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Research Article

Cytopathological Spectrum of Space Occupying Lesions in Liver of the Patients Attending in Tertiary Care Hospital at N.M.C.H, Patna, A Demographic Study

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ABSTRACT

Background: Fine needle aspiration cytology is a rapid, economical and minimally invasive technique without substantial complications for the diagnosis of benign and malignant lesion. The aim of present study was to evaluate the nature of space occupying lesion in liver (hepatic mass) by FNAC under ultrasound guidance as well as to assess the demographic spectrum of the patients. **Material and Methods**: A total of 234 cases presenting with space occupying lesion of liver were included in the study. Ultrasound guidance FNAC was performed from the sol liver in the presence of trained radiologist using 20-22 gauze disposable spinal needle connected to 10 ml disposable plastic syringe with full aseptic precautions. **Results**: The minimum and maximum age of the patients was 6 years and 89 years respectively. However, the mean age of the patient was 54 years with mean ± SD as (54±16 yrs.). Among the females, 75.4% were above the 40 years of age and whereas, 78.6% males were above 40 years of age. A highly statistically significant difference ($p<0.0001$) was found for age greater than 40 years for all categories of disease when compared to age less than 40 years. Occurrences of primary (84.3%), secondary (83.5%) and other (85.7%) malignancies were significantly ($p <0.001$) higher in patients aged above 40 years. Secondary malignancies, metastatic adenocarcinoma (50.0%) was the most common malignancy causing space occupying lesion of liver, followed by primary malignancy of liver (38.46%). Other malignancies were seen in (11.54%) cases. 7 cases (2.99%) were diagnosed as suspicious for malignant due to hypo cellular smear consisting of few atypical cells and 11 cases (4.70%) were non representative (inconclusive), as it contained only few scattered hepatocytes in the background of RBCs. **Conclusion**: Ultrasound guided FNAC from space occupying lesion of liver is highly accurate technique for making the diagnosis of hepatic lesions without any major complications and can accurately distinguish non-neoplastic lesions from neoplastic lesions as well as categorize primary and secondary malignancies, helping in management of hepatic lesions.

Key Words: *Cytopathology, Space occupying lesions of liver (liver mass), US Guided FNAC.*

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INTRODUCTION

Liver is one of the most common sites of metastasis in patients of malignancy as well as it is affected by primary neoplastic lesions and non-neoplastic lesions causing space occupying lesions in liver parenchyma. With the advent of newer radiological techniques like ultrasound, CT scan, MRI scan and nuclear scan (PET scan), even small lesions which were undetected in earlier days, now discovered easily with the help of such advanced radiological techniques. FNAC (Fine needle aspiration cytology) has been proven to be a very effective means of obtaining tissue from the suspected space occupying lesion in liver parenchyma under US/CT guidance and for the Cytological assessment to differentiate its nature whether benign or malignant along with other non-neoplastic conditions. Occasionally inflammatory lesions mimic as mass lesions which may be investigated by FNAC to establish its nature [1].

FNAC is a rapid, less expensive and minimally invasive technique without significant complications for the diagnosis or to differentiate between benign and malignant lesions. Wide bore needle biopsy from the space occupying lesion of liver, although provide greater amount of tissue in comparison to FNAC, it carries greater risk of complications, more expensive, more time consuming and uncomfortable to the patients. With the consideration of minimal discomfort, minimal economic burden, very little liver damage and high level of safety, FNAC often assists as a first choice of investigative technique for the diagnosis of nature of space occupying lesion of liver.

According to literature, the diagnostic accuracy of FNAC for liver lesion is greater than 85% and in malignant lesion its sensitivity is around 90% (67-100%) [2].

The aim of present study is to evaluate the nature of space occupying lesion in liver by FNAC under us guidance as well as to assess the demographic spectrum of patients presenting at our tertiary care hospital.

MATERIAL AND METHODS

The present study was conducted in the department of pathology, Nalanda Medical College, Patna, with the help of department of microbiology, medicine and surgery during the period of January 2015 and December 2018. A total of 234 patients presented with space occupying lesions within the liver parenchyma after ultrasound, were subjected to ultra sound guided FNAC. Clinical details as well as all the routine blood investigations along with prothrombin time index were obtained from the patients. Patients with bleeding diathesis, suspected cases of hydatid cysts and diagnosed cases of Haemangioma by ultrasound or CAT scan were excluded from the study.

FNAC was performed from the SOL of liver with the help of trained Radiologist. The standard technique was applied using 20-22 G disposable spinal needle connected to 10 ml disposable plastic syringe with full aseptic precautions by proper cleaning using antiseptics under the US guidance. Multiple slides were prepared immediately after the aspiration. Both air dried smears as well as slides fixed in absolute alcohol were prepared and stained by H & E stain. All the slides reviewed under the microscope for cytological evaluation.

Gram's staining, Ziehl-Neelsen staining and culture & sensitivity test was done from purulent aspirate as well as wet mount test were done from fresh purulent aspirate to detect trophozoites of entamoebahistolytica. In some cases, other stains such as Giemsa stain, MGG stain and Papanicolaou stain also used for the staining slides.

Results

Table 1 shows, age and sex distribution of patients (n=234) & shows 172cases (73.51%) were male and 62 cases (26.49%) female.

Out of 234 cases, maximum number of suspected cases of SOL in liver was in 51-60 years age group (25.21%); more than three fourth cases were in patients of more than 41 years of age; Among the females, 75.4% were above the 41 years of age and whereas, 78.6% males were above 41 years of age.

In **Table 2** Out of total 234 cases 69cases (29.49%), as hepatocellular carcinoma of which 65cases (27.78%) were male patients. One case (0.43) was diagnosed as hepatoblastoma; total 70cases (29.92%) were found as Primary malignant lesion of liver.

Out of 234cases, maximum number of cases in both sexes were metastatic adenocarcinoma, 91cases (38.89%); of which 48cases (20.51%) were male patients and 43 cases (18.38%) were female patients.

14 cases (5.98%) were found as undifferentiated carcinoma, where the cellular differentiation was so poor that cyto-morphologically it could not be possible to differentiate whether primary hepatocellular carcinoma or metastatic adenocarcinoma. This is why they were named as undifferentiated carcinoma. Biopsy was suggested in such cases for final diagnosis, Further, these cases could not be evaluated as those patients were OPD patients and lost for follow up.

Other malignant tumours diagnosed by FNAC were NHL, 4 cases (1.71%), malignant mesenchymal tumours,3cases (1.28%) possibly either due to metastasis of GIST or primary malignant mesenchymal of liver.

6 cases (2.56%) were diagnosed as benign lesion; of which two cases were diagnosed as Haemangioma and four cases as benign lesions likely to be cirrhotic or regenerative nodule.

28cases (11.97%) were inflammatory pyogenic lesions, of which 15cases of amoebic liver abscess, 11cases of bacterial pyogenic abscess and 2casesdiagnosed as chronic granulomatous pyogenic lesion.

11 cases (4.70%) were non representative (Inconclusive), as it contained few scattered hepatocytes in the background of blood.

A highly statistically significant difference ($p<0.0001$) was found for age greater than 40 years for all categories of disease when compared to age less than 40 years

Table 3showsmaximum number of hepatocellular carcinomas was found after 41years of age 85.51% in both sexes out of total 69 cases and maximum number of Metastatic Adenocarcinoma was found after 41 years of age 84.61% out of 91 cases in both sexes.

Table 4 shows, secondary malignancy, as metastatic adenocarcinoma 91cases (50.0%) out of 182 total malignant cases, was the most common malignant lesion causing space occupying lesion of liver, followed by primary malignancy of liver 70cases(38.46%).Malignancies were significantly($p < 0.001$) higher in patients aged above 40 years. Increasing age showed significant odds (OR (95% CI) i.e., 1.05 (1.03 - 1.07); $p < 0.001$) for developing malignancy, when applying univariate logistic regression analysis.Occurrence of malignancies had no significant ($p = 0.69$) association with gender.

DISCUSSION

Fine needle aspiration cytology is a very useful diagnostic modality to diagnose space occupying lesion of liver and helps to categorize into neoplastic and non-neoplastic lesions. Utility of FNAC in diagnosing hepatic mass lesions was first showed by Lundquist et al in 1971[3]. Ultrasound guided FNAC leads to very little tissue damage and offers accuracy without major complications and minimal intervention at low costs. The only absolute complications of FNAC from SOL liver considered in present study, was patients with haemorrhagic tendency having prolonged prothrombin time, and suspected cases of Echinococcosis and patients with suspected haemangioma at liver surfaces. In our present study, all cases were subjected to ultrasound guided FNAC from SOL liver as it has been reported to be safe, useful and accurate technique for making cyto-pathological Diagnosis [4]. In present study, the patients' age ranged from 6 years to 85years with male predominance (73.5%).Malignant cases were more common after the ages of 41 years in both sexes (83.5%) out of 182 malignant cases.Tailor et al (2016) observed that average age was 59.37 years with a range of 30-80 years; and found more than 94.85% cases after 41 years (in age group of 5th decades onwards)[5]. In present study, malignant cases were found in 84.08% after the age of 41 years (age group of 5th decades onwards).The ages for hepato-cellular carcinoma in present study ranges from 26-80 years.Earlier studies conducted by Nggada et al(2007) described that a total of 47 patients, were studied with a mean age of (SD +/-14.24) years and range between 14 and 75 years[6]. The peak age was between 40-59 years age group.

In present study, the diagnosis was given "Suspicious for malignant" in 3% cases, due to hypocellular smear having few atypical cells in the background of RBCs and necrotic material. Such patients were advised for the repeat FNAC, but the final diagnosis could not be achieved as they were lost to follow up. In 4.7% cases, the cytological diagnosis was inconclusive as the smear shows only few benign looking hepatocytes in the background of RBCs and other blood elements.In our present study, we were able to differentiate the FNAC result into malignant, benign and non-neoplasticinflammatory lesions in 92.3% cases. The diagnostic accuracy in our study was 92.3% which was similar with most of the studies reported in literatures such as Swamy et al [7] 97.5%; Mondal [8] 99.5%; Kuo et al [9] 86.1%; Tsui et al [1] 96%; and Talukder et al [10] 93.5%.Soyuer et al [11] and Wee et al [12] described the criteria to separate WD-HCC from reactive Hepatocytes on the basis of architectural features of the smear showing hypercellularity, arborescent, cohesive clusters, broad trabeculae, transgressing /peripheral endothelium, small monotonous hepatocyteswith nuclear crowding, increased N/C ratio, cytoplasmic hyaline inclusions, atypical naked nuclei and tumour giant cells in comparison to reactive hepatocytes. Bottle *et al*(1988) described in earlier studies three criteria to differentiate HCC from metastatic tumours and the features favouring HCC were polygonal cells with centrally placed nuclei, malignant cells separated by sinusoidal capillaries and bile[13]. Das et al (1997) described cytological features favouring metastatic adenocarcinoma as presence of Dissociated and irregular clusters of malignant epithelial cells along with necrosis and benign hepatocytes[14]. In present study, the cytological features of hepatoblastoma resemble those of small blue round cell tumours of childhood, consisting of small round to oval uniform sized cells with granular cytoplasm and indistinct cell borders. Frequent mitosis seen. Background consists of dirty material along with fragments of capillaries and plump spindle shaped endothelial cells. Rasania et al (2007) found in his study that metastatic tumours were the most common malignancy of liver constituting 70.4% which included all the malignant tumours other than primary HCC[15]. In present study, secondary metastatic adenocarcinoma was the most common malignancy of liver (50%); followed by hepatocellular carcinoma (38%) and other malignancies (11.54%). Benign lesions reported as the smear showed benign looking hepatocytes having granular eosinophilic Cytoplasm with indistinct cell borders. Tsui et al (1998) described in his study that occasionally inflammatory disorders of liver were also Investigated by FNAC when they mimic like a mass lesion [1].

In present study, pyogenic inflammatory lesions diagnosed in 11.97% cases, which included Amoebic liver Abscesses, bacterial liver abscess and chronic granulomatous lesions, likely tuberculous aetiology. Gatphoh et al (2003) described in his study that 68% of granulomatous lesions in liver biopsy were of Tuberculous aetiology in Indian population[16].

CONCLUSION

USG FNAC from SOL liver is very helpful, safe, less time consuming, less cost effective and highly accurate Technique for diagnosis of hepatic lesion with minimal hospital stay and without any major complications.FNAC can

accurately distinguish non-neoplastic lesions from neoplastic lesions and can categorize the different non-neoplastic lesions as well as secondary malignant lesions. It has been proved to be very useful in the management of hepatic lesions.

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TABLE 1 AGE AND SEX DISTRIBUTION OF PATIENTS (N=234)

Age range	No. of cases(%)	No. & % of Males	No. & % of Females
Up to 10 years	3 (1.28%)	2 (0.85%)	1 (0.43%)
11-20 years	3(1.28%)	2 (0.85%)	1 (0.43%)
21-30 years	19(8.12%)	12 (5.13%)	7 (2.99%)
31-40 years	27(11.54%)	21 (8.97%)	6 (2.57%)
41-50 years	40(17.10%)	23 (9.83%)	17 (7.27%)
51-60 years	59(25.21%)	41 (17.52%)	18 (7.69%)
61-70 years	53(22.65%)	48 (20.51%)	5 (2.14%)
More than 71 years	30(12.82%)	23 (9.83%)	7 (2.99%)
TOTAL	234(100%)	172 (73.49%)	62 (26.51%)

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TABLE 2 AGE & SEX DISTRIBUTION OF SOL LIVER IN FNAC (N=234)

DISEASES	No. Of cases	% Of cases	No. Of males	% Of males	No Of females	% Of females
Hepatocellular Carcinoma	69	29.49	65	27.78	4	1.71
Metastatic Adenocarcinoma	91	38.89	48	20.51	43	18.38
Undifferentiated Carcinoma	14	5.98	9	3.85	5	2.13
Non-Hodgkin's Lymphoma	4	1.71	4	1.71	X	X
Mesenchymal Tumour	3	1.28	2	0.85	1	0.43
Hepatoblastoma	1	0.43	1	0.43	X	X
Benign Lesion	4	1.71	3	1.28	1	0.43
Haemangioma	2	0.85	1	0.43	1	0.43
Infective Pyogenic Lesion	28	11.97	25	10.68	3	1.28
Suspicious for Malignant	7	2.99	6	2.56	1	0.43
Inconclusive	11	4.70	8	3.42	3	1.28
Total	**234**	**100**	**172**	**73.50**	**62**	**26.50**

TABLE3 HEPATIC DISEAES IN DIFFERENT DISEASES(N=234)

Age range (years)	Hepato cellular carcinoma	Metastatic adeno car-cinoma	Undiffentiated carcinoma	Non Hodgkins lymphoma	Malignant Mesenchymaltumot	Hepa to-blastoma	Haeman-giom a	Benign-lesion	Inflammatory Pyogenic lesion	Suspicious For malignant	Inconclusive
<10	X	X	X	X	X	1 0.43 %	X	X	2 0.85%	X	X
11-20	X	X	X	1 0.43%	X	X	X	X	2 0.85%	X	X
21-30	3 1.28%	8 3.42%	X	X	X	X	1 0.43 %	1 0.43 %	5 2.14%	1 0.43%	X
31-40	7 2.99%	6 2.56%	1 0.43%	1 0.43%	1 0.43%	X	X	1 0.43 %	5 2.14%	1 0.43%	4 1.71%
41-50	11 4.70%	18 7.69%	2 0.85%	X	1 0.43%	X	X	X	6 2.56%	1 0.43%	1 0.43%

51-60	21 8.97%	21 8.97%	3 1.28%	X	1 0.43%	X	X	1 0.43 %	5 2.56%	3 1.28%	4 1.71%
61-70	18 7.69%	25 10.68 %	5 2.14%	1 0.43%	X	X	1 0.43 %	X	2 0.85%	1 0.43%	X
>70	9 3.85%	13 5.56%	3 1.28%	1 0.43%	X	X	X	1 0.43 %	1 0.43%	X	2 0.85%
Total	**69 29.49 %**	**91 38.89 %**	**14 5.98%**	**4 1.71%**	**3 1.28%**	**1 0.43 %**	**2 0.85 %**	**4 1.71 %**	**28 11.97%**	**7 2.99%**	**11 4.70%**

TABLE 4 COMPARATIVE INCIDENCE & SEX DISTRIBUTION OF PRIMARY & OTHER MALIGNANCIES OF LIVER (N=182)

Malignant Lesion	No. of cases	% cases	Male cases (%)	Female cases(%)
Primary malignant lesion	70	38.46%	66(36.26%)	4(2.20%)
Secondary Metastatic Adenocarcinoma	91	50.00%	48(26.37%	43(23.62%)
Other malignancies(undiff.ca+ NHL + Malignant Mesenchymal Tumour)	21	11.54%	15(8.24%)	6(3.30%)
Total	**182**		**129(70.88%)**	**53(29.12%)**

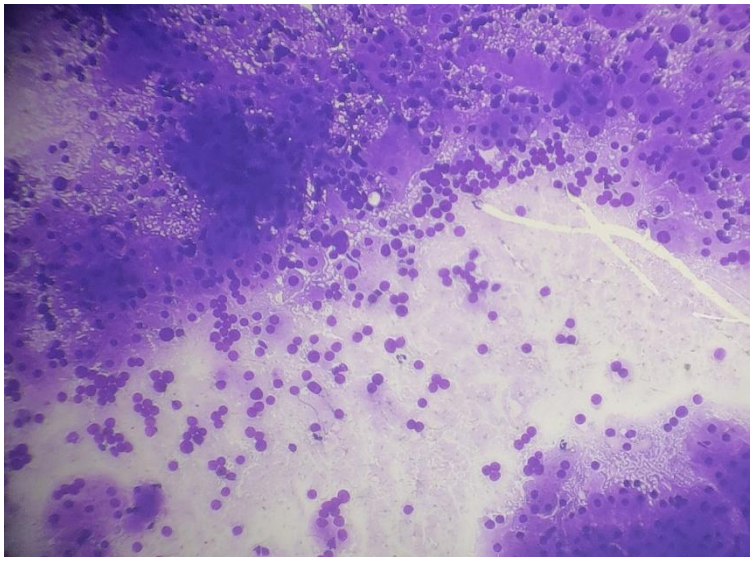

Fig. 1 MICROPHOTOGRAPH OF HEPATOCELLULAR CARCINOMA (Field stain,10x10) (Hypercellular smear, hepatocytes with increased N/C ratio, atypical bare nuclei, Trabecular pattern of cells)

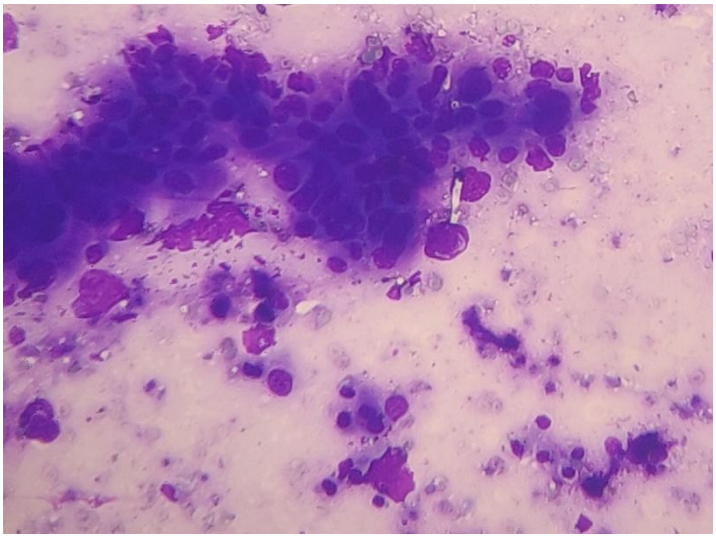

Fig.2 METASTATIC ADENOCARCINOMA (FIELD STAIN)
(Clusters of pleomorphic cells, pleomorphic nuclei, prominent nucleoli, glandular arrangement of cells, necrotic background)

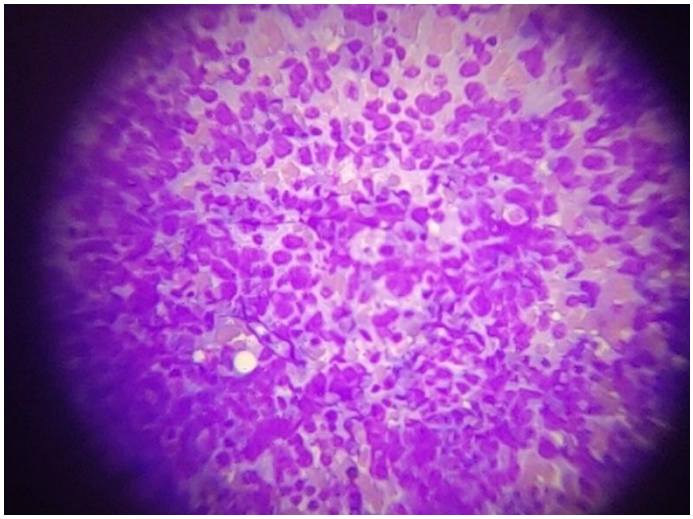

Fig. 3 PHOTOMICROGRAPH OF NON-HODGKIN'S LYMPHOMA
(Monotonous population of small cells with scant cytoplasm

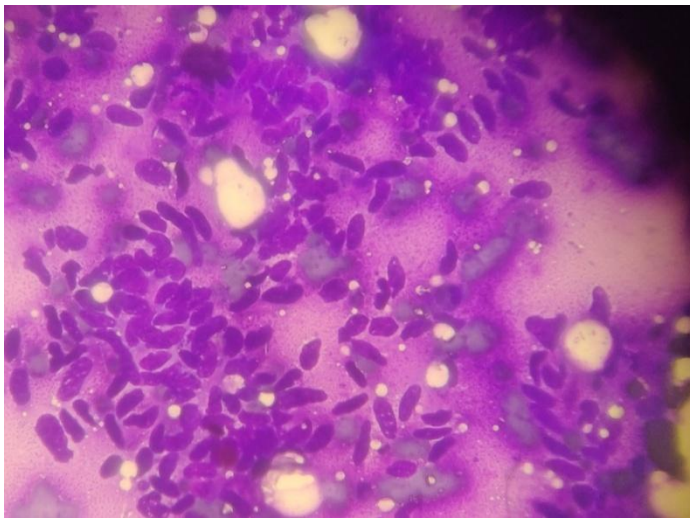

Fig. 4 PHOTOMICROGRAPH OF MALIGNANT MESENCHYMAL TUMOR
(Clusters of spindle shaped cells)

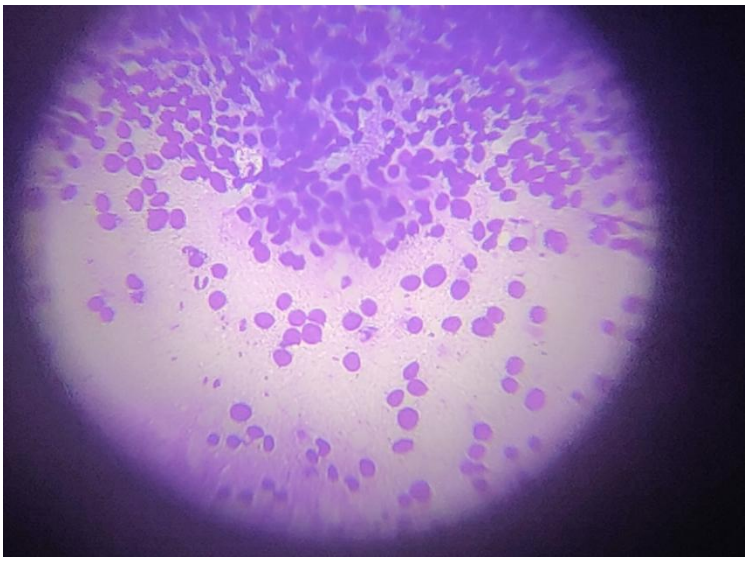

Fig. 5 PHOTOMICROGRAPH OF HEPATOBLASTOMA
(Small round cells with scant cytoplasm)