

ULTRASONOGRAPHIC EVALUATION OF HEPATIC METASTASES OF MALIGNANT DISEASES WITH CYTOPATHOLOGICAL CORRELATION

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Abstract:

Objective: A prospective study was carried out to evaluate the role of ultrasonography in the diagnosis of hepatic metastasis and also to preoperative determination of hepatic metastasis and its validity in diagnostic process.

Methods: A total of 52 patients having hepatic metastasis were enrolled in this study taken from Department of Hepatology of two tertiary level medical institutions. After sonographic evaluation of the metastatic lesion, cytopathology was done in all these patients. With written informed consent they were taken care of from the admission up to diagnosis of the hepatic metastasis, and subsequent management in hepatology unit.

Place and period of study: Department of Radiology & Imaging, Department of Pathology and Department of Hepatology of Bangabandhu Sheikh Mujib Medical University (BSMMU) Hospital and of Dhaka Medical College Hospital (DMCH), during the period between July 2006 and June 2007.

Results: The mean age of the patients was 51.20±11.9 years, ranging from 21 to 69 years. The highest incidence was in 60-69 years age group. The male and female ratio was 3.7:1. The most common symptom was pain with upper abdominal mass (73.1%), and others were anorexia and nausea with weight loss (67.3%), jaundice (28.8%) and ascites (23.1%). Only the right lobe of the liver was involved in 51.9% cases, left lobe in 28.8% and in 19.2% both lobes of the liver were affected. Hepatic metastasis was found as unifocal lesion in 7.7% and multifocal lesions in 92.3% cases. The echopattern was found 57.7% hyperechoic, 28.8% hypoechoic, and rest 13.5% mixed pattern. All cases were metastasis in sonography findings whereas 90.4% cases were metastasis and 9.6% other lesions in cytopathological findings. The validity of ultrasonography were determined by calculating sensitivity, specificity, accuracy, positive predictive value and negative predictive value which were 93.6%, 80.0%, 92.3%, 97.8% and 57.1% respectively.

Key words: Hepatic metastasis, hepatic mass, ultrasonography, cytopathology, validity.

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Introduction

Hepatic metastases are common in the adult and 20 times more frequent than primary malignancy of liver¹. The liver is second in prevalence only to regional lymph node as a site of metastatic disease. Approximately 25% to 50% of all patients who die of malignant disease have metastatic disease to the liver

at autopsy¹. A silent primary neoplasm with hepatic metastases is most often found to be a result of pancreatic, stomach or lung carcinoma². Metastases are nearly always multiple. They are more frequently encountered in the right lobe than the left as large mass of the right lobe and its greater blood flow³. The primary neoplasm is asymptomatic

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in about half the patients⁴. However massive destruction of liver substance or direct obstruction to major bile ducts may occur⁵. There is usually rapid liver enlargement with fever, weight loss and jaundice. Peritoneal dissemination frequently results in ascites⁴. Significant advances in cross-sectional imaging modalities like ultrasound now allow not only detection but often non-invasive characterization of focal and diffuse hepatic process. The presence of metastatic disease to the liver is a *prima determinate* of survival. Over the last decade, there have been tremendous advances in the treatment of metastatic disease of the liver. Liver resection or liver directed therapy is justified to select patients when extrahepatic malignancy is not present and the patients can tolerate therapy³.

In patients with suspected metastatic disease, several imaging procedures are used to detect liver metastases. They include ultrasonography (USG), computed tomography (CT), magnetic resonance imaging (MRI), angiography and radio nuclide scanning. In general, however, USG, CT, and MRI are more accurate than angiography or radionuclide scanning. CT is more specific for detection of tumour nodules but because of its less availability, expense and radiation hazards, it is reserved for complicated cases which can not be detected by other modalities. MRI is also specific but more expensive and lack of its availability makes it more difficult to use as primary modality of investigation. Ultrasound is an excellent screening modality for metastatic liver disease because of its relative accuracy, speed, lack of ionizing radiation and availability⁶. It allows not only detection but often non-invasive characterization of focal and diffuse hepatic process. It is also selected as because it can be done repeatedly and rapidly with least expense. When a patient with previously diagnosed malignancy subsequently develops a liver mass, a fine needle aspiration is performed for histopathological confirmation⁷. Ultrasonographic guidance is usually preferred for its simplicity, capability of real time monitoring and flexible needle tract placement^{6,7}. Cytopathological confirmation is also needed for diagnosis of hepatic

metastasis⁵. Therefore, the aims of the present study were to correlate ultrasonography and cytopathological findings in hepatic metastases and to determine the sensitivity and specificity of ultrasonography to diagnose hepatic metastases of malignant diseases compared with cytopathological findings.

Methods

This was a prospective, cross-sectional and consecutive observational study which was done in the Department of Radiology & Imaging and Department of Pathology and Department of Hepatology of Bangabandhu Sheikh Mujib Medical University (BSMMU) Hospital and Dhaka Medical College Hospital (DMCH), between July 2006 and June 2007. A total of 52 patients were included in this study after taking written informed consent from them, who could fulfill the selection criteria as defined below from Department of Hepatology of BSMMU Hospital and DMCH.

Inclusion Criteria:

- i) Patients with age of 21 to 69 years,
- ii) Patients having clinical manifestations of hepatic metastases of malignant diseases, and
- iii) Patients having a known primary malignancy with sonographic evidence and cytopathological reports.

Exclusion criteria:

- i) Patients unwilling to give consent.
- ii) Patients who has not undergone pathological examination, and
- iii) Patients with abnormal bleeding profile.

At first all these patients were evaluated by detail history, clinical examination with special emphasis on hepato-biliary system. Sonographic examinations were then performed for the evaluation of hepatic metastases. Lobe distribution, multiplicity, echocharacter were evaluated in all the cases. Then fine needle aspiration under ultrasonographic guidance and cytopathological examinations were done and finally were correlated with the sonographic diagnoses.

Data were collected in a predesigned structured data collection sheet. All the relevant collected

data were compiled and statistical analysis were done by using SPSS version 11.0. The results were presented in tables. Z test, Chi-square test and validity test were done where applicable.

Results

This study included 52 patients having metastasis in liver diagnosed clinically. They were divided into five age groups. The mean age of the patients was 51.20±11.9 years, ranging from 21 to 69 years. The maximum patients were in >60 years age group and least was in 21 to 29 years age group (Table-I). Here, 41(78.8%) were male and 11(21.2%) were female (Table-II). The common symptoms in patients, e.g. 38(73.1%) had pain with upper abdominal mass followed by 35(67.3%) anorexia and nausea with weight loss, 15(28.8%) jaundice and 12(23.1%) ascites (Table-III).

Table-I

Age distribution of study subjects (n=52)

Age group (years)	Number	Percentage	Mean±SD (years)
21-29	3	5.8	51.20±11.9
30-39	7	13.5	
40-49	11	21.2	
50-59	14	26.9	
60-69	17	32.7	

Table-II

Sex distribution of patients (n=52)

Sex group	Number	Percentage
Male	41	78.8
Female	11	21.2

*** Z=4.15, P<0.001

Table-III

Presenting features of the patients (n=52)

Features	Number of patients	Percentage
Pain with upper abdomen mass	38	73.1
Anorexia and nausea with weight loss	35	67.3
Jaundice	15	28.8
Ascites	12	23.1

Mainly right lobe of the liver was involved in most cases i.e. 27 (51.9%) patients, and among the others left lobe of the liver involved in 15(28.8%) patients and the rest 10(19.2%) were involved in both lobes of the liver (Table-IV). Among 52 patients, 4(7.7%) were with unifocal lesions and 48(92.3%) multifocal lesions (Table-V). In patients diagnosed by ultrasonography, it was observed that 15(28.8%) were hypoechoic, 30(57.7%) hyperechoic and rest 7(13.5%) mixed pattern (Table-VI). Of total 52 cases, 45(86.5%) cases were metastasis and 7(14.5%) cases were other lesions in sonography findings. On the other hand 47(90.4%) cases were metastasis and 5(9.6%) cases were other lesions in cytopathological findings (Table-VII). Every patient having metastasis which was diagnosed by sonography was correlated with cytopathological diagnosis after collection of the report from the respective case. Of total 52 cases, 45(86.5%) cases were hepatic metastasis and 7(14.5%) cases were other lesions in sonography findings. Only 1 case was found as other lesions in cytopathological among the all hepatic metastasis, which were diagnosed by ultrasonogram. On the other hand, 47(90.4%) cases were hepatic metastasis and 5(9.6%) cases were other lesions in cytopathological findings. Among 7 other lesions cases which were diagnosed by ultrasonogram, 3 cases were hepatic metastasis and the rest 4 cases were other lesions in cytopathological findings (Table-VIII).

Table-IV

Distribution of lesions in different lobes (n=52)

Lobe	Number of Cases	Percentage
Right lobe	27	51.9
Left lobe	15	28.8
Both lobes	10	19.2

Table-V

Metastasis based on unifocal and multifocal lesions by sonographic diagnosis (n=52)

Lesions	Metastasis	
	Number of cases	Percentage
Unifocal	4	7.7
Multi focal	48	92.3

Table-VI
Echopattern of lesions (n=52)

Echogenicity	Number of cases	Percentage
Hypoechoic	15	28.8
Hyperechoic	30	57.7
Mixed	7	13.5

Table-VII
Analysis of metastasis and other lesions (n=52)

Modality	Metastasis	Other lesions
Ultrasonography	45(86.5%)	07(14.5%)
Cytopathology	47(90.4%)	05(9.6%)

Table-VIII
Sonography and cytopathological correlation of metastasis

Sonography	Cytopathological diagnosis		
	positive for metastasis	negative for metastasis	Total
positive for metastasis	44	1	45
negative for metastasis	3	4	7
Total	47	5	52

$\chi^2=21.02, p=0.001, df=1$

The validity of ultrasonography were determined by calculating sensitivity, specificity, accuracy, positive predictive value and negative predictive value which were 93.6%, 80.0%, 92.3%, 97.8% and 57.1% respectively (Table-IX).

Table-IX
Validity test of the ultrasound in diagnosis of metastasis

Validity test	Percentage
Sensitivity	93.6
Specificity	80.0
Accuracy	92.3
Positive predictive value	97.8
Negative predictive value	57.1

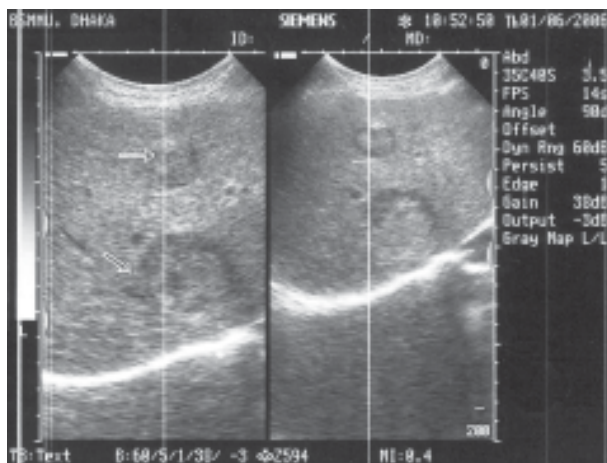


Fig.-1. Sonographic image of multiple metastatic lesions of the liver (Bull's eye appearance) of a 58 years old female patient.

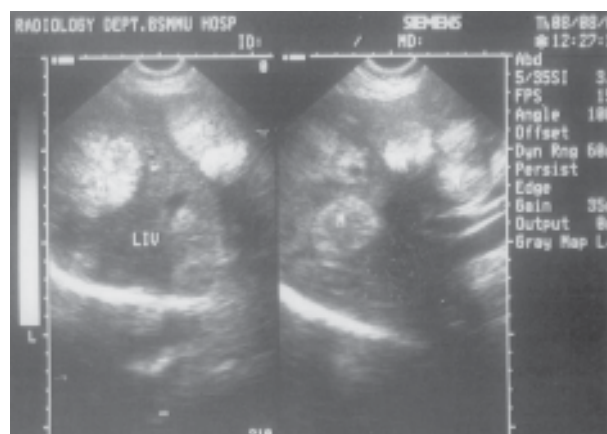


Fig.-2. Sonographic image showing multiple hyperechoic metastatic lesions of the right lobe of the liver of a 40 years old male patient.

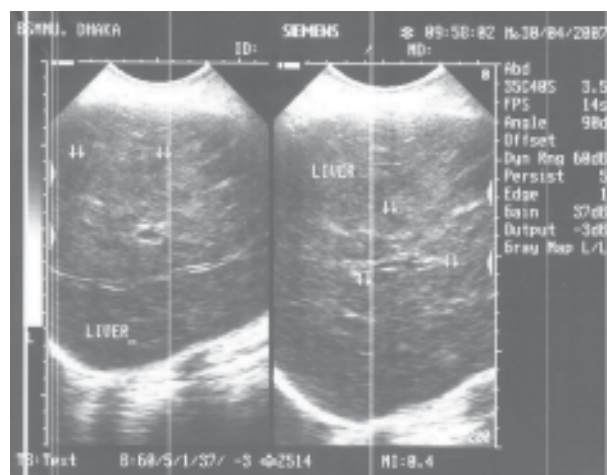


Fig.-3. Sonographic image showing multiple mixed echogenic metastatic lesions of the right lobe of liver of a 55 years old male patient.



Fig.-4. Sonographic image of multiple hypoechoic metastatic lesions of the liver of a 63 years old male patient.

Discussion

Turkay et al.⁸ have shown in their series that the mean age of the patients was 59.7±11.99 years which is slightly higher than that of the present study. Charansangavej et al.⁹ observed that the male female ratio was 3:1 to 4:1 which is in agreement with the present study. Yoshida et al.¹⁰ have shown 85.0% cases of metastases were multiple which is similar with the present study where 92.3% patients were multifocal lesions. This is also similar to the present study. Seheible et al.¹¹ have shown in a prospective study on 76 patients of hepatic metastasis that echographic pattern was found 18.0% hypoechoic, 37.0% hyperechoic, 28.0% was mixed pattern and 17.0% Bull's eye lesions. The results of the present study are not similar to the above mentioned study as they also observed the bull's eye lesions.

Turkay et al.⁸ observed the sensitivity of ultrasonography in diagnosis of hepatic metastasis which was 85-90%. Almost similar value was obtained by Reinhold et al.¹². Both investigations support the results of the present study. Dick and Watkinson¹ found the specificity of ultrasonography in diagnosis of hepatic metastasis was 80%. This finding is similar with the present study where specificity was found 80.0%. Turkay et al.⁸ further correlated the ultrasonographic findings with post-operative cytopathology specimen. They have observed that the positive predictive value was 97.8% with the

histopathology findings. The results of the ultrasonography and cytopathological findings observed in the present study also support the above evidence. Turkay et al.⁸ found accuracy 73% to 94 %. Middleton et al.¹³ and Fisher et al.¹⁴ also found accuracy of ultrasonography, which were 93.0% and 86.0% respectively. The present study strongly supports the above mentioned studies.

It was also observed that the negative predictive value in the present study was 57.1%. However, there is no known evidence of such study on this regard till date in our country. The results of both ultrasonography and cytopathology in the present series are almost similar. Therefore, the inference can be drawn that ultrasonography is a good modality in the evaluation of hepatic metastasis.

Conclusion

As the cytopathological diagnosis of the present study significantly correlated with the ultrasonographic findings and the validity tests are almost identical as observed by other investigators, it can be concluded that the ultrasonography is a useful diagnostic modality in diagnosis of hepatic metastasis. Hence, ultrasonography has definite value in the diagnosis of hepatic metastasis. Moreover, it is simple, non-invasive, rapid diagnostic tool without having any risk of radiation.

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