CASE REPORT

Congenital Chylothorax Complicated with Hemothorax after OK-432 Pleurodesis
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Abstract
Background: Congenital chylothorax is the most common cause of pleural effusion in newborn infants. These infants show signs of respiratory distress at birth. Chemical pleurodesis with OK-432 has recently been proposed for cases of persistent congenital chylothorax as an alternative method to surgery. Here we report a case of neonate with congenital chylothorax who developed hemothorax and shock as received OK-432 pleurodesis. Finally, his congenital chylothorax responded to high dose of octreotide. Although very rare, clinicians should be aware that OK-432 intrapleural instillations may be complicated with hemothorax. (J Pediatr Resp Dis 2014;10:5-7)

Key words: congenital chylothorax, OK-432, hemothorax, octreotide

INTRODUCTION

Congenital chylothorax is the most common cause of pleural effusion in newborn infants.⁴ These infants may show signs of hydrops fetalis or bilateral pleural effusion at birth and respiratory insufficiency. The initial postnatal medical management of congenital chylothorax consists of nutrition control (low-fat high-protein diets with medium-chain triglycerides or total parenteral nutrition), and pleural drainage.⁵ Recently, it has been suggested that somatostatin and octreotide provide benefits for congenital chylothorax therapy.³ Pleurodesis and other surgical interventions such as thoracic duct ligation are alternative choices for intractable congenital chylothorax.³ Chemical pleurodesis with OK-432 has recently been proposed for cases of persistent congenital chylothorax as an alternative method to surgery.⁴ However, the experience of using OK-432 for congenital chylothorax is limited. Here we report a case of neonate with congenital chylothorax who developed hemothorax and shock as received OK-432 pleurodesis. Finally, his congenital chylothorax responded to high dose of octreotide. Although very rare, clinicians should be aware that OK-432 intrapleural instillations may be complicated with hemothorax.

CASE REPORT

A bilateral chylothorax was diagnosed in a fetus at 34 weeks, and emergent induction was arranged. The 3230 g male infant presented with respiratory distress. Bilateral chest tubes were inserted for bilateral massive pleural effusion. Congenital hypothyroidism and fluctuated sinus tachycardia episodes (even over than 230 beats/min.) were also noted but with negative echocardiography finding. He had received a high medium-chain triacylglycerol (MCT) diet, total parenteral...
nutrition and somatostatin infusion as congenital chylothorax therapy for 28 days, but the drainage did not resolve. He was then referred to our hospital for thoracic duct ligation. However, severe bradycardia and cyanosis had occurred during general anesthesia and the surgery could not proceed. Octreotide (Sandostatin®) was then commenced at a dose of 3 μg/kg/h. On day 35, intrapleural instillation of 0.5 Klinische Einheit (KE) of OK-432 (in 5 mL normal saline) was introduced through the right side existing chest tube as chemical pleurodesis for the pleural effusion of more than 150 ml/day. Bilateral chest tubes had stopped draining within 8 h; however his respiratory status worsened 48 h after the OK-432 infusion. Chest echocardiography showed right side moderate pleural fluid accumulation. After removing the occluded chest tubes, massive fresh blood leaked (Figure 1). A new chest tube was inserted for hemothorax drainage. Hypotension, bradycardia, and apnea occurred then. He received endotracheal intubation and ventilator support. After emergent administration of inotropic agents and a blood transfusion, the hemodynamic instability and respiratory status improved 24 h later. Then the bloody pleural drainage turn to clear gradually and the ventilator was weaned off 5 days later. Because of the persistent pleural chylous drainage, the octreotide dose was gradually increased to 10 μg/kg/h over 3 days on day 45, and the pleural effusion was dramatically decreased to less than 5 ml/day (Figure 2). Complete cessation of pleural drainage was rapidly achieved. Weaning from octreotide took place over 5 days at a rate of 1-2 μg/kg/h without obvious side effects. No further pleural effusion was noted during a one month follow-up period after discharge.

**DISCUSSION**

Pleural effusion is rare in the neonatal period. Chylothorax, the leading cause of pleural effusion in newborns, accounts for about 40% of all cases.\(^1\) It results from chyle leakage into the pleural space. The etiology of chylothorax includes congenital, trauma, high central venous pressure, malignancies and miscellaneous.\(^2\) A high proportion of chylothorax in the newborn are secondary to thoracic duct injury following thoracic surgical procedures (cardiac or otherwise). Büttiker et al. established the criteria for chylothorax by the following characteristics of the pleural effusion: total white cell count > 1000 cells/μL with a lymphocyte fraction > 80% and triglycerides

**Figure 1.** Hemothorax and shock developed after OK-432 pleurodesis. There was massive fresh blood leakage from the chest tube (arrow).

**Figure 2.** The pleural effusion was dramatically decreased to < 5 ml/day after the octreotide dose was increased to 10 μg/kg/h.
Congenital chylothorax complicated with hemothorax after OK-432

> 110 mg/dL. Conservative treatment initially with nil per os or a higher percentage of medium chain triglyceride formula leads to complete resolution in approximately 74–80% of cases of chylothorax. However, the cases that do not respond may need further alternative medical or surgical interventions.

Somatostatin and its analog, octreotide, have been proven to be useful in the conservative treatment of chylothorax, however the detailed mechanism of these agents in treating chylothorax is still not clear. It is thought that they have an effect at the vascular somatostatin receptor level, which results in a reduction in chyle production. In treating congenital chylothorax with octreotide, the reported timing of initiation, dose, duration and frequency of dose have varied markedly. Parenteral octreotide at a dose of 80 to 100 µg/kg/day (3.33–4.2 µg/kg/h) intravenously has been used to manage chylothorax. Octreotide was reported to have adverse effects such as supraventricular arrhythmias, injection site pain, nausea, vomiting, constipation or diarrhea, hyperglycemia, hypoglycemia, hypothyroidism, dizziness and fatigue. A higher dose of octreotide of up to 10–12 µg/kg/h has even been reported in treating chylothorax. In our case, an initial octreotide dose of 3 µg/kg/hr was given to avoid worsening the arrhythmia. Subsequently, we gradually increased the octreotide dose to 10 µg/kg/h due to failed OK-432 therapy. No apparent arrhythmia was noted after increasing the dose of octreotide, and a dramatic decrease of the pleural effusion was noted 2 days after the administration of the high dose of octreotide.

Chemical pleurodesis with povidone-iodine, bleomycin and OK-432 have been reported for the treatment of chylothorax. However, there are no recommendations about which agent is the most useful in neonatal patients with congenital chylothorax. In addition, shock and chronic renal failure have been reported as severe side effects of povidone-iodine. OK-432, a lyophilized sclerosing agent prepared from Group A Streptococcus pyogenes, seems to be a safer agent for chemical pleurodesis in patients with chylothorax. Fever, local inflammation, respiratory distress, transient hypertrophy of the pleural membrane and a transient elevated serum C-reactive protein level are the reported side effects of OK-432 therapy. Our case had a hemothorax, which has not previously been reported as a side effect of OK-432 pleurodesis. The mechanism of hemothorax might due to local inflammation but not direct blood vessels injury during OK-432 injection. Because the OK-432 was introduced through an existing chest tube without other invasive procedure.

In conclusion, we report a neonate with congenital chylothorax who responded to a high dose of octreotide but not OK-432 pleurodesis. Although very rare, clinicians should be aware of the possibility of hemothorax and shock during OK-432 pleurodesis.

REFERENCES