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CASE REPORT

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A chylothorax in a young woman: The difficulties of medical management

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Abstract

Lymphangioleiomyomatosis is a rare pulmonary disease affecting women of childbearing age. Whilst chylothorax is a well-recognized complication of the condition, management strategies aren't well-defined, have low success rates and are often only available at tertiary or specialist centres. We describe a case of a young woman referred to pleural clinic with a chylous effusion found to be secondary to lymphangioleiomyomatosis. Initial medical management was unsuccessful and recurrent drainages caused significant complications. Remission was ultimately achieved with a combination of mTOR inhibitors and interventional radiology techniques.

KEYWORDS

chylothorax, lymphangiogram, lymphangioleiomyomatosis, pleural effusion

INTRODUCTION

Lymphangioleiomyomatosis (LAM) is a rare disease affecting women of child-bearing age. Chylothorax is a well-recognized complication yet optimal management has not been well defined. In this report, we describe the presentation and management of a patient with refractory chylothorax secondary to LAM.

CASE REPORT

A 40-year-old lady was referred to the pleural clinic with a new unilateral effusion, from which 1.2 L of milky fluid was aspirated (Table 1, Figure 1A). Her effusion reaccumulated rapidly, requiring 1.5–2 L drainage weekly and drainage of 2 L of chyloascites.

Two years prior, she had undergone excision and biopsy of a large multi-cystic abdominopelvic mass. Her post-operative course was complicated by wound dehiscence and persistent leakage of milky fluid. Histology showed an encapsulated neoplasm comprising myoid cells with round to oval nuclei lining interconnected spaces and diffuse expression of desmin and SMA (Figure 1B). They were positive for HMB45 and oestrogen receptors, confirming perivascular epithelioid cell (PEC) origin (Figure 1C). The histological appearances were of a lymphangioleiomyoma. A computed tomography (CT) scan of the chest showed no evidence of chylothorax, pulmonary cysts or interstitial thickening to suggest pulmonary lymphangioleiomyomatosis. Tamoxifen was initially used to treat the oestrogen receptor positive abdominal mass, as tamoxifen is a partial agonist of oestrogen receptor alpha. She had a good initial response with reduction in the size of the residual abdominal masses.

Given her previous LAM diagnosis, we commenced a low-fat diet and trialled Octreotide, with no reduction in her chyle production. Advice was sought from the National Lymphangioleiomyomatosis Centre in Nottingham, UK. Tamoxifen was stopped in the absence of clinical benefit, and she commenced Sirolimus, with the caveat that improvement could take several months.

She was subsequently admitted with hypoalbuminaemia (17 g/L, normal 35–50 g/L), acute kidney injury and hypovolaemic hyponatraemia, secondary to nutritional losses from repeated drainages. An indwelling peritoneal catheter (IPC) was inserted, and drained 2 L daily with 500 mL of 5% human albumin solution (HAS) supplementation.

She was trialled on total parenteral nutrition (TPN) and kept nil by mouth. This reduced chyle output by 30% but daily outputs remained over a litre.

She underwent a lymphangiogram, which identified a leak from the truncated lymphatic duct in the posterior mid-abdomen, and embolization. Her leak reduced but did not resolve. Surgical intervention was felt likely to reverse the benefits achieved by Interventional Radiology (IR) and medical management. Further embolization was unsuccessful and she was discharged home with regular IPC drainages and HAS supplementation.

Eight months after commencing Sirolimus, and 4 months following embolization, chyle drainage from her IPC reduced and it was removed. She had a persistent, right-sided serous pleural effusion, which resolved following 4 months of drainage via an indwelling pleural catheter. She remains stable on Sirolimus without recurrence after 4 years. We estimate that she drained over 200 L of chyle in the 12–18 months described.

TABLE 1 Pleural fluid biochemistry results.

Biochemistry	Result (normal range)
Protein	52 g/L (<15 g/L)
Lactate dehydrogenase	472 U/L (<50% plasma concentration)
Glucose	2.8 mmol/L (similar to plasma glucose)
Triglycerides	15.3 mmol/L (<2 mmol/L)
Cholesterol	2.8 mmol/L (3.5–6.5 mmol/L)

DISCUSSION

This case report highlights the multiple mechanisms by which chylothorax in LAM can develop, including transdiaphragmatic movement of chylous ascites, following surgical intervention on lymphangioleiomyomata, obstruction of the thoracic duct by smooth muscle cells and ooze from pulmonary lymphatics. This case shows how refractory chylothoraces can be and demonstrates the multiple

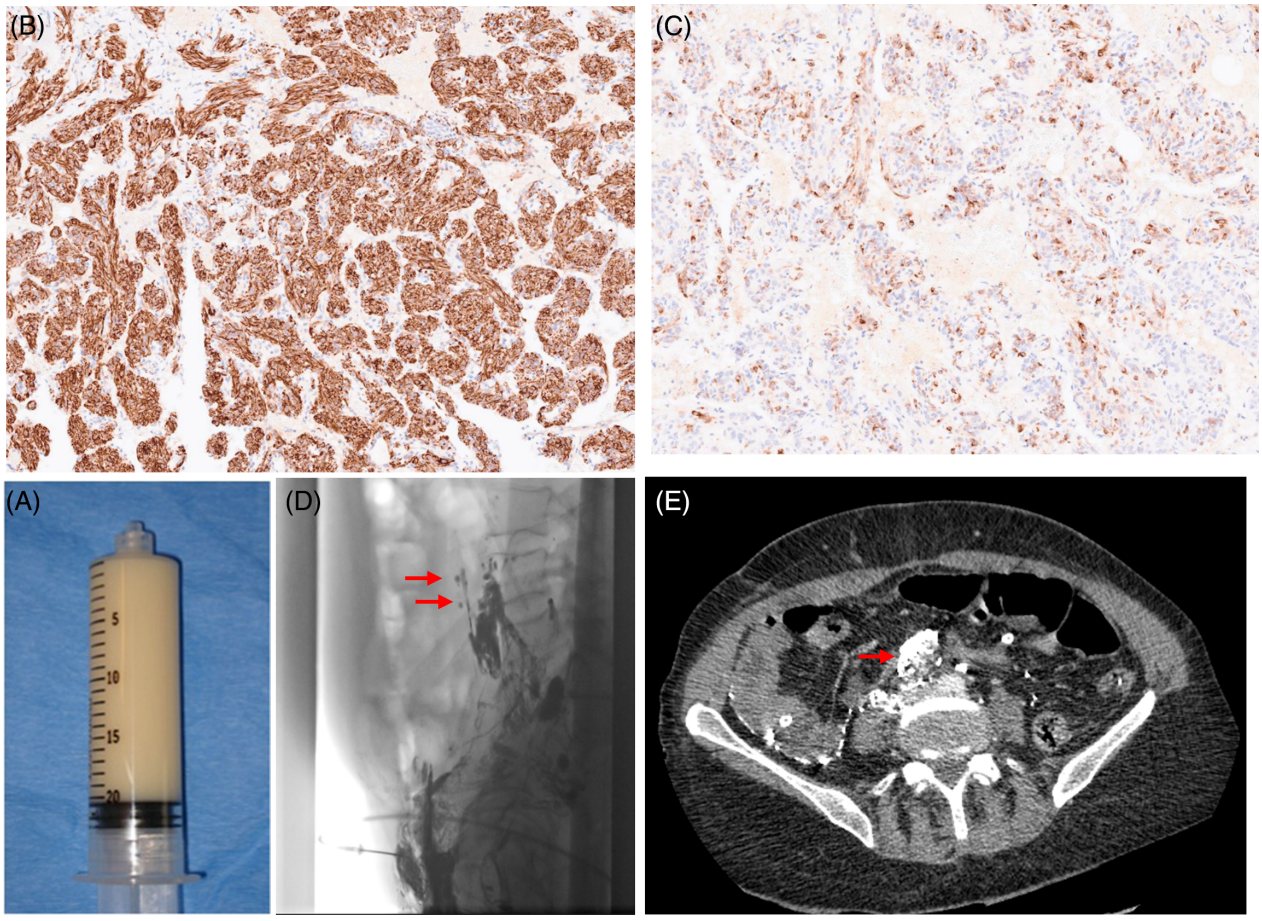

FIGURE 1 (A) A syringe showing the typical appearances of a chylothorax. (B) Tumour cells showing diffuse nuclear expression for desmin receptor (smooth muscle marker). (C) Tumour cells showing patchy HMB45 expression. (D) Image from lymphoscintigraphy showing drops of Lipidiol leaking from defect in lymphatics (red arrows). (E) Image from CT performed post-lymphoscintigram showing glue patch at identified leak in lymphatic duct (red arrow). Traces of lipidiol are seen retroperitoneally and within the adjacent lymphatics.

treatment options available, and how these can be employed sequentially and in combination.

Initial aspiration appearances could be consistent with a chylothorax, pseudochylothorax or empyema. Of note, a small proportion of chylothoraces are not milky in appearance. Sending fluid for cholesterol and triglyceride levels helps differentiate these possibilities.

Histological assessment of lymphangioleiomyomata is challenging in serosal cavities where the tumour surface is lined by mesothelial cells and may be mistaken for mesothelioma. Careful assessment reveals a lack of atypia and a lymphangioma-like growth pattern that should point towards a lymphangioleiomyoma diagnosis. The combination of smooth muscle actin and HMB45 expression is the hallmark of tumours of the PEComa group, securing the diagnosis of LAM.[1]

Around 30% of patients have lymphatic involvement on CT although symptomatic chylous collections are less common.[2] Management is challenging, due to chyle reaccumulation, loss of serum proteins and leucocytes and the risk of infection. mTOR inhibitors cause lymphatic remodelling, overcoming lymphatic obstruction, reducing lymphatic masses and symptoms.[3] As the effect of mTOR inhibitors may take months, starting treatment early and reducing chylous leaks by physical means is recommended. Surgical interventions convey high risk of post-operative leakage, but IR techniques may have more success.

mTOR inhibitors have transformed treatment for women with LAM, but only suppress disease activity. Cessation of treatment is associated with resumption of disease activity[4] therefore sirolimus is currently used indefinitely. Long-term treatment is generally well-tolerated.[5]

Interventional management of ongoing chyle leak is often required. Lymphoscintigraphy, in which a radiotracer is injected into the lymphatics, rarely accurately localizes the leak. Lymphangiogram, in which lipiodol is injected directly into the groin lymph nodes can more accurately localize the leak and allow embolization. Small case series suggest that lipiodol is mildly sclerosant, therefore may be effective alone or in combination with glue. Many cases require multiple attempts, and conservative management should be continued to assess the effects of a procedure prior to considering it further. Lymphangiography is a long procedure; for all but the most stoical, it is better performed under general anaesthesia.

Management of chylothorax can be challenging, and conservative management, such as diet modification, bowel rest and pharmacological options can be insufficient or slow to improve symptoms. More invasive techniques have better outcomes but rely on access to skilled clinicians able to provide this service which may require multiple attempts.

AUTHOR CONTRIBUTIONS

E. Barton drafted and collated the manuscript. S. Johnson provided expert perspective on lymphoangioleiomyomatosis. N. Collin reviewed the radiological images and provided radiologist input for the manuscript. N. Bhatt reviewed the pathological images and provided pathologist input for the manuscript. N. Maskell provided expert opinion on the management of our patient's pleural disease. All authors have reviewed and approved the manuscript.

CONFLICT OF INTEREST STATEMENT

N. Maskell has unrestricted research grants from and sits on paid advisory boards for Rocket Medical Plc and BD. The other authors have no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

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REFERENCES

1. Gupta N, Finlay GA, Kotloff RM, Strange C, Wilson KC, Young LR, et al. Lymphangioleiomyomatosis diagnosis and management: high-resolution chest computed tomography, transbronchial lung biopsy, and pleural disease management. An official American Thoracic Society/Japanese respiratory society clinical practice guideline. Am J Respir Crit Care Med. 2017;196(10):1337–48.
2. McCarthy C, Gupta N, Johnson SR, Yu JJ, McCormack FX. Lymphangioleiomyomatosis: pathogenesis, clinical features, diagnosis, and management. Lancet Respir Med. 2021;9(11):1313–27.
3. Taveira-DaSilva AM, Hathaway O, Stylianou M, Moss J. Changes in lung function and chylous effusions in patients with lymphangioleiomyomatosis treated with sirolimus. Ann Intern Med. 2011;154(12):797.
4. McCormack FX, Inoue Y, Moss J, Singer LG, Strange C, Nakata K, et al. Efficacy and safety of sirolimus in lymphangioleiomyomatosis. N Engl J Med. 2011;364(17):1595–606.
5. Bee J, Fuller S, Miller S, Johnson SR. Lung function response and side effects to rapamycin for lymphangioleiomyomatosis: a prospective national cohort study. Thorax. 2018;73(4):369–75.

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