CASE REPORT AND REVIEW OF LITERATURE

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A comparative study of cytomorphological features of primary and metastatic hepatic lesions - A tertiary care hospital experience

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ABSTRACT

Background: Ultrasonography (USG)-guided fine-needle aspiration cytology (FNAC) of the liver is a primary diagnostic procedure for primary and metastatic hepatic lesions. It is a minimally invasive and accurate technique and renders timely diagnosis for further management. **Aims and Objectives:** The purpose of the study was to evaluate the cytomorphological features of primary and metastatic hepatic lesions. **Materials and Methods:** This retrospective study was conducted in the Department of Pathology of a tertiary care hospital over a period of 2 years. 50 cases of clinically suspicious cases for hepatic malignancy were radiologically confirmed by USG and were subjected to FNAC under USG guidance with simultaneous cell block preparation in 35 cases. Relevant biochemical and serological data were retrieved from laboratory investigation archives. **Results:** The study was conducted on 50 cases of hepatic lesion. Majority of cases were male patients. All liver lesions were diagnosed on USG scan. Out of 50 cases diagnosed cytomorphologically, 8 cases (16%) were diagnosed as hepatocellular carcinoma. Among metastatic lesions, more prevalent lesions were adenocarcinoma 20 (40%). The rest of metastatic deposits included poorly differentiated carcinoma 12 (24%), mucinous carcinoma 4 (8%), malignant lymphoma 3 (6%), neuroendocrine tumor 2 (4%), and malignant melanoma 1 (2%). Primary site for metastatic lesions was diagnosed in 22 cases (52.4%) and unknown in 20 cases (47.6%). **Conclusion:** FNAC is a quick, feasible, and reliable procedure which enables the interpretation of cytological features of malignant hepatic masses.

Key words: Fine-needle aspiration cytology; Hepatic masses; Cytomorphology

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INTRODUCTION

Fine-needle aspiration cytology (FNAC) is a primary method of investigation in patients with suspected malignant hepatic lesions.[1] The accurate and reliable determination by FNAC in conjunction with radiology of the nature of the liver mass is critical for timely diagnosis for the patient.[2] It is a simple and economic procedure. Hemorrhagic diathesis and anticoagulation are few contraindications to this procedure.[3] A few drawbacks associated with this procedure are a small amount of material for examination along with the absence of histological resemblance to tissue patterns in sections. This increases the reliance on the experience of cytopathologist's interpretation.[4] Cell block preparation from a residual material can be a useful alternative for smears for establishing a conclusive diagnosis with increased rates of sensitivity for malignant lesions by cell block method in comparison to conventional smears.[5] The gray zone hepatic lesions which present as a diagnostic dilemma on cytology are dysplastic nodules, focal nodular hyperplasia, hepatic adenoma, and hepatocellular carcinoma (HCC) requiring clinicopathological correlation and application of additional ancillary techniques such as immunohistochemical (IHC) markers. The liver is a common site for metastases from unknown primary and close scrutiny of the smears is the key to arriving at the correct diagnosis.[6-8]

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The aim of this study was to evaluate the cytomorphological features of various primary and metastatic malignant hepatic lesions.

Aims and objectives

This study aims to describe the cytological features of malignant hepatic lesions in patients admitted to a tertiary care center.

MATERIALS AND METHODS

This retrospective study of 2 years included a total of 50 cases clinically and radiologically presenting as liver masses and was subjected to ultrasonography (USG)-FNAC. Relevant clinical, biochemical, hematology, and serological investigations were obtained from archived case files. The procedure was performed under aseptic precautions and aspirates were obtained using a 23-gauge spinal needle under ultrasound guidance and the smears were prepared along with cell blocks prepared simultaneously in 35 cases. Air-dried and wet-fixed (95% alcohol) smears were prepared and stained by May-Grunwald Giemsa and Papanicolaou or Hematoxylin and Eosin stains, respectively. Special stains such as periodic acid–Schiff were used wherever necessary.

Cytomorphological features were studied and a diagnosis was offered by a cytopathologist.

RESULTS

Patients' age ranged from 21 to 90 years with maximum number of patients in the fifth decade. There were 32 (64%) males and 18 (36%) females (Table 1). All the cases were diagnosed as malignant in cytology (Table 2).

Cytomorphologically, liver lesions were categorized into primary HCC 8 (16%) and secondary origin 42 (84%). The most common cytological parameters in HCC were increased nuclear-cytoplasmic ratio, pleomorphism, hyperchromasia, macro-nucleoli, dispersed bare nuclei, intracytoplasmic bile pigment, and trabecular pattern of arrangement followed by traversing capillaries, peripheral endothelial rimming, hypercellularity, and intracytoplasmic inclusions. The least common findings were multinucleation, intranuclear inclusions, bile duct epithelium, and tumor giant cells.

Table 1: Distribution of cases according to age and gender

Age group	Male	Female	Total
21–30	1	1	2
31–40	5	2	7
41–50	7	5	12
51–60	8	6	14
61–70	5	1	6
71–80	3	1	4
81–90	3	2	5
Total	32	18	50

Out of 50 malignant cases, 42 (84%) were metastatic deposits constituted poorly differentiated carcinoma 12 (24%), adenocarcinoma 20 (40%), mucinous carcinoma 4 (8%), malignant lymphoma 3 (6%), neuroendocrine tumor 2 (4%), and malignant melanoma 1 (2%). In all the previously known cases of metastatic lesions, the cytological features were simulating the primary tumor and even the radiological investigations such as USG and CT features confirmed the primary in respective cases which led to surgical resection of the primary.

There were 12 cases of metastatic poorly differentiated carcinoma in our study. The FNAC smears were moderately cellular with cells arranged in small sheets and clusters. The nuclei showed that hyperchromasia and scanty cytoplasm were noted in the cells. Scattered hepatocytes were seen in the background.

The smears of all 20 cases of metastatic adenocarcinomas studied were cellular. Epithelial cells were seen arranged in loosely cohesive flat monolayered sheets, acinar pattern, and dispersed singly with vacuolated and eosinophilic cytoplasm. The cells exhibited mild-to-moderate anisonucleosis with central or eccentrically placed nucleus with dense chromatin with high N/C ratio were noted. Background mainly showed hepatocytes and necrosis.

Four cases of metastatic mucinous carcinomas were encountered in our study. On FNAC smears, the tumor cells were arranged in clusters or as singly and exhibited mild-to-moderate pleomorphism and abundant eosinophilic cytoplasm with intracytoplasmic mucin. Some of the cells showed eccentric nuclei.

We had three cases of malignant lymphoma diagnosed clinically as NHL. The smears were hypercellular and showed atypical lymphoid cells with eccentrically placed cleaved nuclei, speckled chromatin, and pale cytoplasm. Some nuclei were convoluted and mitoses were seen. Background showed hepatocytes and lymphoglandular bodies.

Two cases of metastatic neuroendocrine carcinoma were observed in our study. Smears were showing a few scattered clusters of smaller-sized cells forming glandular arrangement with scanty cytoplasm. Nuclei were showing salt-and-pepper chromatin. Background showed hepatocytes.

In our 45 malignant tumors, there was one case of metastatic malignant melanoma. Smears were hypercellular and showed

Table 2: Categorization of malignant cases (n=50)

Hepatic masses	Malignant cases	No. of cases	Percentage	No of cases	Percentage
Primary origin	Hepatocellular carcinoma	8		8	16
Secondary origin	Poorly differentiated carcinoma	12	24	42	84
	Adenocarcinoma	20	40		40
	Mucinous carcinoma	4	8		8
	Malignant lymphoma	3	6		6
	Neuroendocrine tumor	2	4		4
	Malignant melanoma	1	2		2
	Total	50			100

pleomorphic malignant cells in loose aggregates and in singles. Cells had well-defined cytoplasm, eccentric nucleus, prominent anisonucleosis, and intranuclear vacuoles. Many cells showed intracytoplasmic melanin pigmentation. Background showed melanin pigment granules and hepatocytes. Histopathological correlation was done by cell block in 35 cases.

Clinical history and radiological details were taken to know the primary sites for secondary deposits in the liver. Primary site for liver metastasis was diagnosed in 22 cases (52.4%) and unknown in 20 cases (47.6%). Primary origin included gall bladder (4), GIT (10), pancreas (2), breast (5), and skin (1) (Table 3).

Table 3: Primary site for liver metastasis (n=42)

Liver metastasis	No. of cases	Percentage
Unknown	20	47.6
Known	22	52.4
Gall bladder	4	9.53
GIT	10	23.8
Pancreas	2	4.76
Breast	5	11.9
Skin	1	2.38
Total	42	100

DISCUSSION

USG-guided FNAC as a diagnostic modality has proven to be a low-cost interventional procedure that provides quick and reliable diagnosis with good sensitivity and specificity. It obviates surgical exploration, especially in high-risk patients and facilitating initiation of appropriate therapy and thus saving manpower, time, and reducing the hospitalization. The major problem lies in distinguishing between HCC and metastatic tumor cytology.[9,10] The present study was undertaken to study the cytological features of malignant hepatic lesions.

Majority of the patients in our study were predominantly males in the age group of 21–90 years. Other studies where similar results were observed by Rasania et al., Tandon and Gautam, and Balani et al., which are in concordance with our study.[4,11,12] However, differing results in a study conducted on 50 patients by Jayasree and Jayalaxmi were recorded.[13]

In the present study, majority of the hepatic neoplastic 42 (84%) were cytologically diagnosed as metastatic deposits. Eight cases (16%) were diagnosed as HCC. Our findings were consistent with the studies done by Namshiker et al., Tandon and Gautam, Prasad et al., and Rachana and Rao.[1,4,8,10]

In the present study, definite cytological parameters of HCC were macro-nucleoli, trabecular pattern of cells, hyperchromatic nuclei, increased nuclear-cytoplasmic ratio, and pleomorphism (Figure 1). Wee and Nilsson, Balani et al., and Shruthi and Chavan observed similar cytological features as noted in our study.[12,14,15]

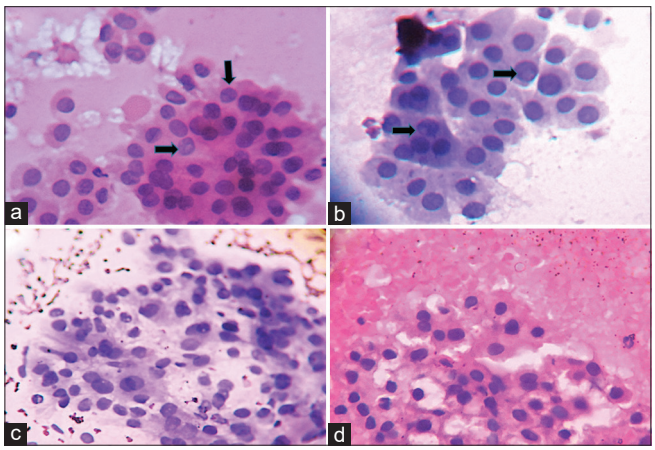

Figure 1: Cytological parameters of HCC (a) HCC – Cytology smear showing malignant hepatocytes exhibiting pseudoacinar formation (H&E, ×40). (b) HCC – Cytology smear showing intranuclear inclusions (Pap, ×40). (c) HCC – Cytology smear showing loosely cohesive irregular clusters of malignant hepatocytes centrally transgressed by proliferating band of endothelium (Pap, ×40). (d) HCC – Cell block showing malignant hepatocytes exhibiting moderate nuclear pleomorphism (HPE, H&E, ×40). H&E: Hematoxylin and Eosin, Pap: Papanicolau stain, HCC: Hepatocellular carcinoma

12 cases of metastatic poorly differentiated carcinoma were cytologically similar as described by Swamy MC et al., who suggested that IHC should be utilized to differentiate PD-HCC from other poorly differentiated carcinomas.[16]

In our study, the predominant metastatic lesions were found to be 20 cases of metastatic adenocarcinoma. Majority of

the patients had primary origin included gall bladder (4), GIT (10), pancreas (2), breast, and skin (1). In the present study, the most common metastatic adenocarcinomas were of unknown primary origin. Similar findings were seen in the studies conducted by Namshiker et al. and Tandon and Gautam.[1,4] HCC was diagnosed in 8 cases. Rasania et al. reported 18 cases of HCC in their study of hepatic lesions.[11] In the study done by Şahin, the majority of metastatic adenocarcinoma cases presented as acinar pattern while the key differentiating features between HCC and metastasis were uniform atypia, increased N/C ratio, hepatocytic appearance, and atypical naked nuclei.[6] The findings of present study were in concordance with these observations.

4 cases of metastatic mucinous carcinoma were encountered in our study. Ahuja et al. concluded that mucin along with a variable cytomorphology depending upon the primary favors metastatic carcinoma.[9]

We also encountered 3 cases of non-Hodgkin's lymphoma diagnosed clinically. Cytological features were similar to those described by Collins et al.[17]

In our study, two cases of metastatic neuroendocrine tumors were diagnosed cytologically. Khalbuss et al., described similar features and also detailed the cytomorphologic spectrum of small-cell tumors of the liver and differential diagnosis and stressed that IHC studies are needed for confirmation and accurate sub-classification.[18]

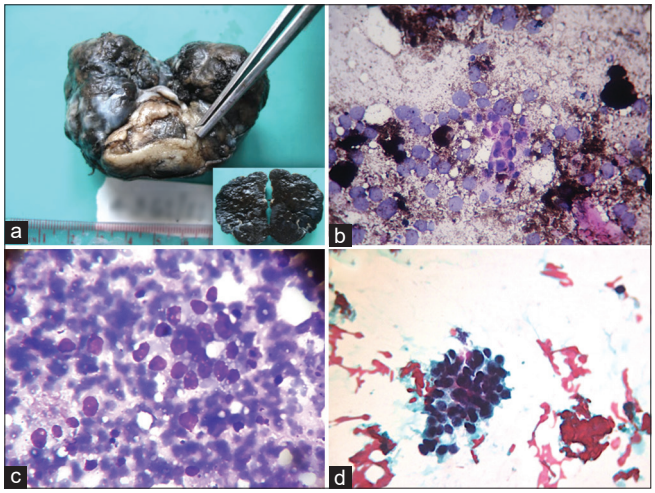

Figure 2: Metastatic lesions (a) Resected surgical specimen of anorectal melanoma. Inset cut section showing brown–black pigmentation. (b) Metastatic malignant melanoma – Cytology smear showing pleomorphic malignant cells in loose aggregates exhibiting anisonucleosis with well-defined cytoplasmic borders and melanin pigment (H&E, ×40). (c) Metastatic breast carcinoma – Cytology smear showing poorly cohesive cluster of malignant ductal cells exhibiting anisonucleosis and hyperchromasia with scanty cytoplasm (Giemsa, ×40). (d) Metastatic poorly differentiated carcinoma – cytology smear showing sheet of neoplastic cells having large hyperchromatic nucleus and scanty cytoplasm (Pap, ×40). H&E: Hematoxylin and Eosin, Pap: Papanicolau stain

The cytological features of a solitary case of metastatic malignant melanoma in our study (Figure 2) were similar to those described by De Casas et al.[19]

Soyuer et al. could determine the primary origin of 193 metastatic adenocarcinomas out of 490 cases. The cytological features of all metastatic tumors included in our study were similar to those described by Soyuer et al. and Centeno et al.[17,20] Cytohistological correlation was done by cell block in 35 cases.

Limitations of the study

The present study had only included a small number of neoplastic hepatic lesions wherein it is not possible to compare cytological features of every tumor and IHC was not done in our study for subtyping of tumors.

CONCLUSION

USG-guided FNAC is a safe, quick, cost-effective, and easily accessible procedure to diagnose liver lesions at an early stage. It offers accuracy without any major complications that can be done on OPD basis.

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