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Treatment of Idiopathic Congenital Chylothorax in Neonates Using Chemical Pleurodesis with Erythromycin

JR ***Pan,*** LP ***Shi,*** MY ***Sun***

Abstract We described the treatment and therapeutic effect of chemical pleurodesis with erythromycin for the three refractory neonates. Chylothorax is a comparatively rare disease with an incidence ranging from 1 in 6000 to 1 in 10000 and a male to female predominance (2:1). Underlying cause is usually attributable to 1 of 4 categories: malignancy, trauma (including surgery), miscellaneous disorders, and idiopathic. We described three neonates who suffered from idiopathic congenital chylothorax. Although rare, congenital idiopathic chylothorax is the most common form of pleural effusion in neonates. Significant long-term morbidity and mortality were reported because of immunologic, metabolic, and nutritional complications in neonates. Many forms of conservative therapy are not always effective in treating idiopathic congenital chylothorax. In our three reported cases, conservative therapy including the provision of total parenteral nutrition and repeated drainage of pleural effusion failed. Eventually all the cases were successfully treated by chemical pleurodesis with erythromycin.

Key words Chylothorax; Erythromycin; Neonate; Pleurodesis

Case Presentations

Case 1

A female neonate was admitted to the neonatal intensive care unit (NICU) of our hospital due to tachypnea on the third day after birth. Bilateral chylothoraces were diagnosed antenatally. The patient was born at 39 weeks gestation and weighed 3800 g at birth. Apgar scores were both 10 at 1 minute and 5 minutes. Her parents were unrelated. There were no hereditary disorders or unexplained infant deaths in family history.

On examination, the pulse was 150 beats per minute, respiratory rate 66 breaths per minute, and the oxygen saturation 99% with no oxygen supplement. The infant appeared dyspnoeic, without crackles audible. There was no cardiac murmur, and the remainder of the examination was normal. Chest computed tomography revealed pleural effusion in the bilateral thoracic cavities (Figure 1). Thoracenteses were made on the first day after admission and chest fluid analysis showed a high number of karyocytes (2.4×10^9/L) with lymphocyte predominance and positive in chyle test. Chemical analysis demonstrated total protein (41.7 g/L), LDH (261 U/L), and glucose (4.21 mmol/L). No microorganisms were found in the culture. Thoracostomy tube drainage was performed because of persistent plural effusion after repeated thoracenteses on the 10th day after admission. Total parenteral nutrition was started on admission. However, the pleural effusion did not improve after eleven days of therapy. The maximal daily volume of pleural effusion reached 100 ml. As result, intrapleural injection of erythromycin was given on the 12th day after admission.

Case 2

A 18-day-old male infant was admitted to the NICU of our hospital because of tachypnea. The patient was born at

Neonatal Intensive Care Unit, Children's Hospital, Zhejiang University School of Medicine, Hangzhou 310003, China

JR **Pan** (潘佳容) *MD*
LP **Shi** (施麗萍) *MD*
MY **Sun** (孫眉月) *MD*

Correspondence to: Dr LP **Shi**

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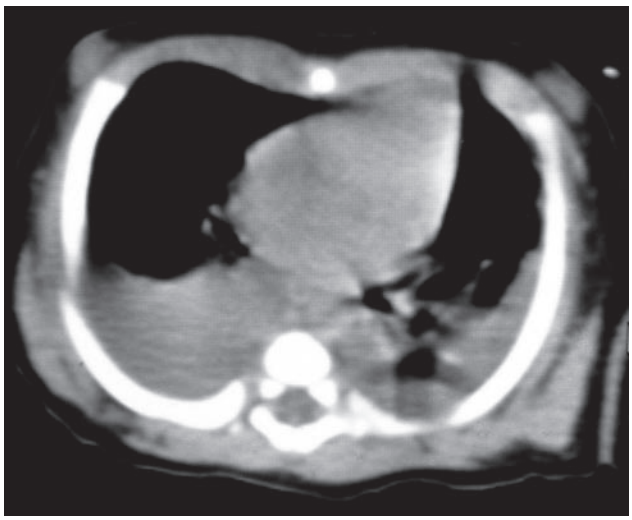

Figure 1 Chest CT demonstrated pleural effusion in bilateral thoracic cavities.

38 $^{1}/_{7}$ weeks gestation. The infant weighed 3100 g at birth and the Apgar scores were both 10 at 1 minute and 5 minutes. Formula feeding was started 3 hours after birth. His mother had a history of induced abortion. There were no hereditary disorders in family history.

On examination, the temperature was 37.0°C, the pulse 140 beats per minute, the respiratory rate 70 breaths per minute, and the oxygen saturation 95% while breathing air. The infant appeared tachypneic and groaned, without crackles audible. Auscultation revealed decreased breath sounds on the right. There was no cardiac murmur, and the rest of the examination was normal. A chest radiograph was obtained immediately and demonstrated pleural effusion in the right thoracic cavity. The diagnosis of chylothorax was confirmed by the predominance of lymphocytes (karyocytes, 0.64×10^9/L; lymphocytes, 80%) and positive in chyle test. After admission, total parenteral nutrition was started. Intrapleural injection of erythromycin was given on the 15th day after admission because of no significant decrease in chest tube drainage.

Case 3

A 15-day-old male infant was admitted to the NICU of our hospital because of cyanosis. The patient was born at 36 $^{6}/_{7}$ weeks gestation. The infant weighed 3000 g at birth and the Apgar scores were not available. Breast feeding started 3 hours after birth. His mother had undergone four induced abortions. There were no hereditary disorders or unexplained infant deaths in family history.

On examination, the temperature was 37.0°C, the pulse 168 beats per minute, the respiratory rate 60 breaths per minute, and the oxygen saturation 80% while breathing room air. The infant appeared tachypneic, without crackles audible. There was no cardiac murmur, and the remainder of the examination was normal. A chest radiograph revealed pleural effusion in the left thoracic cavity. The diagnosis of chylothorax was confirmed by the predominance of lymphocytes (karyocytes, 15.7×10^9/L; lymphocytes, 85%) and positive in chyle test. The amount of pleural effusion did not reduce after 11 days of total parenteral nutrition therapy. Chemical pleurodesis with erythromycin was given.

Chemical Pleurodesis with Erythromycin

Chemical pleurodesis with erythromycin was applied in case 1, case 2, and case 3 on the 12th, 15th, and 11th day after admission, respectively. Erythromycin (0.1 g erythromycin added to 10 ml of 5% Dextrose and 1 ml of 2% lidocaine) was injected intrapleurally in 10 minutes, and intramuscular injection of pethidine 1 mg/kg was given for pain relief. Thoracostomy tubes were clamped for 48 hours. Formula-feeding was given afterwards. Thoracostomy tubes were removed 2 days after complete disappearance of the pleural effusion with formula-feeding.

Results

Case 1

There was no fluid drained after the clamps were taken away from thoracostomy tubes. Repeat chest radiograph demonstrated no pleural effusion in the bilateral thoracic cavities (Figure 2). The pleural effusion did not recur. The infant was discharged 30 days after admission. The infant was followed up, and she was well at 11 months of age.

Case 2

The right pleural effusion completely disappeared on the 19th day after admission with no recurrence. The infant was discharged 26 days after admission.

Case 3

Although the amount of pleural effusion did not reduce significantly five days after chemical pleurodesis with erythromycin for the first time, chemical pleurodesis with erythromycin was given for a second time and the pleural effusion completely disappeared on the 20th day after

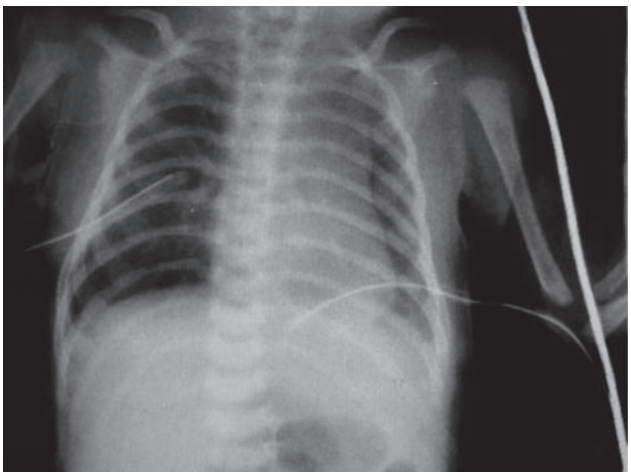

Figure 2 Chest X-ray confirmed that there was no pleural effusion.

admission. The infant eventually was discharged 26 days after admission.

Symptoms of irritability, restlessness, and tachycardia occurred in all cases during the intrapleural injection of erythromycin. These symptoms lasted only a few minutes, and all of them were calmed down very soon after the accomplishments of injections.

Discussion

Neonatal idiopathic congenital chylothorax is a comparatively rare disease which may resolve by cessation of the lymphatic flow in the thorax. The preferred treatment for neonatal idiopathic congenital chylothorax is conservative, with good respiratory, cardiovascular, haemodynamic, and nutritional support as well as infection prevention. For some neonatal idiopathic congenital chylothoraxes, conservative treatment fails. Video-assisted thoracoscopic surgery (VATS) is a recommended approach in child and adult, but it is quite invasive in neonates. Chemical pleurodesis is a method used to treat recurring pleural effusions, especially those in which symphysis between the pleural layers is needed.[1] Intrapleural injection of a sclerosing agent that acts on the mesothelial layer leads to an inflammation and coalesces the parietal and visceral layers, obliterating the pleural space and producing pleurodesis.[2] Although in some clinical trials, erythromycin was effective in nearly 85% of adult cases,[3] there is no report in treating idiopathic congenital chylothorax in neonates. Chemical pleurodesis with erythromycin was successfully used for persistent bilateral chylothoraces in our patients with few adverse effects. The mechanisms of erythromycin responsible for reducing pleural effusions are not completely clear. Apparently, the injection of erythromycin causes damage to the mesothelial layer with the subsequent formation of an inflammatory process, characterised by the production of exudative fluid, resulting in symphysis between the pleural layers. Immediate complications include irritability, restlessness, and tachycardia due to intense pain of the chemical pleurodesis. Intramuscular injection of pethidine and intrapleural injection of lidocaine should be given to attenuate the stress response, alleviate pain and improve compliance with care.

As an ideal sclerosant, erythromycin is inexpensive, effective, and with few side effects. Considering the complications of persistent chylothorax, we believe that chemical pleurodesis with erythromycin can be used as an alternative method to surgery and a treatment of choice for newborn infants, after conservative treatment has failed.

Because of small number of patients, treatment for cases with similar severity needs further evaluation. Data on long term effects of chemical pleurodesis in an immature growing lung is lacking, further review in this area is necessary.

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