

Cytomorphological Patterns of Nodular Lesions of Liver: A 5-year Cross-sectional Study Conducted in Tertiary Care Center of Central India

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Abstract

Background: The liver is one of the most common organs to undergo ultrasonographic (USG) guided fine-needle aspiration cytology (FNAC), and FNAC has become preferred modality for investigation of lesions in the liver.

Materials and Methods: A 5-year retrograde study on cytomorphological patterns of hepatic lesions was performed on total 341 cases. Diagnostic yield was 85.92% (293/341); almost similar results were seen in earlier studies. The main indication was single or multiple nodular lesions demonstrated clinically or by USG finding.

Results: The most common lesion found cytomorphologically was metastatic adenocarcinoma and constituted 41.93% (143/341), whereas hepatocellular carcinoma accounted for 17.5% (60/341) of malignant lesions of liver.

Conclusion: FNAC can be used as the initial modality of choice for the diagnosis of palpable nodular liver lesions as it is quick, safe, simple, and cost-effective.

Key words: Adenocarcinoma, Adenoma, Hepatocellular carcinoma, Fine-needle aspiration cytology

INTRODUCTION

The liver is the second largest organ of the body. Most of the malignancies in the liver are metastatic tumors.¹⁻³ Adenocarcinoma being the most common metastatic tumors to the liver, however, hepatocellular carcinoma (HCC) is the most common primary malignant tumor in the liver.^{4,5} Liver is the most commonly aspirated abdominal organ, i.e., about 55% of the abdominal aspirates.⁶ Ultrasonography (USG) has been used in combination with fine-needle aspiration cytology (FNAC) in the diagnosis of liver diseases.⁷ FNA as diagnostic modality provides accuracy with

little complications, requires minimal intervention, cheap and should be considered early in the investigative sequence.⁸

The differential diagnosis of hepatic mass lesions includes primary liver tumors (benign or malignant), metastatic deposits, cysts, abscesses, and granulomas. Occasionally, inflammatory lesion or diffuse liver diseases may mimic mass-like lesions.

The present study was conducted to describe the cytomorphological features in different nodular lesions of the liver.

MATERIALS AND METHODS

The present study is a cross-sectional study conducted in the Department of Pathology, Pt. Jawaharlal Nehru Memorial Medical College (Pt. JNMHC), Raipur (Chhattisgarh, India). Pt. JNMHC is the major tertiary care center in central India. This is a retrospective study

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conducted during from June 2010 to June 2015 (5 years) and included a total of 341 patients, having nodular lesions including solitary, multiple, and diffuse as detected by clinicians and/or radiologists.

FNAC of liver lesions was conducted using the standard procedure of FNA (both guided and unguided).

Cytological smears were stained by routine hematoxylin and eosin (H and E) stain, May-Grünwald Giemsa stain and Papanicolaou stains (PAP).

Reviews of USG guided cytology slides were also done.

RESULTS

During the period of 5 years, the total number of FNAC performed on liver, i.e., 341 cases (all USG guided) were included in the study. Out of 341 patients, 198 (58%) were male and remaining 143 (42%) were females. Male:female ratio was found to be 1.3:1. Age of the patients ranged from 1 to 80 years with mean age of 40.5 years.

Cytomorphologically, liver lesions were categorized into non-neoplastic lesion, neoplastic lesion, few suspicious cells, and inadequate for interpretation.

Regarding the FNAC diagnosis, 54 cases (15.83%) were non-neoplastic lesions, 220 cases (64.51%) were neoplastic lesions, 19 cases (5.57%) were few suspicious cells, and 48 cases (14.07%) were inadequate for opinion. Out of non-neoplastic lesions, 28 cases showed only normal hepatocytes, 20 cases were pyogenic abscess followed, and 6 cases of amoebic liver abscess.

Around 220/341 cases (64.51%) were neoplastic lesions and the majority of the cases were malignant, i.e., 217/220 cases (98%). Among the metastatic lesions, adenocarcinoma (not otherwise specified) was the most common tumor constituting 143/220 (65%) of all metastatic tumors. The most common primary malignant lesion was HCC 60/220 cases (27.27%). Three cases of each metastatic intraductal carcinoma breast, hepatoblastoma, and adenoma were reported. Two cases of each metastatic renal cell carcinoma and metastatic squamous cell carcinoma were reported. One case of each metastatic non-seminomatous germ cell tumor, metastatic gastrointestinal stromal tumor, malignant melanoma, and undifferentiated carcinoma was also reported.

The primary sites of the metastatic tumor were gallbladder, lung, colon, thyroid, breast, duodenum, cervix, stomach, and kidney (Tables 1-3).

Table 1: Distribution of liver aspirates

Liver aspirates	Number of cases (%)
Benign aspirates	54 (15.83)
Malignant aspirates	220 (64.51)
Suspicious of malignancy	19 (5.57)
Non-representative	48 (14.07)
Total	341 (100.00)

Table 2: Different types of metastatic tumors

Types	Number of cases (%)
Adenocarcinoma (NOS)	143 (65)
Breast	3 (1.36)
SCC	2 (0.90)
RCC	2 (0.90)
NSGCT	1 (0.45)
GIST	1 (0.45)
Malignant melanoma	1 (0.45)
Undifferentiated carcinoma	1 (0.45)
Total	154

NOS: Not otherwise specified, SCC: Squamous cell carcinoma, NSGCT: Non-seminomatous germ cell tumor, GIST: Gastrointestinal stromal tumor, RCC: Renal carcinoma cell

Table 3: Incidence of various types of benign and malignant liver aspirates

Hepatic lesions	Number of cases (%)
Benign	
Normal liver	28 (8.21)
Inflammatory	23 (6.74)
Abscess	3 (1.36)
Adenoma	3 (1.36)
Malignant	
Metastatic	154 (45.16)
HCC	60 (17.59)
Hepatoblastoma	3 (0.87)
Suspicious for malignancy	19 (5.57)
Inadequate for opinion	48 (14.07)
Total	341 (100.00)

HCC: Hepatocellular carcinoma

DISCUSSION

Tissue diagnosis of hepatic masses is very important for early detection of lesion and management. FNAC under image guidance has gained increasing acceptance as the diagnostic procedure of choice and is very effective means of obtaining tissue from many different body sites for cytological diagnosis.⁹ It is predominantly used for diagnosing mass lesions when there is suspicion of a neoplastic process, either primary or metastatic.⁴ Our study emphasizes on cytomorphological patterns of different lesions which are helpful for identification of various lesions. None of the long study of this duration (5 years) with 341 cases of liver FNAC has been performed by this part of the country to best of our knowledge.

The finding of male:female (M: F) ratio in present study came to be 1.3:1, i.e., slight male predominance, whereas Nggada *et al.*¹⁰ found in his study the M: F ratio to be 2.5:1 and Hao *et al.*¹¹ found that the ratio was 2.4:1.

The mean age in the present study came to be 40.5 years while the study done by Talukder *et al.*¹² found the mean age of diagnosing hepatic lesions to be 53 years.

The present study found 15.83 % of non-neoplastic lesion, 64.51% of neoplastic lesion, 5.57% of cases were suspicious for malignancy, and 14.07% cases were inadequate for opinion. Rasania *et al.*⁹ in their study found 23.33% cases of non-neoplastic lesion, 67.77% of neoplastic lesion, 2.23% cases showed suspicious cell, and 6.67 cases were inadequate for opinion. Similarly, Talukder *et al.*¹² found 0.9% of the cases to be non-neoplastic, 93.5% cases to be neoplastic, and 6.5% cases were inadequate for opinion, whereas none of the cases were categorized under suspicious for malignancy.

In the present study, we found neoplastic lesions to be most common finding, which was similar to above studies.

We studied and evaluated the different features in different lesions as described by Ali *et al.*¹³ and Tao *et al.*¹⁴ The cytomorphological features taken in consideration included cellular arrangement, cohesiveness of cells, cell size, N/C ratio, nuclear shape and size, multinucleation, prominent nucleolus, amount of cytoplasm, vacuolation, bile pigment, and hyaline bodies.

In the present study, non-neoplastic benign lesions include pyogenic abscess and amoebic liver abscess. Many times benign hepatocellular neoplasms such as hepatic adenoma and focal nodular hyperplasia can be difficult or impossible to diagnose on FNAC alone because of their similarity with normal liver. In the present study, we found 28/341 aspirates only showing normal hepatocytes which could not be further categorized.

Benign hepatocytes

Needle aspirates of normal liver consist predominantly of hepatocytes, with Kupffer cells and endothelial cells. The hepatocytes are present as single cells or monolayered small cell sheets or groups. These cells are round, polygonal, distinct cell border and dense granular cytoplasm. Hepatocytes frequently contain cytoplasmic pigments such as lipofuscin, hemosiderin, and bile pigments. Nucleus of hepatocytes is round/oval, with regular nuclear membrane, finely dispersed chromatin and conspicuous nucleolus. Occasionally, binucleation may be seen.

Hepatic abscess

Aspirate from abscess shows reactive hepatocytes which showed nuclear size variation, with prominent nucleoli, but the nuclear membrane is regular with normal N/C ratio. Mitotic figure is rare. There may be the background of necrotic debris, histiocytes, and acute inflammatory cells.

NEOPLASTIC TUMOR

- A. Metastatic tumor,
- B. HCC,
- C. Hepatoblastoma.

Metastasis neoplasm

The liver is a common site for metastases, especially from a malignant epithelial tumor in the organs that are drained by the portal venous system, e.g., gastrointestinal tract (GIT). Other common sites are lung, breast, and kidney. Sarcomas, lymphoma, and malignant melanoma can also metastase to the liver. FNA plays very important role in diagnosis of metastatic disease along with history, clinical details, and radiological findings of the patients which could suggest a primary site. Metastatic tumors generally involve liver in form of multiple nodules of variable size.

The most common metastatic tumor is adenocarcinoma. Mainly primary tumor in GIT was found after careful search. Cytomorphological patterns of hepatic aspirate many times suggest the primary site, but in many cases, IHC and serological parameters such as alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA), CA19.9, CA125-like cancer markers are required for definite diagnosis.

Adenocarcinoma

Colonic adenocarcinoma

Necrotic debris often dominates the aspirate. Cells appear columnar or cuboidal. Tumor cell can be arranged in glandular or palisading pattern. Nuclei are elongated and enlarged, hyperchromatic with clumped nuclei (Figure 1a-c).

Breast carcinoma

Usually, the patient is a known case of breast cancer. Tumor cells show the presence of intracytoplasmic lumen formation and intracytoplasmic mucin can be found (Figure 2).

Malignant melanoma

FNA aspirate is black in appearance. Smears reveal high cellularity consisting of dispersed or loosely cohesive cluster of tumor cells. Individual cells are polygonal, may be spindled, small, or anaplastic. Nuclei appear plasmacytoid or eccentric with single prominent nucleoli.

Melanin pigment may obscure nucleocytoplasmic border and appear yellow-brown in PAP stain. Pigment might be dispersed extracellularly as well. Ocular melanomas have greater tendency to metastasize to the liver (Figure 3).

HCC

HCC accounts for 90% of all primary cancers of the liver. Aspirates of HCC show increased cellularity and discohesiveness with crowding and overlapping of cells. The neoplastic hepatocytes are polygonal, present in thick trabecular cords greater than three cells thick. There could be solid sheets, tubular or pseudoglandular arrangement of tumor cells. The nuclei are large round with prominent nucleoli, high N/C ratio. There is moderate to severe nuclear pleomorphism and irregular nuclear membrane. Intracellular inclusions may be present. Spindle, pleomorphic, and multinucleated tumor giant cells may be present. There is also the presence of endothelial cells enclosing or transgressing the tumor cell cluster.

HCC was differentiated from other non-malignant conditions of the liver by the different features such as

cellularity, acinar pattern, trabecular pattern, hyperchromasia, uniformly prominent nucleoli, multiple nucleoli, and high N/C ratio (Figure 4 a-c).

To differentiate poorly differentiated HCC and metastatic adenocarcinoma serum level, AFP and CEA were done.

Hepatoblastoma

Hepatoblastoma is a rare tumor in pediatric age group. It is the most common primary hepatic tumor seen under 3 years of age. Cytological smears show small, blue, and round cell tumors of childhood. Mitotic figures are frequent. The differential diagnosis includes HCC, other small round cell tumors such as neuroblastoma, rhabdomyosarcoma, Wilm tumor, and lymphoma (Figure 5a and b).

CONCLUSION

Guided FNAC plays a key role in differential diagnosis of nodular lesions of the liver. The cytological diagnosis mainly

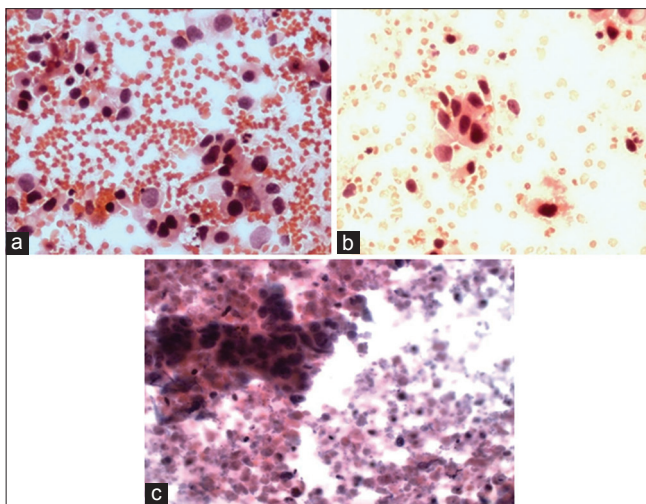


Figure 1: (a-c) Case - 59-year-old male with rectal carcinoma and secondaries in liver

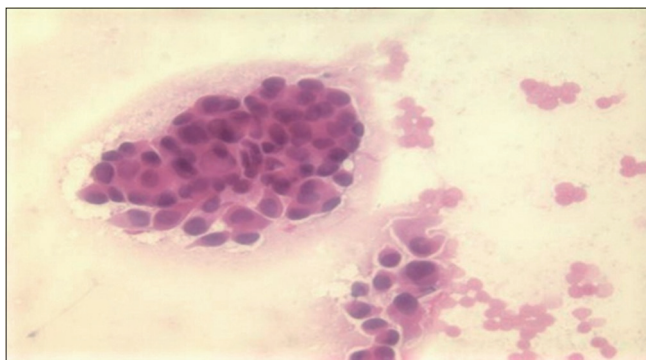


Figure 2: Case - 48-year-old female with carcinoma of breast and secondaries in liver

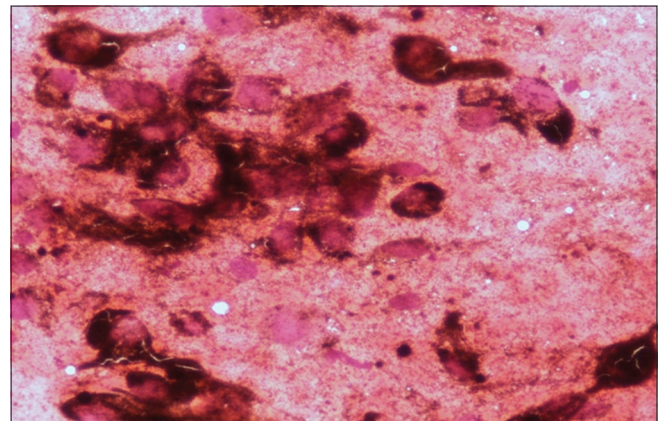


Figure 3: Case - 60-year-old male with malignant melanoma in right eye with metastasis found in liver (aspirate-black)

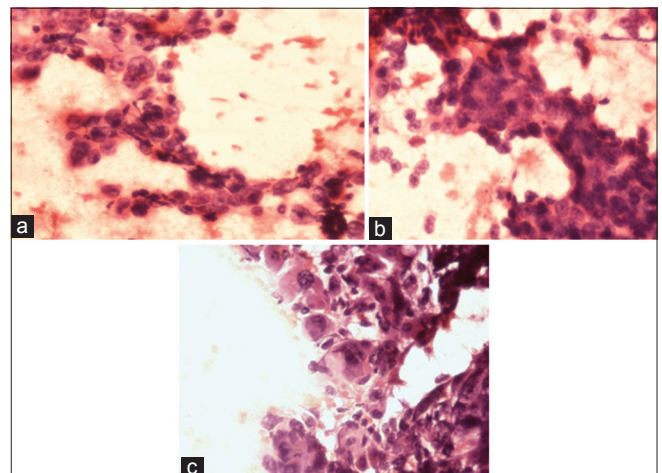


Figure 4: (a-c) Hepatocellular carcinoma

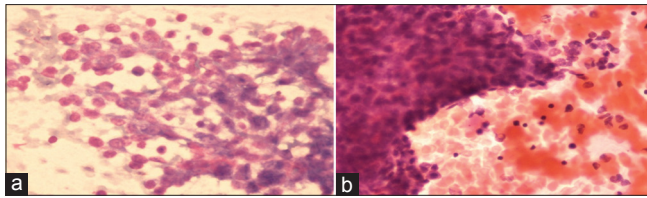


Figure 5: (a and b) Hepatoblastoma

depends on the recognition of distinct cytomorphological features.

The present study emphasized on recognition of unique cytomorphological patterns of distinctive liver lesions for the diagnosis by FNAC.

The present study includes a higher number of case and of long duration which would be more useful in evaluation of cytomorphological changes and in differentiation of a wide spectrum of liver masses.

SUMMARY

FNAC can be used as the initial modality of choice for the diagnosis of palpable nodular liver lesions as it is quick, safe, simple, and cost-effective.

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