

Cytomorphological spectrum of hepatic lesions in image guided fine needle aspiration at tertiary care hospital

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Abstract

Introduction: The majority of malignancies in the liver are metastases. Among the metastatic carcinomas adenocarcinomas are being the most common type. Hepatocellular carcinoma (HCC) is the most common primary malignant tumor in the liver. It is the fifth most common malignant tumor in men and eighth most common in women worldwide. For focal liver lesions Ultrasonography (USG) or computed tomography (CT)-guided fine needle aspiration cytology (FNAC) is an accurate method for a definite diagnosis. The advantage of this technique is its high diagnostic accuracy leading to obsolete use of older technique of blind percutaneous biopsy using a coarse needle. **Aims of the Study:** To describe cytomorphological features of various liver lesions with their clinical correlation and diagnostic accuracy of image-guided FNAC in the diagnosis of liver diseases **Materials and Methods:** The present study was undertaken in a Tertiary Care Hospital of Yenepoya Medical College, Mangaluru and 100 cases were studied over a period of 3 years from 2013 to 2016 **Results:** Of the total diagnosed cases 61 % malignant while only 10% were inflammatory or benign lesions. Among malignant cases (61 cases) majority of the cases were metastatic lesions (41%) and remaining 20 % cases were primary liver lesions. In our study, 20 primary lesions from liver were detected of which 19 were HCC and a single case was intra hepatic cholangiocarcinoma were diagnosed. **Conclusion:** Adenocarcinoma was most common metastatic tumor. While in the primary tumor, HCC were most common **Keywords:** Liver, guided, adenocarcinoma, HCC.

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INTRODUCTION

Liver disease is the third most common cause of death among individuals between age 25 and 59 years¹. Liver is the second largest organ of the body. The majority of malignancies in the liver are metastases. Among the metastatic carcinomas adenocarcinomas are being the most common type². Hepatocellular carcinoma (HCC) is the most common primary malignant tumor in the liver. It is the fifth most common malignant tumor in men and eighth most common in women worldwide³. Fine needle aspiration cytology (FNAC) has been tested and proven

to be a very efficacious means of obtaining tissue from many different body sites for diagnosis. It was applied for liver around 1985⁴ FNAC is a rapid, minimally invasive method that can be practiced for various pathological evaluation of both benign and malignant hepatic lesions. Inflammatory lesions and diffuse liver diseases may mimic mass like lesions or appear as non homogeneous lesions on radiographs. The differential diagnosis of hepatic mass lesions includes primary liver tumors (Benign and malignant), metastatic deposits, congenital and acquired cysts, abscesses and granulomas. Such lesions can also be sampled by FNA to rule out neoplasms and differentiate it from other diagnosis.⁵ For focal liver lesions Ultrasonography (USG) or computed tomography (CT)-guided fine needle aspiration cytology (FNAC) is an accurate method for a definite diagnosis⁶. The advantage of this technique is its high diagnostic accuracy leading to obsolete use of older technique of blind percutaneous biopsy using a coarse needle⁷ Clinical, serological and radiological findings are not reliable to differentiate between a benign and malignant lesion but are useful in making differential diagnosis of various hepatic lesions⁸ Thus, guided FNAC has gained

increasing popularity as the diagnostic procedure of choice. During the procedure, involvement of a cytopathologist increases overall diagnostic accuracy.⁹ It is a valuable tool for identification of malignant lesions and also works as an accessory tool in diagnosis of benign and inflammatory disease of the liver.¹⁰ FNAC is the diagnostic tool with minimum risk, less discomfort to the patient with an added advantage of multiple aspirations at one sitting in the outpatient department. It has proved to be superior to core-needle or open biopsy with an advantage of minimal complications and early diagnosis of the lesion.¹¹ With the real-time imaging by USG, there is no ionizing radiation, puncture is possible in any direction and needle position can be constantly controlled and monitored.¹² USG guided FNAC is a relatively safe procedure in trained and competent hands and it gives fairly accurate results, thereby helping the clinician to plan the best line of treatment. However, occasionally exact diagnosis is not possible with information obtained by FNA cytological material and the possibility of false negative and indeterminate diagnosis always exists. Thus a negative result should always be correlated with the clinical findings and a repeat aspiration may be necessary. An attempt to obtain additional information can be made via the preparation of cell block from any residual material after the conventional smears are prepared. Cell block analysis can obviate the need for repeat needle passes. Also, cell block sections are suited to ancillary techniques like histochemical stains and immunocytochemistry.^{2,3} Liver FNAC is a safe technique with a low rate of serious complications, mostly bleeding or infection. Absolute contraindications for liver FNAC are markedly abnormal coagulation parameters, and relative contraindications include the location of focal lesions in the liver parenchyma that cannot be safely accessed because they are close to large vascular structures.¹³

MATERIALS AND METHODS

Yenepoya Medical College, Mangaluru is one of the largest and well known for diagnosis and management of oncology cases in Dakshina Kannada (Karnataka). The present study was undertaken in a Tertiary Care Hospital of Yenepoya Medical College Mangaluru and 100 cases were studied over a period of 3 years from 2013 to 2016. A thorough clinical history of every patient with particular reference to age, presenting complaints of pain in right upper quadrant of abdomen, weight loss, anorexia, abdominal mass, fever, pruritis and jaundice, abdominal distention with ascites, any of the other malignancy, background cirrhosis were recorded. Few serological parameters (LFT, HBsAg, HCV) and tumor markers (AFP, CEA, CA-125) were recorded.

All patients underwent thorough general physical examination, abdominal examination and majority of the patients were found to have hepatomegaly. The procedure of FNA was explained to the patient seeking, an informed consent and complete co-operation for the procedure. Prothrombin time, bleeding time were checked for each and every patient just before performing the procedure. Under aseptic precautions, FNAC was performed using 20 or 22 gauge, 90 mm spinal needle attached to a 10 ml disposable syringe. The prepared smears were stained with Papanicolaou and Haematoxylin and Leishman stains. Periodic acid-Schiff, Gram's and Ziehl-Neelsen stains were done wherever required. At least 6 smears were made, two air-dried for Leishman and another alcohol fixed for Papanicolaou (PAP) staining which gives better nuclear details. Remaining slides were used for special stains whenever necessary. For cell block analysis, all macroscopically visible tissue fragments in the aspirated material were collected in 10% formaldehyde solution and sedimented by centrifugation and stained by H and E stain.

RESULTS

Fine needle aspiration of a total of 100 cases were studied during three years. Age group ranged from 19 to 80 years with maximum cases in the range of 61-70 years (TABLE 1). Out of 100 cases 61 were male patients and females were comprising of 39% with male to female ratio 1.6:1. The chief complaints were pain in right upper quadrant of abdomen, weight loss, anorexia, abdominal mass and hepatosplenomegaly.

Table 1: Age wise distribution of hepatic lesions

Age	Frequency (No of cases)
0-10	00
11-20	01
21-30	01
31-40	06
41-50	15
51-60	34
61-70	35
71-80	08
Total	100

Of the total diagnosed cases 61% malignant while only 10% were inflammatory or benign lesions. Among malignant cases (61 cases) majority of the cases were metastatic lesions (41%) and remaining 20% cases were primary liver lesions. In our study, 20 primary lesions from liver were detected of which 19 were HCC and a single case was intra hepatic cholangiocarcinoma were diagnosed. Metastatic adenocarcinoma was most common (48%) among metastatic lesions followed by metastatic carcinoma- unclassified (46%), Single cases of other metastatic lesion like small cell carcinoma, metastatic papillary adenocarcinoma were also reported. Majority of

the metastatic adenocarcinomas were from GIT and metastatic small cell carcinomas were from lung. Metastatic lesions were diagnosed on the basis of characteristic features of the primary lesion depending on the type of tumour. And 3 cases of suspicious of malignancy also reported.(TABLE 2)

Table 2: Lesions of liver

Type of tumor	Frequency
1 Primary tumor	
a.Hepatocellular carcinoma	19
b.Intra Hepatic Cholangiocarcinoma	01
2 Secondaries	
a.Metastatic carcinoma - unclassified	19
b.Metastatic adenocarcinoma	20
c.Metastatic – small cell type	01
d.Papillary adenocarcinoma	01
3 Nodular hyperplasia	01
4 Regenerative atypia	01
5 Tuberculosis	02
6 Abscess	03
7 Favouring / suspicious for malignancy	03
8 Reactive changes	08
9 Inadequate sample	21
Total	100

Among 10 cases of benign or inflammatory, each cases of nodular hyperplasia and regenerative atypia, 2 cases of tuberculosis, 3 cases of abscess were reported. 8 cases showed reactive changes and 21 cases were inadequate to opine.

DISCUSSION

The liver is a common site for various non-neoplastic and neoplastic lesions such as primary liver tumors (benign or malignant), metastatic deposits, congenital and acquired cysts, abscesses and granulomas. Liver cancer is the sixth most common cancer worldwide, accounting for 5.7% of the overall incident cases of cancer.^{14,15,16} There is wide geographic variability in incidence with a majority of the cases occurring in developing countries (82%, 366,000 new cases estimated in males in 2002, 147,000 in women) compared with developed countries (74,000 new cases in men and 36,000 women)¹⁷. Surprisingly, in fact, liver cancer is the third most common cancer in developing countries among men after lung and stomach cancer. It is also between two and eight times more common in men than in women¹³. The present study had 79% adequate aspirates Our study shows inadequacy rate of 21 % deep-seated lesions. Other studies like Bell *et al*¹⁸, Talukdar¹⁹ reported inadequacy rate of 13%, 6.5%, and 5.7% respectively. In our study, age range was 19 to 80 years with male predominance M:F ratio being 1.6: 1. In the study done by Naggada *et al*²⁰ and Talukdar age range

from 8 to 80 years with male predominance was reported. Maximum number of malignant cases were found in 61-70 years of age groups with 35 cases next in order of frequency were in 51-60 years with 34 cases. Similar results were seen in the earlier study conducted by Gatphoh *et al*²¹ found out the most common age group of the malignant liver disease was 51-60 years. In our study, among malignancies majority of the cases were metastatic carcinomas (65%). Our results were on nearly concordance with Tao *et al*¹⁰ and Barbhuiya *et al*²² with metastatic lesion being 75% and 74.9% respectively. Some studies have shown metastatic liver malignancy as high as 90%. Metastatic adenocarcinoma was the most common lesion reported in our study. This results are supported by Barbhuiya *et al*. Radiologically multiple liver lesions usually indicates liver metastasis(most commonly from adenocarcinoma of the colon, stomach, lung or prostate).²³ Cytological features used for the diagnosis of liver cell carcinoma over metastatic carcinoma were polygonal cells with centrally placed nuclei, trabecular pattern of growth, cells separated by sinusoidal stroma, nuclear pseudoinclusions, giant cells and bile secretion. Bottles *et al*²⁴ reported the key criteria for the diagnosis of HCC over metastatic malignancies which included polygonal cells with centrally placed nuclei, cells separated by sinusoidal capillaries and bile. Similarly, Soyuer *et al*.²⁵, by stepwise logistic regression analysis showed that centrally located nucleus in an atypical cell, intranuclear inclusion and bile were the three most predictive parameters for the differentiation of metastatic carcinoma from HCC.²⁶ The primary liver malignancy in our study were HCC (19 cases) and a case of intrahepatic cholangiocarcinoma. In this study, HCC was differentiated from other non-malignant conditions of the liver by different distinctive cytological features such as high cellularity, trabecular pattern, acinar pattern, endothelial cells lining or transgressing cell clusters, round to polygonal cells with centrally located hyperchromatic nuclei, single or multiple prominent nucleoli, many atypical stripped nuclei in the background, intracytoplasmic eosinophilic inclusions, intranuclear cytoplasmic inclusions and sinusoidal stroma etc. Cells clusters mainly the trabeculae are seen in better differentiated tumors. With decreasing differentiation single-lying cells become more prominent and endothelial relationships with HCC cell groups are diminished. Cohen *et al*²⁷ put forward that high N/C ratio, trabecular pattern of arrangement and atypical naked hepatocytic nuclei were the three primary criteria for diagnosis HCC and when these three criteria were used, the sensitivity of diagnosing HCC by FNAC was 100% and the specificity was 87%. Kung *et al*.²⁸ suggested that more attention should be paid to the sinusoidal stroma for diagnosis of

HCC by FNA. Soyuer *et al.*²⁵, in their stepwise regression analysis showed that multinucleated tumor giant cells, cytoplasmic hyaline and central sinusoidal stroma as the three most predictive parameters to differentiate reactive hepatocytes from HCC²⁶. In our study we reported 2 tuberculosis cases. smears showed caseous necrosis and granulomas with positive special stain for acid fast bacilli. In one of the study in India showed that 68% of granulomas in liver biopsies were of tubercular etiology.²⁹

CONCLUSION

We found that incidence of malignant hepatic lesions was more than benign. In benign lesions common were reactive changes and cirrhosis. While in malignant liver lesions, metastatic were more common than primary. Adenocarcinoma was most common metastatic tumor. While in the primary tumor, HCC were most common. It is safe, less traumatic, OPD based and costeffective tool.

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