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Orthotopic liver transplantation for massive hepatic lymphangiomatosis

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Abstract

Lymphangiomatosis is a rare malformation of the lymphatic system that causes severe symptoms secondary to progressive growth into or close to vital structures. A case report of liver failure related to this space-occupying intrahepatic mechanism is taken as a starting point for a discussion of the problems of liver transplantation related to large hepatomegalies.

Lymphangiomatosis is a rare malformation of the lymphatic system that may manifest itself in a variety of anatomic locations, including solid organs, serosal space, and soft tissues. Although considered histologically benign, it may produce severe symptoms secondary to continuous growth, with compression of vital structures. Moreover, organ failure may result because of an internal derangement of the parenchyma. This article describes the first known case of massive hepatic and mediastinal lymphangiomatosis treated with total hepatectomy, orthotopic liver transplantation (OLTx), and subsequent excision of tumor from the mediastinal location.

CASE REPORT

A 41-year-old woman with known lymphangiomatosis of the liver was referred to the University of Pittsburgh Health Center for evaluation of massive hepatomegaly. Four years before referral she underwent splenectomy because of severe splenomegaly, and a diagnosis of splenic lymphangiomatosis was made. At that time her liver was noted to be diffusely involved by the same process, but no other sites of the disease were found.

At the time of our initial evaluation the patient showed no symptoms. Physical examination revealed a well-developed, well-nourished woman with no complaints. There was a large right supraclavicular mass that was soft and nontender. The other striking finding was the massive abdominal distention; the liver was palpable at the level of the pubic brim and was soft and nontender. A small amount of ascites was detected. There was also a large umbilical hernia. The remainder of the examination findings were normal. Chest x-ray films revealed a right mediastinal mass that was thought to be an extension of a cervical lymphangioma. The lung fields were clear and the heart shadow was normal. Computed tomographic (CT) scan of the abdomen confirmed that the hepatomegaly was secondary to replacement of the liver

parenchyma by multiple fluid-filled cysts. The results of all liver function tests were within normal limits.

The growth of both the supraclavicular and hepatic masses accelerated over the next 22 months. The patient began to complain of increasing malaise, anorexia, weight loss, back pain, and pedal edema. She also had occasional episodes of dyspnea and recurrent episodes of paroxysmal tachycardia. A course of radiation therapy to the mediastinocervical mass had no effect.

Reevaluation of the patient at that time revealed a significant deterioration in liver function, demonstrated by prolongation of partial thromboplastin time to 38.9 seconds (control, 24 seconds) and prothrombin time to 18 seconds (control, 11 seconds); elevation in total and direct bilirubin level (2.3 mg/dl and 1.1 mg/dl, respectively); and in elevation in alkaline phosphatase level (340 U/dl). The liver volume as assessed by sonogram and abdominal CT scan¹ was 17,960 cc. At this time the patient was activated as a liver transplant candidate, and a suitable donor soon became available.

At the time of OLTx, the peritoneal cavity was explored through a wide transverse incision just above the umbilicus with a long upper-midline extension, which included excision of the xyphoid process. A small amount of bloody ascites, thought to be leakage of fluid from the multiple liver cysts, was drained. The liver had been completely replaced by thin-walled cysts of various sizes, which contained serosanguineous fluid (Fig. 1). The lower edge of the liver was mobilized from the pelvis, and adhesions from the previous splenectomy were carefully divided. The hilar structures were dissected just above the upper border of the pancreas. The bile duct was identified and found to be surrounded by a network of delicate and dilated lymphatic vessels that were filled with clear lymph. The duct and the surrounding lymphatic vessels were ligated *en masse* and divided. The portal vein and hepatic artery were easily identified and were of normal size. Using the principles of early hepatic devascularization and veno-venous bypass, we completed the hepatectomy expeditiously. The remainder of the surgery was carried out routinely. The hepatic artery was revascularized by means of an end-to-end anastomosis between the donor celiac axis and the recipient common hepatic artery. A roux-en-Y choledochojejunostomy over a stent was used for the biliary reconstruction.

Postoperatively, immunosuppression consisted of our standard protocol of cyclosporine and steroids.² The patient's initial course was uneventful, and her liver function was excellent.

On the 11 th postoperative day severe respiratory stridor suddenly developed, and the patient was unable to clear secretions. In spite of aggressive respiratory therapy she could not maintain a clear airway and required intubation. The lung fields remained clear, there was no evidence of pneumonia, and it was thought that the respiratory deterioration was due to acute tracheobronchial compression by the mediastinal mass (Fig. 2). The patient underwent a combined mediastinal and cervical exploration through a median sternotomy and a transverse cervical incision. The mass was intimately attached to every vascular and nervous structure of the mediastinum and lower neck, which resulted in displacement of the right jugular vein, vagus nerves, carotid arteries, and left innominate vein. Many cysts were filled with fresh blood, which probably accounted for the acute enlargement of the mass and the resulting symptoms. Although the tumor was deep-seated, it did not invade any vital structure, and with meticulous dissection it was possible to safely remove it en bloc. The patient also required a tracheostomy because of early postoperative soft tissue swelling.

Postoperatively she recuperated rapidly and was discharged in good condition 2 months after the liver transplant procedure; she is now doing well, 11 months after her discharge, with completely normal liver function.

PATHOLOGY

The liver ($45 \times 26 \times 12$ cm, 16.5 kg) was almost entirely replaced by tumor, which resulted in complete distortion of the normal liver shape. The capsular surface was bosselated because of underlying multiple, semitranslucent cysts. The hilar structures—including the hepatic artery, portal vein, biliary tree, and the gallbladder—were grossly free of cystic distortion, although the gallbladder was slightly edematous (0.3 cm). Sectioning showed multiple smooth-walled cysts up to 6.0 cm in diameter that had replaced most of the hepatic parenchyma, although some intervening normal liver was seen (Fig. 3). The cysts were filled with blood or slightly viscous serous fluid and an occasional thrombus.

Microscopically the tumor consisted of multiple intercommunicating cavernous spaces separated by delicate, thin-walled fibrous septa without smooth muscle (Fig. 4). The cysts were lined with a flattened, innocuous-appearing endothelium and were empty or contained either a faintly eosinophilic proteinaceous fluid or a fluid mixed with blood, presumably resulting from rupture of the expanding lymphatic spaces into the nearby venous channels. Focal organized thrombi with cholesterol clefts were also present, but no areas of solid endothelial cell proliferation, endothelial cell atypia, or mitotic activity were seen (Fig. 5). There were large dilated portal and parportal lymphatic channels in relatively uninvolved areas of the liver, which is also supportive of the conclusion that the tumor arose from lymphatic channels (Fig. 3). Staining for factor VIII-related antigen was focally positive. The uninvolved liver showed focal compression changes with canalicular bile plugging, mild ductal proliferation, and portal inflammation.

The tumors removed from the neck and mediastinum were $13 \times 9 \times 4$ cm and $10 \times 5 \times 3$ cm and consisted of multicystic masses of soft tissue. The cysts ranged from 1 to 4 cm in diameter and were filled with a clear yellow fluid or blood.

The microscopic appearance was similar to that described for the liver tumor.

DISCUSSION

This case report describes the largest liver yet to be replaced by orthotopic liver transplantation. The volume of the liver as measured by CT scan¹ was almost 18 L, which represents a wet weight of more than 40 lb (18.2 kg). The dry weight of the specimen, determined during the pathologic evaluation, was 34 lb (16.5 kg). Previously, the largest liver removed at our institution was a polycystic liver that weighed 28.4 lb (12.9 kg).

Lymphangioma is a rare malformation of the lymphatic system that originates as a congenital malformation of the lymphaticovenous drainage. Most (90%) of these malformations appear by the end of the second year of life.³ Furthermore, progressive lymphangioma that involves the liver alone or is associated with other organ involvement, as described in this case report, is exceptionally rare; since 1970 only 6 cases have been reported in the literature.⁴⁻⁹

This is the first reported case of management of this condition with replacement of the liver; with this case the lymphangiomatosis is demonstrated to be curable by liver transplantation. Thus lymphangiomatosis of the liver becomes a good indication for liver transplantation.

Although the massive size of the liver would seem to make the operation difficult or impossible, this was not the case. In reality, hepatomegaly, even if massive, usually presents fewer technical problems than do small, contracted, end-stage cirrhotic livers.

The characteristics of the largest livers (more than 7 kg in dry weight) in patients who have undergone liver transplantation at the University of Pittsburgh are summarized in Table I. All

the patients were affected by end-stage liver disease mainly due to a space-occupying intrahepatic mechanism, with symptoms related to compression of the vena cava, intra-abdominal organs, nerve roots, or diaphragm. All of them underwent venovenous bypass during the anhepatic phase of the operation; two patients required a rapid and substantial fluid replacement at the time of cross-clamping of the upper vena cava to avoid hypovolemic shock secondary to a massive blood sequestration in the enlarged liver¹⁰. With these precautionary measures, the hemodynamic profiles remained in the usual median values for this procedure.^{11, 12}

Radiotherapy to slow the growth of the mediastinal tumor was attempted, but its only benefit, if any, is limited to the cellular-capillary type of the disease and not the cystic variety found in our patient. (Popper H. Personal communication)

The multicentricity of lymphangiomas, as described in this case, is typical of the previous reported cases, and the rapidity with which a stable, asymptomatic lesion may suddenly become life-threatening is also common. In fact, with only minimal enlargement of the mediastinal mass because of intracystic hemorrhage, our patient had severe, life-threatening respiratory distress. Prompt and aggressive surgical extirpation relieved the tracheobronchial compression and allowed a complete and uncomplicated recovery. It is also important to note that this extensive tumor did not invade any vital structures, which suggests a favorable prognosis.

In summary, lymphangiomas involving the liver is a rare occurrence, often accompanied by involvement of other organs. Most often it will cause progressive hepatomegaly without compromise of liver function. However, as evidenced by our case report, the continued tumor growth to mammoth proportions can cause pressure-related symptoms and subsequent organ failure. Patients with this disease should be evaluated early and followed closely; the judicious use of liver transplantation for this entity appears to be the treatment of choice.

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Fig. 1. Macroscopic intraoperative appearance of liver completely replaced by lymphangiomatosis. The size of the organ was responsible for the progressive organ failure and the multiple compression symptoms.

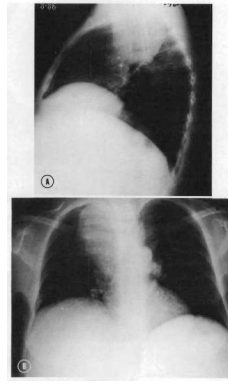


Fig. 2. Chest x-ray film. Lateral (**A**) and posteroanterior (**B**) views show mediastinal lymphangiomatosis that caused tracheobronchial compression with severe respiratory symptoms.

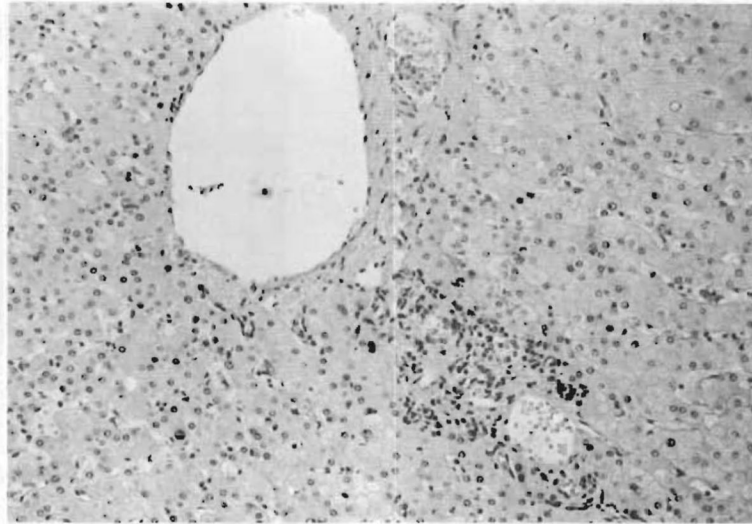


Fig. 3. Section of relatively uninvolved liver shows large dilated portal lymphatic channel that supports the conclusion that the tumor arose from lymphatic channels (Hematoxylin-eosin stain; original magnification $\times 200$.)

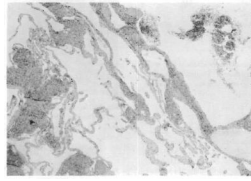


Fig. 4. Photomicrograph of hepatic tumor shows multiple cystlike spaces lined with flattened endothelium and empty or filled with small amount of blood. (Hematoxylin-eosin stain; original magnification $\times 40$.)

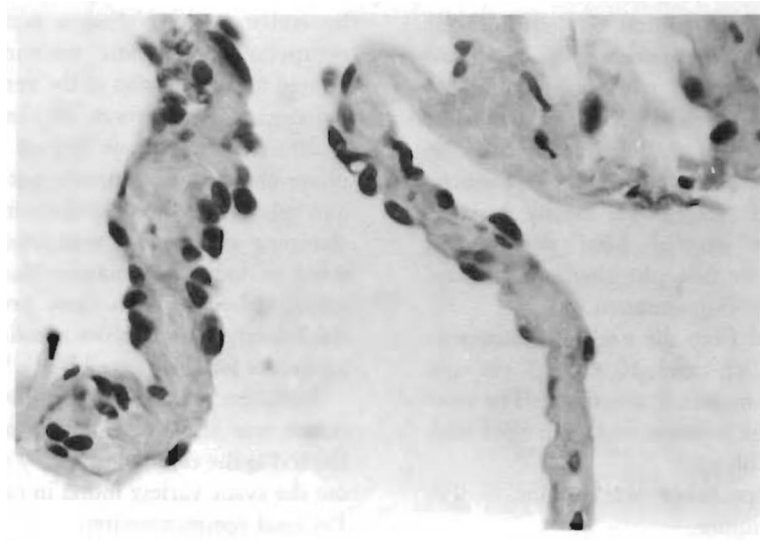


Fig. 5. High-power microscopy of vascular lining cells shows all with benign appearance. No mitotic activity or pleomorphism is seen. (Hematoxylin-eosin stain; original magnification $\times 400$.)

Table 1
Total hepatectomy with orthotopic liver transplantation for hepatomegaly (greater than 7 kg)

Age	Sex	Diagnosis	Liver preoperative volume (cc)	Liver postoperative weight (kg)	Intraoperative problems	Blood loss	Postoperative complications	Survival
41	F	Hepatic lymphangiomatosis	17960	16.5	None	63 U RIS*	Tracheostomy	Alive, well 11 mo; normal liver function
42	F	Polycystic disease (OLTx and KTx)	13400	12.9	Complex artery reconstruction	25 U	Respiratory failure; biliary reconstruction	Alive well 3 yr; normal liver function
51	F	Carcinoid tumor	6950	7.2	None	20 U RIS*	Rejection; re-OLTx	Dead 3 mo; multiorgan failure after re-OLTx
35	F	Hepatic leiomyosarcoma	6700	7.0	None	12 U.	None	Alive with bone metastasis 1 yr; normal liver function

Legend: OLTx, orthotopic liver transplantation; KTx, kidney transplantation.

* Rapid infusion system used during operation.¹⁰