

Triumphs and Tribulations of Cytology in Malignant Hepatic Lesions

Damandeep Kaur¹, Pavneet Kaur Selhi²

^{1,2}Department of Pathology, Dayanand Medical College and Hospital, Ludhiana

Abstract: ***Background:** Guided fine-needle aspiration cytology (FNAC) is an easy, rapid and a minimally invasive diagnostic method for detecting neoplastic and non-neoplastic lesions of liver. Hepatic malignancies, both primary and secondary present as space occupying lesions clinically and radiologically, however, they differ in prognosis and management, hence it is mandatory to distinguish them. **Material and Methods:** All patients, irrespective of age and sex, who presented with nodular hepatic lesions to the hospital from 1st January 2015 to 31st June 2016 were subjected to FNAC under radiological guidance. Rapid onsite evaluation (ROSE) was performed for adequacy of diagnostic material. Haematoxylin and Eosin (H&E), Giemsa stain and Papanicolaou stain were done as per protocol. **Results:** Of the total 100 aspirates, 3% were non-diagnostic, 3% were suspicious of malignancy, 21% were diagnosed as primary epithelial malignancy and 60% were diagnosed as metastatic deposits and 13% as malignant NOS. **Conclusion:** In most hepatic malignancies, surgery is not an option. Thus, differentiation between primary or secondary tumours is extremely important from management point of view. Guided FNAC is a rapid, accurate and cost-effective method not only for detecting malignancy but also subtyping them. Hence, FNAC is a diagnostic technique with high sensitivity & specificity.*

Keywords: FNAC, Liver, hepatocellular carcinoma, chronic hepatitis B, chronic hepatitis C

1. Introduction

Malignant hepatic lesions are common in developing countries and its incidence is on the rise. A leading cause of cancer deaths worldwide accounting for more than 600,000 deaths each year [1] it is a notorious site for developing primary as well as secondary malignancies both of which present as focal space occupying lesion on imaging studies but have different prognosis and treatment.

2. Literature Survey

Primary liver cancer or hepatocellular carcinoma (HCC) is the major cause of mortality in patients with chronic liver disease. About 70%-90% of HCC have been reported worldwide in patients with cirrhosis secondary to hepatitis C, hepatitis B, alcohol, non-alcoholic fatty liver disease and drugs etc. [2] Both alcohol abuse and hepatitis viruses infection can lead to chronic liver disease and hepatocellular carcinomas. [3] The distinction of hepatocellular nodules such as large regenerative nodules and dysplastic nodules from reactive hepatocytes; distinction of well-differentiated HCCs from benign hepatic nodules, and secondary deposits from primary epithelial malignancies remains a diagnostic challenge. [4] Appropriate management of hepatic malignancies depends upon timely and accurate diagnosis which requires distinction of benign from malignant, primary from secondary tumors. Ultrasonography-guided fine needle aspiration cytology (FNAC) is a popular diagnostic technique because it is both precise and reproducible [5] As compared to conventional needle biopsy, guided FNAC is more sensitive and specific technique for diagnosing malignancy with low risk of complications like hemorrhage or biliary leak. [6] The main advantage of FNAC is the possibility of multiple passes which increases the chances of obtaining adequate viable cells even in necrotic tumors. In addition, rapid on site evaluation can be performed to evaluate adequacy of sample and procedure can be repeated if necessary. Cell block technique has been

adopted to make the best use of the available material with possibility of ancillary techniques like cytochemistry and immunohistochemistry. [7] Hence, combination of cytological smears, cell-block, panel of special stains and immunohistochemistry along with close clinico- pathologic correlation optimizes the utility of FNA in the diagnosis of hepatic malignancies [8]

3. Materials and Methods

A total number of 100 USG-guided FNAC were performed on hepatic lesions which were clinically and radiologically suspected as malignant at DMCH, Ludhiana irrespective of age and sex, over a period of 1 year and 6 months. After informed consent, USG guided percutaneous fine needle aspiration (FNAC) was done using 21-gauge spinal needle attached to 20cc disposable plastic syringe in patients with INR not exceeding 1.5. Taking aseptic precautions, needle was introduced in suspended respiration, 6-8 slides were prepared immediately. One of the slide was utilized for rapid on site evaluation for adequacy by doing the Toluidine blue stain. Two of them was wet fixed in 95% ethanol and stained with Papanicolaou stain, Hematoxylin and Eosin and the remaining smears were air dried and stained by May Grunwald Giemsa stain. FNA samples were collected in a separated pass and fixed in 10% formalin, processed and embedded to make cell blocks. Sections were stained by H & E stain. Special stains and IHC were done wherever necessary.

4. Results

During the study period, 100 patients who underwent ultrasound-guided FNAC for focal hepatic lesions were in the age range of 31 to 85 years with maximum cases (33 cases) in the 60-70 years' age group. In each case, clinico-radiological and serological findings were recorded and correlation of cytology was done with histopathology on biopsy. Cell blocks were made in all 100 cases. Male

predominance was found with a MF ratio of 2.1:1. 97% aspirates were cellular and 3% were found poorly cellular on analysing the smears. These were categorised into 5 groups (Table 1)

Table 1: Categorization of malignant hepatic lesions

Groups	Categories	Number	Percentage
Group I	Non-diagnostic	03	3.0%
Group II	Suspicious of malignancy	03	3.0%
Group III	Primary epithelial malignancy	21	21.0%
Group IV	Metastatic deposits	60	60.0%
Group V	Malignant, not otherwise specified	13	13.0%

Group I and II each constituted 3% of the cases. Group IV (metastatic deposits) was the largest group and comprised of 60% cases, followed by group III (primary epithelial malignancy) with 21% of cases. Of the 60 cases diagnosed as metastatic deposits, 50% of cases were categorised as adenocarcinoma deposits, 8.3% as deposits from neuroendocrine tumour, metastatic small cell carcinoma lung constituted 5% of cases, 3.3% cases of metastatic hematolymphoid malignancy and remaining as classified in (Table 2).

Table 2: Cytomorphology of metastatic deposits

Group	Morphology of metastatic deposits	Number	Percentage
Group IV	Metastatic adenocarcinoma deposit	30	50.0 %
	Metastatic neuroendocrine tumor	05	8.4 %
	Metastatic small cell Carcinoma lung	03	5.0 %
	Metastatic hematolymphoid malignancy	02	3.3%
	Metastatic sarcoma	01	1.7 %
	Metastatic, not otherwise specified	19	31.6%

5. Discussion

Guided fine-needle aspiration cytology (FNAC) is an easy, rapid, minimally invasive and a cost effective diagnostic method for detecting neoplastic and non-neoplastic hepatic lesions. It's popularity is attributed to its ability to sample different zones of liver, deep seated lesions, moreover, multiple samples can be taken which improves the accuracy which is further enhanced by ROSE. The sensitivity to pick up malignancy was 97% in our study which is comparable to a study done by Nazir RT et al.^[9]

In our study, 67% of patients were males with a comparatively low incidence in female patients (33%). The male to female ratio of 2:1 which corroborates with studies by Nazir RT et al^[9], Talukder et al^[10] and Sattar A et al^[11] who all observed a M: F ratio of 2:1. The mean age of presentation was 59.56 years comparable to the study of Tailor S et al^[12] where the average age was 59.37 years.

Cytological evaluation was done in all 100 cases and these were categorised these into 5 groups based on their cytomorphological features. Group IV (Metastatic deposits) was the largest group constituting 60% followed by group III i.e. primary epithelial malignancies constituting 21% of the total cases. In our study, metastatic deposits were (60%) more than primary malignancies (21%) which was comparable with studies by Meena S et al^[13], Singh S et al^[14], Chowdhury S et al^[15] and Goel S et al

^[16], Nazir R et al^[9] and Swamy CM et al^[17] found that primary epithelial malignancies were common than the metastatic deposits.

In group I-Cytological smears showed blood mainly with clusters of few reactive hepatocytes. These were considered inadequate for evaluation because of insufficient cellularity. Biopsy was performed in all 3 cases. Two cases were diagnosed as hepatocellular carcinoma on histology and were Hep-par-1 positive on IHC. IHC studies confirmed the diagnosis of metastatic carcinomatous deposits, possibly from stomach with CK 7 positive, CK 20 and Hep-Par1 negative on IHC in third case.

Group II included 3 cases showing atypical cells on cytological smears. Hence, these were categorised under suspicious of malignancy. Biopsy was done in two cases, one was diagnosed as epithelioid hemangioendothelioma and other came out to be metastatic from stomach with CK7 positive(+), CK20 negative(-) and CdX-2 positive(+).

Group III included 21 cases diagnosed as primary epithelial malignancy. The diagnosis was confirmed on histopathology in 17 cases. In the 4 cases where histopathology was unavailable; radiological, clinical and serum tumour markers supported the diagnosis of HCC.

Group IV was further sub categorised into metastatic adenocarcinoma deposits (50%), metastatic neuroendocrine tumour (8.3%), metastatic small cell carcinoma lung (5%), metastatic hematolymphoid malignancy (3.3%), metastatic sarcoma (1.7%) and metastatic deposits, NOS (46.7%).

Of 19 cases diagnosed on cytomorphology as metastatic carcinomatous deposits, NOS, histopathology and IHC of liver SOL in 7 cases determined metastatic deposits from urinary bladder (2), pancreato-biliary tract (4) and prostate (1). On further follow-up, 2 cases had lesions in esophagus which had a morphology of Squamous cell carcinoma esophagus with CK5/6 positivity, 1 was found to be adenocarcinoma from pancreato - biliary tract origin (CK7+, CK20 -) and another one adenocarcinoma stomach (CK7-, CK 20+, MUC 2+) In 1 case clinico-radiological analysis pointed towards primary in gall bladder as biopsy n IHC could not be done. Another 1 case was diagnosed as hepatocellular carcinoma (IHC- Hep-Par 1 +). In 1 case, histological diagnosis of carcinoma was made but IHC was inconclusive hence, the cytological diagnosis was metastatic, NOS. No tissue diagnosis was available in the remaining 5 cases and patients succumbed to the disease on follow up.

6. Conclusion

FNAC plays a decisive diagnostic role in the diagnosis of focal hepatic lesions. Early detection offers the only hope for curative treatment for patients with hepatocellular carcinoma. FNAC has proved to be a sensitive and specific technique for diagnosing malignancy with low risk of complications. The combination of direct smear/cell-block preparation cytology, use of a panel of special stains and immune-stains and close clinico-

pathologic correlation increases the optimization of FNAC in the diagnosis of hepatic malignancies

References

- [1] Dhanasekaran R Et al. Hepatocellular carcinoma: current trends in worldwide epidemiology, risk factors, diagnosis, risk factors, diagnosis, and therapeutics. *J Hepatic Medicine: Evidence and Research*.2012;11:19-37
- [2] El-Serag HB, Rudolph KL. Hepatocellular carcinoma: epidemiology and molecular carcinogenesis. *Gastroenterology*. 2007;132(7):2557–76.
- [3] Dolganiuc A. Alcohol and Viral Hepatitis. Role of Lipid Rafts. *Alcohol Res*. 2015;37(2):299-3094.
- [4] Wee A. Fine-Needle Aspiration Biopsy of Hepatocellular Carcinoma and Related Hepatocellular Nodular Lesions in Cirrhosis: Controversies, Challenges, and Expectations. *Pathology Research International*; 2011:1-175.
- [5] Sumana BS, Muniyappa B. Ultrasonography Guided Fine Needle Aspiration Cytology with Preparation of Cell Blocks in the Diagnosis of Intra- Abdominal Masses. *J Clin Diagn Res*. 2015;9(12):EC08–12
- [6] Asghar F, Riaz S. Diagnostic accuracy of percutaneous cytodagnosis of hepatic masses, by ultrasound guided fine needle aspiration cytology. *Annals*. 2010; 16:184-8
- [7] Kulkarni MB, Prabhudesai NM, Desai SB, Borges AM. Scrape cell block technique for fine needle aspiration cytology smears. *Cytopathology*. 2000; 11:179–84.
- [8] Basnet S, Talwar OP. Role of cell block preparation in neoplastic lesions. *Journal of Pathology of Nepal*. 2012; 2:272.
- [9] Nazir RT, Sharif MA, Iqbal M, Amin MS. Diagnostic accuracy of fine needle aspiration cytology in hepatic tumours. *J Coll Physicians Surg Pak* 2010; 20:373-6
- [10] Talukder SI, Huq MH, Haque MA, Rahman S, Islam SM, Hossain GA, et al. Ultrasound guided fine needle aspiration cytology for diagnosis of mass lesions of liver. *Mymensingh Med J* 2004; 13:25-9.
- [11] Sattar A, Khan AM, Anjum S, Naqvi A. Role of ultrasound guided fine needle aspiration cytology in diagnosis of space occupying lesions of liver. *J Ayub Med Coll Abbottabad* 2014;26(3)
- [12] Tailor SB, Kothari DC. Ultrasound Guided Fine-Needle Aspiration Cytology of Liver Lesions: A Prospective Study. *Int J Sci Stud* 2016;3(11):249-254.Issue 11.
- [13] Meena SP, Patangia P, Rai N. Diagnostic utility of USG-guided FNAC in hepatic lesions. *J. Evid. Based Med. Healthc*. 2016; 3(52), 2699-2702.
- [14] Singh S et al.profile of liver Fine needle aspiration in tertiary care hospital.*Euroasian JHepato-Gastroenterology* 2013;3(1):31-3.
- [15] Chowdhury S et al. A Clinico – Pathological Study of Metastatic Hepatic Lesions with Special Reference to Metastasis from Unusual Primary Sites. p-ISSN: 2279-0861. Volume 14, Issue 2 Ver. VIII (Feb. 2015), PP 46-50
- [16] Goel S, Deepika H, Sharma M. Ultrasound Guided Fine Needle Aspiration Cytology (FNAC) in Diagnosis of Space Occupying Lesions (SOL) of Liver. *Journal of Evolution of Medical and Dental Sciences* 2014; 3: 7480-86.
- [17] Swamy CM et al. Value of ultrasonography-guided fine needle aspiration cytology in the investigative sequence of hepatic lesions with an emphasis on hepatocellular carcinoma. *J Cytol*. 2011 Oct-Dec; 28(4): 178–184.
- [18] Haque S, Dilawar A, Subzwari J. Ultrasound-Guided Fine-Needle Aspiration Biopsy of Metastatic Liver disease: A Comparative Assessment of Histopathological and cytological thechnique. *Biomedica*. 2012;28:49-51.
- [19] Dhameja N, Rai V, Singh R. Fine Needle Aspiration Cytology of Liver Space Occupying Lesions - A Study of 57 Cases from a Tertiary Care Centre. 2016;5(2):287-90.
- [20] Kapadiya DN, Varadharajaperumal R, Santwani PM. Ultrasound guided fine needle aspiration cytology of liver-four-year study. *International Journal of advance Research*. 2015;3(12):523-7.
- [21] Conrad R, Castelino-Prabhu S, Cobb C, Raza A. Cytopathologic diagnosis of liver mass lesions. *Journal of Gastrointestinal Oncology*. 2013;4(1):53-61.
- [22] Rasanía A, Pandey CL, Joshi N. Evaluation of FNAC in Diagnosis of hepatic lesion. *J Cytol*. 2007;24(1):51-4.