Chylothorax in POEMS Syndrome

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Chylothorax results from various causes, such as malignancy, trauma, or infection. POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes) is a multisystemic syndrome that is associated with plasma cell disorder. Pleural effusion is a common manifestation of POEMS syndrome, but the association of POEMS syndrome with chylothorax has not been reported. We report on a 61-year-old female patient who initially presented with dyspnea and bilateral leg edema. Importantly, the patient had normal renal function. Her chest X-ray and computed tomographic imaging showed bilateral pleural effusion, and her chest drainage revealed chylothorax. Detailed examination failed to reveal the definitive cause of the chylothorax. She received several treatments for chylothorax, namely, a low-fat diet or fasting, total parenteral nutrition, a somatostatin analog (octreotide), thoracic duct ligation by video-assisted thoracic surgery, and pleurodesis. However, further examination revealed endocrinopathy, monoclonal plasma cell disorder, peripheral neuropathy, and elevation of the serum level of vascular endothelial growth factor. The patient’s condition was consequently diagnosed as POEMS syndrome. Eventually, her chylothorax was controlled by pleurodesis, and she was transferred to another hospital for stem cell transplantation. Herein, we report on the apparent first case of POEMS syndrome with chylothorax. In some cases of idiopathic chylothorax, the underlying primary disease may be latent, such as in the present patient. POEMS syndrome is rare, but this syndrome should be included in the differential diagnosis of chylothorax with unexplained etiology.

Keywords: chylothorax; pleural effusion; POEMS syndrome; vascular endothelial growth factor; video-assisted thoracic surgery


Introduction

POEMS syndrome is defined by the presence of polyneuropathy (P), a monoclonal plasma cell disorder (M), and paraneoplastic features, specifically organomegaly (O), endocrinopathy (E), and skin changes (S). Other signs are frequently observed in affected patients such as pleural effusion, sclerotic bone lesions, Castleman disease, papilledema, thrombocytosis, peripheral edema, ascites, polycythemia, fatigue, and clubbing. Not all features are required to make the diagnosis (Dispenzieri 2012).

Pleural effusion is a common manifestation of POEMS syndrome; however, there have been no reports about the relationship between POEMS syndrome and chylothorax. To the best of our knowledge, this is the first report of POEMS syndrome associated with bilateral chylos pleural effusion.

Clinical Report

In 2011, a 61-year-old woman presented with dyspnea and only bilateral leg edema, without edema of the upper limbs and face; her chest X-ray film and computed tomographic (CT) image showed bilateral pleural effusion (Fig. 1). Her renal function was normal (serum creatinine: 0.7 mg/dL). She had received routine medical check-ups annually, and her X-ray films showed no abnormality. Her CT image also revealed ascites, but showed no evidence of mediastinal lymph node swelling. Her past medical history included carpal tunnel syndrome, an operation 2 years previously, and previous hospitalization for the treatment of pleural effusions.

Right chest drainage showed pleural effusion, in which the triglyceride (TG) level was 89 mg/dL, the lactate dehydrogenase (LDH) level was 109 IU/L, and the total protein (TP) level was 3.2 mg/dL, indicating exudative chylothorax. A puncture sample of the left pleural effusion yielded a
TG level of 241 mg/dL, and the ratio of pleural-fluid LDH to serum LDH was 0.62, indicating exudative chylothorax. General laboratory values were within the normal range. Ultrasound cardiography showed no evidence of heart failure. There was no cytological evidence of malignancy. The bacterial and mycobacterial cultures of the pleural effusion showed no evidence of infection. Furthermore, upper gastrointestinal endoscopy, colonoscopy, and positron emission tomography/computed tomography (PET/CT) demonstrated no evidence of abnormality. Treatments included a low-fat diet or fasting, total parenteral nutrition (TPN), and a somatostatin analog (octreotide); consequently, the pleural effusion transiently decreased. However, the pleural effusion increased when she resumed a normal diet. She was transferred to our hospital for additional examination and treatment.

A chest X-ray on admission to our hospital showed bilateral pleural effusion and slight collapse of the right lung. Right chest drainage was performed and the pleural effusion yielded 630 mL of serous material, in which the TG level was 15 mg/dL while she was under a low-fat diet. Magnetic resonance thoracic ductography demonstrated a left pleural effusion and a normal thoracic duct (i.e., no evidence of collapse) (Fig. 2).

One hour before the induction of general anesthesia, she was given 50 mL of cream to help identify the leakage of chyle. Video-assisted thoracic surgery (VATS) was performed via the right side (with her body in the left lateral decubitus position). We searched for the thoracic duct in the right thoracic cavity through the 3 ports, but there was no observable chyle leakage. The structure that was likely to be the thoracic duct at the root of the thoraco-abdominal junction was clipped. A chest tube was placed in the right pleural cavity.

Right pleurodesis using picibanil (OK-432) was performed postoperatively, followed by left pleurodesis, because VATS was presumed to be ineffective and it was necessary to control the left pleural effusion without any other treatment. Thereafter, the bilateral pleural effusion did not increase and it was possible to manage the chylothorax.

Endocrinological examination revealed subclinical abnormality (Table 1). The serum thyroid stimulating hormone level was slightly elevated, and the free T3 (FT3) and T4 (FT4) levels were within the normal range. Although the serum luteinizing hormone, follicle stimulating hormone, and estradiol levels were within the normal range, the serum prolactin level was elevated. The serum growth
hormone level was slightly elevated. The serum immunoglobulin levels were all lower than the normal values. Serum and urine electrophoresis revealed monoclonal protein (Bence Jones protein $\lambda$-type), and a bone marrow aspiration specimen showed slight elevation of normal plasma cells (18.0%). She had no thrombocytosis. Serum vascular endothelial growth factor (VEGF) and interleukin-6 (IL-6) levels were elevated (Table 1). A nerve conduction study revealed a decrease in the conduction velocity of the median nerve bilaterally. The condition was eventually diagnosed as POEMS syndrome, and she was transferred to another hospital for stem cell transplantation. Details were not provided, but she appeared to have received autologous peripheral blood stem cell transplantation, and treatment with thalidomide and bortezomib. Ten months afterwards, she had remained well without any signs of recurrence.

**Discussion**

Chylothorax results from disruption of the thoracic duct or its tributaries, leading to the presence of chyle in the pleural space. Approximately 50% of cases are due to malignancy (particularly lymphoma), 25% to trauma (particularly during surgery), and the remainder is from miscellaneous causes such as tuberculosis, sarcoidosis, and amyloidosis (Turton 1987). Chyle contains high levels of triglyceride (110 mg/dL), an essential feature for diagnosis (Maskell and Butland 2003). The methods for imaging the thoracic duct include not only lymphangiography but also magnetic resonance lymphography (Takahashi et al. 2003); magnetic resonance lymphography was used in our patient to evaluate the thoracic duct. Our patient received a low-fat diet, TPN, octreotide therapy, and thoracic duct ligation as treatments for chylothorax, and pleurodesis was finally performed.

POEMS syndrome is a rare disease with unknown cause. In 2012, Dispenzieri published the major and minor diagnostic criteria of POEMS syndrome (Dispenzieri 2012). Plasma and serum levels of VEGF are markedly elevated in patients with POEMS syndrome, and the levels correlate with the activity of the disease. Recently, anti-VEGF monoclonal antibodies have been used therapeutically (Sekiguchi et al. 2013). During the course of the disease, 3%-43% of patients with POEMS syndrome developed pleural effusions (Dispenzieri 2012). However, there was no report of chylothorax associated with the disease. A recent report revealed that POEMS syndrome was related to renal functional impairment, which may result in edema; however, this was not necessarily included in the diagnostic criteria (Nakamura et al. 2013). Our patient met 3 major criteria (polyneuropathy, monoclonal plasma cell proliferative disorder, and VEGF elevation) and 2 minor criteria (extravascular volume overload [pleural effusion, edema] and endocrinopathy), although her polyneuropathy symptoms were mild and her renal function was normal.

Approximately 6% of patients with multiple myeloma (MM) develop pleural effusions, and chylothorax is reportedly associated with MM (Kintzer et al. 1978; Davis and Clark 1986). Pleural effusion in MM is usually benign and are due to congestive heart disease, chronic renal failure, hypoalbuminemia, cardiac amyloidosis, pulmonary infarctions, or infections. On the other hand, malignant pleural effusion is related to pleural involvement secondary to extension of the chest wall, or pleural or pulmonary plasmacytoma; 8 in 958 patients with MM (0.8%) had pleural effusion caused by myeloma involving the pleura (Kintzer et al. 1978). In our patient, there was no cytological or thoracoscopic evidence of malignancy. It was reported that the chylous effusion was bilateral in 16% of the patients and due to the disruption at the level of the thoracic vertebrae or the movement of the chylous ascites following the same
pathways as for the laterality of hepatic hydrothorax (Huggins 2010). Pleurodesis has been successful as a result, and it may have been a reasonable treatment for our patient because chylothorax was possibly a result of the pleural changes caused by long-term inflammation or obstruction of a peripheral lymphatic vessel, not the collapse of the thoracic duct.

In conclusion, we report on the apparent first case of POEMS syndrome with chylothorax. Furthermore, in some cases of idiopathic chylothorax, the underlying primary disease may be latent such as in this case. Thus, POEMS syndrome should be included in the differential diagnosis of chylothorax with unexplained etiology.

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Conflict of Interest

The authors declare no conflict of interest.

References


