

**CYTOLOGICAL TYPING OF LIVER TUMORS AND ITS HISTOLOGICAL CORRELATION**Sharda Balani<sup>1</sup>, Reeni Malik<sup>2</sup>, R. K. Nigam<sup>3</sup>**HOW TO CITE THIS ARTICLE:**

Sharda Balani, Reeni Malik, R. K. Nigam. "Cytological Typing of Liver Tumors and its Histological Correlation". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 13, March 31; Page: 3339-3346, DOI: 10.14260/jemds/2014/2290

**ABSTRACT: BACKGROUND:** The evaluation and management of discrete hepatic masses is a clinical problem. Ultrasound guided fine needle aspiration cytology (FNAC) is a rapid, accurate and safe diagnostic procedure that can be used in various neoplastic and non-neoplastic diseases of the liver. **AIM:** To assess the sensitivity and specificity of ultrasound guided FNAC of liver tumors. **MATERIALS AND METHODS:** Ultrasound-guided fine needle aspiration and true cut liver biopsies were performed on 52 patients clinically suspected of having hepatic lesion. Results of cytology were compared with histology. **RESULTS:** Malignancy was detected in 50 cases. The primary malignancies consisted of 15 cases of hepatocellular carcinoma (HCC), 4 cases of cholangiocarcinoma and 2 of hepatoblastoma. There were 29 metastatic lesions, which included 26 cases of adenocarcinoma, 2 cases of squamous cell carcinoma and 1 of lymphoma. The sensitivity and specificity of FNA for malignancies was found to be 96% and 100% respectively. Accuracy of FNAC was found to be 96.1 % with no false positive diagnosis. **CONCLUSIONS:** FNA of hepatic lesions is an effective, safe and well accepted practice with good sensitivity and specificity. It is recommended that image directed FNAC should be the primary diagnostic modality for assessing potential malignancy in any patient with a localized hepatic mass.

**KEYWORDS:** FNAC; Hepatic malignancies; Metastatic; USG guided.

**INTRODUCTION:** The evaluation and management of discrete hepatic masses is common clinical problem. Appropriate clinical management of these masses depends on obtaining accurate diagnosis. Ultrasound guided FNAC is a rapid, accurate and safe diagnostic procedure that can be used in various neoplastic and non-neoplastic diseases.<sup>1</sup> As diagnosis is readily available on FNAC, appropriate medical or surgical therapy can be started earlier, at the same time avoiding unnecessary expensive and often invasive diagnostic procedures and needless surgery.

**AIMS AND OBJECTIVES:** The study was undertaken to assess the sensitivity and specificity of FNAC of liver tumors.

**MATERIAL AND METHODS:** The study included 52 cases at Gandhi Medical College & associated Hamidia Hospital Bhopal with clinical suspicion of hepatic malignancies with one or more suspicious lesions in previous ultrasound. Ultrasound guided fine needle aspirations were performed by the radiologist with 22 gauge needle for superficial lesions and 18 gauge spinal needle for deep-seated lesions, attached to 20 ml disposable plastic syringe.

Taking all aseptic precautions, area was cleaned, and during suspended respiration, needle was introduced percutaneously into the lesion under ultrasound guidance. Four to five smears were made and immediately fixed in 95% alcohol for 15-20 minutes and then stained with Papanicolaou

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stain. The aspirated material was studied cytologically and the smears were typed as malignant, suspicious of malignancy, negative for malignancy and inadequate.

Similarly true cut biopsies were taken under ultrasound guidance, processed and paraffin embedded sections were stained with H & E.

The cytological features were correlated with histological features.

**RESULTS:** 52 cases ranged in age from 1 to 80 years with maximum number (50%) of cases in age group of 31 to 50 years. Male to female ratio was 1.2:1(28:24).

On cytological examination smears were typed as (table 1).

Cytology diagnosis	No. of cases	Percentage
Malignant	46	88.5
Suspicious	02	3.8
Negative	01	1.9
Inadequate	03	5.8
<b>Total</b>	<b>52</b>	<b>100</b>

**Table 1: Typing of liver aspirates on cytology**

Out of 46 malignant smears 26(56.5%) were metastatic and 20 (43.5%) were primary neoplasms. The most common metastatic tumor was adenocarcinoma 24 (52.2%) cases, 1 (2.2%) case each was of metastatic squamous cell carcinoma, and lymphoma.

Amongst the primary tumors hepatocellular carcinoma (HCC) was most common, 14 (30.4%) cases, followed by 4 (8.7%) cases of cholangiocarcinoma and 2 (4.3%) cases of hepatoblastoma.

SL. NO.	Cytology diagnosis	No. of cases	Histological diagnosis	
			Positive for malignancy	Negative for malignancy
1.	Malignant	46	46	00
2.	Suspicious	02	02	00
3.	Negative	01	00	01
4.	Inadequate	03	02	01
	<b>Total</b>	<b>52</b>	<b>50</b>	<b>02</b>

**Table 2: Comparison of cytologic diagnosis with histological diagnosis**

46 cases typed malignant on cytology correlated well with histopathological diagnosis. Two cases typed suspicious on cytology were found malignant on histological examination. Out of 3 inadequate cytological smears, 2 were malignant and one was focal nodular hyperplasia. One case typed negative for malignancy on cytology was diagnosed as liver abscess.

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SL. No.	Disease category	No. of cases on cytology	No. of cases on histology	Percentage of concurrence in cytology and histology
<b>Primary Liver Neoplasm</b>				
1.	HCC	14	15	93.3
2.	Cholangiocarcinoma	04	04	100
3.	Hepatoblastoma	02	02	100
<b>Metastatic Liver Neoplasm</b>				
1.	Adenocarcinoma	24	26	92.3
2.	Squamous cell carcinoma	01	02	50
3.	Lymphoma	01	01	100
	<b>Total</b>	<b>46</b>	<b>50</b>	<b>92</b>

**Table 3: Typing of liver tumors on cytology and correlation with histology**

Percentage of concurrence in cytology and histology for primary hepatic malignancies was 95.2% and 89.6% for metastatic lesions.

SL.No.	Primary site	No. of cases	Percentage
1.	Gall Bladder	09	34.7
2.	Colon	08	30.8
3.	Breast	01	3.8
4.	Prostate	01	3.8
5.	Unknown	07	26.9
	Total	26	100

**Table 4: Sites of primary in metastatic adenocarcinoma**

Adenocarcinoma was the most common metastatic malignancy diagnosed in 26 cases (52%).9 cases showed primary in gall bladder, 8 were having primary in colon and 1 case each of carcinoma breast and prostate. For 7 cases primary lesion could not be ascertained.

Two cases diagnosed as metastatic squamous cell carcinoma had primary in gall bladder and one case showed metastatic deposits of NHL (Table 4).

Primary tumors constituted 21cases (42%), out of which most common neoplasm was HCC, 15 cases (30%) followed by 4 cases(8%) of cholangiocarcinoma and 2 cases(4%) of hepatoblastoma. (Table 3)

Sensitivity of FNAC of liver tumors came out to be 96%; specificity of the technique was 100%.Accuracy of FNAC was found to be 96.1 % with no false positive diagnosis.

**DISCUSSION:** Malignancy of liver either primary or secondary is one of the commonly occurring neoplasms in the body. Fine needle aspiration under ultrasound guidance has been found to be very useful in diagnosing hepatic tumors.<sup>2,3</sup>

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The most important requirement for cytodiagnosis is to obtain a representative sample. The ultrasound guided FNA of liver lesions increases the accuracy of sampling, even for a deeply seated lesion, and has been proved to be a safe and accurate method for diagnosing primary liver carcinomas and metastases.<sup>4</sup>

Various causes of inadequacy are hemorrhagic, necrotic smears, or smears from non-representative area.<sup>4</sup> In present study causes of inadequacy were hemorrhagic and non-representative smears.

An aspirate that obtains material only from surrounding tissue of the tumor may show reactive and proliferative changes, whereas an aspirate from the center of a large tumor may sample only degenerative and necrotic material<sup>4</sup>. Therefore aspiration to be representative the needle should pass through entire mass which can be achieved in ultrasound guided FNAC.

It is very difficult to differentiate between primary and metastatic tumors on cytology. Difficulty in cytological diagnosis arises at the end of malignant spectrum i.e., distinguishing well differentiated from benign lesions and separating less differentiated from metastatic malignancies.<sup>5</sup>

Important cytological criteria useful in distinguishing HCC from non-neoplastic liver are increased nucleocytoplasmic ratio, arrangement of tumor cells in trabecular pattern and atypical naked hepatocytic nuclei. Other secondary criteria useful in differentiation are nuclear features i.e., irregularly granular chromatin, uniformly prominent and multiple nucleoli.<sup>6</sup>

HCC is characterized not only by the characteristic cells but also by its trabecular pattern with sinusoidal stroma which is consistently present except in the rare variants such as fibrolamellar type.<sup>5</sup>

In the present study cytodiagnosis of HCC was made considering these features (fig. 1 & 2).

The primary cytological features to differentiate HCC from metastatic tumors stated by Bottles et al. include polygonal cells with centrally placed nuclei, malignant cells separated by sinusoidal capillaries and presence of bile.<sup>7</sup> Other secondary criteria useful in differentiating HCC are intranuclear cytoplasmic inclusions and endothelial cells surrounding tumor cells clusters.

The liver is one of the most frequent site of metastases. Malignant tumor originated in any site in the body may metastasize to liver by lymphatic, venous or arterial routes.

As reported in the literature metastatic neoplasms are the most common tumor in the liver.<sup>8</sup> It has been estimated that about 40% to 50% of all cancer patients have metastases in the liver.<sup>9</sup>

Reported frequency of metastatic neoplasms by various authors ranged from 40% to 91.5%, of which adenocarcinoma was the most common.<sup>1, 4, 10-13</sup> In the present study metastatic tumors (58%) were more frequently encountered than primary tumors. Metastatic adenocarcinoma constituted 52%. HCC was the most common primary liver tumor (30%).

The salient features separating HCC from metastatic adenocarcinoma given by Greene et al.<sup>14</sup> were tumor cells in HCC are polygonal or polyhedral, whereas cells are usually columnar or cuboidal in adenocarcinoma; cells in HCC have abundant eosinophilic and granular cytoplasm with one or two macronucleoli, whereas adenocarcinoma cells may show mucin secretion, and presence of more than two nucleoli is common.

Trabecular arrangement is suggestive of HCC, whereas acinar or glandular arrangement is more favorable to adenocarcinoma. Inflammatory background is commonly seen in adenocarcinoma. In our study, metastatic deposits from colon carcinoma showed large columnar cells with eccentric

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large nuclei and prominent nucleoli. Acinar arrangement and intracellular and/or extracellular mucin was frequently observed (figure 3 & 4).

The secondary deposit in the liver may reproduce the histology of primary lesions.

However this is not necessarily so, and in many instances the primary tumor may be well differentiated while the secondary deposit in the liver may be extremely anaplastic and give no hint of their origin. Histology will not always allow the site of primary to be identified especially, if tumor is undifferentiated.

Confirmation of hepatic metastases obviates the need of extensive diagnostic procedures or surgery.<sup>15</sup>

Once a diagnosis of metastatic adenocarcinoma is made, the site of primary tumor is considered to be of less importance in the subsequent prognosis and therapy of the patients<sup>16</sup>.

In present study common sites of primary in cases of metastatic adenocarcinoma were gall bladder and colon.

Various studies have reported sensitivity varying from 67% to 99.5% and specificity 87% to 100%.<sup>3, 4, 11, 17, 18</sup> In the present study, tumor type could be determined by FNAC with specificity up to 100%. FNAC was able to distinguish between neoplastic and non-neoplastic lesions with an overall sensitivity of 96%.

The overall accuracy of procedure in the present study was 96.4%, which was comparable to the rate of accuracy reported in literature (78% to 97.82%).<sup>3,4,11,19</sup> Complications are rarely reported in the literature<sup>15</sup> and were not encountered in our study.

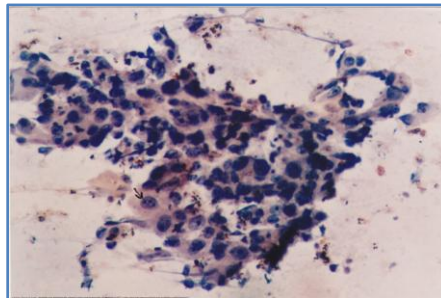
**CONCLUSION:** FNA of hepatic lesions is an effective, safe and well accepted practice with good sensitivity and specificity. The smears obtained under ultrasound guidance are highly representative. It is recommended that image directed FNAC should be the primary diagnostic modality for assessment of suspected liver malignancy.

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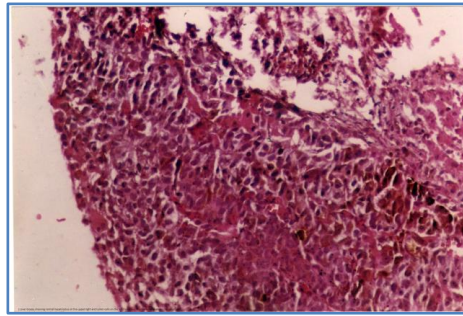
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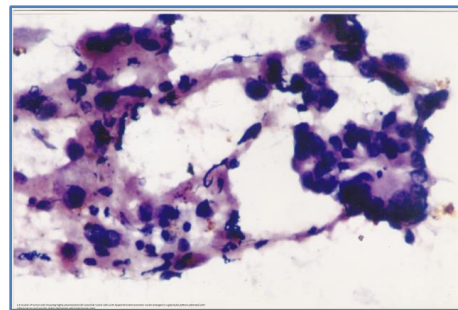


**Figure 1**

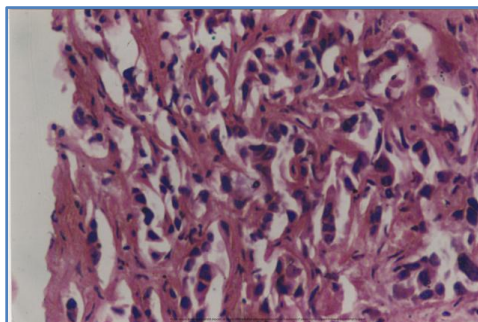
Smear showing both centrally and peripherally placed nuclei, coarse granular chromatin in HCC, nuclei showing macronucleoli and multiple nucleoli (arrow).

**Figure 2**

Liver biopsy showing normal hepatocytes on the upper right and tumor cells on the left. Cells have abundant eosinophilic cytoplasm and increased nucleocytoplasmic ratio-HCC.

**Figure 3**

A cluster of tumor cells showing highly pleomorphic tall columnar tumor cells with hyperchromatic eccentric nuclei arranged in a glandular pattern, admixed with inflammatory and necrotic debris-Metastatic adenocarcinoma colon.

**Figure 4**

Liver biopsy showing metastatic deposits of poorly differentiated adenocarcinoma cells with evidence of pleomorphism, hyperchromasia and attempt to gland formation at several places.

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