Original Article

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Cytology of Malignant Lesions of Liver: An Institutional Study

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Abstract

Background and Objectives: The evaluation and management of various hepatic lesions is a common clinical problem and their appropriate management depends on accurate diagnosis. Aim of the study is to study the cytomorphological features of various neoplastic lesions of liver and role of ultrasonography guided fine needle aspiration cytology (FNAC) in the diagnosis of liver malignancies. *Materials and Methods:* Fifty patients with evidence of liver disease underwent USG guided percutaneous FNAC . Cytomorphologicaldiagnosis were correlated with clinical, biochemical and radiological findings. *Results:* The age of the patients ranged from 6yrs to 75yrs with 40% males and 60% females. Of the 50 patients the cytological diagnosis of malignancies were rendered in 40 patients and smears of the 10 patients were benign, inflammatory and hemorrhagic. The primary liver lesions were more common than the metastatic lesions. The commonest primary liver malignancy was hepatocellular carcinoma followed by cholangiocarcinoma and hepatoblastoma. The metastatic lesion predominantly was adenocarcinoma. *Conclusion:* USG guided FNAC of the liver is a safe, simple, cost effective and accurate method for cytological diagnosis of hepatic malignancies.

Keywords: Hepatocellular Carcinoma; Cholangiocarcinoma; Metastatic Adenocarcinoma.

Introduction

Fine needle aspiration cytology(FNAC) of the liver is widely used well established technique, for the diagnosis of neoplastic lesion particularly to distinguish a primary liver tumor from a metastatic one and also to identify the type of metastatic or primary malignancy [1]. FNAC is done as percutaneous technique under ultrasound guidance (USG) which has revolutionized the procedure [2]. FNAC is an inexpensive, simple, rapid, reliable, sensitive and cost effective technique which helps in the clinical management of hepatic lesions by avoiding unnecessary procedures [3]. USG guidance FNAC of liver is a popular technique as it can be done from multiple sites in the same setting with minimal intervention, minimal complication and in the presence of ascitis.

The aim of the present study is to describe the cytomorphological features of various malignant lesions in the liver and to emphasize the role of USG guided FNAC in the diagnosis of liver malignancies.

Material and Methods

Fifty patients with clinical, biochemical and radiological evidence of liver diseases with normal prothrombin time were subjected to USG guided FNAC with over an one year period from January 2016 to December 2016. The cytological material was obtained using 20 or 22 gauge 90mm spiral needle introduced into the lesion under ultrasound evaluation. The smears are stained using Hematoxylin and Eosin stain, detailed cytomorphological features were studied and then specificity, sensitivity and accuracy of FNAC were evaluated.

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Results

Patients age ranged from 6years to 75 years, out of which 20 (40%) were males and 30(60%) were females. Ultrasound liver revealed solitary mass in 15(30%) cases and multifocal lesions in 35(70%) cases. Out of 50 US guided FNAC from the liver, the lesions are cytomorphologically categorized as nonneoplastic in 10 cases (20%) and malignant lesions in 40 cases (80%).

The nonneoplastic lesions were inflammatory, benign, hemorrhagic and inadequate for interpretation. The malignant lesions were hepatocellular carcinoma (HCC) in 24 cases (60%) cholangiocarcinoma in 2 cases (5%), hepatoblastoma in 2 cases (5%) and metastatic deposits in 12 cases (30%).

Table 1: Distribution of various malignant liver lesions in the present study

Malignant Lesions	Number of cases	Percentage
Hepatocellular carcinoma	24	60
Hepatoblastoma	2	5
Cholangiocarcinoma	2	5
Metastases	12	30
Total	40	100

Hepatocellular carcinoma is the most common malignant liver lesion in our study accounting for 60% of cases. Males were 42% and females were 58% with male to female ratio of 0.7:1. Clinical diagnoses of HCC is made in 10 out of 24 cases while secondary malignancy is suspected in the rest 14. USG showed 20 multifocal lesions and 4 solitary lesions. The largest lesion measured 9x6 cms and the smallest measured 4x3cms. Serum alfa fetoprotein levels were available in 8 out of 24 cases and 3 had high levels, HbSAg was positive in 2 patients.

Cytologically HCC was graded into well differentiated HCC, moderately differentiated HCC and poorly differentiated HCC, using the cytological features such as hypercellularity (83%), trabeculae pattern (37%), peripheral endothelium(26.4%), transgressing endothelium (68%), intracytoplasmic inclusions (28%), bile pigment (20%), bile duct epithelium (15%), pleomorphism (62.2%), increased nuclear:cytoplasmic ratio(90.3%), increased chromatin(34%), intranuclear inclusions(15%), multiple nuclei (16.9%), atypical naked nuclei (88.8%), multiple nucleoli (11%), large nucleoli (7%).

Out of the 24 cases of HCC, well differentiated HCC were 25% and the main cytological features were increased cellularity with cells resembling normal hepatocytes. The tumor cells were arranged in thick trabeculae, acinar, transgressing arborizing pattern and often show peripherally wrapped endothelial cells. Traversing endothelium and a good number of naked nuclei were noted in majority of the cases (Figure 1).

In the present study 50% cases of moderately differentiated HCC have many features of WDHCC. It is found that endothelial rimming or transgressing of cell clusters, large and bizarre tumor cells with moderate to abundant cytoplasm, centric or eccentric nuclei, multinucleation, multiple nucleoli and macronucleoli are associated with this type of HCC. Many atypical naked nuclei and tumor giant cells are also present (Figure 2).

In the present study 12% cases are diagnosed as poorly differentiated HCC which showed cells in sheets, small groups and singles. Transgressing endothelium is seen. Tumor cells of this type of HCC are with distinct cytoplasm, anisocytocysis, highnuclear:cytoplasmic ratio, anisonucleosis, irregular nuclear chromatin, hyperchromasia, multiple nuclei, macronuclei and bare atypical nuclei are seen (Figure 3).

In the present study 2 cases of intrahepatic cholangiocarcinoma were encountered in 2 males of age 65 and 75years. Cytologically the smears showed small cohesive clusters and tiny sheets of small cuboidal cells with round hyperchromatic nuclei with scant cytoplasm(Figure 4).

In the present study 2 cases of hepatoblastomas were reported one in six year old female and the other in forty year old female. USG showed a solitary space occupying lesion in the liver. Cytologically the smears consisted of small round cells as clusters, dissociated cells in acinar arrangement or rosettes. Cells show well defined cytoplasmic border, nuclei showing minimal nuclear pleomorphism and fine granular chromatin (Figure 5).

Metastatic tumors constituted 30% and adenocarcinomas were the commonest type (83%). Primary sites of adenocarcinomas were rectosigmoidalarea (2), ovary (2), pancreas (1), stomach (1) and unknown primary (4) (Table 2). The smears revealed hypercellularity with columnar to cuboidal cells arranged in monolayered sheets, palisade fprms, papillary fragments, acinar pattern

and in singles having vacuolated or granular eosinophilic cytoplasm. The cells showed altered N:C ratio anisonucleosis with central or eccentrically placed nucleus and fine to coarse dispersed chromatin. Metastatic adenocarcinoma of the stomach showed mucin in the background and signet ring cells (Figure 6). Many showed benign hepatocytes in the background. One case of metastatic squamous cell carcinoma from esophagus showed polygonal cells with moderate cytoplasm with enlarged hyperchromaticnucleus .

Table 2: Distribution of metastatic tumors in the present study

Metastatic Tumors	Number of cases	Percentage
Metastatic adenocarcinoma	11	91.5%
Metastatic squamous cell carcinoma	1	8.5%%

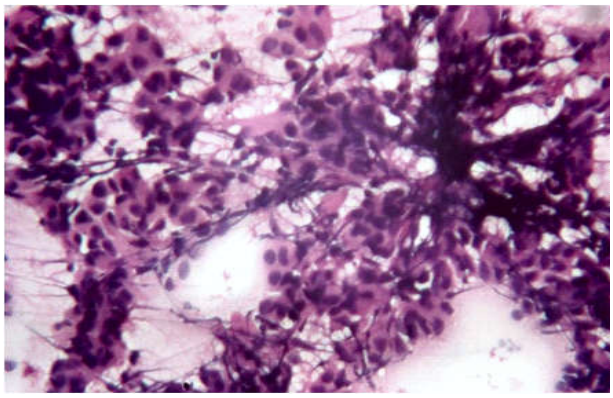

Fig. 1: Well differentiated Hepatocellular carcinoma showing trabecular arrangement with transgressing capillaries

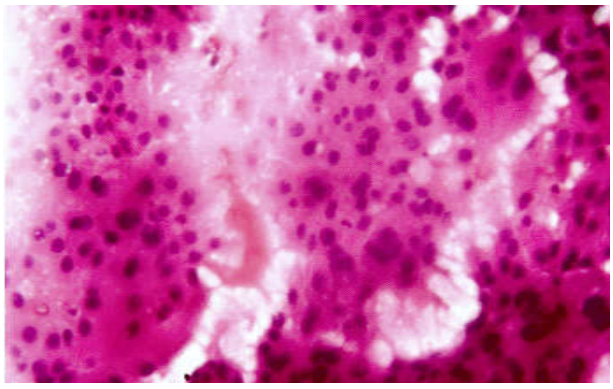

Fig. 2: Moderately differentiated Hepatocellular carcinoma showing nuclear pleomorphism, binucleation and bizarre cells

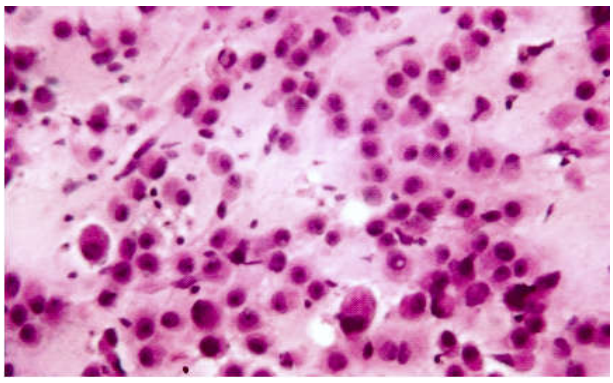

Fig. 3: Poorly differentiated Hepatocellular carcinoma showing singly scattered cells with nuclear pleomorphism, coarse chromatin, prominent nucleoli and intrnuclear inclusions

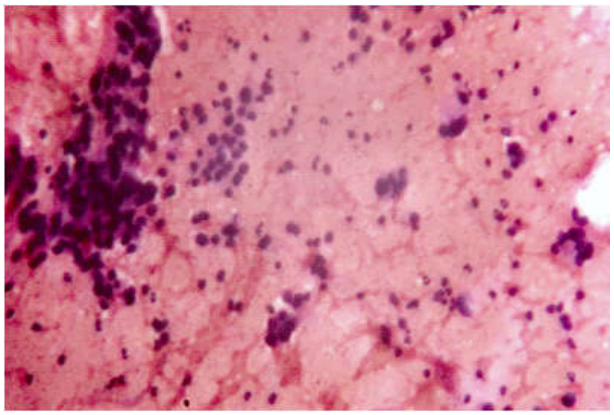

Fig. 4: Cholangiocarcinoma showing cells with foamy cytoplasm and faint acinar pattern

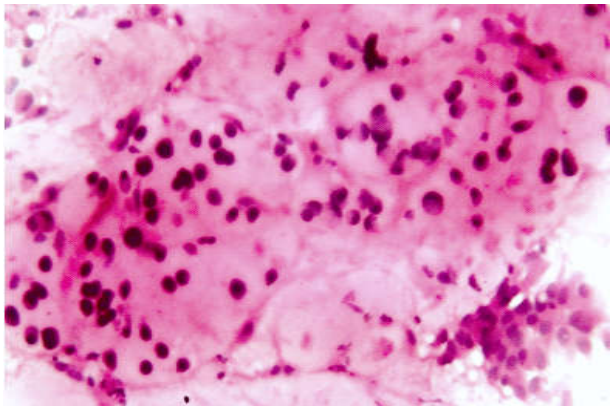

Fig. 5: Hepatoblastoma showing small round blue cells with pseudo rosette arrangement

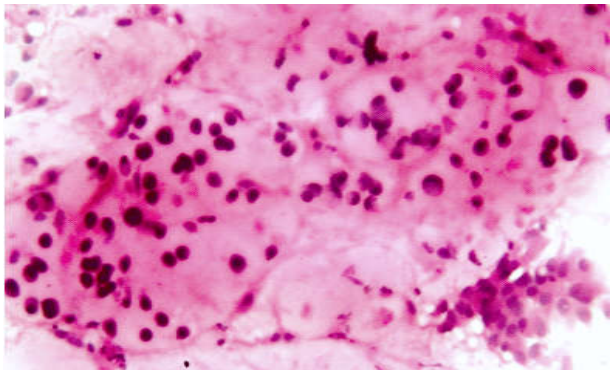

Fig. 6: Metastatic adenocarcinoma showing signet ring ells in the back ground of mucin pool

Discussion

Liver FNAC is used mainly for diagnosing hepatic malignancies primary or metastatic [4]. USG guided FNAC offers accuracy with out major complications and minimal intervention at less cost [5]. In the present study the male to female ratio is 2:3 with slight female preponderance which does not correlate with other studies like Franca et al [6] and Gatphoh et al [7] where the male:female ratio were 2.8:1 and 2:1 respectively.

The malignant lesion was the most commonly encountered pathology in liver in the present study which correlates well with other studies like Rasaniet al [8] and Rosenblatt et al [9]. In the present study primaries of liver is the common malignant lesion which is similar to the study of Kuo et al [9] while the study conducted by Rasani et al [8] show high prevalence of metastatic lesions in liver as shown in Table 3.

An attempt has been made to classify HCC into W-HCC, M-HCC and P-HCC based on the features described by Bottles et al [4] and Pitman et al [10]. Table 4 compares the cytomorphological features of HCC with Wee et al [11].

Table 3: Comparison of malignant lesions of the liver in the present study with other studies

Cytological Diagnosis	Rasania et al(n=43)	Kuo et al(n=523)	Present study(n=40)
Hepatocellular carcinoma	16	427	24
Hepatoblastoma	2	-	2
Cholangiocarcinoma	-	-	2
Metastatic adenocarcinoma	20	52	9
Metastatic squamous cell carcinoma	2	8	1
Metastatic Lymphoma	1	4	-
Metastatic Ovarian adenocarcinoma	1	-	2
Metastaic small cell carcinoma	1	2	-
Metastaic poorly differentiated carcinoma	-	5	-

Table 4: Comparison of cytomorphological features of HCC with other studies

Cytomorphological Features	Wee and Nilson[120]%	Present study %
Hypercellularity	87.1	83
Trabeculae pattern	88.5	66.6
Peripheral endothelium	35.7	26.4
Transgressing endothelium	82.8	68
Intracytoplasmic inclusions	45.7	28
Bile	20	20
Bile duct epithelium	35.7	15
Pleomorphism	80	62.2
Increased N:C ratio	100	94.3
Increased chromatin density	75.7	32.3
Irregular nuclear chromatin	64.2	34
Intranuclear inclusion	35.7	15
Multiple nuclei	57.1	16.9
Atypical naked nuclei	81.4	70
Multiple nucleoli	60	20.7
Large nucleoli	75.1	7

For the majority of hepatic masses the cytodiagnosis and categorization of HCC into 3 grade pose no problems. Hypercellular aspirates composed of cohesive clusters of atypical hepatocytes with arborescent, tongue like projections of broad trabeculae with or without peripheral andothelial rimming are pathognomic of classic HCC. As the tumor grade increases there is corresponding increase in cellular dissociation with less evidence of transgressing and peripheral endothelium and fever trabeculae. Peripheral endothelial rimming is observed less frequently than transgressing endothelium in the broad trabeculae [11,12].

Increased N:C ratio was the single most useful parameter for identifying the malignant hepatocytes. The frequency of eccentric nuclei, irregular nuclear contours and increase chromatin density, increase with higher grades of HCC. Intranuclear inclusions due to invagination of cytoplasm into the nucleus were evident in all the grups with a maximum frequency in WD-HCC. Increased frequency of multiple nuclei and macronucleoli are seen as the grades of HCC increse [11.12]. Atypical hepatocyte naked nuclei are seen in increasing number with increase in grades of HCC which distinguishes highly W-HCC from benign lesion

[13].

Difficulty in cytological diagnosis of HCC arises at the ends of spectrum distinguishing W-HCC from benign lesions and separating less differentiated HCC from metastatic malignancies or other tumors [14]. The most useful criteria to separate highly W-HCC cells from reactive liver cells are architectural features in the smears, hypercellularity, arborescent, cohesive clusters, broad trabeculae, transgressing / peripheral endothelium, small monotonus hepatocytes with nuclear crowding, increased N:C ratio, cytoplasmic hyaline inclusions, atypical naked nuclei and tumor giant cells [15].

Three criteria differentiate HCC from metastatic tumor, polygonal cells with centrally placed nuclei, malignant cells separated by sinusoid capillaries and bile. Two additional criteria namely endothelial cells surrounding tumor cell clusters and intranuclear inclusions are identified as being important secondary for HCC [4].

Two cases of hepatoblastoma are reported in the present study, the cytological features are similar similar to that seen in study by Rasnia et al [5]. Two cases of cholangiocarcinoma are reported in the present study , the cytological features are similar to that seen in study by Kuo et al [9]. The frequency of metastatic liver lesions is lower than the frequencies reported by other studies. The incidence correlates with that reported by Kuo et al.

Adenocarcinoma is the most common metastatic malignancy [17]. Colonic adenocarcinoma is the commonest primary source for liver metastasis. Cytological features of metastatic squamous cell carcinoma are similar to those described by Kuo et al. Ovarian carcinomas frequently metastasize to liver as described by pisto et al [16].

Conclusion

USG guided FNAC is very useful in the diagnosis of hepatic lesions as it is quick, safe, simple, cost-effective and accurate method. Early diagnosis by guided aspiration minimizes further ancillary investigations. FNAC can accurately distinguishes non neoplastic from neoplastic lesions, categorize different neoplastic lesions and differentiate primary from metastatic tumors which is helpful for the management of hepatic lesions.

Ethical Clearance

Obtained from ethical committee VIMS Ballari.

Source of Funding

Self

Conflict of Interest

NIL

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