Fine Needle Aspiration Cytology in the Diagnosis of Focal Liver Lesions

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Fine needle aspiration cytology (FNAC) assisted by cell block examination might be more accurate method for the definitive diagnosis of focal liver lesions (FLL). This study was designed to find out the role of FNAC in the diagnosis of FLLs in comparison to cell block preparations. This cross sectional observational study was carried out in the department of Pathology in collaboration with the department of Radiology & Imaging at Sylhet MAG Osmani Medical College. Study period was from 1 July, 2015 to 30 June, 2016. Clinically & radiologically diagnosed patients of focal liver lesions were study populations. The age of the study patients ranged from 15 to 80 years with a mean of 53.58 years. On FNAC, 10% cases were unsatisfactory, 8% cases were cystic lesion, 4% cases were benign tumor and 78% cases were malignant tumor. Among 39 malignant cases, 30.77% cases were hepatocellular carcinoma (HCC) and 69.23% cases were metastatic adenocarcinoma. Unsatisfactory samples were 18.18%, 6.82% were benign tumors and 75% were malignant tumors. Among the malignant lesions, 18.18% were HCC and 81.82% were metastatic adenocarcinoma. The sensitivity, specificity, positive predictive value (PPV), negative predictive value(NPV) and accuracy of FNAC in the evaluation of FLLs were 100%, 66.67%, 97.06%, 100% and 97.22%, respectively. The sensitivity, specificity, PPV, NPV and accuracy of FNAC in the detection of HCC were 66.67%, 85.18%, 50%, 92% and 81.82% respectively. FNAC of focal liver lesions has high sensitivity and accuracy in the detection of malignancy but it has low sensitivity in the detection of HCC. Cell block preparations were found superior to cytomorphology as immunostaining can be done on cell block preparations.

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Introduction

A focal liver lesion (FLL) is a solid or cystic mass or area of tissue that is identified by radiological or imaging techniques as an abnormal part of the liver. It may be either a benign lesion such as focal nodular hyperplasia, hepatocellular adenoma and hepatic cyst or a malignant lesion such as hepatocellular carcinoma, cholangiocarcinoma, hepatoblastoma and metastatic carcinoma.[1]

Pathological examination is an important aspect in the evaluation of an FLL. FNAC is the preferred method for diagnosis of focal liver lesions and needle core biopsy (NCB) for evaluating diffuse liver diseases where architectural details are important.[2] In recent years FNAC has emerged as an effective tool for diagnosis of a hepatic mass.

Cell blocks prepared from residual materials of fine needle aspirations can be useful adjuncts to smears for establishing a more definitive cytopathological diagnosis.[3] Use of cell blocks improves diagnostic accuracy as it facilitates study of architecture details of multiple sections, use of special stains and immunohistochemistry.[4]

The distinction of moderately to poorly differentiated hepatocellular carcinoma from metastatic carcinoma may be a major problem for cytologists and this distinction is clinically important. Immunohistochemistry is required in this situation to differentiate hepatocellular carcinoma from metastatic carcinoma.[5]

With this background the study was designed to find out the role of FNAC in the diagnosis of focal liver lesions and to correlate its efficacy with cell block preparations using H&E and immunohistochemistry.

Methods

This cross sectional observational study was carried out in the department of Pathology in collaboration with the department of Radiology & Imaging at Sylhet MAG Osmani Medical College from 1 July, 2015 to 30 June, 2016. Clinically and radiologically diagnosed patients of focal liver lesions attending the department of Radiology & Imaging from different departments during the study period were the target population and those who fulfilled the inclusion and exclusion criteria were considered as study population. Patients of all ages and both sexes were included. Patients with bleeding diathesis, suspected liver abscess, hydatid cyst and hemangioma were excluded from the study. 22 gauge needle was placed in the lesion under ultrasound guidance and the material was aspirated with a 10 ml disposable syringe. After placing aspirates on the slides, thin smears were prepared by gentle friction of two slides. Then smears were fixed in 95% ethyl alcohol for at least 30 minutes and stained with Papanicolaou stain. After preparation of smears, the residual material was secured for clot preparation. It was then transferred into 10% formalin and processed as a cell block.[6] Then, the cell blocks were cut at 5 micrometer thickness and were stained with Harri's Haematoxylin and Eosin stain. From the paraffin block 3 micrometer sections were cut and stained for immunohistochemistry with Glypican-3 antibody. The immunohistochemistry was performed in the Immunohistochemistry Laboratory of Bangabandhu Sheikh Mujib Medical University (BSMMU) following their staining protocol. All the data were organized by using scientific calculator and Statistical Package for Social Science (SPSS) version 23.

Results

The age of the study patients ranged from 15 to 80 years with a mean of 53.58 years (SD $\pm$15.32). Out of 50 cases, 33 (66%) were male and 17 (34%) were female with male to female ratio of 1.94:1. Among these patients, the highest number of patients 13(26%) were in the age group 51-60 years (Table I).

Table I: Age and sex distribution of study cases (n=50)

Age Groups (years)	Male No (%)	Female No (%)	Total No (%)
11-20	2(4)	1(2)	3(6)
21-30	1(2)	0(0)	1(2)
31-40	2(4)	4(8)	6(12)
41-50	9(18)	3(6)	12(24)
51-60	7(14)	6(12)	13(26)
61-70	10(20)	2(4)	12(24)
71-80	2(4)	1(2)	3(6)
Total	33(66)	17(34)	50(100)

Out of 50 focal liver lesions, 5 cases were unsatisfactory, 4 cases were cystic lesion, 2 cases were benign tumor and 39 cases were malignant tumor in cytology. Among the malignant cases, 12 were hepatocellular carcinoma (HCC) and 27 were metastatic adenocarcinoma (Figure 1).
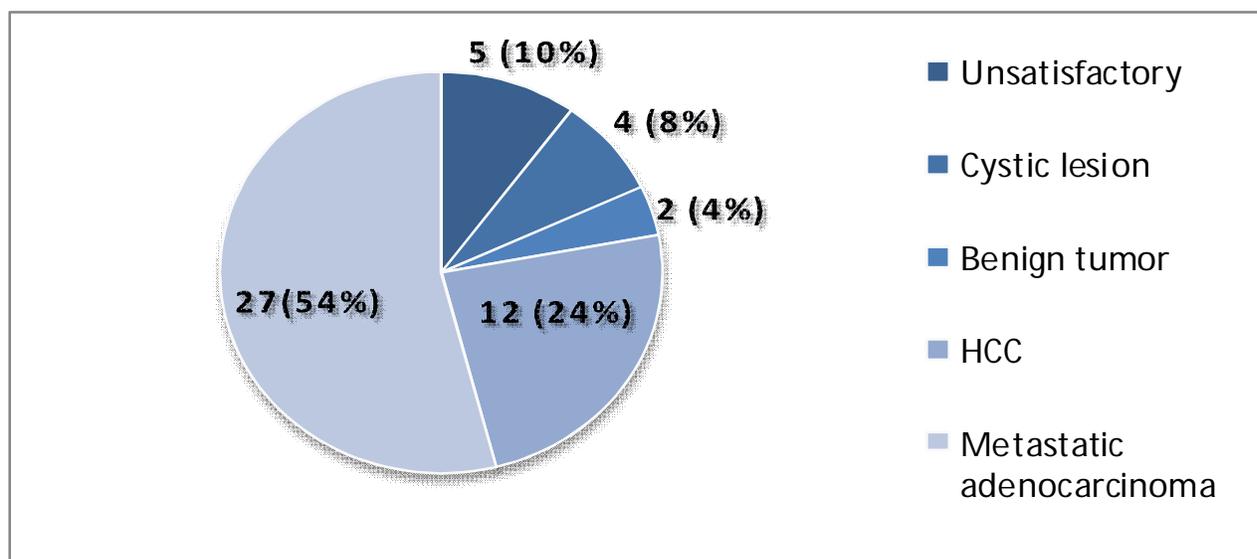

Figure 1. Pie diagram showing distribution of study cases according to FNA cytomorphology

Finally, 8 unsatisfactory, 3 benign and 33 malignant cases were diagnosed in cell block preparations. Among 33 malignant cases 6 were diagnosed as hepatocellular carcinoma (HCC) and 27 were diagnosed as metastatic adenocarcinoma (Figure-2).
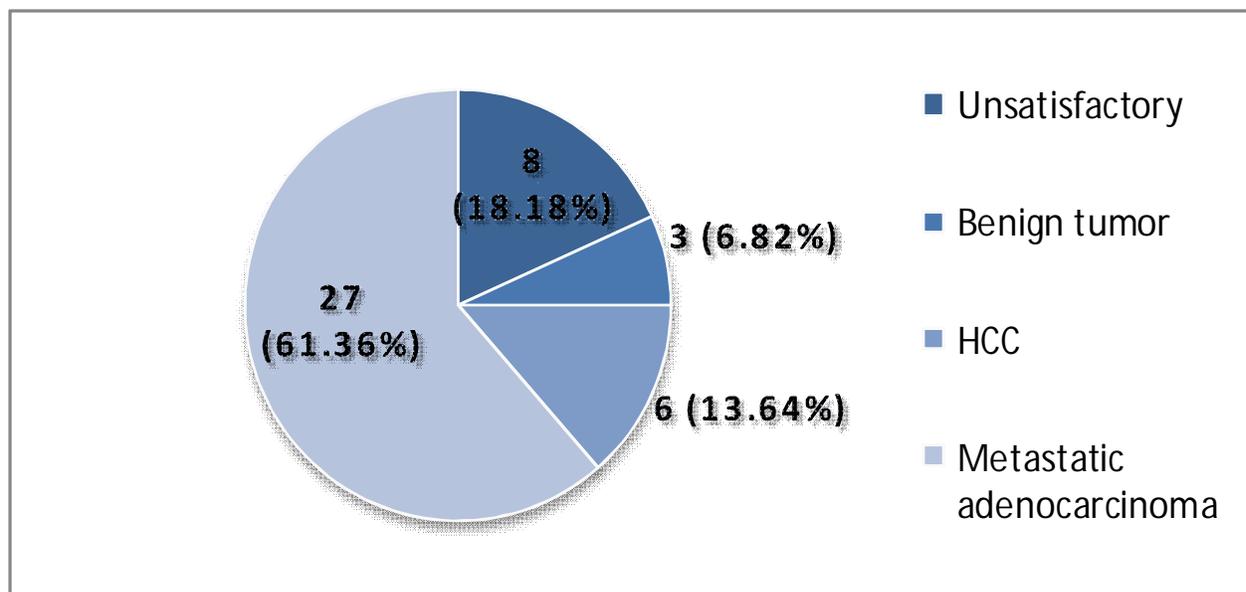
Figure 2. Pie diagram showing distribution of 44 cases according to combined cell block preparations.

36 cases were conclusive on both cytomorphology and cell block preparations. On evaluation of cytomorphological diagnosis of 36 cases, 33 were true positive diagnosis, 2 were true negative diagnosis, 1 was false positive diagnosis and there was no false negative diagnosis (Table II). Sensitivity, specificity, PPV, NPV and accuracy of FNAC in the diagnosis of malignant focal liver lesions were100%, 66.67%, 97.06 %, 100 % & 97.22 %, respectively.

Table II: Statistical evaluation of cytomorphological diagnosis of 36 conclusive cases.

		Cytomorphological diagnosis			
Combined cell block preparations (H&E and IHC)		Disease positive (Malignant)		Disease negative(Benign)	
Positive(Malignant)	33	TP	33	FP	1
Negative(Benign)	3	FN	0	TN	2
Total	36		33		3

TP= True positive, TN= True negative, FP= False positive, FN= False negative

33 cases were diagnosed as malignant by both FNAC and cell block preparations. On evaluation of cytomorphological diagnosis, 4 were true positive, 23 were true negative, 4 were false positive and 2 were false negative in the detection of HCC (Table III). Sensitivity, specificity, PPV, NPV and accuracyof FNAC in the detection of HCC were 66.67%, 85.18%, 50%, 92% and 81.82%, respectively.

Table III: Statistical evaluation of cytomorphological diagnosis in the detection of HCC.

Combined cell block preparations (H&E and IHC)		Cytomorphological diagnosis			
		Disease positive (HCC)		Disease negative (Non HCC)	
Positive (HCC)	6	TP	4	FP	4
Negative (Non HCC)	27	FN	2	TN	23
Total	33		6		27

TP= True positive, TN= True negative, FP= False positive, FN= False negative

Discussion

In the present study, USG guided FNAC was compared with cell block preparations (H&E and immunohistochemistry) in differentiation of focal liver lesions. FNA smears were available in all the 50 cases, but cell blocks were available in 44 cases.

Age of the study patients ranged from 15 to 80 years with a mean of 53.58 years. Nazir et al. (2010) and Kuo et al. (2004) showed 55 and 58.1 years as mean age in their studies which are close to the mean age of present study.[7,8] Highest number of patients (26%) was in the age group of 51-60 years in our study. Nazir et al. (2010) reported that maximum number of cases was seen between 55-65 years of age which is nearly similar to present study.[7] Out of 50 cases, 33 (66%) were male and 17 (34%) were female with male to female ratio of 1.94:1. Similar findings were reported by Swamy et al. (2011).[9] Nazir et al. (2010) showed a male to female ratio of 1.7:1 which is also close to present study.[7]

Out of 50 cases, 5 (10%) cases were unsatisfactory, 4 (8%) cases were cystic lesion, 2 (4%) cases were benign tumor and 39 (78%) cases were malignant tumor on cytomorphology. Further categorization of benign tumors was not done as in Khurana et al. (2009).[6] Among 39 malignant cases, 12 (30.77%) cases were HCC and 27 (69.23%) cases were metastatic carcinoma. All the cases of metastatic carcinoma were adenocarcinomas. Nearly similar findings were found on cytomorphology in the study of Mohmmed et al. (2012), Nazir et al. (2010), Khurana et al. (2009) and Ceyhan et al. (2006).[6,7,10,11] Ozkara et al. (2012) found 9.9% of cases as unsatisfactory on cytomorphology which is similar to the unsatisfactory smear (10%) of the present study.[12]

In final diagnosis of 44 cases by combined cell block preparations (H&E and immunohistochemistry), 8 (18.18%) were unsatisfactory, 3 (6.82%) were benign tumors and 33 (75%) were malignant tumors. Nazir et al. (2010) reported 85% cases as malignant which is nearly close to the malignant cases found in the present study.[7] But Mohmmed et al. (2012) showed 39% cases as malignant which is lower and Khurana et al. (2009) showed 93.75% cases as malignant which is higher than that of present study.[6,10] Among the malignant lesions, 6 (18.18%) were HCC and 27 (81.82%) were metastatic adenocarcinoma in our study. Khurana et al. (2009) found 17.78% cases as HCC and 82.22% cases as metastatic tumor which are concordant with the present study.[6]

The sensitivity, specificity, and accuracy of USG guided FNAC in the evaluation of focal liver lesions were 100%, 66.67% and 97.22%, respectively. Sensitivity of the present study (100%) is similar or close to the sensitivity of studies done by Khurana et al. (2009), Nazir et al. (2010), Swamy et al. (2011) and Mohmmed et al. (2012).[6,7,9,10] Specificity of the present study (66.67%) has concordance with the specificity found by Mohmmed et al. (2012).[10] The specificity shown by Khurana et al. (2009), Nazir et al. (2010) and Swamy et al. (2011) has discordance with that of current study.[6,7,9] The present study showed an accuracy of 97.22% which is similar to that of Nazir et al. (2010) and Swamy et al. (2011).[7,9]

The sensitivity, specificity, and accuracy of FNAC in the detection of HCC were 66.67%, 85.18% and 81.82% respectively in our study. Sensitivity of FNAC in the detection of HCC described by Ozkara et al. (2013) was 68.2% which is similar to the sensitivity of present study.[12] Khurana et al. (2009) and Nazir et al. (2010) showed the sensitivity in the detection of HCC as 72.3% and 96% respectively which are higher than the sensitivity of present study.[6,7] Specificity and accuracy showed by Nazir et al. (2010) were 100% and 97.5% respectively which are also higher than those of the present study.[7]

Conclusion
FNAC of focal liver lesions has high sensitivity and accuracy in the detection of malignancy but it has low sensitivity in the detection of HCC. No significant complication was observed during aspiration. FNAC is a relatively safe, quick, cost effective and patient compliant procedure which has high accuracy in the differentiation between benign and malignant focal liver lesions. Simultaneous cell block preparations can improve the efficacy of FNAC in the subtyping of malignancy.

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