HEPATOVENOCAVAL SYNDROME - A RARE CAUSE OF ASCITES IN THE YOUNG POPULATION

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ABSTRACT

Hepatovenocaval syndrome involves obliteration of the intra-hepatic portion of inferior vena cava. It is a separate entity from Budd-Chiari syndrome with which it is usually confused; however, Budd-Chiari Syndrome involves obliteration of hepatic venous outflow. This case describes a young male patient who presented with a longstanding history of abdominal pain and ascites. His viral screen was negative for Hepatitis B and C. Ascitic fluid routine examination was transudate and an ultrasound scan of the abdomen revealed features of chronic liver disease. He had received anti-tuberculous treatment on a presumption of suffering from abdominal tuberculosis. However, there had been no improvement despite 12 months of therapy. He was thoroughly re-evaluated and a series of advanced investigations were carried out. A computerized tomographic scan of the abdomen revealed solid lesions in the liver suggesting malignancy. Subsequent biopsy was however reported as negative for malignancy. Screening for autoimmune liver disorders and Wilson disease was also negative. The Thrombophilia profile was normal. It is only after the multiphasic magnetic resonance imaging of the abdomen that occlusion of the intra-hepatic portion of inferior vena cava was spotted and a diagnosis of hepatovenocaval syndrome was made. The patient remained on antibiotics and diuretics and reported improvement in condition during hospitalization. Physicians and hepatologists are not much familiar with hepatovenocaval syndrome as a separate entity from Budd-Chiari Syndrome. However, it is of utmost importance to make a correct diagnosis because the management of both conditions differs markedly.

Key Words: Hepatovenocaval syndrome; Budd-Chiari Syndrome; Ascites; Liver.

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INTRODUCTION

Hepatovenocaval syndrome (HVCS) is one of the conditions causing hepatic venous outflow obstruction (HVOO)[1]. It involves mostly idiopathic occlusion of the intra-hepatic portion of inferior vena cava (IVC) and has emerged as an entity slightly different from Budd-Chiari Syndrome (BCS) that involves occlusion of hepatic veins mostly due to congenital or acquired thrombophilias[2]. Correct diagnosis is important because the management of HVCS is different from that of BCS. We outline a case of HVCS that remained undiagnosed for 3 years, partly because of the sub-clinical presentation of the disease and partly because of unfamiliarity with the condition on behalf of practitioners.

CASE REPORT

A 13-year-old male patient presented to the medical ward diagnosed with a case of chronic liver disease on the background of a long history of abdominal distension and bilateral paroxysmal right hypochondrium region pain spanning over 3 years. The pain had started gradually, was dull, and did not radiate elsewhere. However, the intensity of both pain and abdominal distension had progressed over these 3 years. There was no history of fever, abnormal bowel and bladder symptoms, nausea, vomiting, or weight loss. The patient had empirically received anti-tuberculous treatment (ATT) for 12 months based on a suspicion of abdominal tuberculosis. No investigations to diagnose or confirm tuberculosis was performed at that time. The patient achieved only mild improvement in symptoms after initiation of ATT; symptoms returned soon after completion of ATT. The patient's father also gave a history of splenectomy 3 months before presenting to our ward. The reason could not be identified but as per collateral history, the surgery was performed due to intractable pain from a very large spleen.

Clinical examination of the patient revealed gross ascites and visibly distended veins over the abdomen filling from below upwards on obliteration. There was no clinical evidence of jaundice, clubbing, palmar erythema, hepatic flap, lymphadenopathy, jaundice, or pedal edema. Routine and specialized investigations were carried out to reach an ultimate diagnosis, which is tabulated in Table 1.

An ultrasound abdomen performed for evaluation of ascites revealed hepatomegaly (13cm), with coarse

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echotexture and irregular margins. The portal vein measured 8.0mm. Of note was a hypoechoic to the isoechoic area, measuring 6.0 x 5.5cm located at porta hepatis (at the junction of the portal vein and its branches). Gross ascites was also noticed. Further diagnostic modalities were planned. The ascitic fluid routine examination was transudate and predominantly lymphocytic. A computerized tomographic (CT) scan of the abdomen was carried out, which detected multiple nodular areas in both lobes of the liver, the largest measuring 5.0 x 5.2cm in the right lobe of the liver. This aroused the suspicion of malignancy. Alpha-fetoprotein (AFP) as a tumor marker for liver malignancy turned out to be within normal limits ie 1.1ng/ml (<9.0ng/ml). An ultrasound-guided liver biopsy from the suspicious lesions with concomitant esophagogastroduodenoscopy (OGD) was performed under general anesthesia. OGD was inconclusive. Biopsy revealed scanty portal inflammation, fibrous expansion of one of the portal tracts, ballooning degeneration of hepatocytes, and scanty lobular inflammation. There was no evidence of Budd-Chiari Syndrome or malignancy in the biopsy specimen.

An echocardiogram to rule out cardiac causes of ascites was reported as structurally and functionally normal. Doppler ultrasound for portal hypertension showed a portal vein measuring 9.0mm, lifted anteriorly by the hypertrophied caudate lobe. The flow was noted in the hepatic veins and inferior vena cava (IVC) but appeared obliterated. A suspicion of Budd Chiari Syndrome was made. Negative liver biopsy leads to a search for other causes of such presentation. A referral was made to the ophthalmologist to look out for Kayser Fleischer (KF) rings as a manifestation of Wilson's disease; however, they were not present. Subsequent Magnetic Resonance Imaging (MRI) of the brain for CNS manifestations of Wilson disease was also reported as normal. Autoimmune liver profile was also negative. Thrombophilic profile including protein C and S levels, homocysteine levels, anti-thrombin III levels, anti-phospholipid antibodies, and factor V Leiden mutation as a screening test for procoagulant conditions leading to Budd-Chiari Syndrome was reported as normal.

A multiphasic MRI abdomen and pelvis was planned to confirm Budd-Chiari Syndrome. The MRI revealed compression and narrowing of intra-hepatic inferior vena cava (IVC). Portal veins were of normal caliber. Mild compression was noted in left and middle hepatic veins, however, right hepatic vein appeared normal (fig.1). A diagnosis of Hepatovenocaval syndrome was therefore made. The patient was started on antibiotic treatment to improve upon his condition.

DISCUSSION

The hepatovenocaval syndrome (HVCS) is a rare entity usually seen in children and adolescents. It involves complete obliteration of the intra-hepatic portion of the inferior vena cava (IVC). This is as opposed to Budd-Chiari Syndrome (BCS) which involves hepatic venous outflow obstruction[1]. The terms 'Obliterative Hepato-cavopathy', coarctation of inferior vena cava, and 'membranous obstruction of IVC (MOVC)' have also been used for HVCS[2,3]. BCS is a commoner entity in the West, whereas HVCS is more common in Nepal, India, China, and South Africa. A low socio-economic state associated with poor hygienic measures is thought to be the cause of its occurrence in Asia and Africa[4]. Post-partum state, surgery, long-standing fever, diarrhea in nutritionally deprived populations, or alcoholics can lead to HVCS.

The etiology of HVCS is predominantly idiopathic, whereas BCS mostly occurs due to hypercoagulable states. HVCS is believed to occur from recurrent attacks of thrombophlebitis due to repeated bacterial infections which initially cause partial occlusion of the intra-hepatic portion of IVC and ultimately leads to complete obliteration of the intra-hepatic IVC[1].

During an acute attack of thrombophlebitis, a thrombus is deposited at the intra-hepatic IVC, which either gets resolved later on leading to fibrotic bands or may organize causing stenosis of the vein. The process is mostly subclinical so not noticed by the patient or clinician initially. With occlusion or stenosis of the vein, cavo-caval collaterals with upward flow develop, therefore obstructive signs are not evident soon[5]. This is in contrast to BCS, where clinical manifestations of liver failure and decompensation occur rapidly after occlusion of the hepatic vein/s. Liver functions show mild derangement at this stage. Recurrence of such attacks can cause ischemic damage to the liver, ultimately leading to liver cirrhosis and failure[6]. Recurrent loss of hepatocytes from injury due to

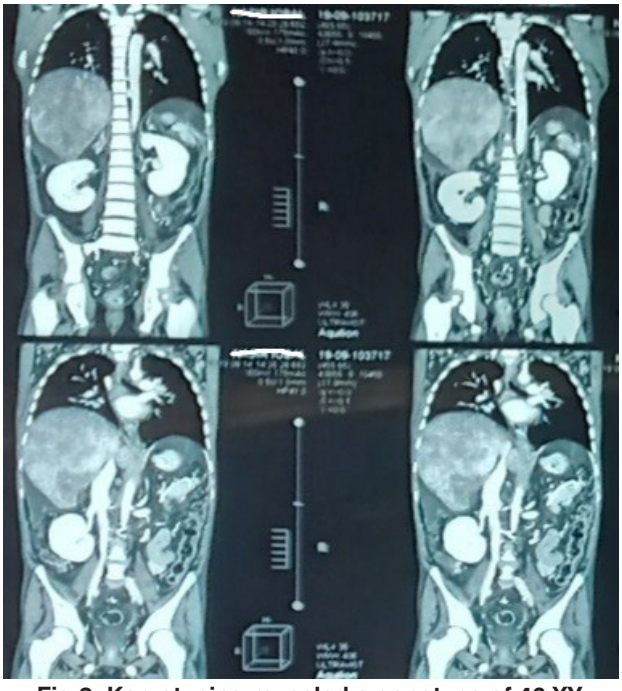

Fig 2: Karyotyping revealed a genotype of 46 XY.

Table 1: Routine and specialized investigations of patients with HVCS

Investigations	Results	Normal Range
Hemoglobin (Hb)	7.6g/dl	12-15g/dl
Blood smear	Microcytic, hypochromic anemia	
Total leucocyte count (TLC)	15,000/cmm	4,000-11,000/cmm
Platelet count	728,000/cmm	150,000 400,000/cmm
Alanine transaminase (ALT)	34U/l	15-40U/l
Aspartate transaminase (AST)	45U/l	15-45U/l
Total bilirubin	1.4mg/dl	0.7-1.5mg/dl
Alkaline Phosphatase (ALP)	1325U/l	300-720U/l
Serial Serum albumin	3.2g/dl, 2.87g/dl	3.5-5g/dl
Prothrombin time (PT)	15 sec, 28 sec	12-16 sec
Serial Activated partial thromboplastin time (APTT)	44.3 sec, 56 sec	30-40 sec
International Normalized Ratio (INR)	1.13, 2.8	0.9-1
Blood urea	32 mg/dl	12-45 mg/dl
Serum creatinine	0.8 mg/dl	0.3-0.7 mg/dl
Hepatitis B Antigen (HBsAg by ELISA)	Non-reactive	
Anti Hepatitis C Antibodies (Anti HCV Abs by ELISA)	Non-reactive	
Lactate dehydrogenase (LDH)	349U/l	225-450U/l
Serum calcium	8.84mg/dl	8.0-10.0mg/dl

thrombophlebitis leads to fibrosis and the development of regenerative nodules. This could be a possible explanation for the multiple nodules seen on radiographs of the patient that had been mistaken for malignancy. Repeated acute exacerbations of thrombophlebitis also lead to splenomegaly or hypersplenism. HVCS has shown an association with hepatocellular carcinoma (HCC)[2]. The development of liver cirrhosis and HCC is directly associated with the severity and frequency of acute exacerbations of thrombophlebitis attacks.

HVCS usually presents with features of chronic liver disease (CLD). Abdominal pain, ascites with pleural effusion, and fever are common presentations. This is characterized by mild elevations in hepatic transaminases[7]. Vascular spiders, palmar erythema, and coagulopathy are uncommon in HVCS-related CLD. Diagnosis can be made by Doppler ultrasound of the IVC. Other advanced tests include inferior vena-cavogram and MRI scans[8,9]. Ascitic fluid usually reveals an exudative predominantly neutrophilic picture. A liver biopsy shows features of CLD with no evidence of HCC[10]. It is diagnosed by real-time ultrasonography and Doppler examination of the liver and IVC. HVCS was previously considered a congenital venous anomaly and treated with surgery or endovascular procedures. It has also been treated on the lines of BCS, however, management of the two conditions is different[11]. Cava-caval shunts (cavo-atrial, meso-atrial, Meso-caval) and surgical procedures have also been instituted in the past but not too many benefits. Currently, treatment mainly aims to reduce the frequency and prevent attacks of acute exacerbation of thrombophlebitis. The treatment involves prolonged antibiotic therapy, diuretics, and other supportive therapy. Thrombolytics and anti-coagulants play no role in the management of HVCS[12]. Circulatory equilibrium is attained in chronic patients by the formation of extensive collaterals; therefore, the need for surgical and/or endovascular procedures is not felt. Liver transplantation has been tried in a few patients with good results, though the cost is the major limiting factor.

HVCS is a rare disease that if not kept in mind might either be missed or confused with BCS. However, both disease conditions have clear differences in their management options.

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Following authors have made substantial contributions to the manuscript as under

Badshah A: Did literature search, article formatting, and compilation.

Humayun M: Conceived the idea, final review.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.