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Refractory chylous effusions in lymphangioleiomyomatosis patient post lung transplant

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Abstract

Lymphangioleiomyomatosis is a rare systemic disorder of unknown etiology that affects young women almost exclusively. Chylous effusions are known to be associated with lymphangioleiomyomatosis and may be difficult to treat. We present the case of a 37-year-old female who received bilateral lung transplantation for lymphangioleiomyomatosis complicated by refractory chylothorax and chylous ascites, ultimately controlled through repeated, open surgical procedures and percutaneous lymphatic embolization interventions. The combined surgical and interventional radiological approach, while not novel in their own right, suggests that a multi-modal interventional approach may be required in refractory cases.

Keywords

Surgery, respiratory medicine, chylous effusions, refractory, lung transplant, embolization

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Introduction

Lymphangioleiomyomatosis (LAM) is a rare cystic disease of the lung that affects women of childbearing age. Although it is true that LAM most commonly affects premenopausal women, LAM has been reported to occur in both preadolescent and elderly women, and there are cases described in men with tuberous sclerosis complex.

The disease is characterized by abnormal smooth muscle proliferation in the lung and lymphatic vessels along the thorax and abdomen.[1] It may occur idiopathically or in 30%–40% of patients affected with tuberous sclerosis complex.[2] Chylothorax is the most common lymphatic complication of LAM (10%–30%), followed by chylous ascites (approximately 4% of LAM patients). It usually results from obstruction or disruption of the thoracic duct or its tributaries.[3] Chylous leaks in LAM can happen without precipitative trauma or as a complication of thoracic surgery, including lung transplantation.[4,5] Chylothorax after lung transplant is a potentially serious complication, management is difficult, and has not been well defined. Here, we described a case of chylous ascites in patient with LAM post lung transplant, controlled by a combination of medical, radiological, and surgical treatment.

Case report

A 37-year-old woman with LAM underwent bilateral lung transplantation on cardiopulmonary bypass for progressive hypoxic respiratory failure despite medical therapy with sirolimus over the preceding 5 years. Sirolimus was held for a total of 9 weeks prior to transplant (3 weeks prior to listing). She was extubated to room air on postoperative day (POD) 3, but developed a right sided chylothorax on day 4. Conservative measures, including no enteral nutrition, total parenteral nutrition (TPN), and subcutaneous octreotide were attempted with no clinical improvement. On POD 26, she required a sub-xiphoid window for a large pericardial effusion. An attempt at lymphangiography to seal the thoracic duct was attempted 6 weeks after transplant but was unsuccessful. She

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developed a chylous leak from the abdominal portion of the thoracic duct, resulting in chylous ascites. On POD 55, she underwent right sided video-assisted thoracoscopy with lysis of adhesions and mass ligation of the thoracic duct, but the chylothorax persisted. Both sirolimus and everolimus were tried after transplant without success. Whereas sirolimus was reasonable well tolerated pre-transplant, she developed anasarca after transplant. Everolimus was started at 5 mg, increased to 10 mg daily, and continued for 6 weeks. However, she developed ill-defined bilateral lung infiltrates and hypoxia not attributable to acute rejection or infection. These resolved after discontinuation of the drug.

Five months after transplant she underwent thoracotomy with repeat ligation of the thoracic duct and two additional large lymphatic tributaries, as well as mechanical and chemical pleurodesis resulting in resolution of the chylothorax. A Denver shunt was placed to control chylous ascites. This shunt would require multiple revisions, manipulations, and replacements over the next 2 years and finally removed. She was referred to a second tertiary care center with a specialized lymphangiography unit for an opinion and possible intervention. Exploratory laparotomy was performed in an attempt to identify and treat culprit vessels. A Denver shunt was placed on the left side, which would continue to require manipulations and revisions and was removed and replaced with an external drainage catheter.

The patient was referred back to the same "specialized in lymphatic interventions" center for additional attempts at percutaneous treatment. Magnetic resonance (MR) lymphangiography demonstrated significant lymphatic leak from the left pelvic and lower retroperitoneal lymphatic masses (Figure 1). Intranodal lymphangiography was then performed with oil-based iodinated contrast (Lipiodol; Guerbet Group, Princeton, NJ, USA) to verify the location of the lymphatic leak. Under fluoroscopy guidance, the retroperitoneal lymphatic masses were accessed transabdominally using a 21G Chiba needle (Cook Inc, Bloomington, IN, USA). The iodinated contrast was then injected through the needle to confirm its position in the masses (Figure 1). The masses leading to the leak, were then embolized through the needle using N-butyl cyanoacrylate (N-BCA) glue (Trufill; Codman Neuro, Raynham, MA, USA) diluted 1:3 with Lipiodol. During embolization a small amount of glue leaked through an iliac vein into pulmonary circulation. The pulmonary emboli were then successfully removed from a right pulmonary vein using an endovascular snare through the right femoral vein approach. The output from the drain decreased over the next few days, and the drain was removed.

Her symptoms would finally be controlled in the following 12 months.

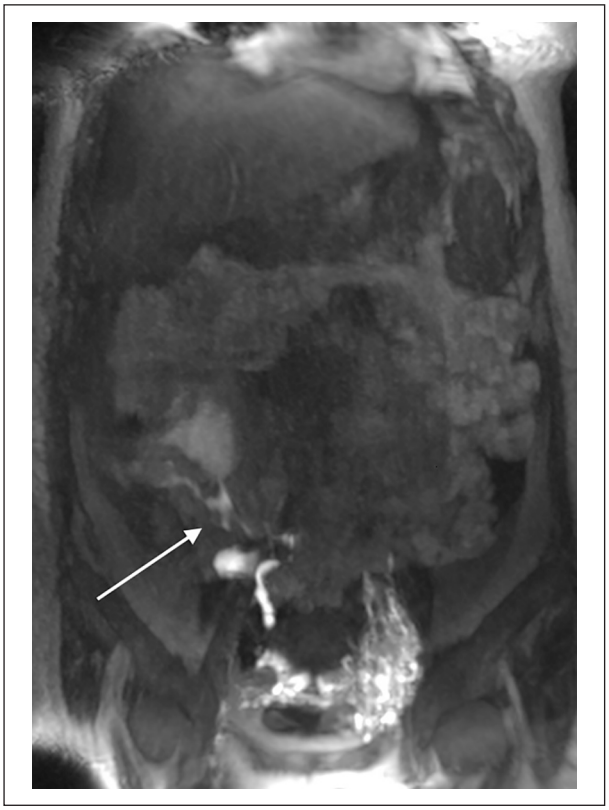

Figure 1. Iodinated contrast to verify the location of the lymphatic leak.

Discussion

LAM is a rare disorder characterized by abnormal proliferation of smooth muscle cells alongside the peribronchial, perivascular, and perilymphatic areas of the lung, which leads to diffuse destructive cystic changes in the lung parenchyma. The pathophysiology of LAM predominantly involves growth and migration of LAM cells identified by pathological staining for receptors such as Human Melanoma Black -45 (HMB-45). Despite a histologically benign appearance, LAM cells can be isolated from peripheral blood; therefore, capable of hematogenous spread to the lung.[6] Furthermore, LAM has recently been characterized as a low-grade, destructive, metastasizing disease. Proliferation of LAM cells may cause lymphatic obstruction. The role of mammalian target of rapamycin (mTOR) inhibitors (sirolimus) for LAM in the immediate pre- and post-transplantation period remains controversial.[7,8] In addition mTOR inhibitors, while sometimes beneficial, have been associated with lung toxicity. In our case, the patient developed bilateral infiltrates, which resolved after drug discontinuation.

In our previous series, we observed significant clinical benefit of sirolimus in patients with symptomatic lymphangioleiomyoma and post-transplant persistent chylous effusions.[9,10] Sirolimus had also been previously described elsewhere as a potential treatment for similar manifestations.[11] Chylothorax after lung transplantation for LAM is a well-known complication with about 10%–30% incidence rate. Lymph collections 3–4 days post transplant suggests a mechanical complication such as thoracic duct trauma, whereas late collections are

likely LAM related. In general, post-operative chylothorax can cause immunosuppression with increasing vulnerability for fatal infections. It may also cause respiratory dysfunction, nutritional deficiencies, and dehydration. The management of post-operative chylothorax is often difficult and sometimes refractory to conservative measures, leading to a prolonged hospital stay. There is no universally accepted algorithm for treatment of chylothorax and the approach remains controversial. Progressive treatment includes modalities of medical, interventional, surgical, and irradiation.

1. Medical treatment: The initial management which consists of (NPO, TPN, and subcutaneous somatostatin) usually fails to stop the drainage. The disturbed integrity of the duct wall leads to massive nutritional loss which is most often compensated by the administration of complete parenteral nutrition which provides an additional benefit as 60%–70% of absorbed fats enter the bloodstream through the thoracic duct.[12]
2. Interventional treatment: In case of unsuccessful conservative management, repeated therapeutic thoracentesis or chest tube drainage may be tried before proceeding to invasive surgical treatment. An indwelling pleural catheter (IPC) may be used and has the advantage of outpatient application.[13] Alternately, more aggressive procedures should be applied to control chylothorax.[14] A successful transabdominal approach to the cisterna chyli has been described in LAM after lung transplantation.[15] In a recent study, management by thoracic duct embolization has proven efficacious in treating chylous effusions with a 62% success rate.[16] For chylothorax, thoracoscopy or thoracotomy with lung decortication, and thoracic duct ligation with or without mechanical pleurodesis is an alternative method and may be more effective than thoracic duct embolization.[17]
3. Surgical treatment: In case of persistent, so-called "high volume" chylothorax with a daily chyle loss of more than 1000 mL lasting 5 days,[18,19] conversion from conservative to surgical treatment is recommended, most often by ligating the thoracic duct which could be combined with mechanical pleurodesis or pleurodesis with sclerosing agents (nitrogen mustard, tetracycline, and talc). Pleurodesis with povidone–iodine was first reported in 2002 and has a 58%–75% success rate in lower output cases. This treatment is controversial due to concerns for renal failure, hyperthyroidism, allergic reaction, and cardiorespiratory failure.[20]

In our case, peritoneovenous shunting for treatment of refractory ascites was attempted with a Denver® shunt (CareFusion Corporation, San Diego, CA, USA) pump with a single-valve. The single-valve pump provides faster flow rates (30–55 mL/min).[21] This device required multiple revisions and replacements (six occasions over 2 years), including multiple thrombolytic applications, predominantly due to recurrent fibrin blockages. Ultimately, symptoms were best controlled by persistent and directed embolization at a center with a specialized lymphangiography unit.

4. Irradiation treatment: One of the less frequent approaches is the irradiation of the thoracic duct which was described by Gerstein et al.[22] Fractional irradiation of the celiac trunk and of the thoracic duct with a dose of 20.4 and 15 Gy, respectively, resulted in the complete remission of chylothorax in a patient with mediastinal lymphadenopathy complicating lymphoma. The major decrease in drained waste was already observed at a dose as low as 7.5 Gy.[23]

Conclusion

Chylothorax and chyloperitoneum may be a devastating complication in patients with LAM who undergo thoracic surgery, and may be refractory to medical, radiological, and surgical treatments. New treatment options have to be considered in this group of patients, including referral to specialized lymphangiography units. The combined surgical and interventional radiological approach, while not novel in their own right, suggest that a multi-modal interventional approach may be required in refractory cases.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Our institution does not require ethical approval for reporting this individual case as it does not include any vital information about the donor or recipient.

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Informed consent

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