Liver transplantation has become the definitive treatment for hepatic failure of various etiologies. Because the procedure is associated with many physiologic changes, the surgical candidate undergoes careful preoperative evaluation with particular emphasis on the cardiovascular system. Patients with end-stage liver disease (ESLD) may have significant, subclinical disease, either as a manifestation of the etiology of liver disease (alcoholic cardiomyopathy, hemochromatosis), as a manifestation of ESLD (high-outcome syndrome), an unclear relationship (pulmonary hypertension in a cirrhotic patient), or as a primary cardiac etiology (coexisting coronary artery disease). We present a patient who underwent orthotopic liver transplantation (OLT) and developed cardiac failure in the perioperative period.

Case Report

A 39-yr-old, 106-kg male diagnosed with ESLD secondary to chronic active hepatitis C and alcoholic cirrhosis was scheduled for OLT. He was listed as United Network for Organ Sharing classification 3, having been hospitalized for 10 days with spontaneous bacterial peritonitis. Sharing classification 3, having been hospitalized for 10 days with spontaneous bacterial peritonitis, and hepatic encephalopathy. His vital signs were: heart rate, 80 beats/min; arterial blood pressure, 100/60 mm Hg; respirations, 22 breaths/min; and temperature, 37.1°C. Cardiac auscultation revealed no significant abnormalities.

Preoperative laboratory values were: Hb, 8.7 mg/dL; platelets, 43,000/mm³; prothrombin time, 15.3 s (normal 11–13); partial thromboplastin time, 43 s (normal 26–38); creatinine, 1.1 mg/dL; glucose, 101 mg/dL; total bilirubin, 3.8 mg/dL (normal 270–380); and iron saturation, 112% (normal 28%–42%).

A liver biopsy performed 4 mo before transplant showed micro- and macronodular cirrhosis with continuing piece-meal necrosis. Lymphoid aggregates, compatible with active hepatitis C infection, were present. Perl’s staining of the liver demonstrated 1–2+ iron deposition in the regenerating nodules using the Sheurer grading system. The amount of iron was classified as hemosiderosis and was considered to be compatible with alcoholic cirrhosis.

Chest radiograph revealed numerous apical bullae, mild diffuse fibrosis, and a normal cardiac silhouette. Electrocardiogram was normal, revealing sinus rhythm with no acute or chronic changes. An echocardiogram performed 4 mo earlier revealed no abnormalities in chamber dimensions, wall thickness, or estimated central venous pressures. The ejection fraction was estimated to be 56%.

Anesthesia was induced with fentanyl, isoflurane, and pancuronium. A pulmonary artery catheter inserted after induction revealed: central venous pressure (CVP), 12 mm Hg; pulmonary capillary wedge pressure (PCWP), 15 mm Hg; cardiac output (CO), 12 L/min; cardiac index, 5.4; systemic vascular resistance (SVR), 491 dynes·s⁻¹·cm⁻⁵; and mixed venous oxygen saturation (SvO₂), 83%. The surgical technique involved the use of venovenous bypass with an anhepatic time of 73 min. Dopamine, 1–2 µg·kg⁻¹·min⁻¹, was used for augmented renal perfusion throughout the procedure and calcium chloride, 0.5–1.0 mg·kg⁻¹·min⁻¹, was used to maintain normal ionized calcium levels during the anhepatic phase. No hemodynamic problems were encountered during the 8-h procedure. The patient remained in sinus rhythm without evidence of ischemia or conduction abnormalities. Total intraoperative fluid administered included 7150 mL of crystalloid, 1000 mL of albumin (5%), 3 U of packed red blood cells, 10 U of platelets, 2 U of fresh-frozen plasma, and 1000 mL of intraoperative salvaged shed blood.

On arrival in the intensive care unit, the patient had the following vital signs: heart rate, 82 beats/min; arterial blood pressure, 146/98 mm Hg; CVP, 13 mm Hg; PCWP, 19 mm Hg; CO, 9.6 L/min; SVR, 815 dynes·s⁻¹·cm⁻⁵; and SvO₂, 86%. Over the next 12 h the patient received 2000 mL of crystalloid, 500 mL of autologous blood, 1 U of packed red blood cells, and 4 U of fresh-frozen plasma. During this time, changes in vital signs were: heart rate increased to 140 beats/min; arterial blood pressure, 131/70 mm Hg; CVP, 14 mm Hg; PCWP, 29 mm Hg; CO, 7.8 L/min; SVR, 1010 dynes·s⁻¹·cm⁻⁵; and SvO₂, 59% (the Fio₂ delivered was reduced from 1.0 to 0.4 during this time). Urine output which had been >1 mL·kg⁻¹·h⁻¹ decreased to 0.5 mL·kg⁻¹·h⁻¹.

Because of the decline in cardiac function, an echocardiogram was performed on postoperative day (POD) 2 revealing decreased overall ventricular contractility and a mildly dilated left atrium and left ventricle. Inotropic support with dopamine, dobutamine, and, eventually, epinephrine was utilized in addition to nitroglycerin in an attempt to improve cardiac function. Despite these therapeutic measures, cardiac function continued to decline and repeat echocardiogram on POD 4 revealed severely decreased contractility of the left ventricle.

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ventricle. Serial electrocardiograms and cardiac enzymes (creatinine phosphokinase and lactate dehydrogenase with isoenzymes) showed no evidence of ischemia or infarction. The patient's condition continued to worsen, and on POD 9 he died of unrelenting cardiac failure.

An autopsy showed the heart to be enlarged, weighing 640 g (normal range 280–340 g). All of the cardiac chambers were dilated markedly. The coronary arteries were free of atherosclerosis and there was no evidence of myocardial infarction. Microscopic findings on all section of myocardium were positive for iron. In addition, the following organs also contained marked iron deposition: kidneys, pancreas, thyroid, pituitary, adrenals, and testes. Based on these findings the diagnosis of hemochromatosis was established.

Discussion

Hemochromatosis is an iron storage disease which results in cellular damage and fibrosis (1). Deposition of iron may occur throughout the body and can include the liver, heart, kidneys, pancreas, endocrine organs, and skin. This is in contrast to hemosiderosis, in which deposition occurs only in the mononuclear phagocytic system (2). The disease can be inherited (idiopathic) or acquired in disorders such as chronic anemias requiring the use of frequent blood transfusions. Classically, these patients present with the triad of cirrhosis, diabetes mellitus, and bronze skin. Laboratory findings of elevated serum iron, iron saturation, and ferritin are indicative of the disease. The definitive test for diagnosis of hemochromatosis is usually a liver biopsy demonstrating 3–4+ iron deposition.

Cardiac involvement is a common complication of hemochromatosis; 15% of patients present with cardiac symptoms (3). In the absence of phlebotomy, cardiac failure is a frequent cause of death. Iron deposition may result in left ventricular hypertrophy or dilation, leading to congestive heart failure or conduction pathway abnormalities, including supraventricular arrhythmias.

The patient in our report had ESLD secondary to hepatitis C and alcoholic cirrhosis. The diagnosis of hemochromatosis was not made despite the elevated ferritin and iron saturation because the liver biopsy was not indicative of this disease. The patient showed no evidence of diabetes mellitus, and his jaundice made it difficult to recognize any bronze pigmentation of the skin. Even if the diagnosis of hemochromatosis had been made preoperatively, additional cardiac evaluation probably would not have been performed, because the electrocardiogram and echocardiogram were normal. Although 70% of patients with idiopathic hemochromatosis have stainable iron in their heart, nearly one-third fail to show iron in the subendocardium of the right ventricle, thereby rendering endomyocardial biopsy less valuable as a diagnostic tool (4). A cardiac stress test might be useful to evaluate a patient with suspected hemochromatosis preoperatively. If the patient was thought to have cardiac involvement, preoperative phlebotomy or chelation therapy with desferroxamine may have been beneficial. Dabestani et al. (5) found that aggressive phlebotomy reversed the cardiac abnormalities in five of seven patients he studied.

This case was unusual in that cardiac problems did not appear until the postoperative period. Intraoperatively the patient did not demonstrate any signs of cardiac dysfunction. In the postoperative period the patient began to show signs of decreased cardiac function. Administration of blood products and fluid in the intensive care unit resulted in an elevated PCWP and resultant reduction in the coronary perfusion pressure. As the cardiac function declined, the coronary perfusion pressure continued to decrease, leading to a vicious cycle of progressive myocardial hypoperfusion, culminating in congestive heart failure and death.

In summary, cardiac failure from unrecognized hemochromatosis resulted in this patient's death following OLT. Although the evaluation of this patient preoperatively included the "gold standard" diagnostic test for hemochromatosis (liver biopsy), in this instance this test was unrevealing. With the established diagnosis of chronic active hepatitis C and alcoholic cirrhosis, no further etiologies were sought for the cause of this ESLD.

If hemochromatosis is suggested by diagnostic tests in a patient undergoing evaluation for OLT, some form of cardiac stress test, such as a dobutamine-stress echocardiography or dipyridamole thallium imaging, may be useful to estimate the cardiac involvement of this disease. If significant hemochromatosis involving the heart is found, the use of phlebotomy and/or chelation therapy should be considered preoperatively.

References