We present a complex case of the Budd-Chiari syndrome due to thrombosis of the hepatic veins in the presence of stenosis of the left hepatic vein and membranous obstruction of the inferior vena cava. The acute thrombosis occurred after laparoscopic surgical removal of the gallbladder. Because we strongly suspected the Budd-Chiari syndrome, hepatic venography was performed. The hepatic venous outflow obstruction was relieved by angioplasty and thrombolytic therapy with use of local infusions of urokinase into the clot. We propose that angiography be performed in patients in whom the Budd-Chiari syndrome is suspected and that angioplasty and thrombolytic therapy be initiated early.


\textbf{REPORT OF CASE}

A 35-year-old woman with ascites and peripheral edema came to our institution 12 days after a laparoscopic cholecystectomy had been performed elsewhere. On pathologic examination, the gallbladder showed cholecystitis and cholelithiasis. The postsurgical course was complicated by an episode of hypotension that persisted for 4 hours on postoperative day 1. Ascitic fluid began leaking from the midline incision on postoperative day 2. The patient was dismissed from the hospital on postoperative day 7; the ascites had decreased only slightly. When the patient was admitted to our hospital, she had abdominal pain, increased abdominal girth, weight gain, and lower extremity edema.

The patient had been taking oral contraceptives for many years. Two years before the current admission and 5 months after normal vaginal delivery of her first child, deep vein thrombosis of her lower extremities had developed. At that time, test results for proteins C and S, antithrombin III, anticardiolipin antibodies, and lupus anticoagulant were normal or negative. Sodium warfarin was administered for 7 months until she became pregnant for the second time; treatment was then changed to subcutaneous administration of heparin for the duration of gestation. Anticoagulant therapy was discontinued soon after the delivery of her second child, 8 months before the current admission.

On physical examination, the patient was obese with a severely distended abdomen and tense ascites, but no distended veins were visible over the abdomen. Pronounced pedal edema was evident.
Laboratory studies yielded the following results: hemoglobin, 16.2 g/dL; total bilirubin, 0.5 mg/dL; aspartate aminotransferase (AST), 203 U/L; lactate dehydrogenase, 223 IU/L; prothrombin time, 13.1 seconds; and albumin, 2.1 g/dL. Results of serologic tests for the hepatitis virus and antinuclear antibody were negative, as were those of the leukocyte alkaline phosphatase stain and Ham test for paroxysmal nocturnal hemoglobinuria. Doppler abdominal ultrasonography showed no abnormality of the hepatic veins, IVC, and portal vein; however, the quality of the examination was compromised because of the patient’s obesity. The liver and spleen were normal in size; moderate ascites was evident. A computed tomographic (CT) scan of the abdomen demonstrated an inhomogeneous parenchymal density of the right lobe of the liver with no detectable mass; the left lobe looked relatively normal. The hepatic veins were not identified.

Two days after admission, the patient’s total bilirubin level increased to 1.3 mg/dL, the AST level increased to 2,890 U/L, and the alanine aminotransferase was 2,340 U/L. Because we strongly suspected the Budd-Chiari syndrome, even though an ultrasound examination of the liver was not suggestive of the diagnosis, venography was performed through the right femoral route. A venacavogram revealed focal stenosis of the IVC just below the anticipated level of the hepatic veins (Fig. 1). Patency of the hepatic veins was not evident. The pressure difference across the caval stenosis was 27 mm Hg. An angioplasty balloon catheter was used to dilate the caval stenosis; after dilation, the gradient was 22 mm Hg. After repeated attempts, only the left hepatic vein could be catheterized through its occluded orifice. The initial injection of contrast medium into this vein revealed a tight stenosis at the orifice and a segment of thrombus within the lumen (Fig. 2). In addition, a network of collateral venous drainage throughout the left lobe of the liver and partially extending to the medial portion of the right lobe was present. The pressure within the left hepatic vein was 47 mm Hg.

Urokinase was infused into the left hepatic vein at a dosage of 4,000 U/min for 4 hours. In addition, the patient was given heparin, 5,000 U as a bolus and then 1,000 U/h. After 4 hours, less than half of the thrombus was dissolved. The stenosis of the orifice of the left hepatic vein was then dilated with a 9-mm-diameter angioplasty balloon, and the infusion of urokinase was continued into the vein at a decreased rate of 10,000 U/h overnight for a total dose of 1.08 million U. By the next morning, additional lysis had occurred, but approximately a third of the original thrombus remained (Fig. 3). Therefore, a latex occlusion balloon catheter was placed deep within the hepatic vein, beyond the residual thrombus, and gently inflated; the thrombus was extracted into the vena cava. No detectable symptom nor alteration of chest roentgenographic findings indicated pulmonary embolism. The final pressure difference across the stenotic site of the IVC was 8 mm Hg, the low vena caval pressure being 13 mm Hg. The left hepatic vein wedge pressure was 16 mm Hg, and the free hepatic vein pressure was 23 mm Hg. Free flow of blood was present in the hepatic vein without evidence of intrahepatic collateral veins (Fig. 4).

Fig. 1. Venacavogram of 35-year-old woman with ascites and edema, showing stenosis (arrow) within intrahepatic portion just below hepatic vein junction. Small dimple (arrowhead) is site of occluded left hepatic vein. The patient experienced no complications from the procedure. Although the serum AST level peaked at 3,640 U/L, it decreased to 263 U/L 2 days after thrombolytic therapy had been initiated. The patient was dismissed 7 days after admission; diuretic therapy was continued (for only 3 weeks), as was sodium warfarin. A CT scan of the abdomen obtained 1 month after the initial scan showed moderate hypertrophy of the left lobe of the liver and mottling of the right lobe, which appeared smaller; the size of the spleen had doubled. At 18-month follow-up, results of the liver tests were normal; no ascites, pedal edema, or esophageal or gastric varices were noted. Ultrasonography showed flow through the right, middle, and left hepatic veins; the size of the spleen was normal.

DISCUSSION
Our patient with the Budd-Chiari syndrome had an acute hepatic venous outflow obstruction that was successfully managed with angioplasty and thrombolytic therapy. Although the ultrasound examination of the hepatic veins and IVC was nondiagnostic, a strong clinical suspicion led to an early, aggressive evaluation of the IVC and hepatic veins.
Fig. 2. Left hepatic venogram obtained after recanalization of occluded orifice. Note large amount of thrombus (arrows) within lumen and intrahepatic collateral veins (arrowheads).

Angioplasty and thrombolytic therapy may have prevented fulminant liver failure and the need for liver transplantation.

Angioplasty has been previously reported in the treatment of thrombosis of the vena cava and hepatic veins. In such studies, it has usually been successful, and associated complications have been minimal. Nonetheless, the rate of restenosis that necessitates repeated angioplasty is high, especially in the hepatic veins. This problem can be prevented by inserting expandable metal venous stents, which have been used after angioplasty and thrombolytic therapy to manage the Budd-Chiari syndrome. Placement of a metallic stent is difficult if the hepatic vein is occluded, a common situation.

Literature on the use of thrombolytic therapy for the Budd-Chiari syndrome is lacking. Application of the thrombolytic agent directly to the clot through a catheter seems likely to be effective. In addition, overcoming increased sinusoidal pressures that would otherwise tend to direct systemically infused agents toward the collaterals and away from the clot is unnecessary. For example, direct application of thrombolytic agents has been claimed to be superior to systemic infusion for the superior vena cava syndrome. Ideally, the lytic agent should be given before the thrombus has organized; otherwise, lysis is less likely to succeed. The thrombolytic agents used are urokinase, streptokinase, or tissue-type plasminogen activator. No studies have addressed the relative efficacy of the various thrombolytic agents for the Budd-Chiari syndrome, and the choice of an agent for a specific patient depends on physician preference. Hemorrhagic risks are minimized by direct application because a lower dose may be administered in comparison with systemic administration. Active bleeding from the gastrointestinal tract is a contraindication to thrombolytic therapy.

Balloon extraction of a thrombus is unnecessary and inadvisable without prior thrombolysis. A thrombus that has been impregnated with urokinase is more likely to dissolve and, thus, less likely to cause a problem if it embolizes to the pulmonary circulation. Ideally, the clot should be extracted through the femoral vein, but this approach is not technically possible.

The events that led to the acute manifestation in our patient are unclear. In fact, in many patients with the Budd-Chiari syndrome, the cause is obscure. No myeloproliferative disorder, lupus anticoagulant, or deficiencies of proteins C and S or antithrombin III were evident. Membranous obstruction of the IVC (MOVCS) was noted but was below the hepatic veins and thus not the cause of the Budd-

Fig. 3. Left hepatic venogram obtained 24 hours after thrombolytic therapy and after balloon catheter dilation of origin of vein. Only a fragment of thrombus remains (arrow).

Fig. 4. Left hepatic venogram obtained after extraction of residual thrombus. Venous flow is now normal, and no intrahepatic collateral veins are identified. Compare with Figures 2 and 3, in which collateral veins are prominent.
Chiari syndrome. MOVC is a syndrome of unknown cause in which outflow of venous hepatic blood is, in some way, obstructed in various sites within the IVC. MOVC is the most common cause of the Budd-Chiari syndrome worldwide, but it is uncommon in the United States. Whether MOVC is congenital or acquired is unknown. Although proof in support of a congenital origin is lacking, evidence shows that webs result from the natural resolution of a thrombus. Histologically, the occlusive tissue has been found to be muscular and elastic, similar to organized thrombi in other sites. All three layers of the vessel wall are present at autopsy, a suggestion of normal initial development of the vessel and subsequent thrombosis that results in a web. Typically, MOVC manifests during the third and fourth decades of life; no cases have been reported in aborted fetuses or during infancy, and it is not associated with other congenital defects. More than 10 variations of MOVC exist. Our patient had a web below the hepatic veins and a large pressure gradient across it. She probably had chronic occlusion of her right and middle hepatic veins and a history of previous venous thrombosis. Possibly, the web represents previous thrombus at this site, now organized, with partial obstruction of blood flow.

CONCLUSION

The algorithmic approach we suggest for patients with acute obstruction of hepatic veins is shown in Figure 5. Aggressive therapy is warranted for such patients because fulminant hepatic failure can be prevented and liver transplantation will be unnecessary. Although thrombolytic therapy may

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**Fig. 5.** Diagram of suggested algorithmic approach for patients with acute obstruction of hepatic veins.
not always be successful, especially if the thrombus is organized, it should be initiated except during active hemorrhage. If the Budd-Chiari syndrome is strongly suspected, we recommend a hepatic venogram both to confirm the diagnosis and to initiate therapy. A CT scan of the liver or a magnetic resonance image cannot conclusively rule out the syndrome; thus, the initiation of thrombolytic therapy will be delayed. Portosystemic shunting, although helpful, is associated with major risks and makes liver transplantation difficult. Thrombolytic therapy and angioplasty seem the most logical combination because they are directed at the site and cause of obstruction.

REFERENCES


