Case Report

Portal vein thrombosis in a young patient of previously asymptomatic hepatocellular carcinoma with Hepatitis-B related cirrhosis

Anup K. Das, Quaisar Jawed[1]

Department of Medicine, Professor of Medicine and I/C Hepatology Unit, [1]Department of Medicine, Post Graduate Trainee, Assam Medical College Hospital, Dibrugarh, Assam, India

ABSTRACT

Portal vein thrombosis (PVT) is a rare condition whose exact prevalence is unknown. In developing countries like India it is most often due to umbilical or intra-abodominal sepsis in young patients. In South-East Asia, PVT is usually seen in middle age and above commonly when due to hepatitis-B related chronic liver disease or HCC, and other malignancies, being extremely rare in those below 30 years. We report a case of abrupt onset PVT with incidentally detected hepatitis-B associated cirrhosis of liver and HCC in a previously healthy young man, presenting with acute hepatic decompensation and some unusual features in the involvement of the portal vein.

Key words: Portal vein thrombosis, hepatocellular carcinoma, Chronic hepatitis B, tumor thrombus

INTRODUCTION

Portal vein thrombosis (PVT) is a rare condition but is associated with serious morbidity and mortality.[1] In contrast to the west, 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.[2]

HBV is the main risk factor for HCC and about 80% are attributable to chronic HBV infection. Chronic carriers are approximately 100 times more likely to develop liver cancer than non carriers. The global incidence of HCC is rising, being the fifth most common cancer and the third most common cause of cancer mortality.[3] Hence, 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.[4] 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 report a young, previously undiagnosed chronic HBV related cirrhotic patient with HCC presenting with PVT and acute hepatic decompensation which is uncommon in India.

Access this article online	
Quick Response Code:	Website: www.ccij-online.org
	DOI: 10.4103/2278-0513.119256

CASE REPORT

A young 23 year old male presented with acute onset anorexia, weakness, rapid weight loss, swelling of abdomen, icterus and moderate pain abdomen radiating to the back for 1 week. Before referral, he was treated outside as acute viral hepatitis but he deteriorated. He was conscious but vomiting frequently, had increasing backache and a low grade irregular fever. He was non-diabetic, non-alcoholic, non-smoker, without any family or past history of jaundice, tuberculosis or abdominal surgery. There was no history of blood-transfusion, tattooing, drug abuse, or recent Non Steroidal Anti Inflammatory Drugs or herbal medication. He had been vaccinated against HBV 7 years ago in a rural vaccination camp.

Address for correspondence: Dr. Anup K. Das, Department of Medicine, Assam Medical College Hospital, Dibrugarh - 786 002, Assam, India. E-mail: anupkrdas@hotmail.com

Examination revealed the presence of icterus, oliguria, ascites, bipedal edema and cachexia. Abdomen was tender and there was a continuous ill localized back-ache. Both the ascites, anorexia and pain progressed throughout his hospital stay. He was ill looking but showed no feature of hepatic encephalopathy.

Investigation reports: HbsAg $^{+}$ve, Hb e Antigen $^{+}$ve (2.29, normal value <1.00), anti- HCV $^{-}$ve, anti-HEV $^{-}$ve, anti-HAV IgM $^{-}$ve, high alpha-feto protein (345.39 ng/ml), chromatogram showed Hemoglobin-E trait (Hb A/E), HIV serology negative. HBV DNA level by polymerase chain reaction was 3280 iu/ml. Chest X-Ray (PA view): Minimal right sided pleural effusion. X-Ray of lumbo-sacral spine was normal. Ultrasonogram of Abdomen [Figure 1]. Liver architecture is markedly coarsened with multiple hypoechoic nodules in both the lobes of liver (cirrhosis). Right lobe shows suspicious lesions suggestive of HCC. Portal vein is dilated with hypoechoic lesion noted within the portal vein suggestive of thrombus with vascularity, extending into left and right portal veins. There is gross ascites and splenomegaly. Ultrasound guided fine needle aspiration cytology of liver [Figure 2]. The cellular aspirates show cells arranged in trabecular and papillary clusters, showing moderate degree of nuclear pleomorphism. Intra-nuclear vacuoles with inclusion bodies are seen and are prominent which is highly suggestive of HCC. The patient refused upper gastrointestinal endoscopy and could not afford a computed tomography scan of the abdomen. We did not do the thrombophilic profile as hereditary thrombophilic disorders such as Factor V Leiden, protein C deficiency, protein S deficiency, and antithrombin deficiency are very rare in the Southeast Asian population.[5] Ascites fluid analysis was not suggestive of tuberculosis or subacute bacterial peritonitis and cytology was negative for malignant cells.

We investigated his family (parents and brother), and his mother was found to be HbsAg and e-antigen positive but asymptomatic.

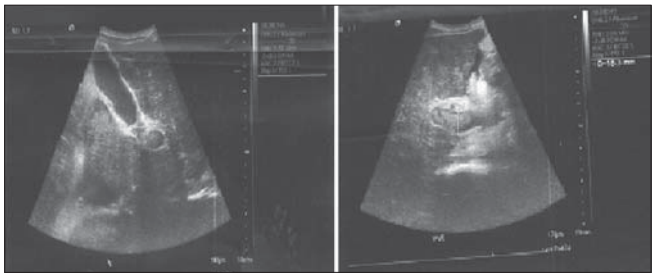

Figure 1: Liver architecture is markedly coarsened with multiple hypoechoic nodules in both the lobes of liver (cirrhosis). Right lobe shows suspicious lesions suggestive of hepatocellular carcinoma. Portal vein is dilated with hypoechoic lesion noted within the portal vein suggestive of thrombus with vascularity, extending into left and right portal veins. There is gross ascites and splenomegaly

He was treated with iv albumin, diuretics, iv glucose, ceftriaxone IV, proton pump inhibitor, tramadol injection (for back-pain). Abdominal paracentesis was done once. He did not improve during 10 days of hospital stay. He was prescribed entecavir 0.5 mg and was discharged against medical advice.

DISCUSSION

This patient illustrates certain differences of the presentation of PVT with HCC in hepatitis B related cirrhosis as compared to the west and other Asia-Pacific regions suggesting a possible geographical variation in HCC with PVT with underlying cirrhotics in the young.

In the west, most common causes of chronic liver disease patients who present with HCC and PVT include hepatitis C and alcohol. In them, chronic HBV carriers who are anti-HbE-positive with long-term inactive viral replication, and who do not have cirrhosis have very low risk of developing HCC.[6,7] In contrast, Asian hepatitis-B carriers without cirrhosis remain at significant risk for HCC regardless of their replication status.[8,9] HCC as initial presentation has a very poor 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 irrespective of the presence of cirrhosis or disease activity as opposed to Caucasians [10] suggesting that only relatively older patients are usually at risk for developing HCC. Our patient was e-antigen positive and already had cirrhosis with portal hypertension with HCC on presentation by 23 years of age, being totally asymptomatic prior to hospitalisation.

PVT is an uncommon but under-recognized disorder, and its true prevalence is presently not definitely known. A large retrospective review of 23,796 autopsies has shown a 1% prevalence of PVT.(11) Remaining asymptomatic

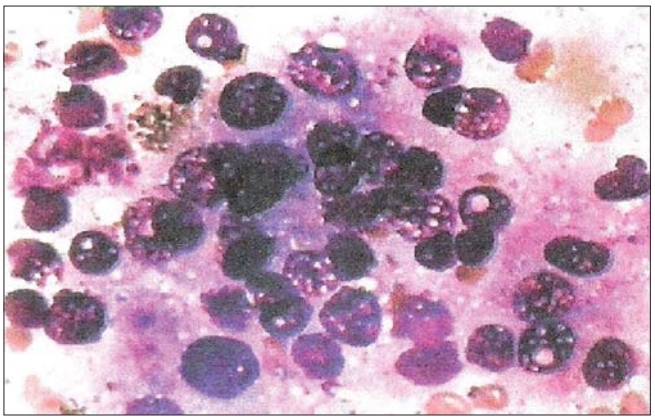

Figure 2: The cellular aspirates show cells arranged in trabecular and papillary clusters, showing moderate degree of nuclear pleomorphism. Intra-nuclear vacuoles with inclusion bodies are seen and are prominent, which is highly suggestive of hepatocellular carcinoma

in many cases, it may be a co-incidental finding in the cirrhosis of liver. In a study of 701 hospitalized cirrhotics who underwent routine ultrasound screening, PVT was identified in 11% of the cases.[12]

In our patient, the risk factors of PVT were two: HBV related cirrhosis and HCC, and both are rare in Asians. In South East Asia most of such cases of PVT with HBV are much older (>40).[2]

The PVT in our patient was due to tumor invasion as per the radio-imaging findings, also supported by rapid development of symptoms. A thrombophilic disorder was unlikely because it is rare in India. A study of 61 patients with PVT from India reported only 1 case of Factor V Leiden and none with prothrombin gene G20210A mutation.[13]

India has intermediate HBV endemicity, with a carrier frequency of 2%-4%. HBV infection in India is acquired in childhood through horizontal transmission, usually before 5 years of age. Vertical transmission of HBV in India is considered to be rare and HCC appears to be uncommon in India than would be expected from the prevalence rates of HBV and HCV.[14] However, this patient presumably acquired the infection vertically (mother HbsAg and e-antigen positive) rather than horizontally (brother and father were HbsAg negative). The rapid onset pain abdomen and ascites can be explained by acute PVT, since in an acute setting of moderate to severe thrombus occlusion, abdominal pain may be the primary feature.[15] The hepatic dysfunction was possibly due to rapid development of HCC and not due to end-stage cirrhosis. Therefore, from the history both HCC and PVT were recent in onset. However, acute PVT can also lead to hepatic dysfunction. PVT in such a young patient with chronic HBV is unusual as per reports from South East Asia. None of PVT patients below 20 years of age were found to be hepatitis-B positive in a large study from Thailand.[2]

His Hb E trait probably was an inconsequential finding, as it is common in the upper part of Assam. Hemoglobinopathies with chronic liver disease have been described in the literature, but since our patient had no history of blood transfusion in the past, we thought it was unlikely of any consequence in this case.

With respect to the sites of thrombus formation, it is of interest to note that the main branch is commonly affected in the younger patients, whereas the right branch is slightly more affected than the left branch in the older patients. In young South-Asian patients aged <20 and 20-39 (79.4%), the main branch was found to be commonly affected; whereas in the older patients, the right branch was slightly more affected than the left and the main branches.[2] The most common distribution of thrombus in patients with cancer and cirrhosis is the right branch whereas in patients with only cirrhosis, it is in the main branch. An Italian study also found that in PVT patients with only liver cirrhosis, the thrombus was situated most commonly in the main portal trunk.[12] For patients without cancer and cirrhosis, the thrombus is equally distributed in all branches.(2) The reason for these differential involvement in different clinical conditions in different age group is not clear. Our patient had main branch plus both right and left branch thrombi, in spite of having both cirrhosis and HCC which is different from that mentioned in literature. Thus, the distribution of thrombi in PVT from our part of the country may differ 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.

The patient was possibly having a low viral load since a long time as he had no other risks for cirrhosis (alcohol, hepatitis-C/HIV co-infections or old age), except being e-antigen positive on presentation signifying viral replication of short duration and a high alfa feto protein due to HCC. It is now established that low viral load does not reduce the risk of HCC in patients from Asia-Pacific region as opposed to in the western population.[16]

This patient illustrates a very uncommon profile of PVT with HCC in our country as different from the west, in terms of risk factors, disease course and age of presentation. It shows that rapidly aggressive HCC at a very young age can be the result of silent, long standing and well-compensated hepatitis-B related cirrhosis, which is vertically acquired, not horizontally, as is the norm in our country. We must be aware of this.

It has been suggested by experts that Asian men should undergo surveillance only from age 40 onwards in the presence of HBV, as the yield from surveillance of all carriers younger than age 40 is likely to be low.[3] On the other hand, recent newer results suggest that younger Asian HBV patients, especially those with a smoking history or family history of HCC, appear to have an increased risk for HCC and should be considered for enrolment in early screening programs regardless of their age.[17] Importantly, a large number of such patients may not have associated cirrhosis at the time of diagnosis of HCC as HBV can cause HCC in the absence of significant liver damage.

However, there are no experimental hard data to indicate at what level of risk or what incidence of HCC should trigger surveillance. We feel that in our regions, HbsAg positive patients may need HCC surveillance at a much younger age as opposed to in the West. Another aspect highlighted in this case report is the hepatitis-B vaccination of children without screening for HbsAg being carried out in many parts of our state, which may miss a vertically acquired

infection as happened in our patient. Proper ante-natal check-up of pregnant women with strict adherence to newborn vaccination should also be mandatory. We think our patient-profile is a case on hand to justify this.

REFERENCES

1. DeLeve LD, Valla DC, Garcia-TsaoG.Vascular disorders of the liver. Hepatology 2009;49:1729-64.
2. Korn Lertpipopmetha, Chirayu U Auewarakul. High Incidence of Hepatitis B Infection-Associated Cirrhosis and Hepatocellular Carcinoma in the Southeast Asian Patients with Portal Vein Thrombosis. BMC Gastroenterol 2011;11:66.
3. El-Serag HB, Rudolph KL. Hepatocellular carcinoma: Epidemiology and molecular carcinogenesis. Gastroenterology 2007;132:2557-76.
4. Jordi Bruix, Morris Sherman. Management of Hepatocellular Carcinoma. Hepatology 2005;5:1208-36.
5. Angchaisuksiri P, Atichartakarn V, Aryurachai K, Archararit N, Rachakom B, Atamasirikul K *et al*. Risk factors of venous thromboembolism in thai patients. Int J Hematol 2007;86:397-02.
6. Fattovich G. Natural history of hepatitis B. J Hepatol 2003;39:S50-8.
7. Hsu YS, Chien RN, Yeh CT, Sheen IS, Chiou HY, Chu CM, *et al*. Long-term outcome after spontaneous HBeAg seroconversion in patientswith chronic hepatitis B. Hepatology 2002;35:1522-7.
8. Huo TI, Wu JC, Lee PC, Chau GY, Lui WY, Tsay SH, *et al*. Seroclearance of hepatitis B surface antigen in chronic carriers does not necessarily imply a good prognosis. Hepatology 1998;28:231-36.
9. Evans AA, Chen G, Ross EA, Shen FM, Lin WY, London WT. Eight year follow-up of the 90,000-person Haimen City cohort: I. Hepatocellular carcinoma mortality, risk factors, and gender differences. Cancer Epidemiol Biomarkers Prev 2002;11:369-76.
10. Beasley RP. Hepatitis B virus as the etiologic agent in hepatocellular carcinoma. Hepatology 1982;2:S21-26.
11. Ogren M, Bergqvist D, Bjorck M, Acosta S, Eriksson H, Sternby NH. Portal vein thrombosis: Prevalence, patient characteristics and lifetime risk: A population study based on 23,796 consecutive autopsies. World J Gastroenterol 2006;12:2115-19.
12. Amitrano L, Guardascione MA, Brancaccio V, Margaglione M, Manguso F, Iannaccone L *et al*. Risk factors and clinical presentation of portal vein thrombosis in patients with liver cirrhosis. J Hepatol 2004;40:736-41.
13. Sharma S, Kumar SI, Poddar U, Yachha SK, Aggarwal R. Factor V Leiden and prothrombin gene G20210A mutations are uncommon in portal vein thrombosis in India. Indian J Gastroenterol 2006;25:236-9.
14. Acharya SK, Madan K, Dattagupta S, Panda SK. Natl Med J India. Viral hepatitis in India. 2006;19:203-17.
15. Sogaard KK, Astrup LB, Vilstrup H, Gronbaek H. Portal vein thrombosis; risk factors, clinical presentation and treatment. BMC Gastroenterol 2007;7:34.
16. Lin CL, Kao JH. Risk stratification for hepatitis B virus related hepatocellular carcinoma. J Gastroenterol Hepatology 2013;28:10-7.
17. 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.

Cite this article as: 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;2:256-9.

Source of Support: Nil, **Conflict of Interest:** None declared.