ORIGINAL ARTICLE

Diagnostic Accuracy of Triphasic CT Scan in Detection of Hepatocellular Carcinoma Versus Metastasis Keeping Histopathology as Gold Standard

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Received: 30-04-2024
Revision : 18-08-2024
Accepted: 27-09-2024

ABSTRACT

Background: The most prevalent primary tumor of liver is hepatocellular carcinoma (HCC) after metastasis, and it is also the 6th most frequent cancer in the world. Since long triphasic CT scan abdomen and serum alphafeto protein levels remains the standard of investigations for confirming HCC. Here we share our experience of appearance of HCC on dynamic liver CT scan, that not all HCC lesions shows typical pattern of enhancement in arterial phase or show washout in venous phase. The pattern of enhancement also differs for different types of HCC. In such cases histopathology gives us the correct answer as it is the gold standard.

Objective: To check the diagnostic accuracy of triphasic CT scan in detection of HCC comparing it with metastatic lesions while keeping biopsy as a gold standard.

Methods: It is a prospective cross-sectional study that was conducted at Radiology department of NORI cancer hospital from 1st Jan 2022 to 31st Dec 2022. Sample size was 50, and the patients coming for CT scan without known primary malignancy were carefully selected. Patient's with hepatic lesions having equivocal pattern of enhancement (differential HCC Vs Metastasis), without any cirrhosis or altered AFP were included in the study. Of these, 39 underwent liver biopsy and were further divided into two groups (HCC Vs Non HCC/ Mets) depending on histopathology report. Patients with typical HCC lesions on Triphasic CT scan, cirrhotic liver morphology, raised AFP levels and benign lesions (e.g. hemangiomas) were excluded from our study.

Results: Our results of the study shows that 64.1 % had the histopathological diagnosis of metastatic disease and 35.9 % had typical HCC. The diagnosis of typical HCC was also confirmed by immunohistochemical marker of Hep-Par. Median age of patients was 40-60 years and the ratio of male: female was approx. 7:3.

Conclusion: There is a high frequency of false negative diagnosis for HCC on triphasic CT in patients with equivocal enhancement pattern and normal alpha feto protein level. This is particularly so in patients without cirrhosis. In such equivocal cases we must rely on biopsy and histopathology which is the gold standard in most of the cases.

Keywords: *Hepatocellular carcinoma, liver, biopsy, cirrhosis, patients, hemangiomas*

INTRODUCTION

Hepatocellular carcinoma (HCC) accounts for the commonest primary liver tumors, which is the sixth commonest cancer worldwide.[1] HCC frequently arises in the background of cirrhosis; the percentage of its development in normal liver parenchyma is approximately 20%.[2] These patients often do not present at an early stage as routine screening/ scrutiny is not done. HCC does not have any specific age predilection and can present at any age peaking at 2nd and 7th decade in a lifetime. It affects men twice as frequently as compared to women and for men there is even more stronger association of its development when the liver parenchyma is diseased by cirrhosis.[3] However there is a variant of HCC, which is Fibrolamellar, that mostly occurs in young peaking in the 2nd and 3rd decades of life and has no sex predilection.[4] These days biopsy is rarely required for HCC diagnosis and favored methods of diagnosis are mostly non-invasive. There are characteristic and typical radiological findings of HCC in patients with background cirrhosis which help in establishing the diagnosis non-invasively.[5] Most of the updated guidelines, including those of the American Association for the Study of Liver Diseases (AASLD)[6] and the European Association for the Study of the Liver (EASL)[7], triphasic CT scan based on liver

dynamic protocol is regarded as the standard noninvasive diagnostic tool for HCC along with magnetic resonance imaging (MRI).[8] MRI is technically more challenging as compared to dynamic CT and is also not widely available.

The mainstay of diagnosing HCCs predominantly in lesions bigger than 1 cm is post contrast, dynamic CT and it carries its sensitivity of up to 94%[9]; But the sensitivity of diagnosis of HCC in lesions less than 1 cm considerably falls low for contrast-enhanced, dynamic CT scan. The characteristic imaging appearances suggestive of HCC on dynamic liver CT are non-rim arterial phase hyper enhancement (APHE), washout on portal venous and sometimes on delayed phase along with marginal/ capsular enhancement in a lesion which measures ≥1 cm.[10] The intense arterial enhancement of the lesion is vital to establish HCC. [11] At present, hepatic liver lesion biopsy is done in only those cases where the diagnosis of HCC remains indeterminate on dynamic CT scan or patients who develop HCC in normal liver without cirrhosis.[12] The washout of lesion on porto-venous phase or delayed phases refers to the presence of hypodensity in lesion when compared with the rest of liver parenchyma and has a specificity of 95–96% for establishing HCC.[11]

Although the specificity of arterial blush and portovenous/ delayed washout is quite high, the sensitivity of these radiological features is quite low and 1/3rd of HCC nodules in the background of cirrhosis do not show the typical pattern of enhancement. This happens generally in cases of well differentiated HCC and in lesions smaller than 2cm. In those indeterminate cases, mostly the international guidelines prefers the use of histopathology for the diagnosis of atypical HCC, nevertheless there is an increasing trend in the use of newer noninvasive/ less invasive diagnostic tools that may increase sensitivity of diagnosis of HCC.[13]

For timely characterization & treatment of focal HCC with non-invasive diagnostic methods, our study focused on determining diagnostic accuracy of Triphasic CT Scan in detection of Hepatocelluar carcinoma versus metastasis keeping histopathology as gold standard.

METHODS

It was a prospective study conducted at NORI Cancer Hospital, Islamabad. The duration of the study was one year from January 1st 2022 to December 31st 2022.

We used consecutive non-probability sampling technique. Sample size was 50 using WHO calculator for sample size. The patients selection criteria were made and only those patients who meet the desired selection criteria were included in the study, rest were excluded.

A lesion is categorized as HCC on triphasic CT scan if it shows arterial phase enhancement (at 17-20 seconds) with washout on portovenous and delayed phases (30seconds, 60 seconds and 5 minutes).

Lesion is considered equivocal if it does not show typical pattern of arterial enhancement and typical wash out on porto-venous and delayed phase, patient does not have any other known malignancy to suggest liver metastasis and size of lesion was more than 2 cm. Equivocal cases were included in the study as it gives the differential of HCC or metastasis. These patients had prior normal liver morphology and normal alpha-feto protein levels.

Patients with typical patterns of enhancement on triphasic CT scan (arterial enhancement and porto-venous wash out), background cirrhotic liver parenchyma, raised AFP levels and benign lesions (e.g hemangiomas) were omitted from the study.

50 patients who undergo triphasic CT scans for malignancy of unknown origin were considered. Of these, 39 underwent liver biopsy and were further divided into two groups (HCC Vs Non HCC/ Mets) depending on histopathology report.

Patients within age group of 38-81 years, presenting with, and malignancy of unknown origin were included. Patients with multiple equivocal lesions in liver on triphasic CT scan were also included. These CT scans were reviewed by senior radiologists having more than 3 years of experience in reading dynamic liver CT scans. All these patients underwent liver biopsy at department of Radiology NORI cancer Hospital and were histopathologically proven as HCC only if shows typical morphology and were Hep Par positive. Metastatic lesions show different morphology and immunohistochemical marker according to origin of tumor.

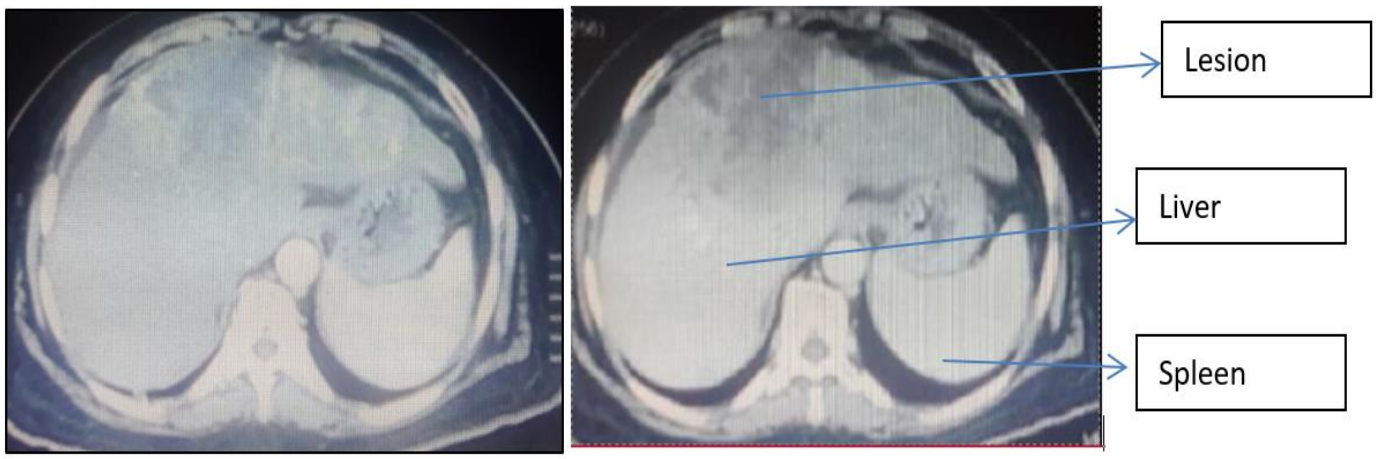
Proforma was established to collect the required data. We used GE Logic S8 ultrasound machine having curvilinear probe for biopsy of hepatic lesions. Patients were biopsied in supine or left lateral position depending upon the segment of liver involved. Statistical analysis was performed using the latest SPSS version of 20. For quantitative variables we measures mean alongwith standard deviation. For qualitative variables we measures frequency as well as percentages. A 2×2 cross table was used to measures the required variables including sensitivity, specificity, PPV, NPV, and diagnostic accuracy.

RESULTS

Sample size was 50 which include male as well as female patients. Out of which 11 were excluded from the study based on exclusion criteria and 39 were included. Eleven (28.2%) were females and twenty eight (71.8%) were males. Mean age of patients were 60.12 years. Viral serology and Alpha feto protein levels of all patients were also recorded. 6 (15.4%) were HCV positive and 33 (84.6%) were HCV negative. 34 (87.2%) had normal AFP levels whereas 5 (12.8%) had raised levels of AFP. The findings on triphasic CT scans and histopathology were also noted. Those who were reported as equivocal cases HCC on triphasic CT scans were analyzed and further biopsy were done on these cases. Histopathology recorded as HCC and Metastasis. On histopathology 14 (35.9%) had HCC and 25 (64.1%) had metastasis. We did not find much different types of HCC in our study and all patients of HCC had typical morphology on standard staining techniques and IHC was applied in all cases which turn out to be Hep Par positive. Chi square test was applied and p value was 0.029.

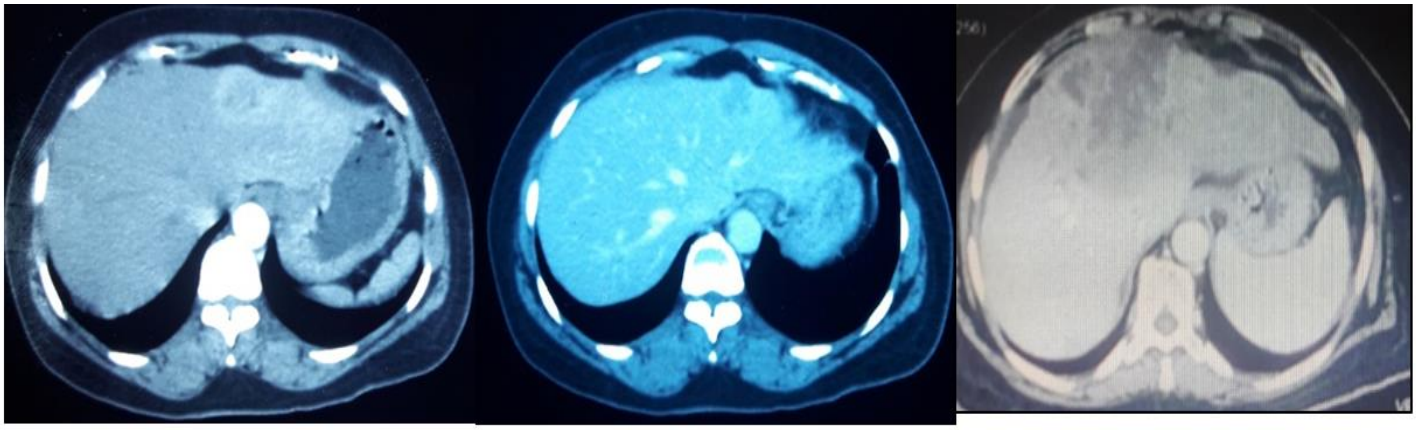
Table 1: Cross Tabulation of Triphasic CT Scan Findings with Histopathology

		Triphasic CT Scan		Total
		Equivocal	HCC	
Histopathology	HCC	13	1	14
	Metastasis	15	10	25
Total		28	11	39



Case 1: A 45 year old young male patient presented with ill-defined large heterogeneous mass in segment IV of liver with no typical arterial enhancement or venous wash out. Histopath showed HCC

Case 2: A 34 year old female presented with multiple arterially enhancing lesions predominantly in left lobe of liver with wash out on venous phase, H/p Metastatic neuroendocrine tumor



DISCUSSION

Hepatocellular carcinoma (HCC) comes at number six in the order of occurrence of cancer in the world and is also the major cause of deaths from cancer accounting to third in cancer mortality worldwide.[14] If it is diagnosed timely, than there are various potentially curable treatment options available which can be offered to the patients and may increase the overall survival of patients thereby improving outcome of disease.[15]

Most of the HCC arises in the background of cirrhosis where diagnosis is usually made easily with triphasic CT scan and raised AFP levels, however not all patients with cirrhotic liver harbor HCC and mostly HCC can occur without the background cirrhosis and in normal hepatic parenchyma.

Chronic hepatitis C viral infection remains the commonest cause of developing cirrhosis in Western countries, whereas chronic hepatitis B viral infection accounts for 60% of HCC in East Asia and Africa; there are also many other causes of chronic liver damage which include mainly usage of excessive alcohol, exposures to aflatoxin, cholestasis, autoimmune diseases, nonalcoholic steatohepatitis and metabolic disorders.[16] If HCC is diagnosed at an early stage, patient can get prompt aggressive treatment, resulting in overall improvement of long-term survival.[13]

Commonly patients present with clinically palpable hepatic lesions or diagnosed incidentally on sonography with hepatic masses however the reason remains unknown. In these two types of scenarios if the findings of triphasic CT scan are confirmatory for HCC than no further investigation is required and treatment can be initiated, however this does not always happen. In our experience we have seen that many a times the findings of dynamic liver scan are equivocal (HCC vs metastasis) with features neither typically favoring HCC nor metastasis. In these scenarios it becomes important to have a biopsy done in order to start a timely treatment. The treatment of HCC can be radiofrequency ablation (RFA), chemoembolization using transarterial pathway called TACE or chemotherapy/ targeted drugs depending upon the size and number of lesions, whereas the treatment of metastasis is entirely different and mainly focuses on targeting the primary organ of origin. In these circumstances it becomes mandatory to find a tissue diagnosis so that oncological treatment can be commenced.

We have seen in our study that CT scan was equivocal in 28 (71.8%) of population whereas it directed to the clue of HCC in 11 (28.2%) of population. Whereas on histopathology 14 (35.9%) patients out of 39 were diagnosed with HCC in the background of normal hepatic parenchyma and 25 (64.1%) had metastasis from various regions of body to liver. In our study 28% of patients had HCC has been detected in normal liver parenchyma as compared to 20% in a study by Aakash Desai et al.[1] Patients with HCC in non-cirrhotic liver presented at an advanced age (median age 60 years). We had more proportion of male patients than females (2.5:1). Majority of these patients were negative for HCV and AFP were normal.

Equivocal cases were those who showed atypical vascular pattern. Top differential were metastasis vs atypical HCC. Non HCC was non arterialized lesion. Majority of patients had larger than 2 cm nodules when diagnosed**.** We also could not find many different types of HCC and our biopsy specimen showed cases of typical HCC which were later on IHC proven. It was not also in our protocol to take biopsy specimen from normal liver for comparison purpose.

Our study has some limitations due to small sample size, larger scale study is suggested. Patient selection was biased as all patients with hepatic lesions mostly with clinical suspicion of HCC were included. Study can be more generalized. The role of MRI can also be explored.

CONCLUSION

There is a high frequency of false negative diagnosis for HCC on triphasic CT in patients with equivocal enhancement pattern and normal alpha feto protein level. This is particularly so in patients without cirrhosis. In this group of equivocal cases we cannot rely much on dynamic liver CT scan and biopsy and histopathology remains the gold standard.

CONFLICT OF INTEREST / DISCLOSURE: Nil.

FUNDING SOURCE: Nil.

AUTHORS' CONTRIBUTION:

ZZ: Acquisition of data, manuscript writing, statistical analysis and data interpretation final approval of manuscript.

UM: Acquisition of data, data analysis and interpretation,

SA: Data analysis and interpretation final approval of manuscript.

MM: Data analysis and interpretation, manuscript writing

AK: Data analysis and interpretation, manuscript writing

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