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### **A 35-year-old man with recurrent pneumonia and whitish sputum**

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#### **Summary conflict of interest statements**

The authors declare that they have no conflict of interest for the submitted work.

**Case presentation:**

A 35-years-old man was admitted for recurrent episodes of pneumonia. He complained of a 2 months history of exertional dyspnea and productive cough with whitish and viscous sputum poorly responsive to antibiotic therapy. He also reported a weight loss of 5kg since the first symptoms appeared. There was no dysphagia, fever, or chest pain. He currently did not use medication and did not have a relevant medical history except a current 10 pack-year smoking history. He did not report any history of trauma or respiratory exposure to fats.

**Physical Examination Findings**

Vital signs were as follows: temperature 36.4°C, BP 125/80 mmHg, heart rate 82 beats/min, respiratory rate 14 breaths/min, and oxygen saturation 95 % on room air without desaturation on exertion. Inspiratory crackles were found in the right lower pulmonary field on chest examination. Cardiac examination revealed normal heart sounds without murmurs, no peripheral edema, and no jugular venous distension. Lymph node examination revealed no lymphadenopathy. Skin and nails were normal.

**Diagnostic Studies**

Lung functional tests revealed a decrease of transfer factor for carbon monoxide (TLCO: 53% of predicted values, carbon monoxide transfer coefficient (KCO: 61%) and lung volumes (TLC: 85%).

Chest tomography showed diffuse interlobular septal thickening and peribronchovascular interstitial thickening associated with patchy ground-glass attenuation mainly in the right lung. No pleural effusion was noted (Fig. 1A).

Echocardiography and neck vessels doppler sonography were normal.

Laboratory test including a WBC count, procalcitonin, CRP, serum creatinine, LDH showed no abnormalities. Antinuclear and anti-granulocyte-macrophage colony stimulating factor antibodies were negative. Blood cultures were negative.

Broncho-alveolar lavage (BAL) revealed a milky liquid, with  $14.4 \times 10^5$  cells/ml, 62% lipid-laden macrophages on hematoxylin and eosin staining and on Oil-red-O staining (Fig. 2, A-B) with weak PAS staining and containing 0.72g/l triglycerides. Testing of this fluid by culture and polymerase-chain-reaction assay for bacterial, fungal, and viral pathogens did not reveal any evidence of infection. Histological examinations of bronchial biopsies showed an infiltrated chorion full of histiocytes, some of which contained a foamy cytoplasm (Fig. 2, C-D). There was no sign of malignancy.

Non-contrast magnetic resonance lymphography revealed excessive proliferation and distension of thoracic lymphatic vessels in both lungs on T2-weighted images (Fig. 1 B-F). Thoracic canal was normal. In addition, excessive proliferation and distension of lymphatic vessels were also seen in cervical and axillary regions. No other extrathoracic abnormalities were found.

**Question: What is the diagnosis?**

**Diagnosis: Chyloptysis due to diffuse pulmonary lymphangiomatosis (DPL).**

### **Discussion**

The diagnosis and management of chyloptysis starts with the recognition of expectoration of milky-white sputum rich in chyle. It is a rare finding and may be challenging, particularly in cases without an accompanying chylous pleural effusion. Chyloptysis in adults should prompt assessment for evidence of lymphatic obstruction from trauma, radiation, and malignancy, and of diseases with known association with chyloptysis as thoracic lymphangiectasis, diffuse

pulmonary lymphangiomatosis (DPL), lymphangiomyomatosis, or yellow nail syndrome.

Diffuse pulmonary lymphangiomatosis involves both lungs and, by definition, is without extra-thoracic lymphatic abnormalities. It appears to be due to a lymphatic developmental abnormality. Pathologic features include a proliferation of complex anastomosing lymphatic channels that markedly expand the typical lymphatic routes within the lungs and mediastinum.

DPL most frequently presents in late childhood but has been described in patients ranging from birth up to 80 years. There is no clear sex predilection. Lymphangiomas may be found within the mediastinum, adherent to the pleura, or within the chest wall. Mediastinal fat may be diffusely infiltrated with anastomosing, dilated lymphatics. The adjacent lung parenchyma may contain collections of hemosiderin-laden macrophages but in contrast to lymphangiomyomatosis, the lung parenchyma is preserved.

The symptomatology is variable including acute dyspnea and chyloptysis when a distended lymphatic ruptures in the bronchial tree, or chylothorax due to a ruptured lung subpleural lymphangiectasis. Chyloptysis may be evaluated for the presence of triglycerides in sputum. Chest imaging can be normal or may show ground-glass opacities and interstitial thickening.

The most relevant examination is magnetic resonance lymphography, in which proliferation and dilation of the lymphatic vessels are identified. In addition, lymphatic leakage may be visible in case of associated effusion (chylothorax, chylopericardium). Finally, this examination allows a detailed study of thoracic lymphatic anatomy, which is essential for therapeutic decision-making and of identification of extra-thoracic lesions.

In patients suffering from DPL, there are no specific treatments. Conservative management should be considered with a diet low in cholesterol and long-chain triglycerides and rich in medium-chain triglycerides. Other options including surgical interventions, systemic treatment (corticosteroids, immunomodulating agents, propranolol and chemotherapy),

radiation therapy, could be considered but are mainly to alleviate clinical symptoms. The value of surgical resection is impaired by the variety of possible lymphatic configurations and by the difficulty to separate lymph collections from normal structures and should be considered for localized intrapulmonary or mediastinal lesions.

### **Clinical course**

Four weeks after a strict fat-free diet, we observed a significant improvement of the symptoms and lung function tests (DLCO: 91%, KCO: 87%, TLC: 92% of theoretical values). Chest X-ray significantly improved with a disappearance of a middle lobar consolidation. After 7 months of follow-up, no recurrence was observed and no further treatments were administered.

### **Pearls**

- Chyloptysis in adults should prompt assessment for evidence of lymphatic obstruction from trauma, radiation, and malignancy, and to exclude diseases with known association with chyloptysis (lymphangiomatosis, yellow nail syndrome, or thoracic lymphangiectasis)
- A lymphangiogram or a magnetic resonance lymphography is recommended to define the abnormality.
- There are no specific treatments for diffuse pulmonary lymphangiomatosis. Patient may respond to either dietary modification.

## **Suggested readings**

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## Figures legends

Figure 1. Imaging of CT scanner and non-contrast magnetic resonance lymphography of the chest. A, CT scanner of the chest showing diffuse interlobular septal and peribronchovascular interstitial thickening associated with patchy ground-glass attenuation mainly in the right lung. B-F, non-contrast magnetic resonance imaging and magnetic resonance lymphangiography of the chest on T2-weighted images showing excessive proliferation and distension of thoracic lymphatic vessels in both lungs, with normal thoracic duct.

Figure 2. A-B, Microscopic examinations showing hypercellular broncho-alveolar lavage rich of lipid-laden macrophages. A, Hematoxylin and eosin staining, original magnification, x40. B, Oil-red-O staining, original magnification, x40. C-D, Bronchial biopsies. C, Hematoxylin and eosin staining showing foamy histiocytes (arrow) infiltrating chorion (original magnification, x20). D, Immunohistological analysis showing positive staining for the histiocytes markers CD68 (original magnification, x2).



