VOLUME - 9, ISSUE - 7, JULY - 2020 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Medicine

PRESENTATION OF PORTAL VEIN THROMBOSIS AS A COMPLICATION OF HEPATOCELLULAR CARCINIMA IN DIFFERENT AGE GROUPS:A CASE SERIES

Dr Rimi Som Sengupta	Associate Professor Department Of Medicine,esi Pgimsr & Esic Medical College,joka,kolkata
Dr Avishek Naskar	Assistant Professor Department Of Medicine,esi Pgimsr & Esic Medical College,joka,kolkata
Dr Anirban Ghosh	Associate Professor Department Of Medicine,esi Pgimsr & Esic Medical College,joka,kolkata
Dr Upal Sengupta*	Assistant Professor,kpc Medical CollegeDepartment Of Medicine,esi Pgimsr & Esic Medical College, joka, kolkata. *Corresponding Author
Dr Samir Chakraborty	Assistant Professor Department Of Medicine,esi Pgimsr & Esic Medical College,joka,kolkata
Dr Anirban Sarkar	Assistant Professor Department Of Medicine,esi Pgimsr & Esic Medical College,joka,kolkata
Dr Tapas Kumar Mondal	Professor And Head Of The Department Department Of Medicine,esi Pgimsr & Esic Medical College,joka,kolkata

ABSTRACT Hepatocellular carcinoma (HCC) is one of the most prevalent cancers worldwide. It is also a major health burden in developing countries like India, where most cases are related to hepatitis B virus infection. Portal vein thrombosis is a well known complication in hepatocellular carcinoma as well as chronic liver disease. The incidence of HCC below 40 years of age is uncommon in India, where the peak age of incidence is between 45 to 55 years. In this study, we present two patients with HCC with underlying chronic hepatitis B and portal vein thrombosis, in different age groups.

KEYWORDS : Hepatocellular carcinoma, Chronic hepatitis B, Portal vein thrombosis

INTRODUCTION

Hepatocellular carcinoma (HCC) is one of the most common cancers in the world, causing 749,000 new cases every year and around 745,000 deaths per year. The incidence is lesser in the Western countries (except southern Europe), being less than 5 cases per 100,000 population, while it is over 20 per 100,000 population in sub-Saharan Africa and Eastern Asia [1, 2]. In India, HCC is the seventh most common cause of cancer-related deaths [3].

About 70 – 80% of all HCC are related to Hepatitis B virus (HBV), 15% to Hepatitis C virus (HCV) and, both HBV and HCV causes HCC in 5% patients. Further, 8% of cases occur due to alcohol alone, and in 10% patients, no direct cause can be found. In some areas of India, Aflatoxin and iron overload are related to HCC cases [4].
Hepatitis B is endemic in India, the prevalence being 2 - 7%, with an average of 4% [5]. There are about 45 million chronic hepatitis B patients in India. Even, the presence of HBV antibodies alone, in absence of hepatitis B surface (HBs) antigen, confers an increased risk of HCC, irrespective of the presence of cirrhosis. Genomic integration of HBV into hepatic tissue causes chromosomal deletions and leads to metaplasia [6].

The incidence of HCC increases with age and peaks between 45 and 55 years. Anorexia, abdominal pain/discomfort and loss of weight are dominant symptoms [4]. Majority of HCC patients in India present in advanced stages, when the tumour is unresectable, leading to high mortality rates [3].

Portal vein thrombosis (PVT) is a common complication of HCC, being present in 10 – 40% patients at time of diagnosis and further 35 – 44% at the time of death or liver transplantation. These patients have mostly metastatic disease at diagnosis, have fewer therapeutic options and shorter overall survival, compared to patients without portal vein thrombosis [7]. Portal venous thrombosis occurs in 4.4 – 15% of cirrhotics [8].

In this case series, we are presenting two patients with HCC with underlying chronic hepatitis B and portal venous thrombosis, with one of them being younger than 40 years of age and the other patient being in the most common age group for HCC in India.

Case 1

A 33 years old previously healthy male presented with history of gradually increasing abdominal distension since 3 months, along with anorexia and weight loss for the same duration. Patient was alcoholic, drank around 60ml whisky every week. There was no history of yellowish discolouration of urine, breathlessness, abdominal pain, any noticeable localized swelling, hematemesis or malena. There was no history of blood transfusion previously, no high risk behaviour, no past history of jaundice and no family history of any liver disorder. Examination showed presence of ascites, mild pedal edema, mild pallor, absence of icterus, mild non-tender, firm hepatomegaly and mild splenomegaly. There was no features of hepatic encephalopathy. Blood reports revealed mild anemia (Hemoglobin 9.8mg/dl), normal total bilirubin level, alanine transminase 75 U/Land aspartate transaminase 65 U/L, normal alkaline phosphatase, normal Prothrombin time, with raised alpha fetoprotein of 4500 ng/ml. Hepatitis B surface (HBs) antigen was positive, envelope (HBe) antigen negative and IgG anti-HBc (anti-core antibody) antibody was reactive. HBV DNA came out to be 2500 units/ml by real time polymerase chain reaction. Ultrasonography of abdomen revealed portal venous thrombosis, with dilated portal vein, with few collaterals, ascites along with enlarged liver and spleen, and a hypoechoic nodular lesion in right lobe of liver. Ascitic fluid study for malignant cells was positive. Contrast

enchanced computed tomography (CECT) of abdomen showed irregular liver surface, a heterodense area in right lobe of liver, portal vein thrombosis, splenomegaly and ascites. CT guided liver biopsy from the lesion revealed hepatocellular carcinoma. So, a diagnosis of hepatocellular carcinoma was made in a patient of chronic liver disease due to Hepatitis B. Sodium restriction was done, Entecavir was started. Oncologist's opinion was to continue conservative management and start Sorafenib, which was followed.

The patient succumbed a few days later from septic shock.

Case 2

A 60 years old male had presented with history of dull aching pain in upper abdomen since last 3 weeks. The pain was localized, spontaneously subsided after few hours, associated with vomiting. He was admitted outside for this pain, where preliminary investigations showed portal vein thrombosis, for which he was referred to our hospital. He says, that he was diagnosed to have hepatitis B surface antigen positive (HBs Ag) 4 years back, but did not have any history of jaundice, abdominal distension, hematemesis or melena. There was no history of abdominal surgery, no drug intake, no familial history of any liver disease. Examination showed mild pallor, no icterus, no edema, no abdominal distension, 1cm hepatomegaly, splenomegaly and no prominent superficial veins. Blood reports showed mild anemia (haemoglobin 9.6 mg/dl), normal leucocytes and platelets, alanine transaminase 78U/L, aspartate transaminase 111 U/L, alkaline phosphatise 479 U/L and normal prothrombin time. Alpha fetoprotein was 3000 ng/ml. Hepatitis B surface antigen (HBs Ag) was positive, HBe was negative, IgG anti-HBc antibody was reactive and HBV DNA by real time polymerase chain reaction came out as 10000 copies/ml. There was enlarged, grossly heterogenous liver, with a large area of altered echotexture in left lobe, along with thrombosed and dilated (21mm) portal vein and enlarged spleen (15.6cm) on ultrasound abdomen. Contrast enhanced computed tomography (CECT) of abdomen revealed irregular liver surface, focal area of heterodensity in segment VI of liver, portal vein thrombosis and splenomegaly. CT guided biopsy from the hepatic lesion was taken, which showed hepatocellular carcinoma. There were no varices on endoscopy. Tenofovir alafenamide (25mg once daily) was given, as per advice of gastroenterologist. Oncologist was consulted and Sorafenib was started. The patient has remained fairly stable on subsequent follow up.

DISCUSSION

Epidemiological data on HCC in India are little, and cancer registries are mostly urban.

Chronic hepatitis B infection is the most important and prevalent risk factor for development of hepatocellular carcinoma (HCC) in Indian patients, whereas it is chronic hepatitis C in Western population and Japan [2, 9]. Around 36 – 74% of patients with hepatocellular carcinoma have hepatitis B surface antigen positive [10]. Many Indian patients with HCC have negative HBe antigen or undetectable HBs antigen. Most patients, around 76%, have features of underlying cirrhosis [6]. Many patients of chronic Hepatitis B in India may present for the first time with HCC [5]. The annual incidence of HCC in HBs antigen positive patients, in South-east Asia, becomes greater than 0.2% at 40 years of age [11].

In this current series, HCC with underlying chronic hepatitis B, has affected 2 individuals at different age groups. In both the patients, HCC occurred on a silently progressed chronic hepatitis B, and both had accompanying portal vein thrombosis. 25% of Indian patients with HCC may develop hematemesis and melena. There is ascites in 60% patients during initial presentation [4]. None of these two patients had hematemesis or melena. The younger patient had ascites at presentation. The younger patient may have acquired HBV in-utero or in childhood, as there was no other risk of acquiring HBV infection and his alcohol intake was too little to have caused chronic liver disease or hepatocellular carcinoma. He had a more aggressive course of disease, presenting with an unresectable tumour mass, and relentless progression to death, despite starting anti-viral and anti-neoplastic agents. Screening for HCC is recommended in high risk individuals above 40 years of age, with chronic hepatitis B and C [6]. Newer studies, like that of Wan et al, suggests earlier enrolment in screening programs for Asian hepatitis B patients, irrespective of age, who have history of smoking or family history of HCC [12]. Currently, there is no screening program for HCC in India.

The older patient, being HBs antigen positive detected few years back, presented with portal vein thrombosis, the investigations for which led to the finding of the underlying HCC. He has not deteriorated as per his last out-patient follow up records.

Both the patients presented at an advanced stage of HCC and with portal vein thrombosis, where therapeutic options are limited as liver transplantation is contraindicated and curative surgical resection is controversial [7]. So, they were given Sorafenib as anti neoplastic therapy and Entecavir for hepatitis B.

Though Hepatitis B vaccination is integrated in the Universal Immunization program (UIP) in India for over 10 years, there exist huge disparities in its coverage in the districts [13]. So, to prevent deaths of thousands of vaccine-preventable hepatocellular carcinoma patients, the coverage of hepatitis B vaccination needs to improve in our resource poor country, where screening programs are still non-existant.

REFERENCES

1. Cerrito L, Annicchiarico BE, Iezzi R, Gasberrini A, Pompili M, Ponziani FR. Treatment of hepatocellular carcinoma in patients with portal vein tumor thrombosis: Beyond the known frontiers. World J Gastroenterol. 2019; 25(31): 4360 – 82.
2. Choo SP, Tan WL, Goh BKP, Tai WM, Zhu AX. Comparison of hepatocellular carcinoma in Eastern versus Western populations. Cancer. 2016; 122(22): 3430 – 46.
3. Lokesh KN, Chaudhuri T, Lakshmaiah KC, Govind Babu K, Dasappa L, Jacob LA et al. Advanced hepatocellular carcinoma: A regional cancer center experience of 48 cases. Indian J Cancer. 2017; 54(3): 526 – 29.
4. Bhattacharyya GS, Govind Babu K, Malhotra H, Ranade AA, Murshed S, Datta D. Chin Clin Oncol. 2013; 2(4): 41.
5. Ray G. Current scenario of hepatitis B and its treatment in India. J Clin Tansl Hepatol. 2017; 5(3): 277 – 96.
6. Kar P. Risk factors for hepatocellular carcinoma in India. J Clin Exp Hepatol. 2014; 4(3): S34 – 42.
7. Quirk M, Kim YH, Saab S, Lee EW. Management of hepatocellular carcinoma with portal vein thrombosis. World J Gastroenterol. 2015; 21(12): 3462 – 71.
8. Ponziani FR, Zocco MA, Campanale C, Rinninella E, Tortora A, Maurizio LD et al. Portal vein thrombosis: Insight into physiopathology, diagnosis, and treatment. World J Gastroenterol. 2010; 16(2): 143 – 155.
9. Sarin S.K.T.V., Guptan R.C., Saigal S., Malhotra V., Thyagarajan S.P., Das B.C. Profile of hepatocellular carcinoma in India: an insight into the possible etiologic associations. J Gastroenterol Hepatol. 2001; 16: 666 – 73.
10. Dhir V., Mohandas K.M. Epidemiology of digestive cancer in India—III: liver. Indian J Gastroenterol. 1998; 17: 100 – 103.
11. Das AK, Jawed Q. Portal vein thrombosis in a young patient of previously asymptomatic hepatocellular carcinoma with hepatitis B-related cirrhosis. Clin Cancer Investig J. 2013; 2: 256 – 59.
12. Wan DW, Tzimas D, Smith JA, Kim S, Araujo J, David R et al. Risk factors for early-onset and late-onset hepatocellular carcinoma in Asian immigrants with hepatitis B in the United States. Am J Gastroenterol 2011; 106: 1994 - 2000.
13. Khan J, Shil A, Mohanty SK. Hepatitis B vaccination coverage across India: exploring the spatial heterogeneity and contextual determinants. BMC Public Health. 2019; 19:1263.