

Report of three cases: congenital chylothorax and treatment modalities

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Chylothorax is the most common cause of pleural effusion in the newborn. We report three patients with congenital chylothorax and discussed the clinical course and treatment options. Cases 1 and 2 with congenital chylothorax were treated by chest tube placement and total parenteral nutrition (TPN), and were fed a formula rich in medium-chain triglyceride. They were discharged home without any sequelae. Our 3rd case with chylothorax did not respond to the conventional therapies. Octreotide infusion was tried without any benefits and necessitated surgical intervention, but the infant developed chronic lung disease requiring nasal oxygen therapy until three months of age. All three patients developed complications of chylothorax treatment like chest tube dysfunction, pneumothorax, nosocomial sepsis, and cholestasis.

Management of congenital chylothorax necessitates a multidisciplinary approach. Treatment options include pleural drainage, cessation of enteral feeding and initiation of TPN. Experience with octreotide treatment is limited. Surgery should be reserved for severe and refractory cases.

Key words: congenital chylothorax, newborn, octreotide, pleurodesis.

Chylothorax is characterized by the accumulation of chylous fluid in the pleural space. It is an uncommon disorder but is the most common cause of pleural effusion in the fetus and neonates. It is classically a disorder of infants at or near term^{1,2}. Males are affected twice as frequently as females and 60% of cases involve the right side of the chest². Congenital chylothorax usually occurs spontaneously due to lymphatic malformations or is associated with birth trauma to the thoracic duct, and it presents a clinical challenge; it produces respiratory compromise, nutritional failure or immunologic depletion contributing to sepsis^{1,3}.

Here, we report three patients with congenital chylothorax and discuss the clinical course, treatment options and complications of chylothorax.

Case Reports

Case 1

A 3290 g term boy was born to a 30-year-old gravida 2 mother. The baby was symptom-free for the first week of life, but minimal respiratory distress was observed later during breast-feeding. Physical examination on admission revealed respiratory difficulty and decreased breath sounds on the left side. The chest radiogram revealed left-sided pleural effusion. Diagnostic and therapeutic thoracentesis removed 50 ml of milky appearing fluid with the following characteristics: protein 3.42 g/dl, lactate dehydrogenase (LDH) 665 U/L, triglycerides 4860 mg/dl, glucose 120 mg/dl, and 85.2% lymphocytes. Chylothorax was diagnosed and chest tube was placed on the left side. Enteral feeding

was discontinued and total parenteral nutrition (TPN) was instituted. Gram stain showed no bacteria and the culture was sterile after seven days. During the clinical course, albumin and intravenous immunoglobulin (IVIG) were given. The daily drainage of fluid gradually decreased. The baby was initially fed by a formula containing medium-chain triglyceride (MCT) (Portagen®, 85% of all dietary fat was MCT) and was discharged home on standard formula.

Case 2

The 2700 g infant was born by cesarean section (C/S) (due to previous C/S) at term, to a 30-year-old gravida 2 mother. She had respiratory distress immediately after birth with diminished breath sounds on the left side. The initial chest radiogram showed left-sided pleural effusion. Thoracentesis revealed that pleural fluid was exudate (glucose 57 mg/dl, total protein 7.5 g/L, triglyceride 48 mg/dl, albumin 4.8 g/dl, total lipid 390 mg/dl, triglyceride 48 mg/dl). The infant was not fed enterally; TPN was started in addition to empirical antibiotic therapy. Chest tube was placed on the left side for drainage. Serum and pleural fluid cultures for *Mycobacterium tuberculosis* and other bacterial and viral infections were negative.

During hospitalization, TPN was continued, and she was then started on MCT-rich formula (Portagen®). The pleural drainage decreased from 120 ml/day to 5 ml/day in two weeks while on this formula. On the 25th day of life, she had a *Candida albicans* sepsis as well as *Klebsiella pneumoniae* wound infection, which were treated with antifungals and antibiotics. Meanwhile, she developed cholestasis, thought to be secondary to TPN, sepsis and antibiotics, which resolved after initiation of enteral feedings and completion of antibiotic therapy.

She was discharged home with a MCT-rich formula (Portagen®) without any medications. A standard formula (Preaptamil®) was used during follow-up which was tolerated well by the infant.

Case 3

The male baby was delivered vaginally at 36 weeks of gestation with a birthweight of 3020 g to a 25-year-old gravida 2 mother and was administered surfactant therapy within the first hour of life due to respiratory distress. Later,

the clinical status of the infant deteriorated and repeated chest radiogram showed bilateral pleural effusion (Fig. 1).



Fig. 1. Chest X-ray of Case 3.

Chest tubes were inserted and analysis of pleural fluid revealed total protein 4.7 g/dl, triglyceride 38 mg/dl, albumin 3.3 g/dl, LDH 233 IU/L, total lipid 220 mg/dl, pH 7.4, and lymphocytes 97%. The color of pleural fluid was clear yellowish since the infant had not been fed. The infection markers of the patient were negative and there was no bacterial growth in the pleural fluid culture. The infant was given antibiotic treatment and TPN was started. Volume and electrolyte hemostasis was maintained and losses of proteins, coagulation factors and immunoglobulins were replaced regularly. Hypothyroidism was diagnosed at newborn screening tests and L-levothyroxine was started. Minimal enteral nutrition with a MCT-containing diet was introduced, but chylous fluid became viscous and prevented the chest tube drainage. The computed scanning of the chest showed bilateral fluid accumulation (Fig. 2). Because of the failure to control pleural drainage, octreotide (Sandostatin®, Novartis), which is a somatostatin synthetic analogue, was started at infusion rate of 1 µg/kg/hr and was increased to 10 µg/kg/hr. No side effects were noted. Clinical status of the infant improved gradually with the cessation of drainage on day 28. With the extubation of the infant, thorax tubes were clamped and octreotide dose was lowered. At the 4th day of extubation, the patient developed respiratory



Fig. 2. Chest computed tomography of Case 3.

distress with reaccumulation of fluid and necessitating intubation, antibiotics and bilateral chest tube reinsertion. The chest X-ray showed signs of chronic lung disease. On the 28th day of octreotide administration, we stopped treatment because of the persistent drainage.

After persistent effusion for six weeks of medical treatment, surgical pleurodesis on the right side of lung was performed and the chylous drainage decreased dramatically in the following days. Additionally, spontaneous improvement was observed on the left side without any surgical intervention. The infant was extubated and started on enteral feedings with MCT-rich formula (Portagen®), which was switched gradually to cow milk-based formula without reaccumulation of pleural effusion. The infant was discharged home at 106 days of life without any respiratory symptoms.

Discussion

Chylothorax is an accumulation of fluid rich in triglycerides in the pleural cavity¹⁻⁴. Criteria for the diagnosis of chylothorax are the following: pleural fluid protein concentration >20 g/L, triglyceride concentration >100 mg/dl, number of cells per milliliter >100 with lymphocyte predominance, and sterile culture⁴. A milky appearance of the fluid (indicates presence of chylomicrons) and positive Sudan III test results are also diagnostic in orally fed infants. In patients not receiving enteral nutrition, elevated triglyceride levels are frequently not detected in pleural fluid analysis. The predominance of lymphocytes in the drainage

fluid is of major utility in the diagnosis since this finding is independent of nutrition^{1,3}. Similarly, the analysis of the pleural fluid in our 2nd and 3rd patients showed high lymphocyte count but triglyceride level was not elevated because they were not fed enterally. Diagnostic thoracentesis gives the patient a transient relief and this occasionally suffices. Usually, the fluid reaccumulates and necessitates thoracostomy tube to keep the pleural space empty²⁻⁴.

A number of therapeutic interventions have been used to reduce chyle production and promote resolution of a chylothorax. The initial management typically includes restriction of dietary fat by using TPN or feeding the baby by a formula rich in MCT^{3,4}.

Ongoing losses further compromise the nutrition of the patients, thus protein replacement, adequate caloric intake, and electrolyte supplementation are all part of standard management. Hypoalbuminemia secondary to excessive chest tube drainage is a common problem as well⁶. In our patients, albumin was added to TPN to keep the plasma level around 3 mg/dl. Loss of large amounts of chyle, which contains prothrombin, fibrinogen, immunoglobulins, and lymphocytes, can predispose the patients to infections and coagulopathy^{1,2,4}. IVIG replacement may be necessary². All three of our patients received IVIG for supportive management.

Beghetti et al.³ reported that 80% of their patients responded to medical treatment. Conservative treatment was effective in our 1st and 2nd patients.

During the last several years, octreotide, a somatostatin analogue, has become another option for management of these patients. Octreotide is prescribed as an antisecretory agent. Although the exact mechanism of the drug has not been defined, it is believed to reduce splanchnic blood flow which results in decreasing thoracic duct flow and triglyceride content of chyle⁶. Over a dozen case reports have been published describing the successful use of octreotide in congenital or postoperative chylothorax in children⁷⁻⁹. For the management of chylothorax in infants and children with octreotide, two approaches have been used. Octreotide may be administered subcutaneously at 20 to 70 µg/kg/day, divided and given as three separate doses, or as an IV infusion

starting at a dose of 1 to 4 $\mu\text{g}/\text{kg}/\text{hr}$ and titrating as needed to 10 $\mu\text{g}/\text{kg}/\text{hr}$. The duration of therapy is typically determined by the reduction in the volume of pleural drainage⁶. Reported durations of octreotide therapy for congenital chylothoraces were longer than in postoperative cases, ranging from 3 to 29 days⁶⁻⁹.

In our Case 3, the use of octreotide showed a transient improvement, but later this effect was abolished. The use of octreotide seems encouraging in the treatment of congenital chylothorax, but the existing literature contains only uncontrolled case reports. Two chylothorax cases unresponsive to this treatment were described by Stefanides et al.¹⁰ and Mikroulis et al.¹¹. Although chylothoraces appear to respond to octreotide, improvement may reflect the natural history of these effusions. The ineffectiveness of the drug in severe cases (such as Case 3) may support this opinion.

Surgical treatment is advocated in resistant cases with either excessive (>10 ml/kg/d or >100 ml/year of age) or prolonged (>3 to 4 weeks) drainage as described in Case 3¹². The surgical options for refractory chylothorax include chemical pleurodesis, pleurectomy, thoracotomy with thoracic duct ligation, intrapleural fibrin glue or pleuroperitoneal shunts². Pleurodesis was reported to be the most frequently used surgical approach and pleuroperitoneal shunts were used in cases with failure of pleurodesis³. Pleurodesis is one way to obtain pleural adhesion, thus obliterating chylous leaks. The clinical condition of Case 3 improved dramatically after surgical pleurodesis with no recurrences and the patient was weaned from ventilatory support after surgery.

In addition to the diagnosis of chylothorax, our 3rd patient also had congenital hypothyroidism. Kessel¹³ reported a newborn with congenital hypothyroidism and nonimmune hydrops fetalis in which the pleural fluid was chylothorax and resolved after thyroid hormone replacement therapy. The mechanism of chylothorax in thyroid hormone deficiency was explained by the reduction in adrenergic stimulation of the lymphatic system. This could result in the engorgement of the lymphatic system and leakage of lymph into pleura¹³. The clinical status of Case 3 did not improve with the addition of thyroid hormone replacement

although thyroid function tests normalized.

Early diagnosis, aggressive initiation of nonoperative management options and a number of surgical procedures have decreased the mortality rate of congenital chylothorax from 50% before the 1950's to 10-20% currently.

Familiarity with the therapeutic options, along with appropriate timing for surgical intervention, can prevent complications. Advances in perinatal and neonatal medicine are changing the natural history of congenital chylothorax with reduction in the morbidity and mortality.

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