Life-threatening Pulmonary Lymphedema Secondary to Thoracic Duct Ligation

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Abstract

We herein report an extremely rare adult case presenting with life-threatening pulmonary lymphedema secondary to generalized lymphedema. A 47-year-old woman with generalized lymphedema from her feet to below her chest, had undergone surgical ligation of the thoracic duct and bilateral pleurodesis for the treatment of intractable idiopathic chylothorax three years earlier. Chest computed tomography demonstrated bilateral ground-glass opacities, air-space consolidation and interlobular septal wall thickening, presenting as a crazy-paving appearance predominantly on the gravity side. Bronchoalveolar lavage revealed marked lymphocytosis. She was treated with long-term oxygen therapy with noninvasive positive-pressure ventilation, followed by lymphovenous anastomoses of the lower extremities.

Key words: chylothorax, crazy-paving appearance, fatal, pulmonary lymphedema, respiratory failure


Introduction

Lymphedema is characterized by an abnormal accumulation of lymphatic fluid in tissues. Secondary lymphedema, which is usually localized, can arise from disruption of the normal lymphatic circulation by trauma, infection, surgery, radiation or cancer. This condition can cause physical discomfort, pain, impaired function and emotional distress due to aesthetic and psychological problems, thereby affecting the patient’s quality of life (1). However, life-threatening problems, such as respiratory failure due to pulmonary lymphedema, are extremely rare. We herein report an adult case of respiratory failure secondary to generalized lymphedema.

Case Report

A 47-year-old woman presented with dyspnea, a productive cough and generalized edema extending from the feet to below the chest. She had a history of thoracic surgery, which had been performed three years earlier at another hospital. She had developed bilateral pleural effusions due to intractable idiopathic chylothorax refractory to management with a fat-restricted diet, and she had undergone surgical ligation of the thoracic duct, followed by bilateral pleurodesis, for the treatment of chylothorax. A positron emission tomography scan before surgery showed no significant uptake of 18F-fluorodeoxyglucose or lymph node enlargement. One month after surgery, the patient developed edema in her lower extremities that gradually worsened, and by 2.5 years after the thoracic duct ligation, it finally extended to below the chest. Combination treatment with furosemide, manual lymphatic drainage and compression bandages was not effective to improve her edema. The patient consulted our university hospital for further evaluation and treatment when dyspnea and a productive cough developed three years after the thoracic duct ligation.

The patient’s body weight had increased from 47 kg at her healthy baseline to a maximum of 92 kg due to extreme lymphedema. Bilateral coarse crackles in the lower posterior portion of her thorax were heard on auscultation of the chest. Chest radiography on admission showed bilateral infiltrative shadows, predominantly in the middle to lower lung fields, which had deteriorated compared to the findings six months before (Fig. 1). Chest high-resolution computed tomography (HRCT) demonstrated bilateral ground-glass opacities, air-space consolidation and interlobular septal wall thickening, showing a crazy-paving appearance, predomi-
Figure 1. Chest radiography at six months before admission (A) showed mild bilateral pulmonary infiltrative shadows, predominantly in the lower lung fields, which had deteriorated up to the middle lung fields on admission (B).

Figure 2. A chest high-resolution computed tomography scan on admission demonstrated bilateral ground-glass opacities, air-space consolidation and interlobular septal wall thickening presenting as a crazy-paving appearance predominantly on the gravity side of the lungs.

An arterial blood gas analysis under 1 L/min of nasal oxygen showed hypoxemia, with a partial pressure of oxygen (PaO₂) of 56.7 mmHg, an oxygen saturation (SaO₂) of 90.4% and an alveolar-arterial oxygen tension difference (A-aDO₂) of 68.0 mmHg. The laboratory data revealed decreased serum levels of albumin (2.5 g/dL) and Na⁺ (130 mEq/L). The serum levels of brain natriuretic peptide (<4.0 pg/mL, normal value <18.4 pg/mL), KL-6 (91 U/mL, normal value <500 U/mL), surfactant protein-A (10.6 ng/mL, normal value <43.8 ng/mL), surfactant protein-D (<17.3 ng/mL, normal value <110 ng/mL), angiotensin-converting enzyme (5.1 IU/L, normal value range from 8.3 to 21.4 IU/L) and carcinoembryonic antigen (<0.2 ng/mL) were within the normal limits.

Bronchoalveolar lavage (BAL) from the right B9 segment (recovery 95 mL/150 mL instilled) with the patient in the back lateral decubitus position revealed a yellow turbid fluid collection (Fig. 3) and markedly increased numbers of total cells at 11.0×10⁵/mL, with lymphocytosis (83.2%), which was CD3⁺ T cell-dominant (96.3%) without clover leaf cells. The CD4/CD8 ratio of BAL lymphocytes was 3.36. The
The color of the bronchoalveolar lavage (BAL) fluid. The first collection of the BAL fluid is shown on the bottom left, and the third collection of BAL fluid is shown on the top left. The control was saline.

The lipid content of the BAL fluid was low at 4 mg/dL for triglycerides and 8 mg/dL for total cholesterol. The total protein and albumin levels in the BAL fluid were 1.2 g/dL and 0.4 g/dL, respectively.

Transbronchial lung biopsy (TBLB) specimens showed the accumulation of acidophilic material by hematoxylin and eosin staining (Fig. 4A), CD68+ foamy macrophages without cholesterol crystals in the alveoli (Fig. 4B) and some lymphocyte infiltration without granuloma formation, which excluded the possibility of sarcoidosis or malignancies, including malignant lymphoma. The periodic acid-Schiff staining and immunohistochemical staining for surfactant protein-A (PE10 antibody, Fig. 4C) of the TBLB specimens were negative, which excluded the possibility of pulmonary alveolar proteinosis (PAP). The lymphatic vessels detected by the D2-40 antibody in the TBLB specimens did not show malignancy or abnormal dilation (Fig. 4D).

The cultures of the BAL fluid were negative for bacteria, including *Mycobacterium spp.* and fungi. These data suggested that the pulmonary edema was secondary to lymphedema and not due to other causes, including PAP, cancer, sarcoidosis or heart failure. Lymphangiography (Fig. 5) revealed severe lymphangiectasia in the lower extremities and accumulation of iodine-based contrast medium in the subcutaneous tissues from the toes to below the chest. The patient was treated with expectorants, a fat-restricted diet and long-term oxygen therapy (LTOT) with noninvasive positive-pressure ventilation (NPPV), followed by repeated surgical lymphovenous anastomoses of the lower extremities in the Orthopedic Department of our university. These treatments led to temporary improvements of her symptoms, oxygenation and opacities on chest radiography. The patient moved to a clinic near her house, but the respiratory failure and lymphedema gradually worsened again. She was admitted to another hospital due to respiratory failure and sepsis. She died of the progression of respiratory failure and septic shock secondary to *Staphylococcus aureus* pneumonia four years after the thoracic duct ligation.

**Discussion**

We treated an extremely rare case of life-threatening pulmonary lymphedema secondary to thoracic duct ligation due to uncontrollable idiopathic chylothorax in an adult. Lymphedema can be categorized as either localized or generalized lymphedema, but generalized lymphedema is rare. Localized lymphedema can be managed by a combination of manual lymph drainage, compression bandages, therapeutic exercises and guidance for self-treatment (2). Our patient was treated with these techniques, but these were not effective due to the massive generalized lymphedema. In general, diuretics are not effective for obstructive lymphedema, although a diuretic had been administered to our patient. Early care for the skin and nails is also important for preventing phlegmon in patients with lymphedema. Supporting the utility of such treatment, our patient was instructed about skin care and did not develop phlegmon. There have been no adult cases of life-threatening pulmonary lymphedema secondary to generalized lymphedema reported in the literature, although a similar case of fatal pulmonary lym-
Figure 4. The transbronchial lung biopsy (TBLB) specimen showed the accumulation of acidophilic material in alveoli by Hematoxylin and Eosin staining (A) and CD68+ foamy macrophages without cholesterol crystals in the alveoli (B) and some lymphocyte infiltration without granuloma formation or malignancy. The immunohistochemical staining of the acidophilic material in the TBLB specimen was negative for surfactant protein-A (PE10 antibody, C). The immunohistochemical staining of the TBLB specimen with the D2-40 antibody showed that there was no malignancy or abnormal dilation of the lymphatic vessels (D). Original magnification, ×200.

Figure 5. Lymphangiography revealed severe lymphangiectasia in the lower extremities and the accumulation of iodine-based contrast medium in the subcutaneous tissues below the chest.

Lymphangiectasia with intractable chylothorax, possibly due to a congenital cause, treated by thoracic duct ligation was reported in a 20-month-old girl (3).

Congenital lymphangiectasia was not the cause of the symptoms in our patient, as this condition always presents in infancy and is fatal. Chylothorax and lower extremity lymphedema can develop in adult patients with lymphangioleiomyomatosis (LAM) (4, 5). However, in our patient, the lymphedema developed after thoracic duct ligation, and thin wall cystic lung lesions, characteristic of LAM or renal angiomyolipomas, were absent, suggesting that LAM was unlikely to be the cause of the generalized lymphedema. Another disease causing lymphedema and chylothorax is yellow nail syndrome, characterized by the triad of yellow nails, lymphedema and pleural effusions (6), but this syndrome was not the cause in our patient.

A crazy-paving appearance on chest HRCT can be observed in patients with PAP, pulmonary alveolar microlithiasis, adult T-cell leukemia/lymphoma, exogenous lipid pneumonia, *Pneumocystis jirovecii* pneumonia, mucinous bronchioalveolar carcinoma, sarcoidosis, organizing pneumonia and adult respiratory distress syndrome (7-11). We excluded the other possible causes of pulmonary edema, including congestive heart failure and PAP, and finally diagnosed the patient with pulmonary lymphedema with generalized lymphedema secondary to thoracic duct ligation. A crazy-paving
appearance with ground-glass opacities, air-space consolidation and interlobular septal wall thickening, predominantly on the gravity side of the chest HRCT, and the serum-like yellow, turbid appearance of the BAL fluid with excessive lymphocytosis suggested abnormal accumulation of lymphatic fluid in the lungs.

Since the alveolar spaces were filled with excess lymphatic fluid, we first tried to treat the patient with LTOT with NPPV to improve the oxygenation, and expectorants to reduce sputum, in addition to a fat-restricted diet; subsequently, the desaturation was improved. However, these treatments were not enough to relieve the dyspnea and the productive cough.

As noted above, congenital generalized lymphangiektasia may lead to pulmonary lymphedema. In a case of congenital generalized lymphangiektasia complicated by pulmonary lymphedema in an infant, percutaneous puncture in the lower extremities was one of the treatments used to discharge the lymphatic fluid (12). This procedure was reported to be safe, easy and effective for improving the quality of life, but it may have side effects such as hypoproteinemia, impaired immune responses and/or infections. Another technique for reducing extremity lymphedema, surgical lymphovenous anastomosis, is effective for symptom improvement and volume reduction (13). Our patient was treated with surgical lymphovenous anastomoses to reduce the lymphatic stream, and this was effective to some extent.

Nevertheless, massive generalized lymphedema is difficult to treat, and the above treatments were only symptomatic treatments. The present patient eventually died of respiratory failure and septic shock due to Staphylococcus aureus pneumonia in another hospital, in spite of intensive treatment with mechanical ventilation and antibiotics, including meropenem and linezolid. To our knowledge, this is the first report of life-threatening respiratory failure due to pulmonary lymphedema in an adult secondary to thoracic duct ligation and pleurodesis.

Lymphedema is usually localized and rarely induces pulmonary lymphedema with respiratory failure; however, physicians and surgeons should nevertheless be aware of this unusual form of lymphedema as a complication of thoracic duct ligation for the treatment of an intractable idiopathic chylothorax.

The authors state that they have no Conflict of Interest (COI).

References