

# Chylous Ascites as a Presentation of Lymphangioliomyomatosis

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## ABSTRACT

A 35-year-old woman presented to the hospital with a 4-week history of large-volume chylous ascites refractory to paracentesis and new-onset dyspnea. Thoracic computed tomography revealed diffuse pulmonary cystic lesions with pleural effusions, and abdominal computed tomography showed ascites with large bilateral retroperitoneal masses displaying positron emission tomography avidity. Biopsy of the masses demonstrated lymphatic invasion by a perivascular epithelioid cell neoplasm, a smooth muscle tumor. The patient was diagnosed as having the sporadic form of lymphangioliomyomatosis and was treated with the mammalian target of rapamycin pathway inhibitor sirolimus with clinical improvement.

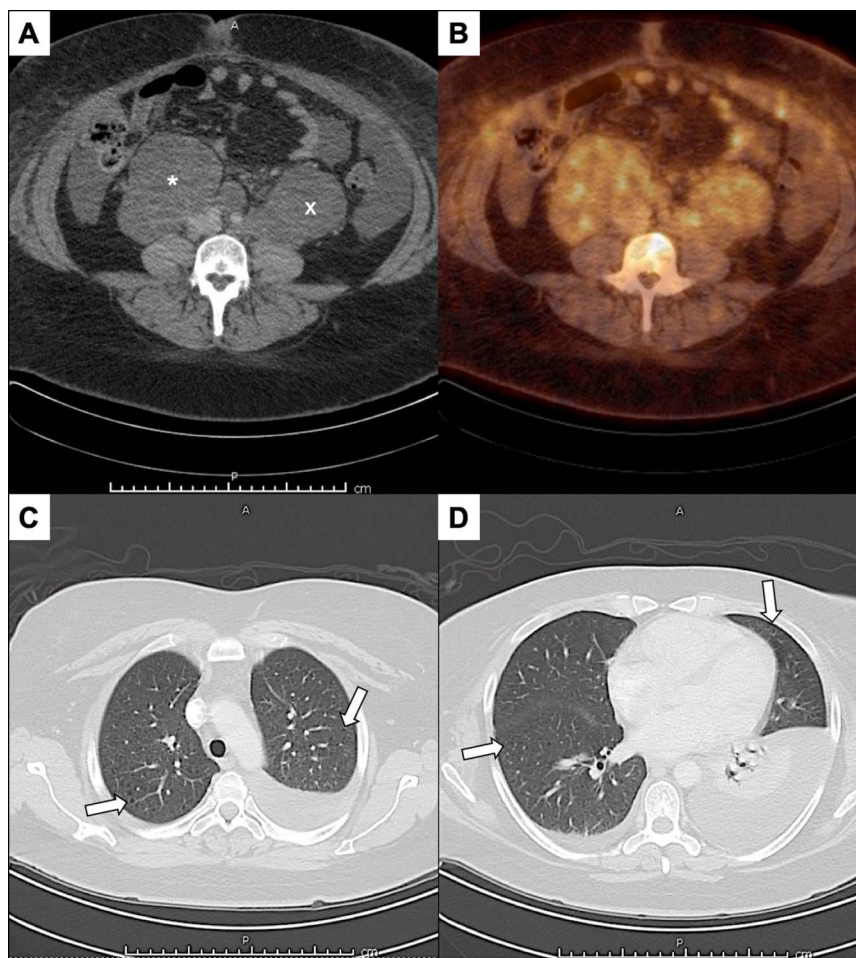
## INTRODUCTION

Lymphangiomyomatosis (LAM) is a rare progressive multisystem disease that almost exclusively affects women of childbearing age as either a sporadic form (S-LAM) or as part of a syndrome linked to the autosomal dominant disorder tuberous sclerosis LAM.<sup>1,2</sup> The incidence for S-LAM is 1–2.6 cases per 1,000,000 women.<sup>3</sup> The disorder is characterized by a diffuse proliferation of abnormal smooth muscle cells characteristic of a group of proliferative tumors termed perivascular epithelioid cell tumors.<sup>4</sup> Patients typically present with pulmonary symptoms such as progressive dyspnea, cough, pneumothorax, hemoptysis, and chylous pleural effusions.<sup>5–7</sup> Clinical suspicion for this disorder can be triggered by extrapulmonary manifestations. Renal angiomyolipomas are a common extrapulmonary finding in S-LAM, but chylous ascites, lymphatic cystic lesions, and axial/retroperitoneal lymphadenopathy can also be seen.<sup>8,9</sup> However, S-LAM presenting with extrapulmonary symptoms alone is uncommon. Here, we present the case of a 35-year-old woman with LAM who presented with progressive abdominal distention and recurrent chylous ascites.

## CASE REPORT

A 35-year-old woman without a significant medical history presented with abdominal distention and associated discomfort for the past 4 weeks. Her symptoms did not progress until 2 weeks before admission, at which time she received a large-volume paracentesis and was instructed to follow-up with her primary care physician. While awaiting that appointment, her symptoms recurred, prompting her to return to the medical center where she was admitted to the hospital. The patient reported that the abdominal discomfort was positional, diffuse, and not associated with oral intake. Associated symptoms included an unintentional 40-pound weight loss over 2 months and dyspnea on exertion. She had no nausea, vomiting, diarrhea, urination changes, decreased appetite, or reduced nutritional intake. The patient denied taking supplements or medications other than aripiprazole for bipolar disorder and levothyroxine for hypothyroidism, without recent dose adjustments. The patient had no known history of cardiac, renal, or liver disease. Social history was notable for lack of alcohol consumption.

On initial presentation, the patient was afebrile, normotensive, had normal sinus rhythm, tachypneic to 26/min, and hypoxemic, with SaO<sub>2</sub> 86% on room air. Her body mass index was 49 kg/m<sup>2</sup>. An abdominal examination revealed a distended abdomen that was



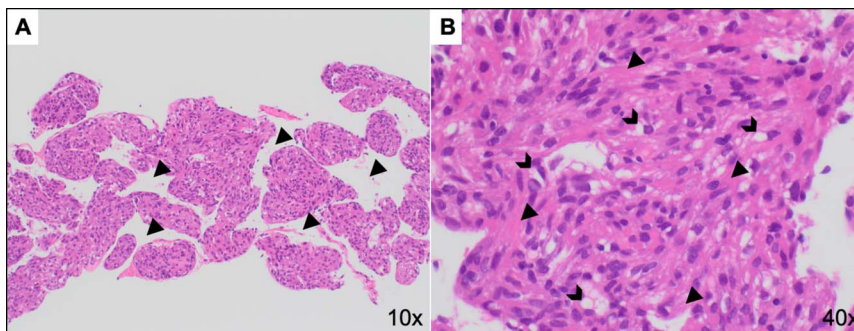
**Figure 1.** Thoracic and abdominal positron emission tomography and computed tomography—(A) A transverse section of the abdomen, showing enlarged retroperitoneal lymphadenopathy, measuring up to 9.3 cm on the right (\*) and 8.0 cm on the left (×). (B) Approximately the same transverse section of the abdomen as seen in panel A, 60 minutes after the administration of  $^{18}\text{F}$ -fluorodeoxyglucose, demonstrating hypermetabolic activity within the enlarged retroperitoneal lymph nodes; SUV max 4.4. A transverse section of the thorax, demonstrating diffuse bilateral cystic changes of the (C) upper and (D) lower lobes of the lung (arrow), and pleural effusions measuring fat attenuation.

diffusely tender to palpation without rebound or guarding and positive for a fluid wave. The pulmonary examination revealed bilateral lower lobe crackles. Laboratory test results were notable for a normal complete blood count and basic metabolic profile, alkaline phosphatase (65 U/L), aspartate aminotransferase (6 U/L), alanine aminotransferase (9 U/L), total bilirubin (0.2 mg/dL), hypoalbuminemia (2.7 g/dL) without an elevated globulin gap, international normalized ratio (1.06), an elevated thyroid stimulating hormone (4.4 mIU/mL), and normal free T4 (1.22 ng/dL). Urinalysis was negative for proteinuria. Serum antinuclear and double-stranded DNA antibodies were negative.

Diagnostic paracentesis revealed a light pink milky ascitic fluid. Analysis of the fluid revealed a nucleated cell count of 399/cumm with 38% neutrophils and markedly elevated triglycerides (1,734 mg/dL). Further analysis of the ascitic fluid included negative body fluid cultures and a negative Gram stain, and acid-fast bacillus stain. Cytology did not demonstrate malignant cells. Serum triglycerides were noted to be within normal

range (86 mg/dL), and serum QuantiFERON-TB Gold was negative. A positron emission tomography and computed tomography demonstrated bilateral hypermetabolic retroperitoneal lymph nodes measuring up to 9.3 cm and small to moderate bilateral pleural effusions, both measuring fat attenuation (Figure 1). Also present were diffuse pulmonary cystic lesions that were well-defined, round, thin-walled, and did not display lobar predominance (Figure 1). A biopsy of the retroperitoneal lymph node showed a smooth muscle tumor, histologically positive for HMB45, SMA, desmin, D2-40, and with a low Ki-67 score consistent with a perivascular epithelioid cell tumor (Figure 2). Based on these findings, a diagnosis of S-LAM was made.

Although the patient's abdominal pain improved after paracentesis, her respiratory status continued to deteriorate. She became progressively more tachypneic (35/min) and had increasing oxygen requirements ( $\text{SpO}_2$  80% on BiPAP). Given worsening pleural effusions, the patient had a chest tube placed with the return of chylous fluid, and she was placed on a high



**Figure 2.** Histopathology of the biopsied retroperitoneal lymph node. (A) A proliferation of epithelioid to spindled cells in nests separated by varying sized clefts (carrot) (hematoxylin and eosin stain, 10× magnification) and (B) muscle fibers can be appreciated in association with the spindled cells while clear spaces, likely representing capillaries/lymphatics are seen in association with epithelioid endothelial cells (chevron). No mitoses or significant atypia are identified (hematoxylin and eosin stain, 40× magnification).

flow nasal cannula. After a workup for infectious causes was negative, the patient was started on sirolimus at 2 mg/d with subsequent improvement in respiratory status, weaning of respiratory support, and removal of her chest tube. The patient was discharged home on sirolimus and did not require further paracentesis. During a follow-up appointment several months later, she was noted to have significant improvement in her symptoms and radiographic evidence of disease with a plan to continue on long-term therapy with sirolimus.

## DISCUSSION

Although S-LAM is rare pulmonary disease, chylous ascites is a well-documented presentation of this disorder.<sup>3,10</sup> S-LAM is caused by somatic mutations in the tuberous sclerosis complex-1 (*TSC1*) and tuberous sclerosis complex-2 (*TSC2*) genes, which indirectly inhibit activity of the mammalian target of rapamycin complex 1 (mTORC1).<sup>11</sup> Overactivity of mTORC1 causes excess cellular growth and proliferation and primes patients to develop the benign tumors characteristic of LAM. These benign tumors can invade into the lymphatic system resulting in obstruction of lymphatic flow, causing chyle to accumulate in the thoracic and abdominal cavity.<sup>12</sup>

LAM is categorized as a cystic lung disease, as reflected by the American Thoracic Society/Japanese Respiratory Society Clinical Practice Guidelines. The only required criterion for diagnosis is a characteristic HRCT of the chest.<sup>13</sup> However, presenting symptoms can be extrapulmonary, and the pulmonary radiologic manifestations of LAM can be subtle and overlooked on initial imaging.<sup>14</sup> The onus for diagnosis of a case presenting with chylous ascites may therefore be the responsibility of the internist or consulting gastroenterologist and argues for greater awareness of this systemic disease.

Treatment options for LAM were advanced in 2011, with the MILES trial showing that therapy with the mTOR inhibitor Sirolimus effectively stabilizes pulmonary function and reduces symptoms.<sup>15</sup> Although long-term outcomes with sirolimus have not been well studied, there is no known cure for LAM and

many patients experience progressive respiratory failure requiring evaluation for a lung transplant.<sup>16</sup>

## DISCLOSURES

Author contributions: All authors contributed equally to this manuscript. JH McLain is the article guarantor.

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