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CASE REPORT

Diagnosis of Vaso-Invasive Hepatocellular Carcinoma Involving the Medial Hepatic Vein and Right Portal Vein in a man presenting with Upper Gastrointestinal Bleeding and Melena

FURQAN UL HAQ[1], MUHAMMAD ALI[2], SANI UL HASSAN[3], DANEET KUMAR[4], YASIR ALI[5], FAROOQUE ISLAM[6], TANVEER HAMID[7], SYED SADAM HUSSAIN[8] , WAQAR ALI SHAH[9], AMAN ULLAH[10]
[1]*Department of Physiology, Swat Medical College, Pakistan*
[2]*Department of Gastroenterology, Hayatabad Medical Complex, Peshawar, Pakistan*
[3]*Department of Oncology, Hayatabad Medical Complex, Peshawar, Pakistan*
[4]*Department of Internal Medicine, Hayatabad Medical Complex, Peshawar, Pakistan*
[5]*Department of IM, Hayatabad Medical Complex, Peshawar, Pakistan*
[6]*Department of Medicine and Allied, Hayatabad Medical Complex, Peshawar, Pakistan*
[7]*Department of Internal Medicine, Sligo General Hospital, Sligo, Ireland*
[8]*General Medicine, Hayatabad Medical Complex, Peshawar, Pakista*
[9,10]*Department of Physiology, Swat Medical College, Pakistan*
Correspondence to Dr. Furqan ul Haq, Email: furqanulhaq459@gmail.com

ABSTRACT

Background: Hepatocellular carcinoma (HCC) is one of the most fatal malignant tumors of the gastrointestinal tract in men as compared to women. It develops in the setting of chronic inflammation and cirrhosis. Major risk factors are hepatitis B and hepatitis C, alcoholic cirrhosis, and non-alcoholic fatty liver disease. It metastasizes to lungs, bones, portal vein and regional lymph nodes. Melena and hematemesis are the common presentations.
Methodology: Case report study done in Swat Medical College, Rahman Medical Institution laboratory and Swat Medical Complex.
Case: We have a confirmed case of HCC initially presenting with coffee color emesis and the previous 06 episodes from August to September 2022 with melena. Computed tomography (CT) abdomen with contrast showed a mass of irregular margins with vascular invasion. Histopathology showed HCC. The rationale of this case report is that we report a HCC case with vascular invasion. This patient is a candidate for systemic therapy, which would be guided by the assessment of financial factors, performance status and other comorbidities.
Practical Implications: This study is going to prove the importance of finding out why the prognosis of HCCa becomes poor when vascular invasion such as hepatic veins, vena cava, portal veins or hepatic artery is present, in this study the invasion was in medial hepatic vein extending to right portal vein, that's why his prognosis is considered to be poor as the disease has vascular invasion, if vessel were not invaded than there was a possible of local chemo and radiotherapy to target the tumor site and patient could have survived normal life.
Results and conclusion: HCC is amongst the most lethal carcinomas with various causes, including hepatitis B and C virus infection, alcohol consumption, non-alcoholic fatty liver disease, *etc*. The risk of HCC recurrence increases many fold in macrovascular invasion as compared to microvascular invasion even after orthotopic liver transplant. Patients diagnosed with HCC should be thoroughly investigated for vascular invasion as it is one of the major factors in making decisions regarding treatment options.
Keywords: Hepatocellular carcinoma, Vaso Invasion, Alpha-Fetoprotein, Cirrhosis, hepatitis B and C, liver masses,

INTRODUCTION

Hepatocellular carcinoma (HCC) is more common in men than women. It is the second leading cause of death in developing countries and a sixth leading cause of death in developed countries[1]. It is usually seen in the 6th and 7th decade of life. The incidence of other cancers in the United States has decreased but that of HCC has increased at the rate of 3.5% annually. About 0.749 Million new cases are diagnosed per year and 0.745 Million cases die per year[2]. Liver lesions rarely occur below the age of 40 years old and are mostly present above 50 years old reaching 70 years of age[3]. In developed countries, approximately 20% of the HCC cases are due to chronic hepatitis B virus (HBV) infection. The incidence in Western countries is rising owing to increasing rates of alcoholic liver disease and hepatitis C infection. If vaso-invasive HCC is symptomatic and left untreated, the five-year survival rate falls below five years. Diagnosis with the use of dynamic gadolinium-enhanced sequences has a sensitivity of 55 to 91% and specificity ranging from 55 to 86%[4]. Portal vein obstruction remains one of the major complications to be considered and it is very difficult to treat once portal vein is involved leading to portal hypertension and splenomegaly and ascites with cardio renal failure, so vaso invasion has been proven to be related very closely to poor prognosis[5].

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At present, surgery is the best curative treatment, either a partial hepatectomy or orthotopic liver transplantation (OLT); the procedure is limited by a smaller number of donors. If surgical resection is done then the survival rate is increased up to 40–50% while the recurrence rate is high, for five years the recurrence rate is 75% to 100%, patients with extra hepatic manifestation have a poor prognosis with a survival rate of less than six months[5]. Liver-focused therapies including transcatheter arterial chemoembolization and percutaneous radiofrequency ablation improve a patient's survival and five-year prognosis, and these are cost-effective therapies. Prognosis-dependent factors are pathological tumor factors (like size, stage, grade, the presence of vascular invasion; prognosis becomes very poor and there is a high rate of recurrence once vessels are invaded, portal vein tumor thrombus and intrahepatic metastases), the patient's hepatitis status, the patient's functional liver reserve and the serum α-fetoprotein level[5]. Insufficient future liver remnant (FLR) or an inadequate surgical margin makes it difficult to undergo hepatectomy especially if the liver is fibrotic[6].

CASE PRESENTATION

A 50-year- old male of Pathan Yusufzai's ethnicity who is a shopkeeper by profession from Pakistan, who was a known case

of decompensated liver disease secondary to chronic hepatitis B infection, presented to our emergency room and complained of coffee ground emesis, frank blood-containing emesis and a change in stool color to tarry black. Upon inquiry, he mentioned that he had six episodes of vomiting and did not lose consciousness. The patient baseline investigations were discussed in Table 1. He started on the appropriate treatment including Sandostatin and his esophagogastroduodenoscopy (EGD) showed large esophageal varices with active ooze. While he was being managed, his ultrasound was ordered and showed a coarse cirrhotic liver with irregular margins, also his alpha-fetoprotein (AFP) was found to be elevated, which was 49.08 ng/ml. Therefore, a computed tomography (CT) scan was ordered, which showed a vaso-invasive HCC within hepatic segments 5 and 8 with maximum cross-sectional dimensions of 64.7×46.7mm with craniocaudal (CC) dimensions of 64.5 mm discussed in Figure 1 and Figure 2 and its report has been discussed in Table 2. Moreover, huge bulky lymph nodes were evident within the hepatic hilar region and paracaval region, a larger one of these measuring up to 45.5 × 49.9 mm (Antero posterior (AP) x Transverse section (TR). His histopathology has been discussed in Figures 3-5.

Table 1: Baseline Investigations. White Blood Cells (WBC), PTH (Parathyroid Hormone). surface antigen; ICT: immunochromatographic test.

Name of Investigation		Results	Normal Range	Unit
Hemoglobin		**8.4**	M=14-18 F=11.7-15.7	mg/dl
W.B.C		**17.0**	4.0-10.0	$X10^3$/dL
Neutrophils		**75**	40-70%	$X10^3$/dL
Lymphocytes		17	20-25%	$X10^3$/dL
Monocytes		04	2-10%	$X10^3$/dL
Eosinophils		02	1-2%	$X10^3$/dL
Platelets Count		**156**	150-400	$X10^6$/L
Sodium		134	136-149	mmol/L
Potassium		3.9	3.8-5.2	mmol/L
Chloride		103.0	98-107	mmol/L
Random Blood Sugar		182	80-140	mg/dl
Blood Urea		65	10-50	mg/dl
Alkaline Phosphatase		**191**	40-129	mg/dl
Serum Calcium (Total)		6.5	8.8-12.0	mg/dl
Total Bilirubin		**2.5**	0.1-1	mg/dl
PTH-Intact		6.01	15-65	pg/ml
Alpha Fetoprotein		49.08	0-6	IU/ml
Physical Examination of Stool	Color	Yellowish	Yellowish	NIL
	Reaction	Acidic	Acidic	NIL
	Consistency	loose	Solid	NIL
	Blood	NIL	NIL	/hpf
	Mucus	NIL	NIL	/hpf
Microscopic Examination of Stool	Ova	Not Seen	NIL	/hpf
	Cyst	Not Seen	NIL	/hpf
	Pus Cells	04-05	NIL	/hpf
	RBCs	NIL	NIL	/hpf

The patient's previous record revealed a hepatitis B virus (HBV) viral load of 2,436,329 in September 2021 and he has since been taking Tab Entecavir 0.5 mg once daily. Additionally, he had an episode of altered sensorium for 48 hours, which was treated as a case of urinary tract infection. Kept on a low sodium diet. He has Child-Pugh Class C liver status. According to Milan's criteria, he is not a candidate for transplant. However, his American Society of Anesthesiologists (ASA) functional status is two, therefore treatment options other than just supportive therapy can be considered[7]. In Past medical history he only has Hepatitis B, no significant family history of any HCC, hepatitis or any other tumor. Psychologically the patient was assessed and found to be oriented normally. His Social history such as diet and appetite were slightly reduced for the past one-year, mild insomnia was also there, used to do his daily routine walk. Sexual history revealed that he is monogamous. In view of the above diagnosis, the patient was counseled about his possible management through a multidisciplinary approach and was referred to a gastroenterologist, followed by a hepatobiliary surgeon and an oncologist. Clinician and patient-assessed outcome was pretty grim keeping in view the vasa invasive nature of the particular carcinoma, while interventions in most such patients are a far cry in our setup because of the affordability and our fragile health system, so most such patients ended up getting medical and palliative treatment in the end. His treatment has been discussed in Table 3.

Abdominal ultrasound: Shrunken liver 13 cm in size with coarse parenchymal echo texture with irregular borders was observed. The spleen was normal in size and measured at 12.3cm. Gross abdominopelvic ascites were seen.

Table 2: CT abdomen with contrast report, CT (computed tomography), HCC (hepatocellular carcinoma), CC (craniocaudal) AP (Anteroposterior), TR (Transverse section).

Structure	Impression
Liver	Hepatic margins are irregular in keeping with cirrhotic morphology, HCC is evident within hepatic segments 5 and 8 with maximum cross-sectional dimensions of 64.7 × 46.7 mm with CC dimensions of 64.5 mm. The lesion is more linearly oriented involving the medial hepatic vein with direct thrombosis of the right portal vein tributary extending up to the main portal vein.
Spleen	Enlarged measuring 13.57 cm with splenic hilar, perigastric and para-aortic varices.
Lymph nodes	Huge bulky lymph nodes are evident within the hepatic hilar region and para caval region, a larger one of these measuring up to 45.5 × 49.9(AP×TR).
Gallbladder and biliary tract	Norma l studies.

Figure 1: CT Scan abdomen and pelvis (with contrast): Done on 15/08/2022**.** Venous phase CT with contrast: red arrows show irregular margins of HCC. CT, computed tomography; HCC, hepatocellular carcinoma.

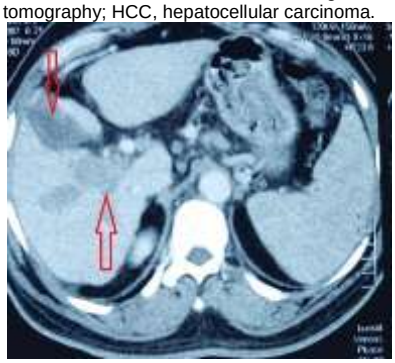

Figure 2: Arterial phase of CT abdomen with contrast showing HCC. Red arrow shows irregular margins of HCC. CT, computed tomography; HCC, hepatocellular carcinoma.

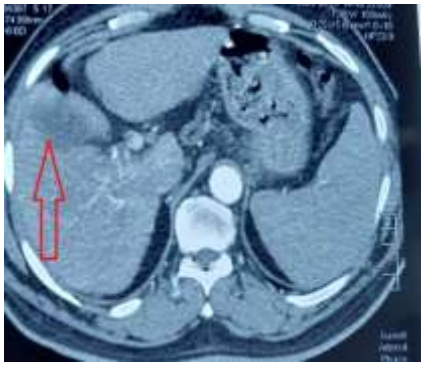

Figure 3: Histopathology of vaso-invasive HCC. Hematoxylin and eosin stain slide of HCC at magnification x40. Hematoxylin and eosin-stained hepatic tissue showing small round cells, with cellular atypia, mitosis and increased nucleus to cytoplasmic ratio. HCC (hepatocellular carcinoma).

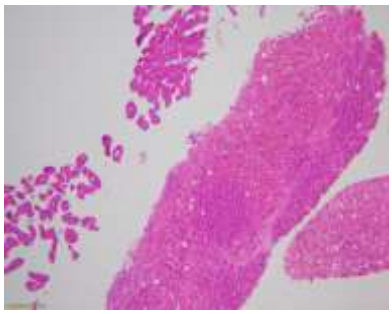

Figure 4: HCC after immunohistochemical staining. Magnification, x40. Immunohistochemical stained tissues with Hepatocyte Paraffin 1 stain. HCC, hepatocellular carcinoma.

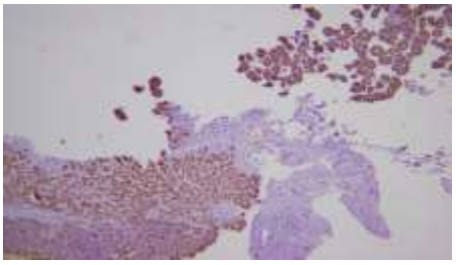

Figure 5: HCC positively stained for Hep Par 1. Magnification, x1,000. HCC positively stained for Hep Par 1 and negatively for CK7 and 20. HCC, hepatocellular carcinoma; Hep Par 1, Hepatocyte Paraffin 1.

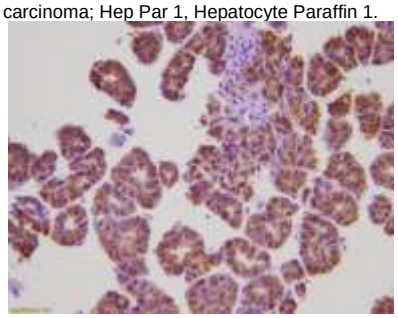

Table 3: Treatment Received. Inj (Injection), Syp (syrup), Inf (infusion), Tab (tablet), IV (Intravenous), PO (per oral); TSF (teaspoon), OD (once daily), TDS (thrice daily), BD (twice daily)

Name of a drug	Route of administration	Dosage	Duration
Inj. Sando	IV	6 Ampules in 1L Normal saline at 40 ml per hour	continuous
Inj. Vitamin K	IV	10 mg	OD
Inj Ceftriaxone	IV	1g	OD
Syp Duphalac	PO	2 TSF	T.D.S
Inf Ringer lactate	IV	1L	BD
Home Treatment:			
Syp. Motilium (antiemetic)	per oral	1 TSF	T.D.S
Syp. Ulsanic (antitussive)	per oral	2TSF	B.D
Tab Spironolactone	Per oral	50 mg	B.D
Syp Cefixime	per oral	250mg	B.D

DISCUSSION

HCC is amongst the most lethal carcinomas with well-known risk factors including hepatitis B and C virus infection, drinking alcohol, hemochromatosis, Wilson's disease, alpha 1 antitrypsin deficiency, primary biliary cirrhosis and autoimmune hepatitis[8]. Screening is recommended in high-risk individuals who have developed cirrhosis from any cause with ultrasonography and serum AFP levels[9]. Diagnosis is based on the typical radiological features of a Triphasic CT scan in the background of high-risk factors for the development of HCC. Usually, biopsy is not recommended in such cases and is indicated only when the radiological features are equivocal or there are no high-risk factors with typical radiological features attributable to other causes[10].

Once the diagnosis is made, further management is based on a multidisciplinary approach. Options for the localized disease include resection, transplant or locoregional therapies. Once there is an invasion of the major vessels then the option of surgery and transplant is hard to practice and curative intent therapy is difficult in such cases[11]. In such cases, patients should be encouraged to participate in Clinical trials or have systemic therapy[12]. Child-Pugh scoring is a very important aspect of the management of HCC because of its prognostic value and as a guide towards the treatment option. A combination of immune checkpoint inhibitors such as atezolizumab and anti-vascular endothelial growth factor receptor (bevacizumab) is the first-line treatment option followed by other kinase inhibitors such as sorafenib and lenvatinib. If there is a progression on these medications then we have the options of Regorafenib, Cabozantinib[13].

In our case, the patient had the risk factor of hepatitis B virus infection. Our patient presented with the manifestations of chronic liver disease in the form of upper gastrointestinal (GI) bleed. Radiology revealed multiple lobes' involvement with vascular invasion and regional lymphadenopathy. Vascular invasion is amongst the various factors that predict the outcome in patients with HCC and is one of the most strongly correlated factors. The risk of recurrence is increased after orthotopic liver transplant (OLT) by 4.4-fold in micro vascular and 15-fold in the macrovascular invasion. This poor prognostic feature along with regional lymphadenopathy precluded the curative intent therapy in our reported case. The Child-Pugh score of our patient has been calculated as nine and is classified as category B[14]. Based on the aforementioned factors, our patient is a candidate for systemic therapy that would be guided by the assessment of financial factors, performance status and other comorbid conditions.

Limitation of the study: The limitations to the study are patient was started on palliative and symptomatic treatment, because he was not able to afford the costs of chemotherapy and second the government setup oncologists denied his treatment as the cancer was advanced to the vascular level, patient could not be followed as he began his treatment from general medicine and gastroenterology department. This study can be useful in consideration of early-stage diagnosis of vaso invasive hepatocellular carcinoma and further research is needed to highlight this issue of vasoinvasion, its definitive treatment and its chemotherapy research-based trials[15].

CONCLUSIONS

HCC is amongst the most lethal carcinomas with various causes, including hepatitis B and C virus infection, alcohol consumption,

non-alcoholic fatty liver disease, *etc*. Patients diagnosed with HCC should be thoroughly investigated for vascular invasion as it is one of the major factors in making decisions regarding treatment options. With major vessel invasion, the option of curative therapy cannot be accomplished. Moreover, vascular invasion is amongst the important poor prognostic factors. Similarly, our case report signifies the importance of vascular invasion in HCC and its role in the prognosis and decision-making regarding the treatment. For every patient who is a candidate for surgery or other curative therapy, the vascular invasion must be ruled out.

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