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Case Report

# Hepatocellular Carcinoma with Portal Vein Thrombosis in an Eight Year Old Boy

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## Abstract

Hepatocellular carcinoma with portal vein thrombosis is rarely seen in young patients. Hepatitis B can lead to HCC with PVT in the absence of cirrhosis. However, it is uncommon in age less than 40 years. Here we present to you a case of an eight year old boy with a family history of hepatitis B who developed HCC with PVT.

**Keywords:** Hepatitis B; Hepatocellular Carcinoma; Portal Vein Thrombosis

## Abbreviation

HCC: Hepatocellular Carcinoma; PVT: Portal Vein Thrombosis; HBV: Hepatitis B

## Introduction

Portal vein thrombosis (PVT) is a rare condition that is not only observed as a complication of liver cirrhosis but also occurs in patients with advanced hepatocellular carcinoma (HCC) and is associated with significant morbidity and mortality [1,2]. Chronic hepatitis B virus (HBV) infection is the main cause associated with cirrhosis/HCC that leads to PVT in South Asian patients who are older than 40 years, but not in young patients [3]. The etiology differs between the malignant and non-malignant portal vein invasion. Non-malignant PVT occurs as a result of portal hypertension and venous stasis, while malignant PVT results from tumor invading portal vein [4]. HBV infection is one of the most common etiology of HCC accounting for approximately 50% of all cases [5]. HCC can occur in HBV patients in the absence of cirrhosis [6]. The chances of development of HCC in patients infected with chronic HBV are relatively higher than in non HBV infected patients and the risk even rises in the presence of high viral load or in cirrhotic patients [7]. Hence, the routine screening for HCC is recommended in chronic HBV patients with cirrhosis and select certain non-cirrhotic HBV populations including Asian males aged ≥40 and females ≥50 years [8]. However, many young chronic HBV patients develop HCC but there have been few studies examining this group as HCC generally is uncommon in young.

Here we present to you a case of an eight years old boy, with a history of undiagnosed chronic HBV related chronic liver disease presenting with HCC with PVT, which is very much uncommon in our part of the world. There has been only one case report from this region prior to this which is from India where HCC was diagnosed in a 16 years old male with HBV infection.

## Case Report

An eight-years old boy presented to us in hepatology clinic with complaints of right hypochondrial pain since last 2 month and abdominal distension since the same duration of time. He also complained of low grade fever since last 15 days, documented to be around 100*F, which was intermittent, occurred mostly in the evening and was associated with decreased appetite. He was born through normal vaginal delivery and has never been admitted in hospital prior to this admission. His family history was positive for Hepatitis B virus (HBV) infection as both of his parents were carriers of chronic HBV infection with history of death of two elder siblings due to complications of chronic liver disease. Apart from this, there was no history of blood transfusion, intramuscular or intravenous injection or any of other risk factors for HBV infection.

On examination, he was pale, cachexic and had bilateral pedal edema. On abdominal examination, there was mild tenderness in right hypochondrium along with distended abdomen and fluid thrill can be elicited.

On laboratory investigations, Hepatitis B surface antigen (HBsAg) and Hepatitis B e Antigen was Reactive, HBV DNA level by polymerase chain reaction was 4650 IU/ml. Chest X-Ray revealed right sided pleural effusion. Ultra-sonogram of Abdomen showed coarse liver texture with irregular margins and multiple hypoechoic nodules in both the lobes of liver. Portal vein was dilated with hypoechoic lesion noted within the portal vein suggestive of thrombus with vascularity on Doppler ultrasound confirming thrombus in main portal vein extending into left and right portal veins along with enhancement of hypoechoic lesions previously seen on plain ultrasound. There was gross ascites and splenomegaly. Ascetic fluid analysis were suggestive of chronic liver disease (high SAAG, low protein) and ascetic fluid was not suggestive of spontaneous bacterial peritonitis (SBP) and cytology was negative for malignant cells. He had Child Turcotte Pugh Score of B9 with advanced MELD of 22 and an advanced BCLC stage C.

In order to rule our benign cause of portal vein thrombosis, thrombophilia profile which included Factor V Leiden mutation, protein C, protein S and antithrombin levels was done which were within normal limits. He then underwent CT Abdomen (triphasic) which showed features of chronic liver disease along multicenteric HCC with portal vein thrombosis (Figure 1).

**Figure 1:** Multicentric Hepatocellular carcinoma with Portal vein thrombosis (PVT). 1(A)- Arterial phase showing lesions in segment III and IV of liver with main portal vein (Blue arrow) and left branch thrombosis (Black arrow). 1(B)- Portovenous phase showing washout of the previous enhancement of the liver lesions and the portal vein suggestive of malignant PVT.

He was advised treatment for ascites which included protein rich diet and dietary salt restriction along with diuretics. His family was counseled regarding the limited treatment options. His survival was four months after the diagnosis of hepatocellular carcinoma.

His other siblings were also tested for HBV and 3 of other siblings out of 5 had HBsAg positive and are undergoing further investigation.

## Discussion

This patient's presentation with HCC as an initial presentation is a rare entity especially considering the age of the patient. This is the first case of presentation of HCC with PVT at such a young age.

In the west, hepatitis C and alcohol intake are amongst most common causes of chronic liver disease in the patients presenting with HCC and PVT. In them, the chronic HBV carrier non-cirrhotic patients with a Hepatitis B e antibody (anti-Hbe) positive disease and long-term inactive viral replication are at a very low risk of developing HCC [9,10]. On contrary, there is an increased risk of HCC in non-cirrhotic Asian hepatitis-B carriers irrespective of their

replication status [11,12]. In HBV- infected individuals, the severity of inflammation, fibrosis, cirrhosis and eventually HCC development is determined by viral load [6,13,14]. The factors found to correlate found to correlate with HCC development include high viral load, cirrhosis, HBe-Anitgen positive disease, HBV genotype "C", and elevated serum HBsAg levels [6]. Patients presenting with HCC as initial finding have a dismal survival rate. The annual incidence of HCC in male hepatitis-B carriers from South East Asia only starts to exceed 0.2% at about 40 years of age regardless of the presence of cirrhosis or disease activity as opposed to Caucasians proposing that only relatively older patients are generally at risk for developing HCC [15]. Our patient was HBe-antigen positive and already had cirrhosis with portal hypertension along with HCC and PVT on presentation by 8 years of age.

PVT is an uncommon but under-recognized disorder, and its actual prevalence is unknown. Portal vein thrombosis (PVT) is more predominant in patients with liver cirrhosis and hepatocellular carcinoma (HCC) than the general population [1]. Benign PVT usually results from portal venous hypertension and venous stasis, whereas malignant PVT results from direct invasion of the portal vein by malignant neoplasms, such as HCC [4]. Malignant PVT is differentiated from benign PVT by several imaging features. Malignant PVT is generally accompanied by parenchymal mass, such as HCC in cirrhotic liver, whereas the presence of PVT alone is considered benign.

In our patient, we found two etiological factors responsible for portal vein thrombosis: one is HBV associated liver Cirrhosis and the other one is HCC. The astonishing feature was that these findings were present in an eight year old boy. The PVT in our patient was due to tumor invasion as per radio-imaging findings and also because all of his thrombophilia profile was unremarkable. There is low incidence of thrombophillic disorders in Pakistan [16]. Overall, incidence of HBV during pregnancy is 1.42% which makes vertical transmission likely the cause of HBV at such an early age [17]. However, most probably HBV infection was acquired through vertical transmission (mother HbsAg and HBe-antigen positive) instead of horizontal transmission (brother and father were HbsAg negative). Acute PVT explains the abrupt onset of abdominal pain and ascites, since in an acute setting of moderate to severe thrombus occlusion, abdominal pain may be the primary presenting complain [18]. Presentation of chronic HBV with portal vein thrombosis at such an early age is very rare in this part of the world (South East Asia).

In case of PVT, the younger patients have main branch which is most commonly affected. However, in cases of older patients, right branch is slightly more affected than the left branch. In young South-Asian patients aged <20 and 20-39, the main branch was found to be commonly affected [3]. Most commonly, right branch of the PV is thrombosed in patients with HCC while, the main branch is likely the one thrombosed in patients presenting with cirrhosis only. European study also found that in cirrhotic patients without HCC but having PVT, the thrombus was situated most commonly in the main portal trunk [19]. In patients with benign disease other than cirrhosis, there is an equal distribution of thrombosis in all branches of PV [3].

On contrary, our patient had main portal vein branch plus both right and left branch thrombi, in spite of having both cirrhosis and HCC which is different from that mentioned in literature. This is likely due to the extensive disease and malignant infiltration of portal vein (PV) by HCC. Also, the distribution of thrombi in PVT from our part of the country may vary from other parts of the world in patients with identical risk factors for PVT and the reason may be some unknown environmental, ethnic, or dietary factors.

Our patient had a very low viral load with no other inciting agent for HCC but was HBeAg Positive and had High serum alpha fetoprotein, which apparently increased the risk of HCC in our patient. Although, it is now recognized that low viral load does not reduce the risk of HCC in patients from Asia-Pacific region as opposed to in the western population [20].

Current recommendations warrant HCC surveillance in HBV positive Asian men aged 40 years, as the yield from surveillance of all carriers younger than age 40 is likely to be low [21]. On the other hand, some studies have recommended the role of early surveillance in younger Asian HBV patients, especially those with a smoking history or family history of HCC [22].

The survival of our patient was four months after the diagnosis of HCC was established. This again relates to the established fact of less than 2.5 years survival in patients with advanced stage HCC. The only management that can be employed at this stage is systemic chemotherapy either in the form of Tyrosine Kinase

Inhibitors or Immune checkpoint inhibitors. These treatment options can only be used in patients having preserved liver function and good performance status [23]. In our patient, he had ascites at the time of presentation. So, it was the major limitation to the commencement of systemic chemotherapy in our patient.

## Conclusion

Considering the case we presented here, we feel that in our region of Indian subcontinent, HbsAg positive patients may need HCC surveillance at a much younger age along with proper ante-natal check-up of pregnant women with strict adherence to newborn vaccination should also be made mandatory.

This is will not only prevent transmission but will also help in reducing the socioeconomic burden caused by the virus on the society.

## Conflict of Interest

None.

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