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CASE REPORT

Challenges of Diagnosis and Management of Congenital Chylothorax in a Low-Resource Setting: A Case Report

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Summary

Chylothorax is a form of pleural effusion. In the neonate, it may be diagnosed in the antenatal or postnatal period. Congenital forms of chylothorax are due to abnormal development or obstruction of the lymphatic system and may be associated with hydrops foetalis; it may also be idiopathic or associated with chromosomal anomalies. The diagnosis is usually based on biochemical analysis of pleural aspirate, and the interpretation of the biochemical parameters depends on whether the baby is feeding. The treatment involves dietary modification, the use of different types of drugs, chest tube drainage, pleurodesis or some other surgical intervention. There are no clinical trials to document the most effective treatment modality. Intrauterine interventions have been reported in some cases. We report a case of neonatal chylothorax to document the diagnostic challenges and management outcomes in a resource-limited setting.

***Keywords:** Chylothorax, Congenital, Lymphatic channels, Neonatal feeding, Octreotide, Pleural effusion, Resource-limited setting.*

Introduction

Chylothorax as a cause of pleural effusion in neonates can be acquired (usually after surgery or some trauma)[1,2] or congenital.[3,4] It is defined as the abnormal accumulation of chyle inside the pleural space.[5] The reported incidence of congenital chylothorax was 1/24,000 births in a population-based study.[6] Congenital forms of chylothorax are due to abnormal development or obstruction of the lymphatic system and may be associated with hydrops foetalis. [3,4] Congenital chylothorax may be idiopathic or associated with chromosomal anomalies.[4,6–8] It is the most common cause of pleural effusion in the perinatal period.[7]

Chylothorax may be diagnosed antenatally (by Obstetric ultrasound scan) or postnatally.[5] It is helpful to ascertain the diagnosis as there are some treatment option variations depending on the aetiology. [3] In the analysis of pleural aspirate for suspected chylothorax, it is important to note that the levels of the analytes depend on whether the infant has been fed or not because the chyle contents of the thoracic duct include triglycerides in the form of chylomicrons coming from the intestines.[9]

The diagnosis of chylothorax is based on the following criteria as applied to the chylothoracic fluid:[10]

a) High concentration of triglycerides (>110 mg/dL [>1.24 mmol/L]) in a patient who is on a normal diet (for example, breast milk in a neonate). It may be lower in a fasting neonate.[9]
b) Cholesterol level is generally less than 200 mg/dL (<5.18 mmol/L).
   A cholesterol level greater than or equal to 200mg/dL (≥5.18 mmol/L) supports a diagnosis of cholesterol effusion and is not typically seen in chylothorax.
c) Appearance – The appearance of fluid from a chylothorax can be milky, sanguineous, or serous, depending on many factors.
d) Glucose, electrolyte and protein levels are similar to plasma levels.
e) pH 7.40 to 7.80
f) Lactate dehydrogenase (LDH) is usually less than two-thirds of the upper limits of the normal serum LDH if the cause is a simple leakage from the lymphatic channels. Otherwise, an associated condition like malignancy should be considered.[9,11]

Other investigations, such as chest Computerised Tomography (CT) scan or Magnetic resonance Imaging (MRI), chromosomal assays, genetic analysis, and echocardiography, are needed to make a firm diagnosis of the aetiology, but they are either unavailable or unaffordable in resource-limited settings.

The treatment of chylothorax involves dietary modification, total parenteral nutrition, the use of different types of drugs like octreotide and midodrine,[8,12] chest tube drainage, pleurodesis [13,14] or some other surgical intervention.[7] There are no clinical trials or consensus to document the most effective treatment modality.[3,7] Intrauterine interventions (thoracentesis and thoracic-amniotic shunting) have been reported in some cases of severe intrauterine chylothorax and appear to improve outcomes.[5,15]

We report this case to document our challenges with establishing a diagnosis and instituting appropriate therapy and the outcome of management in our resource-limited setting.

Case Description

The patient is a male infant who presented at the Babcock University Teaching Hospital, Ilishan-Remo, at the age of 48 hours on referral from a government-owned secondary health facility on account of difficulty with breathing, which was noted soon after birth and jaundice noted about 24 hours after birth. The baby was commenced on intranasal oxygen in the referral centre, and the distress initially subsided, so the baby was commenced on direct breastfeeding at about 38 hours of life. About eight hours after putting the baby to the breast, the difficulty with breathing became noticeable again, with SPO_2 dropping to 77% in room air, which necessitated the referral. The baby was delivered at an estimated gestational age of 38 weeks via elective lower segment Caesarean section on account of a previous uterine scar and breech presentation. The APGAR scores were four at one minute, six at five minutes and six at ten minutes. The birth weight was 3.4kg. The pregnancy was booked in the referral centre, and the last Obstetric USS was done a month before delivery and revealed no abnormality. There was no history of prolonged rupture of membranes, antepartum haemorrhage, peripartum pyrexia, abnormal vaginal discharge, maternal diabetes mellitus or hypertension.

At presentation, he was acutely ill-looking, with central cyanosis, in respiratory distress, afebrile, mildly icteric, not pale, not dehydrated, and with no peripheral oedema. Anthropometric measurements were normal. On the respiratory system examination, he was tachypnoeic with a respiratory rate of 70 cycles per minute and had intercostal and subcostal

recessions. The chest was barrel-shaped, and the breath sounds were bronchovesicular. There were slightly reduced breath sounds at the right lung bases. Other systemic examinations revealed no abnormality. At this point, the working diagnoses were "Term male neonate with severe perinatal asphyxia and hypoxic ischaemic encephalopathy (HIE, Sarnat and Sarnat Stage I) and neonatal jaundice. The differential diagnoses included aspiration syndrome and acyanotic congenital heart disease.

He was commenced on intravenous fluids, intranasal oxygen via an improvised bubble CPAP setup at six cm of water, and intravenous cefuroxime. The serum calcium was normal, but the electrolytes urea and creatinine result showed hypokalaemia (3.1 mmol/L), so he was commenced on maintenance intravenous infusion of 15% potassium chloride. He was also placed on *nil per os* at admission.

On the third day of admission (fifth day of life), his respiratory examination revealed dull percussion notes on both lung zones, worse on the right. The breath sounds were vesicular with coarse crepitations and were markedly reduced on the right. Also, on that day, he had an episode of apnoea, which warranted five minutes of manual positive pressure ventilation before he regained spontaneous respiration. SPO_2 was 92%, and random blood glucose was 142mg/dl. A few minutes after he was resuscitated, he had two brief episodes of tonic-clonic seizures, each episode lasted for about ten seconds, and the duration between the episodes was about 30 seconds. Hyperbilirubinaemia peaked at 14.3mg/dL on the 6th day and was managed with only phototherapy.

On the third day of admission, and on account of the dull percussion notes and reduced breath sounds on the right hemithorax, thoracocentesis was performed on the affected side. The procedure yielded 35mls of free-flowing, golden yellow fluid, which was subjected to chemical and microscopic studies (Figure 1). A plain chest radiograph was done, and it showed homogenous opacity on the right side of the chest with almost no obvious lung tissue markings (Figure 2).

Figure 1: Golden yellow-coloured pleural aspirate obtained when the baby was *nil per os*

A temporary chest drain with a 16G cannula for continuous drainage of the pleural effusion was inserted, while awaiting definitive chest tube drainage to relieve the tension. The respiratory distress subsided after that. Two hundred millilitres of fluid were drained over two days before the temporary drain fell off. The biochemical analysis of the first aspirate is shown in Table I.

Enteral feeding with breastmilk via nasogastric tube was re-commenced on the fifth day of admission when respiratory distress initially subsided significantly. As noted earlier, feeding had been initially withheld at the point of admission on account of respiratory distress. The placement of closed tube thoracostomy drainage could not be done until the seventh day of admission owing to financial constraints with getting the sterile equipment and materials needed for the procedure. When the chest tube was eventually placed, it was noted that the effusion drained had changed in colour and consistency (Figure 3). The biochemical analysis of the new sample is shown in Table I.

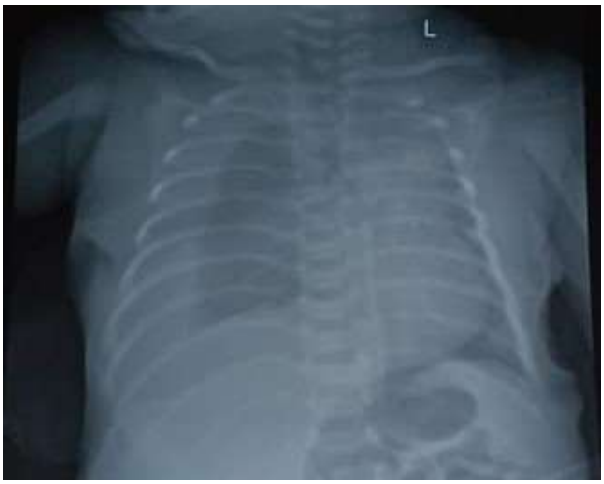

Figure 2: Plain chest radiograph showing massive pleural effusion on the right side with mediastinal shift

Table I: Pleural aspirate parameters before feeding and after commencement of feeding

Parameters	*Clear golden yellow effusion on Day 3 while on Nil per os*	*Chylous effusion on day eight after commencement of feeding on Day 5*
Total Cholesterol	0.9mmol/L	1.4 mmol/L (normal)
Triglyceride	0.5mmol/L	5.3 mmol/L (elevated and diagnostic)
Glucose	6.3mmol/L	4.8 mmol/L
Protein	1.99g/L	2.1 mmol/L
pH	7.0	
Specific gravity	1.010	
Microscopy, culture and sensitivity	Microscopy showed cocci, but no growth.	No organism was reported on microscopy, and culture yielded no growth. White blood cells: 6-8 cells/hpf, no differential count.

When the drainage of chylous fluid persisted actively for a further six days (at that time, the patient had drained a total of 685 mls), the pharmacotherapeutic management of chylothorax was commenced with octreotide infusion based on previous reports about its usefulness in the condition[16,17] at 1 microgram/kg/hr on day 13 of admission. Over the next 72 hours following the commencement of Octreotide infusion, the patient drained only 30 mls of fluid more, and there was no further drainage at all in the following two days.

A grade 2/6 systolic murmur was discovered on the left sternal border on the tenth day of admission; this was suspected to be either an innocent murmur or a ventricular septal defect murmur. This persisted until discharge, but echocardiography could not be done owing to financial constraints. The baby was discharged on the 21st day after admission.

Financial constraints hampered a full evaluation of the baby, hence important investigations (like blood culture, and echocardiography), to exclude likely differentials like sepsis or an acyanotic congenital heart disease could not be done. However, the final diagnosis made in the patient was congenital chylothorax based on the onset of respiratory distress with initiation of feeds initially at the referral centre and the markedly elevated triglyceride levels in the pleural aspirate (which is not a normal constituent of a purely infectious/inflammatory empyema) after resuming feeds in our unit, as described earlier.

The markedly elevated aspirate triglycerides when the patient was on *nil per os* up to four times the upper limit of normal within three days after commencement of enteral feeding with breastmilk, the rapid decline in the previously persistent chylous effusion within 72 hours of the commencement of octreotide infusion, and absence of significant inflammatory cells or bacteria in the pleural aspirate are all in keeping with a diagnosis of congenital chylothorax.

Figure 3: Chylous pleural effusion after the baby re-commenced feeding with breast milk

The infant was not brought for follow-up as planned (because of financial constraints) until he was about two months old and had a new chest radiograph showing clear lung fields and a normal cardiac silhouette. He was again reviewed at eight months; the murmur was no longer audible, and the baby was growing well with appropriate anthropometric measurements and developmental milestones on breastmilk and complementary feeds. His immunisation was up to date at that last visit.

Discussion

The thoracic duct transports chyle (which is a mix of triglycerides in the form of chylomicrons, fat-soluble vitamins, proteins, immunoglobulins, T-lymphocytes, and electrolytes) from the intestine to the bloodstream.[10] It commences at the cisterna chyli, coursing through the mediastinum as it receives non-chylous lymph from tributaries in the pulmonary parenchyma and parietal pleura,[18] and ends at the junction of the left subclavian and jugular veins. This flow increases with dietary fat intake, particularly long-chain triglycerides. Interestingly, long-chain triglycerides constitute 90% of the fatty acid content of breast milk.[19] Any disruption or dysfunction of the flow of chyle across the normal anatomic pathways can result in chylous pleural effusion.[10] Congenital forms are due to abnormal development or obstruction of the lymphatic system.[3,4]

The management of the index case was punctuated at several points by financial constraints that limited the scope of investigations and the required interventions. The delay in diagnosis and commencement of appropriate interventions resulted in lung collapse and eventual apnoea. The ensuing cerebral hypoxia is a likely explanation for the seizures since they did not recur after chest drainage started. A central nervous system infection is another possibility, but the non-availability of funds limited the scope of our evaluation. Notably, the seizures did not recur after the thoracocentesis and subsequent drainage of the pleural effusion commenced. The infant also had no other neurologic symptoms or signs till discharge. The resumption of the distress after the commencement of breastfeeding from the referral centre was probably due to increased thoracic duct flow, which was stimulated by feeding, as described earlier. Another initial problem with establishing the diagnosis was finding normal levels of Triglycerides (TG) in the pleural aspirate. This should have been expected because, in the fasting state, there is no available intestinal TG to traverse and leak through the thoracic duct pathways, based on the normal anatomy and physiology of the thoracic duct.[9,10,18] The respiratory distress necessitated the restriction of enteral feeds, thereby contributing to delayed diagnosis.

The measurement of diagnostic levels of TG depends on feeding on diets containing fats (in this case, breast milk).[9] The goal of treatment is to reduce the volume of lymph/chyle drainage and to allow time for the injured lymphatic vessels to heal (in acquired chylothorax) or develop (in congenital chylothorax).[3] Apart from pleural fluid drainage, the available treatment modalities in order of less likelihood of side effects include feeding with medium-chain triglycerides (MCT) or skimmed milk (having no long-chain triglycerides), restriction of enteral feeds with parenteral nutrition (PN) for some days – these modalities will reduce the thoracic duct flow. The following treatment modalities in order are the use of octreotide (which slows down lymphatic secretion), pleurodesis (to obliterate the pleural space), and surgical ligation (to block the flow through the thoracic duct).[7,8,12] Other interventions in previous reports include high-frequency ventilation, midodrine or etilefrine infusion (which are both alpha-adrenergic agonists and work by vasoconstriction of the lymphatic channels), inhaled nitric oxide, sildenafil (which reduce lymphatic flow by vasodilatation) and glucocorticoids (which may be useful to treat an underlying cause like sarcoidosis). Other surgical modalities include pleuroperitoneal shunt (to divert the accumulated effusion).[20]

In the index case, we could not give skimmed breastmilk, MCT formula or PN with feed restriction owing to non-availability at that time. Therefore, octreotide was the next treatment modality available and was used accordingly. Octreotide is a synthetic analogue of somatostatin, which works by decreasing splanchnic blood flow, inhibiting the release of serotonin, gastrin, vasoactive intestinal peptide, secretin, motilin, and pancreatic polypeptides, and thereby reducing lymphatic flow.[3] No clinical trials have studied the effectiveness of octreotide for the treatment of neonatal chylothorax.[17] A systematic review of the literature suggests that octreotide is safe and effective in 47% of neonatal chylothoraces.[17] Reported side effects of octreotide include persistent pulmonary hypertension, necrotising enterocolitis, and transient hypothyroidism.[16] None of these side effects were noted in the index case. The infant responded well to octreotide in addition to the chest tube drainage, with a rapid slowing down of the effusion. Therefore, we did not need to apply other treatment modalities.

Conclusion

The scope of diagnostic and interventional modalities is still limited in resource-poor settings like ours because of financial constraints and out-of-pocket healthcare payments. Diagnostic findings depend on whether the infant is feeding or not. Initiation of enteral feeding with breastmilk may accelerate the effusion process and worsen respiratory distress, but dietary management is not readily available or sometimes not feasible in our setting. In any case of respiratory distress in a newborn within the first week of life, congenital chylothorax should be considered a possible differential diagnosis. If confirmed, closed-tube drainage and octreotide infusion may result in a successful outcome as they did in the case reported.

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