Bilateral Chylothorax in a Renal Transplant Recipient: Case Report and Literature Review

Osama Gheith, Torki Al Otaibi, M.R. Narayanan Nampoory, Hosam Attia, Medhat Halim, Tarek Said, Prasad Nair, Mohamed Balaha, Waleed Awadein, Zakaria Zakariya, Hasanein Aboatteya, Nawas Moideenkutty

Abstract

Chylothorax is the accumulation of chyle in the pleural cavity as a result of damage to the lymphatic ducts. We treated a young man who was a kidney transplant recipient who had a prior internal jugular vein permanent catheter for hemodialysis, who developed dyspnea and hypoxemia. Chest radiography showed bilateral pleural effusion. Analysis of the white, milky, cloudy, odorless effusion fluid showed cell count > 500/μL; lymphocytes, 60%; total protein, 3.6 mg/dL; urea nitrogen, 45 mg/dL; creatinine, 90 μmol/L; triglycerides, above 2.2 mmol/L (repeatedly high); lactate dehydrogenase, 450 U/L (normal); and cultures, no growth. Magnetic resonance imaging showed thrombosis of the major neck veins, superior vena cava, and azygos vein. Treatment included pleural drains, gut rest, and dietary modification, octreotide, and warfarin. The chylothorax resolved with no relapse. In summary, chylothorax may occur in patients associated with thrombosis of major veins associated with a permanent dialysis catheter.

Key words: Dyspnea, Hemodialysis, Internal jugular vein catheter, Pleural effusion

Introduction

Chylothorax is a pleural effusion consisting of chyle, which is lymphatic fluid enriched with fat and the digestive products of fat absorbed by the intestinal epithelium. Chyle is collected and transported by the thoracic duct to the circulation. Damage to the thoracic duct or tributaries may cause leakage of chyle into the pleural space. In addition, obstruction to the flow of chyle can cause rupture of the lymphatics and chylothorax.

The lymphatic system includes the cisterna chyli, thoracic duct, lymph glands, and lymphatic vessels. The thoracic duct commonly originates from the cisterna chyli and terminates at the junction of the left subclavian and internal jugular veins. The thoracic duct (length, 36 to 45 cm; diameter, 2 to 3 mm) drains intestinal chyle to the bloodstream and the lymphatics of the body, except the right side of the head and neck, right upper limb, right lung, right side of the heart, and convex surface of the liver which are drained by the right lymphatic duct. Normal adult volume of chyle is from 10 to > 100 mL/kg body weight, depending on diet, intestinal absorption, and degree of physical activity.

Chyle contains large quantities of chylomicrons, triglycerides, cholesterol, and fat-soluble vitamins. Central venous catheterization and similar procedures can cause extensive venous thrombosis in the neck. This may impede the drainage of lymph and chyle into the subclavian veins and cause chylothorax.

The diagnosis of chylothorax is made with thoracentesis and pleural fluid analysis. An abundant presence of chylomicrons in the pleural fluid aspirate is diagnostic of chylothorax. When the chylomicron level in the fluid is 50 to 110 mg/dL, lipoprotein analysis is used to evaluate the pleural fluid for
chylomicrons or cholesterol crystals. Fluid triglyceride level > 110 mg/dL may establish the diagnosis, and fluid triglyceride level < 50 mg/dL may exclude the diagnosis of chylothorax. In fasting or malnourished patients, lipoprotein analysis is suggested even when the triglyceride level in the fluid is < 50 mg/dL. In pseudochylothorax—developed with chronic empyema—the cholesterol level is > 200 mg/dL, no chylomicrons are present, and cholesterol crystals are noted on microscopy.

Chylothorax usually is caused by a thoracic duct leak and is suspected in patients with milky effusions and in the presence of specific comorbidities or a history of chest or neck trauma. Transudative chylothorax has been reported when cirrhosis, nephrosis, or heart failure is present. Although most white blood cells in chyle are lymphocytes, chylotroaxes may be neutrophilic, especially after surgery. Typical pleural fluid in chylothorax is a lymphoctic exudate with low lactate dehydrogenase; when atypical fluid is present such as a transudate with high levels of neutrophils or lactate dehydrogenase, there may be additional causes of pleural fluid accumulation.

In a previous report, a 12-year-old patient who had end-stage renal disease and treatment with chronic hemodialysis had a large left pleural effusion that was attributed to multiple hemodialysis access sites in the neck. Repeated reinfusion of chylothorax fluid into the patient was performed in a closed sterile circuit for approximately 7 weeks, to prevent the loss of protein- and T-cell–rich fluid until the chylothorax resolved spontaneously. Reinfusion of chylothorax fluid may be recommended in similar clinical settings. However, literature review showed limited information about chylothorax in young kidney transplant recipients. We treated a patient who had a chylothorax associated with kidney disease and thrombosis of neck veins.

Case Report

An 18-year-old Kuwaiti man had bilateral renal dysplasia and end-stage renal failure, and he had a living-related kidney transplant from his mother in April 1993. After 13 years, the graft was lost because of chronic transplant glomerulopathy, possibly from chronic cyclosporine toxicity. In September 2006, he started hemodialysis and had graft nephrectomy. He developed difficulties with vascular access and benign intracranial hypertension. Therefore, he had a living-unrelated kidney transplant in October 2009, after a desensitization protocol that included immunoadsorption for high panel reactive antihuman leukocyte antigen antibodies (85% for class I and 38% for class II), induction with thymoglobulin, and maintenance with mycophenolate mofetil, corticosteroids, and tacrolimus. The postoperative course was uneventful except for slow graft function because of biopsy-proven acute tubular necrosis and a urinary tract infection (Klebsiella pneumonia) that was treated with levofloxacin. Before discharge from the hospital, mycophenolate mofetil was changed to mycophenolate sodium because of persistent diarrhea, and the right internal jugular vein permanent dialysis catheter was removed.

At 2 months after discharge, he developed dyspnea and hypoxemia. Chest radiography showed bilateral pleural effusion. Drainage of the effusion showed a white, milky, cloudy, odorless fluid consistent with a chylothorax (fluid analysis: cell count > 500/μL; lymphocytes, 60%; total protein, 3.6 mg/dL; urea nitrogen, 45 mg/dL; creatinine, 90 μmol/L; triglycerides, above 2.2 mmol/L (repeatedly high); lactate dehydrogenase, 450 U/L (normal); and cultures, no growth. Echocardiography showed normal ejection fraction, good systolic and diastolic function of both ventricles, and cardiac chambers having average size. Magnetic resonance imaging of the neck showed asymmetry of the right and left internal jugular veins and bilateral pleural effusion (Figures 1A and 1B). Computed tomographic angiography showed a tortuous and thrombosed left internal jugular vein and incomplete thrombi in the right internal jugular and bilateral subclavian and brachiocephalic veins. In addition, incomplete thrombus was observed in the superior vena cava, extending to the right atrium; complete thrombosis of theazygos vein; prominent vertebral veins; and a recanalized umbilical vein that communicated with the mammary veins (Figures 1C and 2).

Bilateral pigtail drains were inserted into the pleural spaces for 3 weeks. Initial treatment included complete gut rest and total parenteral nutrition, and this was changed to a diet containing low fat level or medium-chain triglycerides. After persistence of the chylothorax, he was treated with octreotide (a long-acting somatostatin analog given subcutaneously) and heparin followed by warfarin, and he had a satisfactory response with complete resolution.
In June 2011, the patient was readmitted because of kidney graft dysfunction. Biopsy of the graft showed acute antibody-mediated rejection, and he was treated successfully with plasma exchange through the femoral vein, intravenous immunoglobulin, and rituximab (1 dose). At the most recent follow-up (3 years after he had the chylothorax), graft function was stable, serum creatinine was 152 μmol/L, and he had no relapse of the chylothorax.

Discussion

In June 2011, the patient was readmitted because of kidney graft dysfunction. Biopsy of the graft showed acute antibody-mediated rejection, and he was treated successfully with plasma exchange through the femoral vein, intravenous immunoglobulin, and rituximab (1 dose). At the most recent follow-up (3 years after he had the chylothorax), graft function was stable, serum creatinine was 152 μmol/L, and he had no relapse of the chylothorax.

Discussion

The present patient had bilateral chylothorax, a rare complication in a young kidney transplant recipient, likely because of major vein thrombosis associated with a permanent internal jugular hemodialysis catheter. In the normal adult, the thoracic duct transports approximately 4 L chyle per day, which may enable a rapid and large accumulation of fluid in the chest. Malignancies, either lymphoma (non-Hodgkin lymphoma, 60%) or other malignancies (lung carcinoma), cause > 50% nontraumatic occurrences of chylothorax. 3-6,9,10 Right heart failure with venous hypertension can cause chylothorax. 11,12 Central venous thrombosis and chylothorax may occur in the absence of the usual risk factors—either hereditary thrombophilia or acquired thromboembolic factors—in a patient with septic shock, and procoagulant states such as those induced by sepsis may contribute to the development of chylothorax. 13

In the present patient, oral feeding was associated with marked change in the color and biochemical constituents of the pleural fluid, similar to previously reported findings. 14 Malignancy was excluded with computed tomography and magnetic resonance imaging scans of the chest and abdomen. The patient’s neck veins were used bilaterally for prolonged hemodialysis, which was complicated by thrombosis of both subclavian, internal jugular, and brachiocephalic veins, elevated central venous pressure, and benign intracranial hypertension. Diseases that may increase right-sided central venous pressure, such as restrictive pericarditis, central vein thrombosis, and right ventricular failure, may cause chylothorax. However, not all patients who have right-sided venous hypertension develop chylothorax. 15,16 The development of chylothorax in such cases could be explained by the lymphaticovenous channels within the chest wall, which can contribute to lymphatic drainage in patients who have high central venous pressure. 17 The present patient had an acute clinical presentation, likely because of the large amount of chyle drained by the thoracic duct. 5 The frequency of mortality associated with chylothorax has reached approximately 10% in major medical centers.

Nonoperative treatment may be sufficient in patients who have a small chylothorax, but therapeutic thoracentesis is the initial treatment for a large chylothorax that may cause respiratory distress. Intercostal tube drainage is the preferred method of thoracentesis in most centers. When excessive chyle leak occurs, patients usually are advised to avoid eating or to stay on a low fat diet that is rich in medium-chain triglycerides, which are absorbed directly into the portal circulation. Although dietary changes were attempted, better improvement happened when the patient was treated with...
octreotide.\textsuperscript{18} Somatostatin, or the somatostatin analogue octreotide, has been used successfully in children who had postoperative and iatrogenic chylothorax.\textsuperscript{19} However, care must be taken to monitor the patient for adverse effects of somatostatin therapy, including diarrhea, hypoglycemia, and hypotension.\textsuperscript{20} In addition, the patient with chylothorax is monitored for acid-base and electrolyte problems such as acidosis, hyponatremia, and hypocalcemia.\textsuperscript{21}

Previous reports have noted that patients with chylothorax may have further immunosuppression because of continued loss of proteins, immunoglobulins, and T lymphocytes into the chyle fluid and impaired B-lymphocyte–mediated immune function.\textsuperscript{22,23} These factors may predispose the patient to opportunistic infections.\textsuperscript{24} Therefore, we optimized immunosuppression by decreasing the dosage of mycophenolate mofetil by 50\%, guided by the total lymphocyte count, and by keeping the tacrolimus level approximately 5 ng/mL. The patient initially was anticoagulated with heparin, followed by warfarin with international normalized ratio from 2 to 2.5, and he has had stable graft function without any relapse.

In summary, deep venous thrombosis of neck veins may complicate prolonged permanent catheter placement for hemodialysis and may cause right venous hypertension, which may cause bilateral chylothorax, even after kidney transplant. Successful treatment of chylothorax may be expected after tube drainage, dietary modification, octreotide, and anticoagulation.

References