Original Article

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Pathology Section

The Utility of Fine Needle Aspiration Cytology in the Assessment of Hepatic Lesions

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ABSTRACT

Introduction: Fine Needle Aspiration Cytology (FNAC) is a less invasive, rapid and less expensive diagnostic technique which was initially used for only readily palpable masses and superficial organs. In recent years however, modern imaging techniques like Ultrasonography (USG) and Computed Tomography (CT) have made it possible to use this procedure for inaccessible lesions and deeper organs like the liver.

Aim: To evaluate the utility of FNAC in the assessment of neoplastic and non-neoplastic hepatic lesions and to determine its diagnostic accuracy particularly in malignant hepatic neoplasms.

Materials and Methods: The combined analysis of retrospective and prospective data was conducted over a period of 22 years (from January 1998 to December 2019) in the Department of Pathology, Goa Medical College, Goa, India, on 535 patients who presented clinically and radiologically with hepatic lesions. The Fine Needle Aspirations (FNAs) were performed under ultrasound and CT guidance. The cytology smears were then stained with Haematoxylin and Eosin (H&E) and May Grunwald Giemsa (MGG) stains. A cytohistopathological correlation was performed manually wherever possible with the available data. The overall diagnostic accuracy of FNAC as well as the diagnostic sensitivity of the procedure in detecting malignant hepatic lesions and its positive predictive value was calculated. The chi-square distribution of the categories of cytological reporting and of the various cytopathological diagnosis among the diagnostic aspirates was also studied to find the statistical significance.

Results: Among the 535 patients studied, 386 (72.1%) cases were diagnostic of which 76 were non-neoplastic and 310 (57.9%) were neoplastic lesions. The remaining 149 cases contributed to the non diagnostic category. The distribution of the diagnostic aspirates was statistically significant ($p<0.0001$). This series showed a male preponderance with most of the patients in the 51-60 years age group. Pyogenic abscess of the liver was the commonest non-neoplastic and non malignant lesion (non-neoplastic lesion+Benign neoplasms) and Hepatic metastasis was the commonest neoplastic and malignant lesion. The Chi-square statistics for the same was also significantly high ($p<0.0001$). While adenocarcinoma was the most frequent metastasis morphologically, the commonest site of known primary cancer with hepatic metastasis was the gastrointestinal tract. Cytohistopathological correlation was available in 72 cases. The overall diagnostic accuracy of FNAC in this study was 90% and the diagnostic sensitivity for malignant hepatic lesions was 98% with a positive predictive value of 94%.

Conclusion: Guided FNAC of liver was thus confirmed as a safe procedure that was useful in the successful diagnosis of hepatic lesions especially malignancies.

Keywords: Computed tomography guided, Hepatocellular, Ultrasonography guided

INTRODUCTION

The FNAC is a valuable diagnostic tool for diagnosis of neoplastic and non-neoplastic lesions. Previously inaccessible and deeper lesions are now safely sampled and routinely aspirated using this technique under radiological guidance. Both recent studies as well as older studies have revealed liver to be the most frequently aspirated organ [1-10]. The incidence in percentage of hepatic masses among the intraabdominal masses in these studies ranged from 22% to as high as 72%. The main indication of FNA of the liver is in the diagnosis of focal mass lesions [11]. These include both neoplastic lesions like primary liver cancer, secondary liver cancer, deep hepatic haemangioma and cystic tumours of the liver as well as non-neoplastic lesions like hepatic abscess and circumscribed fatty liver [12]. FNAC is also useful in differentiating neoplasms from inflammatory or diffuse liver diseases which mimic mass like- lesions on radiology. The small diameter of the fine needle used in FNA allows more extensive sampling with few complications [11]. Besides, additional material can be obtained if needed for ancillary diagnostic studies [13]. FNAC of the liver thus is a safe procedure which offers accuracy with minimal intervention at lower costs by avoiding unnecessary exploratory laparotomy. Accurate diagnosis of hepatic masses is important because treatment ranges from supportive care for advanced metastatic lesions to partial hepatectomy for primary carcinoma [14]. Also, as malignancy in the liver is usually inoperable at the time of diagnosis, a diagnostic modality such as FNAC should be considered early in the investigative sequence [15]. This study was thus conducted to evaluate the utility and diagnostic accuracy of FNAC in the assessment of neoplastic and non-neoplastic hepatic lesions and to find its sensitivity in the diagnosis of malignant hepatic lesions. It was conducted over a span of 22 years and includes a large number of cases which adds weightage to the adequacy and usefulness of the procedure especially in advanced stages of malignancy.

MATERIALS AND METHODS

The combined analysis of retrospective and prospective data was studied from early 2019 over a period of 22 years (from January 1998 to December 2019) in the Department of Pathology in a tertiary care centre hospital in Goa, India. The study was approved by the Institution Ethics Committee. Registration number: ECR/83/Inst /GOA/2013/RR-20.

Inclusion criteria: The analysis of 535 patients who presented clinically and radiologically with hepatic lesion where no definite radiological diagnosis were included in this study.

Exclusion criteria: Intrahepatic lesions which involved the biliary system were excluded from this study.

Study Procedure

A detailed workup of patients was carried out including complete patient history, and clinical examination. Some patients presented

with intra-abdominal lump in right hypochondrium, while in others the lesion was detected incidentally during clinical workup. An Informed consent was taken, the coagulation parameters and bleeding time were confirmed to be in the normal range. FNAC under radiological guidance was performed on an in-patient basis using a 22G lumbar puncture needle, 10 mL disposable syringe and a modified comeco syringe piston holder. Smears were prepared and stained with H&E and MGG. A cytopathological opinion was made under light microscopy by correlating with clinical and radiological findings. In most cases, the clinical data, cytopathological, histopathological reports and slides were retrieved from the records of pathology department. Histopathological correlation was carried out where ever possible.

STATISTICAL ANALYSIS

The overall diagnostic accuracy of FNAC was calculated using the formula TP+TN/TP+TN+FP+FN. The diagnostic sensitivity of the procedure in detecting malignant hepatic lesions (i.e., sensitivity for true positive cases) was obtained by the formula, TP/TP+FN×100 and its positive predictive value by using the formula TP/TP+FP×100 (TP=True Positive, TN=True Negative, FP=False Positive and FN=False Negative values). The categories of cytological reporting and the various cytopathological diagnosis among the diagnostic aspirates were also statistically studied manually using the chi-square distribution test.

RESULTS

This series revealed a male predominance with a male to female ratio of 2:1. Majority of the patients were in the age group of 51-60 years, youngest being six years and the eldest 90 years of age. Of the 535 hepatic lesions aspirated, 76 (14.2%) were non-neoplastic and 310 (57.9%) were neoplastic. These were considered as the diagnostic aspirates. The remaining 149 were non diagnostic and included inconclusive cases in which the smears were not representative of the site and mainly comprised of Red Blood Cells (RBCs), neutrophils and normal hepatocytes as well as cases in which the exact nature of the lesion could not be ascertained and hence a differential diagnosis was provided. The chi-square statistics showed that the probability of getting diagnostic aspirates was significantly high (p<0.0001) [Table/Fig-1]. The further analysis in the study was done using these diagnostic cases.

Categories for cytological reporting	Number of cases (n=535)	Percentage (%)	Expected	Chi-square statistics
Diagnostic	386	72.1	267.5	χ^2=52.49, df=1, p-value <0.0001
Non-neoplastic	76	14.2		
Neoplastic	310	57.9		
Non diagnostic	149	27.9	267.5	
Total	535	100		

[Table/Fig-1]: Categories for cytological reporting with chi-square distribution.

Pyogenic abscess was predominant among the non-neoplastic lesions. This was statistically proven with a chi-square value of 192.29 at degree of freedom five and p-value of <0.0001. Neoplastic lesions comprised of five benign neoplasms (three haemangiomas and two haemangioendotheliomas) and 305 malignant neoplasms. The identification of neoplastic lesions and malignant lesions is statistically significant with p<0.0001 at degree of freedom one having a chi-square value of 70.9 and 145, respectively [Table/Fig-2].

Amongst the malignant lesions, metastatic lesions (chi-square statistic=18.44 at degree of freedom two and p<0.0001) were the most frequent followed by hepatocellular carcinoma. The other primaries included hepatoblastoma and lymphoma, the latter being diagnosed in Human Immunodeficiency Virus (HIV) positive patients after ruling out nodal involvement. One case of Solid Papillary Epithelial Neoplasm (SPEN) of liver (carcinoma of low malignant potential) and another of neuroendocrine carcinoma were also considered as primary malignant lesions [Table/Fig-2].

Cytopathological diagnosis	Number of cases (n=386)	Percentage (%)	Expected	Chi-square statistics
Non-neoplastic	76	19.7	193	χ^2= 70.9, df=1, p-value <0.0001
Abscess	62	16.1	12.66	χ^2=192.29, df=5, p-value <0.00001
- Pyogenic abscess	47	75.9		
- Tuberculous abscess	12	19.3		
- Amoebic abscess	3	4.8		
Cyst	5	1.3		
Granulomatous inflammation	4	1.0		
Cirrhosis	2	0.5		
Focal nodular hyperplasia	1	0.3		
Inflammatory lesions (Not specified)	2	0.5		
Neoplastic	310	80.3	193	χ^2= 70.9, df=1, p-value <0.0001
- Benign Neoplasms	5	1.3		
Haemangiomas	3	6		
Haemangioendotheliomas	2	4		
- Malignant neoplasms	305	79	155	χ^2= 145, df=1, p-value <0.0001
Primary	123	31.9		
Hepatocellular carcinoma	114	92.7		
- Hepatoblastoma	5	4		
- Lymphoma	2	1.6		
- Neuroendocrine carcinoma	1	0.8		
- SPEN	1	0.8		
Secondaries (metastasis)	145	37.5	101.7	χ^2= 18.44, df=2, p-value <0.000099
Positive for malignancy	37	9.6		
Grand total	386	100		

[Table/Fig-2]: Cytopathological diagnosis of the diagnostic hepatic lesions with chi-square distribution.
SPEN: Solid papillary epithelial neoplasm

The most frequent metastases were from adenocarcinoma (61.4%) followed by metastasis from poorly differentiated carcinoma (22%) [Table/Fig-3].

The most common site of known primary lesions with hepatic metastasis was the gastrointestinal tract (11%), which contributed to most of the adenocarcinomas [Table/Fig-4].

Morphology of metastasis	Number of cases (n=145)	Percentage (%)
Adenocarcinoma	89	61.4
Poorly differentiated carcinoma	32	22
Small cell carcinoma	9	6.2
Infiltrating duct carcinoma	7	4.8
Squamous cell carcinoma	3	2.1
Malignant melanoma	1	0.7
High grade carcinoma/sarcoma	1	0.7
Pleomorphic sarcoma	1	0.7
Malignant GIST	1	0.7
Neuroendocrine carcinoma/ leukaemic infiltration/lymphoma	1	0.7
Total	145	100

[Table/Fig-3]: Morphology of hepatic metastasis.
GIST: Gastrointestinal stromal tumour

Primary site of metastasis	Number of cases (n=145)	Percentage (%)
GIT	16	11
Breast	7	4.8
Ovary	6	4.1
Lung	5	3.5
Pancreas	5	3.5
Cervix	2	1.4
Oesophagus	2	1.4
Larynx	1	0.7
CBD	1	0.7
Bone	1	0.7
Retroperitoneum	1	0.7
Soft tissue	1	0.7
Unknown	97	66.8
Total	145	100

[Table/Fig-4]: Primary site in case of hepatic metastasis.
GIT: Gastrointestinal tract; CBD: Common bile duct

Of significance is the fact that, of the total number of hepatic metastasis diagnosed cytologically, only 37 were from patients who had previously been treated for known primaries or presented with simultaneous signs and symptoms of a primary tumour with hepatic lesions or revealed radiological evidence of the primary tumour. In the remaining 108 cases, no clinically apparent primary was present, nor were the patients investigated radiologically for the primary mass before the FNAC was conducted. Amongst these cases with unknown primaries, it was possible to suggest primary sites of origin in a few (11 cases).

A cytohistological correlation was available in 72 cases of which five cases were discordant. The correlation was calculated manually using formulae [Table/Fig-5] (r-value of correlation is calculated for quantitative variables, hence cannot be used for this study which includes qualitative data like cytological diagnosis).

Cytopathological diagnosis	Number of cases	Histopathological diagnosis	Number of cases	Correlation*
Non-neoplastic:				
Cirrhosis of liver	2	Cirrhosis of liver	1	True negative
		HCC	1	False negative
Neoplastic:				
Malignant				
HCC	13	HCC	12	True positive
		Regenerative nodules/Cirrhosis of liver	1	False positive
Metastasis/ Secondaries	35	Metastasis	35	True positive
Positive for malignancy	21	HCC	7	True positive
		Metastasis	11	True positive
		Regenerative nodules/Cirrhosis of liver	3	False positive
Inconclusive-Differential diagnosis of Focal nodular hyperplasia and hepatic adenoma	1	Hepatic adenoma	1	True negative
Total	72		72	

[Table/Fig-5]: Cytohistopathological correlation.
True negative-2; False Negative-1; True positive-65; False positive-4; Overall diagnostic accuracy of FNAC=TP+TN/TP+TN+FP+FN=90%; Sensitivity for true positive cases=TP/TP+FN×100=98%; Positive predictive value=TP/TP+FP×100=94%; *histopathology was considered as gold standard; HCC: Hepatocellular carcinoma

The diagnostic accuracy of the procedure was thus 90% with the sensitivity for true positive results (i.e., diagnostic sensitivity for malignant hepatic lesions) and a positive predictive value of 98% and 94%, respectively.

No major complications were encountered in the present study.

DISCUSSION

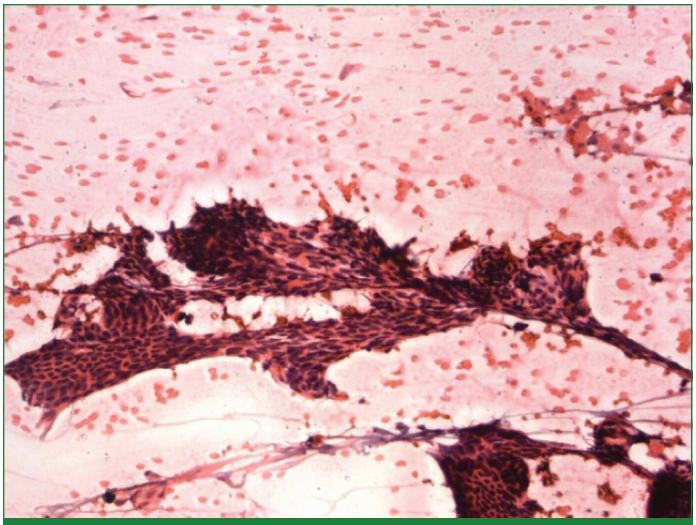
In the present series, among the 535 hepatic lesions aspirated, 14.2% were non-neoplastic, 57.9% were neoplastic while the non diagnostic lesions contributed to 27.9% of the total [Table/Fig-1]. Neoplastic lesions were also predominant in studies conducted earlier [Table/Fig-6] [13,14,16-21]. A male preponderance was observed in this study similar to that observed by other studies [13,14,16,19-21]. The percentage of malignant hepatic neoplasms diagnosed on FNAC was higher than the other lesions diagnosed [Table/Fig-2]. Similar results have been observed in both Western and Indian literature wherein the percentage of malignant lesions was higher than the rest of the lesions diagnosed on cytology [1,5,13,14,17-30]. The slight decrease in the percentage of malignant lesions as compared to the other studies can be attributed to the broader category (28%) of non diagnostic lesions observed in this study. One of the reasons for this being the presence of small deep seated lesions which may have been missed on aspiration. This observation is similar to that demonstrated by Mustafa B et al., and Leiman G et al., [18,28].

Studies conducted	Non-neoplastic lesions (n)	Non-neoplastic lesions (%)	Neoplastic lesions (n)	Neoplastic lesions (n)
Swamy MC et al., [16]	49	68.06	22	30.56
Nasit JG et al., [14]	147	98	3	2
Kaçar Özkara S and Ozöver Tuneli I, [17]	81	80	10	10
Mustafa B et al., [18]	282	98	7	2
Reddy C V et al., [19]	702	92.9	53	7
Tailor SB and Kothari DC, [20]	78	85.90	11	14.10
Sudhakar G and Devi KM [13]	36	78.26	7	58.33
Rastogi N et al., [21]	49/57		8	
Present study	76	14.2	310	57.9

[Table/Fig-6]: Comparison of neoplastic and non-neoplastic lesions in the present and past studies.

Among the malignant hepatic lesions, a higher incidence of metastasis was observed in this study (47.2%) followed by primary hepatocellular carcinoma (37.4%) [Table/Fig-2]. This finding concurred with that reported by some foreign [17,22-24,26-29,30] and Indian studies [9,14,18-21]. The diagnosis of metastatic lesion to the liver was based on the presence of normal hepatocytes amongst neoplastic cells. The cytomorphology of the malignant cells varied based on site of primary tumour. Adenocarcinoma was the most frequent cell type encountered (61.4%) [Table/Fig-3,7]. They were mainly of gastrointestinal origin, this site also being the commonest among the known primary tumour sites with hepatic metastasis [Table/Fig-4]. Zornoza J et al., in their series observed that 72.73% of metastatic hepatic neoplasms were adenocarcinomas [31]. Similar findings were observed by Pinto MM et al., [27] (64.58%), Leiman G et al., [28] (66.67%) and, Mustafa B et al., [18] (67.7%) and Nasit JG et al., [14], Tailor SB and Kothari DC, [20], Rastogi N et al., [21], Swamy MC et al., [16]. Studies have also revealed gastrointestinal tract as the predominant site of primary tumour. These include Ho CS et al., [22] (26.92%) Leiman G et al., [28] (54.29%) and Bognel C et al., [26] (57.14%), Mustafa B et al., [18] (44.2%), Reddy CV et al., [19] Nasit JG et al., [14], and Kaçar Özkara S and Ozöver Tuneli I [17].

Amongst the metastatic hepatic lesions with unknown primaries, it was possible to suggest the primary site from the aspirated material. With a cytological diagnosis of mucinous adenocarcinoma, the



[Table/Fig-7]: FNAC smear of metastasis from papillary adenocarcinoma to liver under higher magnification (H&E, 400X).

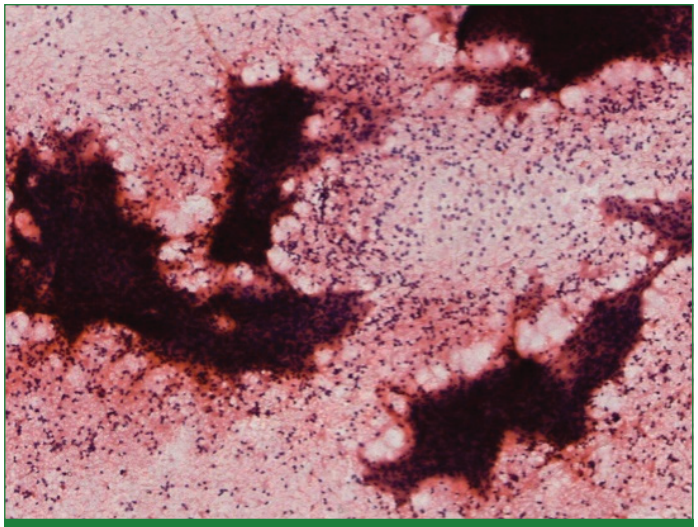
primary sites were restricted to GIT, pancreas and ovaries. Metastasis from small cell carcinoma suggested lung as a probable primary site. In one case of metastasis from squamous cell carcinoma, clinicians were advised to rule out primaries in the oesophagus, lung and cervix while another diagnosis of metastasis from adenocarcinoma to liver indicated lung and GIT as the primary sites. Cytological diagnosis of metastasis from signet ring carcinoma to liver suggested GIT (most probably stomach) and pancreas to be the primary sites. These findings are in concurrence with those of Ho CS et al., and Leiman G et al., [22,28]. Both conducted different studies which favoured the fact that FNA not only provided confirmation of hepatic metastasis but also indicated probable primary sites. It was however not possible to provide the definite primary site for any of the hepatic metastasis with unknown primaries on cytology. In their studies too Hemalatha AL et al., have noted that the primary site of origin of carcinoma could not be determined by aspiration alone [30].

Pinto MM et al., conducted a study and noted the usefulness of FNA in determining the type of hepatic metastasis in patients with history of two primary carcinomas [27]. In this series too, one such case was encountered where a 54-year-old woman, a known case of carcinoma of cervix and carcinoma of breast presented with hepatomegaly. Cytological diagnosis of metastasis from squamous cell carcinoma to liver confirmed the metastatic disease as well as indicated the primary site of origin.

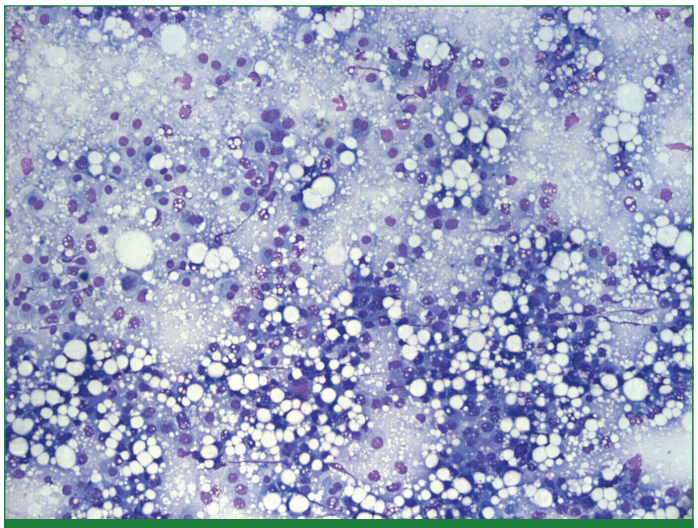
Metastasis has to be sometimes differentiated from benign regenerating hepatic lesions. As reported by Russack V et al., metastatic smears showed absence of nuclear changes in the normal hepatocytes that differentiated it from the latter [32]. Though this study revealed a predominance of metastatic lesions, a higher incidence of primary hepatocellular carcinoma was observed by Sudhakar G and Devi KM, Swamy MC et al., Khodaskar MB et al., Hemalatha AL et al., and Tatsuta M et al., [13,16,25,30,33].

Hepatocellular carcinoma being the commonest primary hepatic tumour in this study, it was cytologically diagnosed based on: 1) Trabercular arrangement of tumour cells as well as the acinar or pseudoglandular pattern [Table/Fig-8]; 2) Individual cellular features- i.e., increased nuclear cytoplasmic ratio, prominent nucleoli (in some cases) [Table/Fig-9]; 3) Presence of intranuclear inclusions [Table/Fig-10]; 4) Presence of atypical hepatocytic naked nuclei; 5) Hepatocytic appearance of tumour cells with central nuclei and eosinophilic/vacuolated cytoplasm; and 6) Presence of tumour giant cells [Table/Fig-11]. Kung IT et al., reported similar observations [34]. They also reported identification of intranuclear inclusions which were seen in majority of cases in this study.

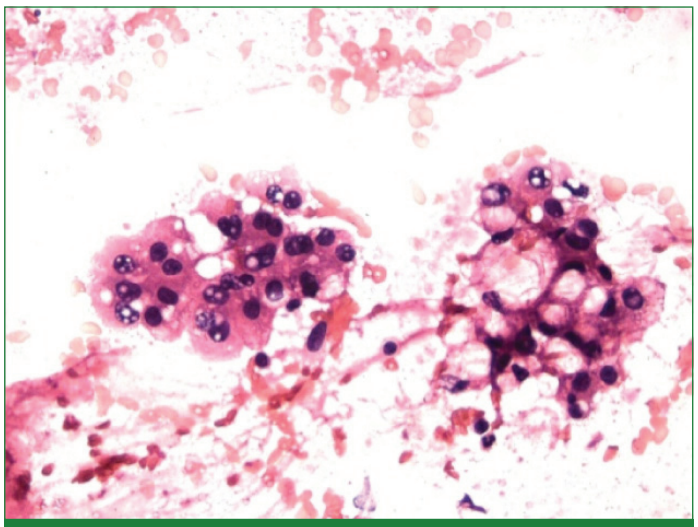
Fatty metamorphosis of HCC can occur in the absence of steatosis in the adjacent liver. It can take the form of large intracytoplasmic



[Table/Fig-8]: FNAC smear of hepatocellular carcinoma showing trabercular arrangement of neoplastic hepatocytes. Many bare/naked nuclei are seen in the background (H&E, 100X).



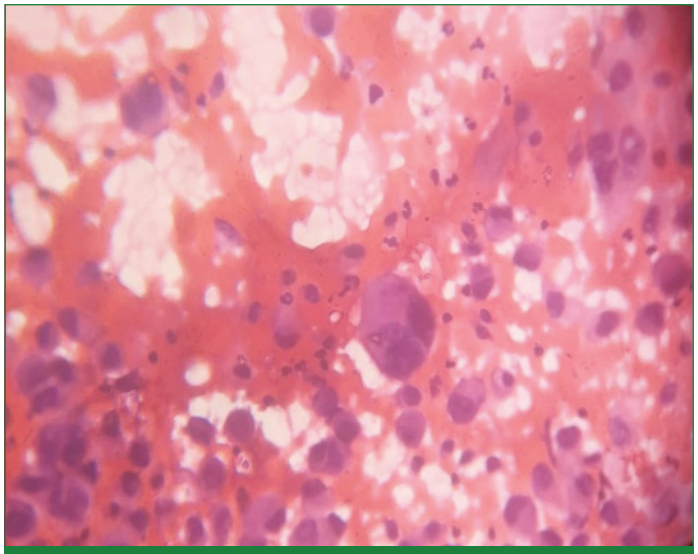
[Table/Fig-9]: FNAC smear of hepatocellular carcinoma showing neoplastic hepatocytes with increased nuclear cytoplasmic ratio (MGG, 200X).



[Table/Fig-10]: FNAC smear of hepatocellular carcinoma showing clusters of neoplastic hepatocytes with intranuclear inclusions and fatty change in cytoplasm (H&E,400X).

vacuoles or smaller bubbly looking vacuoles [35]. A similar feature of fatty change in HCC was observed in one of the hepatic aspirates in the present study [Table/Fig-10].

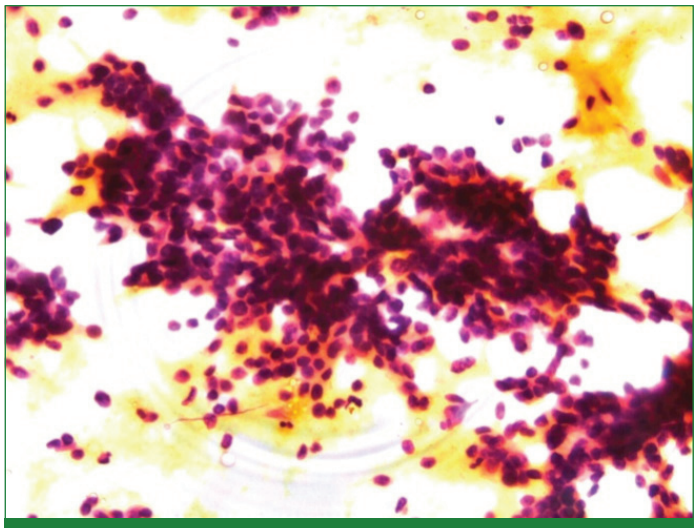
The most common problem was in differentiating between well differentiated hepatocellular carcinoma and other benign conditions like macro-regenerating nodule, focal nodular hyperplasia and liver cell adenoma. It was the combination of the monotony of atypia,



[Table/Fig-11]: FNAC smear of hepatocellular carcinoma showing malignant hepatocytes and tumour giant cells (H&E, 400X).

increased nuclear cytoplasmic ratio, crowding of hepatocytes, prominent nucleoli, presence of atypical naked hepatocytes and the paucity of bile duct epithelium that helped in favouring the diagnosis of well differentiated hepatocellular carcinoma. Similar findings were noted by Cohen MB et al., and Wee A et al., [36,37]. In some cases though, it was impossible to distinguish between well differentiated hepatocellular carcinoma and regenerating nodule. These cases were considered inconclusive and hence non diagnostic.

Distinguishing between a poorly differentiated hepatocellular carcinoma and metastasis to liver may sometimes cause a dilemma. Unlike metastatic smears which revealed presence of normal hepatocytes amongst neoplastic cells, smears of poorly differentiated hepatocellular carcinoma showed malignant polygonal cells with centrally placed nuclei separated by sinusoidal capillaries. Cohen MB et al., and Bottles K et al., revealed similar features with an additional presence of bile pigment as a key cytological feature [36,38]. While a markedly elevated serum Alpha-fetoprotein (AFP) level and the finding of a single lesion with or without satellite lesions on imaging favour a primary tumour over metastatic disease, certain immune cytochemical markers (Hep Par 1, Cytokeratin 5.2, CD10, CEA and endothelial markers positivity and AE1/AE3 negativity) also help to differentiate between a hepatocellular carcinoma (especially well differentiated HCC) and metastasis to liver. Studies therefore emphasise strict clinico-radio-pathological correlation as the first step toward treatment [16]. In some cases it was however not possible to differentiate between the two. These were considered as positive for malignancy [Table/Fig-2].



[Table/Fig-12]: FNAC smear of hepatoblastoma under higher magnification showing uniform atypical hepatocytes with high N:C ratio (H&E, 400X).

The two cases of hepatoblastoma were diagnosed based on hypercellular smears which composed of a uniform population of small to intermediate round to oval cells arranged in truberculae, cords and groups along with individually scattered cells [Table/Fig-12]. The cells had scant cytoplasm a spherical nucleus with inconspicuous nucleoli and stippled chromatin giving a “Salt and Pepper” appearance. Hepatoblastomas were also diagnosed in the studies conducted separately by Khodaskar MB et al., [25] Mustafa B et al., [18], Sudhakar G and Devi KM [13] and Rastogi N et al., [21].

The two cases of primary hepatic lymphoma one in an immunocompromised patient showed smears which revealed a monotonous population of singly arranged lymphoid cell having a hyperchromatic nucleus and scant cytoplasm.

A SPEN of liver and neuroendocrine carcinoma of liver were the other two primaries diagnosed on FNAC. While SPEN was diagnosed based on fairly cellular smears that showed pseudopapille composed of small tumour cells having a round nucleus and moderate amount of fairly granular cytoplasm adherent to delicate fibrovascular core, primary neuroendocrine carcinoma of the liver revealed small round cells with scant cytoplasm and nucleus having a salt and pepper chromatin.

The four benign neoplasms diagnosed in this study were vascular tumours (two haemangiomas and two haemangioendotheliomas) [Table/Fig-2]. Haemangiomas were diagnosed based on the aspirated blood and the few strands of endothelial cells detected. Though considered as a relative contraindication, it is emphasised that FNAC of haemangiomas can supply a definite diagnosis in some cases, as reported by Bree et al., and as found by Solbiati L et al., [39] and Montali G et al., [23]. In a study conducted by Reddy CV et al., [19] of the 14 benign neoplasms 11 were haemangiomas. Nasit JG et al., also revealed two benign hepatic neoplasms one of which was a haemangioma and the other a haemangioendothelioma [14].

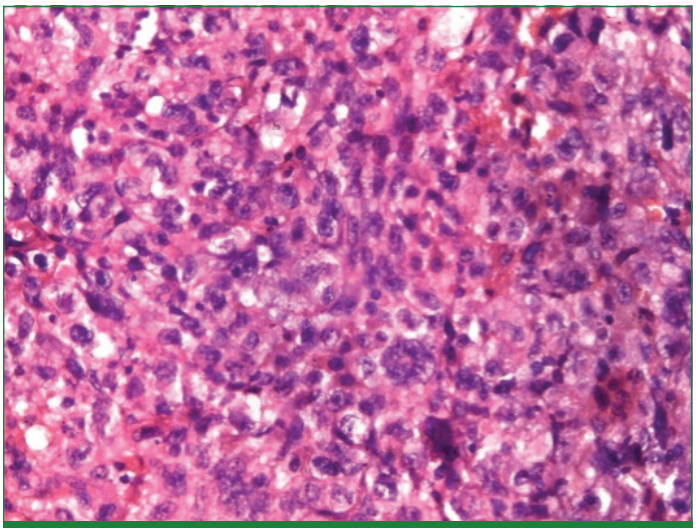
Hepatic abscess was the most commonly aspirated non-neoplastic lesion in this study [Table/Fig-2]. Smears from pyogenic abscess showed necrotic material and marked neutrophilic infiltrate. Tuberculous abscess revealed smears which comprised of caseous necrotic material, clusters of epithelioid cells and dense acute inflammatory infiltrate. However, since hepatocytes from periphery of the abscess or from a healing abscess may show atypia, purulent material obtained has to be subjected to microbiological examination and routine smears have to carefully examined for neoplastic cells and/or subjected to immunocytochemical markers [15].

Rosenblatt R et al., conducted a study wherein hepatic abscess was the commonest non-neoplastic lesion aspirated (20%) [24]. These findings are also similar to those found in Indian studies conducted by Mustafa B et al., [18] Nasit JG et al., [14] and Sudhakar G and Devi KM, [13]. The strikingly increased percentage of hepatic abscess could be attributed to the higher incidence of tuberculous infection in the eastern countries, tuberculous abscess accounting for 15.4% of total number of non-neoplastic lesions in this study. In the present study, hepatic cysts and cirrhosis accounted for 5.8% and 3.8% of the total non-neoplastic hepatic lesions aspirated. When FNAC of hepatic cysts was performed, straw colored mildly turbid fluid was aspirated and smears revealed amorphous materials, macrophages and few uniform cuboidal epithelial cells arranged singly or in monolayered sheets.

In the place, where the study was conducted, considering the increased incidence of alcoholic liver disease, the identification of cirrhosis with atypia and its distinction from well differentiated hepatocellular carcinoma gains significance. Diagnosis of cirrhosis was considered when smears revealed mixture of normal liver cells atypical hepatocytes, bile duct epithelium and absence of naked nuclei in the background. Similar observations were reported by Berman JJ and Mac Nail RE [40].

Among the non-neoplastic lesions aspirated, Montali G et al., [23] reported a higher incidence of hepatic cysts while Fornari F et al., [29] and Swamy MC et al., [16] observed a higher incidence of hepatic cirrhosis. Rastogi N et al., reported equal number of cases of hepatic cirrhosis and hepatic abscess diagnosed on cytology [21]. The single case of focal nodular hyperplasia diagnosed on cytology revealed, sheets of normal hepatocytes arranged singly, in clusters and sheets with interspersed strands of fibro collagenous tissue. These findings are similar to that observed by Rastogi N et al., [21].

In this study, cytohistopathological correlation was available in only 72 cases. [Table/Fig-5,13]. This may be due to fact that the patients diagnosed as having malignant hepatic disease were either referred to oncology institutes for specialised treatment or had convincing evidence of advanced malignancy and hence were not subjected to further histopathological diagnosis. Late diagnosis and socioeconomic status of patients makes it difficult to get operated or even undergo open biopsy [18]; 2) Benign lesions were treated conservatively with antibiotics/antituberculous treatment; while 3) rest of the cases were lost for follow-up.



[Table/Fig-13]: Histopathological section of moderately differentiated Hepatocellular carcinoma (H&E, 400X).

With the available correlation, the overall diagnostic accuracy of FNAC in the assessment of hepatic lesions was 90% similar to that observed in other studies [16,19]. FNA was particularly helpful in the diagnosis of malignant lesions with the sensitivity for true positive results being 98% and the positive predictive value being 94%. Various studies have reported the sensitivity for diagnosis of hepatic malignancies to be ranging from 75.34 to 93% [14,18].

Among the 2611 blind biopsies of the liver by Lundquist A [41] intrahepatic haematoma was the only severe complication observed similar to that noted by Ho CS et al., [22]. However, recent studies have also reported the risk of needle tract seeding in the FNAC of hepatic lesions [14]. Other complications observed include fatal bleeding in a case of chronic liver disease and biliary venous fistula [18]. However in this study, similar to that observed by Mustafa B et al., no complications were encountered [18].

Limitation(s)

In this study, correlation was available in only a few non-malignant cases (non-neoplastic and benign cases). Also, cases where it was a challenge to differentiate between a well differentiated hepatocellular carcinoma and regenerating hepatic nodule were considered non diagnostic. Other diagnostic pitfalls were necrotic aspirates from a malignancy which could have been misinterpreted as hepatic abscess and distinguishing between poorly differentiated hepatocellular carcinomas and hepatic metastasis which were concluded only as positive for malignancy.

CONCLUSION(S)

A FNAC of the liver was thus useful in accurately diagnosing both primary and secondary hepatic malignancies, in determining probable primary sites in patients with unknown primaries, in identifying the type of metastatic carcinoma in patients with a history of two primaries and in suggesting a benign/nonmalignant diagnosis. This study thus shows that FNAC especially that of the liver has stood the test of time over the past few decades. Ancillary techniques like cell blocks and immunocytochemistry have further helped in diagnosis. However, molecular biology biopsies such as in situ hybridisation and PCR are future hot points of FNAC.

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