Case Report

Treatment of congenital chylothorax with octreotide in a hydropic preterm infant

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Congenital chylothorax is rare in preterm infants. While most cases respond to conservative treatment, a few require surgery. Treatment with intravenous octreotide has been reported to have varying success in preterm infants. A fetus was diagnosed with bilateral hydrothoraces at 29 weeks of gestation and repeated thoracocentesis was performed antenatally to allow growth of the lungs. She was delivered electively at 32 weeks by caesarean section. Hydrops fetalis was confirmed and chest tubes were inserted bilaterally soon after birth. Intravenous octreotide was commenced on day 4 of life, titrated to a maximum of 10 μg/kg/hr for a total of 28 days. Hydrothorax resolved at day 30 and total parenteral nutrition was given for a total of 37 days. She was successfully extubated on day 40 of life and discharged on day 80. On review at 6 months of age, she was thriving and developing normally.

Keywords: Congenital chylothorax, Octreotide, Somatostatin, Preterm

Introduction

Chylothorax is the presence of chyle or lymphatic fluid in the pleural space with triglyceride content >1.1 mmol/L, total cell count >1000 cells/ml and lymphocyte predominance >80%.[1] Accumulation of chyle results in pulmonary hypoplasia, the main cause of perinatal death. Complications comprising respiratory failure, infection, electrolyte imbalance and malnutrition occur as a result of loss of proteins, lipids, electrolytes, immunoglobulins and fat-soluble vitamins.[2] Over the past 9 years, a number of case reports have supported the use of intravenous octreotide to treat chylothorax in infants and children.[3–10] However, its use in cases of congenital chylothorax in preterm infants is very limited as it is relatively rare. A preterm infant with hydrops fetalis who responded to octreotide is described.

Case Report

A 31-year-old primigravida was found to have a fetus with bilateral hydrothoraces at 29 weeks of gestation. The fetus underwent serial ultrasound-guided thoracocentesis on the right side as it was the more affected side and easily accessible. The awkward fetal position precluded left thoracocentesis. A total of 11 antenatal thoracocenteses were performed. On each occasion, 80–100 ml of straw-coloured fluid was removed.

The infant was delivered at 32 weeks gestation by elective caesarean section. To facilitate resuscitation, a thoracocentesis was performed 1 hour before delivery. Weighing 1500 g, she was noted to be hydropic with a left pleural effusion and ascites. She was intubated at birth and at 3 hours of life an intercostal chest drain was inserted into the left hemithorax as the first chest radiograph (Figure 1) showed the pleural effusion to be more marked on the left. The intercostal chest tube drained 100 ml of straw-coloured fluid. She required a second chest drain on the right side at 6 hours of life which drained 80 ml of fluid. Analysis of the pleural fluid showed a glucose level of 5.6 mmol/L, triglyceride 0.38 mmol/L (unfed), lymphocytes 160×10^9/L and lactate dehydrogenase 68 IU/L. Results of investigations for causes of hydrops fetalis were normal with normal chromosome analysis and negative viral serology for toxoplasma, rubella, cytomegalovirus, herpes simplex, human immunodeficiency virus and parvovirus. Echocardiogram demonstrated a patent ductus arteriosus which resolved with conservative management and there was no pericardial effusion. Apart from ascites, ultrasound of the abdomen was normal and cranial ultrasound revealed no abnormalities. There was lymphopenia (0.3×10^9/L) which resolved after 4 weeks and serum albumin was 12 g/L.

Owing to worsening carbon dioxide retention, she required high-frequency oscillatory ventilation on day 3 of life and up to 280 ml of pleural fluid was drained. As there was still marked pleural drainage, intravenous octreotide was commenced on day 4 of life with an initial dose of 2 μg/kg/hr, gradually increasing to 10 μg/kg/hr over the next 4 days. Her response to octreotide was most dramatic during the

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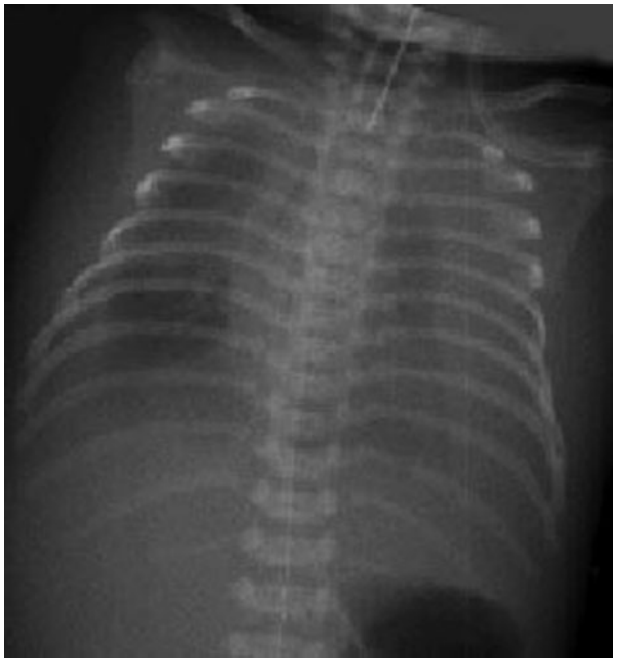

Figure 1 Plain supine chest radiograph showing marked left pleural effusion at 2 hours of life

initiation phase when pleural fluid drainage reduced markedly from 280 ml to 80 ml in 3 days (Figure 2). She was weaned to conventional ventilation on day 6 of life. There was some increase in the amount of pleural fluid on day 9 with expressed breast-milk and on day 19 with a trial of medium-chain triglyceride formula. On both occasions, the pleural fluid turned milky; on day 9, triglycerides were 1.4 mmol/L, glucose 4.1 mmol/L, lactate dehydrogenase 70 IU/L and lymphocytes 12×10^9/L. The marked increase in triglycerides confirmed the chylous nature of the pleural fluid. Octreotide was administered for a total of 28 days and the intercostal chest drain was removed a day later without reaccumulation of the pleural fluid.

Total parenteral nutrition was undertaken from day 3 to day 40 of life and she was ventilated for a total of 40 days. When expressed breast-milk was reintroduced enterally at day 30, there was no recurrence of pleural fluid. No adverse effect from the octreotide was noted. She remained well and was discharged on day 80 of life weighing 2610 g, corresponding to the 3rd centile. On review at 6 months of age, she exhibited normal growth and development.

Discussion

Congenital chylothorax in preterm infants is rare and most cases reported are case reports or case series. Congenital chylothorax associated with hydrops fetalis has an incidence of 1:15,000 pregnancies with a male:female ratio of 2:1.[11] At birth, respiratory function may be compromised with severe asphyxia as a sequela. Antenatal thoracocentesis, pleura-amniotic

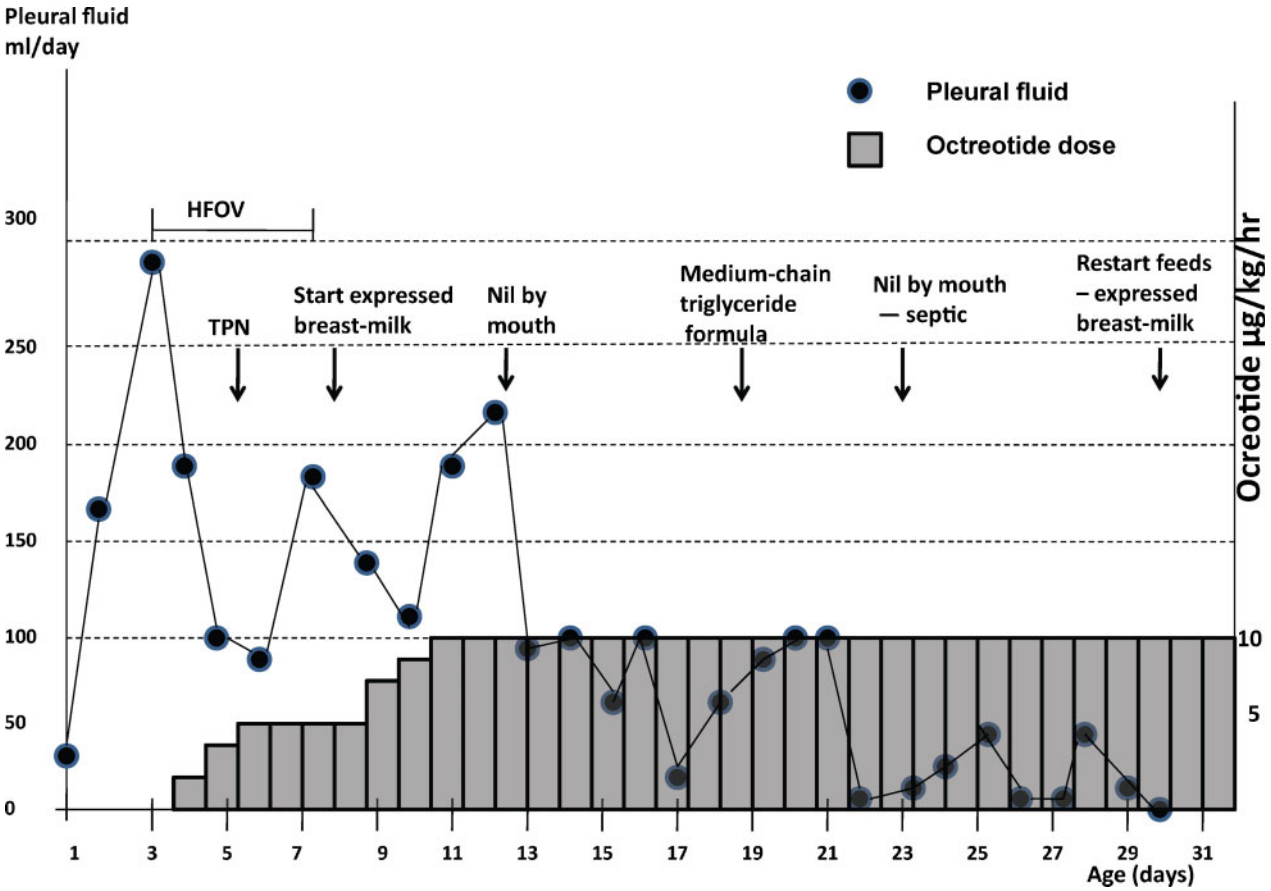

Figure 2 The amount of pleural fluid drained in relation to the dose of octreotide infused. Timing of enteral and parenteral

shunt placement and pleurodesis with *Streptococcus pyogenes*-derived sclerosant OK-432 are interventions to improve respiratory function in the immediate postnatal period and to prevent pulmonary hypoplasia.[12] In this case, antenatal thoracocentesis proved to be effective in delaying the placement of chest tubes in the immediate postnatal period and it allowed time to maximise treatment in terms of respiratory support.

Chylothorax can be primary, either congenital or spontaneous, or secondary following trauma or post-cardiothoracic surgery. The most common type of pleural effusion in the neonatal period is congenital or primary chylothorax. Roehr *et al.* found six reported cases of congenital chylothorax to whom octretotide was given.[13] Somatostatin was used for post-operative chylothorax only while octreotide was used for post-operative, congenital and spontaneous chylothorax.[13]

The pharmacological agent most commonly used to treat chylothorax is somatostatin or its long-acting analogue octreotide with a half-life of 2–6 hours. It reduces chyle flow by causing mild vasoconstriction of splanchnic vessels and hence reduces gastric, pancreatic and intestinal secretions as well as intestinal absorption and hepatic venous flow.

Octreotide has been used increasingly to treat congenital chylothorax. Overall mortality is reported to be 50% with poor prognostic factors associated with hydrops fetalis, congenital anomalies, gestational age <32 weeks, delivery prior to 35 weeks gestation and abnormal karyotype.[2] Rasiah *et al.* reported the youngest patient, a 34-weeks preterm hydropic infant with congenital chylothorax treated with octreotide.[3] The patient in this report was a preterm infant born at 32 weeks gestation who was hydropic with bilateral chylothorax and poor prognostic factors who not only avoided surgery but was successfully treated with octreotide. As this infant was preterm, Table 1 lists most reports of congenital chylothorax in preterm infants only.

Although it took 28 days for the chylothorax to resolve, the initial response to octreotide was good. It has been suggested that in some cases it is worthwhile using a conservative approach with total parental nutrition and enteric rest for over 3 weeks.[1] We chose a conservative approach because of the prematurity and to avoid the complexity of surgery. However, when the pleural drainage increased markedly, octreotide was commenced immediately. Although the response to octreotide was initially dramatic, it might have been coincidental owing to the natural history of spontaneous resolution of chylothorax with time.

Because of the paucity of literature on the use of octreotide in neonatal chylothorax, there is no general concensus on the optimum dose for its use. Rasiah *et al.* noted improvement with doses of 1–2 μg/kg/hr of intravenous infusion of octreotide in other studies but generally a dose of 10 μg/kg/hr appeared to be the threshold dose at which benefit was seen and doses above this did not seem to confer further benefit.[3] Roehr *et al.* found variation in dosages of somatostatin and octreotide used for treatment of

Table 1 Studies reporting the use of octreotide for congenital/spontaneous chylothorax in preterm infants

Author	Patient profile	Age drug commenced	Duration (days)	Maximum dose	Route	Response	Side-effects
Rasiah *et al.*[3] 2004	Preterm 34 wks, hydrops fetalis	Day 32	10	10 μg/kg/hr	i.v.	Resolved day 2	Transient abdominal distention
Sivasli *et al.*[4] 2004	Preterm 34 wks, dysmorphic	Day 22	22	3.5 μg/kg/hr	i.v.	Resolved day 3	Nil
Maayan-Metzger *et al.*[5] 2005	Preterm infant	Day 33	10	60 μg/kg/day	i.v.	Resolved day 2	Transient hypothyroidism
Roehr *et al.*[6] 2005	Preterm 34 wks, hydrops fetalis	Day 53	21	40 μg/kg/day	s.c.	Resolved day 21	Nil
Sahin *et al.*[7] 2005	Preterm 33 wks	Day 15	10	10 μg/kg/hr	i.v.	Resolved day 10	Transient abdominal distention
Lauterbach *et al.*[8] 2005	Preterm 24 wks	Day 103	4	0.3 μg/kg/hr	i.v.	Resolved day 1	Nil
Goto *et al.*[9] 2003	Preterm 26 wks	Day 36	3	0.3 μg/kg/hr	i.v.	Resolved day 2	Nil
Coulter *et al.*[10] 2004*	Preterm 26 wks	Day 103	42	4 μg/kg/day s.c. & 1 μg/kg/hr i.v.	s.c. & i.v.	Resolved day 6	Nil
Ochiai *et al.*[16] 2006	Preterm 29 wks, Trisomy 21	Day 180	22	1–10 μg/kg/hr	i.v.	No response	Nil
Matsukuma *et al.*[17] 2009	Preterm 33^{+6} wks	Day 23	5	0.5–10 μg/kg/day	i.v.	No response	Not specified
Matsukuma *et al.*[17] 2009	Preterm 33^{+6} wks	Day 28	Unknown	10 μg/kg/day	i.v.	No response	Not specified
Current report 2012	Preterm 32 wks, hydrops fetalis	Day 4	28	10 μg/kg/hr	i.v.	Resolved day 28	Nil

* Coulter *et al.* reported convincing evidence of octreotide response where chylothorax ceased during octreotide infusion but recurred after octreotide was stopped and responded completely to a longer course of octreotide.

chylothorax.[13] In their systematic review,[13] somatostatin was used to treat post-operative chylothorax only, whereas octreotide was used for post-operative, congenital and spontaneous chylothorax. In most reports, the effects of octreotide were seen after 5–6 days.[13] In the literature review outlined in Table 1, octreotide dosage ranged from 0.3 to 10 μg/kg/hr. Generally, the maximum optimum dose appeared to be 10 μg/kg/hr.

Somatostatin and octreotide may cause minor side-effects such as 'flu-like symptoms, flushing, nausea, diarrhoea, transient abdominal distension, deranged liver enzymes, transient hypothyroidism and hyperglycaemia. Necrotizing enterocolitis has also been reported and is a potentially fatal side-effect of octreotide.[14,15] In the reports cited in Table 1, the most common side-effect was transient abdominal distention. However, because of the lack of reports in the literature, the long-term safety and adverse effects are not well known.

Although octreotide has been shown to be effective in the treatment of congenital chylothorax in addition to good antenatal care and other conservative measures, clinical improvement may coincide with the natural history of spontaneous resolution with time. We believe this is one of the youngest patients with poor prognostic factors of hydrops fetalis as well as being preterm in whom surgery such as thoracic duct ligation, pleuroperitoneal shunts or pleurodesis was avoided and who improved clinically on octreotide. In view of the infrequent occurrence of this condition, further multi-centre trials are required to ascertain the optimum dosage, duration, safety aspects and long-term sequelae of octreotide.

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