical committee. All of the patients, except one who underwent a HIG scan only, underwent three-phase bone scan and, 48 hours later, HIG scan. Images were acquired with an Elscint Helix dual head gamma camera using a high-resolution, parallel-hole collimator. Imaging parameters were 140 keV photopeak, 20% window and 128x128 matrix. Both examinations were performed in supine position; anterior and posterior images of

the hips or sites of interest were obtained.

Whenever possible, SPECT and 24-hour static images were also acquired with the same gamma camera and collimators. The SPECT acquisition was obtained into 128x128 matrices, 6 degree and 25 seconds per step for 60 steps using body contour orbit. The SPECT images were back-projected and filtered with a Hanning filter (a power of 2 and a cut-off frequency of 2).

THREE-PHASE BONE SCAN

Three-phase bone scan was performed in each patient with 15 mCi of ^{99m}Tc-MDP. Anterior and posterior images of the hips or other sites of suspected infection were imaged. In the first phase, a set of 2-second images was acquired for 1 minute. For the second phase, static planar images of the same site were acquired for 1 minute. Three hours after injection, static images were acquired to signify osseous phase.

^{99m}Tc-LABELLED POLYCLONAL HUMAN IgG

Radiolabelling were performed according to Boonkitticharoen et al. Eighteen mCi of ^{99m}Tc-labelled polyclonal human IgG was administered slowly intravenously. Four hours afterwards images were obtained.

INTERPRETATION

Both three-phase bone and HIG studies were separately evaluated by visual interpretation by a nuclear medicine physician blinded to the final diagnosis and the results of other imaging modalities. The visual findings were graded on a five-point scale of 0-4 according to table 1 and 2 for 3-phase bone scan and HIG scan, respectively. For each modality, sensitivity, specificity, accuracy, positive and negative predictive values were calculated at the optimal scaling threshold. A receiver operating characteristic (ROC) curve was generated and the likelihood ratios at each scaling point were obtained.

Table 1. Descriptions of each grade of HIG scan findings

Table 2. Descriptions of each grade of Bone scan findings

FINAL DIAGNOSIS

Final diagnosis of the 44 sites in 33 patients was assessed by surgery in 22 patients (23 sites), by blood culture in 1 patient (1 site), by aspiration culture in 3 patient (4 sites), by wound swab culture in 4 patients (4 sites), by follow-up in 12 patients (12 sites, median follow-up time of 24 months). The latter included four asymptomatic contralateral prostheses used as negative controls, which were followed 7 to 14 months.

STATISTICAL ANALYSIS

Statistical analysis to show differences between both scintigraphic procedures was performed with a paired test according to Hanley and McNeil.[14] A p-value of <0.05 was considered statistically significant.

RESULTS

According to the final diagnosis (Tables 1 and 2), of the 44 sites investigated, there were 13 infected sites. These included 7 sites of hip infection (3 with prostheses), 2 sites of osteomyelitis, 3 sites of cellulitis (1 accompanying osteomyelitis), and 1 site of tuberculous abscess. The diagnoses of all of the infected lesions were verified by obtaining positive cultures of surgical, aspiration, blood, or wound swab specimen. Of the 31 uninfected sites, the verification procedures were surgery in 16 sites, clinical follow-up in 12 cases (median follow-up time of 24 months),

wound swab culture in 2 cases, and aspiration culture in 1 case.

No adverse reaction to HIG was observed.

Table 3. Individual data for patients with suspected septic hip prosthesis.

Table 4. Individual data for patients with suspected musculoskeletal infection without hip prostheses.

The optimal threshold was chosen from the scaling level where highest accuracy was obtained in each scan. It appeared to be at level 3 for both scans (Table 1 and 2).

Table 1 Description of each grade of HIG scan findings

Positive if Greater Than or Equal to	Increased Activity at Suspected Site
0	none
1	minimal
2	moderate but less than that of vessel
3	equal to that of vessel
4	greater than that of vessel

Table 2 Description of each grade of Bone scan findings

Positive if Greater Than or Equal to	Increased Activity at Suspected Site			
	Soft tissue		Bone	
	Early	Delayed	Early	Delayed
0	none	none	none	none
1	none	mild	none	mild to intense
2	mild	none to moderate	mild	mild to intense
3	moderate	none to moderate	moderate	moderate to intense
4	intense	intense	intense	moderate to intense

With three-phase bone scintigraphy, perfect sensitivity and negative predictive value were obtained. No false negative result occurred. On the other hand, HIG scan dramatically had higher likelihood ratio and moderately increased specificity at the price of sensitivity. There were less false positive results, however, according to the ROC analysis, the accuracy of HIG was not significantly higher than 3-phase bone scintigraphy in the detection of musculoskeletal infection ($p > 0.25$). With HIG scan, there was one false-positive result with a score of 4 (uptake greater than vascular activity) in a patient who turned out to have Ewing sarcoma. This was also one of the 4 false positive cases on 3-phase bone scan. The rest were due to old healed osteomyelitis in 2 case and post-traumatic changes in 1 case.

Table 5. The results, sensitivity, specificity, accuracy, positive predictive ratio, negative predictive ratio, likelihood ratio areas under ROC curves and standard errors of both scans

There was only one false positive result on HIG study, which was also false positve on 3-phase bone study, due to Ewing sarcoma. Three other false positive results with 3-phase bone studies were due to old healed osteomyelitis (patient 2 and 4 in table 4) and healing fracture (patient 1 in table 3).

In those without prostheses (Table 4) patient 2 was presented with a history of on and off discharge from a wound on her right thigh for a few years. She had been put on courses of antibiotic therapy now and then. An active osteomyelitis involving the adjacent Rt. femoral shaft was suspected at the time of examination. Her plain films showed thickening of the adjacent cortical bone and her contrast sinugram showed no connection between the wound and the adjacent bone. The 3-phase bone scan revealed increased activity at the Rt. femoral shaft on both early and delayed images. The HIG study showed focal abnormality of grade 3 (more intense than femoral vein) confining to the lateral aspect of the thigh, suggesting the location of soft tissue rather than bone. Intra-operatively, the bone was sclerotic. There was no evidence to suggest active process of osteomyelitis and the bone culture was negative, while the infection of the soft tissue was verified by a culture from the sinus tract. The increased activity in bone on both early and delayed images can be seen in active remodelling process and does not necessarily signify bone infection. In this case HIG seemed to localise the site of infection more accurately than bone scan.

Table 3. Individual data of patients with suspected musculoskeletal infection with hip prostheses.

Pt	Sex	Age (yrs)	Site of prosthesis	Score		Diagnosis and clinical findings	Verification procedure	Culture	Final Dx	Result	
				Bone	HIG					Bone	HIG
1	F	54	R	3	0	Healing fx femoral shaft & loosening stem and cup	Sx	NG	NI	FP	TN
2	F	59	R	1	1	No evidence of infection	Sx	NG	NI	TN	TN
			L	1	0	Asymptomatic	FU (14m)	-	NI	TN	TN
3	M	43	R	0	0	Loosening, not infected	Sx	-	NI	TN	TN
			L	1	0	Asymptomatic	FU (12m)	-	NI	TN	TN
4	F	63	L	1	0	Loosening stem and cup no evidence of infection	Sx	NG	NI	TN	TN
5	F	70	L	2	0	Decreased pain on conservative	FU (6m)	-	NI	TN	TN
6	M	66	R	0	0	Sx: mild softening of cancellous bone at greater trochanter patho: nondiagnostic	Sx	-	NI	TN	TN
7	F	74	R	4	4	Septic prosthetic hip	Sx	MRSA	I	TP	TP
8	F	41	L	1	0	Severe metallosis, erosion of shaft screw, not loosening	Sx	-	NI	TN	TN
9	F	67	R	4	4	Rt.hip pain with fever 2d improved with ATB Rx	blood	Strep.	I	TP	TP
10	M	63	R	4	4	Septic prosthetic hip	Sx	Strep.D	I	TP	TP
11	M	42	L	1	0	Protrusion of prosthetic head	FU (24m)	-	NI	TN	TN
12	F	67	R	1	0	Sx: no evidence of infection	Sx	NG	NI	TN	TN
			L	1	0	Asymptomatic	FU (7m)	-	NI	TN	TN
13	F	70	R	1	0	Sx: loosening, not infected	Sx	NG	NI	TN	TN
			L	1	0	Asymptomatic	FU (7m)		NI	TN	TN
14	M	60	L	1	0	Improved after conservative Rx	FU (24m)		NI	TN	TN
15	F	44	L	1	0	Dysplastic with flexion contracture	aspiration	NG	NI	TN	TN

ATB = antibiotics; Bone = bone scintigraphy; d = days; Dx = diagnosis; F = female; FU = follow-up; fx = fracture; HIG = HIG scintigraphy; I = infected; L = left; m = months; M = male; MRSA = methicillin resistant Staphylococcus aureus; NG = no growth; NI = not infected; Pt. = patient; R = right; Rx = treatment; Strep. = Streptococci; Strep. D = Streptococci group D; Sx = surgery; TN = true negative; TP = true positive; yrs = years

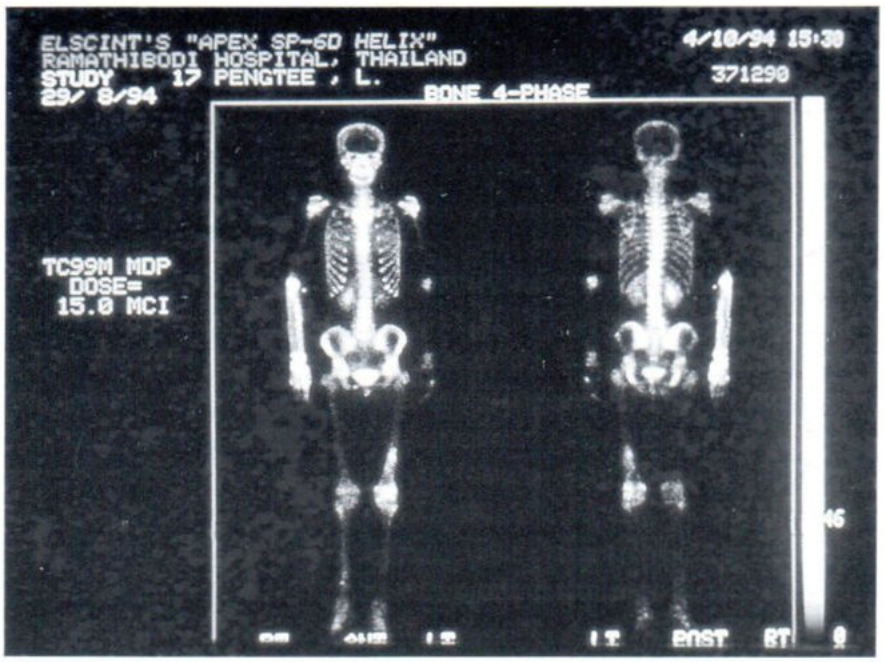
Table 4. Individual data of patients with suspected septic hip prosthesis

Pt	Sex	Age (yrs)	Site	Score on		Diagnosis and clinical findings	Verification procedure	Culture	Final Dx	Result Bone	HIG
1	F	44	Lt. hip	nd	3	Septic hip	Sx	SCN	I	nd	TP
2	F	17	Lt. femoral shaft	3	0	No OM	Sx	NG	NI	FP	TN
			Adjacent soft tissue	3	4	Cellulitis	wound swab	SA	I	TP	TP
3	M	26	Rt. hip	3	3	Septic hip	aspiration	S	I	TP	TP
4	M	37	Rt. fibial shaft	3	1	No OM	Sx	NG	NI	FP	TN
			Adjacent soft tissue	3	3	Cellulitis	wound swab	PA	I	TP	TP
5	M	17	Rt. femoral shaft	4	3	OM	Sx	SA	I	TP	TP
6	F	23	Lt.ischeopubic ramus	4	4	Ewing sarcoma	Sx	-	NI	FP	FP
7	F	53	Rt. hip	4	4	Bilateral septic hips	aspiration	MRSA	I	TP	TP
			Lt. hip	4	4		aspiration	MRSA	I	TP	TP
8	M	41	Rt. femoral shaft	4	4	COM	Sx	SA	I	TP	TP
			Adjacent soft tissue	3	2	Cellulitis	Sx	SA	I	TP	FN
9	M	19	Rt. hip	2	2	Old neglected comminuted fx	Sx	NG	NI	TN	TN
10	F	35	Lt. hip	2	2	SLE with bilateral AVN	Sx	NG	NI	TN	TN
			Rt. hip	2	0		FU (45m)	-	NI	TN	TN
11	F	25	Sacrum	0	0	Ulcer at sacral region	wound swab NG	NG	NI	TN	TN
12	F	71	Rt. hip	0	0	Bursitis improved with NSAID	FU (29m)	-	NI	TN	TN
13	F	31	Lt. hip	0	0	Hip pain, normal CT&MRI Not worsening on FU	FU (36m)	-	NI	TN	TN
14	F	58	Rt. hip	2	2	Hip pain S/P removal of prosthesis	Sx	NG	NI	TN	TN
15	M	31	Rt. hip	1	0	Arthritis secondary from AVN	Sx	NG	NI	TN	TN
16	M	35	Sacrum	0	0	Not involved	FU (10m)		NI	TN	TN
			Rt. Buttock	3	3	Tuberculous abscess	Sx	MTB	I	TP	TP
17	M	77	Low back	0	0	Ulcer at low back	wound swab	NG	NI	TN	TN
18	F	39	Lt. hip	2	2	Chronic hypertrophic synovitis	Sx	NG	NI	TN	TN
19	F	70	Lt. hip	0	1	Arthritis	FU (29m)	-	NI	TN	TN

AVN = avascular necrosis; cart. = cartilage; COM = chronic osteomyelitis; d/c = discharge; FU = follow-up; fx = fracture; I = infected; L = left; m = months; MRSA = methicillin resistant Staphaphylococcus aureus; MTB = M. tuberculosis; ND = not done; NG = nogrowth; NI = not infected; OM = osteomyelitis; PA = Pseudomanas aeruginosa; R = right; Rx = therapy S = Salmonella; SA = Staphylococcus aureus; SCN = Staphylococcus coagulase negative; Sx = surgery

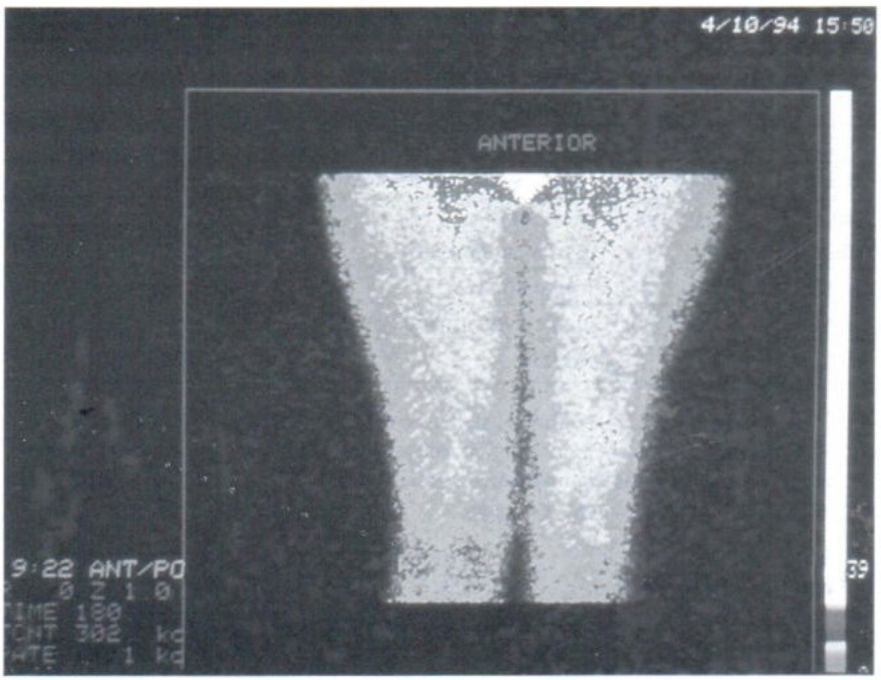
Table 5 Summary of results of both scans

Study	TP	FP	TN	FN	Total	Sensitity	Specificity	Accuracy	P(+)	P(-)	Likelihood Ratio	Area under ROC curve
HIG	12	1	30	1	44	92.31	96.77	95.45	92.31	96.77	28.61	0.971 (0.025)
Bone	12	4	27	0	43	100	87.1	90.7	75	100	7.75	0.957 (0.029)



1A

Fig. 1 Patient 2 from table 4 with on and off discharge from her right thigh had been treated now and then with antibiotics for 2 years. The clinical question was whether there was active osteomyelitis at the time. Three-phase bone scan revealed increased activity at the right femoral shaft on delayed images (A) and increased soft tissue activity around that region on early images (B)



1B

Fig. 1 (B). Increased soft tissue activity around femoral shaft region on early images.

1C

Fig. 1 (C) HIG scan (C) showed focally increased activity at the lateral aspect of the right thigh, the intensity of which was higher than that of the femoral vein.

DISCUSSION

The bone and its surrounding soft tissue were assessed separately on both studies in an attempt to differentiate mere cellulitis form cellulitis with osteomyelitis as their management differs. Clear differentiation between the two was possible only when the soft tissue involvement lied or extended laterally away from the normal osseous locations. In smaller parts of the body, such as hands and feet, this may not be possible. However, there was no such case in our study. This was also a problem with ^{99m}Tc labelled monoclonal antigranulocyte antibody-immunoscintigraphy.[15] Whether SPECT is of value in this setting needs further study to confirm.

In most cases, the intensity of HIG uptake corresponded to the probability of infection. However, the only one false positive case, due to Ewing sarcoma, had most intense uptake. This was likely to be due to increased vascularity in these conditions since it is one of the probable mechanisms of localisation of HIG. Reported conditions causing false positive results with specific and non-specific immunoglobulin are hematoma, recent fracture, pseudarthrosis, osteonecrosis and tumours.[16,17,18]

The exact mechanism of localisation of HIG at the sites of infection is yet to be elucidated and various hypotheses have been suggested. These include binding of the Fc fragment of the immunoglobulin G to Fc receptors on inflammatory cells, binding to bacteria and rheumatoid factors and increased vascular permeability.[19] As the mechanisms of localisation imply, the HIG study cannot differentiate sterile inflammation from bacterial infection. According to Pons et al[20] the HIG study is also an objective test to detect synovitis and to assess the severity of inflammation. They found that the intensity of ^{99m}Tc-HIG

uptake correlated significantly with markers of inflammation in patients with rheumatoid arthritis. In our study it was clearly demonstrated that the intensity of uptake could not distinguish the nature of the lesions in terms of the presence of infection because both true infection and Ewing sarcoma took up HIG avidly. Demirkol et al[21] performed a quantitative analysis of ^{99m}Tc-HIG uptake to detect infection in hip and knee prostheses using target to background ratio and reported no significant difference between the true-positive and false-positive cases.

It was a pity that late HIG imaging at 24 hours was performed in only some cases in this study as it was reported that by which separation the infections from the noninfectious inflammations could be made rather well.[22] In that study a numerical value named the inflammation index was obtained by dividing the average counts per pixel in an area of interest circumscribing the muscoloskeletal foci of accumulation, by the average counts per pixel in an equal size area drawing in an unaffected symmetrical site. Analysis of variance (ANOVA) showed that this index of late HIG study was able to differentiate infections and noninfectious inflammations ($p = 0.016$). However, using the lower limit of 95% confidence interval of the study as a threshold for infection resulted in a sensitivity, specificity and accuracy of 78.57%, 50% and 64.29%, respectively. This may imply that even the performance of the late inflammation index of HIG, which was shown to work statically, was far from ideal practically. The inflammation index of HIG was increased or decreased in late imaging in comparison to its early counterpart in both infection and noninfectious inflammation. As a result this cannot differentiate these conditions.

Despite comparable sensitivity, the specificity in this study were higher than that in the work of Ang et al[23] (86% and 16%) and Demirkol et al[21] (100% and 41%). The apparently good sensitivity, specificity, accuracy, positive predictive value and negative predictive value reported in our study might be partly due to limited sample size and limited number of patients with sterile arthritis. If there had been more patients, particularly those with inflammatory joint diseases, the number of false positive cases might have been higher and the specificity, accuracy, and negative predictive value might have been lower.

The high sensitivity of 3-phase bone scintigraphy in detecting the presence of musculoskeletal infection has been well recognised. However, because the specificity of bone scintigraphy is far from ideal, several radiopharmaceuticals have been investigated for this matter. Some recommended combined labelled leukocytes/marrow scintigraphy and some ^{18}F-FDG. Labelled leukocytes, be it with conventional technique or with monoclonal antigra-nulocyte antibodies are feasible. However, the conventional technique needs blood handling, expensive instrument, and personnel expertise and is time consuming. Despite the fact that labelling with the latter eliminates all the disadvantages of the conventional technique, it is expensive and has a potential to develop HAMA upon repeated use. Moreover, labelled leukocytes are taken up at the bone marrow so in those with post-traumatic or surgical changes, the leukocyte may be misleading and the addition of a bone marrow scan may not always solve the problem.[24] ^{18}F-FDG PET has been reported to detect chronic osteomyelitis with high accuracy. Yet, it is of limited value in discriminating between inflammation and malignancy because tumour cells also show high FDG accumulation.[25] Moreover, it is not available in most part of the world, particularly in Thailand. To date, there is no commercially available radiopharmaceutical that can definitely differentiate infection from sterile inflammation. The only radiopharmaceutical claimed to be specific to bacterial infection was Infecton,[26] ^{99m}Tc labelled ciprofloxacin. However, it is not commercially available.

The HIG study appeared to have comparable sensitivity, specificity and accuracy to that of labelled leukocytes. It is available in a relatively low-priced kit form. Its preparation is easy and safe. The uptake in the bone marrow and HAMA reaction are absent. Considering all these, the HIG study appears it be a good alternative to labelled leukocytes and monoclonal antigranucyte antibodies for localising infection.

At 4 hours most of the ^{99m}Tc-labelled polyclonal human IgG remained in the blood pool, therefore the heart, moderate-sized veins and highly vascular organs such as the spleen, liver and kidneys were seen. Excretion was noted in the urinary bladder. As a result the ^{99m}Tc-labelled polyclonal human IgG may not be used to localise infection in these organs satisfactorily.

CONCLUSION

A HIG study may be used as a screening test of the investigation of painful hip prosthesis and suspected musculoskeletal infection. If no increased activity is seen at the suspected site, it is very unlikely that infection is present. A HIG study appeared to be a safe and convenient method with reasonable sensitivity, specificity and accuracy for the detection of infection. However, differentiation between infection and sterile inflammation cannot be definitely made.

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EFFECT OF RADIOIODINE (^{131}I) THERAPY ON GONADS

Dr. M. A. Taher, Director

Use of radioiodine is, absolutely contra-indicated during pregnancy,[1] although dose to fetal thyroid is small, but it is sensitive and may be of medicolegal consequence. However, gonadal exposure is extremely low (less than a diagnostic radiograph), genetic effects are unlikely, extensive studies have failed to show ^{131}I related neoplasm or birth defects.[2-8] No significant increase in genetic abnormalities has been documented in children of Japanese parents exposed to atomic radiation,[9] and there is an increased tendency to treat young patients with ^{131}I in recent years.[10] In human beings, organogenesis does not begin until the third week after conception. There is no evidence that radiation of a conceptus in the early weeks of pregnancy is more dangerous than irradiation of the ovary before fertilization. The International Commission on Radiological Protection (ICRP) withdrew support for the 10-day rule in 1984. Many agree that pregnancy should be allowed to continue after known exposure of less than 10 centi-Gray (cGy), but some would reduce the upper limit to 5 cGy in the second trimester[11] (1 cGy = 1 rad). Patients treated with ^{131}I are advised to delay conception for at least 6 months after treatment.[12]

Propranolol is also used in the treatment of hyperthyroid patients. It should be avoided during pregnancy as it increases uterine muscle tone which may result in a small placenta and fetal growth retardation. It can also induce neonatal bradycardia, hypoglycemia and impaired response to anoxia.[13-14] Full or partial recovery of dose-dependent spermatic damage of 12 men in 2.5 years is demonstrated after surgery and ^{131}I therapy for thyroid cancer.[15-16] In another study about 25% of patients treated with ^{131}I for thyroid cancer suffered no alterations in FSH levels, whereas the remainder had transient rises in FSH levels. Patients treated repeatedly over a prolonged period had a reduced sperm count.[17] Thyrotoxic patients usually receive much smaller dose of ^{131}I than cancer patients, but anxiety prevails regarding its effect on spermatogenesis. Therefore we like to report a case of healthy boy born to a man treated with ^{131}I for thyrotoxicosis and a case of a healthy daughter born to a woman who inadvertently received radioiodine therapy during early pregnancy.

CASE—1

A man of age 40 years complained of perspirations, weight loss inspite of increased appetite, palpitations, insomnia and was diagnosed as a case of diffuse toxic goitre on 19.6.95 at NMC, Dinajpur (Table 1). He took Carbimazole and thyroxine tablets irregularly from else-where with no improvement. He received radioiodine therapy (5 milliCuries ^{131}I) on 18.1.97 at NMC, Rangpur. He was reluctant to have it as he had only three daughters and no son. However, later on he was improved as seen in the follow ups done on 5.2.98 and 30.8.98, but his wife gave birth to a dead son on 14.6.98. She conceived before her husband' s radioiodine therapy, but both became gloomy as she had three fetal deaths earlier. However, they were assured and fortunately she gave birth to a son on 8.11.99 by Caesarean section. This only son is in good health upto the last followup on 13.2.2000.

CASE— 2

A woman of age 30 years complained of

Nuclear Medical Center, Rangpur, Bangladesh.

increased sweating, weight loss inspite of increased appetite, palpitations, insomnia and was diagnosed as thyrotoxic in February, 1995. She took carbimazole (neomercazole) 45 mg/day for a month with little improvement and received ^{131}I therapy (10 milli-Cuies) on 18.5.95 at Nuclear Med. Institute, Dhaka. At first follow-up, she disclosed that her last menstrual period (LMP) started on 25-5-95 and ultrasonography revealed gestational sac of 10 weeks 2 days, She was advised therapeutic abortion but she did not agree and gave birth to a healthy daughter on 12-3-96. The baby is in good health till 7-9-99, however, her mother is now hypothyroid and on thyroxine (100 microgram daily) therapy (Table-2).

Table 1 Hormone levels of Case-1

Date	T_3 NR 0.8—3.2 nmol/L	T_4 64.—175 nmol/L	TSH 0.4—5 mlU/L
19-06-95	7	219	--- "
17-8-97	8.9	134	0.4 "
13-02-2000	3.1 "	103 "	0.3 "

NR= Normal Range

Table 2 Hormone levels of Case-2

Date	T_3	T_4	TSH
19-3-95	8.89	214	0.09
13-4-95	5.39	213	0.02
5-9-95	0.3	60	0.17
31-3-98	0.48	20	49.9
7-9-99	2.5	50	17.75

CONCLUSION

^{131}Iodine therapy did not damage the gonads in these cases, However, more observations should be continued and we do not recommend the use of radioiodine during pregnancy and lactation. Any how, the present cases show that radioiodine is not teratogenic.

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^{131}IODINE THERAPY IN THYROTOXICOSIS

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ABSTRACT

Radioiodine ^{131}I therapy is becoming popular for treatment of thyrotoxicosis in Bangladesh and well-differentiated thyroid cancers. ^{131}I therapy was started at Rangpur in 1989 (brought from Nuclear Medicine Center, Dinajpur). Up to February, 2000, 161 thyrotoxic patients (F96, M65) of age range 16 to 70 yrs. (diffuse 123, nodular 38), had ^{131}I therapy. Most of our patients are improved by small single dose of ^{131}I therapy and are being followed-up.

Key words : ^{131}Iodine therapy, thyrotoxicosis.

INTRODUCTION

Radioiodine is used in thyroid studies since 1939[1] Beta-rays of ^{131}I (0.606 and 0.33 million electron : volts) ablate thyroid cells and therefore, used as a therapeutic agent in thyrotoxicosis and well-differentiated cancers of thyroid gland. The other options are surgery, antithyroid drugs. (e.g. Carbimazole) or percutaneous ethanol injection of autonomously functioning thyroid nodules[2]

In Britain and USA, mortality from thyrotoxicosis peaked between 1923 to 1940 and incidence remained highest in those areas which once had endemic goitre,[3,4] but in 1977 it came down to 1.9-2.7 % in adult females of North-East England.[5] However, we are still lagging behind in the less developed countries, e.g. in Bandar Abbass (Iran), about 12 % (49 of 381 patients) hyperthyroidism was found in 1994[6] and in Nuclear Medicine Center, Rangpur, 28% of 309 patients were thyrotoxic in 1998.[7]

The ^{131}I dose for thyrotoxicosis is usually computed on the basis of delivering a selected (about 100 micro-Curie, μCi) dose per gm of thyroid tissue.

$$\text{Dose } (\mu Ci) = \frac{\mu Ci/gm \times \text{thyroid wt.(gm)} \times 100}{\%\ ^{131}I \text{ uptake at 24 h.}}$$

Some Centres use high ablative dose. The incidence of post-radioiodine hypothyroidism is almost equal to that following surgery or drug therapy (2-3% per year). The natural history of Graves' disease may be one of a hyperthyroid phase, followed eventually by hypothyroidism.[8] Various dose schedules e.g. as small as 0.5 milliCurie (mCi)[9] to high ablative dose ranging as big as 20 to 100 mCi at the University of Minnesota Hospital U.S.A have been used to treat thyrotoxicosis.[10,11] Thyroid unit of Royal Marsden Hospital[12] (Sutton, UK) uses 2 mCi dose in the treatment of Graves' disease since January 1979, repeated doses are given there after 6-monthly intervals. In Bangladesh, Institute of Nuclear Medicine, Dhaka, Atomic Energy Medical Centre, Chittagong, Nuclear Medicine Centres of Rajshahi and Dinajpur had published results of radioiodine therapy. Here we like to describe initial experiences of radioiodine therapy at Rangpur since 1989.

Nuclear Medicine Center, Post Box No.-16 Rangpur, Bangladesh.

MATERIALS AND METHODS

The patients referred to this centre for suspected thyroid disease were analysed by careful clinical history, physical examination, radioiodine uptake (2,24,48hrs. after oral 10-15 μCi dose of ^{131}I, thyroid scans, and serum levels of triiodothyronine (T_3), thyroxine (T_4) and thyrotropin (TSH) by radio-assays (radioimmunoassay, RIA and/or immunoradiometric assay IRMA).

One hundred and sixty one thyrotoxic patients (F96, M65) were advised to receive oral radioiodine therapy (which did not require any hospitalization), if agreeable to their referring physicians. Regular follow-ups beginning on the 10th week after radioiodine therapy is done in this Centre.

RESULTS

Results are tabulated in Tables 1-3, Only one patients (M50) became hypothyroid 2 years after & 3mCi dose of ^{131}I, however, long-term follow up are being done. Most of the patients are between 30-59 years of age and received single small dose of ^{131}I. Twenty four patients (15%) had carbimazole prior to ^{131}I therapy, amongst them one had severe rash, another had agranulocytosis and others were non-responsive to carbimazole.

DISCUSSION

No serious complication was seen following radioiodine ^{131}I therapy. Long-term follow up is being performed routinely to detect further recurrence (s) and/or hypothyroidism. Treatment of hypothyroidism is quite straightforward and much easier than recurrent thyrotoxicosis.

One of the concerns of radioiodine therapy has been late radiation side-effects. It should not be used during pregnancy. However, extensive studies have failed to show ^{131}I related neoplasm or birth defects. Since the gonadal exposure is extremely low (less than a diagnostic radiograph), genetic effects are unlikely. In the cooperative follow up study[13], comparison of the incidence of thyroid cancer in patients who had surgery (50 cancers in 11,732 patients) compared with those who had radioiodine therapy (19 cancers more than 1 year after ^{131}I in 21,714 patients) showed fewer cancers after the radioiodine therapy. Henneman and colleagues[14] noted that in Graves' disease and toxic multinodular goitre the remission rate is only 40—50 % after antithyroid drugs, these drugs have little effect in toxic adenoma and after ^{131}I (radioiodine) therapy, the risk of malignant diseases and genetic abnormalities is not significantly greater in any age group. Older textbooks mentioned that children and adolescents should not be treated with radioiodine for thyrotoxicosis, but recent research works are in favour of radioiodine, rather antithyroid drugs e.g. carbimazole can give rise to serious side-effects[15].

Since 1997 we are facing scarcity of ^{131}I as AERE (Savar) is not producing it, however, most of our patients are improved by relatively small doses of ^{131}I.

Table 1. Age-Sex distribution.

Age in years	Female		Male	
15 - 20	1		0	
21 - 29	6		3	
30 - 39	28		14	
40 - 49	31		22	
50 - 59	20		17	
60 - 69	6		8	
70 - 79	4		1	
Total =	96	+	65	= 161 patients

Table 2. Number of Doses.

One	133
Two	22
Three or more	6
Total =	161 patients

Table 3. Dose ranges (Total milliCuries)

0.5 - 2 mCi	85 patients
2.1 - 5 mCi	60 "
5.1- 10 mCi	14 "
More than 10 mCi	2 "
Total =	161 patients.

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DIFFERENTIATED THYROID CARCINOMA (DTC) PATIENTS REFFERED FOR RADIOACTIVE IODINE THERAPY AT FIRST PRESENTATION : A 10-YEAR REVIEW

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ABSTRACT

OBJECTIVE: To evaluate the patient characteristics, histological subtype, presenting symptoms and metastatic evidence in thyroid cancer patients referred for radioactive iodine (RAI) therapy at first presentation.

METHODS: A retrospective study of patients with differentiated thyroid carcinoma (DTC) registered at Nuclear Medicine Section, Siriraj Hospital during January 1989 to December 1998 was reviewed.

RESULTS: Five hundreds and sixty-six DTC patients, aged 9-96 years (mean=46.8±16.7), including 440 women and 126 men were analyzed. The overall female/male ratio was 3.5:1. According to the histopathology, 370 papillary carcinomas (65.4%), 191 follicular carcinomas (33.7%), 5 Hürthle cell carcinomas (0.9%) were found. The most common age group was in the range of 31-60 years, accounting for 56% of all patients. There was at least one organ metastasis at first presentation in 235 cases (41.5%). Lymph node is the most often involved organ found in 169 cases (29.9%), followed by lung (52 cases, 9.2%) and bone (49 cases, 8.7%). Ninety-one patients (16.1%) revealed distant metastases at the time of referral. Papillary thyroid carcinomas most commonly metastasize to regional lymph node (39.7%) followed by lung (8.4%), and bone (4.3%), while follicular carcinoma more often metastasize to bone (17.3%) and lung (10.5%).

CONCLUSION: DTC is not uncommon in Thais and affects women rather than men. Papillary carcinoma is the most common histological subtype followed by follicular carcinoma. Since the prevalence of regional node and distant metastases is quite high at presentation, early diagnosis and appropriate treatment are essential for improving the disease outcomes.

Key Words: thyroid cancer, differentiated thyroid carcinoma, radioactive iodine, iodine-131

INTRODUCTION

The thyroid gland is considered a relatively uncommon site of cancer in United States, accounting for 0.6% and 1.6% of all cancers among men and women, respectively.[1] However,

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these figures seem to be higher in Thais. According to the tumor registry at Siriraj Cancer Center from 1989-1998, thyroid cancer accounted for 2% of all new cancer patients, or 1.2% and 2.5% of male and female patient respectively. Fortunately the majority, which is about 89% of thyroid cancers in our institute were differentiated thyroid carcinomas (DTC) and can be treated postoperatively with radioactive iodine (^{131}I).

The objective of this study is to evaluate the patient characteristics, histological subtypes, presenting symptoms and metastatic evidence at first presentation in DTC patients referred for radioactive iodine (RAI) therapy at our institute.

PATIENTS AND METHODS

We retrospectively reviewed the data of 590 new DTC patients referred for RAI treatment at Division of Nuclear Medicine, Siriraj Hospital during January 1989 and December 1998. However, 24 patients who had previous RAI therapy from elsewhere or had incomplete medical records were excluded.

STATISTICAL ANALYSIS

Percentage, mean, standard deviation (SD) and student t-test were used for statistical analysis.

RESULTS

DEMOGRAPHIC FEATURES

Totally 566 DTC patients were included for the analysis. There were 440 women and 126 men with age range 9 - 96 years, mean = 46.8 $\pm$ 16.7 years. The overall female to male ratio was 3.5:1. From 1989 - 1998, the number of DTC patients referred for RAI treatment seemed to be increasing (Figure 1).

The patients' age distribution was displayed in Figure 2. The mean age in both sexes and that in two major types of thyroid cancer i.e. papillary and follicular carcinomas were similar (Table 1). The common age ranges were in between 31 - 60 years old, which accounted for 56% of all DTC patients (318/566). About 39% (222/566) of the patients were 40 or under, which have favorable prognosis. However, the remaining 344 cases (61%), being the majority of the patients, were older.

PATHOLOGY

According to the histopathology, 370 (65.4%) papillary carcinomas (including mixed papillary-follicular carcinomas), 191 (33.7%) follicular carcinomas, and 5 (0.9%) Hürthle cell carcinomas, a follicular variant were found. Therefore, papillary tumors were almost twice as common as follicular carcinomas. The female to male ratio of papillary cancers was 3.2:1 and that of follicular carcinomas was 4.5:1 (Table 2)

PRESENTING SYMPTOMS

The majority of DTC patients presented with thyroid abnormalities, particularly solitary thyroid nodules with or without cervical node metastases. The others may present with metastatic lymph nodes alone, distant metastases, or symptoms related to direct tumor invasion such as hoarseness of voice due to vocal cord paralysis, and upper airway obstruction due to laryngeal or tracheal involvement. Sixty-three (11%) patients were referred for RAI treatment because of recurrent tumor after a variable period of thyroid surgery. On the other hand, the cancer was found incidentally in ten (1.8%), among which eight were operated on hyperthyroidism. The presenting conditions of DTC patients were listed in Table 3.

ORGAN METASTASES

Overall 235 cases (41.5%) showed at least one organ metastasis at first presentation. Lymph node is the most often involved organ found in 169 cases (29.9%), followed by lung (52 cases, 9.2%) and bone (49 cases, 8.7%) (Table 4). Most of the patients (196 cases, 34.6%) had single organ metastasis and the remaining (39 cases, 6.9%) had multiple organ metastases, which the most common combination is lymph node and lung metastasis in 19 cases. When lymph node was not taken into account, ninety-one patients (16.1%) had distant visceral organ metastases at the time of referral. Of these, 45 cases (12.2%) of patients with papillary cancers and 45 cases (23.6%) of those with follicular carcinomas revealed distant metastases. Six patients had uncommon sites of metastases, including brain,[4] liver,[1] and kidney.[1]

For papillary carcinomas, lymph node was most commonly involved organ (147 cases, 39.7%), followed by lung (31 cases, 8.4%), and bone (16 cases, 4.3%). On the other hand, the metastases from follicular thyroid carcinomas were more commonly seen in bone (33 cases, 17.3%) than lymph nodes (22 cases, 11.5%) and lung (20 cases, 10.5%).

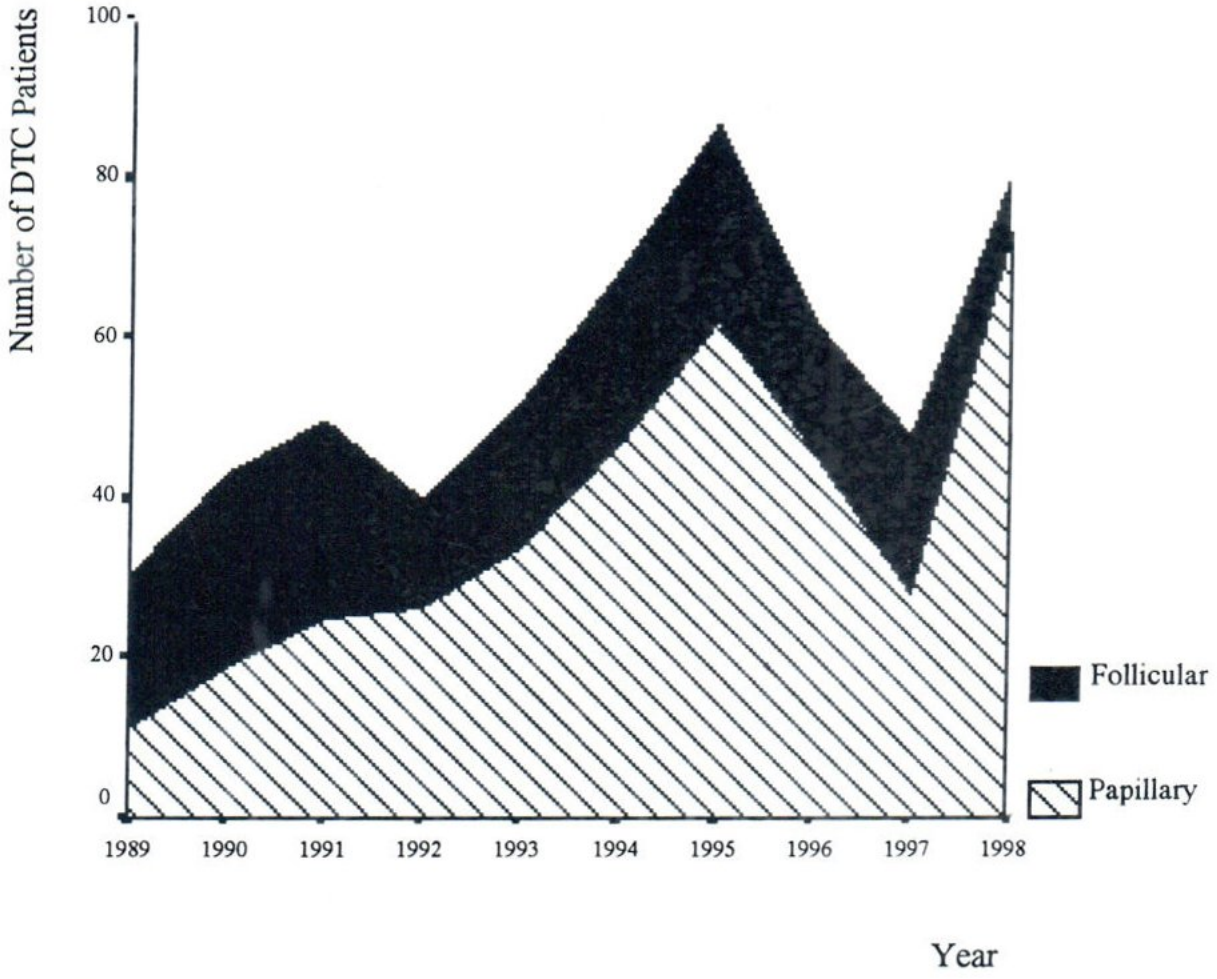

Fig. 1. DTC patients referred for RAI treatment during 1989-1998

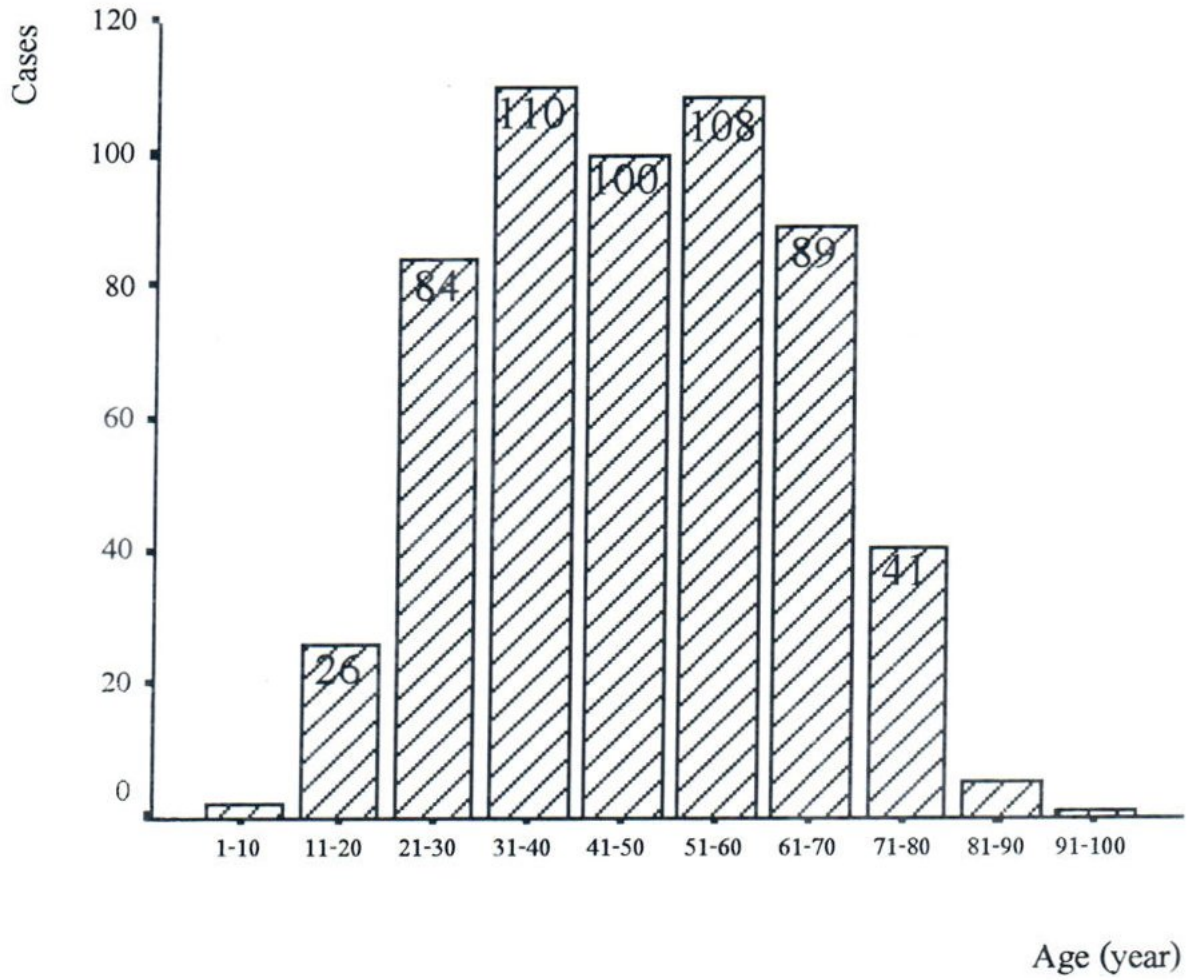

Fig. 2. Age distribution of DTC patients referred for RAI treatment

Table 1. Age ranges of DTC patients referred for RAI treatment

Sex -Type	Cases	Age Range (year)	Mean Age (SD) (year)	p value
Female	440	12-96	46.2 (16.5)	0.1
Male	126	9-81	49.0 (17.3)	
Papillary	370	9-84	46.6 (16.8)	0.7
Follicular	191	12-96	47.2 (16.7)	
All	566	9-96	46.8 (16.7)	

Table 2. Sex distribution of DTC patients according to histological subtypes.

	Papillary		Follicular		Follicular		Hürthle cell		Total	
	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
Female	281	63.9	156	35.5	156	35.5	3	0.7	440	77.7
Male	89	70.6	35	27.8	35	27.8	2	1.6	126	22.3
Total	370	65.4	191	33.7	191	33.7	5	0.9	566	100

Female : male ratio for all DTC patients = 3.5:1,
Female : male ratio for papillary carcinoma patients = 3.2:1
Female : male ratio for follicular carcinoma patients = 4.5:1

Table 3. Presenting Symptoms of DTC Patients Referred for RAI Treatment

Presenting Symptoms	All		Papillary		Follicular	
	Cases	Percent	Cases	Percent	Cases	Percent
Thyroid nodule	384	67.8	255	68.9	126	66.0
Lymph node enlargement	25	4.4	19	5.1	6	3.1
Thyroid and lymph node	10	1.8	8	2.2	2	1.0
Distant metastasis	44	7.8	12	3.2	32	16.8
Recurrent tumor	63	11.1	50	13.5	12	6.3
Invasive property	30	5.3	19	5.1	10	5.2
Incidental	10	1.8	7	1.9	3	1.6
Total	566	100.0	370	100.0	191	100.0

Table 4. Summary of organ metastasis in DTC patients at first presentation

Metastasis/	Papillary		All	Follicular		All	Hürthle Cell		All	Total	
Pathology	Cases	%	%	Cases	%	%	Cases	%	%	Cases	%
Presence of metastasis	173	46.8	30.6	61	31.9	10.8	1	20	0.2	235	41.5
Lymph node metastasis	147	39.7	26.0	22	11.5	3.9	0	0	0	169	29.9
Bone metastasis	16	4.3	2.8	33	17.3	5.8	0	2	0	49	8.7
Lung metastasis	31	8.4	5.5	20	10.5	3.5	1	20	0.2	52	9.2
Other metastasis	2	0.5	0.4	3	1.6	0.5	1	20	0.2	6	1.1

DISCUSSION

From the tumor registry, we found that thyroid cancer in Thailand is somewhat more common than that occurring in USA.[1,2] However, the majority of these tumors is similar, i.e. DTC. As compared to the United States, papillary carcinoma is still the most common histological subtype, but papillary: follicular ratio is lower (2:1 vs 3:1). Thus, follicular tumors are relatively more common among Thais. In addition, DTC is predominant in females with female:male ratio of 3.5:1, which is higher than that observed in US population (2.3:1).[3] Race may be an important factor for these differences.

Since these thyroid tumors arise from thyroid follicular cells, they usually have the ability to concentrate radioactive iodine, and thus, benefit from the RAI treatment. However, in the early years of the study, a few DTC patients were referred for additional RAI therapy following complete surgery. These included in particular follicular carcinomas rather than papillary tumors. Nevertheless, the number of the patients referred for RAI treatment has been recently increasing, exclusively papillary thyroid cancers, which in the past was used to be treated with surgery alone or just combined with thyroid hormone following surgery. This might because more and more clinicians have accepted the role of RAI therapy to treat DTC patients. The benefit of postoperative RAI therapy in papillary tumors was shown by Mazzaferri et al.[4] who found that the recurrence rate had been reduced from 32% in patients treated with surgery alone, to 11% in those given thyroid hormone postoperatively, and to 2.7% in those who received RAI therapy followed by hormonal treatment after surgery. In the patients with follicular carcinoma, there is also significant reduction of recurrence following postoperative I-131 ablation.[5] The reason for this is believed to be due to a direct effect on the micrometastases rather than destruction of residual cancer in the small thyroid remnant.[6] Therefore, it is now generally accepted, that DTC should be treated by near-total thyroidectomy and followed by RAI treatment with long-term follow-up program. As recurrence is twice more commonly found in the patients with nodal metastases than those without node involvement (32% vs 14%), RAI treatment in patients with node involvement is very reasonable.[7] Although combined RAI therapy has important role in most well-differentiated thyroid carcinomas, it may be not necessary in patients with occult primary tumors (less than 1.5 cm in diameter) since they have relatively benign clinical behavior and excellent prognosis.[8,9]

Age at the time of diagnosis and treatment is considered the single most important prognostic factor of patients with DTC.[9] The mean age at initial diagnosis of follicular carcinomas is previously reported to be about 9 years older than that of papillary cancers.[8] In our series, however, there is no any significant difference between age in papillary and follicular carcinomas, and also in both sexes. Nevertheless, the duration of the developing tumors in each patient is quite varied prior to the presentation. Papillary carcinomas may arise for a long time before the patients come to see the doctors because the course of the disease is quite indolent. In contrast, the patients with follicular cancers may be diagnosed earlier due to more common occurrence of distant metastasis. As observed in this study that several patients presented with distant metastases, in particular skeletal metastases.

Another interesting aspect includes the concurrence of thyroid cancer and hyperthyroidism, which has been recently reported to occur in 0.6% to 5.9% of thyrotoxic patients.[10-12] This occurrence raises the importance of studying and excluding the possibility of the neoplastic formation in a more systemic approach.

In contrast to papillary and follicular carcinomas, a follicular variant called Hürthle cell carcinoma rarely collects radioiodine.[13] However, we observed RAI uptake in a case of Hürthle cell carcinoma with bilateral pulmonary metastases. Thus, whole-body I-131 diagnostic scan may guide for the decision of following RAI treatment in this type of tumor.

In terms of tumor spreading, papillary and follicular carcinomas have quite different modes of metastasis. Papillary cancers tend to spread initially via the lymphatic system while follicular carcinomas more often produce hematogenous metastases to bone and lung.[3,6] In our series, lymph node metastases are found in about 40% of patients with papillary cancer and approximately 12 % of those with follicular carcinoma, which is similar to the figures reported by Maxon and Smith[14] (35% and 13% respectively). On the other hand, distant metastases in our study seems to be higher, which are 12.2% in patients with papillary carcinoma and 23.6% in those with follicular cancer, as compared to 3.8% and 16.4% respectively as previously reported.[14] A reason for this may be associated with delayed consultation, which leads to delayed diagnosis and treatment of the patients. Thus, the patients who have thyroid-related symptoms should go to see their doctors sooner and clinicians or surgeons should also be alert for malignant condition and not delay the diagnosis. Furthermore, many patients have inadequate previous thyroid surgery and/or lack of combined RAI treatment for their tumors, which results in recurrent or metastatic disease. Therefore, early diagnosis with prompt and appropriate treatments after the diagnosis including surgery followed by radioiodine, and hormonal therapies in each patient should be attempted.

CONCLUSION

DTC is not uncommon in Thais. Although it has quite favorable prognosis, they can metastasize to lymph node, bone, lung, etc. Presence of these metastatic evidences at first presentation of course, results in increase in morbidity and mortality. To improve the disease outcomes, early diagnosis with appropriate treatments should be warranted.

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ADENOCARCINOMA OF THE CERVICAL CANCER : RADIATION TREATMENT IN SIRIRAJ HOSPITAL 1993 – 1995

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ABSTRACT

Objective : To evaluate the incidence and the results of the radiation treatment in adenocarcinoma and adenosquamous cell carcinoma of the cervical cancer.

Study design : A retrospective review of 125 patients with adenocarcinoma and adenosquamous cell carcinoma of the cervical cancer who had the primary radiation treatment in between 1993 – 1995.

Result : After the completion the radiation treatment, there were 35 patients (28.0 %) who had residual disease. The median follow up time was 43.5 months, 61 patients (48.8 %) still had no evidence of disease, 16 patients (12.8%) had local recurrence and 23 patients (18.4 %) developed distance metastasis.

Conclusion : The radiation treatment is the primary treatment for stage II and stage III adenocarcinoma of the cervical cancer. The total abdominal hysterectomy is recommended after the completion of radiation treatment to improve the local control. For stage I diseases, radiation treatment can be used as the primary treatment especially for bulky lesions. The adjuvant hysterectomy is also recommended to improve local control. The concurrent chemo-radiation is suggested for locally advanced lesions to improve the tumor control. The adjuvant chemotherapy should be benefit for the residual tumor, which is not suitable for surgery and also recommended for improving the survival in lymph nodes positive patients. Any how, a further study should be done.

INTRODUCTION

Cervical cancer is the most common malignancy in Thailand. The histology type of squamous cell carcinoma is the most common, while adenocarcinoma and the subset, adenosquamous cell carcinoma are relatively rare. The incidences of adenocarcinoma and adenosquamous cell carcinoma of all cervical cancer are only 4-12.6 percent and 2-3.6 percent, respectively. [1-5]

Due to the number of reports has been limited, the management of adenocarcinoma and adenosquamous cell carcinoma is still controversial. The purpose of this study is to evaluate the response of primary radiation treatment, especially for stage II and III diseases and stage I that is not suitable for surgical treatment.

MATERIALS AND METHODS

This study was the retrospective review of the 131 patients who came for primary radiation treatment at the Division of Radiation Oncology, Department of Radiology, Faculty of Medicine Siriraj Hospital, between January 1993 to December 1995. The mean age was 47.77 years (range 26-74 years). The clinical staging was applied

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according to the International Federation of Gynecology and Obstetrics (FIGO) classification. Seventeen patients (12.97 %) had stage I, 67 patients (51.14 %) had stage II, 44 patients (33.58 %) had stage III, and 3 patients (2.29 %) had stage IV disease.

The primary radiation treatment planning was the combination of the external radiation 50 Gy in 5-6 weeks and a setting of medium dose-rate (Cesium) intracavitary brachytherapy which the *TDF at point A was 81.* The external beam radiation was given by using Cobalt machine or Linear accelerator (10 MV.) machine, anterior-posterior field technique, 1.8-2 Gy conventional fraction.

The criteria of the results to be studied were the residual disease, the local recurrence and the distance metastasis.

RESULTS

For the 3 – year period from 1993 – 1995, we excluded 7 patients who did not have complete treatment (Stage I; n = 1, Stage II; n = 1, Stage III; n = 1 and Stage IV; n = 3). This study included 125 evaluated patients. There were 96 patients who had pure adenocarcinoma and 29 patients who had the subset adenosquamous cell carcinoma. Most of the patients were stage II (n = 66) and stage III (n = 43) diseases. There were some of stage I disease who was not suitable for surgery (n = 16). The stage distribution by histology is shown in Table1.

***TDF** = Time-Dose-Fractionation

***Remark :** TDF 81 at point A medium dose-rate (Cesium) intracavitary brachy therapy is equivalent to 2800cGy / 3 weeks external radiation.

Table 1. Stages distribution by histology

	Stage I	**Stage II**	**Stage III**
Adenocarcinoma (n = 96)	12 (12.50 %)	51 (53.12 %)	33 (34.37 %)
Adenosquamous cell carcinoma (n = 29)	4 (13.79 %)	15 (51.72 %)	10 (34.48 %)
Total (n = 125)	16 (12.8 %)	66 (52.8 %)	43 (34.4 %)

After the completion of radiation treatment, there were 35 patients who had residual disease (stage I; n = 1, stage II; n = 10 and stage III; n = 24). Fourteen patient (stage II; n = 8 and stage III; n = 6) were treated with a second course of intracavitary radiation after the completion of external radiation within 6-8 weeks. Twelth patients showed well local control. Four patients who had stage III disease still had residual disease and 3 of them developed distance metastasis. The adjuvant chemotherapy had been used in 16 patients and they all still had residual diseases

after completion of the course of treatment, and 6 of them developed distant metastasis.

Most of the patients were planned to have radiation treatment alone. However, there were 16 patients who have further elective total hysterectomy (stage I; n = 5 and stage II; n = 11) after radiation therapy had been completed. Four pathological sections showed positive microscopic residual disease at the cervix, but all lymph node sampling were negative for malignancy. Eleven patients had no evidence of disease, 3 patients had local recurrence and 2 patients had distant metastasis while the primary site was well controlled. The result of treatment comparing radiation alone and combined radiation and surgery is shown in Table 2.

Table 2. The result of treatment : Radiation alone and combined radiation and surgery.

	Radiation alone		Radiation → Surgery	
	No	Disease control	No	Disease control
Stage I	11	9 (81.81 %)	5	4 (80.00 %)
Stage II	55	30 (54.54 %)	11	7 (63.63 %)
Total	66	39 (59.09 %)	16	11 (68.75 %)

The median follow up time was 43.5 months (range from 2 – 72 months). The patients who were alive without evidence of disease were 61 patients (48.8 %). Thirty-five patients (28.0 %) had residual disease. Sixteen patients (12.8 %) had local recurrence. The median time to recurrence was 21.5 months (ranged from 8 – 42 months). Twenty-three patients (18.4 %) developed distant metastasis. The median time to have distant metastasis was 14 months (range from 2 – 53 months). There were 10 patients who had residual disease and then developed distant metastasis. The median time to have distant metastasis was 11 months (range from 2 – 30 months). Compared to 13 patients who had distant metastasis with the primary cancer well controlled, the median time to have distant metastasis was 14 months (range from 4 – 53 months). The reported organ metastasis were lung (n = 8), liver (n = 1), bone (n = 1), brain (n = 1), supraclavicular lymph nodes (n = 4) and para -aortic lymph nodes (n = 3). The histology type and the end result of the follow up are shown in Table 3.

Table 3. The histology type and the end result of the follow up.

	Residual disease	Local recurrence	Distance metastasis	Disease control
Adenocarcinoma (n = 96)	28 (29.16 %)	12 (12.50 %)	17 (17.70 %)	48 (50.00 %)
Adenosquamous cell carcinoma (n = 29)	7 (24.13 %)	4 (13.79 %)	6 (20.68 %)	13 (44.82 %)
Total (n = 125)	35 (28.00 %)	16 (12.80 %)	23 (18.40 %)	61 (48.80 %)

For stage I disease, the median follow – up time was 44 months (ranged from 1 – 67 months). The patients who were alive without evidence of disease were 13 patients (81.25 %). One patient had residual disease and 1 patient had local recurrence and 1 patient developed distant metastasis.

For stage II disease, the median follow up time was 43.5 months (range from 2 – 71 months). The patients who were alive without evidence of disease were 37 patients (56.06 %). Ten patients had residual disease and 9 patients had local recurrence and 12 patients developed distant metastasis. One patient had HIV positive and died at the 24th month after treatment. Two patients had ovarian cancer at the 13th and the 14th month.

For stage III disease, the median follow up time was 43 months (range from 6 – 72 months). The patients who were alive without evidence of disease were 11 patients (25.58 %). Twenty-four patients had residual disease and 6 patients had local recurrence and 10 patients developed distant metastasis. Two patients had febrile sepsis and died at the 2nd and the 6th month during the courses of palliative chemotherapy. One patient had breast cancer at the 25th month. The stage distribution by histology and the end result of the follow up are shown in Table 4, 5 and 6.

Table 4. Stage I and the end result of the follow up.

	Residual disease	Local recurrence	Distance metastasis	Disease control
Adenocarcinoma (n = 12)	1 (8.3 %)	1 (8.3 %)	1 (8.3 %)	9 (75.0 %)
Adenosquamous cell carcinoma (n = 4)	0 (0 %)	0 (0 %)	0 (0 %)	4 (100 %)
Total (n = 16)	1 (6.25 %)	1 (6.25 %)	1 (6.25 %)	13 (81.25 %)

Table 5. Stage II and the end result of the follow up.

	Residual disease	Local recurrence	Distance metastasis	Disease control
Adenocarcinoma (n = 51)	8 (15.68 %)	7 (13.72 %)	7 (13.72%)	30 (58.82 %)
Adenosquamous cell carcinoma (n = 15)	2 (13.33 %)	2 (13.33 %)	5 (33.33 %)	7 (46.66 %)
Total (n = 66)	10 (15.15 %)	9 (13.63 %)	12 (18.18 %)	37 (56.06 %)

Table 6. Stage III and the end result of the follow up.

	Residual disease	Local recurrence	Distance metastasis	Disease control
Adenocarcinoma (n = 33)	19 (57.57 %)	4 (12.12 %)	9 (27.27 %)	9 (27.27 %)
Adenosquamous cell carcinoma (n = 10)	5 (50.00 %)	2 (20.00 %)	1 (10.00 %)	2 (20.00 %)
Total (n = 43)	24 (55.81 %)	6 (13.59 %)	10 (23.25 %)	11 (25.58 %)

The tumor size is the important prognostic factor for the treatment of cervical carcinoma. There were 101 patients whose tumour sizes of the primary lesion had been recorded. Thirty-eight patients (37.62 %) had a lesion less than or equal to 3 cm and 78 patients (72.27 %) had a lesion greater than 3 cm. There was higher chance of residual disease and developed distant metastasis in a lesion greater than 3 cm group. The size of lesions and the end result of the follow up are shown in Table 7.

Table 7. The size of lesions and the end result of the follow up.

Lesion (n = 101)	Residual disease	Local recurrence	Distance metastasis	Disease control
$\leq$ 3 cm (n = 38)	7 (18.42 %)	5 (13.15 %)	4 (10.52 %)	23 (60.52 %)
> 3 cm (n = 73)	16 (21.19 %)	7 (9.58 %)	16 (21.91 %)	33 (45.20 %)

DISCUSSION

From the Tumor Registry, Siriraj Hospital, between 1993-1995 the number of cervical cancer patients was 1786 patients. Among theses, 259 patients (14.5%) were adenocarcinoma and 43 patients (2.4%) were adenosquamous cell carcinoma.[6-8] The incidence of adenocarcinoma and adenosquamous cell carcinoma appears to be increasing.[9] It was difficult to draw conclusion about the influence of histology on prognosis. The patients with adenocarcinoma did not have worse prognosis than squamous cell carcinoma.[10,11] The size of the lesions and the lymph node metastasis were the important prognostic factors. Some studies showed the evidence that the patients with adenocarcinoma have a poorer prognosis than the patients with squamous cell carcinoma of the same stages.[4,12,13] The rate of lymph node metastasis and distant metastasis were more commonly found for the patients with adenocarcinoma. The combination of radiotherapy and surgery has been controversy. The survival in patients who underwent adjuvant hysterectomy did not significantly improve and the combination of two modalities was also associated with a relatively high risk of treatment complications.[12,14]

Among the adenocarcinoma groups, adenosquamous cell carcinoma was considered a subtype of adenocarcinoma. There is no statistical significant difference in survival between adenocarcinoma and adenosquamous cell carcinoma.[3] In our study, we found no difference in stage distribution, and response of treatment.

For stage I disease, the radical abdominal hysterectomy and pelvic lymph node dissection has been the primary treatment. Adjuvant whole pelvic irradiation might decrease the risk of local recurrence but did not improve survival.[9] For the bulky lesions, the regression is more slowly or less completely after radiation treatment alone. The addition of a hysterectomy was helpful to improve the local control but did not improve the survival.[10,14] From this study, there is no difference in disease control between patients who had adjuvant hysterectomy after radiation treatment compared to patients who had radiation treatment alone. The poor prognosis of stage I disease is associated with the lymph node metastasis.[2,9,12,15] The 5 year survival fell from 81.3% to 42.7% when tumor had lymph node metastasis.[3] The CT-scanning or MRI could detect the lymph nodes metastasis as well as measured the lesion size.[16-17] We suggest to use the CT-scanning or MRI to find the evidence of lymph node metastasis which is the poor prognostic factors of the disease. To date it is unclear which treatment modalities are the most efficacious as adjuvant therapy for stage I disease. The cisplatin – base concurrent chemo-radiation therapy and adjuvant chemotherapy was suggested to imorove survival.[15,18]

For stage II disease, we also recommend adjuvant hysterectomy after the completion of radiation treatment as for stage I disease. The disease control of the combined treatment group was better than that receiving radiation treatment alone. Several authors reported the attempts to improve the outcome of radiation treatment with an extrafascial hysterectomy.[1,10,14]

For stage III disease and the patient with a lesion greater than 3 cm., we found that most of the patients had the residual disease after the completion of radiation treatment and developed distant metastasis. From many studies, for the locally advanced diseases, the ciplatin – base chemotherapy was suggested to use as concurrent chemo-radiation to improve local control and adjuvant chemotherapy to improve the survival.[19-23]

CONCLUSION

The radiation treatment is the primary treatment of the cervical cancer in every histologic type and every stage of disease (except stage I that is suitable for surgery). The adjuvant treatments that might improve the local control and survival should be further investigated in randomized control trial to show the results.

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ABDOMINAL WALL COMPRESSION AND PRONE POSITION EFFECTIVELY DISPLACE PELVIC SMALL BOWEL AND REDUCE IRRADIATED VOLUME

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ABSTRACT

Objectives: Small bowel is a dose limiting structure for pelvic irradiation, which is commonly used in several cancers. Moving the small bowel out of the pelvic irradiated field results in decreasing complications. In this study, we evaluate the efficacy of abdominal wall compression and prone position in displacing the small bowel out of the pelvic irradiated field, reducing patient thickness, decreasing the irradiated volume and increasing dose uniformity.

Material and Method: Ten cervical cancer patients with at least 20 cms separation at center of pelvic field were entered into this study. Oral contrast medium was used to visualize pelvic small bowel. Volume of irradiated tissue and small bowel area within the treatment ports was measured in supine position before and after abdominal wall compression and in prone position. The study was performed twice in each patient.

Results: The distance between the Anterior and Posterior field at center of pelvic field was decrease by about 3.8 cms after abdominal wall compression and 1.6 cms in prone position. Average of reduced irradiated volume after compression and prone position was 13.14% and 5.51% respectively ($p<0.005$). Better dose uniformity was obtained. Additionally, 49.49% of the mean small bowel area was diminished by abdominal wall compression whereas 26.40% by prone position ($p<0.005$).

Conclusion: Abdominal wall compression and prone position were effectively able to displace small bowel and reduce irradiated volume within pelvic treatment field. These simple, safe, inexpensive and reproducible techniques may decrease complications from pelvic irradiation.

INTRODUCTION

Pelvic irradiation is commonly used for several cancers such as gynecological, rectal, prostate and bladder malignancies. Survival benefit has been recently illustrated from chemoradiation in cervical and rectal cancer. [1-6] However, acute and chronic small bowel complication is a limiting factor for aggressive combined modalities. Small bowel is a mobile structure that could be relocated by a variety of techniques. Several approaches, both surgical and non-surgical options, have been employed to reduce the small bowel volume in the irradiated field[7-15]. Such

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methods, however, are not often feasible and practical. Another concern of radiation therapy planning is the dose homogeneity, which is influenced by the patient thickness. For parallel opposing fields, as the patient thickness increases the central axis maximum dose near the surface increases relative to the midpoint dose, especially when decreasing beam energy. This study was designed to evaluate the efficacy of abdominal wall compression and prone position in displacing small bowel out of the pelvic treatment area and reducing patient thickness and irradiated volume in patients who have abdominal thickness more than 20 centimeters. Reduction of patient thickness will improve dose homogeneity which may decrease complicaitons.

MATERIAL AND METHODS

Ten cervical cancer patients treated at the Division of Radiation Oncology, Department of Radiology, Chulalongkorn Hospital were included. All patients must have at least 20 cms separation at center of pelvic field. Patient having previous abdominal surgeries were excluded. Oral contrast was used to locate the pelvic small bowel. Approximately 30 minutes before simulation, patients were informed to drink two glasses (about 300-400 ml) of oral contrast medium containing 1:1 barium sulfate. Radiograph of pelvic field was taken after contrast medium filled the pelvic small bowel. Upper and lower border of pelvic field was placed at upper sacroiliac joint and bottom of obturator foramen, respectively. Two-cm margin lateral to the bony pelvis was defined. The pelvic field size was approximate 16x16 to 16x19 cm^2.

Square-shape foam (figure 1) was used for abdominal wall compression. The dimension of the foam was 15x17x5 cm^3, which was closed to the field size. The foam was placed on the abdominal wall on top of the irradiated field and taped firmly to the table. The patient was encouraged to relax the abdominal wall so that the maximum compression could be accomplished (figure 2). Another radiograph of the pelvic field was taken after compression for comparison with the pre-compression film.

The distance between the Anterior and Posterior fields of the tissue at three levels, upper border, center and lower border of the pelvic field, were recorded before and after the abdominal wall compression.

After removing the foam, the patient was placed in prone position. Radiograph of the pelvic irradiated field was taken and the tissue separations at the three levels were noted as well. Irradiated volumes of the pre and post compression and prone position were assessed by multiplying the field size with the average value of pelvic fields separation.

The study was conducted twice in each patient. Compression of the abdominal wall corresponding to the first time was attempted. Body contour of a patient's lower abdomen in sagittal and transverse planes was made for illustration of isodose distribution.

Small bowel areas in the pelvic irradiated field were evaluated by delineation contrast-filling small bowel in the simulation films in each position. Small bowel areas were determined by dividing the area of opacification into 1-cm segments and summing the results of each segment. Correction of magnification factor of each film was attained. Difference of small bowel area and pelvic irradiated volume were compared and calculated using pair t-test. Comparison of the two studies in each patient was also made to study the reproducibility of the processes. We also studied transverse isodose distribution in each position to assess the homogeneity.

RESULTS

The characteristics of treated patients are listed in table 1. The average of the reduced small bowel area was 49.49% ($p<0.0005$) and 26.4% ($p<0.0005$) after abdominal wall compression and prone position respectively. Additionally, the reduction was reproducible as shown in table 2. An example of films is demonstrated in figure 3.

The distance between the Anterior and Posterior fields at the center of pelvic field ranged from 20 to 24 cm. The mean reduction were 3.8 cm and 1.6 cm after compression with foam and prone position, respectively. Therefore, The distance between the Anterior and Posterior fields at the upper border, center and lower border in each patient was more uniform. The irradiated volume was reduced 13.14% after compression ($p<0.0005$) and 5.51% in prone position ($p<0.005$) as compare to supine position as shown in table 3.

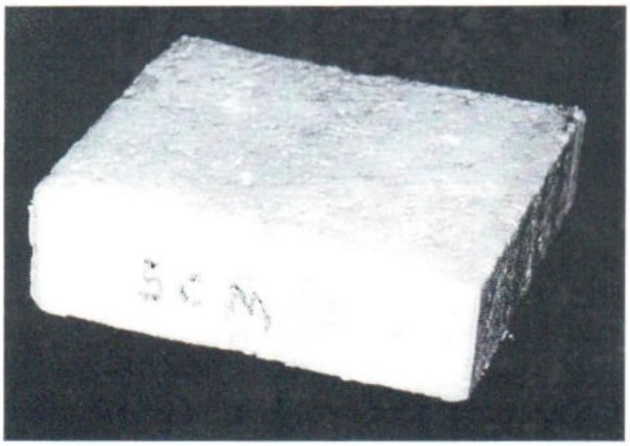


Fig. 1. The 15x17x5 cm^3 foam used for abdominal wall compression

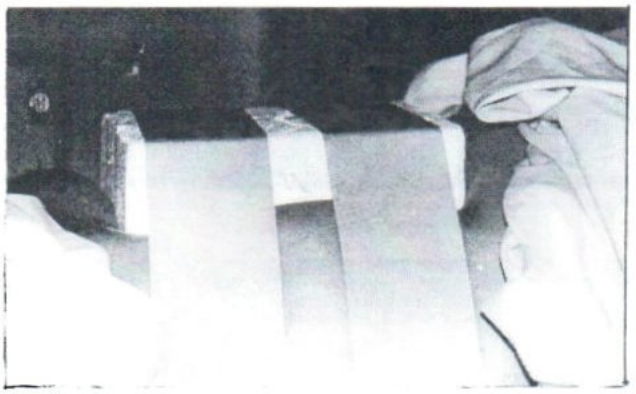
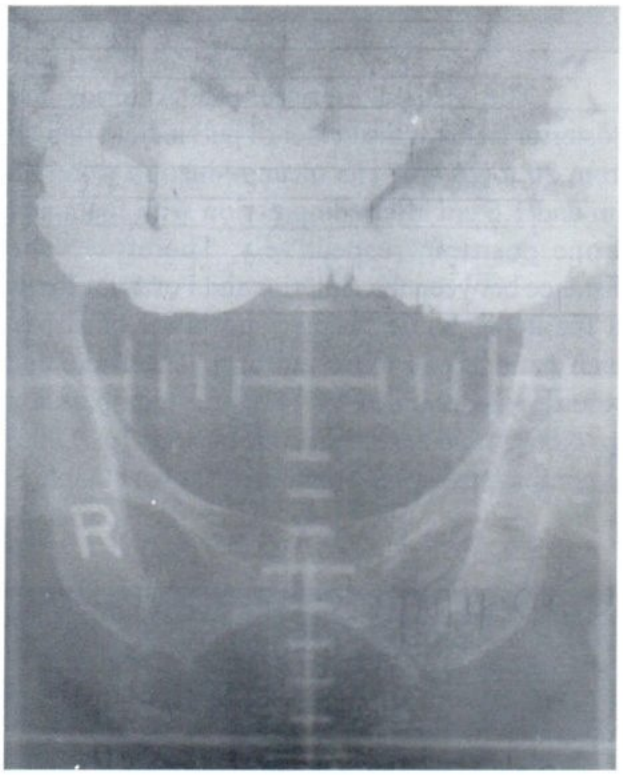


Fig. 2. The foam was placed on top of the pelvic irradiated field and taped firmly to the treatment table.



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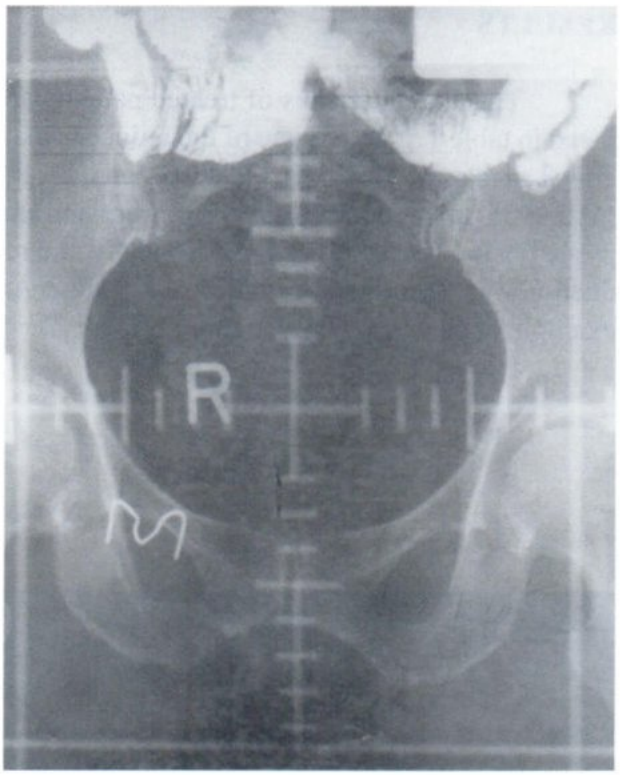

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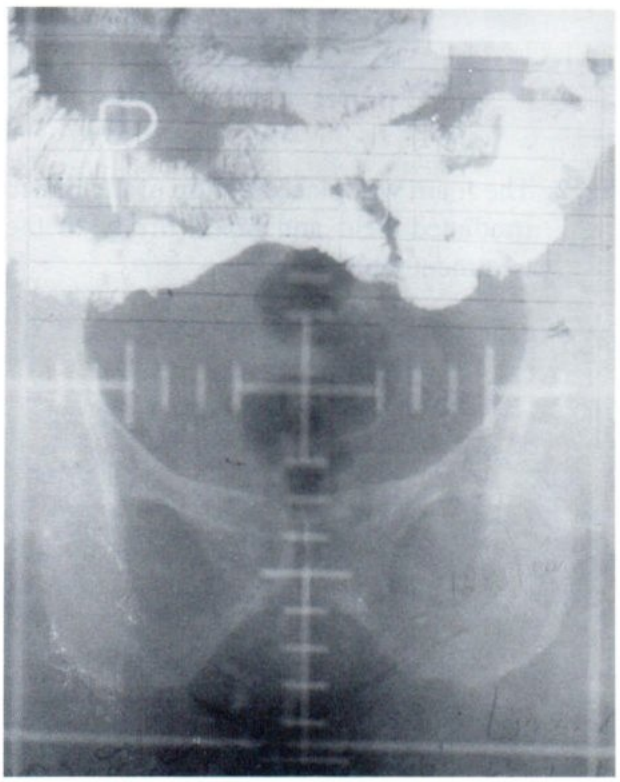

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Fig. 3. Simulation films illustrate the contrast-filling small bowel in the pelvic irradiated field. A. Supine position before abdominal wall compression. B. Supine position after compression. C. Prone position.

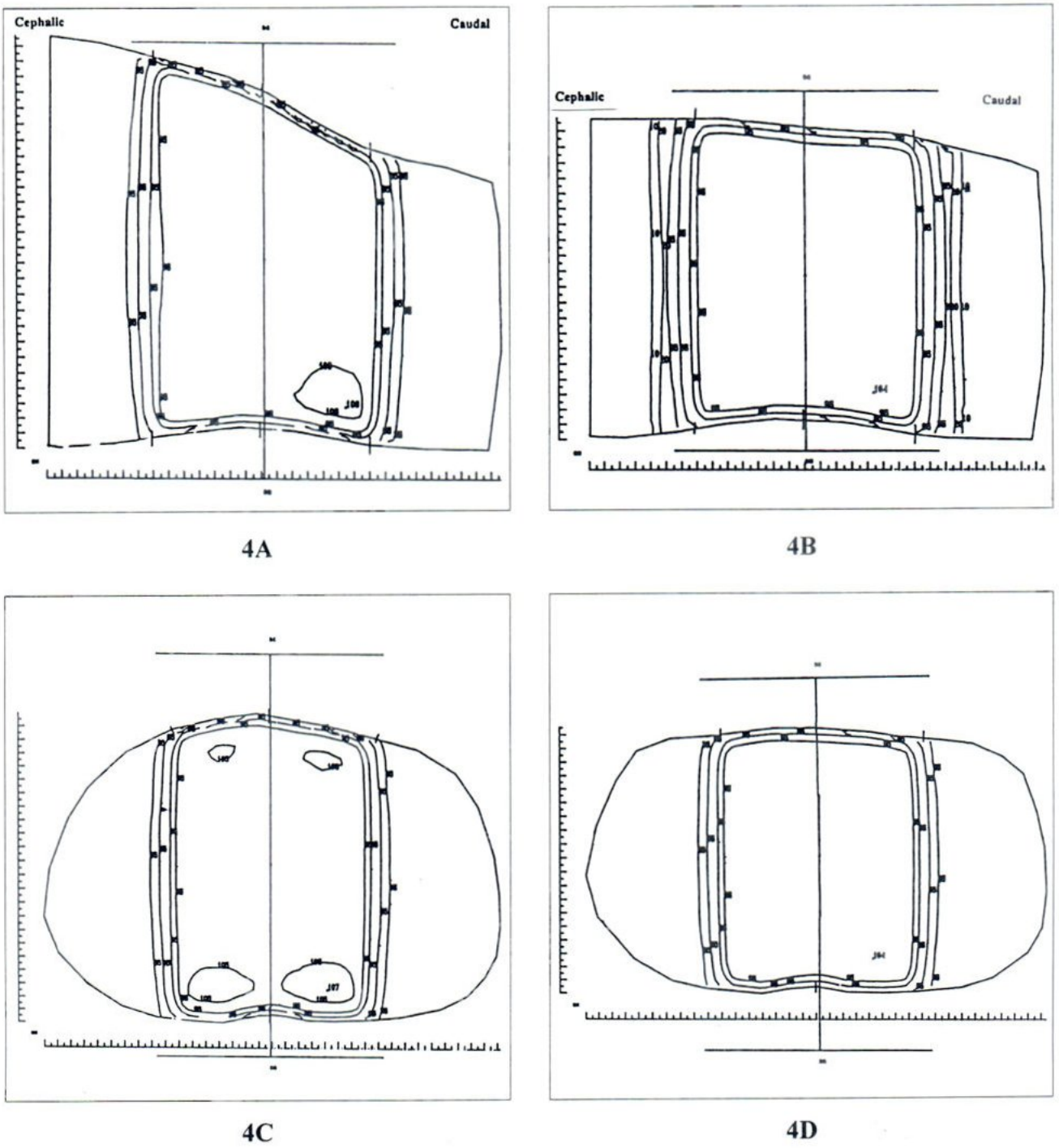
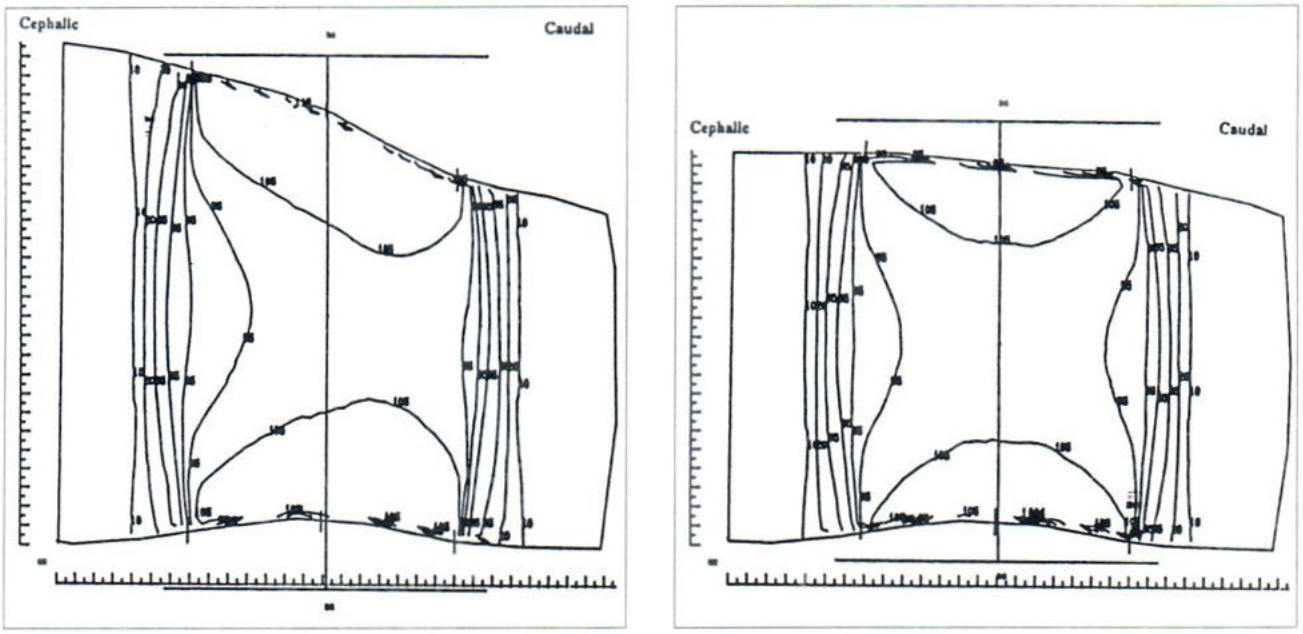


Fig. 4. The isodose distribution in the pelvic irradiated field using 10 MV photon. Field size 17x16 cm^2, SAD at 100 cms.
A. Sagittal view before abdominal wall compression. (Thickness at the center 22 cms.), B. Sagittal view after abdominal wall compression. (Thickness at the center 18.5 cms.), C. Axial view at the center of pelvic field before compression, D. Axial view at the center of pelvic field after compression.



5A 5B

Fig. 5. The isodose distribution in the pelvic irradiated field using Co-60 machine. Field size 17x16 cm^2, SAD at 80 cms.
A. Sagittal view before abdominal wall compression (Thickness at the center 22 cms.), B. Sagittal view after abdominal wall compression (Thickness at the center 18.5 cms.)

Table 1. Characteristics of studied patients.

No.	Age	Staging	Field size (Y x X)	Thickness of the tissue at the pelvic fields (cms)*		
				Precompression	Postcompression	Prone
1.	40	IIA	19x17	21.5-20-16	18.7-17-16	-
2.	55	IIIB	19x16	25-23-18	21.5-19.5-18	22-22-19
3.	61	IIIB	17x16	24-22-19	19-18-19	21-20-20
4.	59	IIIB	17x18	21.5-21-17.5	17.5-17.5-17.5	20-20-18
5.	70	IIIB	19x18	22-20-18	18-17-18	20-19-18
6.	59	IIB	16x17	25-23-18	19.5-19-18	21-21-20
7.	58	IIB	17x17	23.5-22-19	18.5-18-19	21-20-20
8.	54	IIIB	17x17	26-24-20	20-19-20	22-22-21
9.	30	IIB	16x16	24-22-19	18-18-19	21-21-20
10.	60	IIIB	17x17	25-23-20	20-19-20	21-21-21

* Three values are thickness at the upper, center and lower border of the pelvic field, respectively.

Table 2. The small bowel area in the pelvic irradiated field.

Patient No.	Investi-gation	A	B	A-B(%)	C	A-C(%)	C-B(%)
1.	1st	111.9	37.2	74.7 (66.76)	0*	-	-
	2nd	68.5	65.8	2.7 (3.94)	80.4	-11.9 (-17.37)	14.6 (18.16)
2.	1st	126.5	34.4	92.1 (72.81)	98.5	28 (22.13)	64.1 (65.08)
	2nd	80.2	22.9	57.3 (71.45)	47.8	32.4 (40.40)	24.9 (52.1)
3.	1st	160.8	109.3	51.5 (32.03)	129.4	31.4 (19.53)	20.1 (15.53)
	2nd	165.3	67.5	97.8 (59.17)	76.1	89.2 (53.96)	8.6 (11.3)
4.	1st	149.1	57.8	91.3 (61.23)	83.2	65.9 (44.20)	25.4 (30.53)
	2nd	130.5	62.5	68 (52.11)	114.4	16.1 (12.34)	51.9 (45.37)
5.	1st	116.7	106.5	10.2 (8.74)	115.8	0.9 (0.77)	9.3 (8.03)
	2nd	152.1	126	26.1 (17.16)	178.8	-26.7 (-17.55)	52.8 (29.53
6.	1st	146	108.5	37.5 (25.68)	127.4	18.6 (12.74)	18.9 (14.84)
	2nd	138.6	69.4	69.2 (49.93)	116.1	22.5 (16.23)	46.7 (40.22)
7.	1st	157.2	42.2	115 (73.16)	131.7	25.5 (16.22)	89.5 (67.96)
	2nd	79.69	34.46	45.23 (56.76)	39.23	10.46 (13.13)	34.77 (88.63)
8.	1st	52.14	12.85	36.29 (75.35)	19.68	32.46 (62.26)	6.83 (34.71)
	2nd	141.54	72.3	69.24 (48.92)	88.56	52.98 (37.43)	16.29 (18.4)
9.	1st	141.54	72.3	69.24 (47.75)	88.56	52.98 (29.65)	16.26 (18.36)
	2nd	101.44	53	48.44 (47.83)	71.36	30.08 (31.07)	18.36 (25.73)
10.	1st	173.92	77.54	96.38 (55.42)	118.33	55.59 (31.96)	40.79 (34.47)
	2nd	94	34.31	59.69 (63.50)	48.17	45.83 (48.76)	13.86 (28.77)

A: The small bowel area before abdominal wall compression (cm^2)
B: The small bowel area after abdominal wall compression (cm^2)
C: The small bowel area in prone position (cm^2)
* The prone position was performed only once in patient number 1.

Table 3. Reduced irradiated volume after abdominal wall compression and prone position (%)

Patient number	Compression	Prone
1.	10.09	-
2.	10.61	4.55
3.	13.85	6.15
4.	12.5	3.33
5.	11.67	5.0
6.	14.39	6.06
7.	13.95	5.43
8.	15.71	7.14
9.	15.38	4.62
10.	13.24	7.35
Average	**13.14**	**5.51**

DISCUSSION

Cervical carcinoma is the most common cancer in Thai female.[16] It is ranked to be the first in patients who were diagnosed to have cancer in Chulalongkorn hospital in 1998.[17] Radiation therapy has been considered a standard treatment in locally advanced cervical cancer. Recently, survival was shown to be improved from concurrent chemoradiation. Moreover pelvic radiation is also utilized in rectal, prostate, bladder and endometrial cancer to improve local tumor control. However, one of the normal tissues which is the dose limiting structure is small bowel (TD 5/5=4500cGy). Increased stool frequency is commonly seen during pelvic irradiation. Chronic complications include small bowel obstruction, malabsorption and perforation. There are several factors predisposing to late small bowel complications, including total radiation dose, dose per fraction, irradiated small bowel volume, previous surgery and combined chemoradiation. The severity of acute small bowel complications was associated with irradiated small bowel volume whereas late complication was related to small bowel volume receiving more than 45 Gy.[9]

Several surgical and non-surgical techniques have been employed to reduce pelvic small bowel volume.[7-15] Surgical options include omental sling, absorbable synthetic mesh sling, temporary intrapelvic tissue expander, intrapelvic prosthesis and reperitonizing pelvic floor. Such methods, however, are not often feasible. Variety of positions has been studied and shown to have a benefit of small bowel displacement from pelvic treatment field. These include prone, trenderlenburg, bladder distension, abdominal wall compression and belly board devices.

Due to their safety, simplicity, practicability and applicability to Thai patients, we chose to evaluate the abdominal wall compression and prone position techniques. The foam used for abdominal wall compression has little effect on quality of radiation. The reductions of the small bowel area in the pelvic irradiated field (49.49% and 26.4% after abdominal wall compression and prone position respectively, $p<0.0005$) should be

resulted in decreasing the complications.

Furthermore, we found that reducing thickness of pelvic tissue at the upper border and center of the field made isodose distribution in the pelvic irradiated volume more homogeneous. The dose and the area of the hot spot was lower after abdominal wall compression and prone position as shown in the figure 4. Using Co-60 beam, instead of higher Megavoltage photon beam, would make this benefit more significant especially in patients who have thickness more than 20 cms at the center of pelvic field. (figure 5). After abdominal wall compression, the irradiated volume was reduced 13.14% compared to 5.51% from prone position. Cautiously, the reducing irradiated volume might not mean that the tissue was displaced from the pelvic irradiated field but in fact part of it was compressed. However, decreasing the hot spot dose and the area of hot spot combined with the increasing dose homogeneity would reduce normal tissue complications. Clinical significance of these procedures in reducing acute and late small bowel complications remains to be verified.

Assessing these two techniques, we discovered that abdominal wall compression was more effective than prone position in terms of reducing small bowel area and irradiated volume. One disadvantage of prone position is the difficulty in setting up body alignment which can make the treatment area shifted. We also studied the efficacy of the procedures twice in each patient. Using pair t-test, we found that there is no significant difference between first and second investigation confirming the reproducibility.

In conclusion, either abdominal wall compression or prone position is effective in reducing small bowel area in pelvic irradiated field. The simple, safe, inexpensive and reproducible techniques may decrease complications from pelvic radiation.

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JUNCTION PLANE DOSIMETRY IN DIFFERENT TECHNIQUES OF COBALT-60 HEAD AND NECK IRRADIATION

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Vinai POLWATSATIAN, BSc.*

ABSTRACT

Study of dose at the junction between lateral and anterior field in irradiation technique of head and neck cancer with a Cobalt-60 teletherapy machine was performed in anthropomorphic rando phantom with TLD-100 chips as dosemeters. Doses were compared in three different techniques ; straight field (Technique 1), couch turntable in lateral field (Technique 2) and couch turntable in lateral field with a half beam block device in anterior field (Technique 3). When normalize dose at any point of the junction as a percentage of the dose at the center of lateral field, the mean doses in Technique 1 , Technique 2 and Technique 3 are 112.56±13.51%, 103.69 ± 12.29% and 97.20 ± 12.25% respectively. Measurements were done three times in each technique to assess for the setup reproducibility. It was found that only the reproducibility in Technique 1 and 2 was acceptable. This report is an attempt to investigate the dosimetry at the junction plane in different techniques of head and neck irradiation and suggest an appropriate technique which provides a reproducibly uniform dose distribution across the junction of head and neck irradiation with the Cobalt-60 teletherapy machine.

INTRODUCTION

The irradiation technique of head and neck cancer commonly performed with the lateral and anterior field to treat the primary tumor and the draining lymphatics. Because of an overlapping of the beam divergence of these adjacent fields makes the dose at the junction to be non-uniform. Many studies have been reported to solve this problem. These included the use of couch and collimator rotation in lateral field,[1] the gantry rotation in anterior field (with the couch rotated 90^0).[2] More recently, the introduction of asymmetric collimators in linear accelerator machine has allowed a treatment to be performed in the monoisocentric technique.[3,4] The advantage in this technique is a couch movement not being required. Therefore it is theoretically more accurate and setup reproducibility can be acquired. In our institution, the main treatment unit for head and neck irradiation is Cobalt-60 teletherapy machine due to its appropriate energy, less cost and easy maintenance. But there is a disadvantage from a large penumbra that makes the problem of the matching field overdosage being more severe. Moreover, with a symmetric collimating system, the monoisocentric technique cannot be performed by this unit. In this work, we proposed to investigate for the junction plane dosimetry in different techniques of head and neck irradiation and determine a suitable technique that may provide both a good dose uniformity at the junction and setup reproducibility to be considered as our routine treatment technique.

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MATERIALS AND METHODS

Firstly, the lateral and anterior treatment fields were defined on a rando phantom by the Shimadzu conventional simulator with 80 cm. source–skin–distance. From simulation, junction was shown at the level of a thyroid notch. Measurments of dose at the junction were performed with the TLD-100 chips (LiF:MgTi, 3.2x3.2x0.9 mm,Harshaw Chemical, Germany). Because its appropriate thickness represented a good dose resolution at the junction. A 2 mm. thick of perspex sheet was trimmed to match with the neck contour of the rando phantom and thirty-seven holes were drilled in a regular pattern of six rows with a spacing of 1.5 cm. This 2 mm. perspex sheet was covered by the phantom and allowed the TLDs to be fitted and removed during the measurements.

Then the phantom was treated in Cobalt-60 treatment room with three different techniques. Each time a position of the phantom was carefully reproduced from the simulation. The details of each setting-up technique are described in the following.

TECHNIQUE 1-STRAIGHT FIELD

In this technique, phantom was firstly treated with the two lateral opposing fields. Dose delivered to the reference point (at a half of separation at a level of field center) in each field was 100 cGy. Anterior field was given a dose of 200 cGy at depth 4 cm. All fields were treated with 80 cm SSD. Positions of the collimator and couch were confirmed to be at 0 angle in every measurement. Measuring of dose in this technique will illustrate the dose at the junction when an overlapping of beam divergence between the two fields existed.

TECHNIQUE 2- COUCH TURNTABLE IN LATERAL FIELD

The couch turntable was introduced when phantom was treated in lateral field to eliminate the lower border of beam that diverged into the superior border of an anterior field. The couch was turned in the direction of the beam to create a transverse match with the anterior field. The angle of couch turntable depends on the length of treatment field and SSD. It can be calculated from the following equation.[5]

$$\text{Tan}\,\theta = \frac{\text{field length}}{\text{distance}} \qquad \text{.....(1)}$$

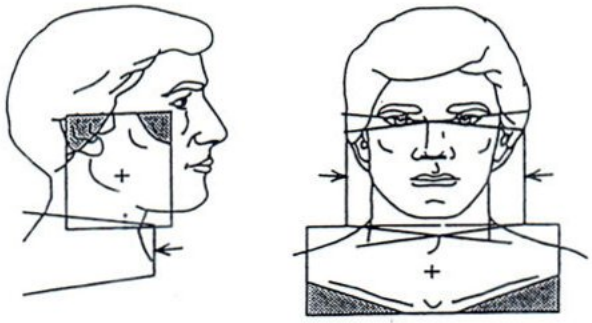
In this experiment, the angle of couch turntable is 4^{0}.

TECHNIQUE 3-COUCH TURNTABLE IN LATERAL FIELD WITH A HALF BEAM BLOCK IN ANTERIOR FIELD

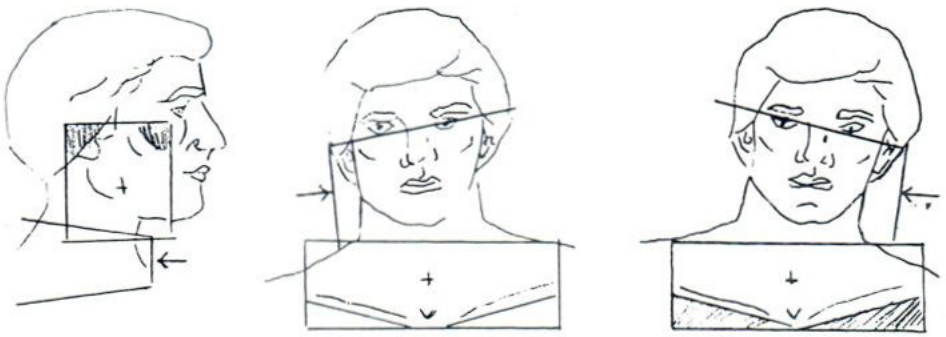
A half beam block device provides a mean to reduce a penumbra on one side of the beam by shielding half of the beam at a field central axis. Therefore, when it was introduced to the anterior field, it will match with the lower border of lateral field that the couch turntable is being used. With this device, the field length of the anterior field has to be double and block the upper half of the field.

RESULTS

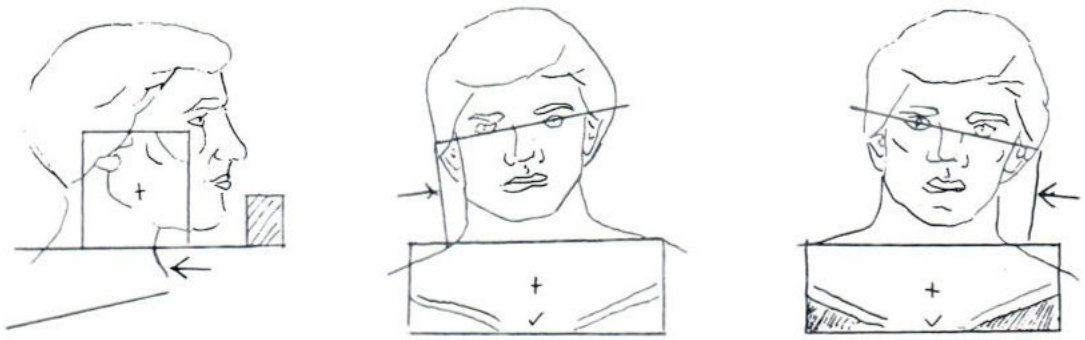
The results of junction plane dosimetry in three different techniques of head and neck irradiation were presented in Fig. 3 - Fig. 5. Dose at each point was normalized as a percentage of dose at the reference point. Mean dose at the junction, dose variation (determined from a standard deviation of the mean dose) and also a setting-up reproducibility (assessed from a mean of the standard deviation from 3 measurements) are summarized in Table 1.



a)



b)



c)

Fig. 1. The diagram illustrate a) Technique 1-straight field, b) Technique 2-couch turntable in lateral field c) Technique 3 –couch turntable in lateral with a half beam block in anterior field

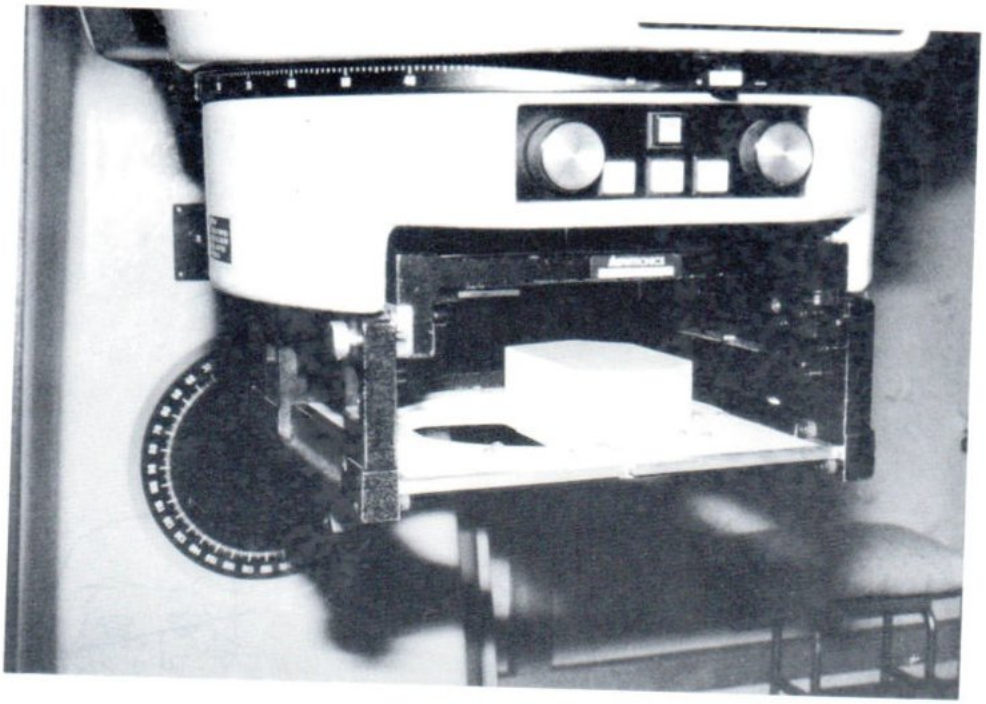


Fig. 2. A half beam block device

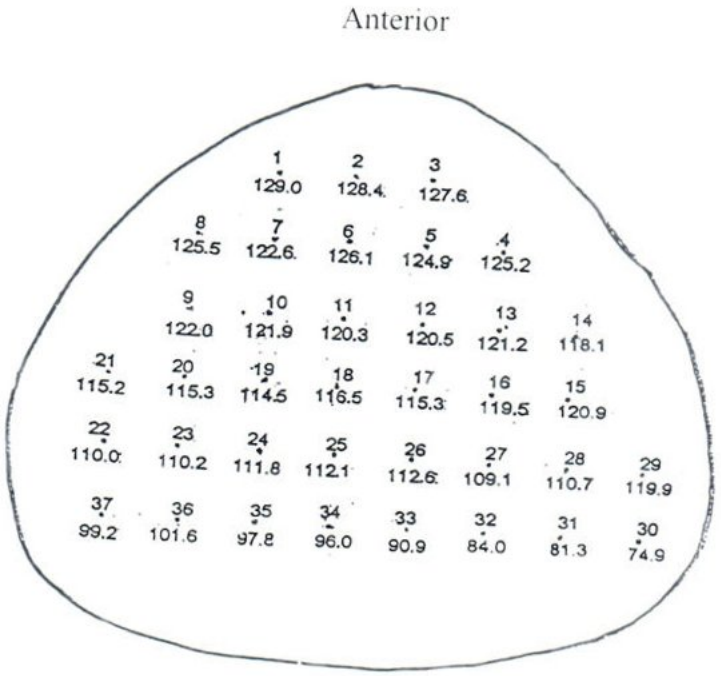


Fig 3. Dose distribution at a junction plane in the technique of straight field.

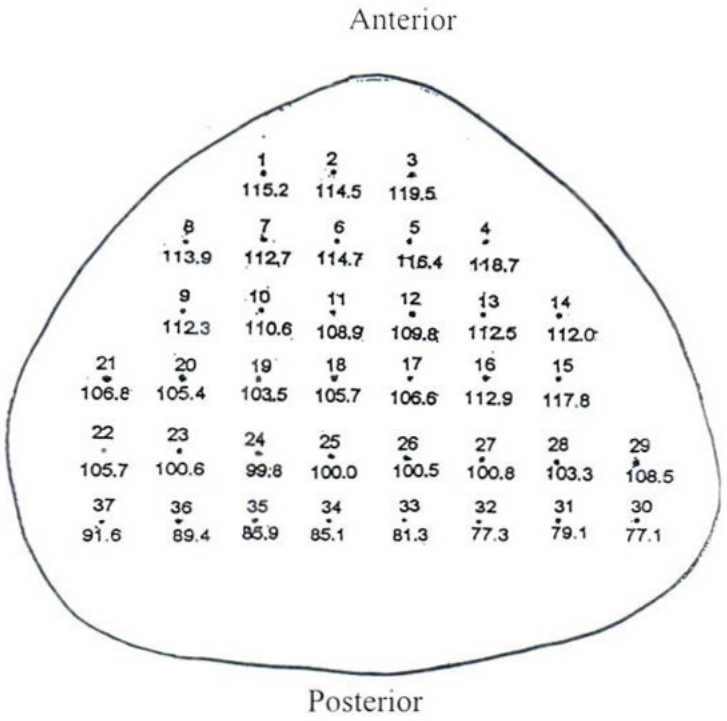


Fig 4. Dose distribution at a junction plane in the technique of couch turntable in lateral field.

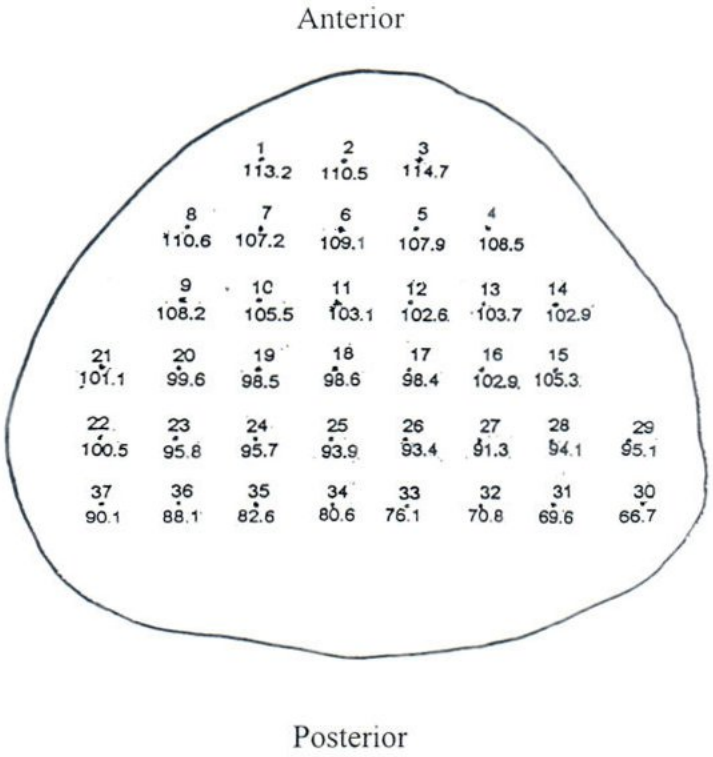


Fig 5. Dose distribution at a junction plane in the technique of couch turntable in lateral field with a half beam block in anterior field.

Table 1. Summary of junction plane dosimetry in three techniques.

Techniques	Mean Dose	Dose variation	Reproducibility
Straight field	112.56	13.51	2.09±1.03
Couch turntable	103.69	12.29	3.11±1.15
Couch turntable+HBB	97.20	12.25	7.72±4.55

HBB = half beam block

DISCUSSION AND CONCLUSION

Numerous methods have been introduced for solving a problem of non-uniformity of the dose at a field junction.[1,2,6,-8] Recently, the technique of monoisocentric utilizing asymmetric collimation showed a potential advantage of more accurate and reproducibly dosimetry.[3,4,9] It also reduced a number of setup factors that are subjected to error by an operator. But it is a technique available with the linear accelerator unit only. In the institute that Cobalt-60 teletherapy machine still be the main treatment unit for head and neck cancer, dosimetry at the junction was required to assess for a magnitude of a field matching problem. Efforts to study a dose distribution at the junction of various techniques available with the Cobalt-6o machine was proposed. In this study we used a technique of couch turntable to solve for the divergence of lateral beam. Actually a half beam block device has a limitation in a field dimension. From simulation, the length of lateral field was 14.5 cm. That means, if a half beam block is applied, the field length required to set is at 29 cm. Since the maximum field size available for this device was 20x20 cm and when was half blocked a field was reduced to 10x20 or 20x10 cm, therefore it is not enough for the lateral field length. We found that applying a couch turntable in lateral field can minimize both area and level of high dose. Measurements in Technique 1 clearly demonstrated a level of high dose (up to 110-130%) at the junction in a large portion of anterior neck. With a couch turntable, this high dose region was decreased and presented a maximum dose not greater than 120%. Also, a mean dose in technique 1 and 2 was shown to improve from 112.56% to 103.69%. Among these techniques, the best uniformity of dose distribution was seen in technique 3. A mean dose at the junction in this technique (97.20%) was very close to a prescribed tumor dose. Moreover, the overdose was seen in a small area of neck and not greater than 115%. This high dose is still exist in the anterior neck due to the contour irregularity that we can not improve by using a compensator.

More interesting findings are dose variation and setup reproducibility. No difference in dose variation was seen in three techniques. It is unlikely in the setup reproducibility that only Technique 1 and 2 that provided an acceptable value. Reproducibility was worse in Technique 3. This may arise from a half beam block device. It required a correct position when fitted with a collimator to accurately provide the half blocked beam. Thus, it is easily subject to error by both an operator and the mechanic of the machine. In this technique, we tried to confirm the data by carefully repeating the measurements 5 times and the results were shown in Table 1.

In summary, the study of junction plane dosimetry in head and neck irradiation technique performed with Cobalt-60 suggested the technique of couch turntable in the lateral field to be

appropriate. It presented both the acceptable good dose uniformity and setup reproducibility. Even though, the application of a half beam block in the anterior field had the best dose uniformity at the junction but its reproducibility was not satisfied. However, not only the junction plane but also a whole treatment volume including critical organ such as lens, thyroid and brain that dosimetry should be carefully verified prior to the application in the routine clinical uses.

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Message from

Professor Dr. Kawee Tungsubutra

Editor-in-Chief, The Asean Journal of Radiology

Dear Friends ,

Happy New Year to you all. I hope this journal had passed the critical period. We can stand on our feet and hope that our younger generation will start to run!

Kawee Tungsubutra
January - April 2001.

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