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Ultra-Sound Guided Fine Needle Aspiration Cytology in Diagnosis of Space Occupying Lesions of Liver with Special Emphasis on Hepato-Cellular Carcinoma

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Abstract

Background

The evaluation and management of various hepatic lesions is a common clinical problem and their appropriate clinical management depends on accurate diagnoses.

Aims:

To study the cytomorphological features of distinctive non-neoplastic and neoplastic lesions of the liver and to evaluate the sensitivity, specificity and diagnostic accuracy of ultrasonography (USG)-guided fine needle aspiration cytology (FNAC) in the diagnosis of liver diseases.

Materials and Methods:

The study was performed on patients who came with SOL in liver on ultrasonography, with normal range of prothrombin time index in SMS hospital, Jaipur. Procedure was performed on 172 patients from 2 January 2016 to 16 sepetember 2016. USG Guided FNAC performed after getting an informed consent & with the help of a radiologist. Relevant clinical and serological details were obtained from every patient .

Results:

The mean age at presentation 56.47 years (25-95 years), ratio was almost equal male to female , male patient were 91(52.9%) and female were 81(47.09%) out of 172. Adequate sample were 148(86.04) and inadequate sample were 24 out of 172 patients. The cytological diagnosis of non neoplastic lesion were total 10 in which granuloma 01(10%),liver abscess 4(40%),regenerating nodule 1(10%) , fatty liver 2(20%), cystic lesion 1(10%) and inflammatory lesions 1(10%). Neoplastic lesion were(135) more common than non neoplastic lesions . The majority of neoplastic lesion were metastatic tumor 104(77.03%), followed by primary HCC23 (17.3%), unclassified malignancies 4(2.96%), cholangiocarcinoma 4 (2.96%) out of total 135 cases. The overall diagnostic accuracy of FNAC was 97.82% with a sensitivity and specificity of 96.87 and 100% respectively.

Conclusion - USG-guided FNAC of the liver is a safe, simple, cost-effective and accurate method for cytological diagnosis of hepatic diffuse, focal/nodular and cystic lesions with good sensitivity and specificity.

Introduction

The liver is involved by many non-neoplastic & neoplastic diseases. Evaluation & management of hepatic lesions is a common problem & their appropriate clinical management depends on accurate diagnosis. Liver remains one of the most common organ for the lodgement of metastasis. Differentiation between benign and malignant, primary or secondary tumours is extremely important for management point of view . Presence of metastasis usually rules out surgery whereas if HCC is diagnosed at an early stage, surgical resection is possible and may assure cure. The clinical and radiological presentation of both

primary and metastatic tumours can be similar – as a space occupying focal mass. Here FNAC can play a major decisive diagnostic role. Differential diagnosis of hepatic mass lesions - Primary Liver Tumors Metastatic Deposits, Cysts (Congenital/ aquired), Abscesses, Granulomas

MATERIALS AND METHODS

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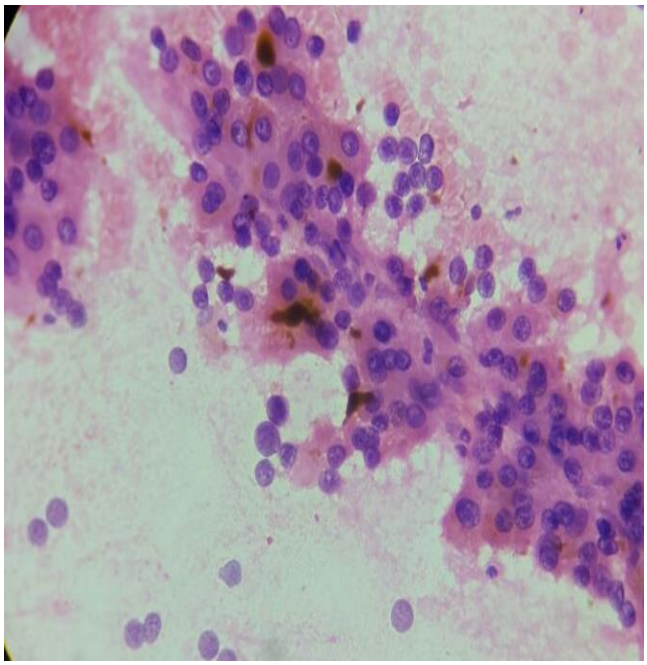
OBSERVATIONS AND RESULTS –

The mean age at presentation 56.47 years (25-95 years), ratio was almost equal male to female , male patient were 91(52.9%) and female were 81(47.09%) out of 172. Adequate sample were 148(86.04) and inadequate sample were 24 out of 172 patients. The cytological diagnosis of non neoplastic lesion were total 10 in which granuloma 01(10%),liver abscess 4(40%), regenerating nodule 1(10%), fatty liver 2(20%), cysticlesion 1(10%) andin flammatory lesions 1 (10%). Neoplastic lesion were (135) more common than non neoplastic lesions . The majority of neoplastic lesion were metastatic tumor 104(77.03%), followed by primary HCC23 (17.3%), unclassified malignancies 4(2.96%), cholangiocarcinoma 4 (2.96%) out of total 135 cases

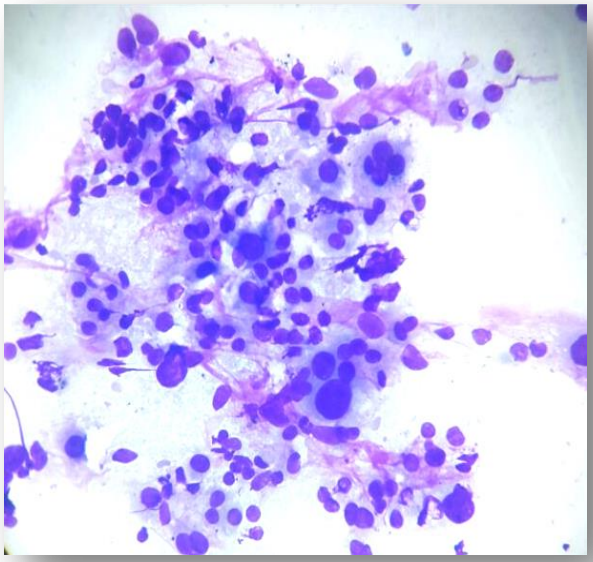
The distribution of hepatocellular carcinoma, well differentiated HCC were 7 (30.4 %), moderately differentiated HCC 5 (21.73%) % poorly differentiated HCC were 11 (47.8%) out of total 23 cases.

The distribution of metastatic carcinoma of total 104 cases. The metastatic adenocarcinoma were more common 71 (68.2%) than metastatic malignant epithelial neoplasm , metastatic malignant squamous cell carcinoma and metastatic small cell carcinoma each were 6 (5.76%), metastatic renal cell carcinoma, neuroendocrine tumor , metastatic mesenchymal tumors and metastatic malignant melanoma cases were 2 each. Metastatic ductal carcinoma (breast) , metastatic small round cell tumor , metastatic sarcoma, metastatic adrenal cortical tumor and metstatic from lungs each were 1(0.96%). The overall diagnostic accuracy of FNAC was 97.82% with a sensitivity and specificity of 96.87 and 100% respectively.

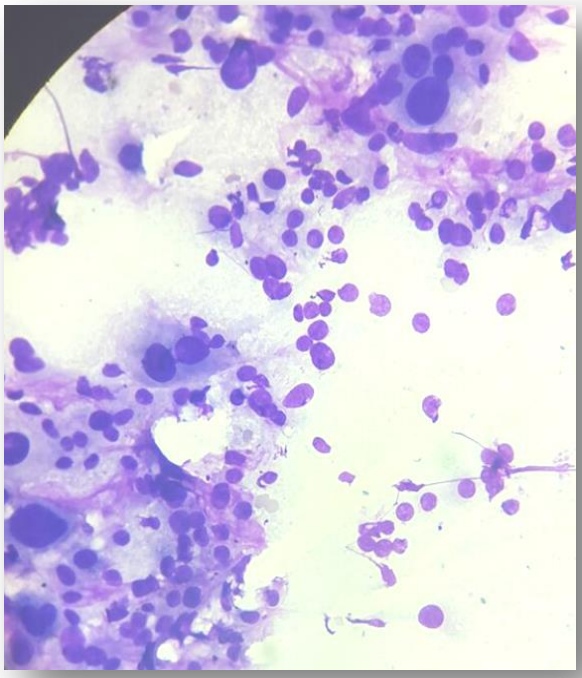
(A) Well Differentiated-HCC - Hypercellular smear with broad trabeculae ,endothelial transgression of vessels in the cell clusters, bare atypical nuclei, large polygonal cells with abundant eosinophilic granular cytoplasm, intracytoplasmic bile, increased nucleus to cytoplasm (N:C) ratio, central round nucleus and intranuclear inclusions.



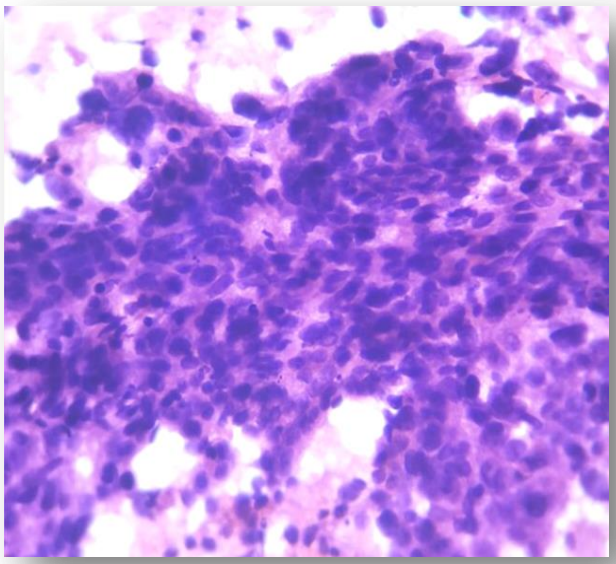
(B) Moderately differentiate-HCC - Endothelial rimming or transgressing of cell clusters, eccentric nuclei, multinucleation , multiple nucleoli and mcronucleoli



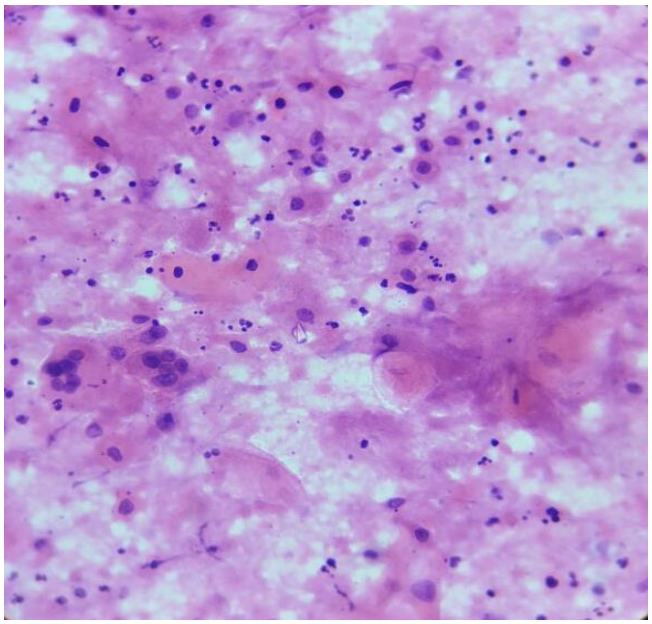
(C) Poorly differentiated –HCC - Cells have no resemblance to hepatocytes , having relatively scanty cytoplasm. Nuclei show variation in size & shape, have granular chromatin (Marked nuclear pleomorphism). Nucleoli irregular, numerous bare malignant nuclei lying in the background



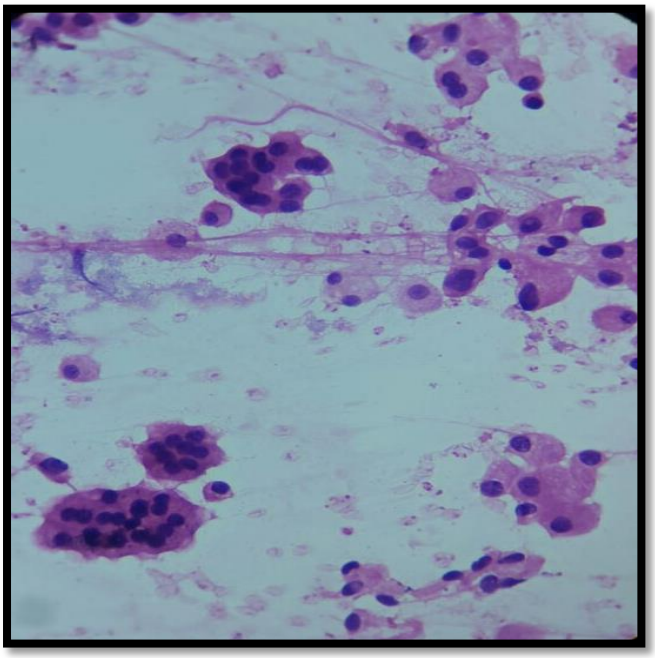
(D) Metastatic Adenocarcinoma – Hypercellular smear with columnar to cuboidal cells arranged in sheets ,attempt to form glands,at places acinar pattern with palisading also observed . cytoplasm is granular eosinophilic at places showing evidance of mucin secretion. N: C ratio is altered. Anisonucleosis with central / eccentrically placed nucleus . Fine-coarse dispersed chromatin.



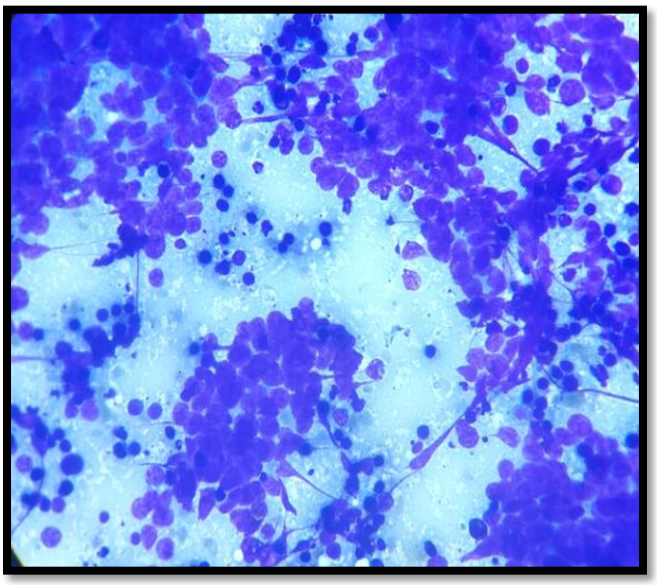
(E) Metastatic Squamous Cell Carcinoma - Squamoid, tadpole-like and spindle-shaped cells ,well-defined abundant keratinized cytoplasm ,pleomorphic and hyperchromatic nuclei



(F) Cholangiocarcinoma - Sheets, clusters & microglandular arrangement nuclear crowding & overlapping, decrease Cell Cohesion, small cuboidal/ columnar Cell, variable nuclear enlargement & pleomorphism & delicate cytoplasm with fine vacuolization.



(G) Metastatic Small Cell Carcinoma(Oat cell carcinoma) - Highly pleomorphic cells, fragile cytoplasm ,high N:C ratio, irregular nuclear membrane, fine stippled chromatin, multinuceation of nuclei numerous mitotic figures and occasional reactive hepatocytes in background



Discussion –

USG-guided FNAC offers accuracy without major complications and minimal intervention at less cost.[5] Although imaging techniques have helped greatly with the early and accurate diagnosis of liver abscess, the appearances are often non-specific. There is some overlap between the radiologic features of liver abscesses, HCC and metastases. Tumors, primary or secondary, may undergo extensive necrosis, with the resultant radiologic image of the cavitary neoplasms mimicking abscesses; abscesses are accompanied by proliferative reactive changes, making radiologic differentiation from a neoplastic process almost impossible. In these situations FNAC plays an essential complementary role.[6]

In non-pyogenic abscesses, further investigation for amoebae should be carried out if the cytological examination reveals much necrotic debris notably lacking neutrophils. Amoebae are unlikely to be detected in the smears unless tissue from the walls of the abscess cavity is examined.[6] However, trophozoites of *E. histolytica* were evident in our case. Amoebic liver abscess can also be diagnosed by the presence of serum anti-amoebic antibodies.[6,7]

The presence of hepatocytes entangled within fibrous strands, increased numbers of bile duct epithelium, Kupffer cells, dysplastic and mildly pleomorphic hepatocytes favors diagnosis of cirrhosis.[8] The presence of fibrous strands, intranuclear vacuoles and large nucleoli and absence of characteristic transgressing and peripheral endothelium favored the cytological diagnosis of cirrhosis in one case, but was concluded as HCC on tissue section.

The diagnostic value of cytological findings indicating granulomatous disease of the liver may be of variable clinical value and significance since granulomas are found in a wide variety of conditions. Indian studies have shown that 68% of granulomas in liver biopsies are of tuberculous etiology.[8,12]

Liver FNAC is used mainly for diagnosing hepatic malignancies, primary or metastatic.[13] .We have made an attempt to classify HCC into W-HCC, M-HCC and P-HCC based on the features described by Bottles *et al*.,[13] and Pitman *et al*.,[14] compares the cytomorphological features of HCC with the Wee *et al*.,[15] study.

For the majority of hepatic masses, the cytodiagnosis and categorization of HCC into three grades pose no problems. Hypercellular

aspirates composed of cohesive clusters of atypical hepatocytes with arborescent, tongue-like projections of broad trabeculae, with or without peripheral endothelial rimming are pathognomonic of classic HCC. As the tumor grade increases, there is corresponding increase in cellular dissociation, with less evidence of transgressing and peripheral endothelium and fewer trabeculae. Peripheral endothelial rimming is observed less frequently than transgressing endothelium in the broad trabeculae.[15]

Intracytoplasmic eosinophilic inclusions were present in 22-25% HCCs. Though the presence of intracytoplasmic inclusions strongly supports HCC, they have also been reported in ovarian, breast, lung and adrenal gland tumors and in asbestosis lung.[16] The presence of intracytoplasmic bile is a well-established diagnostic feature of HCC.Anisocytosis and anisonucleosis were prominent features (>80%) in M-HCC and P-HCCs. Increased N:C ratio was the single most useful parameter for identifying the malignant hepatocytes. The frequency of eccentric nuclei, irregular nuclear contours and increased chromatin density increases with higher grades of HCC. Intranuclear inclusions due to invagination of cytoplasm into the nucleus were evident in all the groups, with a maximum frequency in WD-HCC. Increased frequency of multiple nucleoli and macronucleoli are seen as the grades of HCCs increase.[15] Atypical hepatocytic naked nuclei were seen in increasing numbers with increase in grades of HCC, which distinguishes highly W-HCC from benign lesions.[17]

Difficulty in cytological diagnosis of HCC arises at the ends of the spectrum—distinguishing W-HCC from benign lesions and separating less-differentiated HCC from metastatic malignancies or other tumors.[1,18] A stepwise logistic regression analysis has been used to distinguish HCC and reactive liver cells[19] and between HCC and metastatic tumor cells.[13] The most useful criteria to separate highly W-HCC cells from reactive liver cells are: Architectural features on the smears/cell block sections, hypercellularity; arborescent, cohesive clusters; broad trabeculae; transgressing/peripheral endothelium; small, monotonous hepatocytes with nuclear crowding, increased N:C ratio, cytoplasmic hyaline inclusions, atypical naked nuclei and tumor giant cells. Well-defined cytoplasmic borders, abundant thick and monotonous cytoplasm, eccentric nuclei, thick nuclear membranes, irregular nuclear contours, increased chromatin density, irregular chromatin distribution and macronucleoli were not always detectable in highly W-HCC. In fact, some of them were seen in dysplastic hepatocytes.[18,20]

Three criteria differentiate HCC from metastatic tumor: Polygonal cells with centrally placed nuclei, malignant cells separated by sinusoidal capillaries and bile. Two additional criteria, namely, endothelial cells surrounding tumor cell clusters and intranuclear inclusions were identified as being important secondary criteria for HCC.[13] However, in our study, two metastatic malignancies reported as P-HCC on FNAC, were histopathologically identified as poorly differentiated carcinomas. The presence of transgressing endothelium and intranuclear inclusions misled the diagnosis of P-HCC in these cases.

Although primary carcinomas may be poorly differentiated the cytological features which favoured metastatic poorly differentiated carcinoma were the presence of benign hepatocytes, necrosis along with irregular clusters and dissociated malignant cells. Immunohistochemistry might be of value in differentiating P-HCC from other poorly differentiated tumors.

The frequency of metastatic liver lesions was higher than the frequencies reported by other studies.[3,21] Adenocarcinoma is the most common metastatic malignancy[3] and colonic adenocarcinoma is the commonest primary source for liver metastasis.[2] Pinto *et al*.,[21] observed two cases of metastatic RCC. Cytological features of metastatic SCC were similar to those described by Kuo *et al*.[1]

The diagnostic accuracy of FNAC of liver in our study is on par with other series [Kuo *et al*.,[1] (86.1%), Ramdas *et al*.,[22] (87.5%), Cochand-Priollet *et al*.,[23] (82.6%) and Franca *et al*.,[24] (78%)]. With an accuracy of 97.82% for liver lesions, FNAC is a valuable method that allows rapid diagnosis.

Conclusion

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

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