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CASE REPORT

Congenital Chylothorax in a Late Preterm Infant and Successful Treatment With Octreotide

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Chylothorax is defined as abnormal accumulation of lymphatic fluid in the pleural space and is a rare condition in neonates. Chylothorax causes respiratory and nutritional problems and a significant mortality rate. Octreotide is a long-acting somatostatin analog that can reduce lymphatic fluid production and has been used as a new strategy in the treatment of chylothorax. Here, we report a premature baby with severe bilateral pleural effusion diagnosed by prenatal ultrasound and subsequently confirmed to be congenital chylothorax after birth. This newborn baby was initially treated with bilateral chest tube insertion to relieve severe respiratory distress. However, the chylothorax recurred after a medium-chain-triglyceride-enriched formula was initiated. The accumulation of chylothorax diminished after the administration of octreotide. Therefore, octreotide may allow the patient to avoid invasive procedures, such as reinsertion of chest tubes or surgery.

1. Introduction

Chylothorax is defined as abnormal accumulation of lymphatic fluid in the pleural space and is a relatively rare condition in newborns. In neonates, chylothorax occurs in situations causing damage to the thoracic duct, such as cardiothoracic surgery, birth trauma, and great vessel thrombosis.[1] It also occurs in dysmorphic syndromes, such as Turner or Noonan syndrome. However, in many situations, the etiology of the chylothorax is uncertain and is believed to be caused by abnormality of thoracic or pulmonary lymphatic system. This is termed idiopathic congenital chylothorax.[2] Regardless of the underlying mechanism, chylothorax causes respiratory, nutritional,

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and immunological complications.[3,4] The mortality rate has been reported to be as high as 50% depending on gestational age, presence of abnormal karyotype, additional congenital anomalies, hydrops fetalis, and the duration and severity of the chylothorax.[3]

Octreotide is a long-acting somatostatin analog that acts on somatostatin receptors in the splanchnic vessels to inhibit lymphatic fluid production. Octreotide has been used in the treatment of postoperative or spontaneous chylothorax in infants and older children.[5,6] It has also been used for the treatment of congenital chylothorax in term neonates.[7,8] However, the experience of octreotide use in premature babies with congenital chylothorax is limited.[6,9–14]

Here, we report a female premature baby identified with prenatal severe bilateral pleural effusion and subsequently diagnosed with congenital chylothorax after delivery. She was initially treated with emergent chest tube insertion because of severe respiratory distress and was successfully treated with octreotide when the chylothorax reaccumulated. Octreotide avoided the baby needing reinsertion of the chest tube or surgery.

2. Case Report

This female neonate was delivered at 35 weeks of gestation to a primigravida mother by means of cesarean delivery for severe bilateral pleural effusion. The birth weight was 1904 g, and the Apgar scores were 1 at 1 minute and 4 at 5 minutes. The parents were nonconsanguineous, and the pregnancy was uneventful until 2 days before the delivery, when bilateral severe pleural effusion was detected by routine prenatal ultrasound (Figure 1). After delivery, the neonate was intubated because of severe respiratory distress and admitted to the neonatal intensive care unit. The patient had generalized edema but no dysmorphic features. A chest X-ray revealed severe bilateral whiteout of the lung field (Figure 2), and bilateral pleural effusion was confirmed by ultrasound.

Bilateral chest tube insertion was performed immediately because of severe respiratory distress and deterioration of O_2 saturation. The drained pleural effusion revealed straw-colored fluid. The cell counts of the pleural effusion revealed the following: red blood cells, 1750 cells/mm^3 and white blood cells (WBCs), 1950 cells/mm^3 with 100% lymphocytes. Biochemical analysis of the pleural effusion revealed the following: glucose, 54 mg/dL; total protein, 3.1 g/dL; lactate dehydrogenase, 97 IU/L; total cholesterol, 17 mg/dL; and triglyceride, 10 mg/dL (before feeding). The cell counts of the peripheral blood revealed the following: WBC, 12,300 cells/mm^3 with 42% neutrophils and 30% lymphocytes (absolute lymphocyte count, 3690 cells/mm^3). The albumin level of the plasma was 2.0 g/dL. Total parenteral nutrition (TPN) was initiated. Follow-up chest X-ray and ultrasound revealed no pleural effusion accumulation. On Day 4, the endotracheal tube was removed, and feeding was initiated. To observe the change of triglyceride level after feeding but avoid worsening of the chylothorax, we started a small amount of feeding with 2 mL of half-strength regular formula every 12 hours. The output of pleural effusion continued to decrease, but the color became turbid. The cell counts of the pleural effusion revealed the following: red blood cells, 4300 cells/mm^3 and WBC, 7029 cells/mm^3 with 66% lymphocytes and 34% neutrophils, and the biochemical analysis revealed the following: total cholesterol, 28 mg/dL and triglyceride, 170 mg/dL. The cell counts of the peripheral blood revealed the following: WBC, 9300 cells/mm^3 with 69% neutrophils and 10% lymphocytes (absolute

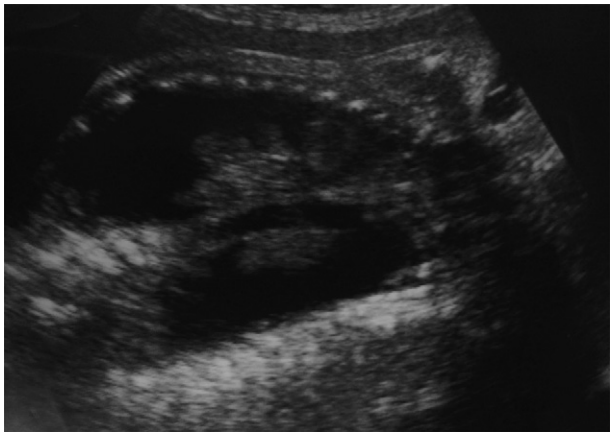

Figure 1 Prenatal ultrasound demonstrating the presence of bilateral large amount of pleural effusion.

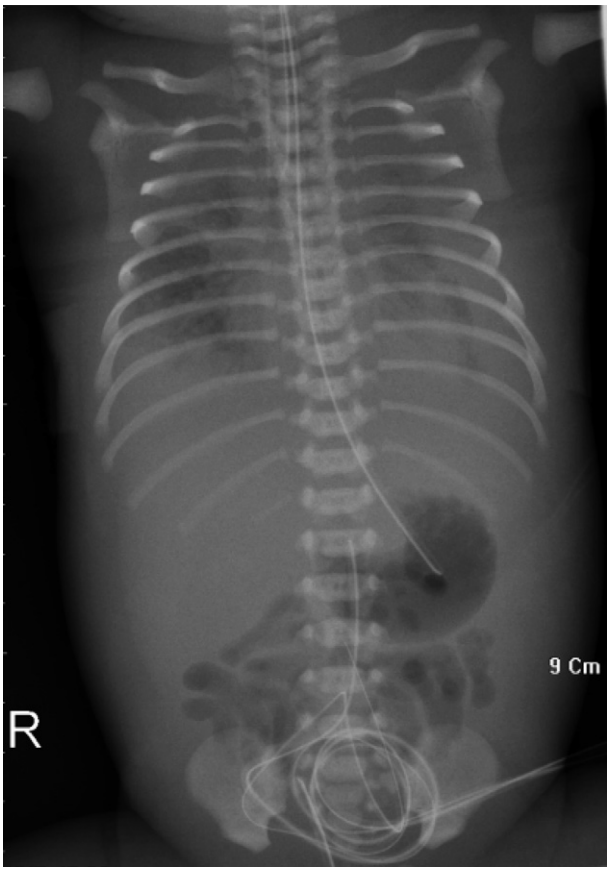

Figure 2 X-ray picture showing the presence of bilateral large amounts of pleural effusion, ascites (centralized bowel loops), and subcutaneous edema.

lymphocyte count, 930 cells/mm^3). The left and right chest tubes were removed on Day 10 and Day 18, respectively, because of malfunction. Enteral feedings with a medium-chain-triglyceride (MCT)-enriched formula (Alfare; Nestle, Vevey, Switzerland) were initiated on Day 15.

After the removal of the chest tubes, ultrasound was performed daily, and no reaccumulation of pleural effusion was detectable till Day 20. On Day 21, minimal pleural effusion was detected by ultrasound on the right side, and by Day 23, the pleural effusion thickness reached 9 mm, measured by ultrasound. There was also gradual respiratory deterioration. Instead of reinsertion of chest tubes or surgery, we decided to try octreotide. It was started at a beginning dose of 16 ug/kg/d subcutaneously in two divided doses and gradually increased to 48 ug/kg/d, and a 7-day course was completed. After the commencement of octreotide, right-side pleural effusion gradually subsided, along with respiratory improvement. By Day 33, the pleural effusion was no longer detectable by ultrasound. The relationship among amount of pleural effusion, nutrition types, and octreotide use is summarized in Figure 3. No side effects of octreotide, such as nausea, vomiting, diarrhea, hyperglycemia, hypotension, or liver dysfunction, were observed during the period of treatment. No reaccumulation of pleural effusion was detected thereafter. The chromosome analysis revealed normal female karyotype.

3. Discussion

The strategy of treating chylothorax is the same regardless of the etiology of chylothorax. The first step is aspiration of the pleural fluid for initial drainage and diagnostic purpose. However, continuous drainage of the chyle with a chest tube is indicated if the effusion causes respiratory distress or the accumulation of effusion recurs.[5] Chest tube may be required for a period of time because it takes time for chyle leakage to heal. However, long-term insertion of chest tube has been reported to be associated with hypoproteinemia, lymphopenia, hypogammaglobulinemia, infection, and prolonged ventilator use and its associated lung injury, leading to prolonged hospitalization and emotional stress to the family.[2,4]

Nutritional support in the management of chylothorax is aimed at providing adequate caloric intake while minimizing the chyle flow in the thoracic duct to wait for spontaneous healing of the leakage site. This is usually achieved by feeding with a formula high in MCT, which bypasses the intestinal lymphatic system and is absorbed directly to the portal vein.[15] It is noteworthy that even water intake by mouth can produce thoracic lymph flow,[16,17] and a formula containing MCT with up to 87% of fat can also cause reaccumulation of pleural effusion.[3] Therefore, complete enteric rest using TPN is suggested by some authors.[18,19] A practical approach is to use TPN until the output of pleural effusion is minimal and the cardiopulmonary status is stable. Then, a trial of feeding with MCT-enriched formula can be given with close monitoring of reaccumulation of pleural effusion, either by chest tube drainage or ultrasound.[3]

Surgical interventions of chylothorax, including direct ligation of the thoracic duct, pleural abrasion, pleurodesis, or pleural-to-peritoneal shunts, should be considered if medical treatment fails to decrease chyle flow and allow healing of the thoracic duct. The timing of surgery is not uniformly defined. Most authors suggest at least 3—5 weeks of medical therapy before proceeding to surgery.[2,20,21] However, if a chyle-leaking site could be well identified and the flow is high, which makes spontaneous healing less likely, early surgery is suggested.[22] Successful surgery shortens the duration of chest tube insertion and, thus, reduces the risks of its complications and shortens the duration of hospitalization.

In this case, left and right chest tubes were removed on 10 days and 18 days of life, respectively, because of obstruction of the chest tube. When the chylothorax reaccumulated and the patient had significant respiratory distress, instead of reinsertion of chest tubes or surgery, we decided to try octreotide. After treatment with octreotide,

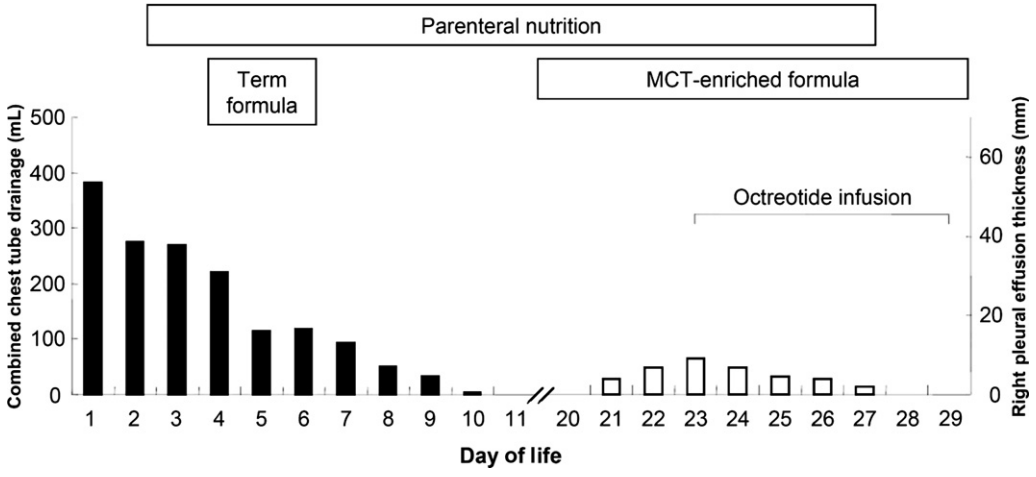

Figure 3 Graph showing the amount of pleural effusion, nutrition types, and octreotide infusion duration. After Day 20, when both chest tubes had been removed, the amount of right-side pleural effusion was detected by ultrasound through the eighth intercostal space at the posterior axillary line. No pleural effusion accumulation was detectable by ultrasound on the left side. MCT = medium-chain triglyceride.

the chylothorax subsided. We could not exclude the possibility that the improvement of chylothorax was because of natural history of the disease. However, we measured the accumulation of chyle by ultrasound daily, and the improvement of the chylothorax coincided with the initiation of octreotide; it is likely that the subsiding of pleural effusion was because of octreotide treatment.

Somatostatin is a polypeptide secreted from the paraventricular nucleus of the hypothalamus. It has an inhibitory effect on the secretion of growth hormone, glucagon, and insulin. Octreotide, a synthetic somatostatin analog, is more potent in inhibiting endocrine system and has a much longer half-life. In gastrointestinal tract, somatostatin and octreotide act on somatostatin receptors to reduce intestinal blood flow by vasoconstriction of the splanchnic vessels; decrease gastrointestinal motility; and inhibit gastric, pancreatic, and biliary secretions, thus reducing intestinal fat absorption and lymphatic flow in the thoracic duct.[6,23–26] Somatostatin and octreotide have been used to treat a variety of diseases, including acromegaly, carcinoid syndrome, secretory diarrhea, severe gastrointestinal bleeding, postgastrectomy dumping syndrome, chemotherapy-induced diarrhea, and persistent hyperinsulinemic hypoglycemia.[27–30] Octreotide has been used in the treatment of postoperative or spontaneous chylothorax in infants and older children.[5,6] It has also been used for the treatment of congenital chylothorax in term neonates.[7,8] The experience of octreotide use in premature babies with congenital chylothorax is limited.[6,9–14] There is no consensus on the route, dosage, and duration of octreotide administration for chylothorax. It could be administered as a continuous intravenous infusion or given twice daily as an intravenous bolus or subcutaneously. The effective daily doses were from 7.2 ug/kg to 240 ug/kg (median, 68 ug/kg) for intravenous infusion and from 2 ug/kg to 68 ug/kg (median, 40 ug/kg) for subcutaneous administration. The duration of administration ranged from 3 days to 43 days.[6] We started subcutaneous octreotide at a lower dose of 16 ug/kg/d for safety reason and reached a final dose of 48 ug/kg/d.

Octreotide is generally considered to be safe, with only occasional side effects. The side effects of octreotide are mainly related to its vasoconstrictive and antisecretory actions. The reported adverse reactions include cramps, flatulence, nausea, diarrhea, necrotizing enterocolitis, hyperglycemia, transient hypothyroidism, and liver dysfunction.[6,26] No aforementioned side effects of octreotide were observed in our patient.

In conclusion, octreotide in the treatment of a premature baby with congenital chylothorax appears to be a safe and effective adjunct therapy. It prevented our patient from undergoing reinsertion of chest tubes or surgery. However, further studies in a larger number of patients are required to determine the effectiveness, proper dosing, and side effects of this drug in the treatment of congenital chylothorax.

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