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Case report

Successful treatment of a patient with chyluria due to lymphangioleiomyomatosis using sirolimus

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ABSTRACT

Lymphangioleiomyomatosis (LAM) is a rare and progressive neoplastic disease of young woman, characterized by the proliferation of abnormal smooth muscle-like cells (LAM cells) in the lungs and axial lymphatics. A 44-year-old woman was referred to our hospital because pleural effusion was detected during a health checkup. She had chylothorax, chylous ascites, and chyluria, and her computed tomography scan showed a solid tumor in the pelvis. Surgical biopsy was performed; she was diagnosed as having LAM. We could not control the fluid collection and chyluria using standard medical treatments. Therefore, we chose to administer sirolimus, and her symptoms dramatically improved. The mechanism of chyluria presumably involved LAM cell infiltrates in the ureter via the lymphatic vessel flow, which causes LAM to develop because of ureter wall exposure.

1. Introduction

Lymphangioleiomyomatosis (LAM) is a rare disease that affects 3.4–7.8 persons per 1 million [1], and it occurs exclusively in women of reproductive age [2]. Pathologically, it is characterized by the proliferation of abnormal smooth muscle-like cells (LAM cells) in the lungs and axial lymphatics, including the mediastinum and retroperitoneum, and lymphangiogenesis in the lesion [3]. Patients with LAM often develop respiratory symptoms and signs, such as exertional dyspnea, pneumothorax, and hemosputum [4]. Approximately 15% of patients with this disease have been diagnosed based on the presence of chylothorax, chylous ascites, renal angiomyolipomas, and lymphangioleiomyomatosis of the retroperitoneum and pelvis [4].

We herein describe our experience with one patient with LAM who had chylous ascites and chyluria due to LAM cells infiltrating the ureter. Her condition remarkably improved after administering sirolimus.

2. Case report

A 44-year-old woman was found to have pleural effusion on a chest radiograph during an annual health checkup in July 2016. Her computed tomography (CT) scan showed pleural effusion, ascites fluid, and a nodular lesion of the pelvis; therefore, we suspected peritoneal cancer. There was no familial history of tuberous sclerosis complex. She had a history of tonsillectomy at 28 years of age and lumbar disc herniation at 36 years of age.

The physical examination at the initial visit revealed that her height was 156 cm, body weight was 48.6 kg, body temperature was 36.1 °C, blood pressure was 104/62 mmHg, radial pulse rate was 80/min, and respiratory rate was 18/min. No superficial lymphadenopathy was identified on palpation. She had neither anemia nor jaundice. Auscultations of her heart and lung sound were normal. The abdomen was slightly distended, which indicated the presence of ascites.

Results of the biochemical examination of blood at the initial visit were normal, except for the hemoglobin level of 10.5 g/dL (reference range 11.6–14.8 g/dL). Regarding tumor markers, the carbohydrate antigen 125 level was 628 U/mL (reference range 0.0–35.0 U/mL). As for results of the pulmonary function test, percentage vital capacity (% VC) and 1% forced expiratory volume (FEV1.0%) were within normal range (%VC: 83.8%; FEV1.0%: 98.4%), but the percentage diffusing capacity of the lung carbon monoxide (%DLco) and percentage diffusing capacity of the lung carbon monoxide/alveolar ventilation (%

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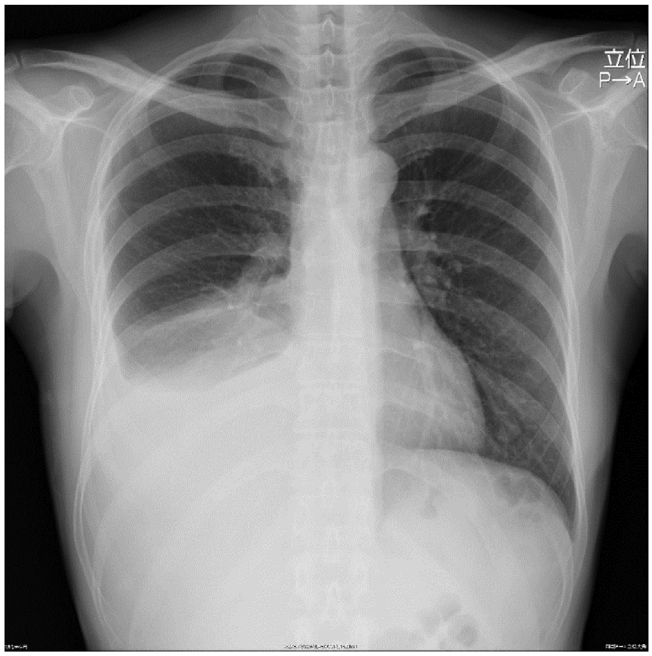

Fig. 1. Radiological findings on admission. Chest radiograph revealing right pleural effusion.

DLco/VA) were slightly decreased (%DLco: 76.0%; %DLco/VA: 72.0%). The chest radiograph revealed right pleural effusion with mild to moderate retention (Fig. 1), and the chest CT scan showed moderate accumulation of the right pleural effusion with multiple thin-walled cysts in both lung fields (Fig. 2A). The enhanced abdominal CT scan demonstrated ascites and slightly heterogeneous tumorous lesions of the right pelvis (Fig. 2B). However, there was no evidence of any renal angiomyolipomas. Even the magnetic resonance imaging scan of the pelvic area showed similar findings.

The patient's clinical course is presented in Fig. 3. She did not have an appetite because of the presence of ascites fluid with severe retention at the initial visit. The ascites fluid was chylous ascites (Fig. 4A). Despite the use of diuretics (furosemide and spironolactone), albumin therapy, abdominocentesis, and cell-free and concentrated ascites reinfusion therapy, we could not control the ascites fluid, and the patient

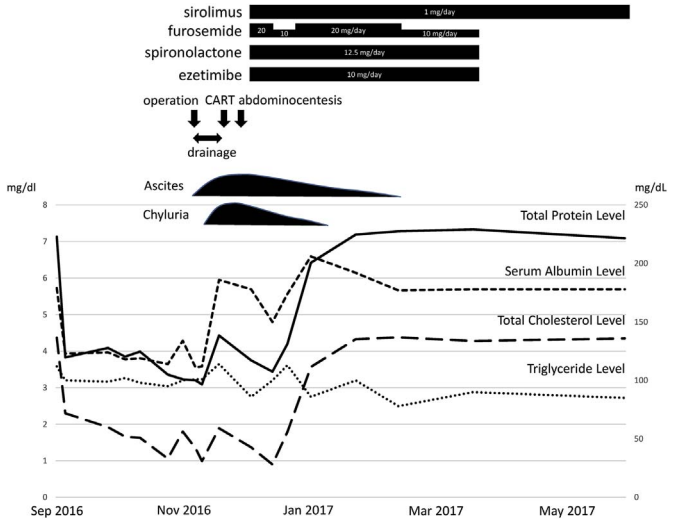

Fig. 3. Patient's clinical course.

developed significant hypoproteinemia and hypoalbuminemia. In November, enucleation of the right retroperitoneal tumor was performed. According to the histopathological examination, the cell that had a kind of circular nucleus from a uniform circle in acidophilic cytoplasm stained by hematoxylin-eosin formed a strand from a vacuole nest and multiplied (Fig. 5A). Additionally, a part of the same type of cell became spindle-shaped and was complex (Fig. 5B). The immunohistochemical stain was positive for smooth muscle actin (Fig. 5C), HMB45 (Fig. 5D), and MelanA (Fig. 5E), leading to the diagnosis of LAM. Postoperatively, we noticed that chyluria (Fig. 4B) had worsened, and a diagnosis of nephrotic syndrome was made (daily urinary protein level: 11,258 mg/day; daily urinary albumin level: 4675.45 mg/day). There was no oval fat body or fatty cast with urinary sediment, so the cause of nephrotic syndrome was regarded as chyluria due to lymphatic vessel obstruction with LAM, not a glomerular abnormality. Although lymphangiography was performed to confirm the position of the fistula in the thoracic duct, we could not detect it. We hypothesized that stenosis or occlusion of the lymphatic vessel by tumor invasion within the pelvis would exist.

Next, the oral administration of 1 mg/day each of sirolimus and

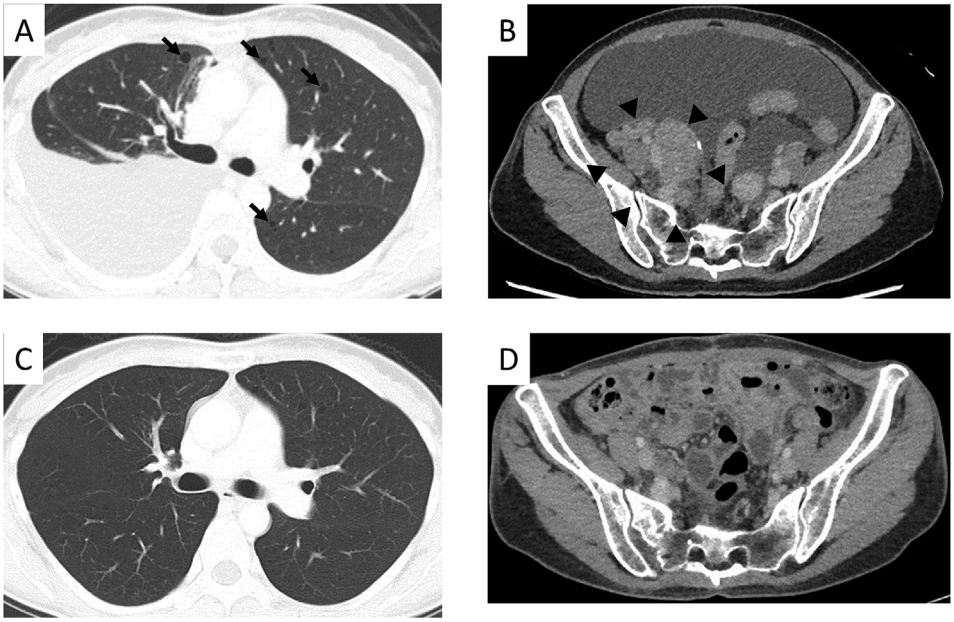

Fig. 2. Computed tomography (CT) scans (1.25-mm slice) on admission (A, B) and after 2 months of sirolimus treatment (C, D). A: Chest CT scan revealing moderate accumulation of the right pleural effusion and multiple thin-walled cysts (arrows) in both lung fields. B: Enhanced abdominal CT scan demonstrating ascites and a solid tumor (arrowheads) in the right pelvis. C: Chest CT scan revealing that the multiple small cysts in both lungs are stable and pleural effusion retention is decreased. D: Enhanced abdominal CT scan showing that the quantity of ascites fluid and size of the tumor lesion are smaller.