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ORIGINAL ARTICLE

ULTRASOUND GUIDED FINE NEEDLE ASPIRATION CYTOLOGY (FNAC) IN DIAGNOSIS OF SPACE OCCUPYING LESIONS (SOL) OF LIVER

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ABSTRACT: TITLE: Ultrasound guided fine needle aspiration cytology (FNAC) in diagnosis of space occupying lesions (SOL) of liver. **INTRODUCTION:** Liver is an important organ for metabolism of body and is also a drainage site for many organs, therefore it becomes affected in many benign, malignant and inflammatory conditions and performing ultrasound guided FNA helps to diagnose cases with 90-95% accuracy and minimizing the requirement of biopsy. **AIMS**: To evaluate the efficacy of ultrasound guided FNA and to look for spectrum of diseases affecting liver. **MATERIAL AND METHODS:** The study is performed on patients who came with lump abdomen and had SOL in liver on ultrasonography in SMS hospital, Jaipur. Ultrasonography guided FNAC was performed on 360 patients in one year period from January 2013 to December 2013. Majority of the patients were males and most of them were middle to elderly age group. Samples were adequate in 324 (90%) and inadequate in 36 (10%). Out of 360 patients 7 had benign lesions, rest all had malignant tumors. Of all the malignant tumors, metastatic tumors were commonest accounting for 68% cases, hepatocellular carcinoma accounted for 15% and the rest 17% were unclassified malignancies. **CONCLUSION:** Ultrasonography guided FNAC is a simple, safe, cost effective and accurate diagnostic method for cytological diagnosis of hepatic lesions. It can be practiced in any centre where ultrasound facility and specialist pathologists are available. Cell blocks can be prepared from FNAC material which is of great help especially in cases who have unknown primaries and present with metastasis in liver.

KEYWORDS: Space occupying lesions (SOL), Fine needle aspiration cytology (FNAC), Ultrasonography.

INTRODUCTION: Liver is an important organ for metabolism of body and is also a drainage site for many organs; therefore it becomes affected in many benign, malignant and inflammatory conditions. Cancers spreads to liver because liver filter most of the blood from the body. Kupffer cells in the body are regarded as most powerful defence mechanism against the development and lodgement of cancers, [1] however under long term ischemic hypoxic stress Kupffer cells can secrete a variety of pro-inflammatory cytokines to promote the development of carcinogenesis.[2, 3]

The clinical and radiological presentations of both primary and metastatic tumors can be similar–as a space occupying focal mass, occasionally inflammatory lesions or diffuse liver diseases may mimic mass like lesions or appear as non-homogeneous regions on radiographs. Here, FNAC can play a major decisive diagnostic role and performing ultrasound guided FNA helps to diagnose cases with 90-95% accuracy and minimizing the requirement of biopsy. The present study is being conducted to evaluate the role of US guided FNA and to look for spectrum of diseases affecting liver.

MATERIALS AND METHODS: All patients coming to SMS hospital, Jaipur from January 2013 to December 2013 with SOL in liver on ultrasonography were subjected to ultrasound guided FNAC

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over a period of one year after getting an informed consent. Relevant clinical and serological details were obtained for every patient. Patients with bleeding diathesis, suspected hydatid cyst, hemangioma or already diagnosed cases were excluded from the study. FNAC was performed under ultrasound guidance with the help of a radiologist.

A disposable spinal needle (22/23 gauge), connected to 10 ml plastic syringe was used. In case of multifocal lesions, the largest or the most easily accessible lesion was selected. The slides were prepared bedside and immediately fixed in absolute alcohol, for cytological evaluation. The smears were stained by May-Graunwald-Giemsa, hematoxylin and eosin (H and E) stains. Periodic acid-Schiff (PAS), Gram's and Ziehl-Neelson (ZN) stains were done whenever needed. Visible tissue fragments whenever obtained during FNA were studied as cell blocks in some cases.

OBSERVATIONS AND RESULTS: During the study period, 360 patients were reported for aspiration of liver masses, after fulfilling the inclusion criteria. The mean age at presentation was 53.3 years with age ranging from 29-75 years. The maximum number of cases were in between 50-60 years of age showing a male predominance with a male to female ratio of 2:1.Serum alpha-feto protein was assessed in 116 cases, out of which it was raised in 40% cases. Ultrasonography of liver revealed solitary mass in 55% cases, multifocal lesions in 40%, diffuse parenchymal disease in 5%.

Cytologically, liver lesions were categorized into: Non-Neoplastic lesions (2%), neoplastic lesions (88%) and Non-Diagnostic/Acellular (10%).

Non-Neoplastic Cases	No. of Cases
Granulomatous lesion	2
Regenerating Nodule	2
Liver Abscess	3
Total	**7**

Table 1: Distribution of Non-Neoplastic cases

Non-neoplastic lesions included liver abscess, granulomatous lesion and regenerating nodule liver. The smears from liver abscess predominantly showed neutrophils. The smears from granulomatous hepatitis showed epithelioid histiocytes in singles and small clusters along with foreign body and Langhan's type of multinucleated giant cells and lymphocytes. The smears from regenerating nodule liver showed regenerating hepatocytes with presence of bile duct epithelium.

Figure1: Microphotography of a granulomatous lesion in liver with arrow showing clusters of epithelioid cells.

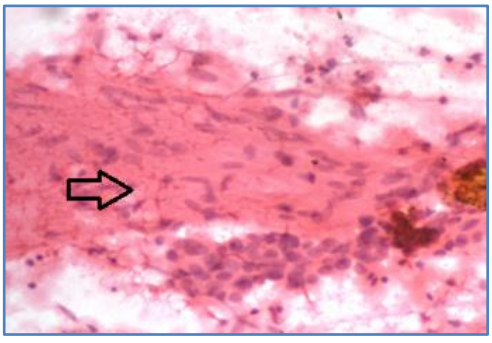

Figure 1

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Neoplastic cases	No. of cases
Primary(HCC)	47(15%)
Metastatic tumors	216(68%)
Unclassified malignancies	54(17%)
Total	**317**

Table 2: Distribution of Neoplastic cases

Metastatic tumors constituted the majority (68%) of neoplastic tumors. Hepatocellular carcinoma was present in 15% of cases, however unclassified malignancies constituted a large group accounting for 17% cases. Final diagnosis of cytologically diagnosed unclassified malignancies could not be evaluated as the patients were lost to follow-up.

Primary tumors	No. of cases
Well- Differentiated HCC	7(15%)
Moderately differentiated HCC	32(68%)
Poorly Differentiated HCC	8(17%)
Total	**47**

Table 3: Distribution of primary tumors

Cytologically, HCC was classified into well, moderately and poorly differentiated types (W-, M- and P-HCC) which accounted for 7 (15%), 32 (68%) and 8 (17%) cases of total HCC cases respectively. The main cytological features in W-HCC were hypercellularity with broad trabeculae, endothelial rimming/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.

M-HCC had many features of W-HCC. Endothelial rimming or transgressing of cell clusters, eccentric nuclei, multinucleation, multiple nucleoli and macronucleoli were more associated with M-HCC. P-HCC showed cells in sheets, small groups and singles. Anisocytosis, anisonucleosis, irregular nuclear chromatin, hyperchromasia, multiple nuclei, macronucleoli and bare atypical nuclei were seen in all the patients. Transgressing endothelium, inflammation, necrosis and giant cells were seen in 40% of cases. Multinucleated giant cells with three or more atypical nuclei were seen in all grades of HCC.

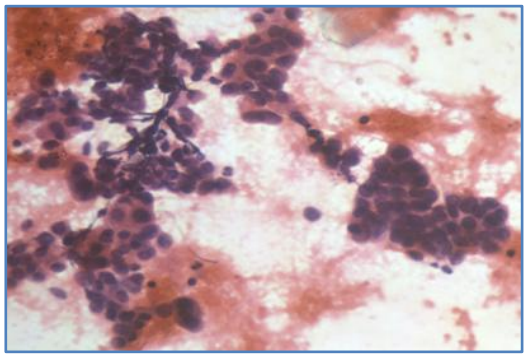

Figure 2: Microphotography of a moderately differentiated HCC

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Metastatic diseases	No. of cases
Metastatic adenocarcinoma	96 (44%)
Metastatic malignant epithelial neoplasms	53
Metastatic squamous cell carcinoma	38
Metastatic small cell carcinoma lung	14
Metastatic ductal carcinoma(Breast)	4
Metastatic small round cell tumor	4
Metastatic carcinoid tumor	2
Metastatic renal cell carcinoma	2
Metastatic from ovary	1
Metastatic malignant melanoma	2

Table 4: Distribution of metastatic cases

Metastatic tumors constituted 68% of cases and adenocarcinoma was the commonest type. The smears from metastatic adenocarcinoma revealed hypercellularity with columnar to cuboidal cells arranged in monolayered sheets, palisade forms, acinar pattern and in singles having vacuolated or granular and eosinophilic cytoplasm. The cells showed altered N: C ratio, anisonucleosis with central or eccentrically placed nucleus and fine-coarse dispersed chromatin.

Many showed benign hepatocytes in the background. Inflammation, necrosis and fibrosis were prominent in some cases. In metastatic squamous cell carcinoma (SCC), smears showed squamoid, tadpole-like and spindle-shaped cells with well-defined abundant keratinized cytoplasm and pleomorphic and hyperchromatic nuclei.

In some tumors (24.5%) it was not possible to differentiate squamous from adenocarcinoma and were reported as malignant epithelial neoplasms. Various others metastatic tumors included metastatic small cell carcinoma lung, metastatic renal cell carcinoma, metastatic medullary carcinoma thyroid, metastatic melanoma, metastatic carcinoid, metastatic round cell tumor, metastatic breast cancer, metastatic ovarian cancer respectively. Primaries were not known in 46% cases.

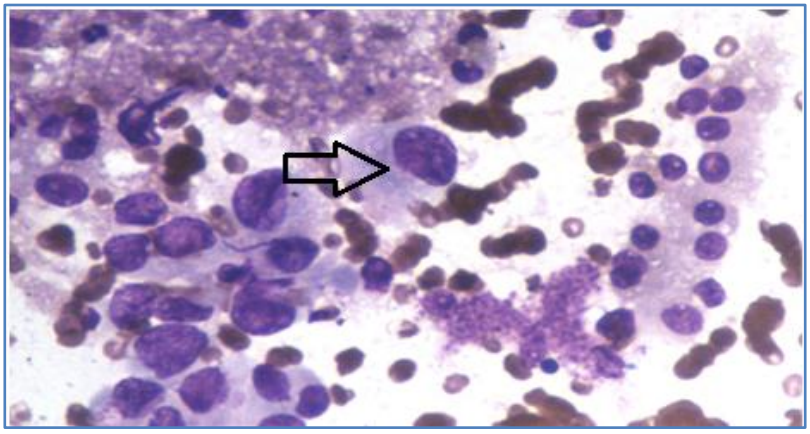

Figure 3: Microphotograph of a metastatic adenocarcinoma (see arrow)

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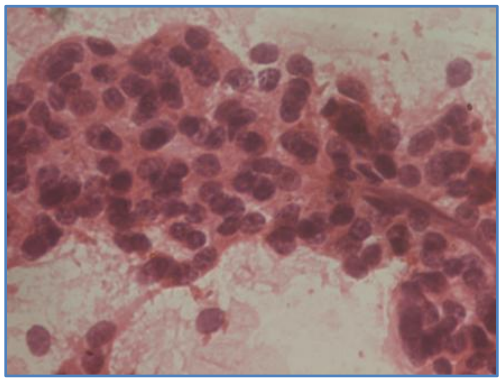

Figure 4: Microphotograph of a metastatic carcinoid tumor

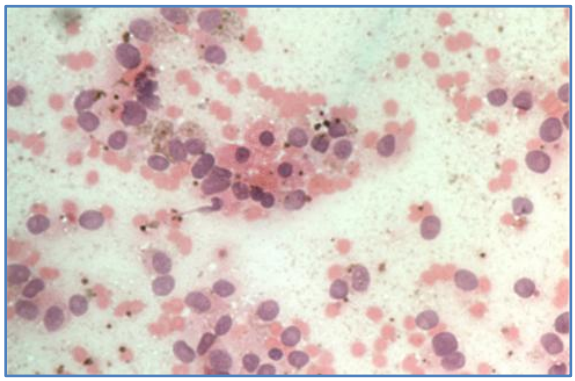

Figure 5: Microphotography of metastatic malignant melanoma

DISCUSSION: Ultrasonography guided FNAC offers accuracy without major complications and minimal intervention at less cost.[4] Although imaging techniques have helped greatly in diagnosing majority of hepatic lesions but 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.[5] In our study USG guided FNA was diagnostic in 90% cases. Among the few diagnosed non neoplastic diseases, the diagnostic value of granulomatous disease of the liver may be of variable clinical importance 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.[6, 7]

Liver FNAC is used mainly for diagnosing hepatic malignancies, primary or metastatic.[8] Attempts to classify HCC into W-HCC, M-HCC and P-HCC were based on the features described by Bottles et al and Pitman et al.[8, 9] 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.[8, 10]

The 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.[10, 11]

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.[8]

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Although primary carcinomas may be poorly differentiated the cytological features which favored 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 similar than the frequencies reported by other studies.[12, 13]

Adenocarcinoma is the most common metastatic malignancy[12] and colonic adenocarcinoma is the commonest primary source for liver metastasis.[14] Pinto et al[15] observed two cases of metastatic RCC. Cytological features of metastatic SCC were similar to those described by Kuo et al.[4] Unclassified malignancies constituted a large bulk in our study; however attempts were made to categorize them by cell block in tissues wherever available. Unclassified malignancies constituted a bulk in our study. Out of 54 unclassified malignancies, Cell blocks were made in 8 cases and 5 out of them were adenocarcinomas and one was metastatic melanoma.

CONCLUSION: USG-guided FNAC is a quick, safe, simple, cost-effective and accurate method for diagnosing hepatic lesions. Early diagnosis by guided aspiration minimizes further ancillary investigations and decreases the length of hospital stay.

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