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Diagnosis and management of congenital chylothorax

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ABSTRACT

Congenital chylothorax, the accumulation of lymph in the pleural space, is a rare and serious condition that can appear alone or accompany congenital anomalies. Ultrasonography and pleural fluid analysis can diagnose it early from the fetal period. Both prenatal and postnatal therapeutic interventions improve the fetal prognosis and decrease the rate of complications.

Keywords: pleural effusion, fetal hydrothorax, chylothorax, lymph

INTRODUCTION

Congenital chylothorax is the accumulation of lymphatic fluid in the pleural space diagnosed antenatally, at birth, or in the first 28 days postpartum [1], with a prevalence of 1:10000 [2] to 1:24000 live births [3]. The male sex is affected 2 times more frequently [1].

It can occur as a result of abnormalities of the lymphatic vessels or defects of the thoracic cavity [1,2], or it can also be secondary to the trauma of the thoracic duct at the time of birth through the sudden hyperextension of the neck or stretching of the thoracic wall [4]. The pulmonary effusion in most cases is bilateral (86.2%), followed by the right side due to the positioning of the thoracic duct along the right posterior mediastinum [1,2]. Fluid accumulation prevents the normal development of the lungs and, thus, affects fetal pulmonary and cardiovascular function [4].

Chylothorax can accompany congenital anomalies such as trisomy 21, pulmonary hypoplasia, X-linked centronuclear myopathy, lymphangiectasia, Noonan syndrome (PTPN11 mutation), myotonic dystrophy, chylous-pharyngeal fistula [1,5,6]. These associated anomalies negatively influence the evolution of the cases [1,4].

Prenatal diagnosis can be made by ultrasound from 17 to 38 weeks, usually at 30 weeks [1,7]. After the diagnosis, the pleural effusion is monitored by weekly ultrasound to evaluate its evolution. In cases with large pleural effusions, intrauterine intervention with intraamniotic drainage of the chylothorax is recommended to avoid the occurrence of hydrops, pulmonary hypoplasia, and fetal heart failure [4]. The birth is usually premature, around 34 weeks [1]. Congenital chylothorax is a life-threatening condition in newborns with a mortality rate of 20-63.6%, most commonly due to pulmonary hypoplasia [4,5,8].

Therapeutic intervention is necessary to prevent the prolonged leakage of the chyle and secondary complications such as infection, malnutrition, dehydration, bleeding, and prolonged hospitalization [2,5]. In the long term, pulmonary function and neurodevelopment are appropriate for the age of children who have congenital chylothorax [9].

DIAGNOSIS

In intrauterine life, during fetal ultrasounds, chylothorax can be detected as a unilateral or bilateral hypoechoic fluid in the pleural space [4,10]. (Figure 1)

In utero, thoracocentesis and examination of pleural fluid are performed. Chylothorax is diagnosed as a milky pleural effusion that contains > 1.1 mmol/L (> 110 mg/ml) triglycerides and a total cell

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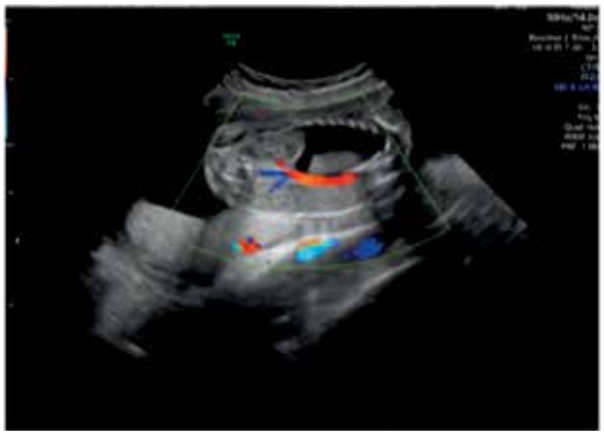

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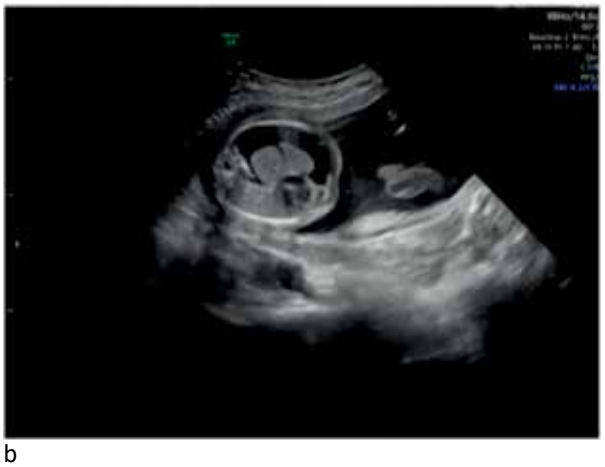

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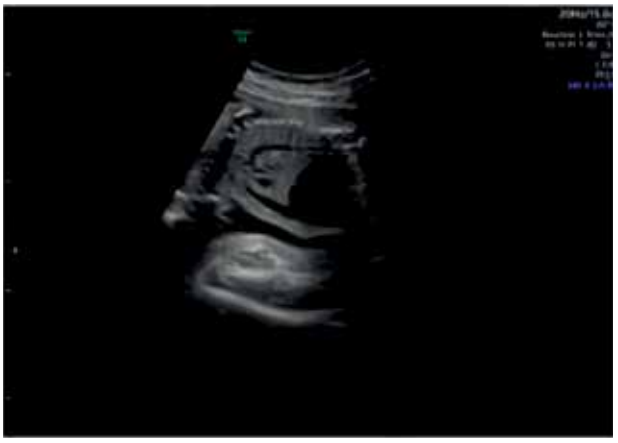

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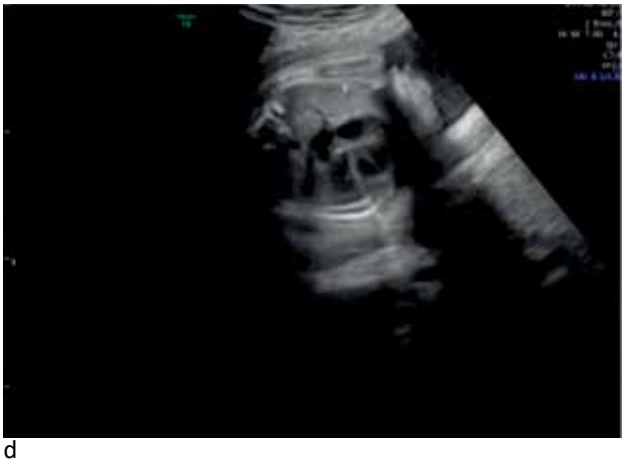

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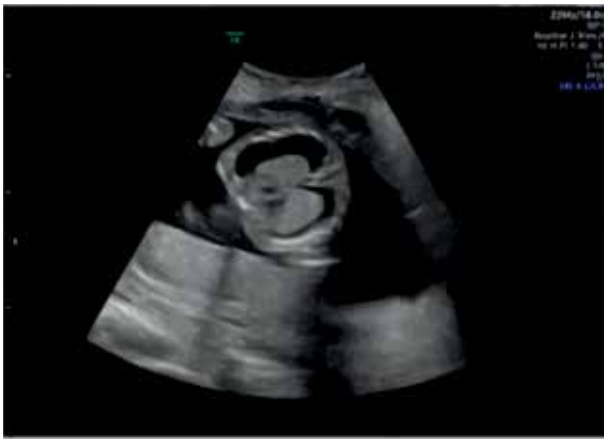

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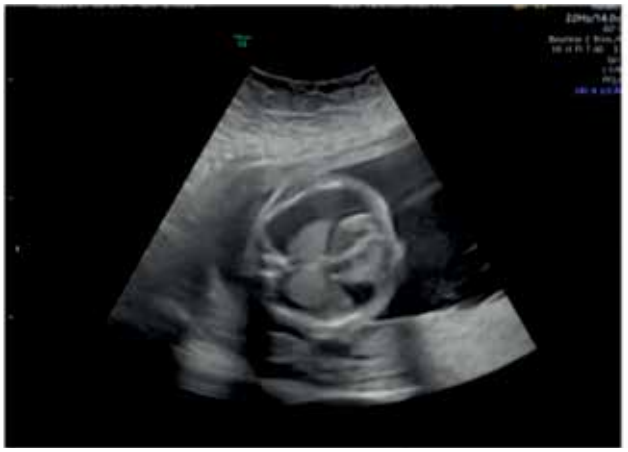

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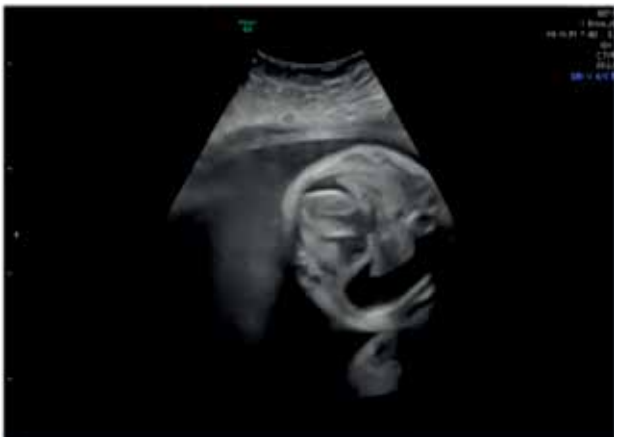

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FIGURE 1. Ultrasonography findings of a unilateral (a,b,c,d) and bilateral chylothorax (e,f,g). (a) sagittal (b) transversal (c) coronal image shows a unilateral hypoechoic fluid in the pleural space at 23 weeks of gestation. (d) thoracoamniotic shunt at 34 weeks (arrow). Transversal images show a bilateral hypoechoic fluid in the pleural space at (d) 18 weeks and (e) 22 weeks of gestation. (f) Transversal image show a bilateral hypoechoic fluid, ventricular hypertrophy, and polyhydramnios at 26 weeks.

count >1,000 cells/microL, with a lymphocyte fraction > 70% [11].

In addition, pleural effusion can also be associated with polyhydramnios due to intrathoracic pressure that affects fetal swallowing [7]. In severe cases with fetal hydrops, ascites and subcutaneous edema may be encountered [10].

A morphological fetal ultrasound must be performed to highlight or exclude other anomalies. Amniocentesis is also recommended to perform the fetal karyotype and rule out cytomegalovirus infection. In these situations, it is recommended to carry out screening for TORCH and parvovirus infections to eliminate other causes of fetal hydrops [12,13].

MANAGEMENT

Prenatal management

Prenatal intervention in the case of chylothorax aims to evacuate the accumulated lymph in the pleural cavity, thus allowing fetal lung development. The management of chylothorax depends on the gestational age at which it is diagnosed. Thus, in the case of diagnosis at a gestational age under 34 weeks, weekly ultrasound monitoring is recommended in mild unilateral chylothorax to see its progression or regression. If the pleural effusion progresses or fetal hydrops appear, serial transabdominal thoracentesis or the installation of a thoraco-amniotic shunt is recommended to reduce fetal cardiac and pulmonary damage. In contrast, diagnosis at a gestational age greater than 34 weeks requires thoracentesis and immediate delivery [1,2,4].

As the lymph is produced by the absorption of fats in the small intestine, a maternal diet low in fat and rich in high medium-chain triglycerides is recommended, which seems to reduce the volume of the drained fetal chyle [14].

By performing thoracentesis as a therapeutic method, the liquid accumulates again quickly, in 24-48 hours, which requires frequent punctures, with an increased risk of spontaneous abortion or premature birth. Instead, thoracentesis immediately before birth avoids neonatal asphyxia and favors the newborn's adaptation to extrauterine life [4].

The thoracoamniotic shunt ensures continuous drainage of the pleural fluid in the amniotic cavity, thus allowing lung expansion, making it the optimal treatment method in the case of fetal chylothorax [7,15,16]. The technique of shunt insertion is difficult, depending on the placental insertion, the fetal position, and the amount of amniotic fluid, and requires a learning curve and an experienced operator. It is also not without complications, including failure or wrong placement, bending, blocking, or migration of the tube, damage to organs and intrathoracic vessels, and recurrence of pleural effusions [7].

In utero, pleurodesis is another method tested over time for treating congenital chylothorax, especially in case the insertion of the shunt fails, or technical difficulties arise. This consists of chyle aspiration and fetal intrapleural instillation of non-teratogenic, sclerosing, and immuno-stimulating substances (OK-432 - Picibanil). Sometimes it may require repeating the procedure depending on the gestational age, the dose of the instilled substance, and residual pleural fluid at the time of the procedure. The response to the treatment is good in many cases, with the reduction of pleural effusion [12,17,18].

Prenatal treatment techniques are invasive methods and are at risk of causing spontaneous abortion, preterm birth, fetal death, premature rupture of membranes, intra-amniotic infection, and placental abruption [12].

However, prenatal interventions improve the evolution of fetal chylothorax, with the Apgar score being higher, pneumothorax being less frequent, and ventilatory parameters being better at birth. In addition, prenatal therapy also increases the survival rate to 76.9%, compared to 11% in newborns who did not receive prenatal therapy [1,2].

Postnatal management

Prenatal interventions improve the fetal prognosis, but neonatal interventions such as mechanical ventilation, thoracic drainage, and pleurodesis are necessary in most cases until the pleural fluid production stops [7,12].

Respiratory distress and asphyxia are complications that can occur at birth in infants with congenital chylothorax. Thus, endotracheal intubation and mechanical ventilation may be required for a mean duration of 7 days (1-16 days) to treat neonatal respiratory failure. Premature neonates, in particular, may develop pneumothorax requiring the instillation of surfactant. Thoracocentesis immediately after birth may be necessary in cases of fetal asphyxia [7].

Continuous pleural drainage may be necessary to reduce the pressure on the lungs in case of reaccumulating of the chyle to avoid repeated thoracentesis [8].

Nutrition increases lymphatic flow 2-10 times, and it is recommended to initiate total parenteral nutrition after birth and avoid enteral nutrition for an average of 6 days (5-10 days) to reduce flow. Oral feeding is started in the absence of ultrasound signs of pleural effusion, and milk formulas based on medium-chain triglycerides are recommended [1,2,5].

Lymph contains lymphocytes, chylomicrons, proteins, antibodies, immunoglobulins, coagulation

factors, nutrients, and fluids. Loss of lymph through pleural drainage requires the replacement of lost albumin and globulins by therapy with albumin, immunoglobulin, and fresh frozen plasma [4,7].

Octreotide is a somatostatin analog used to treat chylothorax and chylous ascites in newborns through its effects of reducing portal pressure, lymphatic flow in the thoracic duct, and fat absorption. Treatment begins between the 4th and 30th day of life, on average the 16th day, in cases with persistently increased tube drainage. It is administered by continuous intravenous infusion in doses of 1 μg/kg/h and progressively increased up to the maximum dose of 10 μg/kg/h for an average duration of 17.5 days [5,19]. The effectiveness of the therapy is measured by the reduction of drained chiles until complete remission and can be influenced by the underlying genetic conditions, as well as by the associated comorbidities. Studies show the efficiency of octreotide administration in approximately 36.3-53.3% of newborns with congenital chylothorax [5,19]. Adverse effects are usually mild and transient, the most common being hypoglycemia, hyperglycemia, bloody stools, abdominal distention, or changes in thyroid function tests [5,19]. Midodrine, an oral agonist of alpha-1 adrenergic receptors, and etilefrine, a sympathomimetic agent, are drugs with promising results in refractory chylothorax [20,21].

Surgical pleurodesis can be performed in case of prolonged lymphatic drainage beyond 6 weeks to prevent secondary complications [1]. Thus, intrapleural injection of povidone-iodine, OK-432, or talc has proven its effectiveness in treating fetal pleural effusion [4,12,18,22]. In severe cases, refractory to the therapeutic methods described previously, surgical interventions such as ligation or embolization of lymphatic vessels, excision of localized lymphangiomatosis, or formations that cause increased central venous pressure may be necessary [2].

CONCLUSIONS

Congenital chylothorax is a condition with potentially severe effects on pulmonary development and fetal cardiac function. Early diagnosis, followed by therapeutic interventions from the intrauterine period, improves fetal outcomes without leaving long-term sequelae.

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