Treatment of refractory lymphangioleiomyomatosis–associated chylous effusion with a pleuroperitoneal window and omental flap

Subroto Paul, MD, a Stacey Su, MD, a Heather Edenfield, BA, a David J. Kwiatkowski, MD, b and Raphael Bueno, MD, a Boston, Mass

Lymphangioleiomyomatosis (LAM) is a rare progressive cystic disease of the lung that predominantly affects women. Clinical features of the disease include spontaneous pneumothoraces, dyspnea, cough, as well as the formation of chylous effusions. These effusions are often refractory to treatment. We describe a case of a 74-year-old woman with LAM associated chylous effusions that was refractory to standard treatments including bowel rest with total parental nutrition (TPN), thoracic duct ligation, and pleurectomy but was successfully managed with a novel combination of oral progesterone, rapamycin, and doxycycline combined with the creation of a pleuroperitoneal shunt with omental flap placement in the pleural cavity.

CLINICAL SUMMARY

A 74-year-old woman presented with recurrent chylothorax. Thirty years earlier, she had 3 left pneumothoraces treated by means of pleurodesis, with findings of “blisters” on her lungs. At age 71 years, she experienced abdominal discomfort, abdominal computed tomographic scanning showed a complex retroperitoneal infiltrative mass, and biopsy showed lymphangioma. Three years later, she presented with dyspnea and was found to have bilateral pleural effusions, a pericardial effusion, and diffuse cystic parenchymal changes on chest computed tomographic scanning (Figure 1, A). Echocardiographic analysis revealed pericardial tamponade, which was drained for 600 mL of chyle. Her pericardial effusion recurred, and she was referred for surgical intervention. Abdominal magnetic resonance imaging showed a complex retroperitoneal mass extending to the aortic bifurcation (Figure 1, B). Lymphangiographic analysis showed dilated tortuous lymphatic channels (Figure 1, C). Review of her previous abdominal mass biopsy (Figure 1, D) confirmed lymphangioma. A diagnosis of abdominal lymphangiomyoma and pulmonary lymphangioleiomyomatosis (LAM) was made.

She underwent creation of a subxiphoid pericardial window and laparoscopic ligation of thoracic duct tributaries in the retrocrural area. Bilateral chylous effusions worsened, particularly on the right, given her previous left pleurodesis. Drainage of 2 to 3 L/d chyle from the right pleural space persisted despite treatment with total parenteral nutrition and bowel rest. Subsequent right thoracotomy with pleurectomy, talc poudrage, and mass thoracic duct ligation failed to prevent recurrent chylothorax. Attempted thoracic duct cannulation failed, and thoracic duct embolization could not be performed.

The patient’s urine had increased levels of matrix metalloproteinases, and oral doxycycline was administered. Based on preliminary reports of its benefit in LAM, oral rapamycin was started (trough level, 7–15 ng/mL). Progesterone (400 mg administered intramuscularly every month) was added empirically, and she was re-fed the chylous chest tube output to restore immune function.

Despite surgical and medical therapy, the chest tube output remained high, requiring prolonged inpatient care. She underwent creation of a transdiaphragmatic window by means of laparoscopic resection of a portion of the diaphragm to the right of the crus and posterior to the liver. An omental flap was placed into the right pleural space connecting the right pleural cavity to the peritoneum, with the hope that the omentum might absorb chyle and maintain the patency of the pleuroperitoneal channel. The patient was maintained on a clear liquid diet and total parenteral nutrition. Chest tube and abdominal drain outputs decreased, and tubes and drains were removed within 7 days. The patient was discharged on a regular diet. The patient continues to do well 16 months afterward. Follow-up chest films show minimal bilateral effusions. She continues on doxycycline and rapamycin (goal trough levels, 3–5 ng/mL).

DISCUSSION

LAM chylous effusions are often refractory to medical treatment and can be severely debilitating, leading to cachexia, immunosuppression, and death. There is no standard effective medical or surgical therapy for LAM-associated chylothorax, particularly when pleurodesis fails.1 Our case is the first to describe the successful treatment of a refractory LAM-associated chylothorax using a combination of drugs...
aimed at various aspects of the pathogenesis of this disease combined with the creation of a pleuroperitoneal window and an omental flap.

Although the benefit of drug treatment in this patient is uncertain, we have continued them at present, given the patient’s improvement and tolerance of this regimen. Doxycycline has been shown to be inhibit matrix metalloproteinases in experimental models and appeared to have benefit in previous patients with LAM.2 Rapamycin is used because its target, mammalian target of rapamycin complex 1 (mTORC1), is constitutively activated in LAM. A recent publication indicates therapeutic promise for rapamycin in LAM.3 Based on the discovery of estrogen receptors in LAM cells, progesterone has been used to treat LAM. However, clear evidence of its benefit is lacking, and in this patient it was discontinued without any clinical effect.

Externalized pleuroperitoneal shunts have been described as a method to control refractory chylous effusions in children. Device placements to prevent shunt closure are rarely performed because these become clogged, infected, or both. Omental flaps are used in the repair or prevention of bronchopleural fistulae and empyema cavities. Only a single report in Italian has previously described a similar procedure: the placement of an intrathoracic omental flap to successfully treat chylothorax after failed partial pleurectomy in a patient with LAM.5 It is unclear whether the omental flap assisted in controlling the effusion through active absorption of fluid or by maintaining the patency of the pleuroperitoneal shunt. There remains no clear mechanism for fluid absorption attributed to the omentum.

Refractory chylothorax in patients with LAM remains a challenge. As shown in this report, pleuroperitoneal shunt creation with omental flap placement combined with multi-drug therapy should be considered in the armamentarium for this often desperate condition.

References