Ultrasound/computerized tomography guided fine needle aspiration cytology of liver lesions

Lekha. M.B.[1,*], D.C. Prabhu[2], A.H. Nagarjappa[3]

[1]Assistant Professor, Dept. of Pathology, Dr. B. R. Ambedkar Medical College and Hospital, Bangalore, Karnataka, [2,3]Retired Professor, Dept. of Pathology, Bangalore Medical College and Research Institute, Bangalore, Karnataka, India

***Corresponding Author:**
Email: dr_lekha@rediffmail.com

Abstract

Introduction: Malignancy in the liver, primary or metastatic, is usually inoperable at the time of diagnosis and as such, portends an ominous prognosis. A diagnostic modality such as FNAC, which offers accuracy with minimal complications and requires minimal intervention at low cost, warrants consideration early in the investigation sequence.

Objectives: The study has been undertaken to evaluate the diagnostic efficacy of ultrasonography (USG)/ computerized tomography (CT) guided FNAC in the diagnosis of liver lesions, to correlate FNAC diagnosis with histopathology wherever possible, to correlate FNAC diagnosis with radiology diagnosis and to study the cytological patterns of liver lesions.

Materials and Methods: A prospective study of 60 patients was conducted between November 2008 and October 2010. After obtaining the detailed clinical and radiological data, patients were subjected for FNAC under USG or CT guidance.

Results: Cytodiagnosis of 60 cases were categorized into 6 (10%) Non-neoplastic lesions, 53 (88.33%) malignant neoplastic lesions and 1 (1.66%) as suspicious of carcinoma. The different neoplastic lesions were 21 (39.62%) hepatocellular carcinoma, 21 (39.62%) metastatic adenocarcinoma, 6 (11.32%) metastatic poorly differentiated carcinoma and 5cases (9.43%) of unclassified malignancy. Histopathological correlation was available in 11 malignant neoplastic lesions which confirmed the diagnosis. Nineteen cases of multiple lesions described by ultrasonography and suggested differential diagnosis of metastasis and HCC proved to be metastatic in 10cases (52.63%) and HCC in 9 cases (47.36%) by cytological examination. Overall diagnostic accuracy of the FNAC of liver to detect malignant lesions was 93.75%.

Conclusion: USG/CT guided FNAC of liver permits the categorization of more frequent non-neoplastic lesions and neoplastic primary and secondary metastatic malignancy in a simple and rational manner which is helpful for the management of hepatic lesions. Ultrasound guided fine needle aspiration of liver has a promising role to play in the diagnosis and classification of liver disease than ultrasonography alone, as it requires greater degree of precision to reach diagnostic accuracy.

Keywords: Ultrasound guided, Fine needle aspiration cytology, Core needle biopsy, Hepatic lesions.

Introduction

The various types of space occupying lesions of the liver are metabolic, infectious and neoplastic (malignant or benign). They present radiologically either as a focal lesion or as a diffuse involvement.[1] Although a differential diagnosis can be made clinically, biochemically and radiologically, histopathological examination of the tissue from the lesion is often required for a definite diagnosis.[1] Most of these lesions are easily assessable by fine needle aspiration cytology (FNAC). Further, it is important to establish if the lesion is malignant, and in that case, whether primary or metastatic in nature. An FNAC aids in making a quick diagnosis, thus saving valuable time and enables early initiation of treatment.[2]

FNAC is gaining popularity as a diagnostic technique for space occupying lesions of the liver, because it is quick, inexpensive and minimally invasive, when compared to core-needle or open biopsy.[1,3] However, blind aspiration has the inherent drawback of poor lesion localization and lower diagnostic accuracy. This has led to the usage of various radiologically guided FNAC, which is done either using ultrasonography (USG) or computerized tomography (CT).[1,4]

The present study has been conducted to evaluate the efficacy of ultrasound guided percutaneous FNAC in the diagnosis of liver lesions and to assess the feasibility of using this technique as a routine diagnostic procedure for liver lesions.

Aims and Objectives

The objectives of the study were to categorize the lesions of liver observed at FNAC – Inflammatory or non-inflammatory, malignant or benign, primary or secondary, to establish the various cytological patterns of the lesion of liver, to correlate the radiological findings with cytology, to correlate histopathologically in available cases and to correlate findings of radiology with combined cytology and imaging alone.

Materials and Methods

The present study was conducted on subjects with a radiologically confirmed hepatic mass, who were in-patients as well as those visiting the outpatient department of Victoria hospital and Bowring and Lady Curzon hospital from November 2008 to October 2010. After obtaining a detailed clinical and radiological data, the patient was subjected to FNAC under USG or CT guidance. Written informed consent was obtained from

the patient before undertaking the procedure. The study was approved by the Institutional Ethics Committee.

The area (based on the clinical examination and radiological finding) was sterilized with spirit. The length of the needle used was 15-20cm. A 22-23 cm G disposable needle was fixed on a 10 mL disposable syringe that was pre-fixed to the FNAC gun.

Under USG guidance, the needle was introduced and its position was checked before aspiration. The tissue specimen was collected, expressed on to a glass slide and then, spread. Two dry smears and two smears fixed in alcohol 95% were prepared. Excess specimen was fixed in formalin and preserved for cellblock, which were later processed and sections taken for histopathology examination. Alcohol fixed smears were stained with Papanicolaou (PAP)/ hematoxylin and eosin (H&E) and dry slides were stained with May-Grünwald Giemsa (MGG) /Leishman's stain. Statistical data of age and sex, cytological diagnosis, histopathological correlation, radiological correlation and diagnostic accuracy was studied.

Results

A total of sixty cases were included in the study. On all these subjects FNAC of the liver was carried out under USG/CT guidance, and cytological analysis was done. Of these, core needle biopsy/cell block preparations were available for histopathological examination in 16 cases. A correlation between FNAC and histopathological study findings was done.

The age of the patients ranged from 28 to 90 years with a mean age of 57.28 years. The majority were male patients in their fifth decade. Males accounted for 43 cases (72%) and females 17 cases (28%) with a male to female ratio of 2.5:1.

Pain abdomen in the right hypochondrium was the most common presenting symptom. The other frequently reported symptoms were mass per abdomen, loss of appetite, loss of weight, vomiting, jaundice and fever.

Ultrasonography findings revealed solitary mass in 25 cases (41.66%), multifocal lesion in 34 cases (56.66%) and diffuse parenchymal lesion in one case (1.6%). In 55 (91.66%) cases, aspirates were hemorrhagic, and purulent in the remaining 5 (8.33%) cases.

Of the 60 cases, in 53 (88.83%), the lesion was neoplastic, in 6 (10.16%) non-neoplastic and in one (1.66%), it was inconclusive, but suspicious of carcinoma. The diagnosis based on FNAC findings are described in (Table 1).

Table 1: FNAC diagnosis in 60 patients

Diagnosis	No. of cases	Percentage
Non-neoplastic lesions	**6**	**10%**
Pyogenic liver abscess	5	8.33%
Granulomatous hepatitis	1	1.66%
Neoplastic lesions	**53**	**88.33%**
Hepatocellular carcinoma	21	35%
Metastatic adenocarcinoma	21	35%
Metastatic poorly differentiated carcinoma	6	10%
Unclassified malignancy	5	8.33%
Suspicious of carcinoma	1	1.66%
Total	**60**	**100**

Graph 1: Percentage FNAC diagnosis in 60 patients

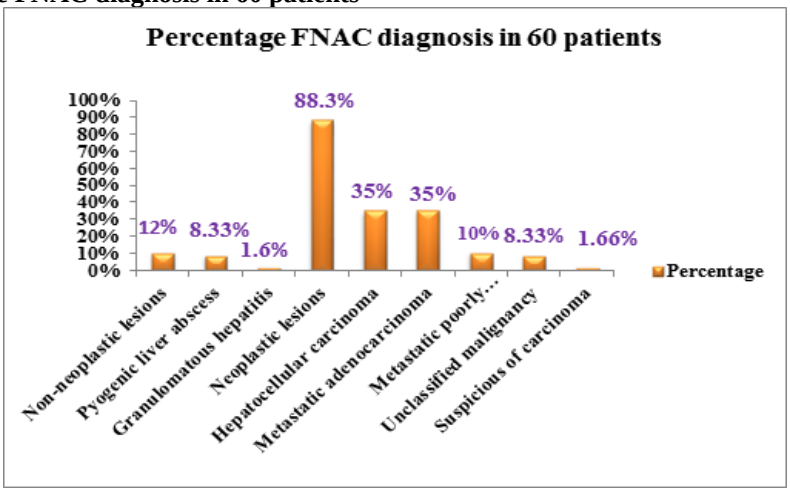

Table 2: Cytological diagnosis compared with histopathological diagnosis

Cytological diagnosis	Follow-up biopsy/cell block	Histological diagnosis	
		Malignant (No. of cases)	Non-Neoplastic (No. of cases)
Malignant (53)	10	10	0
Non -Neoplastic (6)	5	0	5
Suspicious of carcinoma	1	1	
Total	**16**	**11**	**5**

Table 3: Comparison of metastatic lesions with different studies

Cytological Diagnosis	Rasania et al.[6](n=43) (52.40%)	Kuo et al.[10] (n=76) (14.53%)	Present study (n=27) (50.94%)
Metastatic adenocarcinoma	37(86.04)	52(68.42)	21(77.77)
Metastatic squamous cell carcinoma	2(4.68)	8 (10.52)	-
Metastatic lymphoma	1(2.32)	4 (5.26)	-
Metastatic malignant melanoma	-	1 (1.31)	-
Metastatic- ovary	1(2.32)	-	
Metastatic –kidney	1(2.32)		
Metastatic sarcoma	-	4(5.26)	-
Metastatic small cell carcinoma	1(2.32)	2 (2.63)	-
Metastatic poorly differentiated carcinoma	-	5(6.57)	6(22.22)

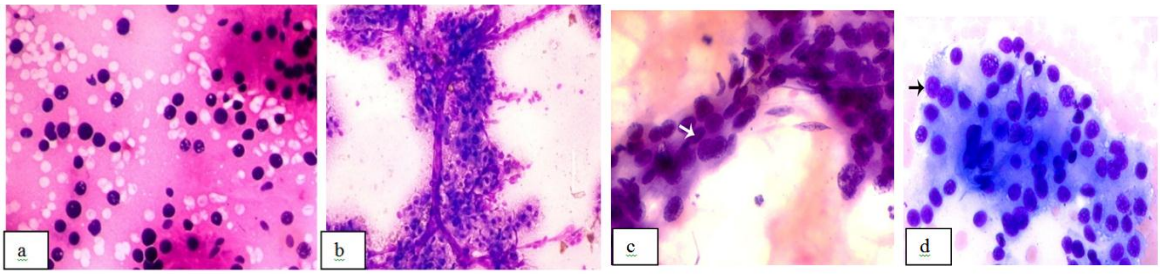

Fig. 1a: WDHCC, traversing blood vessels with well differentiated tumor cells. (MGG 20x); 1b: WDHCC showing atypical naked nuclei (H&E; MGG 20x); 1c: MDHCC showing with endothelial cells and tumor cells (H&E; MGG; 1d: MDHCC showing intranuclear inclusion (MGG 40x)

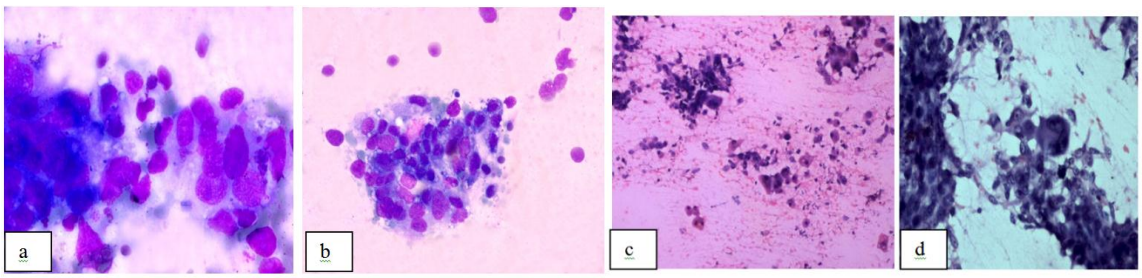

Fig. 2a: PDHCC showing high (N/C) ratio and large hyperchromic nucleus (MGG 40X); 2b: PDHCC showing high N/C ratio and large hyperchromtic nucleus (MGG 20X); 2c: Metastatic adenocrcinoma showing vaguely formed acinar pattern (H&E MGG 10X); 2d: Metastatic adenocarcinoma showing tumor giant cell (H&E; MGG 40x)

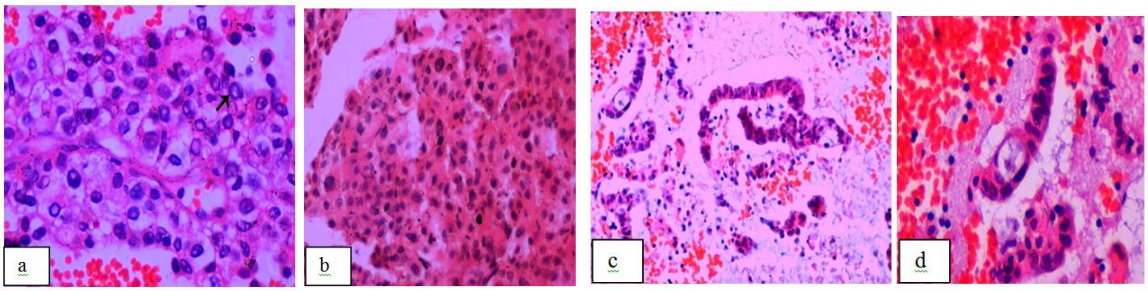

Fig. 3a: WDHCC showing traversing blood vessel and intranuclear inclusion (H&E: MGG); 3b: MDHCC showing nuclear pleomorphism and high N/C ratio (H&E; MGG 20x); 3c: Metastatic adenocarcinoma showing glandular pattern and mucin in background (H&E; MGG 20x); 3d: Metastatic adenocarcinoma showing signet ring cell (H&E; MGG 40x)

Non-neoplastic Lesions: Five cases of pyogenic liver abscesses were diagnosed cytologically. One subject was in the third decade of life, while two were in their fifth decade and one in the sixth decade. The subjects presented with abdominal pain, fever and jaundice. Ultrasonography showed a solitary lesion in all subjects, with a maximum size of 9 x 8 cm. Aspiration yielded thick purulent material. The smear showed plenty of neutrophils accompanied by necrotic cells and debris. Few macrophages, reactive fibroblasts and degenerating hepatocytes were also present.

In one subject who was diagnosed to have granulomatous hepatitis, there was moderate hepatomegaly. Ultrasonography showed diffuse parenchymal lesion. The smears were moderately cellular and showed epithelioid histiocytes in singles and small tight clusters along with foreign body and Langhan's-type of giant cells. A few benign hepatocytes and bile duct epithelial cells were present. Background showed hemorrhage.

Neoplastic Lesions: Malignant lesions of the liver constituted 53 cases (89.33%) of the 60 aspirates. Primary, metastatic and unclassified malignancies constituted 21 (39.62%), 27 (50.94%) and 5 (9.43%) cases respectively. Of the malignant tumors, majority were metastatic (50.94%), followed by hepatocellular carcinoma (HCC; 39.62%).

Of the 21 cases of HCC diagnosed on cytologic examination, there were 17 males (80.95%) and 4 females (19%) with a male to female ratio of 4.2:1. The age of the patients ranged from 31 to 90 years with a mean age of 59.71 years. The patients presented with pain abdomen in the right hypochondrium, mass per abdomen, loss of appetite and loss of weight. Ultrasonographically, 12 cases showed solitary lesions and 9 showed multifocal lesions. The largest lesion measured 14 x 14 cm and the smallest measured 5x 4 cm.

Cytologically, HCC was graded into well-differentiated HCC (WDHCC), moderately differentiated HCC (MDHCC) and poorly differentiated HCC (PDHCC). Out of the 21 cases, 10 cases were diagnosed as WDHCC; smear showed increased cellularity with cells resembling normal hepatocytes. The tumor cells were arranged in thick trabecular, acinar, transgression of blood vessels in cell clusters, bare atypical nuclei, large polygonal cells with abundant eosinophilic granular cytoplasm, increased nucleus to cytoplasm ratio, central round nucleus and intranuclear inclusions. Further, several naked nuclei were noted (Fig. 1a & 1b). Five cases of MDHCC also had many features of WDHCC. It was found that endothelial rimming or transgressing of cell clusters, eccentric nuclei, multinucleation, multiple nucleoli and macronucleoli were associated more with this type of HCC (Fig. 1c & 1d). Six cases were diagnosed as PDHCC showed cells in sheets, small groups and singles. Transgressing endothelium was seen. Anisocytosis, anisonucleosis, irregular nuclear chromatin, hyperchromasia, multiple nuclei, macronuclei and bare atypical nuclei were seen (Fig. 2a & 2b).

Twenty one cases of metastatic adenocarcinoma were diagnosed in our study with 13 males and 8 females with a male to female ratio of 1.6:1. The age ranged from 42 to 80 years with a mean age of 55.42 years. The primary tumor was colorectal in 5, ovary in 1, breast in 2, pancreas in 1, gall bladder in 1, stomach in 2 and cervix in 2 patients. In 7 patients, the primary tumor was not established. Similar to HCC, the common symptoms were pain abdomen followed by mass per abdomen, loss of appetite, loss of weight and fever. USG showed multifocal lesions in 25 patients and solitary lesion in 2 patients. The largest lesion measured 8 x 6 cm and smallest measuring 2x 2 cm.

The smear studied revealed high cellularity. Cells were columnar, cuboidal or round to oval and arranged in flat monolayered sheets, palisade forms, acinar pattern and in singles having vacuolated or granular and eosinophilic cytoplasm. The cells showed mild to moderate anisonucleosis with central or eccentrically placed nucleus and fine to coarsely dispersed chromatin pattern. Some cases showed multinucleation (2-3 nuclei) irregular hyperchromatic nuclei with prominent nucleoli. Altered N: C ratio was noted (Fig. 2c & 2d). Mitotic figures were often present. In many cases

normal hepatocytes were present and inflammation, necrosis and fibrosis were prominent in some cases.

There were 6 cases of metastatic poorly differentiated carcinoma (PDC) in our study. The FNA smears were moderate-to-highly cellular with the cells arranged in dicohesive sheets, clusters, palisades and in singles. The nuclei showed mild to marked pleomorphism with finely-to-coarsely granular chromatin. Normal and reactive hepatocytes were also noted.

One case of liver aspirate was suspicious of malignancy as smear showed well differentiated hepatocytes and absence of necrosis; it was difficult to differentiate into hpatocellular adenoma or HCC.

Cyto-Histopathological Correlation: In 16 cases, the cytological diagnosis was correlated with core needle biopsy/cell block histopathological diagnosis. The histopathological diagnosis was taken as standard for comparison (Table 2).

Of the 5 cases reported as non-neoplastic lesions on FNAC, histopathological examination confirmed the non-neoplastic nature in all cases. Of the 10 cases diagnosed as malignant on cytological examination, all the cases were reported as neoplastic (Fig. 3 a-d). In one case which was inconclusive on cytology, smear showed well differentiated heptocytes and absence of necrosis. It was difficult to differentiate into hepatocellular adenoma or HCC. On histopathology, the features were conclusive of HCC.

Correlation of ultrasound findings with USG-guided FNAC Findings: Ultrasonographic findings of liver were correlated with cytological findings. Five cases of solitary lesions described by ultrasonography as abscess were proved as such in cytology in 100% cases. A single case of diffuse parenchymal lesion revealed cytological findings as granulomatous hepatitis. Nineteen cases of multiple lesions described by ultrasonography with a suggested diagnosis of metastasis or HCC proved to be metastatic in 10 cases (52.63%) and HCC in 9 cases (47.36%) by cytological examination. A total of 15 cases of multiple lesions which were suggested to be metastatic lesions in ultrasonography were proven as such in cytology. Ten cases of solitary lesions suggested as HCC by ultrasonography was proven to be the same. Of the nine cases of solitary lesion suggested as neoplastic on ultrasonography, 5 cases were of unclassified malignancy, 2 cases of metastasis and 2 cases of HCC on FNAC.

Discussion

Lundquist was the first to report the reliability of FNAC in the diagnosis of intrahepatic malignant tumors in a large study population of 2611 subjects.[5] USG-guided FNAC offers accuracy with minimal invasiveness and cost-effectiveness, without major complications.[6] In our study, all 60 cases were subjected to USG-guided FNAC.

The age of the patients ranged from 28 to 90 years with a mean age of 57.28 years. The males accounted for 43 cases (71.66%) and females 17 cases (28.33 %) with a male to female ratio of 2.2:1. In a study by Dhameja et al.,[1] the age of subjects ranged from 2 to 70 years, and the male to female ratio was 4:1. In another study by Swami et al.,[7] the age of subjects ranged from eight months to 90 years and the male to female ratio was 2:1.

In our study, USG revealed a solitary mass in 34 cases (56.66%), multifocal lesions in 25 (41.66%), diffuse parenchymal disease in 1 (1.66%) case. Swamy et al.[7] reported solitary mass in 37 cases (51.38%), multifocal lesions in 26 (36.12%), diffuse parenchymal disease in eight (11.12%) and normal echogenicity in one (1.38%). Bell et al.[8] reported multiple focal hepatic lesions in 92 patients and single focal lesion in 58 patients by USG. However, the number of detected lesions was not specified in 25 patients.

In our study, there were a total of 6 cases (10%) of non-neoplastic lesions, 53 cases (89.33%) of neoplastic lesion and 1 case (1.66%) which was suspicious of carcinoma. Similar findings of high incidence of malignant lesions were seen in study done by Rasaniaet al.[6] and Rosenblatt et al.[9] In the study by Swamy et al.,[7] neoplastic lesions (68.06%) were more common than non-neoplastic lesions (30.56%). However, in the study by Dhameja et al.,[1] 94.7% of cases were neoplastic lesions while 3 (5.3%) were non-neoplastic.

Of the neoplastic lesions, we found no benign lesions, similar to the findings of the study by Dhameja et al.[1] However, Rosenblatt et al.[9] report 47 of 59 FNACs to be malignant. Rosenblatt et al.[9] observed 5 HCCs (8.47%) and 47 (71.8%) of metastatic carcinoma. In the present study there were 21 HCCs (35%), and 27 metastatic tumors (50.94%) and 5 (8.33%) cases of unclassified malignancy and one case (1.66%) suspicious of carcinoma.

Majority of cases had metastasis 27 (50.94), followed by HCC 21 (39.62) similar to the study done by Rasania et al.,[7] where there was a higher prevalence of metastatic lesions in liver (70.4% cases), while study conducted by Kuo et al.[10] showed a higher prevalence of HCC (81.64%) among the malignant liver lesions.

We classified the HCC cases into WDHCC, MDHCC and PDHCC similar to the description by Rasania et al.[6] as grades I, II, and III. In the present study, WDHCC and PDHCC (30.09% each) were more common in comparison to the study by Rasania et al.[6] which showed higher number of MDHCC or Grade II cases (56.2%).

Previous studies have shown that about 75% of the FNAC cases are metastatic cancers.[2] In our study 50.94% (27 of 53 cases of malignancy) were metastatic cancers. In the study by Barbhuiya et al.,[2] the most common primary tumors were GIT adenocarcinoma (44.2%) followed by gallbladder adenocarcinoma (15.9%). In our study, colon adenocarcinoma was the

most common source of liver metastasis. Metastatic adenocarcinoma was the most common metastatic malignancy in the present study (Table 3). Similar observations have been made by Rasania et al.[6] and Kuo et al.[10]

Although imaging techniques (USG and CT) have helped greatly with the early and correct diagnosis of liver abscess, the appearances are often non-specific.[11]

There is some overlap between the US and CT features of liver abscesses, HCC and metastases. Two situations may occur. (1) Tumor masses, primary or secondary, undergo extensive necrosis, with the resultant radiologic image of the cavitary neoplasm mimicking abscesses; (2) abscesses are accompanied by proliferative reactive changes, making radiologic differentiation from a neoplastic process almost possible. Here aspiration cytology or FNAC plays an essential complementary role.[11]

In the present study, 5 cases of pyogenic liver abscesses were seen. The smears showed plenty of neutrophils and nuclear debris along with few degenerating hepatocytes. Histopathology was available for all cases which confirmed the cytological diagnosis. There was one case diagnosed as granulomatous hepatitis in the present study (1.69%) in which the smears showed epithelioid histiocytes in singles and small clusters along with multinucleated giant cells and few benign hepatocytes. Caseous necrotic material or acid-fast bacilli were not seen in our case. Radhika et al.[12] reported the findings of 4 patients with tuberculosis of the liver diagnosed by FNAC. The aspirates showed epithelioid granuloma admixed with benign hepatocytes and bile duct cells.

Studies by Herszenyi et al.[13] and Shah et al.[14] have demonstrated the sensitivity of FNAC in diagnosing hepatic malignancy to be ranging from 75.34 to 93%. Other studies have reported a specificity ranging from 69% to 100%.[2,9,10,15-17] In our study, we observed a 93.75% accuracy in the diagnosis as there was one case which was inconclusive on FNAC, and was proven to be HCC on histopathology. With high diagnostic accuracy of 93.75% for liver lesions in our study, upholds the unquestionable value of guided FNAC as a mandatory diagnostic procedure in the assessment of hepatic lesions. Thus, FNAC is a valuable method that allows rapid diagnosis. However, its sensitivity depends on the site and depth of the lesion and the skill of the person performing the procedure, as well as the experience of the pathologist.

We did not observe any complications in our study, similar to the observations by Ramdas and Chopra[16] and Barbhuiya et al.[2] However, in studies by Mingoli et al.[18] and Patel and Shapiro[19] complications like fatal bleeding have been reported in a case of chronic liver disease, needle tract tumor seedling and biliary-venous fistula. Lundquist[5] reported only one significant complication, an intrahepatic hematoma among the 2611 cases studied.

Conclusion

Ultrasound-guided fine needle aspiration cytology of liver is a safe, simple, cost effective and accurate method for cytological diagnosis of hepatic lesions. In the present study, USG/CT-guided FNAC was useful in distinguishing non-neoplastic from neoplastic lesions, and further assessing the type of neoplastic lesion. This is particularly helpful because malignant tumors of the liver are very common, and an early diagnosis is quintessential for improving the treatment outcomes. Therefore, USG/CT-guided FNAC is a promising technique for early diagnosis of hepatic lesions, with a very high diagnostic accuracy.

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