COMPARISON OF IMAGE FINDINGS WITH HISTOPATHOLOGICAL DIAGNOSIS ON ULTRASOUND GUIDED PERCUTANEOUS LIVER BIOPSY IN RELATION TO HEPATOCELLULAR CARCINOMA

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ABSTRACT

OBJECTIVES: To compare the image findings with histopathological diagnosis on ultrasound guided (USG) percutaneous biopsies of liver lesions in relation to hepatocellular carcinoma (HCC) and to assess the role of hepatitis B virus (HBV) and hepatitis C virus (HCV) in evolution of HCC.

METHODS: This descriptive cross-sectional study included biopsies performed on patients reporting to Kuwait Teaching Hospital, Peshawar, Pakistan from 01-07-2017 to 30-09-2017. The patient selection was based on findings on various image modalities like triphasic liver computed tomography (CT) or dynamic magnetic resonance imaging (MRI), in which percutaneous liver biopsy was indicated. The biopsies were routinely processed for histological examination on hematoxylin and eosin stain and application of immunohistochemical stains for detecting HCC.

RESULTS: A total number of 82 USG percutaneous biopsies were performed on various sites out of which 41 (50%) were performed on liver lesions. On imaging 12 (30%) were diagnosed as hepatocellular carcinoma whereas 16 (39%) cases were confirmed on histopathology, which either showed Hep-Par-1 or arginase positivity. On imaging 11/16 (68.75%) were either diagnosed as HCC or were suspicious of it. A sensitivity of 75% and specificity of 95% was calculated for diagnosis of HCC on imaging. The correlation between image and biopsy diagnosis of HCC was statistically significant (p value 0.05).

CONCLUSION: The present study concludes that image findings are helpful in the initial diagnosis of HCC which shows an increasing trend to be associated HCV as compared to HBV with a remarkably declining trend.

KEY WORDS: Image-Guided Biopsy (MeSH); Ultrasonography (MeSH); Liver (MeSH); Carcinoma, Hepatocellular (MeSH); Hepacivirus (MeSH); Hepatitis B virus (MeSH); Immunohistochemistry (MeSH); Histology (MeSH).

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INTRODUCTION

The first percutaneous liver biopsy was performed by Paul Ehrlich in 1883 in Germany.[1] Ultrasound guided (USG) needle biopsy was reported in 1958 by Menghini.[2]

Traditionally the liver biopsy has been used for diagnosis of hepatic disease. This expanded to assessment of extent of fibrosis and inflammation that helps in staging and predicting prognosis in liver disease so that clinical management decisions become easier.[3] While serological tests for fibrosis (Fibro Test) and non-invasive tests (elastography) have been introduced, they have not been uniformly standardized nor are widely available.[4,5] Histology based on liver biopsy continues to be the most acceptable test.[6]

Worldwide nearly 50% of liver biopsies are still performed without imaging guidance. The use of USG reduces complications and increases the likelihood of specimen adequacy and procedural success.[3] Nearly 50% of liver biopsies in the United States are performed by radiologists and USG is the favored modality.[7]

At national level in a hospital based prospective study the efficacy of 16 and 18-guage needle was assessed on 426 patients of either gender who underwent USG percutaneous liver biopsy for histopathological evaluation of space occupying lesion of liver or diffuse liver disease. It was concluded that USG percutaneous liver biopsy using either 16 or 18-gauge core biopsy needle was safe and effective method to characterize liver pathology with very low rate of complications.[8]

On the global scale, primary liver cancer is a major contributor to both cancer incidence and mortality. It is the sixth most commonly occurring cancer in the world and the third largest cause of cancer mortality. The most common histologic type of primary liver cancer, hepatocellular carcinoma (HCC), is a malignant tumor arising from hepatocytes, the liver's parenchymal cells.[9]

Hepatocellular carcinoma differs from most malignancies because it is commonly diagnosed based on imaging features alone, without histologic confirmation. This is because overt hepatocellular carcinoma does not have a portal blood supply; it is supplied solely by abnormal, unpaired hepatic arteries. This results in a characteristic vascular enhancement pattern that can be used to make a definitive radiologic diagnosis.[10]

TABLE I: DETAILS OF ULTRASOUND GUIDED PERCUTANEOUS LIVER BIOPSIES

Histopathology Findings	No. of Cases	Percentage
Hepatocellular Carcinoma	16	39
Metastatic Carcinoma	13	32
Benign Non-Neoplastic Lesions	6	14.6
Cholangiocarcinoma	2	4.8
Neuroendocrine Tumor	1	2.4
Lymphoproliferative Lesions	1	2.4
Hemangioendothelioma	1	2.4
Adenoma	1	2.4
Total	41	100

The highest liver cancer incidence rates in the world are reported by registries in Asia and Africa. In contrast to these high rate HCC areas, low rate areas include northern Europe as well as North and South America.[9]

In Pakistan due to the absence of a national cancer registry and screening programs, the data primarily comes from single center experiences or scattered regional registries. Therefore, the prevalence of hepatitis and HCC can only give a rough estimate of the real magnitude of this problem.

Incidence of HCC in Pakistan is on a rise and correlates well with increasing exposure to risk factors for HCC in our population. According to available hospital-based data, age standardized rate for HCC in Pakistan is 7.6 per 100,000 persons per year for males and 2.8 for females.[11]

In a study of 410 patients of liver cirrhosis in Khyber Pakhtunkhwa (former NWFP), Pakistan, HCC was found in 45 (10.98%) patients with predominance of males. Out of which 77.78%, were positive for hepatitis C virus (HCV) and only 4.44% for hepatitis B virus (HBV) infections.[12]

The aim of the study is to compare the image findings with histopathological diagnosis on USG percutaneous biopsies of liver lesions in relation to hepatocellular carcinoma (HCC). The role of HBV and HCV in evolution of HCC was also assessed.

METHODS

This prospective cross-sectional study was carried out in Kuwait Teaching Hospital, Peshawar, Pakistan from 01-07-2017 to 30-09-2017 on patients referred to Radiology Department, Kuwait Teaching Hospital from various hospitals in the city and Khyber Pakhtunkhwa province. The patient selection was based on findings on various image modalities, triphasic liver computed tomography (CT) or dynamic magnetic resonance imaging (MRI), in which percutaneous liver biopsy was indicated. Prior to biopsy the patients were evaluated for the procedure and an informed written consent was taken from them.

The skin site was sterilized and draped to ensure asepsis and the area was anesthetized with xylocaine 2%. Under USG, the deep soft tissues and liver pericapsular areas were also infiltrated with the local anesthetic. We used 18-G Bard Magnum Gun and ensured that the length of biopsy obtained remains between 15 mm to 20 mm to maintain the adequacy for histological diagnosis. The biopsies were routinely processed for histological examination on haematoxylin and eosin (H&E) stain and application of immunohistochemical stains for detecting HCC.

The patients were also assessed serologically by ELISA method for the presence of HCV antibodies and hepatitis B surface antigen (HBsAg).

The data was analyzed in Excel 2016 and SPSS version 19.

RESULTS

A total number of 41 USG percutaneous liver biopsies were performed on patients with liver lesions referred to Kuwait Teaching Hospital, Peshawar. These biopsies were sent to Shaukat Khanum Cancer Hospital & Research Center Laboratory, Lahore and Agha Khan University Hospital Laboratory, Karachi for immunohistochemical markers and ultimate diagnosis.

The age ranged from 17 to 75 years with a mean of 51.4±11.70 years. Thirty-seven patients were 40 years or older. Males were 26 and females 15 with a ratio 1.6:1.

Out of these 41 liver biopsies 16 (39%) were diagnosed as hepatocellular carcinoma (HCC) on histopathology with 6 of them being HCV positive and 1 showed HBV positivity. Out of 16 cases of HCC 15 (93.7%) had age range from 40-65 years whereas only one (6.3%) was under 40. Among them 13 (81.2%) were males and 3 (18.7%) females with a ratio 3.2:1. On imaging 12 (75%) of them were either diagnosed as HCC or were suspicious of it but all the 7 cases of HCV or HBV were diagnosed as HCC (Table I).

The next common tumor was metastatic carcinoma with 13 (31.7%) cases diagnosed. Metastatic adenocarcinoma in this group was the most common with 11 (85%) cases followed by metastatic neuroendocrine tumor 2 (15%) cases (Table I).

Other primary malignant tumors included cholangiocarcinoma 2 cases and one each of neuroendocrine tumor, lymphoproliferative disorder and epithelioid hemangioendothelioma.

Among benign tumors a single case (2.43%) of adenoma was diagnosed.

The next group consisted of 6 (4.63%) benign lesions like cirrhosis 3 (50%) cases out of which 2 were HCV positive, fibrosis 2 (33.3%) cases and an abscess (16.6%). In this group, 03 cases were strongly suggestive of HCC on imaging, but the corresponding biopsy could not reveal malignancy perhaps due to extensive fibrosis and collagenization in cirrhosis leading to nonrepresentative biopsy. In these 03 cases clinico-radiological correlation or a repeat biopsy was recommended.

TABLE II: CORRELATION BETWEEN IMAGE AND HISTOPATHOLOGY DIAGNOSIS OF HEPATOCELLULAR CARCINOMA

Histopathology	Image Positive	Image Negative	Row Total	p Value
Positive	13	4	17	0.05
Negative	2	0	2	
Column Total	15	4	19	

In this study the HCV positivity came out to be 14.6% whereas HBV positivity only 2.43%. Out of HCV positive cases 66.7% developed HCC and 33.3% developed either cirrhosis or extensive fibrosis. The only HBV positive case turned out to be HCC.

All the 16 cases of HCC either showed Hep-Par-1 or arginase positivity which is a novel marker for lesions arising from hepatocytes. All the metastatic tumors were Hep-Par-1 or arginase negative. The individual tumors diagnosed were positive according to their cell type, e.g., cholangiocarcinoma showed positivity for CK7 and CK19, neuroendocrine tumor for CDX-2, lymphoproliferative disorder for CK-30 and CD4 and epithelioid hemangioma for CD34.

The correlation between image and biopsy diagnosis of HCC was statistically significant (p value 0.05) (Table II). A sensitivity of 75% and specificity of 88% was observed.

DISCUSSION

Liver disorders which require a percutaneous liver biopsy commonly occurs in older age group with an average of 51.4 years in our setup. Usually the male population is affected, and the common lesions are HCC, metastatic carcinoma, cirrhosis and fibrosis. HCC, cirrhosis and fibrosis may be related to HCV infection.

These findings correspond with Poynard T, et al, and Thabut D, et al. who concluded that the age of a patient at the time of HCV infection diagnosis has proven to be a risk factor for the progression of liver fibrosis, liver cirrhosis and hepatocellular carcinoma. If a patient is more than 40 years old at the time of diagnosis of HCV infection, their progression of liver fibrosis is much faster than those under 40 years,[14] and for those aged more than 65 years, the relative risk of severe liver fibrosis is 3.78 times higher than that of those under 65 years.[15]

The prevalence of the HBsAg in a western, European hospital remained stable over the period 1993-2003, at 0.7%.[16] In our study we observed that among positive cases 6 out of 7 were HCV positive whereas only 1 case was HBV positive which reflects a rising trend for HCV and a decline in HBV infections in our population.

In contrast, in our study the diagnosis of HCC on imaging was made in 12 (30%) cases out of which 9 (75%) turned out to be HCC on histology whereas 3 (25%) cases were diagnosed as metastatic carcinoma, cirrhosis and fibrosis. A sensitivity of 75% and specificity of 88% was observed. These values are a bit higher than Lin MT, et al. who obtained overall diagnostic sensitivity of HCC by single imaging as approximately 65-80% (liver CT or MRI).[17] Earlier in 2006 Colli A, et al. reviewed HCC diagnosed on histopathology and compared findings on CT and MRI from 1966 to 2004 and found that for the 10 CT studies sensitivity was 68% and specificity 93%; and for the nine MRI studies sensitivity was 81% and specificity 85%.[18]

Metastatic carcinoma can mimic HCC whereas in cases of advanced cirrhosis and overwhelming fibrosis especially if the lesion is small, the percutaneous needle biopsy is likely to miss it. Therefore, in cases where there is strong suspicion of malignancy a repeat biopsy must be advised. This is supported by Kim TK, et al. who concluded that although imaging techniques have markedly improved in detecting small liver lesions, they often detect incidental benign liver lesions and non-hepatocellular malignancy that can be misdiagnosed as HCC.[19]

CONCLUSION

The present study concludes that image findings are helpful in the initial diagnosis of HCC which shows an increasing tendency to be associated with HCV as compared to HBV with a remarkably declining trend.

REFERENCES

1. El-Shabrawi MH, El-Karaksy HM, Okahsa SH, Kamal NM, El-Batran G, Badr KA. Outpatient blind percutaneous liver biopsy in infants and children: is it safe? Saudi J Gastroenterol 2012 Jan-Feb;18(1):26-33. DOI: 10.4103/1319-3767.91735.
2. Menghini G. One-second needle biopsy of the liver. Gastroenterology 1958; 35(2): 190-9.
3. Vijayaraghavan GR, David S, Bermudez-Allende M, Sarwat H. Imaging-guided Parenchymal Liver Biopsy: How We Do It. J Clin Imaging Sci 2011;1:30. DOI: 10.4103/2156-7514.82082.
4. Shaheen AA, Wan AF, Myers RP. FibroTest and FibroScan for the prediction of hepatitis C-related fibrosis: a systematic review of diagnostic test accuracy. Am J Gastroenterol 2007 Nov;102(11): 2589-600. DOI:10.1111/j.1572-0241.2007.01466.x.
5. Piscaglia F, Salvatore V, Mulazzani L, Cantisani V, Schiavone C. Ultrasound Shear Wave Elastography for Liver Disease. A Critical Appraisal of the Many Actorson the Stage. Ultraschall Med 2016 Feb;37(1):1-5. DOI: 10.1055/s-0035-1567037.
6. Alswat KA, Mumtaz K, Jafri W. Liver biopsy for histological assessment: The case in favor. Saudi J Gastroenterol 2010 Apr-Jun;16(2):133-9. DOI: 10.4103/1319-3767.61245.
7. Rockey DC, Caldwell SH, Goodman ZD, Nelson RC, Smith AD; American Association for the Study of Liver Diseases. Liver Biopsy. Hepatology 2009 Mar;49(3):1017-44. DOI: 10.1002/hep.22742.
8. Iqbal J, Sattar A, Al-Qamari N, Hussain M, Rashid S. Compare the efficacy and complications of 16 gauge vs 18 gauge core biopsy needle in ultrasound guided percutaneous liver biopsies. J Dow Univ Healt Sci 2017;11(2):41-5.
9. McGlynn KA, Petrick JL, London WT. Global epidemiology of hepatocellular carcinoma: an emphasis on demographic and regional variability. Clin Liver Dis 2015 May;19(2):223-38. DOI: 10.1016/j.cld.2015.01.001.
10. McEvoy SH, McCarthy CJ, Lavelle LP, Moran DE, Cantwell CP, Skehan SJ, et al. Hepatocellular carcinoma: illustrated guide to systematic radiologic diagnosis and staging according to guidelines of the American Association for the Study of Liver Diseases. Radiographics

2013 Oct;33(6):1653-68. DOI: 10.1148/rg.336125104.

11. Hafeez Bhatti AB, Dar FS, Waheed A, Shafique K, Sultan F, Shah NH. Hepatocellular Carcinoma in Pakistan: National Trends and Global Perspective. Gastroenterol Res Pract 2016;2016:5942306. DOI: 10.1155/2016/5942306.

12. Farooqi JI, Farooqi RJ. Prevalence of Hepatocellular Carcinoma in Patients of Liver Cirrhosis: An Experience in North West Frontier Province (NWFP). J Coll Physicians Surg Pak. 2000;10(2):54-5.

13. Yan BC, Gong C, Song J, Krausz T, Tretiakova M, Hyjek E, et al. Arginase-1: a new immunohistochemical marker of hepatocytes and hepatocellular neoplasms. Am J Surg Pathol 2010 Aug;34(8):1147-54. DOI: 10.1097/PAS.0b013e3181e5dffa.

14. Poynard T, Ratziu V, Charlotte F, Goodman Z, McHutchison J, Albrecht J. Rates and risk factors of liver fibrosis progression in patients with chronic hepatitis c. J Hepatol 2001 May;34(5):730-9. DOI 10.1016/S0168-8278(00)00097-0

15. Thabut D, Le Calvez S, Thibault V, Massard J, Munteanu M, Di Martino V, et al. Hepatitis C in 6,865 patients 65 yr or older: a severe and neglected curable disease? Am J Gastroenterol 2006 Jun;101(6):1260-7. DOI: 10.1111/j.1572-0241.2006.00556.x.

16. Frith J, Jones D, Newton JL. Chronic liver disease in an ageing population. Age Ageing 2009 Jan;38(1):11-8. DOI: 10.1093/ageing/afn242.

17. Lin MT, Chen CL, Wang CC, Cheng YF, Eng HL, Wang JH, et al. Diagnostic sensitivity of hepatocellular carcinoma imaging and its application to non-cirrhotic patients. J Gastroenterol Hepatol 2011 Apr;26(4):745-50. DOI: 10.1111/j.1440-1746.2010.06501.x.

18. Colli A, Fraquelli M, Casazza G, Massironi S, Colucci A, Conte D, et al. Accuracy of ultrasonography, spiral CT, magnetic resonance, and alpha-fetoprotein in diagnosing hepatocellular carcinoma: a systematic review. Am J Gastroenterol 2006 Mar;101(3):513-23. DOI: 10.1111/j.1572-0241.2006.00467.x.

19. Kim TK, Lee E, Jang HJ. Imaging findings of mimickers of hepatocellular carcinoma. Clin Mol Hepatol 2015 Dec;21(4):326-43. DOI: 10.3350/cmh.2015.21.4.326.

AUTHORS' CONTRIBUTIONS

Following authors have made substantial contributions to the manuscript as under:

AM: Acquisition of data, final approval of the version to be published.

MMK: Concept & study design, final approval of the version to be published.

AAZ: Analysis & interpretation of data, drafting of manuscript, final approval of the version to be published.

SA: Analysis & interpretation of data, critical review, final approval of the version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

Authors declared no conflict of interest

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