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FINE NEEDLE ASPIRATION CYTOLOGY OF LIVER IN COMPARISION WITH HISTOPATHOLOGY IN A TERTIARY CARE CENTRE

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ABSTRACT

Fine needle aspiration cytology (FNAC) is a simple, rapid, out-patient investigation procedure for the diagnosis of palpable lumps of many organs in the body. It is a valuable pre-operative investigation of choice as it helps in precise and appropriate patient management. The study was undertaken to evaluate the diagnostic efficacy of the FNAC in neoplastic and non neoplastic lesions of the liver and to correlate the FNAC diagnosis with histopathology. An analysis of 65 fine needle aspiration biopsies of the liver has been presented. In the present study, males constituted 73.84% and females 26.15% with Male to Famale ratio of 2.8:1. Majority of the patients presented between 3rd and 5th decades with the peak incidence in 4th decade. The diagnostic yield in the present study was 97%. Out of 65 cases, 4.61% were found to be inadequate for reporting. Of the 65 cases, normal aspirate accounted for 15.38%, benign 46.15% and malignant 33.84% of cases. Of the 22 malignant aspirates, 45.45% were primary

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and 54.55% were metastatic lesions. The diagnostic accuracy of liver aspirations in the present study was 95.24%. False negative rate in the present study was 7.14% and False positive rate was 3.57%. No complications were encountered during the procedure, in the present study. The present study shows that fine needle aspiration cytology, is one of the best investigation with a fairly good accuracy which can be achieved with greater experience and expertise. Hence we conclude that FNAC of liver is a safe, simple and rapid method that can be done in the diagnosis of wide range of diseases.

Keywords: Liver, cytology, aspiration.

INTRODUCTION

Fine needle aspiration cytology (FNAC) is a simple, rapid, out-patient investigation procedure for the diagnosis of palpable lumps of many organs in the body. It is a valuable pre-operative investigation of choice as it helps in precise and appropriate patient management.

FNAC initially originated in Scandinavian countries and currently has become an important diagnostic tool. Though initially, the procedure was applied to superficial palpable masses, it is also used for detection of deep-seated lesions in the body including the liver.

The main indications of FNAC of liver are single or multiple nodular lesions, detected by palpation or radiographic imaging. The procedure is often assisted with the help of ultrasound (US). Findings on cytology are best correlated with radiological diagnosis for a precise diagnosis. Appropriate clinical management of a hepatic lesion or mass depends on an accurate diagnosis on FNAC. We aimed to evaluate sensitivity, specificity and accuracy of US guided percutaneous fine needle aspiration cytopathology (FNAC) in the diagnosis of liver masses in our center.

AIMS AND OBJECTIVES

The study was undertaken with the following aims and objectives

1. To evaluate the diagnostic efficacy of the FNAC in neoplastic and non neoplastic lesions of the liver.
2. To correlate the FNAC diagnosis with histopathology
3. To compare the data with other studies in assessing the diagnostic efficacy of FNAC liver.
4. To highlight the limitations if any.

MATERIALS AND METHODS

A prospective study was conducted in a tertiary care centre, from November 1991 to July 1993. A total of 65 cases of US guided liver FNACs were evaluated cytologically and the findings were compared to the histopathological biopsies in 52 of these cases. Majority of patients presented with either mass per abdomen and or distension of abdomen. Prior to the FNAC procedure the patients were examined in detail which included recording of pertinent clinical histoy and a through physical examination to arrive at a clinical diagnosis. The routine investigations were carried out including bleeding time, clotting time and pro-thrombin time. Ultrasound examination was also carried out.

After brief explanation of the technique, an informal consent was obtained from the patient. In cases of diffuse liver lesions, FNAC was done from right lobe of liver, in 8^{th} or 9^{th} intercostal spaces, in the mid axillary line. In localised lesions, it was carried out from the site of the lesion.

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The material obtained after the procedure was stained with Papanicolaou's stain, Haematoxylin and eosin stain and May Grunwald-Giemsa's stain. In 52 cases, liver biopsy was done under local anaesthesia and biopsies was subjected to histopathological examination.

RESULTS

The results of 65 consecutive needle aspirations were analysed. The clinical data as per performa and histological sections were reviewed from all patients. The following observations were documented.

Age distribution

Out of 65 cases, 48 (73.84%) were males and 17(26.15%) were females. The maximum no of male patients were in 3rd decade and maximum no of females patients were in 2nd decade. The youngest patient was 4months old, a case of Gaucher's disease. The oldest patient was 80 years old. [Table 1]

Table 1-Age group of patients

Age group	Males		Females	
	Number	Percentage %	Number	Percentage
1M – 10	2	3.08	3	4.62
11-20	1	1.54	1	1.54
21-30	1	1.54	6	9.20
31-40	17	26.15	2	3.08
41-50	11	16.92	2	3.08
51-60	11	16.92	2	3.08
61-70	2	3.08	1	1.54
71-80	3	4.62	0	0
Total	48	100	17	100

On cytological examination, majority were non neoplastic aspirates (30 cases, 46.15%) followed by malignancy in 22 cases (33.84%). In 10 cases (15.38%), the aspirate was normal. In 3 cases (4.61%), the material for inadequate for reporting. [Table 2]

Table 2 : Cytological diagnosis of liver aspirate

Cytological diagnosis	No of cases	Percentage %
1. Normal	10	15.38
2. Non neoplastic	30	46.15
3. Malignant	22	33.84
4. Inadequate	3	4.61
Total	65	100

Cytological features of liver aspirate:

1. Normal aspirate – Majority of smears reported as normal aspirate showed small clusters of benign hepatocytes. They were round to oval to polygonal with abundant, pink, granular cytoplasm. They were arranged in groups, singly or in cord pattern. The nuclei were central, round and vesicular with finely distributed granular chromatin. Mitosis were not seen. Bile duct epithelial cells and macrophages were seen in few cases.

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2. Fatty change- Four cases were diagnosed as “fatty change” on cytological examination and confirmed on histological examination. The smears showed many cells in groups and scattered singly. The characteristic finding were the presence of cytoplasmic vacuoles and the nuclei pushed to the periphery
3. Cirrhosis of liver- Cytologically 8 cases were diagnosed as cirrhosis of liver and confirmed subsequently by histological examination. Most of the smears in these cases showed moderate cellularity with the cells arranged in large groups. There were increased no of fibrous strands with many cells entangled within them. The cells showed mild atypicality in size and shape. Occasional binucleation was seen. Increased no of Kupffer cells (macrophages) were also seen.
4. Granulomatous hepatitis – Cytologically 3 cases were diagnosed as granulomatous hepatitis and confirmed as granulomatous hepatitis on hitopathological examination. The smears from these cases showed moderate cellularity. The cells were in clusters, cords and ill formed granulomas. Few hepatocytes showed bi-nucleation. Kupffer cells were seen prominently. The background showed lymphocytes.
5. Miliary tuberculosis – Two cases of miliary tuberculosis were diagnosed cytologically and confirmed on histopathology. On cytology, the hepatocytes were arranged in clusters and singles. Occasional binucleated cells were seen. Aggregates of epitheloid cells were seen amidst the hepatocytes. The background showed good number of lymphocytes.
6. Hepatitis: Two cases of "Hepatitis" were dignosed cytologically. One case was infective hepatitis which was confirmed by histopathology, the other was clinically diagnosed as alcoholic hepatitis in which biopsy was not done. The smear from infective hepatitis case showed occasional cluster of benign hepatocytes. A few clusters showed degenerative and regenerative changes which were in the form of ballooning of cells and double nuclei in a background of neutrophils, lymphocytes and necrotic debris.The smears studied from alcoholic hepatitis case showed hepatocytes, kupffer cells and few fibrous strands. Few hepatocytes showed fatty change. Amidst these hepatocytes were seen neutrophils. Rest of the hepatocytes were normal.
7. Storage Disorder - Two cases were diagnosed as "Storage disease” (Probably glycogen storage disease) on cytological examination were subsequently confirmed as storage disease on histopathological examination. The smears showed hepatocytes in clusters and cords. The cells were distended with vacuolated cytoplasm and small nuclei placed centrally or eccentrically. Both the smears were positive on PAS staining (Diastase sensitive).
8. Suppurative lesion - One case of "suppurative lesion" diagnosed cytologically showed sheets of polymorphs, few cells with degenerative changes and necrotic material.
9. Reactive changes- Diagnosis of "Reactive changes “ on cytological examination was given in 8 cases which showed moderate cellularity with hepatocytes arranged in clusters, cords & trabecular pattern. The hepatocytes showed mild anisonucleosis. Some of the nuclei were large with prominent nucleoli. In addition, normal looking hepatocytes were also seen along with bile duct epithelial cells. Few binucleated hepatocytes, naked nuclei and lymphocytes were also seen.

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Table 3: Cytological diagnosis of Non neoplastic aspirate

Cytological diagnosis	No of cases	Percentage %
1. Fatty change	04	13.33
2. Reactive changes	08	26.66
3. Cirrhosis of liver	08	26.66
4. Granulomatous hepatitis	03	10.00
5. Miliary tuberculosis	02	6.66
6. Storage disorder	02	6.66
7. Infective hepatitis	01	3.33
8. Alcoholic hepatitis	01	3.33
9. Suppurative lesion	01	3.33
Total	30	100

22 Cases (33.84%) were diagnosed as malignant on FNAC. Majority of these were metastatic carcinomas (54.55%), in which metastatic adenocarcinoma were 11 (50.00%), and squamous cell carcinoma was 1(4.55%) case. Primary hepatocellular carcinoma comprised 10 cases (45.45%) of the total malignant aspirates.

Table 4: Cytological diagnosis of malignant aspirate.

Cytological diagnosis	No of cases	Percentage %
Primary hepatocellular carcinoma	10	45.45
Metastatic:		
1. Adenocarcinoma	11	50.00
2. Squamous cell carcinoma	1	04.55
Total	22	100

In 52 cases, the cytological diagnosis correlated with histopathological diagnosis. The histological diagnosis was taken as the standard for comparison. Of the 28 cases reported as non neoplastic lesions on FNAC, the histopathological examination confirmed the non neoplastic nature in all but one case which, however turned out to be malignant. Of the 14 cases reported as malignant on cytological examination, one case was normal on histopathology. Of the 7 cases reported as normal, on histopathological examination, 2 cases were storage disorders and one was miliary tuberculosis. The remaining 4 cases were consistent with the cytological report.

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Table 5: Cyto-histomorphological correlation

FNAC diagnosis (52 cases)		Histopathology (52 cases)		
		Non neoplastic lesion	Malignant	Normal
Non neoplastic	28	27	01	-
Malignant	14	00	13	1
Normal	07	03	00	4
Inadequate for interpretation	03	02	00	1
Total	52	33	14	5

Table 6: Analysis of FNA cytodiagnosis

	Non neoplastic	Malignant
True positive (TP)	27	13
False positive (FP)	01	01
True negative (TN)	13	27
False negative (FN)	01	01

Hepatocellular Carcinoma

Ten cases of "Hepatocellular Carcinoma" were diagnosed on cytological examination. The diagnosis was confirmed in 8 cases on histopathological examination. In one in case, biopsy could not be done and in the other the histological examination was normal. Cytological features in hepatocellular included cell rich aspirate with cells arranged in large, loose cohesive clusters, cords, trabecular pattern and in one case acinar pattern was noted. The cells showed hyperchromatic nuclei and pleomorphism with 1-2 prominent eosinophilic nucleoli. Binucleated and multinucleated giant cells were seen. Occasional mitotic figures were present.

Metastatic Adenocarcinoma

The diagnosis of "Metastatic adeno carcinoma" was offered in 11 cases on cytological examination. In 5 cases histopathological correlation was available which confirmed the diagnosis. The smears from these cases showed a cellular aspirate. The cells were columnar, cuboidal or round to oval. They were arranged in flat monolayered sheets, palisade forms, acinar pattern or cell balls. The cytoplasm was vacuolated or granular cell and weakly cyanophilic. The cells showed mild to moderate anisonucleosis with centrally or nuclei and finely dispersed chromatin Some cases showed eccentrically placed, irregular hyperchromatic nuclei with prominent nucleoli. Altered N/C ratio was noted. Mitotic figures were aften present.

Metastatic Squamous Cell Carcinoma : One case of "Metastatic Squamous Cell Carcinoma" was diagnosed on FNAC was confirmed by histopathology. The smears showed high cellular yield. The cells were in sheets, groups and also singly scattered. These cells were large oval to polygonal with large irregular hyperchromatic nuclei. The cytoplasm was moderate and

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eosinophilic. Many bizarre, spindle and caudate cells were also noted. The cells showed increased N/C ratio and keratinization. The background was necrotic.

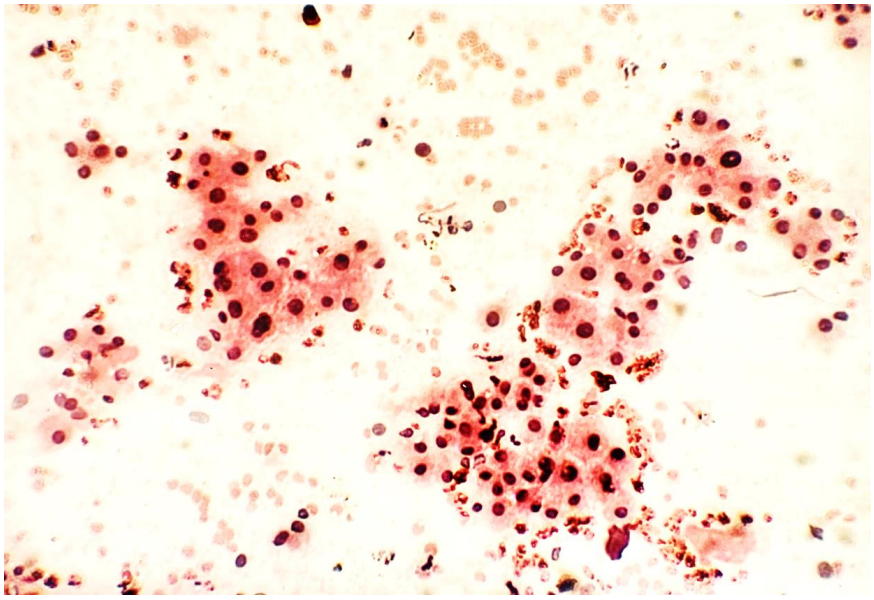

Figure 1 : Reactive changes – Hepatocytes in cords and clusters with mild anisonucleosis. [H&E x100]

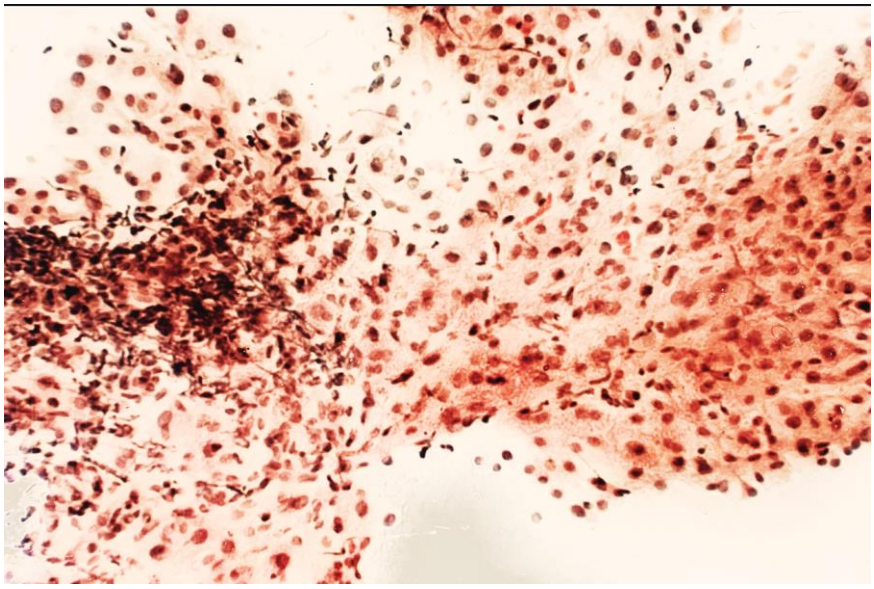

Figure 2 : Cirrhosis of liver – Hepatocytes showing mild anisonucleosis, increased fibrous strands. Few hepatocytes entangled in fibrous strands. [H&E x100]

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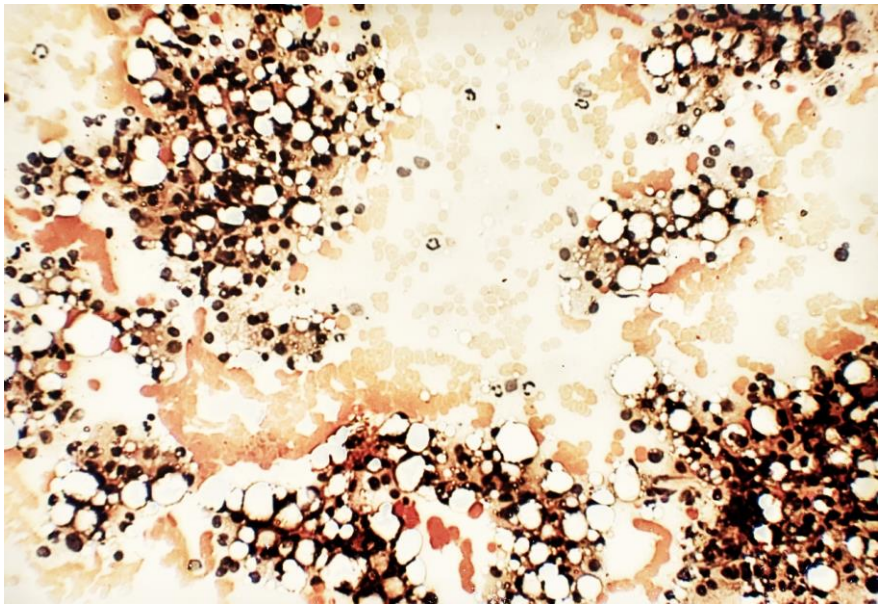

Figure 3: Fatty change – Hepatocytes with vacuolated cytoplasm and peripherally pushed nuclei. [PAP x400]

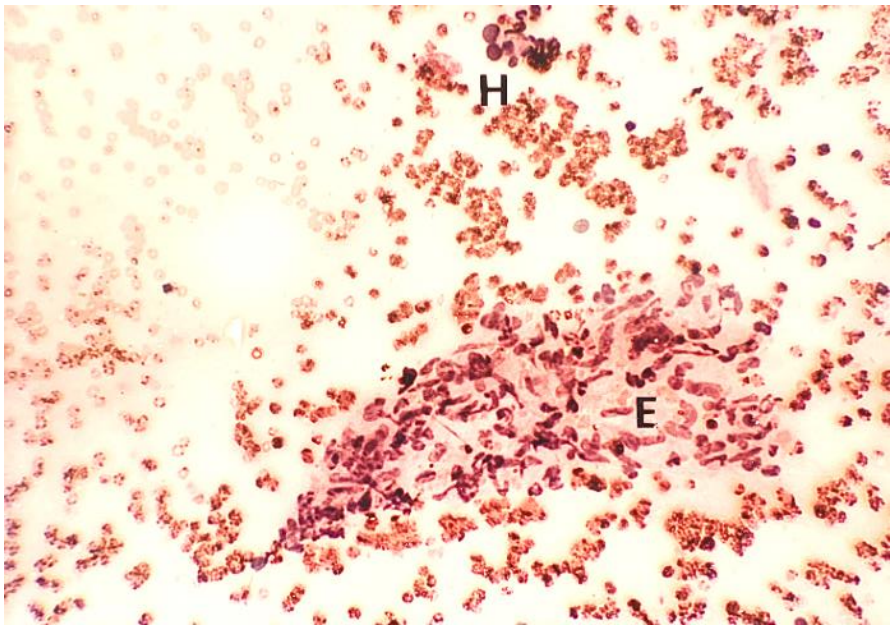

Figure 4: Tuberculosis-Liver. Aggregate of epithelioid cells[E]. Also seen are clusters of hepatocytes. [PAP x100]

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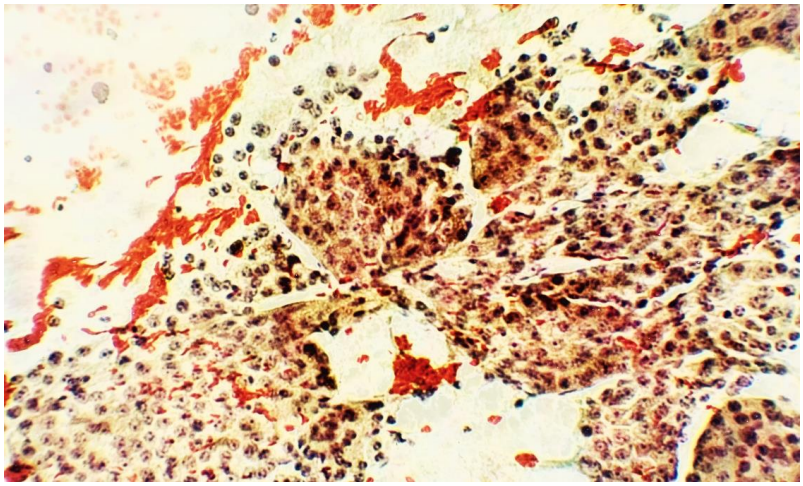

Figure 5: Hepatocellular carcinoma-Neoplastic cells in trabecular pattern showing hyperchromatic and prominent nucleoli. [PAP x100]

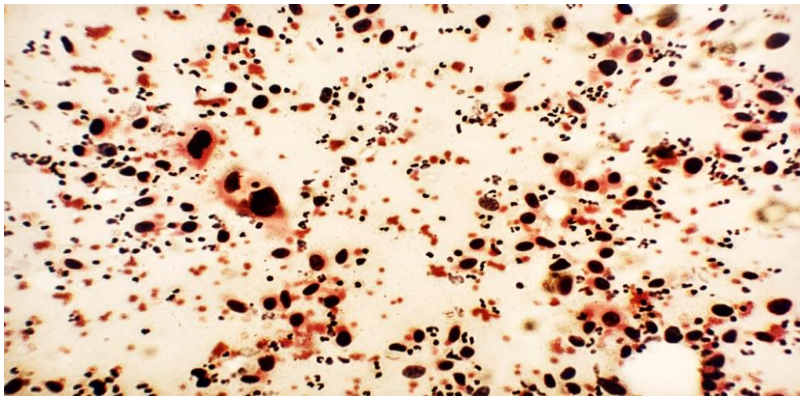

Figure 6 : Metastatic squamous cell carcinoma – Neoplastic cells singly scattered, large cells with pleomorphic , hyperchromatic nuclei. Lymphocytes and neutrophils are also seen in the background.

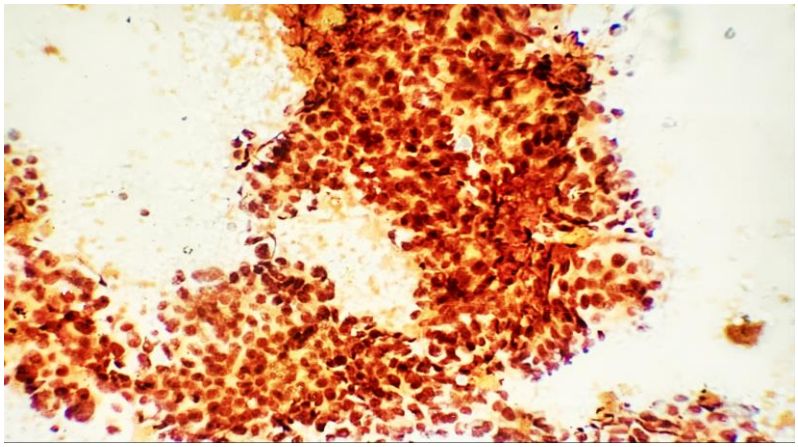

Figure 7 – Metastatic Adenocarcinoma – Cells in large loose cohesive clusters. Round to oval cells with hyperchromatic nuclei [PAP x100]

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DISCUSSION

In the late 19th century, Leyden and Menetrier tried using needles to obtain cells and tissue fragments from various tissues and tumours. As early as 1920 Josefson performed puncture of various abdominal organs, including liver with a rather fine needle. By means of puncture, Waldenstrom has demonstrated amyloidosis of the liver in cases of chronic suppuration. The first work on liver FNAC, was reported by the Italian investigator, Lucatello, in 1895.

European literature contains several reports usefulness of liver cytology in diffuse liver disorders. Stormby and Akerman had good success in the diagnosis of granulomatous disease of liver, of which they described seven cases. They noted however that the diagnostic cells (epithelioid histiocytes) were often difficult to detect and careful screening was warranted. Fine needle biopsy followed by cytologic examination has been proved to be a reliable method for the diagnosis of hepatic malignancy. The usefulness of liver cytology in the evaluation of jaundiced patient was asserted by Hennqver and the Hasselstrom. They were able to separate obstructive from non-obstructive jaundice; obstruction presented as increased amounts of proliferating biliary epithelium, with granulocytic infiltration, cholestasis (22). undamaged hepatocytes and Marguerite M. Pinto et al in their five year study of 81 transhepatic fine needle aspiration biopsies of liver 78 patients, reported a sensitivity for malignancy of 91% and a specificity of 100%.

An analysis of 65 fine needle aspiration biopsies of the liver has been presented. All the aspirations were unguided. In the present study males constituted 73.84% and Tel females 26.15% with Male to Famale ratio of 2.8:1. 4. Majority of the patients presented between 3rd and 5th decades with the peak incidence in 4th decade. The diagnostic yield in the present study was 97%. 6. Out of 65 cases, 4.61% were found to be inadequate for reporting. Of the 65 cases, normal aspirate accounted for 15.38%, benign 46.15% and malignant 33.84%. Of the 22 malignant aspirates, 45.45% were primaray 54.55% were metastatic lesions. The diagnostic accuracy of liver aspirations in the study was 95.24%. present. False negative rate in the present study was 7.14% and False positive rate was 3.57%. No complications were encountered during the procedure, in the present study. A comparison of the findings of the present study has been compared with various other studies in Table 7.

Table 7 : Comparison of the findings of the present study with other studies.

Cytological diagnosis	**No of cases**					
	Present study	**Reddy, et al-2015**	**Khanna M et al-2016**	**Lekha. M.B. et al-2018**	**Rajyalakshmi and Rajani-2020**	**Sujitha, et al-2023**
Non neoplastic						
1. Fatty change	04	06	4	0	-	-

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2. Reactive changes	08	0	0	0	-	-
3. Cirrhosis of liver	08	0	0	0	-	-
4. Granulomatous hepatitis	03	0	3	1	-	-
5. Miliary tuberculosis	02	0	0	-	-	-
6. Storage disorder	02	0	0	-	-	-
7. Infective hepatitis	01	0	0	-	-	-
8. Alcoholic hepatitis	01	0	0	-	-	-
9. Suppurative lesion	01	0	0	5	-	-
10. Abscess	0	20	6	-	-	-
11. Simple / hydatid cyst		27	0	-	-	-
Neoplastic						
Benign	-	14	3	-	-	-
Primary hepatocellular carcinoma	10	148	51	21	11	8
Metatstatic carcinoma						
Adenocarcinoma	11	400	83	21	14	20
Squamous cell carcinoma	1	3	2	0	1	-
Others	0	121	8	12	11	22
Inadequate	3	0	6	0	1	0
Total no of cases	65	755	169	60	38	50

CONCLUSION

FNAC of liver offers a simple method of diagnosis of neoplastic and non-neoplastic lesions of the liver. be performed repeatedly It helps to It can as it is safe and easy procedure. distinguish between primary and metastatic lesions, in most of the cases. It serves as a complementary diagnostic procedure to Histopathological examination. The present study has made it clear that fine needle aspiration cytology, is the best investigation one can ask for with a fairly good accuracy which can be achieved wiith greater experience and expertise. Hence we conclude that FNAC of liver is a safe, simple and rapid method that can be done in the diagnosis of wide range of diseases

CONFLICT OF INTEREST

The authors declare NO conflict of interest.

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