2 nd Case Presentation for the Course in Clinical Nutrition

GESKES/ SSNC

Case of Congenital Chylothorax and its Nutritional Treatment

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1. Summary

The management of congenital chylothorax with hydrops encompasses basic and advanced life support at birth, preparation for immediate chest tube placement, followed by continuous pleural drainage until chylous flow has ceased. Chylous replacement needs to be tailored and replaced 1:1. The infant needs specific dietary measures (especially TPN for 5-7 days and special fat-free formula thereafter) with slow introduction of enteral feeds. Once full feeds are established, special care needs to be taken to administer long chain fatty acids without provoking recurrence of chylothorax. If conservative measures fail over a prolonged period or TPN associated complications arise, pharmacological treatment with somatostatin or even surgery must be evaluated.

2. Key Words

Chylothorax; individualized diet; fat-free formula.

3. Abbreviations

Total parenteral nutrition (TPN), Medium Chain Triglycerides (MCT)

4. Introduction

Congenital chylothorax is defined as an accumulation of chylous fluid in the pleural space often detected by antenatal ultrasound. It is a very rare disorder, estimated to occur in 1 of 10-15'000 births (range 0,75-5,5 per 10'000 births) and usually is an isolated finding.[1, 2, 3] In even rarer cases it can be associated with chromosomal or cardiac anomalies or certain syndromes. [4] The finding can be from incidental to presenting as respiratory distress, and in pronounced circumstances even lead to the development of fetal hydrops. In the latter case perinatal mortality is rather high ranging from 15-50 %. [3, 4] Since this is such a rare clinical situation, there is no strict consensus in management. [1,4,5] Many cases can be managed conservatively via fat-free nutrition and parenteral support in addition to the chest tube placement.

5. Case Presentation

J.S. was born to a healthy second gravid 1st parity mother of 39 years. The pregnancy was uneventful until the 35th week, when a fetal hydrops with pleural and abdominal effusions were diagnosed by ultrasound. The mother was immediately transferred to our tertiary care centre for further management. Since the mother also presented with polyhydramnios and irregular contractions, the baby was rapidly delivered by elective cesarean section at 35 1/7 weeks gestational age with a birth weight of 2560 g (P 50). Immediately after she was born, the infant was intubated and thoracocentesis performed bilaterally. Drainage fluid amounted to about 100 ml on both sides. This is an enormous quantity when considering the circulatory volume to be about 200-260 ml of blood. Primary adaptation was limited because of restricted ventilation and difficulty intubating due to generalized oedema. Cardio-vascular compromise necessitated cardiac massage as of 4 minutes of age. Her Apgar values were 1, 2 and 3 at 1, 5 and 10 minutes respectively. She developed arterial hypotension, necessitating volume replacement and then vasopressor

treatment with dopamine. She required considerable ventilatory support for her size and age. During the ensuing days the pleural drainage continued to flow at a rate of 200 ml/d (which corresponds to approximately 3,5 ml/kg body weight/h). The diagnosis of chylous fluid was highly probable with a total white cell count of 9100 x 10^6/L that showed 80% lymphocytes on the first analysis. The abdominal sonogram revealed a small amount of ascites without any other pathology. Head ultrasound showed a normal anatomy. On echography the heart had a normal structure and function. The arterial hypotension was transient, and probably due to the chronic intrauterine intravascular depletion as well as the circulatory compromise that the pleural effusions had on the great vessels. Dopamine was weaned over 48 hours and blood pressure remained normal as long as volume losses were replaced. Apart from the hydropic signs the clinical status was normal as was the karyotype, ruling out chromosomal syndromes associated with chylothorax (such as Trisomy 21 or a Turner Syndrome). Maternal serologies were non-contributory. The aetiology of the congenital chylothorax remains unclear and is most likely due to a congenital malformation of the intrathoracic lymphatic system.

Because of the continued pleural drainage, the infant developed a marked hypoproteinaemia, hypalbuminaemia, as well as hypogammaglobulinaemia, both of which we proceeded to replace at regular intervals (see figure 1 for course of total protein). The large volume losses also meant considerable electrolyte losses that needed close monitoring and replacement.

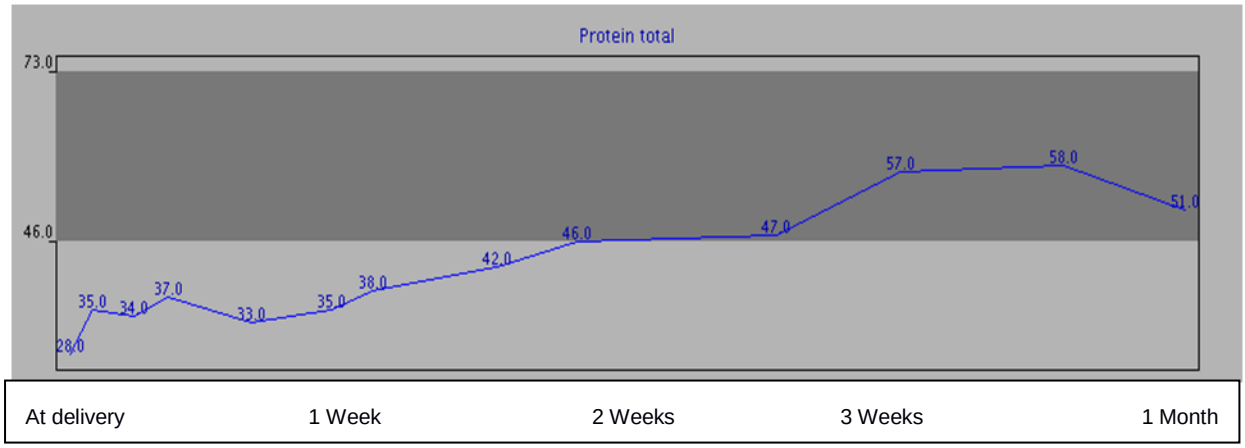

Fig 1: Course of total serum protein content in g/L from delivery to 4 weeks of age

In regards to the nutritional management, we exposed the infant to expressed breast milk within hours of delivery. The results in the pleural effusions were prompt, with the appearance of a milky colour (the first pleural drainage fluid was transparent and honey-coloured), elevated triglycerides at 5,51 mmol/L as well as a marked leucocytosis of now 14 450 x 10 6 cells/L with lymphocytic predominance (80% in the differential). Because the enteral nutrition with breast milk lead to an increased production of chylous fluid, we switched within one day to a formula called basic F (Milupa®), a special 'fat free' formula for the management of disorders in fat metabolism or chylothorax, as in our case (see Table 1). The remaining required fluid was given as parenteral nutrition. Over a period of 10 days the chylous drainage decreased to 100, then gradually to 60 and finally to 15 ml/day.

Composition per 100 ml			
	Basic F (Milupa ®)	Human Milk	Standard Infant Formula
Energy (kcal)	49	65-70	66
Protein (g)	1,8	0,7-1	1,3
Fat (g)	< 0,1	4-5	3,4
Carbohydrates (g)	10,2		7,4
Lactose (g)	4,1	6	7

Table 1) Comparison of Special Formula with Human Milk and Regular Formula. [15,16]

The infant was extubated on the 8th day of life. She tolerated advancing enteral feeds with basic f all the while receiving intravenous lipids as well as all vitamins according to her body weight. The pleural tubes were removed on the 12th day of life. Within 8 days though she redeveloped a chylothorax, necessitating new bilateral pleural tubes. This time we managed to maintain spontaneous respiration, solely administering oxygen via a nasal cannula and indwelling chest tube under morphine analgesia and chloral hydrate sedation. Enteral feeds were completely withheld for 6 days. In order to decrease intravascular volume, and thus indirectly reduce lymphatic volume, she was also given furosemide for 3 weeks duration. All the while, the pleural replacement was continued 1:1 with differing liquids, according to her laboratory results of total protein, immunoglobulins and albumin.

Despite the dysproteinaemia with considerable hypalbuminaemia (minimally at 17,7 g/L; norm 38-54 g/L), the risk-benefit ratio was deemed too unfavorable to justify thrombosis prophylaxis.

After 6 days of TPN, the baby was gradually re-introduced to basic f (Milupa ®) special formula up to a total volume of 160 ml/kg/day. According to enteral tolerance, the parenteral nutrition was slowly reduced over the duration of 10 days. Once full feeds had been re-established, the infant was given increasing amounts of Liquigen® (20% medium chain triglycerides) to a maximum of 3 g/kg body weight/ day. Once the parenteral nutrition ceased, she no longer received the essential long chain fatty acids, which is why we very gradually added walnut oil to the milk to a maximum of 2 ml total per day. We also added a multivitamin preparation at the usual dose of 2x 6 drops. She remained stable without clinical or radiological evidence of a recurrent pleural effusion. After a total of 6 weeks of this special diet, the baby was successfully re-exposed to maternal breast milk. After a further 10 day observation period, she was discharged on demand full breast feeding.

She is currently 18 months old, weaned from breast milk, developing normally and thriving.

6. Discussion

As stated above our infant was born with fetal hydrops due to congenital pleural effusion, which had accumulated bilaterally in the thorax to such an extent as to become haemodynamically significant. This is an extremely rare condition with an incidence ranging from 0,7-5,5 per 10'000 births. [1, 2, 3] The diagnosis of congenital chylothorax is established by exclusion and through the clinical course. In our case, the infant's chromosomes returned normal in number, thus excluding Trisomy 21 or Turner Syndrome. Clinically there were no signs of a syndromal disorder. The additional exams revealed a normal echography of the heart, normal ultrasound of the brain and abdomen, largely excluding a Noonan Syndrome. There were no signs of increased venous pressure of the superior caval vein, nor was there any evidence on clinical, radiological nor laboratory exams of any malignancies or benign tumors in the thorax. Some congenital viral infections can lead to foetal hydrops and secondarily to pleural effusions. [5] Our infant had no clinical, nor laboratory evidence of a congenital infection. Given the antenatal occurrence of the pleural effusion without antecedents of either surgical interventions, or trauma, post traumatic etiologies could be ruled out.

In light of the laboratory findings (absolute cell count >10 ^{6}/L, with a lymphocyte fraction >80% and triglyceride levels >1,1 mmol/L) [4, 5, 7] in the pleural effusion as well as the clinical course, we conclude that our infant had a congenital chylothorax, that responded favourably to conservative management. What ultimately led to the pleural effusion remains unclear. A more important anomaly of the lymphatic system such as a primary lymphangiectasy seems improbable given the favourable respiratory response. Usually infants presenting with primary lymphangiectasy show a profound respiratory insufficiency and usually succumb with postmortem confirmation of diagnosis.

On first analysis the pleural effusion showed an elevated cell count with lymphocytic predominance. In the absence of enteral nutrition and thus the appearance of chylomicrons and elevated triglycerides, this is highly suggestive of a chylous pleural effusion. Once the infant was challenged with enteral feeds the chylous promptly showed elevated concentrations of triglycerides.

Chyle transports lipids and lipid soluble vitamins which have been absorbed from the small bowel and incorporated into chylomicrons. [6] The chyle collects in lymphatic capillaries, accumulating excessive interstitial fluid, extravasated proteins and lymphocytes. The chyle then is transported in the lymphatic system through the lymphatic duct to rejoin the venous system at the venous angle. Any interruption in the anatomical course of the lymph system can lead to chylous accumulation in the thorax. In the newborn this is most frequently observed after cardiac surgery for congenital anomalies or after diaphragmatic hernia repair. [1, 4, 6, 7]

Given the above functions of chyle, the chronic removal thereof can lead to considerable morbidities (restrictive lung disease with pleural effusion, protein-energy malnutrition because of large protein and lipid losses, increased risk of infection because of lymphocyte loss and hypogammaglobulinaemia, hypovolaemia and electrolyte derangements) and increase mortality. [4,12]

We opted to initially replace removed chyle 1:1 with normal saline, fresh frozen plasma, and then, once concentrations were proven to be low, also to replace immunoglobulins and albumin accordingly.

The basal flow rate of chyle is around 1,4 ml/kg body weight/ h and can increase tenfold after fat-containing meals. [2, 4] Even after enteral ingestion of liquids containing carbohydrates and protein the flow rate can increase. Thus, a first approach in treating chylothorax, apart from pleural drainage, is to administer total parenteral nutrition (TPN) to reduce chylous flow and allow spontaneous healing of the lymphatic system. [4, 5, 6] There is no consensus on the duration of TPN, since all the experience in neonatology comes from case series. [4, 5, 6, 7]

In our infant, when the chylothorax recurred, we also added a diuretic to reduce intravascular, and thus also lymphatic volume. [12] Once again, there is no strict treatment protocol to indicate diuretics. Once the chylous flow has diminished satisfactorily the gut is rechallenged with a fat-free diet, in our case a fat-free formula. MCT is added as caloric source since MCT consists of triglycerides with short enough fatty acids to be directly absorbed into the venous system, thus bypassing the lymphatic pathway. [4,5, 6,] In the second attempt, once the infant was on full enteral feeds, we added walnut oil to the diet. This was done to substitute the long chain fatty acids. Walnut oil was chosen over other healthy vegetable oils for its favourable properties in regards to long chain fatty acids. [8,9] Little is known about the development of walnut allergies after exposure during the neonatal period. What is of concern though, is that walnut oil, cold pressed more so, can lead to allergies in susceptible individuals and that tree nut allergies seem to be morepersistent than other food allergies (i.e. egg white or cow's milk). [17, 18]

The mother of the infant was a second time mother, who had previously successfully breast fed her child. She was motivated to do so with her second-born and diligently expressed her milk. There are case reports where skimmed expressed human milk was given to infants with chylothorax. [13,14] We considered doing this for our infant, since human milk has many nutritional advantages over industrially-produced formula. We were unfortunately met with logistical and hygienic problems. We nevertheless encouraged the mother to continue expressing breast milk with the aim of switching back from formula to human milk once the chylothorax had resolved.

Increasing numbers of case reports are being observed where patients with chylothorax (congenital and postoperative) are being treated in refractory situations with Octreotide, a somatostatin analogue, which reduces chylous flow. [4,5, 6, 10] Unfortunately, no randomised trials have been conducted due to the low number of cases. Currently, the case reports allow no conclusions as to the safety and the efficacy of this approach. Furthermore, the doses used in the case reports vary greatly, from 0,3-10 ug/kg/h as continuous infusions or 10-70 ug/kg/day subcutaneously. [10] The advantage of using Octreotide is in reducing the duration of TPN and its associated complications. [4, 5, 6, 10, 11] We declined the use of Octreotide, since our infant was premature and thus at risk of developing some of the feared side effects, such as necrotizing enterocolitis, hyperthyroidism, reduced retinal neo-vascularization, or even persistent pulmonary hypertension of the newborn . [4, 6, 10, 11] Furthermore, our infant responded promptly to our nutritional intervention, even the second time around.

Surgical interventions are reserved for refractory cases where chyle continues to be produced or complications of TPN appear. [7, 6, 12] Once again, however, there is no consensus on the timing of surgery, nor the best surgical approach to take (i.e. lymphatic duct ligation at multiple sites, pleurodesis or lastly pleuro-peritoneal shunting). [5, 6, 12]

7. Learning points

1. Congenital chylous effusions can be managed conservatively via nutrition, thus avoiding surgery.
2. Total parenteral nutrition during prolonged periods can be therapeutic, but bears a high risk of secondary cholestasis, respectively hepatopathy.
3. Fat-free enteral nutrition is feasible but needs special attention to essential long chain fatty acids.
4. Special fat-free infant formula is available. However, skimmed expressed maternal breast milk is a desirable alternative.
5. Chronic chyle loss without appropriate replacement can lead to medical complications, such as hypovolaemia, dyselectrolytaemia, dysproteinaemia and generalized edema, malnutrition and immunosuppression to name the most frequent.
6. Second line treatment options are medication with Octreotide or surgical management with thoracic duct ligation, pleurodesis or pleuro-peritoneal shunt.

8. Literature

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