CASE REPORT

Hepatocellular Carcinoma With Presentation of Budd-Chiari Syndrome

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Budd-Chiari syndrome is defined as hepatic venous outflow obstruction at any level from the small hepatic veins to the junction of the inferior vena cava and the right atrium independent of the underlying disease. We report here a 40-year-old male patient who complained of abdominal fullness and bilateral lower leg edema for 1 month. A physical examination disclosed bilateral lower leg edema. Abdominal sonography revealed a small amount of ascites with thrombosis of the inferior vena cava and right hepatic vein. Viral hepatitis marker tests showed positive hepatitis B surface antigen. Tumor markers showed elevated serum α-fetoprotein levels. Computed tomography and magnetic resonance imaging confirmed hepatocellular carcinoma with inferior vena cava and right hepatic vein thrombosis. Therefore, hepatocellular carcinoma with Budd-Chiari syndrome was diagnosed. The patient was treated with intravenous heparin, which was then changed to oral warfarin. Although it is relatively rare, clinicians should be aware of hepatocellular carcinoma with Budd-Chiari syndrome when leg edema occurs without hypoalbuminemia in patients with chronic hepatitis B, because these patients are in the high-risk group for developing hepatocellular carcinoma. Regular follow-up of chronic hepatitis B, including biochemical and sonography surveillance, should be performed. [*J Chin Med Assoc* 2010;73(2):93–96]

Key Words: Budd-Chiari syndrome, hepatitis B virus, hepatocellular carcinoma

Introduction

Budd-Chiari syndrome (BCS) was first described by George Budd in 1845 as a classic triad of abdominal pain, hepatomegaly and ascites.[1] In 1899, Hans Chiari, a pathologist, further documented the pathological features of the disease.[1] It is currently defined as hepatic venous outflow obstruction at any level from the small hepatic veins to the junction of the inferior vena cava (IVC) and the right atrium independent of the underlying disease.[2] We report here a case of hepatocellular carcinoma (HCC) with the initial presentation of bilateral lower leg edema and BCS.

Case Report

A 40-year-old male from Myanmar complained of abdominal fullness and bilateral lower leg edema for 1 month. He visited our outpatient department for further evaluation. A physical examination disclosed bilateral lower leg edema. The patient's blood counts were as follows: white blood cells were 8,300/mm^3 (normal, 4,800–10,800/mm^3), hemoglobin was 14.6 g/dL (normal, 12–16 g/dL), and platelets were 215,000/mm^3 (normal, 130,000–400,000/mm^3). Serum biochemistry test results were as follows: alanine aminotransferase levels were 216 IU/L (normal, 0–40 IU/L),

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E-mail: cwsu2@vghtpe.gov.tw • Received: May 26, 2009 • Accepted: November 10, 2009
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aspartate aminotransferase levels were 200 IU/L (normal, 5–45 IU/L), albumin levels were 3.9 g/dL (normal, 3.7–5.3 g/dL), total protein levels were 7.0 g/dL (normal, 6.4–8.4 g/dL), and total bilirubin levels were 1.8 mg/dL (normal, 0.2–1.6 mg/dL). Abdominal ultrasound (Figure 1) showed the disappearance of Doppler flow in the intrahepatic segment of the IVC and the right hepatic vein. Therefore, the patient was admitted for further evaluation.

After admission, 24-hour urine protein collection showed only 0.567 g/day. The possibility of nephrotic syndrome was unlikely. Abdominal computed tomography revealed a hypoattenuated mass in hepatic segment 7 (S7) that measured 3.7 cm, adjacent to the IVC. The mass had dense contrast enhancement in the arterial phase and rapid washout in the portal venous phase. There were contrast-filling defects within the right hepatic vein (Figure 2A) and intrahepatic segment of the IVC (Figure 2B), compatible with tumor thrombus. In addition, a wedge-shaped hypodense lesion was found in hepatic S6 and S7, indicating liver infarction due to thrombosis of the right hepatic vein. Abdominal magnetic resonance imaging revealed a mass in hepatic S7 that measured 4.4 cm. The lesion showed low intensity on T1-weighted imaging (Figure 3A), high intensity on T2-weighted imaging (Figure 3B), early global contrast enhancement in the arterial phase (Figure 3C), and rapid contrast washout in the portal venous phase (Figure 3D). All of the imaging findings confirmed HCC. Thrombosis in the intrahepatic segment of the IVC and right hepatic vein were also observed, compatible with BCS.

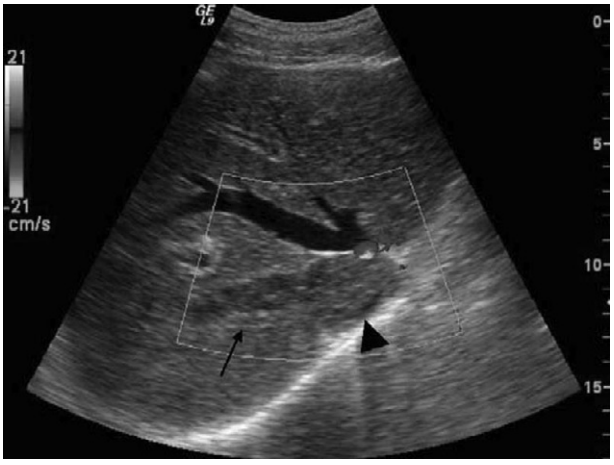

Figure 1. Abdominal ultrasound shows the disappearance of Doppler flow in the intrahepatic segment of the inferior vena cava (arrowhead) and the right hepatic vein (arrow).

Viral hepatitis marker tests showed positive hepatitis B surface antigen (HBsAg), but antibody against hepatitis C virus was negative. Tumor markers showed elevated α-fetoprotein levels of 31,158 ng/mL (normal, < 20 ng/mL), but carcinoembryonic antigen levels were normal (2.39 ng/mL; normal, < 6 ng/mL). Coagulation factors [protein C, 67% (normal, 80–140%); protein S, 117% (normal, 60–130%)] were within normal limits. Antiphospholipid antibody–immunoglobulin G (IgG), cardiolipin–IgG, disseminated intravascular coagulation profile, paroxysmal nocturnal hemoglobinuria marker and antinuclear antibody were all negative.

Initially, the patient was treated with intravenous heparin, which was then changed to oral warfarin. Subsequently, we discussed the therapeutic modalities including radiotherapy or target therapy with the patient. However, he decided to receive traditional herbal medicine and went back to Myanmar. Therefore, we were unable to follow him up after the diagnosis was established. The final diagnosis was HCC with BCS.

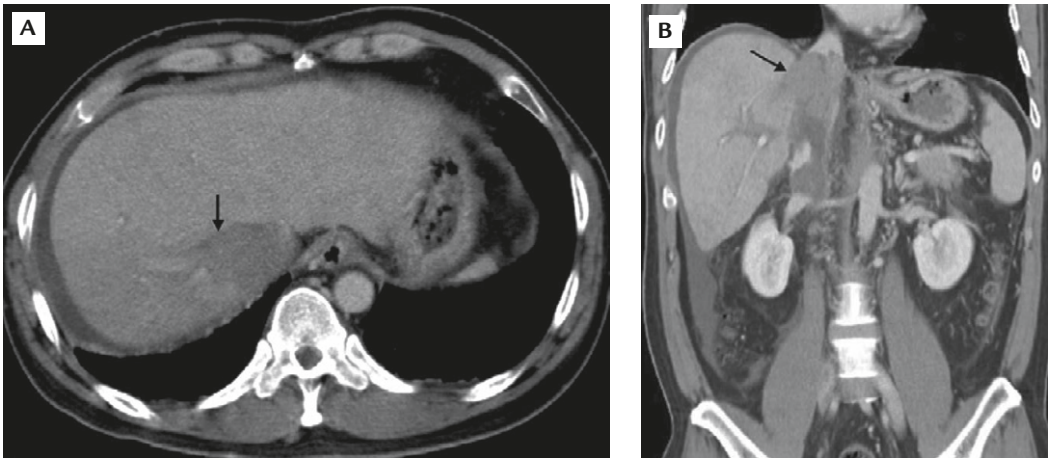

Figure 2. Abdominal computed tomography shows contrast-filling defects within the (A) right hepatic vein (arrow) and (B) intrahepatic segment of the inferior vena cava (arrow), compatible with tumor thrombus.

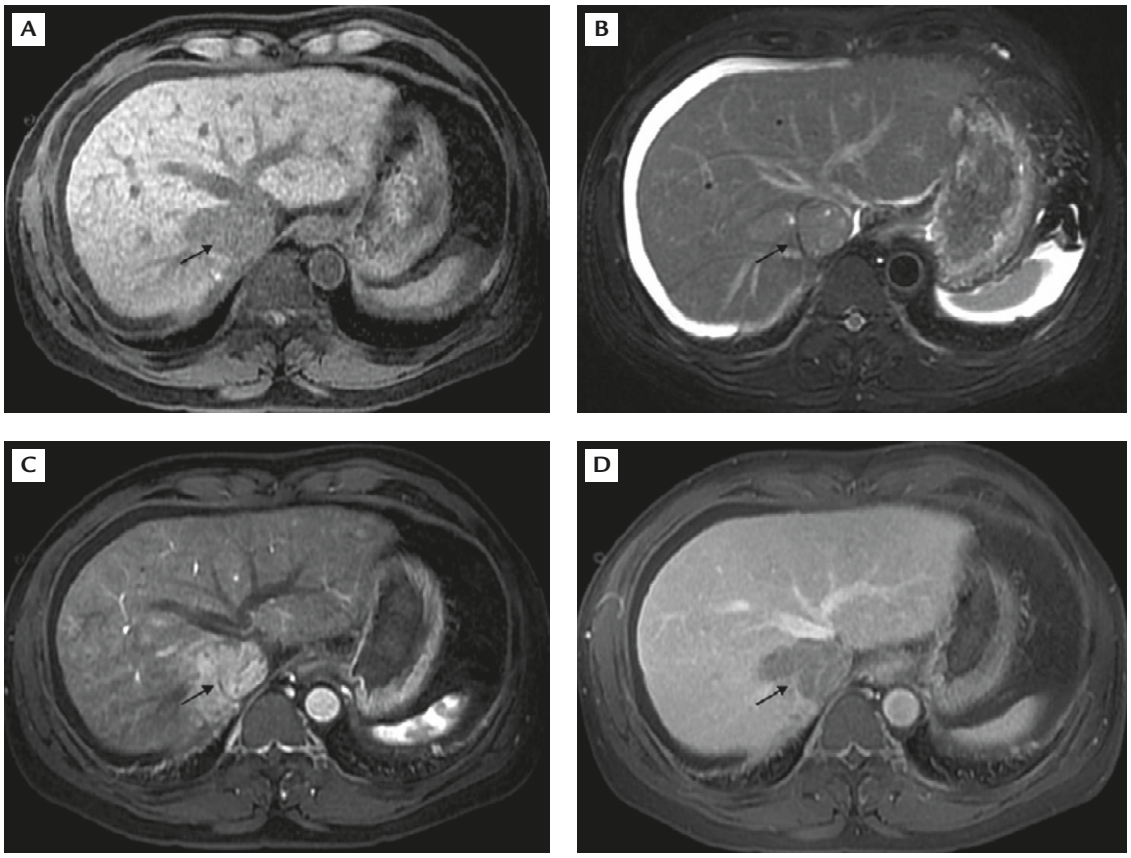

Figure 3. Abdominal magnetic resonance imaging demonstrates a hepatic mass in segment 7: (A) low intensity on T1-weighted imaging (arrow); (B) high intensity on T2-weighted imaging (arrow); (C) early global contrast enhancement in the arterial phase (arrow); (D) rapid contrast washout in the portal venous phase (arrow).

Discussion

HCC is the 5th most prevalent cancer in the world, causing 300,000–500,000 deaths per annum.[3,4] In Taiwan, it is the leading cause of cancer mortality in males and is second in females.[3] The common organs of metastasis from HCC are lung, bone, brain, and adrenal glands.[5] Although HCC with microscopic invasion is common and occurs in 60–90% of patients with tumor size >5 cm,[5,6] BCS is found in <1% of all HCC patients.[7,8] The clinical manifestations for HCC with invasion to the main vessels and BCS are diverse, from asymptomatic status to abdominal pain, chest pain, dyspnea, hematemesis, hemoptysis, anorexia, lower leg edema, and syncope.[7] Resection surgery, systemic chemotherapy, target therapy with sorafenib, radiotherapy, and transcatheter arterial chemoembolization have been reported as therapeutic modalities for HCC patients with main portal vein invasion or BCS.[7–9] However, the long-term outcome is quite dismal, with a median survival of approximately 2–20 months in spite of therapy.[7–9]

In most cases, BCS can be diagnosed solely on the basis of imaging without liver biopsy.[10] Doppler ultrasonography of the liver has a sensitivity and specificity of 85–90% for the diagnosis of BCS.[10] Bargallo et al classified the ultrasound signs of BCS into 3 categories: specific signs (hepatic vein obstruction manifested in different ways); suggestive signs (intrahepatic venovenous, portovenous or portacaval collateral and caudate vein >3 mm in diameter); and nonspecific signs (caudate lobe hypertrophy, extrahepatic collaterals, portal vein thrombosis, regeneration nodules, inhomogeneous liver parenchyma, and ascites).[11] Alterations of the hepatic (71.1%) and/or caval (28.9%) veins are the most frequent ultrasound signs of BCS, and the combination of the 2 signs (97.8%) with caudate lobe hypertrophy (66.7%) exhibits the highest positive predictive value for the diagnosis of BCS.[10] Computed tomography scans further allow for the detailed evaluation of patency of the hepatic vein and IVC, as well as the degree of caudate lobe hypertrophy.[1] In addition, magnetic resonance imaging may help to differentiate chronic from acute disease and provide further delineation of vascular anatomy.[1]

The treatment modalities for BCS include treatment of underlying disease, anticoagulation, percutaneous

angiography, transjugular intrahepatic portosystemic shunt, and liver transplant.[2] Early initiation of anticoagulant therapy is recommended for all patients regardless of whether or not an underlying prothrombotic disorder has been identified.[12] However, a surprisingly high incidence of heparin-induced thrombocytopenia with unfractionated and low-molecular-weight heparin has been reported.[12] If the patient does not improve with medical treatment, percutaneous angiography with or without a stent should be considered. Transjugular intrahepatic portosystemic shunt is an effective treatment for patients with BCS uncontrolled by medical therapy.[13] In the 10–20% of patients in whom the therapies mentioned above are unsuccessful, liver transplantation is the remaining treatment option for BCS.[14,15] Since recurrent BCS after transplantation has been reported, life-long anticoagulation is recommended.[16] Although the mortality rate of BCS at 3 years is as high as 90% if untreated, excellent survival can be achieved when prompt therapeutic procedures are performed.[2,16] Nevertheless, if BCS is caused by HCC, the prognosis is very poor in spite of aggressive therapies.

In our case, a 40-year-old male patient presented with ascites and bilateral lower leg edema without proteinuria and hypoalbuminemia. Nephrotic syndrome and liver cirrhosis were unlikely candidates after an initial evaluation and, therefore, decreased venous return of IVC was considered in the differential diagnosis. Laboratory studies were carried out to exclude autoimmune and hematologic disorders. The patient had no systemic prothrombotic risk factors of BCS such as myeloproliferative diseases, antiphospholipid syndrome, paroxysmal nocturnal hemoglobinuria, and Behcet's disease.[2] Nevertheless, he had chronic hepatitis B, which placed him in the high-risk group for developing HCC. Alpha-fetoprotein levels were extremely high. The imaging modalities, including dynamic computed tomography and magnetic resonance imaging, both demonstrated typical vascular characteristics to establish a definite diagnosis of HCC. All the findings mentioned above suggested that BCS in our patient was secondary to HCC.

Although the combination is relatively rare, clinicians should be aware of HCC with BCS when leg edema occurs without hypoalbuminemia in patients with chronic hepatitis B, who are in the high-risk group for developing HCC. More importantly, regular surveillance by abdominal sonography is crucial for the early detection of small HCC in high-risk patients. If small HCC can be detected early, the incidence of vessel invasion and BCS would be diminished. Long-term cancer-free survival could then be expected with curative therapy modalities.

Acknowledgments

This study was supported by a grant (V97B1-015) from Taipei Veterans General Hospital.

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