Report of a case of neonatal chylothorax that responded to long-term octreotide treatment, and review of the literature

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SUMMARY: Çakır U, Kahvecioğlu D, Yıldız D, Alan S, Erdeve Ö, Atasay B, Arsan S. Report of a case of neonatal chylothorax that responded to long-term octreotide treatment, and review of the literature. Turk J Pediatr 2015; 57: 195-197.

Chylothorax is a relatively uncommon condition defined as an abnormal collection of lymphatic fluid within the pleural space. Morbidity of congenital chylothorax (CC) is high, and prognosis is very poor if CC is associated with hydrops fetalis. Although the optimal treatment of CC has not been determined, conservative treatment and surgical intervention are employed. However, there is still little experience with the use of octreotide therapy for this condition, and optimal duration of the treatment for response evaluation is not known. We report a newborn with CC who presented with intrauterine bilateral pleural effusion and was resistant to conservative treatments. Octreotide (6 μg/kg/h) infusion was started on the 10th postnatal day due to ongoing pleural drainage. Although the patient improved rapidly with continuous administration of octreotide, we had to continue the drug for 151 days, even subcutaneously on outpatient follow-up. To the best of our knowledge, this patient is unique in receiving octreotide treatment for such a long time, with a successful outcome and a safe profile.

Key words: newborn, congenital chylothorax, fetal pleural effusion, octreotide.

Chylothorax is the accumulation of lymph fluid or chyle in the pleural space. Although congenital chylothorax (CC) is an uncommon disorder, it is the most common cause of pleural effusion in the neonatal period. Chylothorax may be either congenital or acquired due to thoracic surgery. Most cases of CC, however, occur without a clear etiology. These have been termed "idiopathic congenital chylothorax"; or, if expressed up to several weeks after birth, the term "spontaneous neonatal chylothorax" can be used. The prevalence of idiopathic CC is about 51/15,000 births, and accounts for 8% of chylothoraces in children. CC may be associated with lymphangiomatosis, lymphangiectasia, congenital heart disease, chromosomal abnormalities (Turner Syndrome, Noonan Syndrome, Down Syndrome), mediastinal malignancies or H-type tracheoesophageal fistulas. The diagnosis of chylothorax is classically established via pleural fluid analysis and entails a triglyceride content of 1.1 mmol/L or more and a total cell count of 1000 cells/ml or more with 80% lymphocytes. The optimal treatment of CC has not been determined, and conservative treatments combined with pleural drainage and surgical intervention have been employed. Recently, in a few studies, continuous infusion of somatostatin (or its longer-acting synthetic analog, octreotide) has been reported successful in the treatment of CC[1]. We herein report a patient with idiopathic CC who presented with intrauterine bilateral pleural effusion and had chylothorax resistant to conservative treatment. Although the patient improved rapidly with continuous administration of octreotide, we had to continue the drug for 151 days, even subcutaneously (s.c.) on outpatient follow-up. To the best of our knowledge, this patient is unique in receiving octreotide treatment for such a long time, with a successful outcome and safe profile.

Case Report

A 2570 g male newborn with a gestational age of 34 weeks was born by cesarean section to a 28-year-old mother from her first pregnancy. Pleural effusion was detected on follow-up at the 32nd week of gestation and was drained twice, at one-week intervals. The biochemical characteristics of the drained fluid were consistent with those of chylous fluid (Table I). Congenital infections (toxoplasmosis, rubella, cytomegalovirus, syphilis, herpes and parvovirus B19) were ruled out. Fetal echocardiography and chromosomal analysis were found to be normal. In order to exclude fetal anemia, middle cerebral artery-peak systolic volume (MCA-PSV) was measured by Doppler ultrasonography (US) and also found to be normal. Bilateral pleural effusion was detected on chest X-ray after delivery, and the patient required respiratory support in the form of mechanical ventilation. Bilateral chest tubes were inserted, which resulted in the drainage of chylous fluid. On the 2nd postnatal day, feeding with a formula rich in medium-chain fatty acids (MCT) was started. The use of bilateral chest tubes was continued, and approximately 80-120 ml of chlyous drainage was obtained daily. Consequent to increased respiratory distress on the 8th postnatal day, thorax computed tomography (CT) was scheduled; it revealed ongoing bilateral pleural effusion (Fig. 1). No microorganisms were found to have grown on the pleural fluid culture. An infusion of the somatostatin analog octreotide (Somatosan, DEM, Istanbul, Turkey) at a dosage of 4 μg/kg/h was initiated; this was increased to 6 μg/kg/h on the 10th postnatal day on the basis of the daily drainage volume. The patient's need for respiratory support ended on the 11th postnatal day, but oxygen support was continued. The chest tubes were removed on the 19th postnatal day, and the octreotide dosage was reduced to 5 μg/kg/h. This was again decreased, to 4 μg/kg/h, on the 24th postnatal day, and continued as 0.1 mg/kg/day, s.c., beyond the 60th day. Follow-up thoracic ultrasonography, which was performed weekly, demonstrated the presence of bilateral effusion in progressively decreasing amounts.

On the 68th postnatal day, the patient was discharged with MCT formula and oxygen support, and the family was trained to administer octreotide at 0.03 mg/kg/dose t.i.d. His need for oxygen ceased one week after discharge from the hospital. The octreotide dosage was decreased 50% every three weeks and eventually withdrawn on the 160th postnatal day (for a total of 151 days of therapy). During octreotide therapy, no adverse effects (hyperglycemia, vomiting, diarrhea, constipation, reaction at the injection site, ECG changes, gallstones) were observed. The patient was healthy and neurodevelopmentally normal at his 18-month follow-up.

Discussion

Routine management of CC involves treatment of the underlying condition, draining of fluid, insertion of a chest tube until all the fluid is drained and, rarely, surgery. Octreotide is a drug that may reduce the production and accumulation of fluid and allow babies to recover faster. Although no trials have evaluated the safety and efficacy of this drug in infants, a limited number of case reports are available. The mechanism of action of octreotide in chylothorax is uncertain. It is suggested that octreotide causes mild vasoconstriction of splanchnic vessels, including those involved in hepatic venous flow. This leads to a reduction in gastric, pancreatic and intestinal secretions as well as intestinal absorption. However,

Table I. Biochemical and Microbiologic Results of Pleural Fluid

	Intrauterine	1st postnatal day	6th postnatal day	8th postnatal day
Density	1020	1022	1021	1025
LDH: Lactic dehydrogenase (U/L)	122	157	135	626
Protein (g/dl)	1.5	1.8	2.5	2.4
Triglyceride (mmol/L)	6.8	10.1	46.3	50
Cholesterol (mg/dl)	21	29	28	30
Cells (cells/ml)	1080	1170	1350	1410
Lymphocytes (%)	88	84	92	90

octreotide use is associated with adverse effects such as arrhythmias, injection site pain, nausea, vomiting, constipation, diarrhea, hyperglycemia, hypoglycemia, dizziness and fatigue; in neonatal case reports, a few adverse effects have been reported[2].

A Cochrane meta-analysis in 2010 identified 19 CC cases in which octreotide was used either subcutaneously or intravenously. Fourteen case reports described successful use (resolution of chylothorax), four reported failure (no resolution), and one reported equivocal results following use of octreotide[2]. The timing of initiation, dosage, duration and frequency of doses varied markedly. The longest duration was 35 days, reported by Coulter et al.[3] One unresponsive case was treated with OK-432, while 3 cases had surgery after 3, 5 and 22 days of octreotide treatment respectively[2]. In case reports published after 2010, 35 days was the longest duration of octreotide treatment indicated; unresponsive cases were generally treated surgically after 10 days[4,5]. Gastrointestinal intolerance and clinical presentations suggestive of necrotizing enterocolitis and transient hypothyroidism were reported as side effects in the Cochrane analysis. No practice recommendation could be made based on the evidence identified in this review.[2] A prospective registry of chylothorax patients and a subsequent multicenter randomized controlled trial to assess the safety and efficacy of octreotide in the treatment of chylothorax in neonates were suggested.

Antenatal management of chylothorax consists of thoracentesis or pleuroamniotic shunts to prevent pulmonary hypoplasia. Our patient's pleural effusion was drained twice in utero, and the patient was followed with conservative treatment, including continuous drainage, dietary modifications (MCT diet or total parental nutrition) and use of positive end-expiratory pressure during mechanical ventilation. In unresponsive cases, the surgical approach includes thoracoscopic pleurodesis, pleuroperitoneal pump, surgical abrasion, ligation of the thoracic duct and creation of a thoracic duct to azygous vein anastomosis. Octreotide, a somatostatin analog, is used for the management of patients with refractory chylothorax not responding to conservative management, in order to prevent surgery[2].

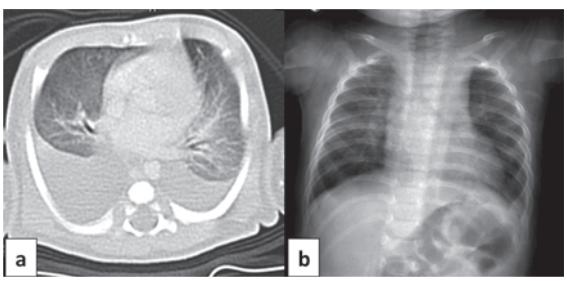

Fig. 1. a) Thorax computed tomography demonstrating bilateral pleural effusion. **b)** Chest X- ray in addition to ultrasonography performed weekly on follow-up revealed pleural effusion to have been completely resolved by the 160th postnatal day.

The use of octreotide in the treatment of chylothorax in infants and children has been reviewed. In cases published in the literature, octreotide has been used at a dosage of 0.3-12 μg/kg/h and, in general, for up to 10 days[2,3,6]. In our patient, we administered octreotide treatment at 6 μg/kg/h (IV) for 16 days, and continued with 0.05 mg/dose t.i.d. (s.c.) for 151 days. The patient was discharged on the 68th postnatal day, and family was trained to give s.c. injections. During the course of this treatment, no adverse effect was observed. To the best of our knowledge, our patient is the only newborn reported in the literature who has been treated with octreotide for such a lengthy period, without side effects. We suggest that octreotide seems to have a good safety profile in newborn infants and remains a promising alternative to surgery for cases of CC. Further multicenter studies are required to ascertain optimal dosing and duration of use for octreotide in the treatment of CC.

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