SEPT. - DEC. 2001
Volume VII Number III

ISSN 0859 144X

THE ASEAN JOURNAL OF RADIOLOGY

Published by The Radiological Society and
The Royal College of Radiologists of Thailand,
Bangkok, Thailand

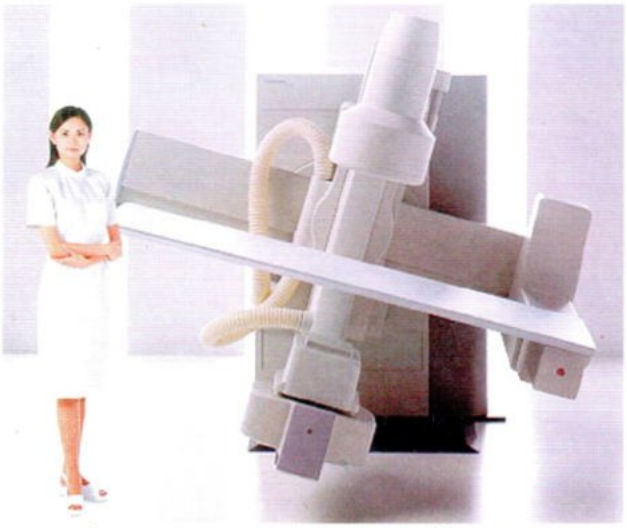
Started through an educational grant from Bracco since 1995

TOSHIBA

GLOBAL IMAGING •MEDICAL SYSTEMS

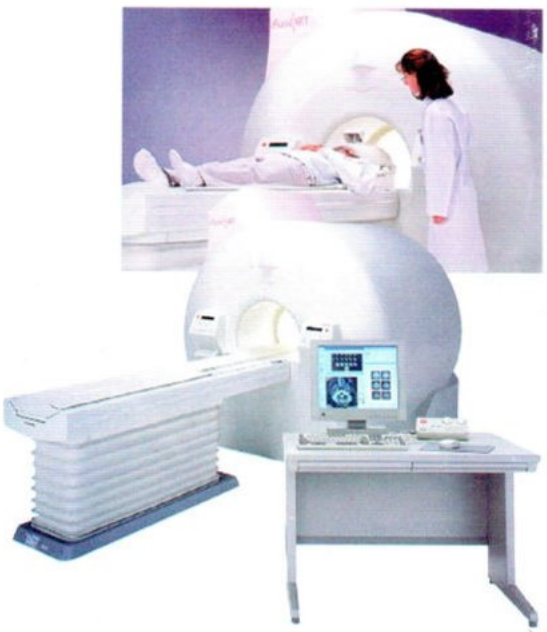
Medical Equipment and Systems

Since the development of our X-ray tube in 1914,Toshiba Medical Systems Company has grown into one of the world's leading diagnostic imaging manufacturers, contributing to the advancement of medicine. Our operations include Research & Development, design, production, sales, services and support of diagnostic imaging equipment and systems. These and other activities have won the highest praise in the global medical market. The trust of our customers is a major factors in charting our course towards a new future in medicine.

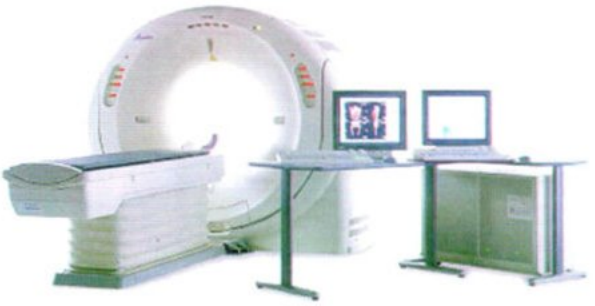


Multipurpose X-ray System : Model ULTIMAX

Toshiba's vision is to provide solutions to the medical professionals that help save patients' lives while offering reliable products with a long service life.



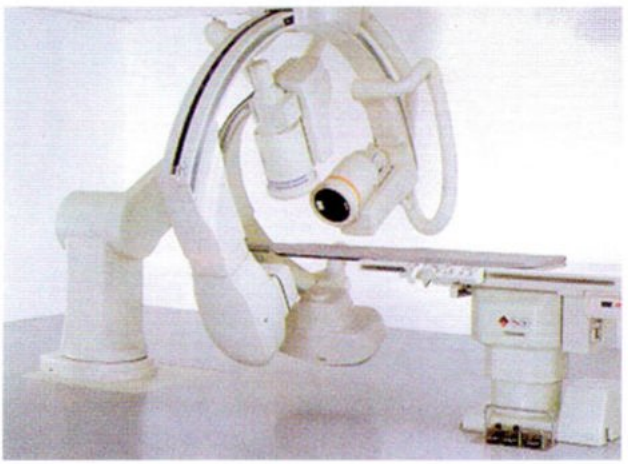
MRI Scanner : Model Excelart



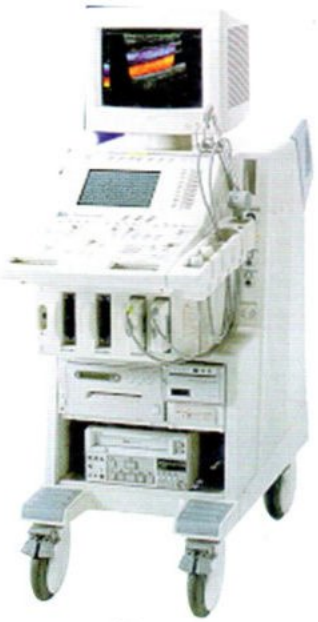
Multislice CT Scanner : Model Aquilion MULTI

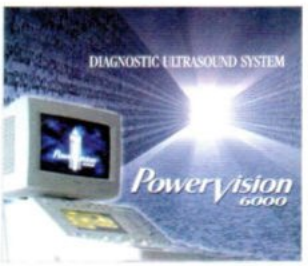
Whether the most appropriate solution is a single product or a complex combination of multiple modalities and imaging networks, Toshiba's philosophy is to be a long-term reliable partner with our customers.

That's why we say " Toshiba, Made for Life "



Biplane Angiography System : Infinix CB





Powervision 6000

Made for Life

(SOLE DISTRIBUTOR)

CMC BIOTECH CO., LTD.
364 Muban Town-in-Town, Soi Ladphrao 94, Ladphrao Road, Wangthonglang, Bangkok 10310
Tel. 66(0) 2530-4995 (automatic 8 lines) Fax: 66(0) 2539-6903
Northern Branch (Chiangmai) Tel. 66(0) 5328-3261 Fax. 66(0) 5320-4463 Mobile Phone (01) 445-3766
North Eastern Branch (Khon Kaen) Tel. 66(0) 4334-1642 Fax. 66(0) 4334-1643 Mobile Phone (01) 431-3385
Southern Branch (Songkhla) Tel. 66(0) 7442-9803 Fax. 66(0) 7442-9804 Mobile Phone (01) 573-4937

SEPT. - DEC. 2001
Volume VII Number III

ISSN 0859 144X

THE ASEAN JOURNAL OF RADIOLOGY

**Published by The Radiological Society and
The Royal College of Radiologists of Thailand,
Bangkok, Thailand**

Started through an educational grant from Bracco since 1995

www.bracco.com/imaging

Chief Editor

Professor Kawee Tungsubutra
Kaweevej Hospital, 318 Taksin Road, Dhonburi, Bangkok 10600, Thailand.

Asean Journal of Radiology.
Instructions for Authors.

1. The Asean Journal of Radiology publishes the papers on Radiological Sciences, such as research work, review articles, case reports, innovations in Medical Sciences related to all branches of Radiology, and letters to the editor. The aforementioned materials can be written in English only.

2. The authors have to submit 2 copies of the manuscript and a diskette: **to Prof. Dr. Kawee Tungsubutra.** 318 Kaweevej Hospital, Taksin Road, Dhonburi, Bangkok 10600, Thailand.

3. The original copy to be submitted must be typed in a double space on one side of the page of 8.1/2" x 11.1/2" paper.

4. The format of the article must include :

a. Title page and address of the author (s)
b. Abstract
c. Introduction (Background)
d. Material and Method
e. Results and discussion (Tables and Illustrations)
f. Acknowledgement (if any)
g. References (Follow the Vancouver style developed by ICMJE)

5. We will provide 5 copies of reprints for the author (s) who submit (s) an article for publication in the Asean Journal.

6. The illustrations and tables must be clearly prepared with legends in English as they are the art works to be reproduced.

7. The authors are responsible for the contents of the article as to its facts and findings.

8. Ethics.

Paper reporting studies which might be interpreted as human experimentation (e.g. controlled trials) should conform to the standards of the Declaration of Helsinki (see British Medical Journal 1964:2:177) and should indicate that, approval that such studies may proceed, has been granted by the local or hospital Ethics Committee.

When reporting experiments on animals indicate whether the institution's or the National Research Council's guide for, or any national law on, the care and use of laboratory animals was followed.

THE ASEAN JOURNAL OF RADIOLOGY

Volume VII Number III SEPT. - DEC. 2001

CONTENTS

THE ASEAN JOURNAL OF RADIOLOGY

Volume VII Number III SEPT. - DEC. 2001

CONTENTS

DETERMINATION OF ALPHAFETOPROTEIN (AFP) LEVEL IN THE HEPATITIS B CARRIERS WITH DIFFERENT MALIGNANT DISEASES BY RADIOIMMUNOASSAY TECHNIQUE (A PILOT STUDY)

Viroj WIWANITKIT, M.D.[1]
Jamsai SUWANSAKSRI, M.Sc.[2]

ABSTRACT

Alpha-fetoprotein (AFP) , is a commonly used tumor marker in the present day. In the Individuals with chronic hepatitis B are at increased risk for the development of hepatocellular carcinoma. Although precise recommendations do not exist, it is reasonable for such individuals to undergo periodic screening for cancer. Screening procedures include measurement of serum alpha-fetoprotein (a tumor marker that is elevated in about 85% of individuals with hepatocellular carcinoma) and ultrasound examination. Here we reported the study of serum AFP levels determined by radioimmunoassay technique in the hepatitis B carriers with various malignant diseases. This study was designed as a descriptive pilot study. The serum AFP levels from 7 hepatitis B carriers with different malignant diseases, 3 with hepatoma (Child Class C) and 4 with non-hepatoma, were used in this study. All were the confirmed cases of hepatitis B infection without concomitant of other hepatitis. The radioimmunoassay kit used in this study was ELISA-AFP (CIS Bio International). It was noted that a great variations of the AFP levels among the hepatoma subjects were observed although we used the patient in the same Child classification. However, comparing to the other 10 selected non hepatitis B carriers with hepatoma (Child Class C), wide range of serum AFP was also observed. Furthermore, some overlapping of the AFP levels between hepatoma and non-hepatoma group was observed. We also studied the serum AFP levels among the other 10 hepatitis B silent carriers without evidence of liver structural pathology (from ultrasonography study) and revealed that the average AFP level was comparable to the malignant group. Furthermore, using the ANOVA analysis, there was no significant difference among the four groups of subjects ($P = 0.176$). Hence, the serum AFP level may not be a good screening tool for hepatoma in the hepatitis B carriers.

Key words: alpha fetoprotein, hepatitis B carrier, radioimmunoassay

INTRODUCTION

Alpha-fetoprotein (AFP) is a glycoprotein with a molecular weight of approximately 70 KD.[1] AFP is normally produced during fetal and neonatal development by the liver, yolk sac, and in small concentrations by the gastrointestinal tract.[2] After birth, serum AFP concentrations decrease

[1] Department of Laboratory Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok Thailand;
[2] Department of Clinical Chemistry, Faculty of Allied Health Science, Chulalongkorn University, Bangkok Thailand

rapidly, and by the second year of life and thereafter only trace amounts are normally detected in serum.[3] Elevation of serum AFP to abnormally high values occurs in several malignant diseases,[4-7] most notably nonseminomatous testicular cancer and primary hepatocellular carcinoma. In the case of nonseminomatous testicular cancer, a direct relationship has been observed between the incidence of elevated AFP levels and the stage of disease.[8-9]

Elevated AFP levels have also been observed in patients diagnosed with seminoma with nonseminomatous elements, but not in patients with pure seminoma.[6,8,10,11] In addition, elevated serum AFP concentrations have been measured in patients with other noncancerous diseases, including ataxia telangiectasia, hereditary tyrosinemia, neonatal hyperbilirubinemia, acute viral hepatitis, chronic active hepatitis and cirrhosis.[12-15] Elevated serum AFP concentrations are also observed in pregnant women.[16-17] Therefore, AFP measurements are not recommended for use as a screening procedure to detect the presence of cancer in the general population.

However, in the Individuals with chronic hepatitis B are at increased risk for the development of hepatocellular carcinoma. Although precise recommendations do not exist, it is reasonable for such individuals to undergo periodic screening for cancer. Screening procedures include measurement of serum alpha-fetoprotein (a tumor marker that is elevated in about 85% of individuals with hepatocellular carcinoma) and ultrasound examination. Here we reported the study of serum AFP levels determined by radioimmunassay technique in the hepatitis B carriers with various malignant diseases.

MATERIALS AND METHODS

This study was designed as descriptive pilot study. The serum AFP levels from 7 hepatitis B carriers with different malignant diseases, 3 with hepatoma (Child Class C) and 4 with non-hepatoma, were used in this study. All were the confirmed cases of hepatitis B infection without concomitant of other hepatitis. The radioimmunoassay kit used in this study was ELISA-AFP, purchased from the CIS Bio International. Briefly, it is a solid phase two-sited immunoturbidimeteric assay. Two monoclonal antibodies were prepared against sterically remoted antigenic sites on the AFP molecules, the first one is coated in the ELISA solid phase, the second one radiolabelled with iodine 125 is used as a tracer. The AFP molecules present in the standards or the samples to be tested are "sandwiched" between the two antibodies, following the formation or the coated antibodies/antigen/iodinated antibody sandwich, the unbound tracer is easily removed by a washing step.

All collected data were analyzed using descriptive statistical analysis. Comparison was performed at the statistical significant level equaled to 0.05.

RESULTS

The result from AFP determination was shown in Table 1. The AFP levels among the hepatoma group ranged from 3 to 800 ng/mL while the AFP levels among the non-hepatoma group ranged from 4 to 9.5 ng/mL (Figure 1).

Table 1. Serum AFP levels among the hepatitis B carrier subjects

No	Disease	Serum AFP level (ng/ml)
1	Hepatoma, Child Class C	800
2	Hepatoma, Child Class C	8
3	Hepatoma, Child Class C	3
4	Non Hodgkin's lymphoma	6.5
5	CA esophagus	9.5
6	CA cervix, stage III B	4.5
7	Cholangiocarcinoma	4

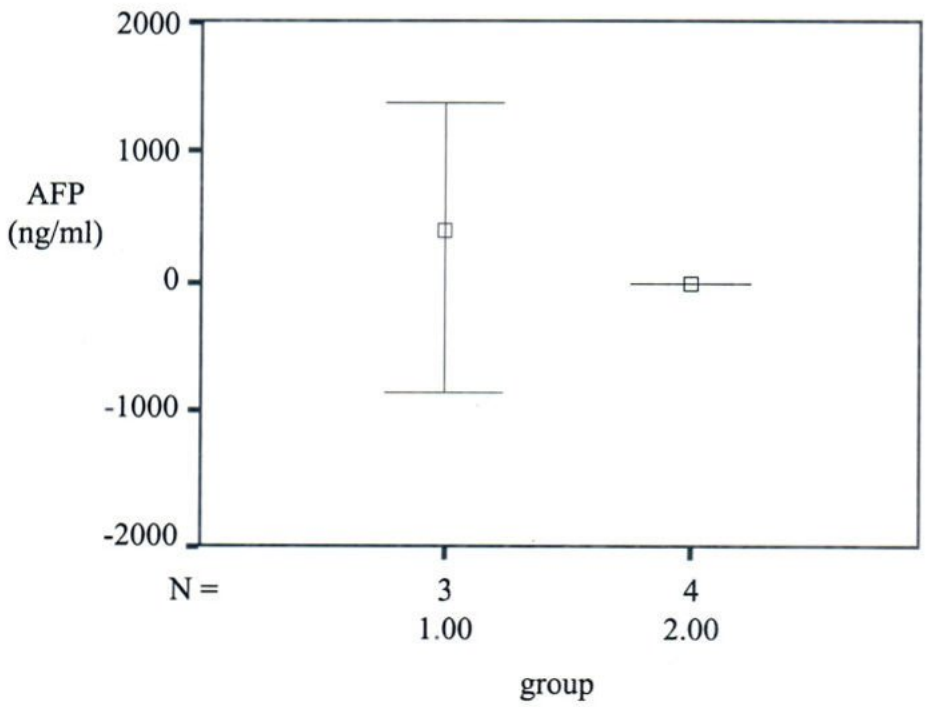


Fig. 1. Show 95% CI of serum AFP levels in each group
Group 1 = hepatitis B carriers with hepatoma
Group 2 = hepatitis B carriers with non hepatoma malignant diseases

Table 2. Average (mean ± SD) and 95 % CI of serum AFP level in different groups of patients

Group	Average (ng/ml)	95 % CI (ng/ml)
1. hepatitis B carriers with hepatoma (n = 3)	270.33 ± 458.71	0 - 1409.84
2. hepatitis B carriers with non hepatoma malignant diseases (n = 4)	6.13 ± 2.50	2.15 - 10.10
3. silent hepatitis B carrier (n = 10)	5.50 ± 1.58	4.37 - 6.63
4. non hepatitis B carriers with hepatoma (n = 10)	146.40 ± 182.69	15.71 - 277.09

DISCUSSION

HBV is a mostly double-stranded DNA virus in the Hepadnaviridae family. HBV causes hepatitis in human and related virus in this family cause hepatitis in ducks, ground squirrels and woodchucks. Although relatively rare in the United States, hepatitis B is endemic in parts of Asia where hundreds of millions of individuals may be infected. HBV is transmitted horizontally by blood and blood products and sexual transmission. It is also transmitted vertically from mother to infant in the perinatal period which is a major mode of transmission in regions where hepatitis B is endemic.[18-20]

HBV causes acute and chronic hepatitis. The chances of becoming chronically infected depends upon age. About 90% of infected neonates and 50% of infected young children will become chronically infected. In contrast, only about 5% to 10% of immunocompetent adults infected with HBV develop chronic hepatitis B.[18-20] These patients, who are still potentially infectious, have no symptoms and no abnormalities on laboratory testing. Nonetheless, some of these patients will have evidence of hepatitis on liver biopsy. Some individuals with chronic hepatitis B will have clinically insignificant or minimal liver disease and never develop complications. Others will have clinically apparent chronic hepatitis. Some will go on to develop cirrhosis. Individuals with chronic hepatitis B, especially those with cirrhosis but even so-called chronic carriers, are at an increased risk of developing hepatocellular carcinoma (primary liver cancer). This type of cancer is the leading cause of cancer death in the world, also in Thailand.

Therefore, every carrier needs a yearly check-up with the doctor to find the possible complications. A panel of liver enzymes (e.g., AST, alkaline phosphatase), liver function tests (e.g., PT) and a complete blood count should be checked yearly.[21] A baseline AFP and ultrasound are usually obtained at the first clinical visit, no matter what the patient's age is. In cirrhosis, yearly or twice yearly testing is begun as early indicators of hepatocellular carcinoma (HCC). The AFP is a tumor marker and is increased in 85% of individuals with HCC, often before clinical evidence of cancer is present. Ultrasound may show small cancers at a time when they can be resected completely.

Here, we performed a pilot study to obtain the level of serum AFP in hepatitis B carriers from different malignant diseases. Interestingly, the great variations of the AFP levels among the hepatoma subjects were observed although we used the patient in the same Child classification. However, comparing to the other

10 selected non hepatitis B carriers with hepatoma (Child Class C), wide range of serum AFP was also observed (Table 2). Furthermore, some overlapping of the AFP levels between hepatoma and non-hepatoma group was observed.

We also studied the serum ALP levels among the other 10 hepatitis B silent carriers without evidence of liver structural pathology (from ultrasonography study) and revealed that the average AFP level was comparable to the malignant group (Table 2). Furthermore, using the ANOVA analysis, there was no significant difference among the four groups of subjects ($P = 0.176$). Hence, the serum AFP level may not be a good screening tool for hepatoma in the hepatitis B carriers. However, our study is only a pilot study with only a few subjects, therefore, further larger study is recommended.

REFERENCES

1. Ruoslahti, E. and Seppala, M., Studies of Carcino-Fetal Proteins: Physical and Chemical Properties of Human Alpha -Fetoprotein. Int. J. Cancer 7:218, 1971
2. Gitlin, D., Perricelli, A. and Gitlin, G. M., Synthesis of Alpha-Fetoprotein by Liver, Yolk Sac, and Gastrointestinal Tract of the Human Conceptus. Cancer Res. 32:979, 1972.
3. Masseyeff, R., Gilli, G., Krebs, B., Bonet, C. and Zrihen, H., Evolution en Fonction de I'Age du Taux Serique Physiologique de I'Alpha-Foetoproteine chez I'Homme et le Rat. (French) in Alpha-Feto-Protein (Masseyeff, R., ed.) p.313. INSERM, Paris, 1974.
4. Silver, H. K. B., Gold, P., Feder, S., Freedman, So. O. and Shuster, J., Radio-immunoassay for human alpha-fetoprotein. Proc. Nat. Acad. Sci. U.S.A. 70:526, 1973.
5. Waldmann, T. A. and McIntire, K. R., The use of a radioimmunoassay for alpha -fetoprotein in the diagnosis of malignancy. Cancer 34:1510, 1974.
6. Kohn, J., Orr, A.H. McElwain, T.J., Bentall, M. and Peckham, M. J., Serum alpha-fetoprotein in patients with testicular tumors. Lancet 2:433, 1976.
7. Abelev, G.I., Alpha-fetoprotein in oncogenesis and its association with malignant tumors. Adv. Cancer Res. 14: 295, 1971.
8. Scardino, P. T., Cox, H. D., Waldermann, T. A., McIntire, K. R., Mittemeyer, B. and Javadpour, N., The value of the serum tumor markers in the staging and prognosis of germ cell tumors of the testis. J. Urol. 118:994, 1977.
9. Bosl, G.J., Lange, P. H., Fraley, E. E., Goldman, A., Nochomovitz, L. E., Rosai, J., et al., Human chorionic gonadotropin and alpha-fetoprotein in the staging of non-seminomatous testicular cancer. Cancer 47:328, 1981
10. Lange, P.H., McIntire, K.R. and Waldmann, T. A., Hakala, T.R. and Fraley, E. E., Serum alpha-fetoprotein and human chorionic gonadotropin in the diagnosis and management of nonseminomatous germ-cell testicular cancer. Medical Intelligence 259:1237, 1976.
11. Javadpour, N., McIntre, K. R. and Waldmann, T. A., Human chorionic gonadotropin (HCG) and alpha-fetoprotein (AFP) in sera and tumor cells of patients with testicular seminoma. Cancer 42:2768, 1978.
12. Waldmann, T.A. and McIntire, K. R., Serum Alpha-Fetoprotein Levels in Patients with Ataxia-Telangiectasia. Lancet 2:1112, 1972.

13. Belanger, L., Tyrosinemie Hereditaire et Alpha-1-Fetoproteine. II. Recherche Tissulaire Comparee de I'Alpha-Foetoproteine dans Deux Cas de Tyrosineimie Hereditaire. Considerations sur I'Ontogenese de la Foetoproteine Humain (French). Pathol. Bio.21:457, 1973.
14. Kew, M. C., Purves, L.R. and Bersohn, I., Serum Alpha-Fetoprotein Levels in Acute Viral Hepatitis. Gut 14:939, 1973.
15. Endo, Y., Kanai, K., Oda, T., Mitamura, K., lino, S. and Suzuki, H., Clinical Significance of alpha-Fetoprotein in Hepatitis and Liver Cirrhosis. Ann. N. Y. Acad. Sci. 259:234,1975.
16. Purves, L. R. and Purves M., Serum Alpha-Fetoprotein. VI. The Radioimmunoassay Evidence for the Presence of AFP in the Serum of Normal People and During Pregnancy. S. Afr. Med. J. 46:1290, 1972.
17. Sepalla, M. and Ruoslahti, E., Alpha -Fetoprotein: Physiology and Pathology During Pregnancy and Application to Antenatal Diagnosis. J. Perinat. Med. 1: 104, 1973.
18. Tang ZY. Hepatocellular carcinoma. : J Gastroenterol Hepatol 2000;15 Suppl:G1-7
19. Kane SV, Ganger DR. Management of hepatocellular carcinoma: staging and treatment. Am J Ther 1997;4:39-45
20. Kreczko S, Lipska A, Wysocka J. Alpha-fetoprotein: diagnostic value in hepatic disorders. Pol Merkuriusz Lek 2000;8: 420-3
21. Lok AS, Heathcote EJ, Hoofnagle JH. Management of hepatitis B: 2000-summary of a workshop. Gastroenterology 2001;120:1828-53

OUTCOME OF RADIOIODINE TREATMENT IN GRAVES' DISEASE PATIENTS AT SRINAGARIND HOSPITAL

Charoonsak SOMBOONPORN, M.D.
Krisana ROYSRI, M.D.

ABSTRACT

Background: Although being an effective and convenient means in the treatment of Graves' hyperthyroidism, radioiodine-131 (^{131}I) therapy usually provides unpredictable results with a major disadvantage of permanent hypothyroidism.

Objective: The study was conducted with the aim to explore the treatment outcomes of ^{131}I in the patients with Graves' disease. The obtained data would to be used in the evaluation and improvement of current management in this group of patients in our unit.

Design: Retrospective, descriptive study
Setting: Srinagarind Hospital, Faculty of Medicine, Khon Kaen University
Study methods: Reviewing medical records of patients with Graves'disease referred for ^{131}I therapy at our unit between June 1994 to August 2000 was performed. Three treatment outcomes were analyzed including efficacy of ^{131}I in the treatment of hyperthyroidism with the first dose, the number of ^{131}I dose used to cure hyperthyroidism and thyroid status of patients at the specific points of time after the last treatment dose.

Results: Nine hundred and eighty-four Graves' disease patients (793 females, 191 males) were analyzed. In the 693 cases who were followed up and evaluated for the result of treatment with determinable outcome, 247 cases (35.6%) were cured from hyperthyroidism with the first dose of ^{131}I. Of all 449 cases with adequate follow-up, 291 (64.8%) and 116 cases (25.8%) were cured by one and two doses of ^{131}I respectively, leaving nearly 10% of patients having to be retreated with additional dose. In evaluating thyroid status, incidence of persistent hyperthy- roidism decreased from 45.6% after the first year to 13.9% at the end of the fifth year while incidence of permanent hypothyroidism tended to rise from 9.3% after the first year to 28.1% and 22.2% at the end of the forth and the fifth year respectively.

Conclusion: Our study revealed that outcomes of ^{131}I therapy in patients with Graves' disease were rather unpredictable. We think that the aim of treatment should be more stressed on the earlier cure of hyperthyroidism rather than the avoidance of inevitable permanent hypothyroidism. Our dosage regimen therefore should be reconsidered to achieve a higher dose of radioiodine to cure hyperthyroidism within an earlier period and by a lower number of treatment dose.

Key words: Graves' disease, Radioiodine, Treatment outcome, Hypothyroidism

Division of Nuclear Medicine, Department of Radiology, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand.

INTRODUCTION

Radioactive iodine, ^{131}I, has been used in the treatment of hyperthyroidism for more than half of a century. The major advantages over other treatment modalities, antithyroid drug (ATD) and thyroidectomy, lies in its simplicity, convenience, safe, relatively low cost, high effectiveness and absence of significant complication.[1] The ideal outcome of ^{131}I treatment is to make patient be euthyroidism by a single administered dose and to remain this thyroid status as long as possible. However, this goal is usually unlikely and unpredictable in the clinical practice. Reciprocal relationship is usually obtained by the failure of treatment and the incidence of hypothyroidism.[2-4] The outcome varies from institution to institution and from country to country depending on the indications for treatment, criteria in patient selection and regimen of dose selection.[5] Moreover, pretreatment with ATD, methods and experience in the estimation of thyroid gland weight and regimen in the follow-up of patients are also important factors affecting the treatment outcome.[6-7]

Although our thyroid clinic at Nuclear Medicine Division, Srinagarind Hospital has been the largest one of its kind providing ^{131}I therapy for hyperthyroid patients, mostly from the northeast Thailand, the results of treatment has never been reported. The treatment outcomes of ^{131}I therapy in Graves' disease patients during the past 7 years therefore were studied with the ultimate goal to improve medical services of our unit by using the data obtained from the study. Three aspects of outcome were analyzed including efficacy of the first ^{131}I dose, number of doses needed to cure hyperthyroidism and patient's thyroid status after the specific points of the follow-up time.

MATERIALS AND METHODS

Medical records of consecutive hyperthyroid patients referred for ^{131}I treatment at Division of Nuclear Medicine, Department of Radiology, Srinagarind Hospital, Faculty of Medicine, Khon Kaen University from June 1994 to August 2000 were reviewed. After patients with toxic adenoma and toxic multinodular goitre were excluded, 1,032 Graves' disease subjects were enrolled into the study. Clinical diagnosis of Graves' disease was determined by experienced physicians and was supported by the elevation of serum thyroxine or triiodothyronine level with or without serum thyroid stimulating hormone (TSH) measurement. Euthyroidism and permanent hypothyroidism in the follow-up visits were determined clinically, mostly with simultaneous thyroid function test results. Data regarding age at the time of the first ^{131}I treatment, sex, indication for ^{131}I therapy, history of ATD allergy or co-morbidities prior to ^{131}I therapy, weight of thyroid gland estimated by palpation, date of each ^{131}I treatment, date of established euthyroidism and permanent hypothyroidism occurring following ^{131}I treatment and date of the last follow-up were collected by one nuclear medicine physician, the first author. The last evaluation was at the end of July 2001.

^{131}I TREATMENT

Contraindications for ^{131}I treatment, such as women during pregnancy or lactation, were excluded, not giving treatment. Radioiodine thyroid uptake test was performed in all cases to confirm the diagnosis and, more importantly, to help in the calculation of the administered doses. ATD was stopped at least 7 days before ^{131}I therapy. Other drugs and foods known to affect iodine uptake by thyroid gland were also refrained for their appropriate periods of time.[8] At least 4-hour fasting before ^{131}I administration was recommended in all subjects to make sure that

radioiodine was properly absorbed by gastrointestinal tract. In determining ^{131}I dose for individual patient, 24-hour thyroid uptake value and estimated thyroid gland weight were used for the calculation to achieve 100 microCuries of ^{131}I per gram of thyroid tissue. Some patients with history of cardiac failure or concomitant cardiac arrhythmia were treated with a higher dose regimen of 150 microCuries per gram of thyrold. There were two nuclear medicine physicians involving in the treatment during this period. Thyroid scintigraphy with technetium-99m pertechnetate was not routinely performed but was considered only in some cases suspected of nodule on palpation.

ATD and beta-blocker were prescribed as needed after ^{131}I treatment to individual case according to the justification of physicians. Although there was no exact follow-up schedule after ^{131}I treatment, each follow-up time was usually between 3 months and one year mostly according to the severity of hyperthyroidism. Retreatment with ^{131}I was considered in persistent hyperthyroid cases in no shorter than 3 months after the previous dose. Thyroxine replacement therapy was administered in those who developed permanent hypothyroidism.

TREATMENT OUTCOMES

There were 3 outcomes aimed to be explored. Firstly, the percentage of successful treatment after the first dose of ^{131}I. Subjects were classified into one of the three results including success, failure or undetermined. The success was determined at 6 months after treatment with patients having no symptoms and signs of hyperthyroidism even not taking ATD. The failure was defined as the patients still had symptoms and signs of hyperthyroidism at least 6 months after treatment or retreatment with ^{131}I was administered. The undetermined subjects were defined for those whose follow-up time was less than 6 months and the subjects were not retreated during this time.

Secondly, the number of ^{131}I doses needed to cure hyperthyroidism in each subject. In determining this outcome, the subjects to be analyzed were those who had an adequate follow-up that their last follow-up time showed euthyroid or permanent hypothyroid status. The subjects that still were hyperthyroidism, classified as inadequate follow-up, were excluded.

The last outcome was the incidence of thyroid status-hyperthyroidism, euthyroidism and permanent hypothyroidism-documented after the specific points of time,1, 2, 3, 4 and 5 years respecfively following the last treatment dose. The subjects who were evaluated at one point of time had to be followed up at the next point of time, otherwise were excluded.

DATA HANDLING

Data entry and editing were performed before the raw and edited data were prepared for analysis. The data analyses were performed using the Statistical Package for the Social Sciences (SPSS) program for Windows, version 9.0.

For descriptive analysis of patient' s characteristics, continuous variables including age, thyroid gland weight and ^{131}I administered dose were reported as mean $\pm$ standard deviation (SD) or median (minimum, maximum) as proper, whereas ratio or percentage was used to present categorical variables including sex and indication for ^{131}I therapy. All outcomes were shown as the percentage. This study was approved by the Ethics Committee of Faculty of Medicine, Khon Kaen University.

RESULTS

DESCRIPTION OF THE STUDY POPULATION

Of all 1,032 Graves' disease subjects treated by radioiodine during the time of study, 48 cases were excluded due to incomplete data obtained. The rest 984 cases were enrolled for analysis. Almost all subjects lived in the northeast Thailand. Characteristics of subjects including age, sex, estimated thyroid gland weight and indications for ^{131}I treatment-new cases without prior ATD treatment, medical failure within 6-month ATD treatment, failure between 6-month and 2-year ATD treatment, failure after 2-year ATD treatment, relapse of hyperthyroidism within 2 years after ATD cessation, relapse beyond 2 years after ATD cessation and relapse after thyroidectomy-were shown (Table 1). The documented co-morbidities before ^{131}I therapy included 68 cases of congestive heart failure and/or cardiac arrhythmia, 2 cases of thyroid storm and a case of hypokalemic periodic paralysis. There were 31 cases having history of allergy to ATD. A cold thyroid nodule was found in 5 cases, documented by thyroid scintigraphy and a thyroid nodule was clinically palpated in other 5 subjects without the result of thyroid scintigraphy.

TREATMENT OUTCOMES

In determining the outcome after the first dose of ^{131}I treatment, 291 of 984 cases (29.6%) were excluded since the outcome could not be definitely determined due to less than 6-month follow-up time according to the criteria. As a result, the outcome of the rest 693 cases was evaluated and defined as success or failure. Characteristics of subjects who could and could not be evaluated for this outcome were comparable (Table 2). The success rate after the first dose of treatment was found in 247 of 693 cases (35.6%) as shown in Table 3.

Regarding the number of ^{131}I administered dose needed to cure hyperthyroidism, 449 of 984 cases (45.6%) whose follow-up times were long enough to render euthyroidism or permanent hypothyroidism were analyzed. Characteristics of subjects who were and were not adequately followed up were comparable (Table 4). It was noted that the majority of subjects (64.8%) were cured by a single dose. The distribution of the number of administered dose was shown in Table 5.

In determining thyroid status of subjects after the last dose of treatment of all 984 subjects, there were 441, 257, 132, 64 and 36 subjects that could still be followed up at 1, 2, 3, 4 and 5 years respectively. The incidence of hyperthyroidism, euthyroidism and permanent hypothyroidism at these follow-up periods was shown (Fig. 1). It was noted that the incidence of hyperthyroidism decreased from 45.6% at the end of the first year down to 26.8%, 22%, 17.2% and 13.9% at the end of 2, 3, 4 and 5 years respectively. On the contrary, the incidence of permanent hypothyroidism tended to rise progressively from 9.3% at the end of the first year to 19.1%, 22%, 28.1% and 22.2% respectively.

TABLE 1. Characteristics of all subjects.

Characteristics	Number
Female: male ratio	793: 191 (4.2 : 1)
Mean age ± SD (y)	40.9 ± 11.6
(range)	(14 -80)
Median thyroid weight (g)	35
(min, max)	(20, 200)
Indications	
New	19 (1.9%)
ATD < 6 m	145 (14.7%)
ATD 6 m - 2 y	276 (28%)
ATD > 2 y	384 (39%)
Relapse < 2 y	79 (8%)
Relapse > 2 y	35 (3.6%)
Relapse after surgery	46 (4.7%)

TABLE 2. Characteristics of subjects in the determinable and undeterminable treatment outcome groups for the first dose.

Characteristics	Determinable outcome (N = 693)	Indeterminable outcome (N = 291)
Female: male ratio	558: 135 (4.1:1)	235: 56 (4.2:1)
Mean age ± SD (y)	40.3±11.6	41.6±11.6
(range)	(15-75)	(14-80)
Median thyroid weight (g)	40	35
(min, max)	(20, 200)	(20, 120)
Median ^{131}I dose (mCi)	5	5
(min, max)	(3, 27)	(3, 20)
Indications		
New	12 (1.7%)	7 (2.4%)
ATD < 6 m	84 (12.2%)	61 (20.9%)
ATD 6 m - 2 y	200 (28.9%)	76 (26.1%)
ATD > 2 y	287 (41.4%)	97 (33.3%)
Relapse < 2 y	52 (7.5%)	27 (9.3%)
Relapse > 2 y	27 (3.8%)	8 (2.7%)
Relapse after surgery	31 (4.5%)	15 (5.2%)

TABLE 3. Treatment outcome of the first dose of ^{131}I.

Outcome	Number
Success	247 (35.6%)
Failure	446 (64.4%)
Total	693 (100%)

TABLE 4. Characteristics of subjects who were and were not adequately followed up to determine the number of administered doses of ^{131}I to cure hyperthyroidism.

Characteristics (Total = 938)	**Adequate FU** (N = 449)	**Inadequate FU** (N = 535)
Female: male ratio	388: 61 (6.4: 1)	405: 130 (3: 1)
Mean age ± SD (y)	40.6 ± 11.6	41.3 ± 11.5
(range)	(16 – 75)	(14 – 80)
Median thyroid weight (g)	35	40
(min, max)	(20, 200)	(20, 150)
Indications		
New	9 (2%)	10 (1.9%)
ATD < 6 m	64 (14.3%)	81 (15.1%)
ATD 6 m – 2 y	128 (28.5%)	148 (27.7%)
ATD > 2 y	173 (38.5%)	211 (39.4%)
Relapse < 2 y	38 (8.4%)	41 (7.6%)
Relapse > 2 y	21 (4.7%)	14 (2.6%)
Relapse after surgery	16 (3.6%)	30 (5.6%)

TABLE 5. Distribution of the number of administered doses of ^{131}I in the adequately followed-up group.

Number of ^{131}I administered dose	**Number of subjects** (Total = 449)
1	291 (64.8%)
2	116 (25.8%)
3	37 (8.2%)
4	4 (0.9%)
5	1 (0.2%)

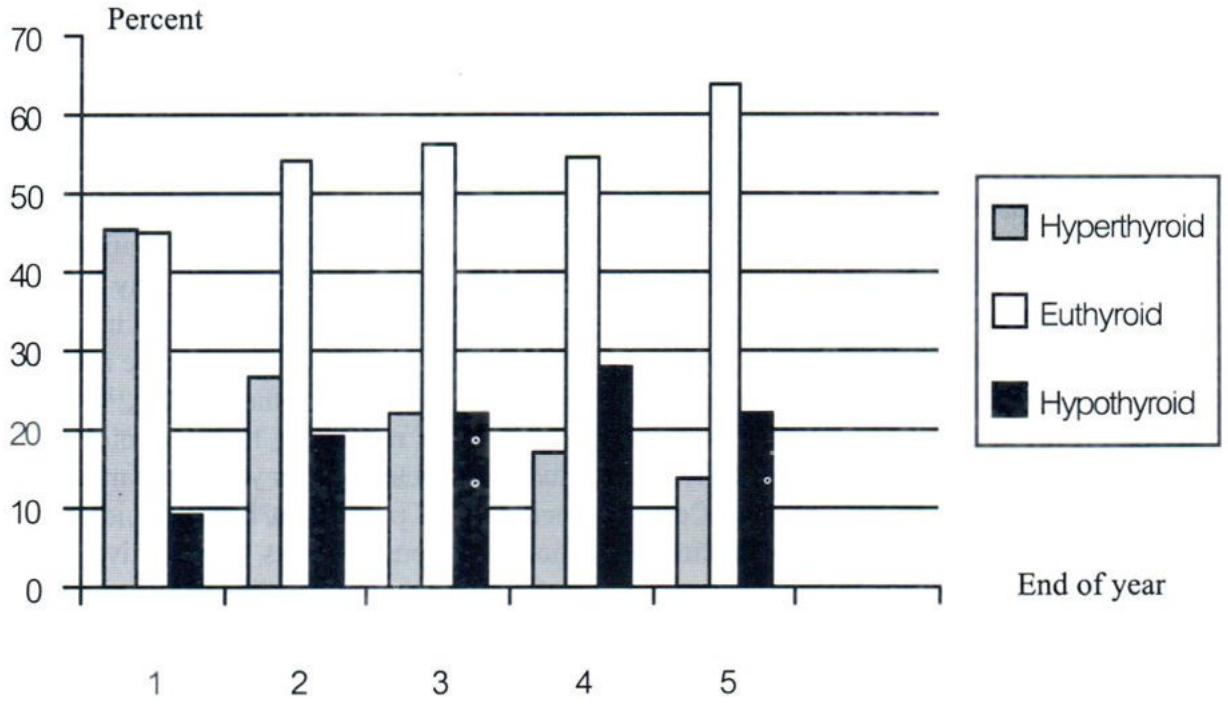


Fig. 1. Incidence of thyroid status at the specific points of time after the last ^{131}I treatment.

DISCUSSION

The aim of radioiodine therapy in hyperthyroidism is to destroy sufficient thyroid tissue to cure hyperthyroidism by rendering the patient either euthyroidism or hypothyroidism. Despite more than half a century of experience, there is little agreement regarding the most appropriate dose regimen.[9-10] Although several studies have attempted to determine the optimal dose of radioiodine for curing hyperthyroidism and avoiding the development of permanent hypothyroidism,[11-12] the results of treatment is still unpredictable.

Our study revealed the outcomes of ^{131}I treatment in Graves' disease patients who mostly resided in the provinces of northeast Thailand. Female sex predilection of the subjects was about 4:1 and was comparable to those in the literatures.[11-13] It was noted that the majority (81.7%) of indications for ^{131}I therapy was the medical failure after being treated by ATD.

About one-third of patients were cured from hyperthyroidism by only one dose of ^{131}I while hyperthyroidism was still existed in almost two-third and was subsequently considered for retreatment. The follow-up time of 6 months after treatment was used to determine the success of ^{131}I therapy since most of the patients who were successfully treated usually rendered euthyroid or hypothyroid state within this period and those who still were hyperthyroidism beyond this period were considered as the candidate for retreatment. Although nearly 30% of subjects were lost to follow-up, resulting in undeterminable outcome of the first ^{131}I dose, the characteristics of these subjects were comparable to those who could be adequately followed up. The success rate of the first treatment dose in our study was rather low compared with those in some studies.[5,14] Apart

from the difference in dose selection regimen used,[5] this was probably because most of our study population (81.7%) had received ATD before radioiodine treatment. Some studies suggested that there was a relative radioresistance in those prescribed ATD before or after radioiodine.[6-7,15-16] Another possible reason was the error in the estimation of thyroid gland weight, which was performed by palpation. This method was somewhat subjective and interpersonal error could be very high in a large gland. Since we calculated the treatment dose according to the 24-hour radioiodine uptake value and estimated thyroid gland weight to achieve about 100 microCuries per gram of thyroid tissue, the underestimation of gland weight could lead to the underdose of radioiodine administered. A more objective and clinically probable method using the ultrasound technique in the calculation of thyroid volume could be used.[17] Moreover, more sophisticated but probably not practical techniques in measuring metabolically active volume of the thyroid were also recommended including ^{123}I single photon emission computed tomographic (SPECT) imaging or ^{124}I positron emission tomographic (PET) imaging.[18-20] Apart from the accuracy in estimation of thyroid gland size, the thyroid gland size itself might relate to the outcome after ^{131}I treatment. It was found that large thyroid, over 26 grams, was one of the main predictors of non-response to radioiodine therapy if the dose range of 60-90 Grays was aimed to thyroid tissue.[5]

Curing patients from hyperthyroidism with a single dose is the goal of ^{131}I therapy, we thus explored the number of subjects who were cured by a single dose. It was revealed that about 65% of our subjects in the adequately followed-up group needed only single dose while about one-third of subjects required more than a single dose to achieve euthyroidism or hypothyroidism. This proportion, again, could varied and was depended significantly on the dosage regimen used.[5,13]

The major drawback of ^{131}I therapy is the significant incidence of hypothyroidism, which is cumulative. One of the large studies exploring the long-term incidence of hypothyroidism after ^{131}I treatment in 4,473 hyperthyroid patients during 26-year period reported 6% hypothy-roidism developed within the first year with increasing to 72% within 26 years, or an average rise of 2.6% per year.[21] Like some other studies,[13,22] while the incidence of remaining hyperthyroidism in our study was declining over years after treatment, the incidence of permanent hypothyroidism, which should be considered as the negative end point rather than the complication of treatment, tended to rise progressively. In our study, a significant number of subjects, about 22%, still remained hyperthyroidism even after the third year of follow-up. The occurrence of permanent hypothyroidism within the first four years after treatment was at the average rate of 7% per year. At the end of the fifth year, the incidence of hypothyroidism was lower than that at the end of the forth year likely because a significant number of subjects who already developed hypothyroidism were lost to follow-up between the end of the forth and the end of the fifth year after the last dose. Besides the dose regimen selected, the use of sensitive assay for TSH, resulting in earlier recognition of hypothyroidism, could determine the incidence of hypothyroidism.[22]

Because of this study was done in the retrospective way, therefore it had some limitations. Details of the data depended highly on the accuracy and consistency in recording patient's data by the physicians during the routine services. The subjects who were lost to follow-up definitely affected the outcome. In addition, there was also a limitation regarding the financial status in some subjects. Hence, thyroid status was sometimes documented clinically without simultaneous confirmation by thyroid

function test. However, our study population was one of the largest ever been reported. In addition, a recent study postulated that genetic and cultural factors might also be associated with the treatment response rate.[5] Our patients were mostly the people in the northeast Thailand. Therefore their outcomes were the beneficial data in auditing the treatment of the patients from this region. Further study should be conducted to clearly explore possible factors affecting favorable outcomes of treatment in this population such as age, sex, initial thyroid weight, radioiodine uptake value or prior treatment modalities.

In conclusion, although being an effective means in the treatment of hyperthyroidism, ^{131}I showed rather unpredictable outcomes in our study population. Some patients may remain hyperthyroidism even more than two doses of ^{131}I administered and in a significant follow-up time, whereas all patients had a chance to develop permanent hypothyroidism increasingly with time. However, since thyroxine is generally available and cheap, replacement therapy in permanent hypothyroidism following ^{131}I therapy is easy and usually acceptable. We think that our dosage regimen should be reconsidered to give a higher dose of radioiodine to get cure of hyperthyroidism within an earlier period and by a lower number of treatment doses without increasing rate of hypothyroidism.

REFERENCES

1. Solomon B, Glinoer D, Lagasse R, Wartofsky L. Current trends in the management of Graves' disease. J Clin Endocrinol Metab 1990; 70: 1518-24.
2. Hamburger JI, Paul S. When and how to use higher ^{131}I doses for hyperthyroidism. N Engl J Med 1968; 279: 1361-5.
3. Holm LE, Lundell G, Dahlqvist I, Israelsson A. Cure rate after ^{131}I therapy for hyperthyroidism. Acta Radiol 1981; 20: 161-6.
4. Sridama V, McCormick M, Kaplan EL, Fauchet R, DeGroot LJ. Long-term follow -up study of compensated low dose ^{131}I therapy for Graves' disease. N Engl J Med 1984; 311: 426-32.
5. Howarth D, Epstein M, Lan Linda, Tan P, Booker J. Determination of the optimal minimum radioiodine dose in patients with Graves' disease: a clinical outcome study. Eur J Nucl Med 2001; 28: 1489-95.
6. Tuttle RM, Patience T, Budd S. Treatment of propylthiouracil before radioactive iodine therapy is associated with a higher treatment failure than therapy with radioactive iodine alone in Graves' disease. Thyroid 1995; 5: 243-7.
7. Sabri O, Zimmy M, Schulz G, et al. Success rate of radioiodine therapy in Graves' disease: the influence of thyrostatic medication. J Clin Endocrinol Metab 1999; 84: 1229-33.
8. Mettler FA Jr, Guiberteau MJ. Essentials of nuclear medicine imaging 4th ed. Philadelphia: W.B. Saunders, 1998: 109.
9. Franklyn JA. The management of hyperthyroidism. N Engl J Med 1994; 330:1731-8.
10. Shapiro B. Optimization of radioiodine therapy of thyrotoxicosis: what have we learned after 50 years? J Nucl Med; 34: 1638-41.
11. Allahabadia A, Daykin J, Sheppard MC, Gough SC, Franklyn JA. Radioiodine treatment of hyperthyroidism-prognostic factors for outcome. J Clin Endocrinol Metab 2001; 86: 3611-7.
12. Nordyke RA, Gilbert FI Jr. Optimal iodine -131 dose for eliminating hyperthyroidism in Graves' disease. J Nucl Med 1991; 32: 411-6.

13. Tavintharan S, Sundrum FX, Chew LS. Radioiodine ^{131}I therapy and the incidence of hypothyroidism. Ann Acad Med Singapore 1997; 26: 128-31.
14. Sabri O, Zimmy M, Schreckenberger M, et al. Characterization of therapy failures in radioiodine therapy of Graves' disease without simultaneous antithyroid agents. Nuklearmedizin 2001; 40: 1-6.
15. Sabri O, Zimmy M, Schreckenberger M, Reinartz P, Ostwald E, Bull U. Radioiodine therapy in Graves' disease with large diffuse goiter with or without carbimazole at the time of radioiodine therapy. Thyroid 1999; 9: 1181-8.
16. Koroscil TM. Thioamides alter the efficacy of radioiodine treatment in patients with Gravs' disease. South Med J 1995; 88: 831-6.
17. Bockisch A, Jamitzky T, Derwanz R, Biersack HJ. Optimized dose planning of radioiodine therapy of benign thyroidal diseases. J Nucl Med 1993; 34: 1632-8.
18. Frey P, Townsend D, Flattet A, et al. Tomographic imaging of human thyroid using ^{124}I. J Clin Endocrinol Metab 1986; 63: 918-27.
19. Ott RJ, Batty V, Webb S, et al. Measurement of radiation dose to the thyroid using positron emission tomography. Br J Radiol 1987; 60: 245-51.
20. Crawford DC, Flower MA, Pratt BE, et al. Thyroid volume measurement in thyrotoxic patients: comparison between ultrasonography and iodine-124 positron emission tomography. Eur J Nucl Med 1997; 24: 1470-8.
21. Holm LE, Lundell G, Dahlqvist I, Israelsson A. Incidence of hypothyroidism occurring long after iodine-131 therapy for hyperthyroidism. J Nucl Med 1982; 23: 103-7.
22. Holm LE. Changing annual incidence of hypothyroidism after iodine-131 therapy for hyperthyroidism, 1951-1975. J Nucl Med 1982; 23: 108-12.

SONOGRAPHIC INCIDENCE OF CONGENITAL ANOMALIES OF THE KIDNEY- A STUDY IN BANGLADESH

Ashoke Kumar Paul[1], Hosne Ara Rahman[2], Nafisa Jahan[3], Md. Sayedur Rahman Miah[4]

ABSTRACT

To assess the sonographic frequency of congenital renal anomalies, we retrospectively reviewed the results of whole abdominal and genitourinary ultrasound studies of 12005 cases performed over a period of 6 years between January 1995 to December 2000. The study was done among the patients who came to Ultrasound unit of the Nuclear Medicine Centre, Khulna, Bangladesh for ultrasound examination. Ultrasound revealed renal anomalies in 44 patients for an incidence of 1: 273 (0.36 percent). Males were more affected than females, the ratio being 1.4: 1. Of these anomalies, Unilateral renal agenesis dominates the list with the incidence of 1: 750 (0.13 percent). Ectopic kidneys were found in 12 patients with the incidence of 1: 1000 (0.10 percent). Adult polycystic kidneys were found in 11 patients with the incidence of 1: 1091 (0.09 percent). 3 patients (0.02 percent) had hypoplastic kidney and 2 cases (0.02 percent) with crossed fused ectopia. No apparent serious discrepancy is noted for each of the above anomalies in comparison to other studies.

Key words: Renal anomalies, Ultrasonography

INTRODUCTION

Congenital anomalies of the kidney comprise a diversity of abnormalities, ranging from absence to aberrant location, orientation and shape. The urinary organs may be maldeveloped owing to genetic defects or to environment. However, the etiology of majority of malformations is not known[1]. Most of the renal anomalies are clinically asymptomatic. The diagnosis is usually not suspected or remains undetected unless an imaging study done for other reasons[2]. In the past the usual method of detection had been excretory urography but now-a-days ultrasonography is available in most of the places in Bangladesh. As ultrasound is a safe, non-invasive and less costly it becomes a popular investigation modality as a routine procedure for any doubtful condition in our country and ultrasound examination for unrelated reason have been discovering more asympatomatic renal anomaly cases incidentally. There are several studies regarding the incidence

[1] Ashoke Kumar Paul MBBS, DNM Senior Medical Officer Nuclear Medicine Centre, Khulna
[2] Hosne Ara Rahman MBBS Medical Officer Nuclear Medicine Centre, Khulna
[3] Nafisa Jahan MBBS Medical Officer Nuclear Medicine Centre, Khulna
[4] Md. Sayedur Rahman Miah MBBS, DNM Senior Medical Officer Nuclear Medicine Centre, Khulna

For Correspondence: Dr. Ashoke Kumar Paul Senior Medical Officer Nuclear Medicine Centre, Khulna Khulna Medical College Hospital Campus G P O Box 12, Khulna 9000 Bangladesh
E-mail<akpaul65@hotmail.com>

of various renal anomalies[2,3,4] but no such studies have been undertaken in this region. The aim of our study was to evaluate the incidence of various congenital anomalies of the kidneys in Bangladeshi population.

MATERIALS AND METHODS

The results of whole abdominal and genitourinary sonographic studies of 12005 patients performed at the Ultrasound Unit of the Nuclear Medicine Centre, Khulna, Bangladesh, between January 1995 to December 2000, were reviewed. Sonographic studies were done through transabdominal approach using a Siemens Sonoline SL-2 real time ultrasonogram equipped with both 3.5 MHz linear and sector transducer. The usual preparation was done in all the cases and genitourinary ultrasound was done with full urinary bladder. Renal ultrasound examinations are routinely performed with the patients in both the supine and the prone positions at our institution.

RESULTS

Of the total 12005 cases, 44 patients were found to have congenital renal anomalies of which 26 were male and 18 were female. The overall frequency of renal anomalies was 0.36 percent. We found 5 types of renal anomalies with male : female ratio being 1.4:1 (Table-I). Of these anomalies, 16 patients (0.13 percent) had unilateral renal agenesis with male female ratio 1.6:1. Left kidney was found to be absent in 9 cases and right kidney was absent in 7 cases. Ectopic kidneys were found in 12 patients (0.10 percent) of which 7 were female and 5 were male with female male ratio 1.4:1. Left kidney was ectopic in 7 cases and right kidney was ectopic in 5 cases. 9 were pelvic kidney and 3 kidneys were placed in iliac region. A 27 years young man presented with palpable pelvic mass and was interpreted as gross hydronephrotic pelvic kidney (left), which was confirmed on surgery; the right kidney was normal.

11 patients (0.09 percent) had adult polycystic kidneys with male female ratio 2.6:1. Among these, 7 cases were diagnosed at the age of 35-40 years, 3 cases at 50-55 years and 1 case at 60 years. Associated liver cyst was present in 3 cases. 3 patients (0.02 percent) had congenital hypoplastic kidney of which 2 were male and 1 was female. Crossed fused ectopia was found in 2 cases (0.02 percent) and fusion takes place at right side in both the cases. There were 2 cases of associated anomalies of the genitalia in patients with solitary kidney; 1 patient with bicornuate uterus and 1 patient with hypoplastic uterus.

Table-I. Sonographic incidence of congenital anomalies of the kidneys

Anomaly	Number of patients	Percentage	Incidence	Sex		Position of anomaly		
				Male	Female	Right	Left	Bilateral
Unilateral agenesis	16	0.13	1:750	10	6	7	9	-
Ectopic	12	0.10	1:1000	5	7	5	7	-
Polycystic	11	0.09	1:1091	8	3	-	-	11
Hypoplastic	3	0.02	1:4000	2	1	2	1	-
Crossed fused ectopia	2	0.02	1:6000	1	1	2	-	-
Totals	44	0.36	1:273	26	18	16	17	11

DISCUSSION

Congenital anomalies of the kidneys are not uncommon. Before the advent of modern diagnostic modalities, the majority of cases, though small in number were usually undetected and now-a-days its diagnosis is enhanced in our country due to vast use of ultrasonography. The ultrasound service at our institute does not take selected cases and the patients may considered a good cross section of urology and the findings in this study can be regarded as an excellent index of renal anomalies. Malformations of the kidneys and ureters are of great clinical importance and account for about 40 percent of all pathological conditions akin to these organs[3]. In the study, we have found 44 instances of congenital anomalies of kidneys with the incidence of 1:273 (0.36 percent); this seems to be lower than that of other studies[5,6] and the reason may be that , here, in the study, we have considered only the anomalies of the kidney proper. A consideration of the individuals in this study shows that males were more affected than females, the ratio being 1.4:1 and there was no apparent predilection for either the left or right side, as it occurred 17 times on the left side, and 16 on the right side.

The most frequent anomaly observed in this study was that of absence of one kidney which occurred 16 times for an incidence of 1:750, that is almost close to other studies[5,6,7]. The kidney was found to be absent more on the left side than the right, the ratio being 9 to 7. The next most frequent anomaly was that of renal ectopia, which occurred 12 cases with the incidence of 1 in 1000, that is consistent with other studies[3,7]. The left side is favored over the right, the ratio being 7 to 5 which is also correlate with other study[7]. The ectopic kidney may be found in any of the locations of its normal ascent with just equal frequency[4]. Most ectopic kidneys are clinically asymptomatic but it may appear initially with abdominal pain, urinary infection or a palpable mass. Here, one case was detected as grossly hydronephrotic pelvic (left) kidney that mimicking colonic mass.

Adult polycystic kidney disease was found in 11 patients with the incidence of 1 in 1091, that is almost similar to other studies[6,8]. All the cases were bilateral. It is an autosomal dominant trait and the patient's children have a chance of

inheriting the condition. An early diagnosis either by ultrasound or intravenous urography is very important before starting their family life. Renal hypoplasia occurs sporadically and is probably due either to a deficiency of metanephrogenic tissue or to defective branching of the ureteric bud. This abnormality was found in 3 cases with good renal function. There were 2 cases of crossed fused ectopia for an incidence of 1 in 6000 in this study. Both the cases present with an asymptomatic abdominal mass without any functional impairment. The occurrence of associated anomalies of the genitalia has been variously reported. We found 2 cases of associated anomalies in patient with solitary kidney; 1 patient with bicornuate uterus and 1 patient with hypoplastic uterus.

CONCLUSION

This preliminary study shows the local incidence of various congenital anomalies of the kidneys and we found no apparent serious discrepancy for each of the described anomalies in comparison to other studies. The patient with renal anomalies should be kept under observation to assess renal function and to ensure therapeutic measures when needed.

REFERENCES

1. Stephens FD: Embryopathy of malformations. J Urol (Guest editorial) 1982; 127: 13
2. Walsh PC, Retik AB, Stamey TA, Vaughan ED (editors) Campbell's Urology, 6th ed. Philadelphia, W. B. Saunders Company 1992; 1357-1388
3. Smith EC, Orkin LA: A clinical and statistical study of 471 congenital anomalies of the kidney and ureter. J Urol 1945; 53: 11-26
4. Dretler SP, Olsson C, Pfister RC: The anatomic, radiologic and clinical characteristics of the pelvic kidney: an analysis of 86 cases. J Urol 1971; 105: 623-627
5. Weatherall DJ, Ledingham JGG, Warrell DA (editors) Oxford Textbook of Medicine, 2nd ed. Oxford: ELBS, Oxford University Press 1987; 18.168-18.170
6. Edwards CRW, Bouchier IAD, Haslett C, Chilvers ER (editors) Davidson's Principles and Practice of Medicine, 17th ed. London: ELBS, Churchill Livingstone 1995; 659-661
7. Rains AJH, Ritchie HD (editors) Bailey and Love's Short Practice of surgery, 19th ed. London: ELBS, H. K. Lewis & Co Ltd 1985; 1120-1126
8. Sweny P, Farrington K, Moorhead JF (editors) The Kidney and its disorders, 1st ed. Oxford: Blackwell Scientific Publications, 1989; 753-760

THE RADIOLOGY OF HIRSCHSPRUNG DISEASE

Pannee VISRUTARATNA, MD

Constipation is a very common problem in childhood, accounting for 6% of pediatric outpatient visits.[1] It is also one of the most frequent reasons for a barium enema examination in pediatric patients.[2] Constipated children are frequently referred to a radiologist for a barium enema to exclude Hirschsprung disease, which is one of the most serious identifiable causes of constipation.[1] The aim of this article is to review the pathogenesis, clinical manifestations, preparation of patients for barium enema studies, barium enema technique, imaging findings seen in Hirschsprung disease, and differential diagnosis.

PATHOGENESIS OF HIRSCHSPRUNG DISEASE

Hirschsprung disease or congenital aganglionic megacolon is now recognized as one of several disorders of intestinal innervation. Collectively known as "dysganglionoses", these disorders include aganglionosis of the bowel wall, hypoganglionosis, neuronal dysplasia (hyperganglionosis), absence of intrinsic innervation of the colon, and absence of innervation of the intestine.[3]

Hirschsprung disease is characterized by a congenital absence or deficiency of the ganglion cells in the myenteric (Auerbach's) and submucosal (Meissner's) plexuses of the rectum and the distal part of the colon, together with hyperplasia of cholinergic nerve fibers in the circular muscle layer, muscularis mucosae, and mucosa with a high activity of acetylcholinesterase.[4] This is due to a lack of the normal caudal migration of the neurons of the neural crest along the intestinal branches of the vagus nerve in utero. The region of aganglionosis is almost always continuous; the existence of "skip areas" is extraordinarily rare.[5] Absence of intramural ganglion cells interferes with the normal relaxation of peristalsis in the bowel wall and the internal anal sphincter. The aganglionic segment of the colon becomes hypertonic and behaves as a functional stenosis leading to partial or complete colonic obstruction. Immediately proximal to the aganglionic segment the intestine becomes markedly dilated with feces and gas.[4]

The rectosigmoid region is the most common transition site from normal to abnormal bowel. The transition zone is located in this region in 75% of patients. It is in the left colon in 12% of patients, splenic flexure in 4%, transverse colon in 4% and right colon in 3%.[3,6] There is total colonic aganglionosis with or without small intestinal involvement in 2% of patients. When the transition zone is in the rectosigmoid region, it is called short segment disease. When it is proximal to the sigmoid, it is called long segment disease. Ultrashort segment disease with aganglionosis limited to the region of the internal sphincter is very rare, as is aganglionosis involving the entire alimentary tract.[6,7]

CLINICAL MANIFESTATIONS

Hirschsprung disease occurs in one of 5,000 to 8,000 live births.[3] According to the American Academy of Pediatrics Surgical Section Survey the ratio of male to female patients with short segment Hirschsprung disease is 3.8 to 1. The ratio is 2.8 to 1 in long segment disease and 2.2 to 1 in total colonic aganglionosis.[6] Familial incidence is significant only in very long

Department of Radiology, Faculty of Medicine, Chiang Mai University Chiang Mai 50200, Thailand

segment disease of the colon.

70-80% of patients with Hirschsprung disease become symptomatic within the first week of life. Most affected children are term neonates.[8] They usually present with distal bowel obstruction. Hirschsprung disease is responsible for approximately 15% to 20% of cases of neonatal bowel obstruction.[9] Ninety percent or more of normal neonates pass meconium in the first 24 hours of life, and 99% pass meconium by 48 hours of life. Any infant who fails to pass meconium by 48 hours of life should be considered as having Hirschsprung disease until proven otherwise.[10] A minority of patients with Hirschsprung disease are found later in infancy or childhood, usually with chronic, severe constipation.

Up to a third of patients with Hirschsprung disease have or develop enterocolitis, either as a presenting feature, before, or after surgery.[11] Enterocolitis is most frequently seen during the first 3 months of life.[6]

Hirschsprung disease has been associated with various congenital defects, such as Down syndrome, cardiac anomaly, genitourinary anomaly, gastrointestinal anomaly, and Ondine's curse (congenital hypoventilation syndrome).[3,5,8] Anorectal malformation has reported as an association.[12]

On examination, a child with Hirschsprung disease usually has a distended abdomen and may have palpable solid stool in the colon. Rectal examination may result in the explosion of foul-smelling liquid, virtually pathognomonic for Hirschsprung disease with early enterocolitis. Diagnosis before the onset of enterocolitis is critical in reducing mortality.[11]

IMAGING FINDINGS

1. Plain abdominal films

Plain abdominal films in neonates with Hirschsprung disease show a distal bowel obstruction, often with markedly dilated loops of bowel[5,9,10] (Figs. 1, 2). There is little or no rectal gas. A prone lateral cross table film can be taken to assess the amount of air in the rectum.[13] In the older child, plain abdominal films may show stool in an obvious megacolon. A lack of air in the distal colon and rectum is usually seen. Newman et al. have found that 4.4% of infants less than 1 year old with Hirschsprung disease present with pneumoperitoneum secondary to perforation.[14] Most of these patients have total colonic aganglionosis. Calcification in the lumen of distal small bowel has also been found on plain abdominal films of patients with total colonic aganglionosis.[15] Pneumatosis intestinalis or an abnormal mucosal pattern is sometimes seen on plain abdominal films of patients with Hirschsprung disease and enterocolitis.[8,10]

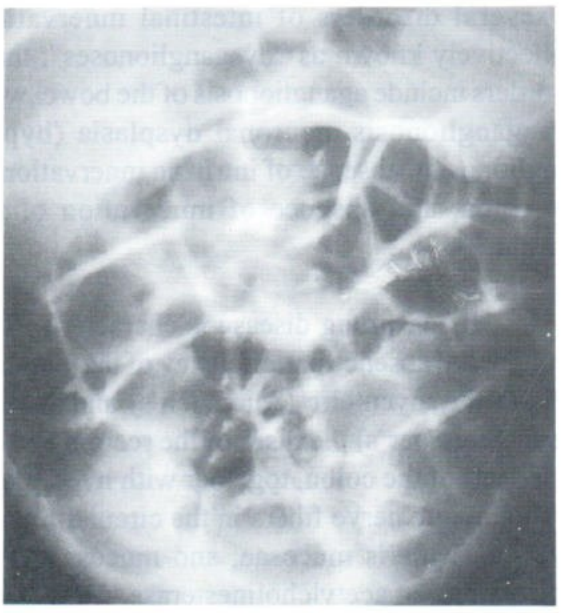


Fig. 1. Plain abdominal film shows dilatation of multiple bowel loops with no rectal gas.

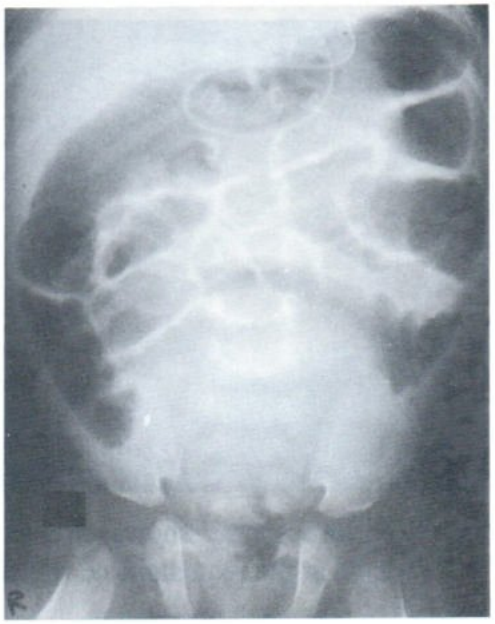


Fig. 2. Plain abdominal film shows dilatation of multiple bowel loops with a little rectal gas.

2. Contrast Enema

Of the available methods for diagnosing Hirschsprung disease, a contrast enema is used to determine the proximal extent of aganglionosis, to exclude other diseases, and to alert the surgeon if the patient has developed enterocolitis.[8,16] The other methods are rectal biopsy and rectal manometric examination. Rectal biopsy is the gold standard for diagnosis of Hirschsprung disease. Rectal manometric examination has been most useful in differentiating ultrashort segment Hirschsprung disease from psychogenic constipation.[8]

Barium enema is less accurate in cases of Hirschsprung disease with total colonic aganglionosis, very-short segment aganglionosis, in infants younger than one month of age, and in patients who have had a colostomy.[3] Overall, barium enema has a false-negative rate of 5% to 40% and a false-positive rate of up to 27%, depending on which combination of radiographic signs is present.[3]

Barium enema is contraindicated if plain films reveal pneumoperitoneum, pneumatosis intestinalis, or an abnormal mucosal pattern of enterocolitis.[8] Administering an enema to a patient with active colitis may precipitate sepsis and secondary circulatory collapse.

PATIENT PREPARATION

Although Rosenfield et al. have found that rectal examination and a cleansing enema prior to the study appear not to obscure visualization of a transition zone,[17] no cleansing enemas should be performed for several days before the contrast enema. Bowel cleansing prior to contrast enema is contraindicated because it makes the transition zone less obvious, and more importantly, bowel evacuants may precipitate fulminant colitis. The tendency of affected children to retain cleansing enemas may also cause serious electrolyte imbalance.[8]

IMAGING TECHNIQUE

O'Donovan et al. have found that a water-soluble contrast enema has a sensitivity and specificity equal to those of a barium enema for the detection of Hirschsprung disease and avoids the problems associated with barium spillage into the peritoneal cavity with perforation.[18] In addition, other causes of low intestinal obstruction such as meconium plug and meconium ileus are better studied with water-soluble contrast media than with barium.[10] At our hospital, barium sulfate is still used for a contrast enema because it is much cheaper than water-soluble contrast media.

Balloon catheters should never be used because of the likelihood of rectal trauma in a spastic and narrowed rectum, and they may obscure the aganglionic segment and the transition zone.[4,5,8] Only the tip of a soft catheter should be inserted into the anus to insure complete visualization of the contrast-filled

rectum.

The examination is begun with the lateral projection to detect a distal transition zone. Barium is introduced slowly to best demonstrate denervation hyperspasticity.[4,5,8] Rapid overdistention of the colon with barium is the most common reason for missing both the spasm and the transition zone.[8] The procedure has to be done slowly to leave enough time for the bowel to adapt to the volume of barium. Some time is needed for the aganglionic segment to contract to its former diameter.[4] When the transition zone has been identified, the proximal colon does not need to be examined because no additional information is likely to be obtained and because the predictably poor ability of the colon to empty will leave it needlessly filled with barium, which may complicate the procedure for the surgeon performing a diverting colostomy.[8]

If initial films of the colon show no spastic segments or transition zone, delayed lateral and frontal views of 24 or 48 hours may reveal the transition zone.

Abnormalities seen on barium enema

1. Transition zone between the normal or slightly small distal aganglionic bowel and the dilated ganglionic proximal bowel (Figs. 3, 4). Presence of a transition zone in the rectosigmoid is a highly reliable diagnostic feature of Hirschsprung disease; however absence of this sign does not rule it out.[17] The transition zone may be abrupt or gradual (Fig. 5) and is mostly at the rectosigmoid junction. This finding is present in approximately 65% of neonates.[17] A transition zone and a megacolon can be seen usually after 4-6 weeks of age.[4]

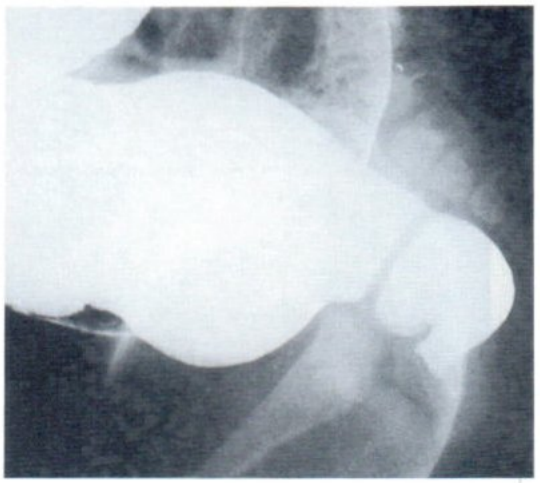


Fig. 3. Barium enema shows a transition zone at the rectosigmoid region.

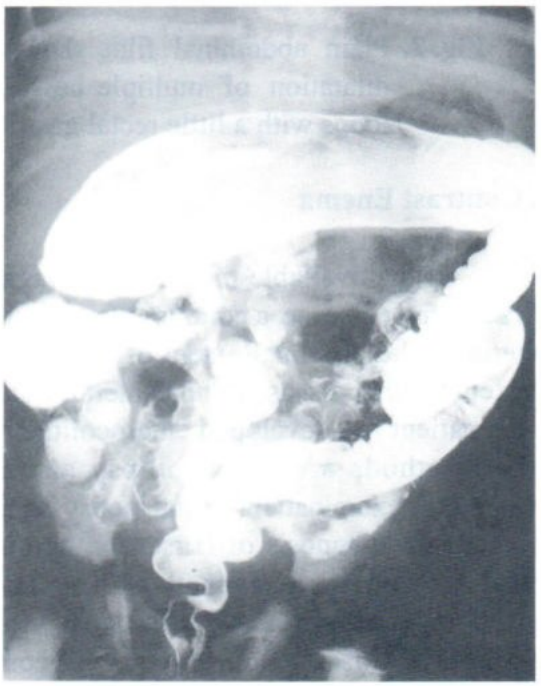


Fig. 4. Barium enema shows a transition zone at the splenic flexure.

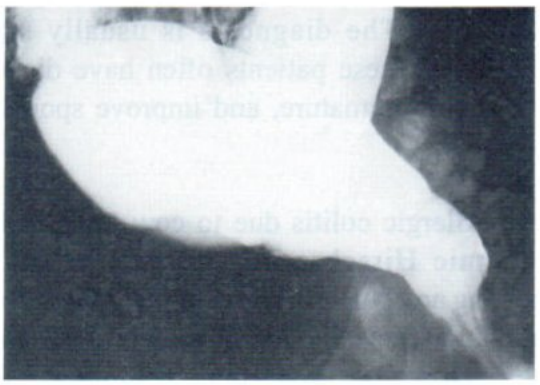


Fig. 5. Barium enema shows a gradual transition zone at the rectosigmoid region. The rectosigmoid index is 0.5

2. Abnormal contractions and peristaltic activity with pointed serrations or "saw-tooth" appearance of the aganglionic segment (Fig. 6). This is infrequently seen in the aganglionic segment but is a reliable sign of Hirschsprung disease. It has been reported in 26% of barium enemas of infants with Hirschsprung disease.[17]

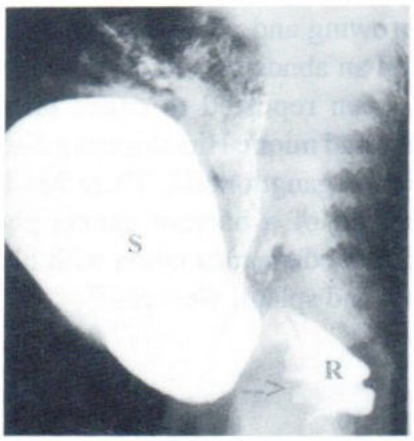


Fig. 6. Barium enema shows a transition zone in the rectosigmoid region and abnormal contraction (arrow) of the rectum (R). S = sigmoid.

3. Retention of barium proximal to the aganglionic segment at 24 hours after the examination. This is the most sensitive sign, presenting in over 80% of neonates with Hirschsprung disease. However it is less specific, because it can be seen in patients without Hirschsprung disease,[17,19] and a good evacuation does not rule out Hirschsprung disease.

A pattern of barium mixed with stool is infrequently seen on a 24-hour delayed film but has been reported as a highly reliable sign of Hirschsprung disease.[17]

4. Rectosigmoid index. This is obtained by dividing the widest diameter of the rectum by the widest diameter of the sigmoid colon when the colon is fully distended. The widest rectal diameter is measured at any point below the third sacral vertebra.[20]

In normal newborn infants, as well as cases of meconium plug syndrome and other causes of low intestinal obstruction, the rectum is commonly found to be wider than the sigmoid loop. The rectosigmoid index is normally greater than or equal to 1.0. In Hirschsprung disease the widest rectal diameter is usually less than the widest diameter of the sigmoid loop, even in the absence of a transition zone. A rectosigmoid index of less than 1.0 is suggestive of Hirschsprung disease. It is obviously unnecessary when a transition segment is clearly evident.[20,21] It is not a useful measurement in long segment or total colonic aganglionosis.[21]

5. Work hypertrophy (jejunization). In a child older than 3 months, the proximal colon develops hypertrophy of the circular and longitudinal muscle fibers in response to obstruction of the aganglionic segment. This causes a prominence of the muscle fibers that radiographically resembles the plicae circulares of the jejunum[8] (Fig. 7). This jejunization is a useful supportive

sign of aganglionosis.

6. In children with Hirschsprung disease and colitis, the enema may show **mucosal nodularity, mucosal irregularity,** and **spiculation**[17] (Fig. 7). Clearly, enemas should not be performed in newborns who are critically ill with colitis.

7. The radiologic diagnosis of total colonic Hirschsprung disease is very difficult. Findings include a normal barium enema, **a short colon of normal caliber**, a **microcolon**, and a **transition zone in the ileum**[22,23] (Fig. 8). Additional findings include **easy, extensive reflux far back into small bowel**[24] and a **pseudotransition zone in the colon.**[22] Bowel shortening is seen as loss of the redundancy of the sigmoid colon that is seen in normal infants. The colon has been described as resembling a question mark.[8] There is also prolonged retention of barium.[23]

DIFFERENTIAL DIAGNOSIS

The most important disease to be considered in differential diagnosis is functional immaturity of the colon (meconium plug syndrome or neonatal small left colon syndrome). In contrast to Hirschsprung disease, in the first days of life the barium enema shows a marked narrowing of the distal colon up to the left colonic flexure with an abrupt transitional zone in the area of the left colonic flexure,[4] and in a patient with functional immaturity of the colon, the rectum is usually quite distensible.[4] The diagnosis is usually made clinically, as these patients often have diabetic mothers, are premature, and improve spontaneously.[10]

Allergic colitis due to cow milk protein can mimic Hirschsprung disease; it causes narrowing and mucosal irregularity of the rectum, an abnormal rectosigmoid index, and a transition zone.[25] However, pronounced mucosal fold thickening and irregularity are constant findings in allergic colitis, reflecting the inflammatory response of the rectum to the antigenic proteins. In comparison, the rectal mucosa in Hirschsprung disease is usually intact, with the serrated appearance of the contrast column due to intermittent spasm.[25] In addition, the location of the mucosal abnormality is atypical for Hirschsprung enterocolitis, in which mucosal abnormality is seen predominantly above the level of the transition zone.[11]

Salmonella colitis has been reported to cause narrowing and mucosal irregularity of the rectum and an abnormal rectosigmoid index.[26] It has also been reported to cause large bowel obstruction and mimic Hirschsprung disease with total colonic aganglionosis. There has been one case reported of a barium enema showing a narrowed and edematous colon with blunting of the hepatic and splenic flexures.[27]

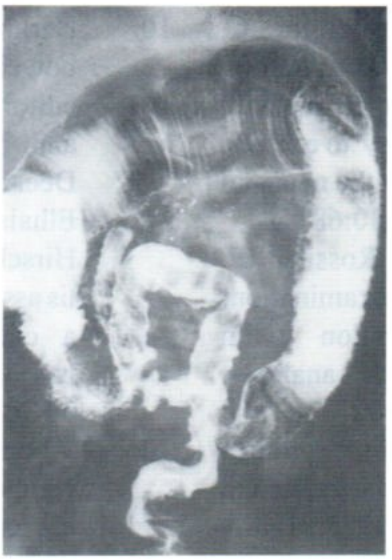


Fig. 7. Barium enema shows long segment Hirschsprung disease. The transition zone is at the junction of the distal descending colon and sigmoid. Note mucosal irregularity of the descending colon from colitis and jejunization at the transverse colon.

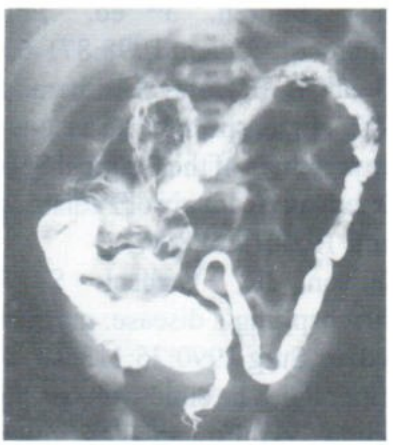


Fig. 8. Barium enema (left) shows narrowing of the rectum, sigmoid, descending colon, and transverse colon; and reflux of barium into the small bowel. A 24-hour delayed film (right) shows diffuse narrowing of the colon and dilatation of the distal small bowel. At surgery total colonic aganglionosis was found.

REFERENCES

1. Reid JR, Buonomo C, Moreira C, Kozakevich H, Nurko SJ. The barium enema in constipation: comparison with rectal manometry and biopsy to exclude Hirschsprung's disease after the neonatal period. Pediatr Radiol 2000;30:681-4.
2. Kanterman RY, Siegel MJ, Rossiter JE. Pediatric barium enema examination: optimizing patient selection with univariate and multivariate analyses. Pediatr Radiol 1994;24:288-92.
3. Worman S, Ganiats TG. Hirschsprung's disease: a cause of chronic constipation in children. Am Fam Physician 1995;51:487-94.
4. Fotter R. Imaging of constipation in infants and children. Eur Radiol 1998;8: 248-58.
5. Buonomo C, Taylor GA, Share JC, Kirks DR. Gastrointestinal tract. In: Kirks DR, Griscom NT, editors. Practical pediatric imaging: diagnostic radiology of infants and children. 3rd ed. Philadelphia: Lippincott-Raven, 1998:871-6.
6. Kleinhaus S, Boley SJ, Sheran M, Sieber WK. Hirschsprung's disease-a survey of the members of the Surgical Section of the American Academy of Pediatrics. J Pediatr Surg 1979;14:588-97.
7. Neilson IR, Yazbeck S. Ultrashort Hirschsprung's disease: myth or reality. J Pediatr Surg 1990;25:1135-8.
8. Miller KE. The child with constipation. In: Hilton SvW, Edwards DK, editors. Practical pediatric radiology. 2nd ed. Philadelphia: W. B. Saunders, 1994: 219-31.
9. Hernanz-Schulman M. Imaging of neonatal gastrointestinal obstruction. Radiol Clin North Am 1999;37:1163-86.
10. Berlin SC, Sivit CJ, Stringer DA. Large bowel. In: Stringer DA, Babyn PS, editors. Pediatric gastrointestinal imaging and intervention. 2nd ed. Hamilton: BC Decker, 2000:486-91.
11. Elhalaby EA, Coran AG, Blane CE, Hirschl RB, Teitelbaum DH. Enterocolitis associated with Hirschsprung's disease: a clinical-radiological characterization based on 168 patients. J Pediatr Surg 1995; 30:76-83.
12. Watanatittan S, Suwantanaviroj A, Limprutithum T, Rattanasuwan T. Association of Hirschsprung's disease and anorectal malformation. J Pediatr Surg 1991;26:192-5.
13. Lorenzo RL, Harolds JA. The use of prone films for suspected bowel obstruction in infants and children. AJR Am J Roentgenol 1977;129:617-22.
14. Newman B, Nussbaum A, Kirkpatrick JA Jr. Bowel perforation in Hirschsprung's disease. AJR Am J Roentgenol 1987;148: 1195-7.
15. Fletcher BD, Yulish BS. Intraluminal calcifications in the small bowel of newborn infants with total colonic aganglionosis. Radiology 1978;126:451-5.
16. De Bruyn R, Hall CM, Spitz L. Hirschsprung's disease and malrotation of the mid-gut. An uncommon association. Br J Radiol 1982;55:554-7.
17. Rosenfield NS, Ablow RC, Markowitz RI, et al. Hirschsprung disease: accuracy of the barium enema examination. Radiology 1984;150:393-400.
18. O'Donovan AN, Habra G, Somers S, Malone DE, Rees A, Winthrop AL. Diagnosis of Hirschsprung's disease. AJR Am J Roentgenol 1996;167:517-20.

19. Taxman TL, Yulish BS, Rothstein FC. How useful is the barium enema in the diagnosis of infantile Hirschsprung's disease? Am J Dis Child 1986;140:881-4.
20. Pochaczevsky R, Leonidas JC. The "recto-sigmoid index". A measurement for the early diagnosis of Hirschsprung's disease. AJR Am J Roentgenol 1975;123:770-7.
21. Siegel MJ, Shackelford GD, McAlister WH. The rectosigmoid index. Radiology 1981;139:497-9.
22. Sane SM, Girdany BR. Total aganglionosis coli. Clinical and roentgenographic manifestations. Radiology 1973;107:397-404.
23. De Campo JF, Mayne V, Boldt DW, De Campo M. Radiological findings in total aganglionosis coli. Pediatr Radiol 1984; 14:205-9.
24. Chandler NW, Zwiren GT. Complete reflux of the small bowel in total colon Hirschsprung's disease. Radiology 1970; 94:335-9.
25. Bloom DA, Buonomo C, Fishman SJ, Furuta G, Nurko S. Allergic colitis: a mimic of Hirschsprung disease. Pediatr Radiol 1999;29:37-41.
26. Bhatt R, Rickett A. Salmonella colitis: a mimic of Hirschsprung disease. Pediatr Radiol 2000;30:431-2.
27. Gross E, Engelhard D, Katz S. Large bowel obstruction: an unusual presentation of salmonella enterocolitis in infancy. Pediatr Surg Int 2000;16:525-6.

BRACCO EDUCATION

Asia - Oceania

AO

Asian-Oceanian Seminars on Diagnostic and Interventional Radiology 2002

Uroradiology and Obstetrics & Gynaecology Imaging: current issues and new modalities

May 18 - 19
Seoul, Korea

Programme Leader:
Prof K S Cho

For further information please contact:

ASDIR Secretariat
Huntington Consultancy Pte Ltd
47 Hill Street #06-04
S.C.C.C.I. Building
Singapore 179365
Tel: +65-339 2883
Fax: +65-339 2272
E-mail: asdir.secretariat@huntington.com.sg

BRACCO
THE IMAGE OF INNOVATION

www.bracco.com/imaging

STONE DISEASES IN CHILDREN

Dr. M. A. Taher

ABSTRACT

Cholelithiasis and Urinary calculus are very rare in childhood. Therefore we present two cases of gallstones and four cases of urinary calculi.

Key words : Cholelithiasis, urolithiasis, childhood, ultrasonography (USG).

INTRODUCTION

Cholelithiasis is more common in children than previously supposed in the phrase---"fat, female, fertile, forty, fat intolerance". Prenatal or fetal gallstones are reported rarely[1,2] e.g. at 36 weeks of gestational age. Udeshi et al. reported a fetal stag-horn renal calculus detected by Ultrasonography between 18 & 20 weeks of gestation. Sonography is the initial test of choice as it is painless, non-ionizing and relatively cheap. In some cases, isotope renogram is needed to assess individual kidney functions.

CASE REPORTS

Case 1

A boy aged 11 years presented with pain in right hypochondrium and was treated with antacids and antispasmodic drugs, but was not cured completely. Abdominal ultrasonography revealed a small calculus in gallbladder, but there was no history of fat intolerance. Spontaneous disappearance was noticed in a month, but recurrence of the gallstone was found after one year. To avoid the risk of obstructive jaundice, cholecystectomy was done and the sonographic finding was confirmed.

Case 2

A boy aged 3 years 8 months complained of painful hematuria on 15th August, 1994. Ultrasonography revealed a 5 X 10 mm calculus in right kidney. The patient did not have surgery and was lost to follow-up, but came again on 17th April, 1995 with recurrent painful hematuria. His father told that he was symptom-free during this interval of eight months. Repeat ultrasonography revealed bilateral nephrolithiasis and the patient was referred to uro-surgeon, but could not be followed-up.

Case 3

A boy aged 10 years came with complain of dysuria. Ultrasonography revealed small right kidney (6 cm long), normal left kidney (8.5 cm long) and a vesical calculus (4.8 cm diam.). He was also lost to follow-up.

Case 4

Recurrent urinary calculi was found in a boy. At 9 years of age he was operated to remove vesical calculus. After 1year i.e. at 10 years of age he again came with loin pain and ultrasonography revealed a 17 mm stone in the right kidney. Gamma Camera renogram using intravenous 1 milliCurie 99m Tc-DTPA showed normal left kidney and obstructive nephropathy in the right side. He had right nephrolithotomy and was improved clincically.

Director, Nuclear Medicine Centre, Post Box No.-16 Rangpur-5400, Bangladesh.

Case 5

A boy aged 7 years came with abdominal pain and severe vomiting. Ultrasonography showed a gallstone. Other investigations revealed no any abnormality. Surgery confirmed the ultrasonic finding---cholecystectomy made the patient symptom free.

Case 6

A boy of 6 years complained of dysuria for 2 years and was neglected due to poverty. A plain X-ray of abdomen showed a big calculus in the urinary bladder. Ultrasonography revealed 2.5 X 1.5 cm vesical calculus and bilateral pelvicaliectasis in both kidneys. (Fig.1)

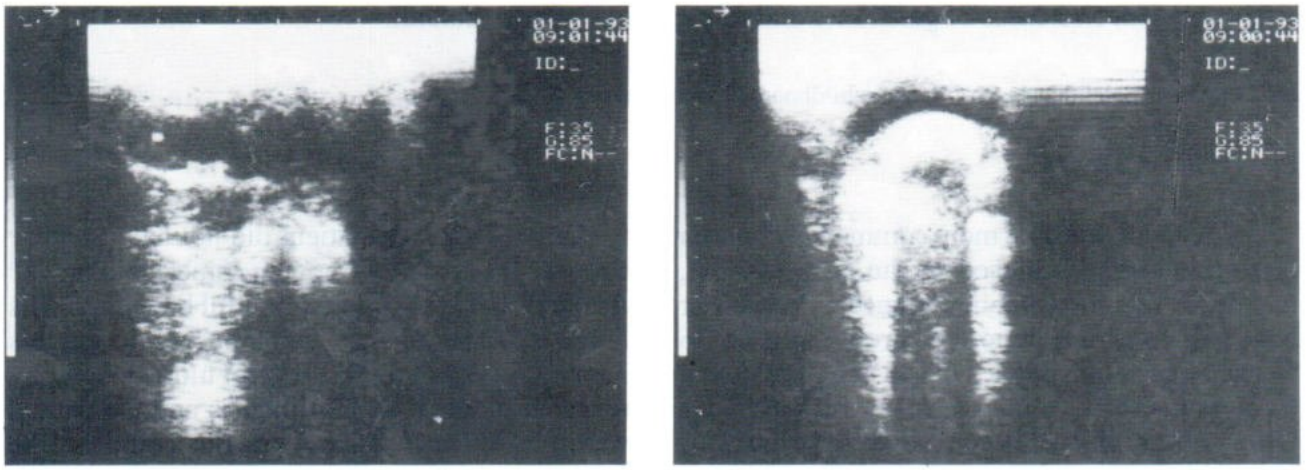


Fig. 1. Vesical calculus (Case 6)

DISCUSSION

In children, gallstone and urolithiasis are rare, but it is important to be diagnosed early and non-invasively e.g. by ultrasound and isotope renogram. People are afraid of surgery especially in children and may be the reason of failure to follow-up. Infantile gallstones often disappear spontaneously over time, the exact mechanism of disappearance is unknown.[3] The causes of gallstones in children include hemolytic disease (e.g. sickle cell disease), prematurity, total parenteral nutrition, furosemide, biliary and cardiac malformations, hepatolenticular degeneration (Wilson disease), genetic factors (e.g. Pima Indians), liver diseases, abnormal enterohepatic circulation (due to ileal disease, cystic fibrosis, pancreatic insufficiency, bacterial overgrowth, short gut), obesity, gallbladder disease and oral contraceptive.[4] The total incidence of obstructing or potentially obstructing uropathy of the lower urinary tract in childhood is about 1 in 1000 general pediatric admissions.[6] A small renal stone may dissolve by diuresis therapy, bigger stones need percutaneous removal or extracorporeal shock wave lithotripsy or nephrolithotomy ; bilateral renal calculi may indicate a metabolic disorder and should be investigated vigorously.

REFERENCES

1. Abbitt PL, McIlhenny J : Prenatal gallstones. J Clin Ultrasound 18:202, 1990.
2. Beretsky I, Lankin DH : Diagnosis of fetal cholelithiasis using real time high resolution imaging employing digital detection. J Ultrasound Med 2: 381-383, 1983.
3. Keller MS, Markle BM, Laffey PA at. al. : Spontaneous resolution of cholelithiasis in infants. Radiology 157 : 345-348, 1985
4. Stringer DA : Pediatric Gastrointestinal Imaging. B. C. Decker Inc. Toronto, 1989.
5. Udeshi UL, Sowerby T, Cope D, Tristram L, Brady T. Post-natal outcome of prenatally detected mild fetal pelvicalyceal dilatation, Eur. J. Ultrasound 3 : S21, 1996.
6. Ringertz HG. Lower urinary tract obstruction in children. Pp. 311-319. In Margulis AR, & Gooding CA(eds.) Diagnostic Radiology 1984, University of California.

DOUBLE GALLBLADDER : CASE REPORTS

Dr. M. A. Taher

ABSTRACT

Over the last few months we found two cases of double gallbladder which is quite rare.

CASE REPORT (1)

A 65 years old man complaining of acute abdominal pain, vomiting and lump in the right upper abdomen, was referred to us for sonographic evaluation. Abdominal ultrasound scan revealed two cystic structures in the right hypochondrium at the gallbladder fossa, both of which contained multiple stones showing posterior acoustic shadowing (Figure 1). Cholecystectomy was planned.

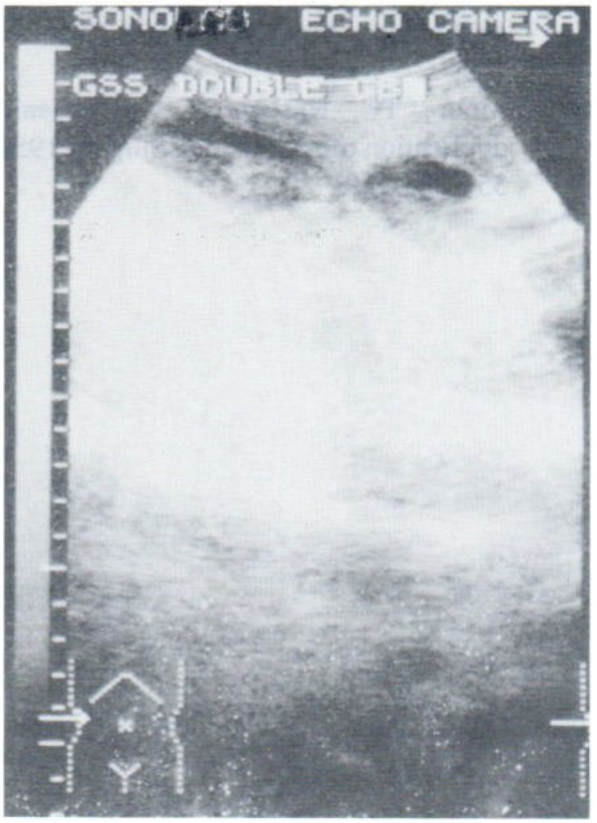


Fig. 1. Sonography showing duplication of gallbladder with stones in both lobes.

CASE REPORT (2)

A girl of 9 years complained of fluctuating jaundice and abdominal pain since last 4 years. USG revealed double gallbladder with a tiny calculus in the cystic duct.

DISCUSSION

Double gallbladder is a rare finding : 1 in 4000 autopsies by Boyden[1] ; about 150 cases have been described in the literature.[2-5] Sonographic findings in double gallbladder with cholelithiasis of both lobes have been described in other countries,[6,7] but not yet in Bangladesh to our knowledge.

Director, Nuclear Medicine Centre, Post Box No.-16 Rangpur-5400, Bangladesh.

REFERENCES

1. Boyden EA. The accessory gallbladder-an embryological and comparative study of aberrant biliary vesicles occurring in man and the domestic mammals. AM J Anat 1926 ; 38 : 177-231.
2. Cunningham JJ : Empyema of a duplicated gallbladder : echographic findings. J. Clin. Ultrasound 1980 ; 8 : 511-512.
3. Gross RE : Congenital anomalies of the gallbladder. Arch Surg. 1936 ; 32 : 131-159.
4. Moore TC, Hurley AG : Congenital duplication of gallbladder. Surgery 1954 ; 35 : 283-289.
5. Guyer PB. McLoughlin M. Congenital double gallbladder. A review and report of two cases. Br. J. Radiol. 1967 ; 40 : 214-219.
6. Garfield HD, Lyons EA, Levi CS. Sonographic findings in double gallbladder with cholelithiasis of both lobes. JUM 1988 ; 7 : 589-591.
7. Chouhan AL, Chouhan S, Chouhan MK. Duplication of gallbladder associated with cholelithiasis : Sonographic detection. J Clin Ultrasound 1995 ; 23 : 556-557.

COST-EFFECTIVENESS OF ABDOMINAL ULTRASONOGRAPHY IN APPENDICITIS

Dr. M. A. Taher, Director,

The objective of this study was to find out the cost-effectiveness of ultrasonographic examination in patients with lower abdominal pain to diagnose acute appendicitis. During July, 1991 to August 2000, we have performed abdominal ultrasonography in 4289 patients of lower abdominal pain by Puylaert's graded compression technique[1] for acute appendicitis using Pie Medical 3.5-5 Mega-Hertz linear transducer, Aloka 210, SSD 500/1100 curvilinear probe, Fukuda 1000/3500 linear, Siemens SL 2 sector and linear probes. Among the 100 patients (M51, F49, ages 9 to 75 years) suspected of having acute appendicitis, 29 actually had appendicitis. Interpretation of appendiceal sonographic results was 98% accurate. The sonographic result led to changes in the treatment of 52 patients, and prevention of unnecessary appendectomy in 13 patients, providing a savings of about Takas 65000 ($ 1300) and prevented unnecessary hospital admission for 69 patients, thus saving approximately Tk. 7800/-. The cost of performing the 100 sonographic examinations was about Tk. 35000/- and thus the overall savings was about Tk. 500/- ($ 9.45) per patient. It is concluded that ultrasonography performed in patients with suspected acute appendicitis improves diagnostic accuracy, thus leading to more appropriate selection of patient treatment and with reduction of expenditure.

Key words: Ultrasonography, vermiform appendix, appendicitis.

Diagnosis of acute appendicitis is not simple as numerous other conditions including ascending diverticulitis, mesenteric adenitis, and genitourinary diseases show similar symptoms. Sonography has become an important tool in the investigation and diagnosis of many abdominal pathologic entities. Since 1986, 14 studies including more than 9956 patients have been published to diagnose acute appendicitis by ultrasound showing an overall sensitivity of 85% and specificity of 96% if the sonography was done by expert.[2,3] In a study of 609 patients clinically suspected to be having appendicitis, 426 cases turned out to be appendicitis on ultrasound examination and the rest (173/609) had a broad spectrum of gastrointestinal, gynecologic, biliary and urologic diseases.[4] However, the overall efficacy of appendiceal sonography in the clinical management of patients with suspected acute appendicitis in respect to effective use of resources has not yet been studied in Bangladesh. Here, we examine the cost-effectiveness of sonography in relation to improved diagnostic accuracy in patients with acute appendicitis.

Nuclear Medicine Centre, Post Box No.-16 Rangpur-5400, Bangladesh.

MATERIALS AND METHODS

From July 1991 to August 2000 we performed sonography on 4289 patients at Nuclear Med. Centers (NMC), Dinajpur and Rangpur, and private clinics at Kurigram, Gaibandha and Lalmonirhat. Of these, 100 consecutive patients (51 male and 49 female, ages 9 to 75 years) with clinically suspected acute appendicitis participated in this study. None of the patients had undergone appendectomy. The follow-up duration was 1 to 14 days (average 7 days), during which time none of the patients was lost. The 100 patients were attended to by one of 10 physicians, consisting of 5 surgeons, 1 gastroenterologist, 1 pediatrician and 3 general practitioners, who determined whether hospitalization for suspected acute appendicitis was necessary on the basis of the clinical information. Appendiceal sonography was indicated for all 100 patients. Before sonography was performed, the attending physicians determined the likelihood of acute appendicitis based on the following scale: definitely appendicitis (indication for immediate surgery), probably appendicitis (indication for immediate hospitalization and possible surgery). The patients' medical history was taken and physical examination was performed, followed immediately by sonography. The patients did not undergo and prior preparations, such as fasting or instillation of fluid into the intestines. The sonography operator received no prior information about the laboratory test results of the patients, and examined the hepatobiliary and urogenital systems routinely to rule out any calculus for focal lesion, and followed the technique using graded compression proposed by Puylaert.[1] A swollen appendix diameter of 6 mm or more was considered pathologic. The appendix was differentiated from the terminal ileum on sonography based on the absence of peristalsis. Other important signs in acute appendicitis are appendicolith, increased echogenicity of the periappendicular fat, loss of the submucocal layer, pericecal abscesses, lymphnodes and extraluminal gas. The ultrasonic features of the layer stratification of the pathologic appendix were used to classify the pathologic appendix into the following three types:

(1) Catarrhal: abnormal wall thickening, mainly of mucosa with distinct layer stratification,

(2) Phlegmonous: abnormal wall thickening, mainly of the submucosa with distinct layer stratification,

(3) Gangrenous: abnormal wall thickening with blurred layer stratification. Other pathologic findings included abscess formation and thickening of the mesoappendix. Clinically, we considered type 1 is compatible with early appendicitis, type 2 is non-perforating appendicitis, and type 3 is perforating appendicitis. We indicated conservative treatment for patients with catarrhal appendicitis on sonography, whereas immediate surgery is indicated for patients with phlegmonous or gangrenous appendicitis.

After sonography the operator estimated the likelihood that the patient had acute appendicitis on the following scale: definitely appendicitis (swollen appendix could be seen on sonography), or definitely not appendicitis (no pathologic finding indicative of appendicitis could be seen), We used sonographs (Pie Medical, Fukuda 1000/3500, Aloka 210,SSD 500/1100, Siemens SL 2) sector, linear and curvilinear probes with 3.5—5 Mega-Hertz frequency. (Figs 1+2)

Definitive diagnosis was established at surgery in 25 patients and at the clinical follow-up examination in 75 patients. The patients were diagnosed as having acute appendicitis, other specific conditions or nonspecific abdominal pain. Changes in patient care were determined by comparing the planned treatment (hospitalization for observation or emergency appendectomy) with the actual treatment (discharge from hospital,

hospitalization for observation, treatment for an alternative condition, emergency appendectomy or other surgery) received after the sonographic findings had been taken into account. We assumed that each patient who avoided hospitalization for observation would have been hospitalized for only one day of observation if sonography had not been done.

The mean cost of appendectomy and of one day of observation in the hospital were determined from the data of the patients. The cost of sonography ranged form Tk. 100 to Tk. 400 per patient during the study period. Changes in hospital resources used were determined by comparing the treatment plans made before sonography with the actual treatment regimen the patient underwent. The number of unnecessary appendectomies avoided was multiplied by the cost of removing pathologic appendix. The number of hospital observation days avoided was multiplied by the cost of one hospital day excluding incidental charges. The overall cost savings as a result of using routine sonography was determined by subtracting the cost of performing 100 appendiceal sonography from the savings that resulted from incorporating the sonographic results into treatment decisions.

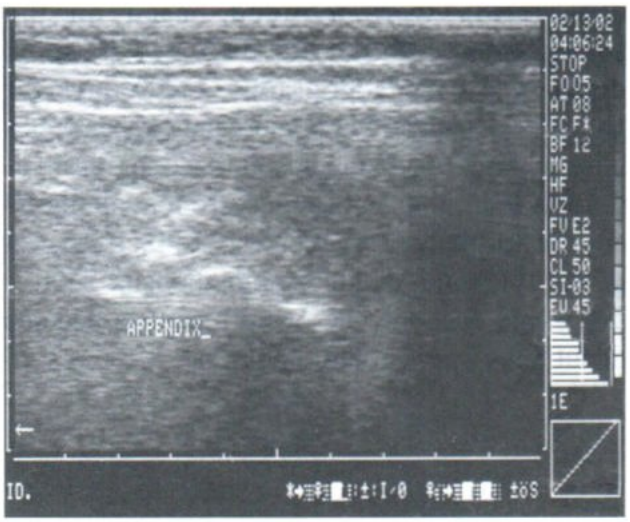


Fig. 1. Nromal appendix at USG.

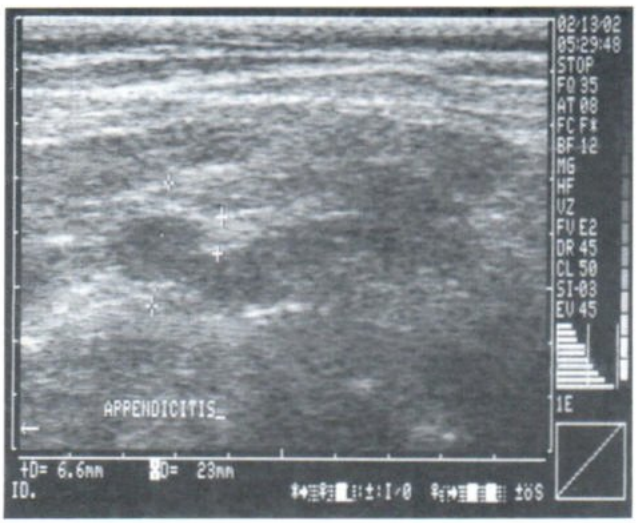


Fig. 2. Appendicitis at USG.

RESULTS

Typical sonographic features of acute appendicitis are shown in figures 1 and 2. Acute appendicitis was the definitive diagnosis in 29 of the 100 patients (29%). Of these, diagnosis of 4 patients having suspected caterrhal-type acute appendicitis was confirmed during follow-up hospitalization, while the other 25 patients were confirmed at surgery by pathologic examination. In 71 patients (71%) acute appendicitis was ruled out during clinical follow-up examination including additional imaging results such as radionuclide scans, endoscopy with biopsy and barium contrast studies. The results of sonography were positive in 27 patients (23 patients with surgical and pathologic evidence of phlegmonous or gangrenous type acute appendicitis and 4 patients with follow-up evidence of catarrhal-type acute appendicitis) and negative in 71 patients (all negative throughout clinical follow-up examination). Sonography produced false-negative results

in two patients with surgical and pathologic proof of phlegmonous or gangrenous-type acute appendicitis and no false-positive result. Overall sonographic interpretation had 95% sensitivity, 100% positive predictive value, 98% negative predictive value, and 98% overall accuracy for diagnosing or ruling out acute appendicitis.

Definitive diagnosis was made in 42 of the patients (42%) (Table 1). Sonography revealed the correct diagnosis in 40(95.2%) of these patients. Nonspecific abdominal pain was diagnosed in 58 patients. Of this group, no organic disease was included in the definitive diagnosis.

A comparison of clinical likelihood versus the sonographic likelihood of acute appendicitis with respect to the final diagnosis of this disorder is shown in Table 2.

The sonographic results prompted 52 changes in treatment strategy. These changes involved prevention of unnecessary appendectomy in 13 patients whose diagnoses were established as definitely appendicitis' sonographically (6 with gynecologic disease and 7 with urinary disease), unnecessary hospitalization in 60 patients who were established as probably or possibly appendicitis' clinically but definitely not appendicitis' sonographically (57 patients with nonspecific pain, 1 with gynecologic disease and 2 with urinary disease). On the other hand, 9 patients were admitted for emergency appendectomy based on sonography that were considered definitely appendicitis' contrary to the clinical findings of probably or possibly appendicitis. The mean cost of necessary appendectomy was $100(range 90-110). Thus the overall cost savings from avoiding appendectomy in 13 cases was $1300. The mean cost of one day observation was approximately $5. At least 69 hospital days of observation were avoided based on the sonographic results: 60 days for patients discharged after sonography and 9 days for patients who underwent emergency appendectomies without first being hospitalized for observation. In total, the cost savings from avoiding 69 days of hospital observation was $ 345. If the cost of the 100 sonographic examinations at $700 is taken into account, the overall savings become about $ 9.45 per patient (Table 3).

TABLE 1. Definitive Diagnosis of our patients

Definitive Diagnosis	Number of patients
Appendicitis	29
Catarrhal	4
Phlegmonous, gangrenous	25
Urinary diseases	7
Gynecologic diseases	6
Nonspecific abdominal pain	58

Total =100

TABLE 2. Estimated clinical and sonographic likelihood of acute appendicitis compared with definitive diagnosis

	Definitive diagnosis	
	Appendicitis confirmed	Appendicitis ruled out
Clinical likelihood		
Definitely appendicitis	20	13
Probably appendicitis	9	58
	Total = 29	71
Sonographic likelihood		
Definitely appendicitis	27	0
Probably not appendicitis	2	71
	Total = 29	71

TABLE 3. Cost Savings because of incorporation of sonography in the diagnosis of acute appendicitis

Treatment changes	Number of patients	Savings or Costs per Patient ($)*	Overall saving or Costs ($)*
Savings			
Avoided unnecessary appendectomy	13	100	1300
Avoided observation for 1 day before Appendectomy / discharge	69	5	345
Costs			
Sonography	100	7	700
Total cost savings		9.45	945

*Dollar estimates reflect exchange rate of $1=Tk.39 --56/-

DISCUSSION

The present results demonstrate that sonography had a high diagnostic accuracy for acute appendicitis. Moreover, its use led to improved patient care and reduced use of hospital resources. Sonographic diagnosis is useful in patients clinically suspected of having acute appendicitis, including those who are ultimately diagnosed as having other conditions. The normal appendix is seen in less than 30% of patients. Occasionally a mass consisting of inflamed appendix, periappendiceal fluid and thickened omentum may be seen in the right iliac fossa.[5] Sometimes degenerated uterine leiomyoma may mimic acute appendicitis,[6] and sonographic findings of carcinoid appendix has also been described.[7] Sonography is also excellent in showing an abscess and may demonstrate an appendicolith, a 'coffee-bean' sign, a hyperechogenic finger-like projection (inflamed appendix) extending into a cystic mass (pus) with or without scattered internal echoes may be seen in an appendix abscess.[8] Rarely a radionuclide scan (Gallium-67 citrate or Technetium-99 metastable monoclonal antibodies against granulocytes) is required to demonstrate an occult abscess in right iliac fossa or a 'hot' appendix.[9-10]

Appendicitis is still a fascinating subject. It is a common disease and still difficult to understand, to diagnose and to treat. Does ultrasound have a role in the management of patients suspected of having appendicitis? Some will say it has a limited yet positive impact.[11] Surgeons do not find the use of ultrasound nor CT scan valuable in the diagnosis of appendicitis.[12,13] They recommend laparoscopy instead.[12] The problem is even more complicated when special new pathological techniques will show appendicitis in otherwise normal looking appendices.[14] This article may be of value for it shows how in countries where access to technology is limited the use of ultrasound may be cost-effective. The cost saving may look trivial when compared to what has been published for rich countries,[2] but should have a positive impact in health care.

The cost savings in the present study may have been overestimated because of the lack of false-positive data. Patient selection by clinical history and physical examination may further optimeze the situation.

REFERENCES

1. Puylaert JBCM. Acute appendicitis: Ultrasound evaluation using graded compression. Radiology 158:355-360, 1986.
2. Fujii Y, Hata J, Futagami K, Hamada T, Mitsuoka H, Teramen K, Konemori G, Suenaga K. Ultrasonography improves diagnostic accuracy of acute appendicitis and provides cost savings to hospitals in Japan. J Ultrasound Med 19: 409-414, 2000.
3. Shyamkumar N K, Justus A, Davis VS, Koshi T. Role of ultrasound in the evaluation of acute appendicitis. Bangladesh J Ultrasonography 4: 55-59, 1997.
4. Simonovsky V. Ultrasound in the differential diagnosis of appendicitis. Clin Radiol 50: 768 - 773, 1995.
5. Abu-Yousef MM, Franken EA. An overview of graded compression sonography in the diagnosis of acute appendicitis. Sem Ultrasound CT MR 10: 552,1989.
6. Yacoe ME, Jeffrey RB Jr.Degenerated uterine leiomyoma mimicking acute appendicitis: sonographic diagnosis. J Clin Ultrasound 23: 473 -475, 1995.

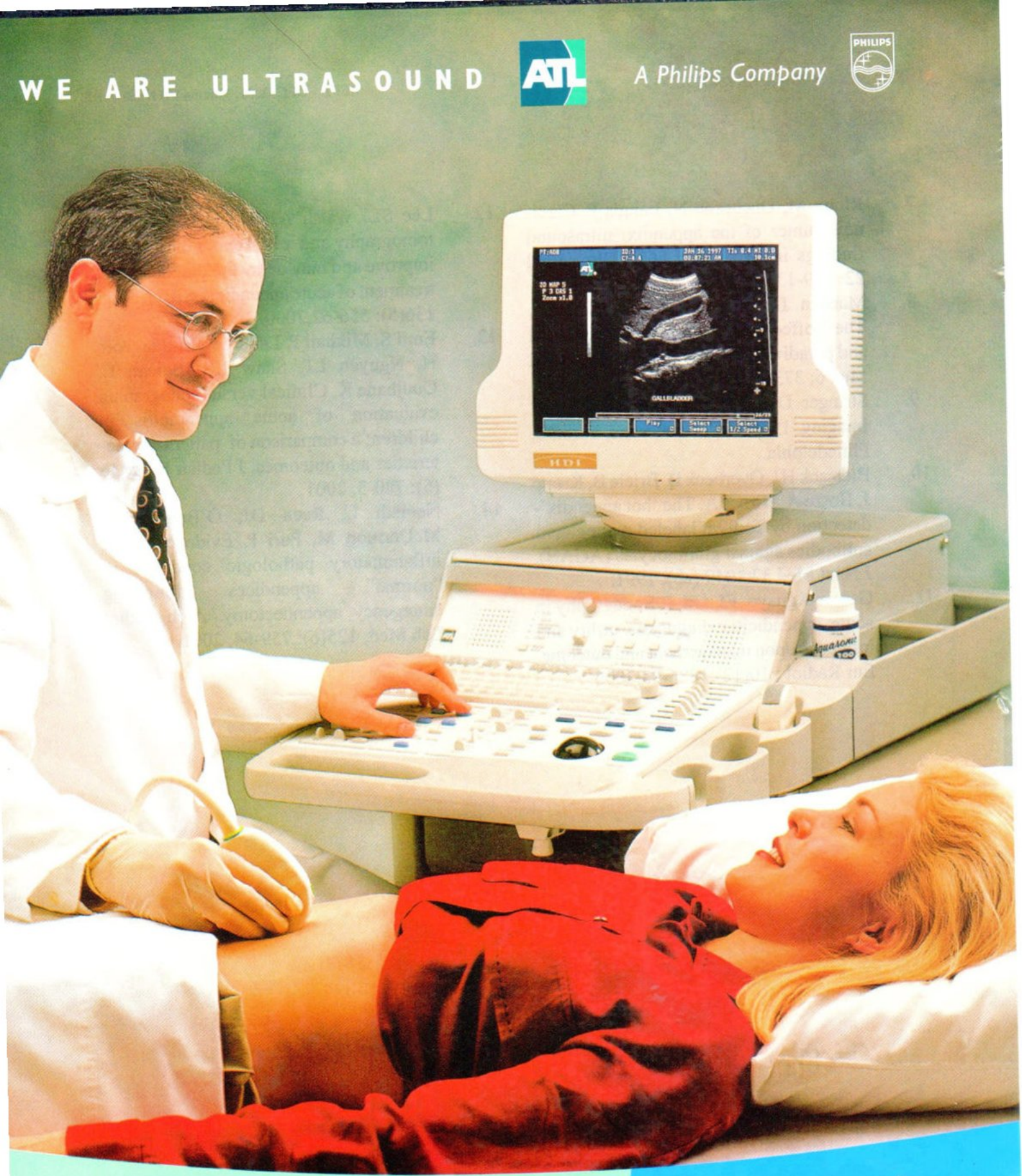
7. Rioux M, Duchesne N, Langis P. Carcinoid tumor of the appendix: ultrasound findings in two cases. J Clin Ultrasound 22: 129-133, 1994.
8. Machan L, Pon MS, Wood BJ et al. The 'coffee-bean' sign in periappendiceal and paradiverticular abscess. J Ultrasound Med 6: 373-375, 1987.
9. Stringer DA. Pediatric Gastrointestinal Imaging. 1989 B.C. Decker Inc, Toronto, Philadelphia.
10. Biersack HJ, Overbeck B, Briele B, Kropp J, Hotze A, Hirner A. The 'hot appendix'-detection by Tc-99m labeled monoclonal antibodies against granulocytes (AGAB). J Nucl Med 32:1049 (ab), 1991.
11. Garcia-Aguayo FJ, Gil P. Sonography in acute appendicitis: diagnostic utility and influence upon management and outcome. Eur Radiol ; 10(12):1886-93,2000.
12. Lee SL, Walsh AJ, Ho HS. Computed tomography and ultrasonography do not improve and may delay the diagnosis and treatment of acute appendicitis. Arch Surg; 136(5): 556-62,2000.
13. Emil S, Mikhail P, Laberge JM, Flageole H, Nguyen LT, Shaw KS, Baican L, Oudjhane K, Clinical versus sonographic evaluation of acute appendicitis in children: a comparison of patient characteristics and outcomes. J Pediatr Surg; 36 (5): 780-3, 2001.
14. Nemeth L, Reen DJ, O'Briain DS, McDermott M, Puri P. Evidence of an inflammatory pathologic condition in "normal" appendices following emergency appendectomy. Arch Pathol Lab Med; 125(6): 759-64, 2001.

WE ARE ULTRASOUND

ATL

A Philips Company

PHILIPS



FOR MORE INFORMATION PLEASE CONTACT

PHILIPS MEDICAL SYSTEMS

- TEL. 745-4090 Ext. 3332
- FAX. 398-0792

Philips Electronics (Thailand) Ltd.
209/2 Sanpavuth Road, Bangna, Bangkok 10260

ฆพ. 78/2542

PHILIPS

Let's make things better.

IDIOPATHIC ACUTE TRANSVERSE MYELITIS ; MR MANIFESTATION

Montanan ROHITOPAKARN, M.D., Siriporn HIRUNPAT, M.D.
Wiwatana TANOMKIAT, M.D.

ABSTRACT

The purpose of this report is to describe the MR manifestations of patients who were diagnosed as idiopathic acute transverse myelitis (IATM).

Eleven patients seen in a 4–year-period at Songklanagarind Hospital with clinically proved to be IATM were retrospectively reviewed. The location, size, pattern, segmental length of abnormal hyperintensity on T2-weighted images and pattern of abnormal enhancement were determined.

The findings are summerized as followed : No abnormality was detected in one case (9%). The region of involvement was mostly in the thoracic cord (85%). Most of the lesions (84%) were longer than 1 vertebral segment. The most sensitive images were T2 weighted images and the most common pattern of abnormal signal intensity in the spinal cord was the holocord (47%). Abnormal enhancement was seen in 57% of post contrast enhanced cases and all of them showed diffused vague enhancement.

Conclusion : MR manifestations of IATM are variable and non –specific. Most of them are seen as areas of hyperintensity on SE T2 weighted images without significant cord expansion. The lesions usually extend beyond one vertebral segment. Post Gadolineum study may show vague diffused enhancements or may not be enhanced at all. All these findings are similar to other previous studies.

INTRODUCTION

Idiopathic acute transverse myelitis (IATM) is an interesting, well–recognized but poorly understood inflammatory disorder in the spinal cord. Its origin is unclear although most authors implicate an autoimmune disease.[1]

IATM is characterized by acute rapidly developing progressive lesions that affect both halves of the spinal cord in the absence of compression from any other known neurologic disease. IATM therefore is often a diagnosis of exclusion.

IATM should be distinguished from the broader category of acute transverse myelopathy that has also, sometimes confusingly, been referred to as IATM. Acute transverse myelopathy refers to any disorders that acutely affect function on both sides of the spinal cord regardless of the longitudinal extent. There are many

Department of Radiology. Songkhlanakarind Hospital, Faculty of Medicine, Prince of Songkhla University , Tel-Fax 074 429-927 Hadyai, Songkhla, 90110 , Thailand. Correspondance to S. Hirunpat

other causes of acute transverse myelopathy, such as multiple sclerosis, neoplasm, infarction and trauma, which are beyond the scope of our study.

Although the major role of MR imaging is to identify treatable conditions that can mimic IATM such as acute disc herniation, hematoma, epidural abscess or compression myelopathy, there are many interesting manifestations of IATM on MR images and the cumulative cases in world literature are still few. We add our experience and describe our MRI findings.

MATERIALS AND METHODS:

The spinal MRI of 11 patients who were clinically diagnosed as idiopathic acute transverse myelitis during May 1996 – July 2000 were studied.

In all patients, clinical data including age, sex, prodomal history, date and length of symptom on set were reviewed. Prodomal history included recent illness, vaccination or trauma within 6 weeks of the onset of symptoms.

Objective clinical data from the neurological physical examination and cerebrospinal fluid profile were also recorded.

Our routine MRI technique for evaluation of suspected spinal cord lesions includes Sagittal and Axial SE T1 weighted images, T2 weighted images (1.5 T MRI unit, Magnetom-Vision : -Siemens). Additional post intravenous contrast studies (Magnevist 0.1mmol / kilogram of body weight) were obtained in eight cases in order to exclude the possibility of spinal cord tumor.

Results of all MRI examinations were reviewed by 2 radiologists and the lesions were characterized on the basis of signal intensity, morphology, location and the vertebral segmental length.

In the patients who underwent axial T2- weighted imaging, lesions were further classified into three categories[1] based on the location of the abnormal signal intensity seen on axial T2-weighted image:(Fig2,3.4)

1) Holocord with or without peripheral sparing
2) Non-holocord

Degree and pattern of enhancement with gadolinium were recorded.

RESULTS

Of the 11 patients, 6 patients (55%) were female and 5 patients (45%) were male. The mean age was 35 years (range 15-53 years). Prodomal symptoms were present in 8 patients (Table 1).

With respect to clinical presentation , all patients had paraplegia and sensory deficit. Length of symptom onset to a maximal level was between 4 hours and 4 weeks.

Nine of eleven patients had cerebrospinal fluid (CSF) studies. Abnormal CSF studies were noted in 4 patients(45%) which were abnormal in 4 patients (36%) (Table1).

TABLE 1. Clinical Findings in Patients with IATM

Patient No./age(y) /sex	Length-of Symptom Onset	Prodomal Symptom and Time	Level of Sensory Deficit	CSF profile			
				Protein (mg/dl)	Sugar (mg/dl)	WBC Cell/mm^3	Differential Cell count (cell)
1. 47 F	14 d	Upper respiratoty tractinfection (URI) 2 wk. Earlier	C7-C8	-		-	-
2. 53 F	1 d	- None	T8	Normal	Normal	0	-
3. 15 M	1 d	- URI 2 wk. Earlier	T4	Increased (61 mg/dl)	Normal	55	L52, PMN 3
4. 30 F	7 d	- None	L2	Increased (64 mg/dl)	Normal	2	L2
5. 34 F	20 d	- Fever 1 mo.earlier	T4-T5	Normal	Normal	0	-
6. 34 F	30 d	- Minor trauma 2 mo. Earlier	T6	Normal	Normal	2	L2
7. 43 F	2 d	- Recurrent ATM (twice) 2 yr earlier	L1	Increased (77 mg/dl)	Normal	20	L18, PMN 2
8. 19 M	4 d	- URI 1 mo earlier	T8	-	-	-	-
9. 19 M	1 d	- Diarrhea 7 d. earlier	T10	Normal	Normal	0	-
10. 52 F	4 hr.	- None	L1	Normal	Normal	0	-
11. 43 M	9 d	- URI 2 wk. Earlier	-	Increased (145 mg/dl)	Increased (85/144)	1	L1

Normal CSF protein < 50 mg/dl
Normal CSF sugar < half of blood sugar level
Normal CSF white blood cell < 5 lymphocytes/mm^3)
L : lymphocyte,
PMN: Polymorphonuclear cell

The spinal cord MR findings were abnormal in 10 of 11 patients (91%);8 patients had a single lesion, 1 patient had two non-contiguous lesions and 1 patient had three non-contiguous lesions (Fig 1). No abnormality could be detected by MRI in one case. (Table 2)

Among 13 lesions from 10 patients, 11 lesions (85%) occurred in the thoracic cord, 1 lesion occurred in the cervicothoracic and 1 lesion involved the lower thoracolumbar cord.

Seven of 13 lesions (54 %) were more than two vertebral segments long. Three lesions were less than two vertebral segments long. Three lesions were one vertebral segment long.

Four (4/13) lesions (31%) had slight cord expansion, 8 lesions (69%) had no cord expansion and the other one showed cord atrophy.

The axial SE T2W image of the patient number 3 was disppeared. Twelve lesions in axial T2W images could be studied 8 lesions (67%) involved the majority of the cord in the cross

sectional area (holocord pattern) (Fig 2), 4 lesions (33%) involved focal non-specific region (non holocord pattern) (Fig 3,4).

Seven lesions were furthur evaluated with Gadolinium enhanced MR imaging. There was no evidence of enhancement in 3 lesions (43%). Four lesions (57%) had abnormal enhancement and all of them (100%) were diffused vague enhancement.

TABLE 2. MR Imaging Finding in Patients with IATM

Paitent	Spinal cord		Sl on T1W	Length (number of vertebral body)	Pattern on axial T2W	Contast enhancement pattern
No	Lesion location	Expansion				
1	T4-T5,T7,T9-T10	No	isointense	1 - 2	Holocord	-
2	T9-T10	No	isointense	2	Posterior cord but both GM and WM	None
3	T2-T8	No	isointense	8	No axial T2W	Diffuse vague
4	T11-T12	Yes	isointense	2	Holocord	-
5	C7-T1,T12	No	isointense	1 - 2	Holocord	None
6	Upper T	No	isointense	4	Holocord	Diffuse vague
7	T1-T4	Atrophy	isointense	4	Holocord	Diffuse vague
8	T5-T10	Yes	isointense	6	Holocord	-
9	T7-T8	Yes	isointense	1	Holocord	None
10	T12-L1	Yes	isointense	3	Anterior Gm	Diffuse vague
11	Invisible	No	isointense	0	-	None

Si = Signal intensity
GM = Gray matter
WM = White matter

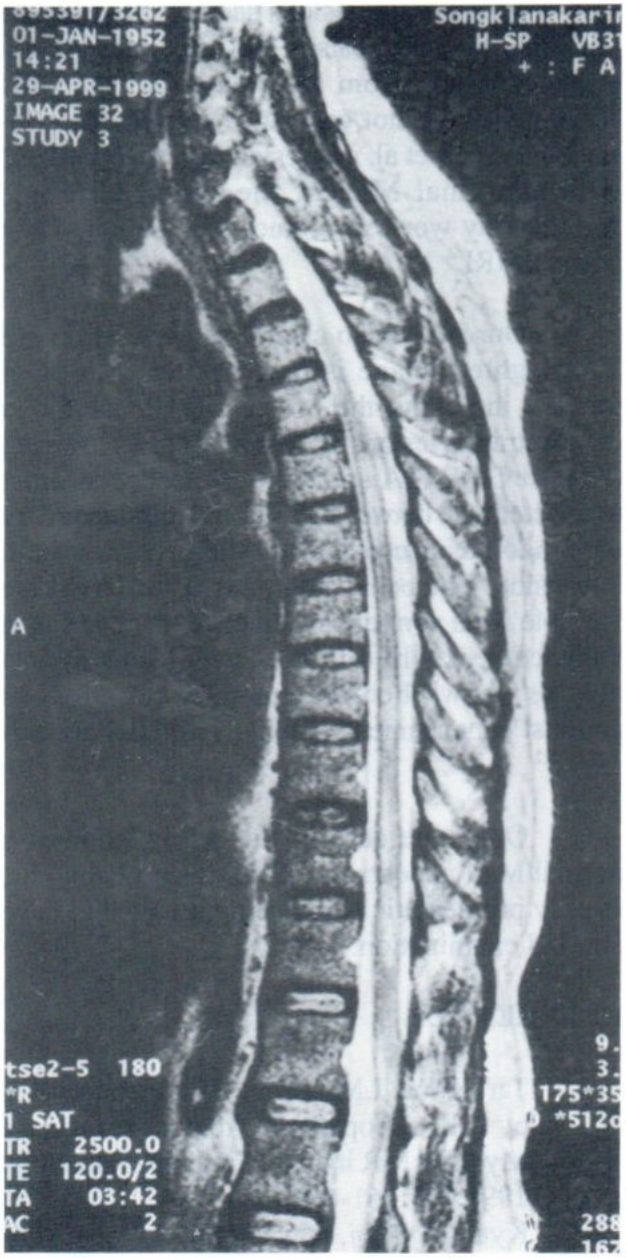


Fig. 1. Sagittal SE T2w image shows multiple non-contiguous hyperintensity lesion in mid and lower thoracic cord.

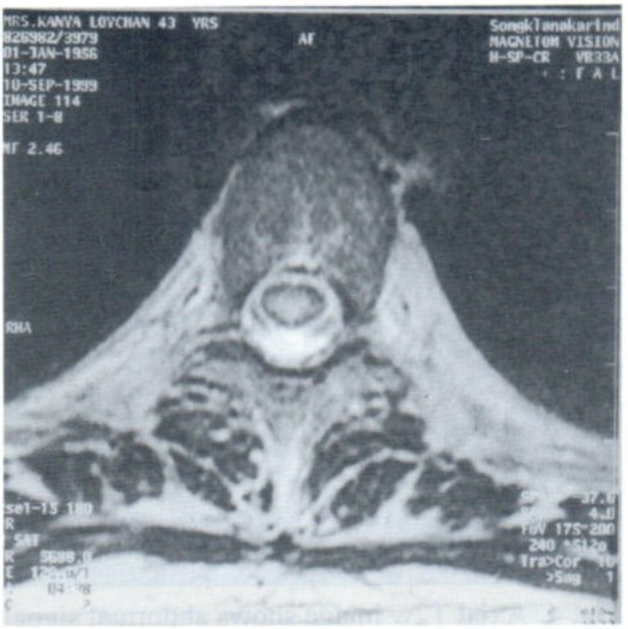


Fig. 2. Axial T2w image shows a holocord signal intensity abnormality in upper thoracic cord.

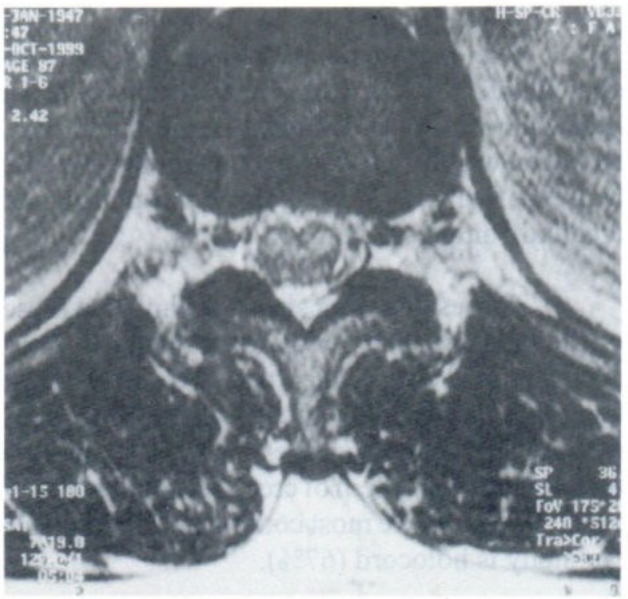


Fig. 3. Axial T2w image shows abnormal signal intensity predominate anterior gray matter in lower thoracic cord.

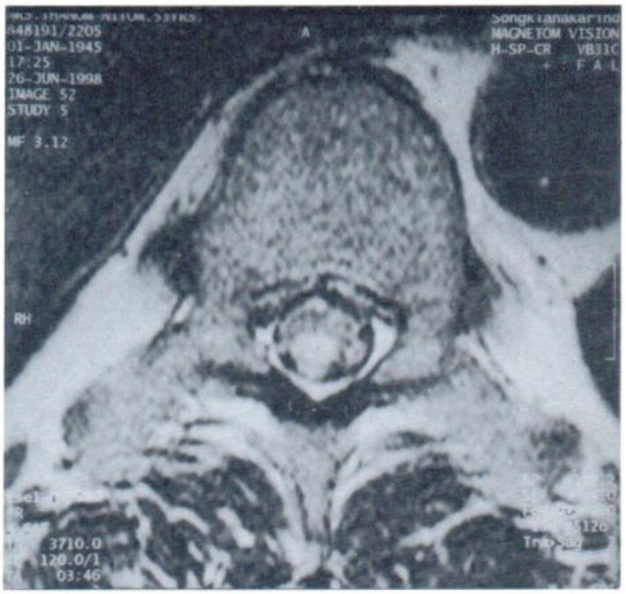


Fig. 4. Axial T2w image shows abnormal signal intensity involving predominate posterior cord in lower thoracic cord.

DISCUSSION

The diagnosis of IATM is based on clinical information. MRI, the best non-invasive imaging modality to demonstrate the spinal cord, has been widely used to exclude other possible causes of myelopathy such as neoplasm and epidural compression.

The results of our study are similar to those of previous reports.[1,2] Variable patterns from normal spinal cord appearance to abnormal high signal intensities within the affected cord are seen on axial T2 weighted images. There is no definite or characteristic pattern of cross-sectional involvement. However, the most common pattern seen in our study is holocord (67%).

Demonstration of the disease extending longer than 1 vertebral segment in the spinal cord was seen in most cases (86%). Differential diagnosis of a long spinal cord lesion may include syringomyelia, however clinical manifestations of these entities are different and syringomyelia can usually be clearly seen on both T1W and T2W images similar to a water signal intensity.

Whether the lesions seen by MRI can be related to the prognosis is still uncertain. Austin et al. conclude from their data that the MRI abnormality did not correlate with the prognosis,[3] but Scott et al. suggested that their patients with abnormal MRI of the spinal cord had significantly worse outcomes than patients with normal MRI.[4]

Our study also clearly shows that the SE T2 weighted image is much better than other images, including the post Gd-DTPA study, in demonstrating lesions in the spinal cord. However, the post Gd-DTPA study is still needed in order to differentiate between IATM and intramedullary cord neoplasm especially when there is cord expansion. The enhancing patterns of IATM are variable from non- enhancement to diffuse vague enhancement while that of neoplasms almost always shows heterogeneously pronounced contrast enhancement or focally nodular appearance.[1,2]

Only one case in our study, showed a normal MRI appearance. This was probably due to only problematic cases being selected to have an MRI examination.

REFERENCES

1. Tartaglino LM, Croul SE., Flanders AE, et al. Idiopathic Acute Transverse Myelitis: MR imaging findings. Radiology 1996;201:661-669.
2. Kyu Ho Choi, Kwang Soo Lee, Sun Ok Chung, et al. Idiopathic Transverse Myelitis : MR Characteristics. AJNR 1996;17:1151-1160.
3. Austin SG, Chi-Shing Zee, Waters C. The Role of Magnetic Resonance Imaging in Acute Transverse Myelitis. Can. J. Neurol. Sci. 1992;19:508-511.
4. Scott T, Weikers N, Hospodar M, Wapenski J. Acute Transverse Myelitis : A Retrospective Study Using Magnetic Resonance Imaging. Can. J. Neurol. Sci. 1994;21:133-136.

PARAPHARYNGEAL SYNOVIAL SARCOMA: MR IMAGING

M. PUVANESWARY MB,BS, FRCR[1]
P. DAVIDSON MD, FRACS, FRCP, FRCS[2]

SUMMARY

Synovial sarcoma is a rare, malignant soft-tissue tumour, which usually arises in the extremities of a young adult. They are rare in other areas of the body including the neck. We present a case of synovial sarcoma occurring in the neck with MR findings. A heterogeneous multiloculated tumour with fluid-fluid levels, calcification and haemorrhage occuring in a young adult, should raise the suspicion of a synovial sarcoma.

Key words: magnetic resonance, synovial sarcoma, neck

CASE REPORT

A 11- year old female presented with gradual enlargement of a lump in the left side of the neck over a period of several months. The patient's general health was good. On examination the patient was afebrile with a firm mass measuring approximately 4 cm in diameter palpable in the left side of the neck beneath the angle of the mandible. There was no lymphadenopathy. The spleen and liver were not palpable and the skin and mucosa of the head and neck region were normal.

Magnetic resonance imaging of the neck was performed with axial T1-weighted and T2-weighted spin-echo, and coronal short TI-inversion recovery sequences (STIR). Gadolinium-enhanced (Gd-DTPA) images in the axial and coronal planes were also obtained. T1- weighted axial spin-echo images (Fig1) demonstrated a lobulated mass with intermediate signal intensity and focal region of higher signal intensity suggesting the presence of subacute haemorrhage.

Coronal STIR (Fig2) and axial T2-weighted (Fig3) images revealed a heterogeneous but predominantly high signal intensity mass with internal septation and multiple fluid-fluid levels. There were a few foci of signal void within the mass suggesting the presence of haemosiderin or calcification. Gadolinium-enhanced images (Fig4) demonstrated heterogeneous nodular and septal enhancement. The tumour measured 4.5x3.5 x2.5cm. The main bulk of the tumour was located in the left parapharyngeal space, with extension inferiorly to the paralaryngeal space. Tumour extended inferiorly to the level of the superior pole of the left thyroid gland with displacement of the larynx and upper airways to the right. Superiorly the tumour extended to the level of the palatine tonsil. The posterior tonsillar pillar (palatopharyngeus muscle) was displaced anteriorly and the posterior belly of the digastric muscle laterally. On retrospective review the margins of the posterior belly of the digastric muscle and longus capitis muscle were ill-defined. The tumour appeared inseparable from the pharyngeal constrictor muscle. There was distortion, rotation and displacement of the oropharynx and hypopharynx which was displaced to the right. The left pyriform sinus was obliterated. The left

[1] Department of Medical Imaging and Paediatric Surgery
[2] John Hunter Hospital, N.S.W. AUSTRALIA

Correspondence : M. Puvaneswary JOHN HUNTER HOSPITAL Locked Bag No1. Hunter Mail Centre NSW 2310 Phone 49213383 Fax 49213949

submandibular gland was displaced antero-inferiorly, the carotid sheath and sternocleido-mastoid muscle were displaced laterally.

At surgery an encapsulated mass extending to the base of the skull was excised. This contained liquefied haemorrhage and some soft, pale gelatinous tissue in part of the mass.

Histology of the mass revealed a monophasic synovial sarcoma with poorly differentiated areas. Immunostains demonstrated spotty keratin-reactivity, with little or no labelling for desmin or S100 protein. There was diffuse strong CD99 staining of the tumour consistent with the diagnosis of synovial sarcoma.

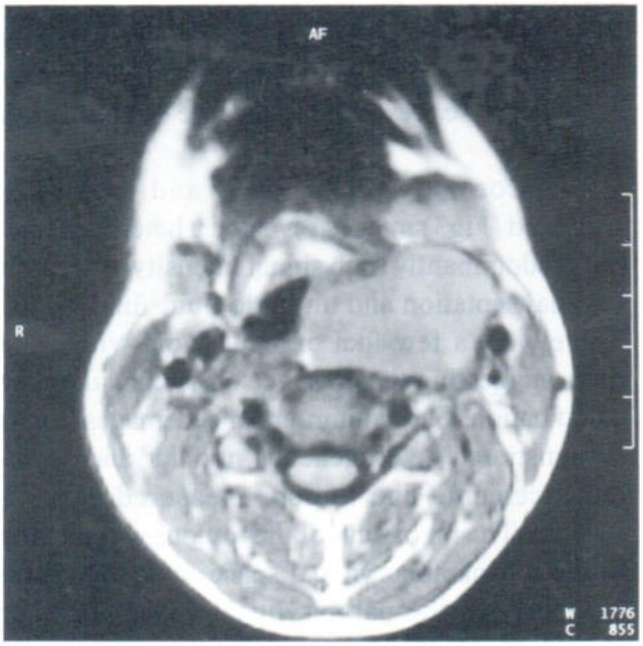


Fig 1. T1-weighted spin-echo axial image shows a well-defined lobulated mass with intermediate signal intensity. On the lateral aspect the mass demonstrated higher signal intensity suggesting the presence of haemorrhage.

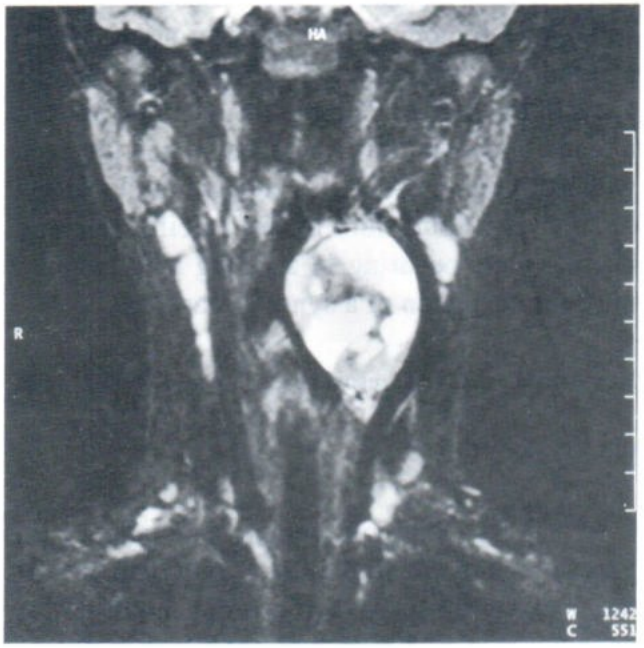


Fig 2. Coronal STIR MR image demonstrated heterogeneous but predominantly high signal intensity mass with several foci of signal void suggesting the presence of calcification or haemosiderin.

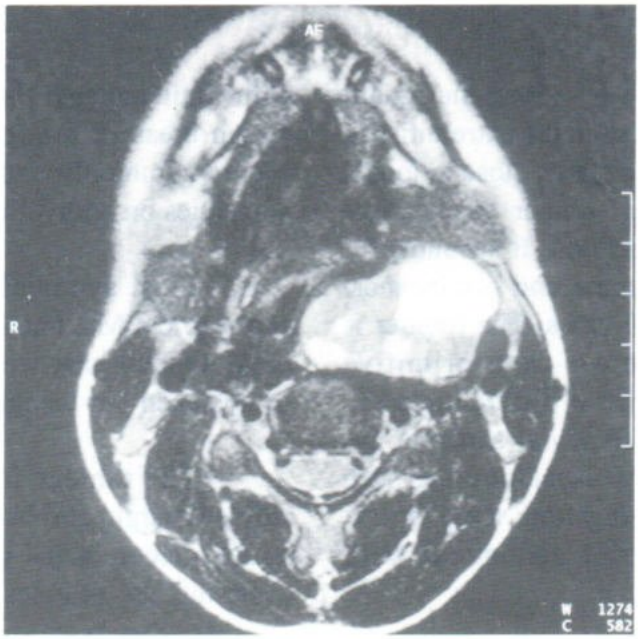
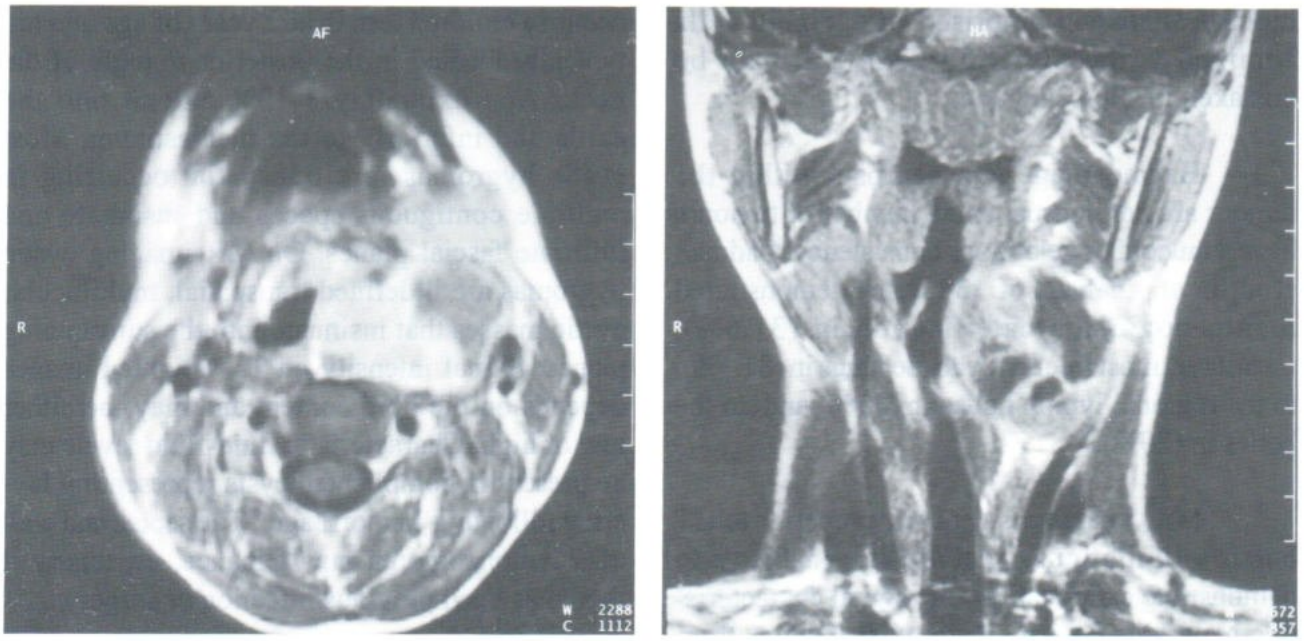


Fig 3. T2-weighted spin-echo axial image reveals a multilocular mass with fluid-fluid levels.



4A. **4B.**

Fig 4. A) Axial and B) coronal gadolinium-enhanced MR image displays nodular and septal enhancement.

DISCUSSION

Synovial sarcoma is a rare malignant tumour and frequently arises in the extremities in young adults more often distally, close to joints, tendon sheaths and bursae. Tumour rarely arises from an intra-articular location. It accounts for 8-10% of soft tissue sarcoma and occurs most commonly between 20-40 years. The tumour is considered to arise denovo from primitive mesenchymal cells that have differentiated to resemble synovial cells. Synovial sarcoma has been reported to occur in unusual locations such as the cervical region arising from the pharynx, larynx, chest wall, anterior abdominal wall, gluteal region and vagina.[1,2,3]

Tumours rarely arise in the cervical region. The first case of hypopharyngeal and laryngeal synovial sarcoma was reported by Jernstrom in 1954.[1] The tumour is usually characterised by a biphasic pattern comprised of spindle cells admixed with epitheloid cells and may be mistaken for fibrosarcoma.[4]

Haemorrhage and necrosis within the tumour are not unusual and a number of tumours have a mucoid or gelatinous consistency. Cadman et al, in an analysis of 134 cases demonstrated roentgenographic calcification in (31.6%), metastases most frequently to the lungs in (81.1%), to the regional lymph nodes in (23%) and to the bones in (20%).[4]

MR imaging is generally superior to CT but it's limitations include it's inability to demonstrate calcification and signal characteristics generally do not distinguish benign from malignant tumours.[5]

On MR imaging synovial sarcomas have predominantly heterogeneous signal intensity multiloculated masses with internal septation and multipile fluid-fluid levels.[6] The signal intensities of the fluid indicate the presence of haemorrhage within areas of cyst or necrosis.[7] Calcification occurs commonly and manifests as low signal intensities on both T1 and T2-weighted images.

Most synovial sarcomas enhance with contrast. On MR imaging approximately a third of the tumours have well defined margins and can be mistaken for benign tumours.[8]

The tumour in our patient had an ill-defined margin and had enlarged cervical lymph nodes. Secondaries to regional lymph nodes occur in 23% of cases.[4]

The differential diagnosis of multiloculated cystic masses in the neck includes thymic cyst, cystic hygroma/lymphangioma and cervical teratomas. The majority of cystic hygromas, occur in children less than 2 years of age and are typically located in the posterior triangle of the neck. Approximately 3-10% extend into the axilla and inferiorly to the mediastinum. Most cystic hygromas are transpatial occurring in multiple contiguous spaces and insinuate and infiltrate fascial planes. On MR imaging cystic hygromas are illdefined transpatial, multilocular cystic masses that insinuate into the surrounding planes. Signal intensity on T1-weighted images depends on the lipid content and may be either low or high. Characteristic fluid-fluid levels may be present in complicated cysts representing layering following hemorrhage.[9] The septae and wall of a lymphangioma may enhance, especially if there has been previous infection or surgery.

Thymic cysts are rare and the majority occur between 2 and 13 years of age and are located in the lower half of the neck and mediastinum. On imaging, thymic cysts are generally thin-walled unilocular or multilocular masses closely associated with the carotid sheath.

The mass is frequently elongated at one or both ends, tapering into a tract or cord.[10]

Three percent of teratomas are found in the neck. Cervical teratomas are multilocular, heterogeneous masses containing both solid and cystic components with scattered calcification.[11]

Other parapharangeal non-mucosal neck masses include neurogenic tumours and other soft -tissue sarcomas. Fluid-fluid levels within a cystic mass have been described in a schwannoma and a neurofibroma.[12] Extracranial schwannomas are most commonly found in the mid-neck. On MR imaging, schwannomas are of intermediate signal intensity on T1-weighted images and hyperintense on T2-weighted images depending on the cellularity. Twenty percent of schwannomas have cystic degeneration and may mimic other cystic masses. Some older schwannomas (ancient schwannomas) have degenerative changes with haemorrhage, haemosiderin and fibrosis.

CONCLUSION

Although signal characteristicS of synovial sarcomas are non specific, MRI is useful to demonstrate the extent of the tumour and pressure effects on adjacent airway. The MRI findings of a heterogeneous, multiloculated tumour in a young adult with fluid-fluid levels, calcification, and haemorrhage suggest synovial sarcoma

REFERENCES

1. Jernstrom P. Synovial sarcoma of the pharynx: Report of a case. Am J Clin Pathol 1954;24:957-961.
2. Gatti WM, Strom CG, Orfei E. Synovial sarcoma of the laryngopharynx. Arch Otolaryngol 1975;101:633-636.
3. Chellam VG and Varghese. Parapharyngeal synovial sarcoma. A case report and review of literature. Indian J of Cancer 1979;16:87-89.
4. Cadman NL, Soule EH, Kelly PJ. Synovial sarcoma : An analysis of 134 tumours. Cancer 1965 ;18:613- 627.
5. Kransdorf MJ, Jelinek JS, Moser RP et al Jr. Soft-tissue masses: Diagnosis using MR imaging. AJR 1989;153:541-546.
6. Morton MJ, Berquist TH, McLeod RA, et al. MR imaging of synovial sarcoma. AJR 1991;156:337-340.
7. Mahajan H, Lorigan JG and Shirkhoda A. Synovial sarcoma : MR Imaging. Magn Reson Imaging 1989;7:211-216.
8. Blaksin MF, Siegel JR, Benevenia J et al. Synovial sarcoma:. Frequency of nonaggressive MR characteristics. J. Comput Assit Tomogr 1997;21:785-789.
9. Koeller KK, Alamo L, Adair CF et al : Congenital cystic masses of the neck: Radiologic - pathologic correlation. Radiographics 1999; 19:121-146.
10. Nguyen Q, de Tar M, Wells W, et al: Cervical thymic cyst: Case and review of the literature. Laryngoscope 1996;106: 247-252
11. Rothschild MA, Catalano P, Urken M, et al : Evaluation and management of congenital cervical teratoma. Arch Otolaryngol Head Neck Surg 1994;120: 444- 448
12. Catalano P, Fang Hui E, Som PM. Fluid - fluid levels in benign neurogenic tumours. AJNR. 1997;18: 385-387

PRIMARY BILATERAL ADRENAL LYMPHOMA: A CASE REPORT

Boonyaporn VASURATNA, Rachanee LESTSIRICHOK, Laddawan VAJRAGUPTA

ABSTRACT

Primary lymphoma of both adrenal glands in a 59-year-old man is reported. The patient presented with fever and weight loss for 5 months. Computed Tomography (CT) scan of the abdomen revealed bilateral adrenal masses. Opened biopsy at right adrenal gland was done and immunostaining histologic report revealed large cell type of malignant lymphoma, whereas the bone marrow aspiration was negative. After initiation of chemotherapy, the patient developed febrile neutropenia, which was complicated by pneumonia and expired shortly thereafter. Literature about imagings of primary adrenal lymphoma was reviewed.

INTRODUCTION

Adrenal masses rarely result from involvement by lymphoma. Diffuse non-Hodgkin's disease is the most common type.[1-4] This may be found at presentation or at follow-up. In CT series, about 1-4% of patients being followed for lymphoma developed adrenal involvement.[2-4] Adrenal involvement is most commonly seen in conjunction with an extra-adrenal disease site particularly retroperitoneal adenopathy.[1, 5] Involvement of the adrenal glands were demonstrated up to 25% of patient with lymphoma in an autopsy series.[6] Primary adrenal lymphoma is rare and is believed to arise from hematopoietic cells in the adrenal glands.[7] The true incidence of these neoplasms is not known.[8] To our knowledge, this is the first reported case of primary adrenal lymphoma in Thailand.

CASE REPORT

A 59-year-old man, who had had underlying NIDDM type II for 10 years, presented with prolonged fever and weight loss for 11 kilograms in 5 months. The patient developed freguency of fever with chill, sweating, and pain at periumbilical area in the last 2 months. Neither splenomegaly, hepatomegaly nor lymphadenopathy was present. The computed tomography of the abdomen demonstrated bilateral adrenal masses (Fig 1,2). The right and left adrenal masses were 7x4.5 cm and 5x3 cm in size respectively, measured about 25 to 34 HU on non-contrast enhanced images. On enhanced images, these masses were inhomogeneously enhanced to about 73 to 79 HU.

The symptoms were not improved, so the patient was referred to King Chulalongkorn Memorial Hospital. At presentation, the patient looked chronically ill without cushingnoid appearance. The body temperature was about 39°c, whereas the pulse rate, respiratory rate and blood pressure were normal. No lymphadenopathy, hepato-splenomegaly or abdominal mass was detected. Routine laboratory tests were within normal limits.

NIDDM = Non-insulin dependant Diabetes Mellitus.

Department of Radiology, Faculty of Medicine, Chulalongkorn University.

Bone marrow aspiration was performed on the 3rd day of admission and the result was negative for hypercellular bone marrow. Unsatisfied specimens were obtained from 2 times of fine needle aspiration of the adrenal glands so the opened biopsy at the right adrenal gland was performed on the 20th day of admission and the histological examination revealed large cell type of malignant lymphoma by immunostaining for LCA (Leukocyte Common Antigens and Vimentin).

After initiation of chemotherapy, the patient developed febrile neutropenia and sepsis and was complicated by pneumonia on the 35th day of hospital course. The patient expired 3 days later.

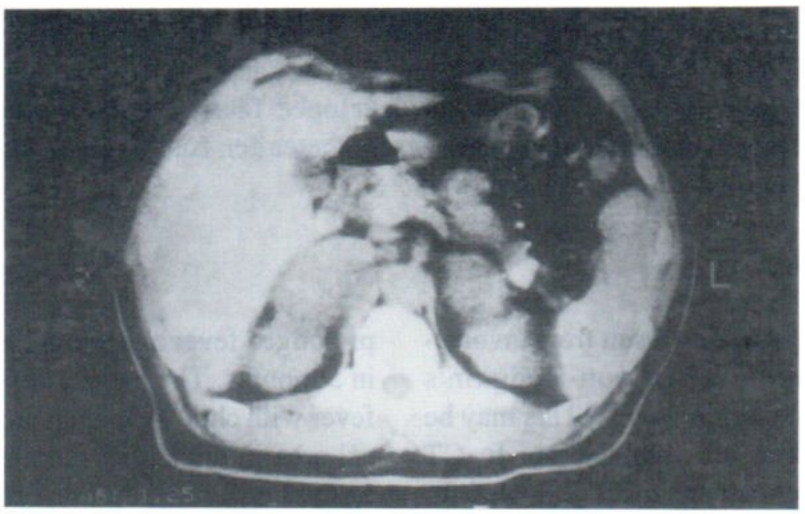


Fig. 1. Unenhanced CT scan shows bilateral adrenal masses. The masses are slightly hypodense than renal parenchyma.

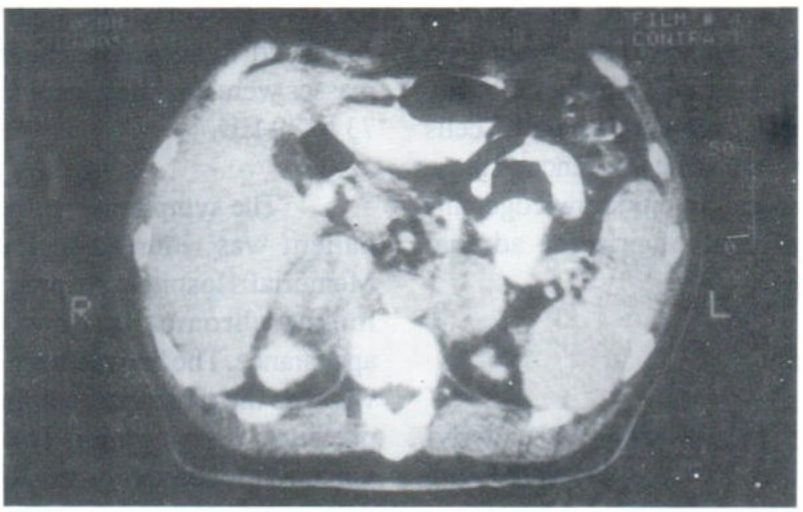


Fig. 2. Constrast-enhanced CT scan shows inhomogeneous enhancement of bilateral adrenal masses.

DISCUSSION

Bilateral adrenal enlargement can be associated with hyperfunction or normal to diminished function of the gland. Hyperplasia and pheochromocytoma are causes of enlargement with hyperfunction. If the function of the gland is normal or diminished, common causes are granulomatous infection (tuberculosis and histoplasmosis), metastasis and hemorrhage.[9] Metastasis to the adrenal glands are most common from lung and breast cancer.[1]

Primary lymphoma of the adrenal gland is rare. Since lymphoma arises from hematopoietic tissue which may be present in the adrenal glands, primary lymphoma arising in the adrenal gland can be expected.[7] The presenting symptoms are non-specific which may include fever, anorexia, malaise and a palpable abdominal mass. Over 70 cases were reported in the literature over the past 40 years and bilateral primary adrenal lymphoma appears to predominate over unilateral.[8,10-12] The definite diagnosis of adrenal lymphoma is by electron microscopic examination with immu-nostaining techniques. Review of the literature indicates diffuse histiocytic lymphoma to be the most common histology of primary adrenal lymphoma.[1-4, 7]

There is no pathognomonic appearance on the imaging findings. Neither ultrasonography, CT scan nor Magnetic Resonance Imaging (MRI) can indicate lymphomatous involvement of the adrenal gland. The sonographic appearance of primary adrenal lymphoma may vary from anechoic or hypoechoic to mixed hypoechoic and hyperechoic lesions. The hypoechoic variety is the most common pattern. Variable sonographic appearances is probably due to the presence of hemorrhage or necrosis.[7]

Using CT, adrenal lymphomas usually are seen as large soft tissue masses (46 to 60 HU) replacing the adrenal glands. They usually alter the shape of the adrenal glands, but the glands may markedly expand while retaining a somewhat adrenaliform shape.[1] The growth pattern sometimes can suggest lymphoma, as it is more likely to infiltrate or insinuate around the upper pole of the kidney rather than displace it, as would be typical for carcinoma.[1] Mild to moderate enhancement is seen after intravenous administration of iodinated contrast. The primary adrenal lymphoma tends to have necrosis and hemorrhage which may cause a cystic appearance on computed tomography.[7] However, CT appearances of adrenal enlargement due to lymphomas are non-specific and may mimicked by metastases.[13] In general, calcification in untreated lymphoma is uncommon, but a case of primary adrenal lymphoma with CT appearace of a cystic mass with multiple punctate calcifications has been reported.

MR imaging has considerable promise in the evaluation of adrenal glands.[14] In some cases, such as pheochromocytoma and adrenal adenoma, MRI helps to increase imaging accuracy by using the signal characteristics of the masses.[1,15] MRI is better than CT to demonstrate IVC patency and periadrenal blood vessels can be easily distinguished from adrenal nodules.[14,15] However, MR appearance of adrenal lymphomas are in distinguishable from other malignancies.[1] They are usually heterogeneous, with low signal on T1-weighted images (less intense than normal liver, but more intense than muscle) and more intense than fat on T2-weighted images. Kato et al. described a case of primary non-Hodgkin's B-cell lymphoma of diffuse large cell type at both adrenal glands, which MRI revealed bilateral adrenal masses with some enhancing septa.[16]

In conclusion, primary adrenal lymphoma is a rare disease, which has no specific appearance on sonography, CT nor MRI. However, in a

patient with unilateral or bilateral adrenal enlargement even in the absence of lymphadenopathy, primary adrenal lymphoma should be included in the differential diagnosis.

REFERENCES

1. Kenney PJ, Lee JKT. The adrenals. In : Lee JKT, Stanley RJ, Sagel SS, Heiken JP, editors. Computed body tomography with MRI correlation. Vol.2. 3rd ed. Philadephia: Lippincott - Raven, 1998: 1171-208.
2. Glazer HS, Lee JKT, Balfe DM. Non-Hodgkin's lymphoma. computed tomographic demonstration of unusual extranodal involvement. Radiology 1983; 149:211-7.
3. Jafri SZ, Francis IR, Glazer GM, Bree RL, Amendola MA. CT detection of adrenal lymphoma. J Comput Assist Tomogr 1983;7: 254-6.
4. Paling MR, Williamson RJ. Adrenal involvement in Non-Hodgkin's lymphoma. AJR Am J Roentgenol 1983; 141:303-5.
5. Moulton JS. CT of the adrenal glands. Semin Roentgenol 1988;23:288-303.
6. Rosenberg SA, Diamond HD, Jaslowitz B, Craver LF. Lymphosarcoma: a review of 1269 cases. Medicine (Baltimore) 1961; 40:31-53.
7. Falchook FS, Allard JC. CT of primary adrenal lymphoma. J Comput Assist Tomogr 1991;15:6:1048-50.
8. Salvotore JR. Ross RS. Primary bilateral adrenal lymphoma. Leuk Lymphoma 1999;34:111-7.
9. Davidson AJ, Hartman DS. Radiology of the kidney and urinary tract. 2nd ed. Philadelphia : W.B. Saunders, 1994:715-48.
10 Wang J, Sun NC, Renslo R, Chuang CC, Tabbarah HJ, Barajas L, et al. Clinically silent primary adrenal lymphoma. a case report and review of the literature. Am J Hematol 1998; 58:130-6.
11. Sasagawa I, Sadamori N, Itoyama T, Tsukasaki K, Nakamura H, Tomonaga M, et al. Primary adrenal lymphma with chromosomal abnormalities. Acta Hematologica 1995;94:156-62.
12. Al-Fiar FZ, Pantalony D, Shepherd F. Primary bilateral adrenal lymphoma. Leuk Lymphoma 1997;27: 543-9.
13. Alvarez-Gastelles A, Pedraza S, Tallada N, Castella E, Gifre L, Torrents C. CT of primary bilateral adrenal lymphomas. J Comput Assist Tomogr 1993;17:3:408-9.
14. Glazer GM. MR Imaging of the liver, kidneys and adrenal glands. Radiology 1988;166:303-12.
15. Lee FT Jr., Thornbury JR, Grist TM, Kelcz F. MR Imaging of the adrenal lymphoma. Abdom Imaging 1993;18:95-6.
16. Kato H, Itami J, Shiina T, Uni T, Arimizu N, Fujimoto H, et al. MR Imaging of primary adrenal lymphoma. Clin Imaging 1996;20:126-8.

CASE REPORT: CARCINOMA OF THE MALE BREAST

Dr.M.A. Taher, Director

Cancer of the male breast is a rare condition with an incidence of 0.5/100,000 per year in Denmark[1] and about 1000 men in the world.[2] It may be more serious than in female owing to much less amount of tissue between the carcinoma and the chest wall, and may fungate quite early.[3] The risk of breast cancer in men is proportional to the amount of breast tissue present and therefore is increased in patients with substantial gynecomastia.[4] In this report we present a case of carcinoma of the male breast.

CASE REPORT

A 68 years old man with left breast enlargement sine 1992 was operated on 1993. Biopsy revealed ductal carcinoma in situ with papillary pattern. Because in situ carcinoma was diagnosed, a left simple mastectomy was performed. Pathological examination of the specimen revealed infiltrating ductal carcinoma. The patient had radiotherapy, combination chemotherapy including tamoxifen, but developed multiple metastases confirmed by isotope bone scan and died on 7th November, 1998.

DISCUSSION

Gynecomastia, the most frequent lesion of the male breast, occurs mainly in peripuberty and around 50 years of age and may rarely harbour an intracystic carcinoma.[5] The adolescent gynecomastia is usually bilateral and seems to disappear spontaneously within 1 to 2 years.[6] The gynecomastia of older men may be caused by hormonal imbalance, may accompany systemic disorders (advanced alcoholic cirrhosis or renal failure), or may be drug-induced. The idiopathic gynecomastia persists after puberty in normal, healthy men and is usually unilateral.[6]

Gynecomastia is not thought to be associated with the development of male breast cancer unless the gynecomastia is part of Klinefelter's syndrome.[7,8] Gynecomastia is found in 0% to 20% of males with breast cancer.[9,10] A recent study showed that ductal carcinoma in situ may appear on high-resolution sonography(10-13 MHz) as calcifications, masses or focally dilated ducts.[11] Ultrasound can guide aspiration of cyst fluid as well as aspiration of cells directly from the papilloma. In the case of intracystic carcinoma, the cystic fluid is often hemorrhagic and dark brown. However, cytology of cystic fluid may be falsely negative.[12]

REFERENCES

1. Storm HH, Manders T, Friis S et al: Cancer incidence in Denmark 1988. Danish Cancer Society, Copenhagen, 1991.
2. Taber's Cyclopedic Medical Dictionary, New Delhi, 1993
3. Das S: A manual on Clinical Surgery 13 Old Mayor's Court, Calcutta, 1986.
4. Andreoli T E, Carpenter C C J, Plum F, Smith L H Jr. (eds.): Cecil/Essentials of Medicine, WB Saunders/Igaku-Shoin, Tokyo 1986.

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

5. Fallentin E, Rothman L: Intracystic carcinoma of the male breast. J Clin Ultrasound 22: 118-120, 1994.
6. Kapdi CC, Parekh N J. The male breast, Radiol Clin North Am 21: 137, 1983.
7. Ouimet-Oliva D, Hebert G, Ladouceur J. Radiology of breast tumors in the male. J Can Assoc Radiol 28: 249, 1977.
8. Borgen P I: Male breast cancer, Semin Surg Oncol 7: 314, 1991.
9. Reuter K, D'Orsi C J, Reale F: Intracystic carcinoma of the breast: The role of ultrasonography. Radiology 153: 233, 1984.
10. Weshler Z, Sulkes A: Contrast mammography and the diagnosis of male breast cysts. Clin Radiol 31: 341, 1980.
11. Hashimoto B E, Kramer D J, Picozzi VJ: High detection rate of breast ductal carcinoma in situ calcifications on mammographically directed high-resolution sonography. J Ultrasound Med 20: 501-508, 2001.
12. Hilton SvW, Leopold GR, Olson LK et al: Real-time breast sonography: Application in 300 consecutive patients. Am J Roentgenol 147: 479, 1986.

COMPARATIVE STUDY OF STANDARD FRACTIONATION AND REDUCED FRACTIONATION RADIOTHERAPY IN UTERINE CERVICAL CANCER.

S. PENPATTANAGUL M.D.

ABSTRACT

During the first of January 1998 to 30th of September 2000, new uterine cervical cancer patients were double-blinded randomly devided into 2 groups to receive a daily radiation dose fraction of 200 cGy or 250 cGy. In the standard treatment group, 20 fractions of 200 cGy were given to the pelvis and 5 fractions of 200 cGy were given to the parametria in addition. Three more fractions were given to boost the parametrial doses in stage IIIB patients. In the reduced fractionation group 15 fractions were given for the whole pelvis and 4 fractions for the parametria. Two booster doses to the parametria were given in stage IIIB. Both groups were treated 5 fractions per week. Time-dose-fraction calculation formular (TDF) was used to determine the number of fractions. Both groups were given intracavitary radiation with Cesium LDR machine 24-26 Gy by single insertion. Residual tumor, local recurrent tumor, metastasis and complication were compared by T-test evaluation with 95 % confidence interval. The study showed worse local control in the reduced fractionation group in stage IIIB patients. Better local control in the reduced fractionation group in stage IB patients. No significant difference was seen in the early and late complication of radiation of both groups.

INTRODUCTION

Uterine cervical cancer is the most common cancer in female in THAILAND. Estimated number of new cases is 5590 cases per year.[1] Radiotherapy is the treatment of choice in both early and advanced stages of the patients. The result of treatment in advanced stages is poor.[2] There are about 21 radiotherapy centers in Thailand. 9 centers are in the capital city. The radiotherapy centers and number of beds for treatment of uterine cervix cancer is not enough. The patients have to wait about 3-12 weeks to start the treatment. Altered fractionation radiotherapy of tumor was studied in many centers from 1976 to 2000.[3,4,5,6,7] Table 1 shows each type of altered fractionation. The reduced fractionation was selected to be used in our department due to shortened total treatment time and we hope to get a better result with acceptable complication.

MATERIAL & METHOD

The study was started from 1st January 1998 to 30th September 2000. Only stage IB to stage IIIB patients were selected for double blind randomised study. Two groups were divided and treated by a standard fraction of 200 cGy/day and reduced fractionation of 250 cGy/day. In the 200-cGy group, 20 fractions were given to the whole pelvis and 5 fractions more were added to the parametria (midline block field). Three

DEPARTMENT OF RADIATION ONCOLOGY UDORN REGIONAL CANCER CENTER THAILAND

fractions of booster doses were added to the parametrium in stage IIIB. The 250-cGy group received 15 fractions to the whole pelvic and 4 fractions of midline blocked field. Two fractions of booster doses were added in stage IIIB. All cases received 5 fractions / week of AP and PA pelvic field alternatively with Cobalt teletheapy machine with additional brachytherapy by Cesium intracavitary insertion 24-26 Gy in single insertion. Table 2 shows the number of fractions, total doses and overall treatment time of each group. Table 3 shows the TDF of the treatment of each group. Amount of blood transfusion, level of cystitis and diarrhea for each case was recorded during irradiation period. The early response was evaluated at the last external irradiation day. The result of radiotherapy was evaluated at 3 months after Cesium insertion. The recurrent tumor and late complication were evaluated at 3-30 months follow-up period (the mean follow-up time is 19.65 months). Three significant late complications (subcutaneous fibrosis, radiation proctitis and radiation-cystitis) were grading with RTOG radiation morbidity scoring criteria. The T-test (Levene's Test of Equality of Variences) was used to evaluate the different results of both groups with 95 % confidence interval.

RESULTS

There are 234 uterine cervical cancer patients that received treatment at the radiotherapy unit Udorn Regional Cancer Center. 56 patients were not included in the study: 7 cases were recurrent or metastatic post treatment from other centers, 8 cases were post operation, 32 cases were stage IVA or IVB, 9 cases received external irradiation with other regimen due to severe bleeding.

After completion of the treatment, the number of patients for evaluation is 146 cases. 32 cases were excluded from the study: 1) no brachytherapy (19 cases), 2) delay brachytherapy (5 cases), 3) incomplete external irradiation (7 cases), 4) early death from other disease (1 case).

The patients in conventional dose group were 68 cases and in the reduced fractionation group were 78 cases (table 4). The result of the study was shown in table 5-8. Table 10 and table11 show the Radiotheapy Oncology Group (RTOG) criteria for grading of radiation morbidity. Severe complication grade 4-5 was not detected in both arms. No definite different in the number of blood transfusion and the complication of treatment in both groups. But there is significant difference in result of tumor control in stage IIIB patients. The number of residual tumor and recurrent tumor in the reduced fractionation group (250 cGy) is significantly higher (p value=0.005). Therefore, good result in the reduced fractionation group was seen in stage IB patients (p value = 0.002).

TABLE 1. Type of altered fractionation radiotherapy.

	Dose /F. (cGy)	F./day	Treatment days/week	Total dose (cGy)	Total time (days)
1. standard fractionation	180-200	1	5	6500-7000	45-56
2. hyperfractionation	110-125	2	5	More	Equal
	70-80	3	5	More	Equal
3. accelerated hyperfractionation	130-170	2	5	More	Less
4. accelerated fractionation	180-200	1	6-7	Less	Less
	180-200	2	5	Less	Less
5. hypofractionation	>210	1	<5	Less or equal	Less or equal
6. accelerated hypofractionation	>210	>1	1-5	Less	Less
7. concomittent boost field					
8. mixed fractionation					
9. split course external irradiation					
10. reduced fractionation	>200	1	5	less	less

TABLE 2. Radiation treatment plan of each group.

		Whole pelvis (fractions)	Parametrium (fractions)	Boost RT at Pm.	Total F.	Total dose (cGy)	Total day
Standard fraction	Stage IB, IIA, IIB, IIIA	20	5	-	25	4000+ 1000	33-35
	Stage IIIB	20	5	3	28	4000+ 1000+ 600	38
Reduced fractionation	Stage IB,IIA,IIB,IIIA	15	4	-	19	3750+ 1000	25
	Stage IIIB	15	4	2	21	3750+ 1000+ 500	29

TABLE 3. Time-dose-fractions table (TDF).

		Whole pelvis	parametrium	Boost Pm	Total TDF
Standard fraction	Stage IB,IIA,IIB,IIIA	65.36	16.34	-	81.70
	Stage IIIB	65.36	16.34	9.80	91.50
Reduced fractionation	Stage IB,IIA,IIB,IIIA	69.09	18.42	-	87.51
	Stage IIIB	69.09	18.42	9.21	96.72

TABLE 4. Staging of tumor.

	200 cGy	250 cGy
Stage IB	15	25
Stage IIA	25	28
Stage IIB	14	16
Stage IIIA	-	2
Stage IIIB	14	17
Total cases	68	78
age	31-68 years mean 48.59 ,SD 9.15	31-72 years mean 49.67,SD 10.75
no significant difference in stage (p= 0.95)		

TABLE 5. Number of local residual tumors and recurrent tumors.

	200 cGy		250 cGy		P value (95%CI)
	cases/total	%	cases/total	%	
Stage IB	4/15	26.7	2/25	8.0	.002*
Stage IIA	9/25	36.0	5/18	27.8	.26
StageIIB	5/14	35.7	5/16	31.3	.625
Stage IIIA	-	-	1/2	50.0	-
Stage IIIB	7/14	50.0	14/17	82.3	.005*
Total cases	25/68	36.7	27/78	34.6	.594

TABLE 6. Early complications and late complications.

		200 cGy	250 cGy	P value	95 %CI	
					lower	upper
1. early cystitis	Grade 1	36	38	.950	-.11	.27
	Grade 2	4	3			
	Grade 3	-	-			
2. early diarrhea	Grade 1	23	19	.378	-.41	.23
	Grade 2	17	28			
	Grade 3	6	6			
3. blood transfusion				.935	-.27	.25
4. subcutaneous fibrosis	Grade 1	10	18	.211	-.30	.12
	Grade 2	5	3			
	Grade 3	-	2			
5. late cystitis	Grade 1	6	2	.130	-5.48E-02	.13
	Grade 2	-	1			
	Grade 3	-	-			
6. late proctitis	Grade 1	10	12	.892	-.16	.17
	Grade 2	3	3			
	Grade 3	-	-			
7.comparing total late complications				.554	-.37	.28
*No grade 4,5 complication detected in this study						

TABLE 7. Number of metastatic cases (medium follow up time 19 months).

stage	200 cGy		250 cGy	
	Cases/total	%	Cases/total	%
All stage	6/68	8.8	7/78	9
Stage IB	2/15	13.3	0/25	0
Stage IIA	1/25	4	3/28	10.71
Stage IIB	2/14	14.28	0/16	0
Stage IIIA	-	-	0/2	0
Stage IIIB	1/14	7.1	4/17	23.5

TABLE 8. Survival of the patients (with and without tumor).

Stage	Survival	200 cGy		250 cGy	
		Cases/total	%	Cases/total	%
Stage IB	6 months	15/15	100	25/25	100
	12 months	15/15	100	18/18	100
	18 months	12/12	100	12/12	100
	24 months	6/6	100	5/5	100
Stage IIA	6 months	25/25	100	18/18	100
	12 months	21/22	95	15/16	94
	18 months	15/18	83	11/13	85
	24 months	7/8	87	2/3	67
Stage IIB	6 months	14/14	100	16/16	100
	12 months	9/10	90	10/11	91
	18 months	4/5	80	4/7	57
	24 months	2/3	67	1/3	33
Stage IIIA	6 months	-	-	2/2	100
	12 months	-	-	1/1	100
	18 months	-	-	1/1	100
	24 months	-	-	1/1	100
Stage IIIB	6 months	13/14	93	16/17	94
	12 months	11/12	92	12/12	100
	18 months	7/8	87	5/8	62
	24 months	4/5	80	3/4	75
All stages	6 months	67/68	98	77/78	99
	12 months	56/59	95	56/58	96
	18 months	38/43	88	33/41	80
	24 months	19/22	86	12/16	75

TABLE 9. Possible factor in pelvic failure [5]

Patient-related
1. low socioeconomic level
2. age younger than 35 years
3. anemia
4. Karnofsky performance status below 90
5. high stage of tumor
6. bulky tumor
7. nodal metastases
8. small cell histologic type
Treatment-related
1. low-energy teletherapy
2. lack of brachytherapy
3. single brachytherapy insertion versus two or more
4. prolong rest period between teletherapy and brachytherapy
5. insufficient radiation dose
6. persistent of tumor at end of radiation therapy

TABLE 10. Acute Radiation Morbidity Scoring Criteria (RTOG).

	Score	Clinical signs and symptoms
1. acute radiation cystitis	Grade 1	Frequency of urination or nocturia twice pretreatment habit; dysuria, urgency not requiring medication
	Grade 2	Frequency of urination or nocturia less frequent than every hour; dysuria, urgency, bladder spasm requiring local anesthetic.
	Grade 3	Frequency with urgency and nocturia hourly or more frequently; dysuria, pelvic pain, or bladder spasm requiring regular, frequent narcotic; gross hematuria with or without clot passage
	Grade 4	Hematuria requiring trasfusion; acute bladder obstruction not secondary to clot passage, ulceration, or necrosis
2.acute radiation proctitis	Grade 1	Increased frequency or change in quality of bowel habits not requiring medication; rectal discomfort not requiring analgesics
	Grade 2	Diarrhea requiring parasympatholytic drugs; mucous discharge not necessitating sanitary pads; rectal or abdominal pain requiring analgesics
	Grade 3	Diarrhea requiring parenteral support; severe mucous or blood discharge necessitating sanitary pads; abdominal distention (flat plate radiograph demonstrates distended bowel loops)
	Grade 4	Acute or subacute obstruction, fistula or perforation, GI bleeding requiring transfusion, abdominal pain or tenesmus requiring tube decompression or bowel diversion

TABLE 11. Late Radiation Morbidity Scoring Criteria (RTOG).

	score	Clinical signs and symptoms
1. subcutaneous fibrosis	Grade 1	Slight induration (fibrosis) and loss of subcutaneous fat
	Grade 2	Moderate fibrosis but asymptomatic, slight field contracture
	Grade 3	Severe induration and loss of subcutaneous tissue; field contracture> 10 % linear measurement
	Grade 4	necrosis
2. radiation cystitis	Grade 1	Slight epithelial atrophy, mild telangiectasia
	Grade 2	Moderate frequency, generalized telangiectasia, intermittent macroscopic hematuria
	Grade 3	Severe frequency and dysuria, sever generalized telangiectasia (often with petechiae), frequenct hematuria, reduction in bladder capacity
	Grade 4	Necrosis, contracted bladder (capacity< 100 cc), severe hemorrhagic cystitis
3. radiation proctitis	Grade 1	Mild diarrhea, mild cramping, bowel movement 5 times daily, slight rectal discharge or bleeding
	Grade 2	Moderate diarrhea and colic, bowel movement > 5 times daily, excessive rectal mucous or intermittent bleeding
	Grade 3	Obstruction or bleeding requiring surgery
	Grade 4	Necrosis, perforation, fistula

DISCUSSION

Uterine Cervical Cancer is the most common female cancer in Thailand. Early detection of the tumor is in the process of highly motivated in the attempt to reduce the number of advanced stage tumors. Poor result of radiotherapy is in the late stage cancer.[2] There are many new lines of treatment in the process of investigation to get better local control. Altered fractionation radiotherapy is used in many centers.[8,9] But the results are not satisfactory. Reduced fractionation radiotherapy was used in this study because of the benefit of decreasing the overall treatment time and the tumor response rate may be increased. In many studies no significant benefit had been shown.[8,9] The disadvantages of reduced fractionation with increased dose per fraction are the increasing of early and late complications of radiation. The 250 cGy dose /fraction that were used in our study is not a very high dose. The treatment was given daily as the conventional treatment. TDF calculation is used to decide the number of fractions. TDF of reduced fractionation in this study is slightly higher than standard fraction (table 3). The total treatment days were 10 days shorter than the standard group. Number of blood transfusion and degree of early

complications were in our interest during radiotherapy. But no significant difference was detected. Late complication of radiation at the time of evaluation also shows no significant differences.

The result of treatment in the advanced stage (IIIB) was opposite to our expectation. The lower total tumor doses that had been given may be the reason of the poor results in the late cases.

On the contrary a better result was seen in stage IB. In this study, we didnot take the sizes of the tumor as a criteria for evaluation of the result of the response to treatment. Tumor size is, in fact, one important factor of tumor control.[10] Larger dose fraction of reduce fractionation group may be more effective to the tumor than the standard dose fraction. The result of stage IB is different from the study of Perez.[11] Total number of patients in this study is not large enough. Further larger study is needed to confirm the result.

REFERENCES

1. Vatanasapt V, et al.: Cancer in Thailand 1988-1991. IARC Technical Report no 16,1993:59-60.
2. Jampolis S, Andras J, Fletcher GH: Pelvic failure in Ca Cervix after radiation: Radiology 1975; 115: 681-685
3. Greenberg M, Eisert DR, Cox JD: Initial evaluation of reduced fractionation in the irradiation of malignant epithelial tumors. Am J Roentgen Radium Ther Nucl Med 1976; 126: 268-278
4. Byhardt RW, Freenberg M, Cox JD: Local control of squamous cell carcinomas of the oral cavity and oropharynx with 3 vs 5 treatment fractions per week, Int J Radio Oncol Biol Phys 1977;2:415-420
5. Marcial VA: Radiation Therapy of cervical cancer: present at the National conference of Gynecologic Cancers, Orlando, Florida, April 2-4,1992
6. Harwood AR, Beale FA, Cummings JB, et al: Supraglottic laryngeal carcinoma: An analysis of dose-time-volume factors in 410 patients: Int J Radio Oncol Bio Phys 9:311,1983
7. Wang CC: Altered fractionation radiation therapy for gynecologic cancers. Cancer 60:2064-2067,1987
8. Marcial VA, Amato D, Marks RD, et al: Split-course versus continuous pelvis irradiation in carcinoma of the uterine cervix: A prospective randomized clinical trial of the radiation therapy oncology group. Int J Radiat Oncol Bio Phys 9:431-436,1983
9. Marcial VA, Komaki R, : Altered fractionation and extended field irradiation of carcinoma of cervix.Cancer 76 (suppli) : 2152-2158, 1995
10. Perez CA, Grigsby PW, Nene SM, Camel HM, Galalatos A, Kao MS, Lockett MA; Effect of tumor size on the prognosis of carcinoma of the uterine cervix treated with irradiation alone: Cancer 62: 2796-2806,1992
11. Perez CA, Breaus S, Madoc-Jones H, et al: Radiation therapy alone in the treatment of carcinoma of uterine cervix.I.Analysis of tumor recurrence. Cancer 51: 1393-1402,1983