Case Report

A Bolt Out of the Blue: A Case of Unexpected Acute Liver Failure

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Abstract

Introduction: We describe an unusual case of acute hepatitis leading rapidly to acute liver failure. Clinical Picture: Our patient had known chronic hepatitis B with a regenerating nodule confirmed on imaging and histology. He was admitted initially for abdominal discomfort after a trip to China, and investigations showed acute hepatitis with alanine transaminase (ALT) and aspartate transaminase (AST) at 678 and 557 U/L, respectively. Initial differential diagnoses were acute exacerbations of chronic hepatitis B, and viral hepatitis A or E. However, acute Budd-Chiari syndrome was diagnosed on computed tomography (CT) scan of the abdomen, which showed extensive thrombosis of the hepatic vein, all the intrahepatic branches, inferior vena cava, up to the right atrium. Treatment: Due to the extensive nature of the thrombus, radiological or surgical intervention could not be performed. Outcome: The patient was managed conservatively but progressed rapidly and died of acute liver failure 16 days after presentation. Conclusion: Our case highlights the rapidity of progression of acute Budd-Chiari syndrome. Diagnosis and management of Budd-Chiari syndrome are discussed.

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Key words: Budd Chiari syndrome, Hepatic vein, Hepatitis B, Liver neoplasm, Thrombosis

Introduction

Acute hepatitis could result from viral, autoimmune or drug-reaction causes, among others. In areas endemic with hepatitis B, acute exacerbations of chronic hepatitis B (CHB) are the commonest cause.[1,2] Hence, in Singapore where 4% of the population are hepatitis B carriers,[3] when faced with acute hepatitis in a patient with known CHB, hepatologists often consider acute exacerbations of CHB as the most likely aetiology, which may lead to a delay in diagnosis in cases not caused by CHB. We hereby report a case of acute hepatitis in a patient with CHB, which turned out to be due to an unusual cause.

Case Report

The patient, a 64-year-old Chinese man with known CHB for more than 20 years, first presented on 4 December 2004 with abdominal discomfort, without fever, vomiting, or changes in bowel habit. The patient denied consuming alcohol regularly, or any recent intake of new medication or herbs. However, he had been to China for a few weeks prior to his presentation. Clinically there was no jaundice, pallor, hepatomegaly, shifting dullness, elevated jugular venous pressure waveform, or ankle oedema. Initial liver panel showed acute hepatitis (Table 1). He had been an inactive hepatitis B carrier, with normal liver panel and alpha fetoprotien level last tested in July 2004. His HBeAg and HBV DNA by hybridisation assay (Digene®, lower detection limit 1.4 x 10^5 cop/mL) were last tested in March 2004, and were negative.

The initial clinical diagnosis was acute exacerbations of CHB, with differential diagnosis of acute viral hepatitis A or E. HBV DNA titre, anti-HAV IgM, and anti-HEV IgM testing were performed and the patient was discharged with an early outpatient review.

Ten months prior to this acute presentation, a screening ultrasound scan had shown a 1-cm hypoechoic nodule in the left lobe of the liver but his liver panel and alpha-fetoprotein level had been normal. Computed tomography (CT) of the abdomen showed no arterial enhancement or portal venous washout to suggest hepatocellular carcinoma, with normal-looking hepatic vessels (Figs. 1a and 1b). Subsequent hepatic lipoidal angiography showed no tumour

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brush, and lipoidal CT showed no abnormal uptake of lipoidal, which would have suggested hepatocellular carcinoma. An image-guided biopsy of the lesion which showed features of a regenerative nodule was also performed in April 2004. A repeat CT done in July 2004, 4 months after the last CT scan, showed no interval changes (Figs. 2a and 2b).

The patient underwent an outpatient CT of the abdomen on 14 December 2004, but was re-admitted on the same day with worsening abdominal distension. Physical examination showed jaundice, moderate ascites, hepatomegaly, and ankle oedema. Laboratory investigations revealed worsened liver panel (Table 1). His HBV DNA titre, anti-HAV IgM, and anti-HEV IgM, which were dispatched on 6 December, were negative. Delta virus superinfection was considered unlikely, as delta virus is rare in Singapore, as well as many hepatitis B-endemic areas.[4] CT performed on 14 December showed extensive hepatic vein thrombosis, extending from all intrahepatic branches, through the inferior vena cava, to the right atrium, with moderate ascites. The left lobe lesion had increased in size from 1 cm in March 2004 to about 4.5 cm (Figs. 3a, 3b, and 3c). The thrombosis was not seen in prior images of his CT abdomen when they were reviewed.

The overall diagnosis was extensive thrombosis of the hepatic vein and inferior vena cava, i.e., acute Budd-Chiari syndrome. Surgical thrombectomy, infusion of thrombolytics, insertion of transjugular intrahepatic porto-systemic shunts (TIPPS), or liver transplantation were considered but deemed infeasible. Systemic anticoagulants were not given as the patient had a worsening coagulopathy. The patient deteriorated rapidly into acute hepatic failure, and died 10 days after admission, or 16 days after his first presentation.

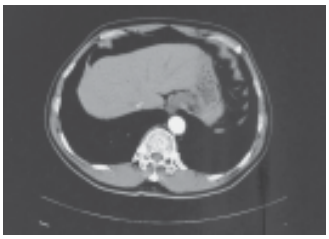

Fig. 1a.

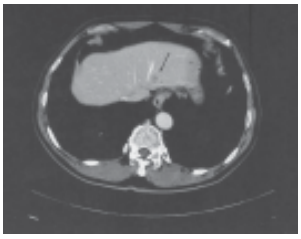

Fig. 1b.

Fig. 1a. CT abdomen performed 10 months before his acute presentation in the arterial phase. No arterially enhancing lesion was noted.

Fig. 1b. In the portal venous phase, a mild area of washout was noted in the left lobe (marked by an arrow).

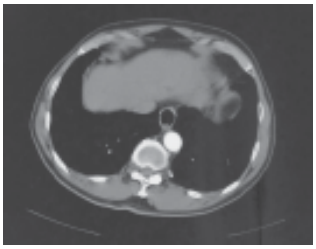

Fig. 2a.

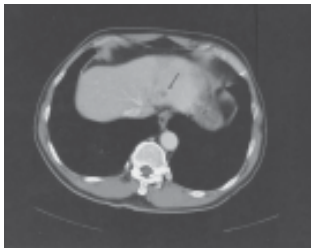

Fig. 2b.

Fig. 2a. CT abdomen performed 4 months after the initial CT, which showed no arterially enhancing lesion in the arterial phase.

Fig. 2b. CT abdomen in the portal venous phase, showing the same lesion in the left lobe (marked by an arrow).

Discussion

Budd-Chiari Syndrome (BCS) is defined as a hepatic venous outflow obstruction at any level from the small hepatic veins to the junction of the inferior vena cava and the right atrium.[5] It is an uncommon disease, and usually presents as chronic liver failure, with subacute onset of ascites, ankle oedema, and tender hepatomegaly. However, up to 20% of patients present acutely with a well described clinical picture of right upper quadrant pain, hepatomegaly, rapidly developing jaundice and acute hepatitis with fulminant liver failure.

Unfortunately, diagnosis of acute BCS is usually difficult. The presenting complaints and initial laboratory investigations are non-specific.[6-8] Most patients present

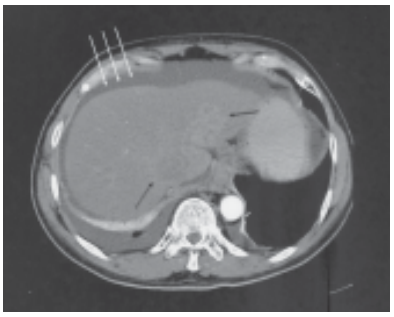

Fig. 3a.

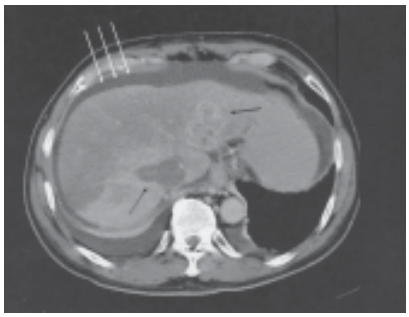

Fig. 3b.

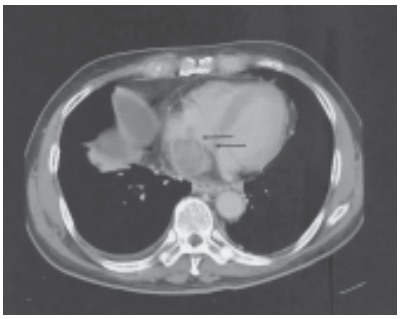

Fig. 3c.

Fig. 3a. CT abdomen in the arterial phase done on 14 December 2005 showing the same lesion in the left lobe (marked by dark arrow), but with new onset of ascites (marked by white arrows). A thrombus can be seen at the hepatic vein (marked by dashed black arrow).
Fig. 3b. CT abdomen in the portal venous phase showing the left lobe lesion (marked by dark arrow), and ascites (marked by white arrows). The hepatic vein and inferior vena cava thrombus is better seen in this phase.
Fig. 3c. CT of the chest showing the thrombus (marked by dark arrow) extending to the right atrium.

Table 1. Laboratory Results of the Patients from 5 Months Prior to Presentation

Laboratory results	Normal range	28 July	6 December	14 December	22 December
Bilirubin, uM	<30	11	16	78	238
Albumin, g/L	>35	42	31	33	24
ALT, U/L	<70	35	678	1675	775
AST, U/L	<50	30	557	1879	602
LDH, U/L	<700	465	1149	5300	2328
ALP, U/L	<130	94	136	189	151
Alphafetoprotein, ug/L	<15	4.6	3.4		
Creatinine, uM	<130		108	131	145
White cell count, $x10^9$/L	4-11		8.1	9.52	9.88
Haemoglobin, g/dL	13-16		13.5	14.7	13.0
Platelets, $x10^9$/L	130-400		102	62	42
Prothrombin time, s	9.8-13.3		17.1	23.7	44.3

with an acute hepatitic picture, with elevation of bilirubin and transaminases, which is non-specific and could also be seen in other types of acute liver injury.[9] Diagnosis is usually made radiologically, by either Doppler study of the hepatic vein, or multiphasic CT of the liver, with or without confirmation with venogram. In addition, multiphasic contrast-enhanced magnetic resonance imaging (MRI), which typically reveals caudate lobe hypertrophy with contrast enhancement, and obliteration of hepatic veins, has presented itself as a promising new tool in replacing inferior vena cavography as an non-invasive means of confirming the diagnosis.[10] Radionuclide imaging of the vena cava, which typically reveals a sharply truncated inferior vena cava with extensive collaterals, caudate lobe enlargement, and delayed visualisation of the heart, has been proposed as a diagnostic means in the past but it has been found to be less accurate than Doppler study and is not routinely performed nowadays.[11,12]

Most BCS cases are related to hypercoagulable states or invasion by malignant tumour.[11] When diagnosis was made in our patient, he was already in liver failure with grim prognosis so no further procoagulation screening was done. Although BCS associated with hepatocellular carcinoma was possible in our patient, his prior extensive workup, including biopsy and serial CT, showed a non-malignant regenerating nodule. Regenerating hepatic nodules have been found to be associated with BCS, resulting from ischaemia from hepatic outflow obstruction.[13] In our patient, the regenerative nodule was small in size, and was unlikely to have created the requisite amount of obstruction to have caused BCS.

Management of BCS includes medical, radiological, and surgical options.[14,15] Medical options include anti-coagulation to prevent thrombus extension, and diuretics to relieve ascites. Radiological treatment includes angioplasty with direct infusion of thrombolytics, and placement of transjugular intrahepatic portal-systemic shunt. Surgical treatment includes thrombectomy, portal-systemic shunting, and liver transplantation. Unfortunately, none was appropriate for our patient, as the extensive nature of the thrombosis was not amenable to thrombolysis, angioplasty or embolectomy, bypass, or transplantation. Our patient was already auto anti-coagulated from the rising prothrombin time, so heparin was not given.

In our patient, his known history of CHB, and recent travel history to China led us to consider acute exacerbations of CHB and acute viral hepatitis A or E as the top 3 differential diagnosis, which could have led to the delay in his diagnosis. This case highlights the rapidity of progression of acute BCS, and more importantly, the need for having an open mind in managing patients with acute hepatitis and in considering all differential diagnosis.

In conclusion, we presented a case of acute BCS in a patient with chronic hepatitis B. The patient's underlying CHB and recent travel history led us to consider acute exacerbations of chronic hepatitis B, and acute viral hepatitis A or E as the likely diagnoses. Clinicians ought to keep an open mind in considering all causes of acute hepatitis.

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