The Hidden Diagnosis: Uncovering LAM Behind Dyspnea and an Elevated ANA

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- A 23-year-old woman presented with progressive shortness of breath unrelieved by significant weight loss. Workup showed a pericardial effusion, elevated ANA, diffuse cystic lung changes on CT, and a chylous pleural effusion. Retroperitoneal lymphangioleiomyomas and elevated VEGF-D confirmed the diagnosis of sporadic lymphangioleiomyomatosis (LAM). She was started on sirolimus with early symptom improvement.
- LAM is an uncommon multisystem disorder in which abnormal smooth muscle–type cells grow within the lungs and lymphatic tissues. This process causes progressive cystic changes in the lungs, recurrent fluid collections such as chylous effusions, and tumors in abdominal or retroperitoneal sites. Diagnosis is often delayed because symptoms mimic more common conditions (4).
- This case highlights the importance of considering LAM in young women with unexplained dyspnea or pleural effusions. Early recognition and sirolimus therapy can stabilize disease. An osteopathic approach addressing respiratory mechanics and lifestyle support is essential for long-term care.

Case Description

- A 23-year-old woman presented with progressive shortness of breath over several months, despite losing 50 pounds through increased activity.
- Initial evaluation revealed a moderate pericardial effusion. (figure 1)
- Rheumatologic screening showed a markedly elevated ANA titer (>1:1280, speckled pattern).
- Chest CT demonstrated diffuse cystic lung changes and a moderate to large right pleural effusion. (figure 2 and QR code)
- Thoracentesis removed 1 liter of chylous pleural fluid.
- Abdominal CT showed revealed retroperitoneal lymphangioleiomyomas (figure 3)
- Lab work showed VEGF-D 1,365 pg/mL (elevated).
- Based on these findings, sporadic LAM was diagnosed.
- Sirolimus therapy was initiated, alongside pulmonary rehabilitation and close follow-up. Patient experienced early improvement in dyspnea and stabilization of effusions. She remains under multidisciplinary follow-up, with continued pulmonary rehabilitation and oxygen support as needed.

Literature Review

- Lymphangioleiomyomatosis (LAM) is a rare, progressive lung disease that primarily affects women of reproductive age. It is caused by abnormal smooth muscle-like cells infiltrating the lungs and lymphatics, leading to cystic lung destruction, pneumothorax, chylous effusions, and retroperitoneal tumors (1).
- Prevalence is estimated at 3–8 per million women but is likely underdiagnosed due to symptom overlap with asthma and COPD (3).
- LAM occurs in two forms:
  - **TSC-LAM**: in patients with tuberous sclerosis complex
  - **Sporadic LAM**: in women without TSC
- Mutations in **TSC1/2** activate the **mTOR pathway**, driving proliferation and lymphangiogenesis. **Diagnosis** is based on high-resolution CT showing characteristic cysts, plus one confirmatory feature (e.g., angiomyolipoma, chylous effusion, elevated VEGF-D ≥800 pg/mL) (5).
- **Management** has advanced with mTOR inhibitors (sirolimus, everolimus), which stabilize lung function and reduce lymphatic complications (2). Remaining challenges include optimizing long-term therapy, tracking progression, and developing curative treatments.

Conclusions/Discussion

- **Early initiation of sirolimus** stabilizes lung function, reduces recurrence of chylous effusions, and improves quality of life.
- This case underscores how overlap with autoimmune disease (high ANA, effusions) can delay recognition and highlights the need for persistent, integrative clinical reasoning. The generalized symptomology of LAM can delay a proper diagnosis.
- **Multidisciplinary care** (pulmonology, radiology, rheumatology, cardiology) and referral to specialized centers are essential for optimal management.
- From an osteopathic perspective, supporting respiratory mechanics, lifestyle optimization, and patient empowerment are key strategies in managing chronic rare lung disease.
- **Future directions:** improved biomarkers, optimized long-term use of mTOR inhibitors, and the pursuit of remission-inducing therapies.

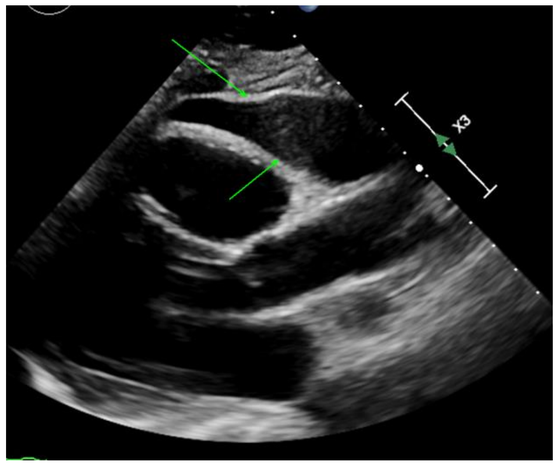

Figure 1: Parasternal long axis view on transthoracic echocardiogram showing an anterior pericardial effusion adjacent to the right atrium and right ventricle

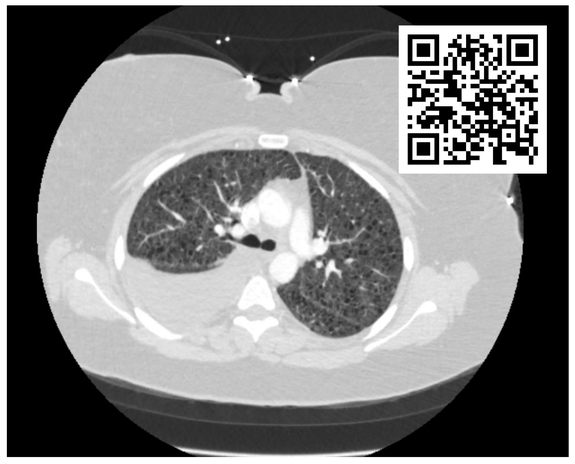

Figure 2: CT chest with lung windows showing large right-sided pleural effusion and diffuse cystic changes throughout the lungs (scan QR code for video)

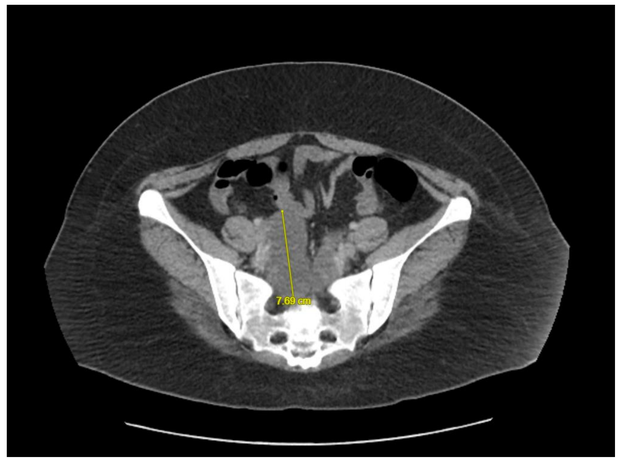

Figure 3: Abdominal pelvic CT revealing multiple low-density masses in the retroperitoneum and bilateral pelvis along the iliac vessels suggestive of lymphangioleiomyomas. A reference mass in the right iliac region spans approximately 7.7 cm.

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