

Primary fetal pleural effusion – a case of successful prenatal intervention

Derrame pleural fetal primário – um caso de sucesso da terapêutica pré-natal

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Abstract

Fetal pleural effusion is a rare condition whose prognosis is highly variable. Most primary cases are chylothorax and prenatal interventions can significantly alter its natural course. Some authors defend thoracoamniotic shunting as the preferred intervention but in few cases the effusion may resolve or stabilize after a single transabdominal thoracentesis. The authors present a case of primary bilateral pleural effusion identified at the 31st gestational week. A thoracentesis was performed at the 32nd week. A little effusion was maintained, with no reaccumulation. The newborn had an appropriate respiratory response at delivery and no thoracentesis was required in the neonatal period.

Keywords: Primary hydrothorax; Prenatal management; Therapeutic thoracentesis.

INTRODUCTION

Fetal pleural effusion (also referred as fetal hydrothorax) is an accumulation of fluid in the pleural space, which can present either uni- or bilaterally. It is a rare condition that affects 1 in 10 000 to 15 000 pregnancies, being more frequent in males than females (2:1)¹. Recent data suggests it can be more common than originally described². It may occur as an isolated finding or in association with several conditions, namely as part of nonimmune hydrops or severe anemia. There is a well-established association with chromosomal anomalies, mainly Down syndrome, and genetic syndromes, including Noonan's syndrome, Opitz-Frias hypertelorism hypospadias syndrome and Caffey's cortical hyperostosis¹. Congenital infections, cystic hygroma, congenital pulmonary lymphangiectasias and car-

diac malformations can also be associated with this condition^{1,3}.

Bilateral effusion is the most common clinical manifestation²⁻⁴. The median gestational age at diagnosis and at delivery is around 30-32 weeks and 34-35 weeks, respectively^{1,3-5}. Most primary pleural effusions are lymph accumulation (chylothorax) and it probably results from abnormalities of the lymphatics vessels^{1,3,6}.

The clinical course of this condition is variable and difficult to predict. It ranges from spontaneous resolution to progressive increase and development of hydrops with high risk of preterm delivery or fetal death^{1,2}. Perinatal overall mortality between 22 and 53% has been reported, reaching 75% in untreated pleural effusions associated with hydrops^{1,3-5}.

The available evidence about prenatal management is based essentially on retrospective studies of case series or case reports. Although there is no consensual recommendations, recent data supports that prenatal intervention can significantly alter the natural course of primary pleural effusions³⁻⁵.

The authors describe a case of primary bilateral pleural effusion identified at the 31st gestational week which had a good neonatal outcome after a single pre-

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natal thoracentesis. The therapeutic option and the facts that eventually predict a good prognosis will be briefly discussed.

CASE REPORT

A 44-year-old patient, gravida 5 para 1 (1 vaginal delivery, 3 first trimester spontaneous abortions after age 40) with no relevant medical history, was referred to our obstetric department by a first trimester combined screening with high risk for trisomy 21 (1:30). No structural anomaly was detected and nuchal translucency was below 95th percentile in the first trimester ultrasound, which was performed in another hospital. Despite the advanced gestational age at the first appointment (19th gestational week), she underwent an amniocentesis whose result revealed a normal male karyotype. Due to maternal age, she maintained pregnancy surveillance in our department. At the 24th

week, gestational diabetes was diagnosed. Blood glucose values were controlled with dietary plan and insulin injections. Morphological ultrasound (Figure 1-A,B) and fetal echocardiogram, at the 21st and 27th weeks respectively, were unremarkable. The fetal echocardiogram was requested as an insurance, considering the maternal age and the early onset of insulin to control the glucose blood values.

On the third trimester ultrasound, performed at the 31st week, bilateral pleural effusion with lung atelectasis (Figure 2-A,B) and polyhydramnios (amniotic fluid index of 27,8 cm) were identified. No other structural abnormalities were detected. There were no signs of fetal anemia (peak systolic velocity in the middle cerebral artery was normal) or hydrops, namely pericardium effusion, ascites, subcutaneous edema or placentomegaly. Fetal biometry was compatible with gestational age and cervical length evaluation was normal (35mm).

Antibody screening, including red cell antibodies,

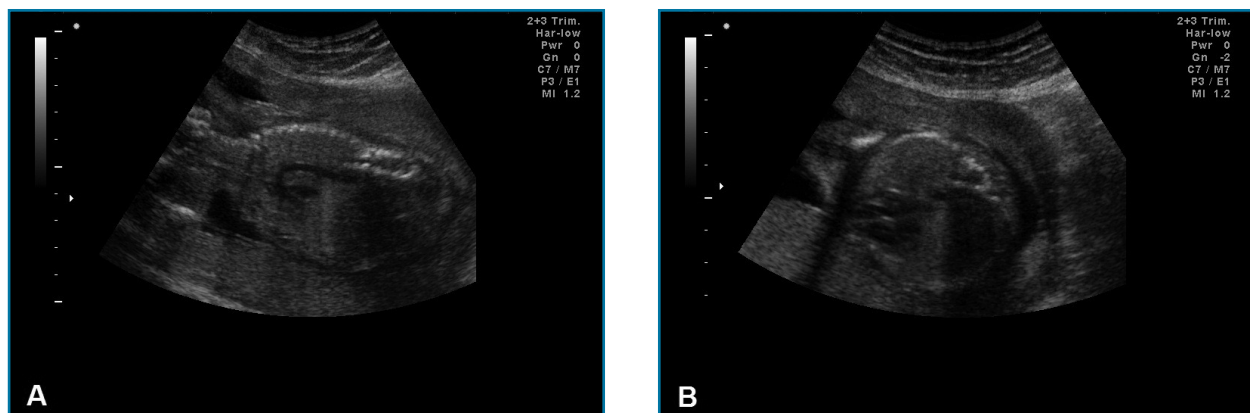


FIGURE 1. Aortic arch (A) and fetal heart four chamber view (B) on morphological ultrasound

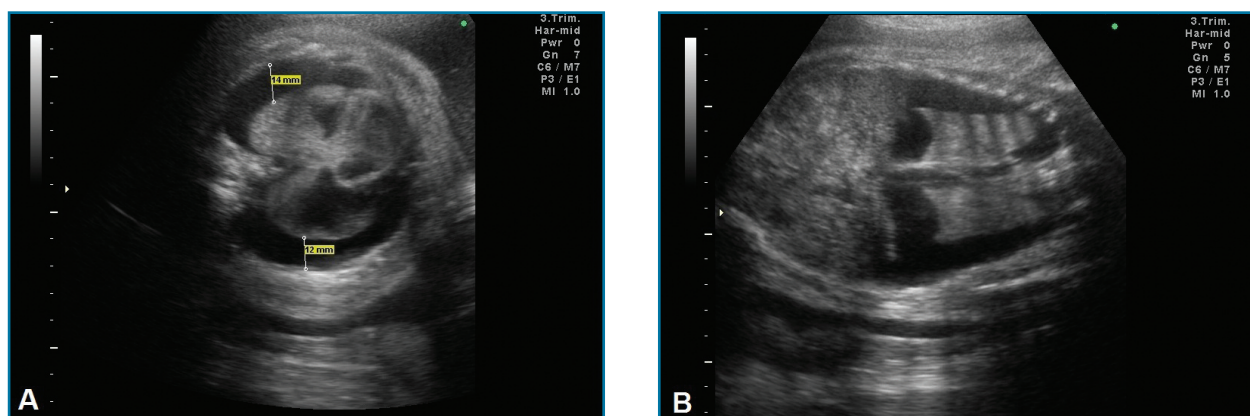


FIGURE 2. A,B – Bilateral pleural effusion at the 31st week (diagnostic ultrasound)

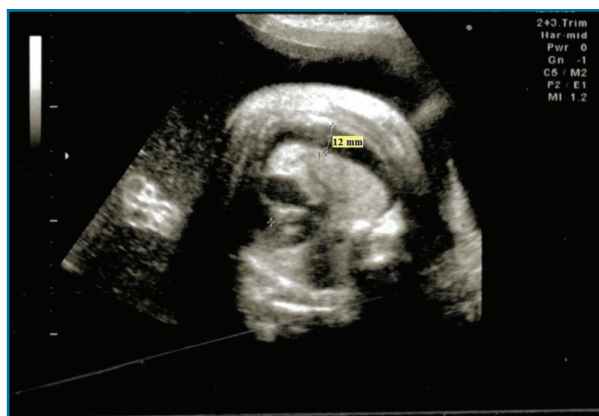


FIGURE 3. Mild and stabilized pleural effusion at the 33rd week (10 days after thoracentesis)

and screening for congenital infections (toxoplasmosis, syphilis, rubella, cytomegalovirus and herpes simplex virus) were negative.

A transabdominal thoracentesis under ultrasound control was performed at the 32nd week, using a 20-gauge spinal needle. A turbid fluid was removed, which composition suggested the diagnosis of chylothorax (no erythrocytes, total white blood cells count of $5.20 \times 10^3/\mu\text{L}$, with lymphocyte proportion of 97%). Serial ultrasound evaluations confirmed the success of the treatment and revealed only a little and stabilized bilateral effusion (Figure 3). Polyhydramnios was maintained. Fetal growth assessment was normal, with estimated fetal weight between the 60th and 70th percentiles. After the intervention antenatal corticosteroid therapy for pulmonary maturation was performed with intramuscular injection of 12 mg of betamethasone re-

newed 24 hours later.

At the 33rd week, the pregnant woman was admitted with threatened preterm labor. She went into spontaneous labor and a cesarean section was performed at the 34th week (12 days after thoracentesis) for non-reassuring fetal status. The newborn weighing 2632 grams required transient ventilator support with appropriate respiratory response (Apgar score of 6, 9 and 10 at 1, 5 and 10 minutes, respectively). The chest x-ray revealed a little right-sided pleural effusion that spontaneously resolved (Figure 4-A,B), with no need of thoracentesis in the neonatal period.

During the first 2 years of life, the infant had three episodes of mild acute bronchiolitis. Four years post-partum follow-up evaluation confirmed he was a healthy child and had a normal development for his age.

DISCUSSION

The authors present a case of successful prenatal management of a primary pleural effusion identified at the 31st gestational week.

On the etiological investigation we did not offer screening of Noonan's syndrome. However, there is growing evidence that late presenting pleural effusions (after fetal viability) are commonly associated with that condition, so genetic testing should be considered for those cases².

The fluid removed by transabdominal thoracentesis suggested the diagnosis of chylothorax. In newborns the diagnosis of chylothorax is confirmed by thora-

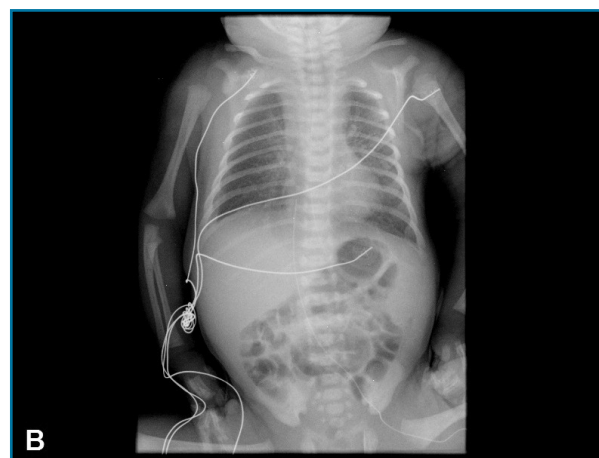
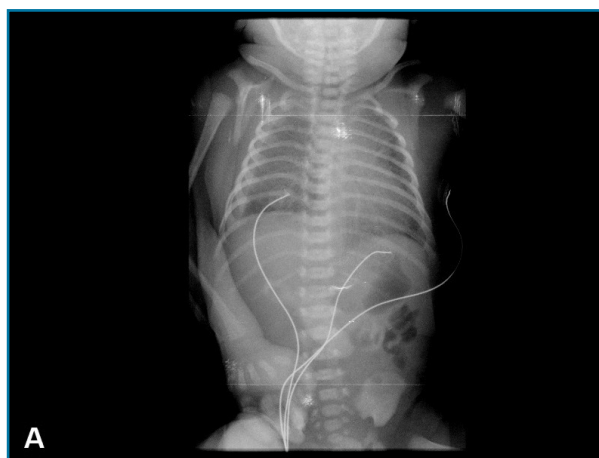


FIGURE 4. Chest x-ray after birth (A) showing a little right-sided pleural effusion, not perceptible at the 5th day of life (B).

centesis when the fluid contains triglyceride levels > 1.1 mmol/L (with oral fat intake) and total white blood cells count $> 1000/\mu\text{L}$, with lymphocyte proportion $> 80\%$ ^{1,3,6}. Although the normal mean percentage of lymphocytes in the fetal blood is usually $> 80\%$, several authors adapt this criteria to confirm the diagnosis *in utero* with transabdominal thoracentesis^{3,5-7}.

There is no consensus about prenatal management of primary pleural effusions. Some authors had proposed therapeutic recommendations, particularly in patients for whom a diagnosis is made before or at 34 weeks^{1,6}. Prenatal management includes serial ultrasounds, transabdominal thoracentesis, thoracoamniotic shunt placement and, rarely, *in utero* pleurodesis^{1,8}. Severe pleural effusions can compromise normal lung maturation leading to pulmonary hypoplasia with a high rate of perinatal mortality. So, the main goal of those interventions is to prevent pulmonary hypoplasia and facilitate the respiratory management in the delivery room and neonatal period. Recent studies show that prenatal therapy significantly improves survival of newborns, particularly in the setting of fetal hydrops³⁻⁵. Some authors defend thoracoamniotic shunting as the preferred intervention since it provides a permanent drainage of the pleural effusion with a single procedure. There is growing evidence that it is the most effective intervention, especially in cases of fetal hydrops or rapid effusion progression^{1,4,5,9}. The most common complication is shunt migration or obstruction, which may occur in more than 20% of the procedures^{1,4}. On the other hand, some authors choose thoracentesis at first, because it establish the diagnosis, is technically easier to perform and is potentially therapeutic. Its main limitation is the risk of rapid effusion reaccumulation, occurring generally within 1 hour to 10 days^{1,10}. In few cases the effusion may resolve or stabilize after a single thoracentesis, especially in non-hydrotic fetuses^{1,4,5,10}. However, there are studies reporting a high rate of repeat intervention after the first thoracentesis or disappointing survival rates after an antepartum thoracentesis to facilitate neonatal resuscitation^{9,10}. It is important to note that those series included a high proportion of hydrotic fetuses. Both thoracentesis and thoracoamniotic shunting appear to be well tolerated and the global incidence of complications is low. Nevertheless, its potential benefits should be balanced against the risk of prematurity and premature rupture of membranes, which remain the greater concerns⁴.

Despite prenatal management, after delivery some newborns remain asymptomatic or experience only mild respiratory distress, while others need immediate resuscitation, possibly requiring urgent pleural drainage^{1,3}. Several factors have been associated with a poor prognosis after prenatal detection of pleural effusions, including the presence of a secondary cause, structural anomalies, fetal hydrops, low birth weight, preterm birth less than 34 weeks, multiple or large effusions^{4,8}. On the other hand, spontaneous resolution seems to be more common in primary unilateral cases diagnosed in the second trimester^{1,2,10}.

In the present case, important secondary causes were excluded even before the diagnosis. The performance of amniocentesis ruled out the possible association with chromosomal aneuploidies, namely Down syndrome, which are described in 11 to 14% of congenital pleural effusions^{2,4,9}. The association with congenital heart defects seems to be around 15 to 20%^{4,9}. A normal morphologic ultrasound and fetal echocardiogram were against this hypothesis. After the diagnosis, autoimmune or infectious etiology were also excluded. Furthermore, the absence of hydrops or other structural anomalies, the moderate severity of the pleural effusion at diagnosis and the appropriate birth weight for the gestational age seem to have promoted the positive neonatal outcome^{4,8,10}. The corticosteroid therapy completed more than 24 hours before the delivery may have been an important contributor for the good respiratory response. In case series of primary pleural effusions, polyhydramnios seems to be a relatively frequent finding and has no established prognostic impact^{2,7,10}. On the other hand, in this case the pregnant woman was diagnosed with gestational diabetes, which represents a well established etiology of polyhydramnios¹¹.

During the first 2 years of life, the infant had three episodes of acute bronchiolitis, one of them with hospitalization. Interestingly, a retrospective study of congenital chylothorax with a minimum 3-years postpartum follow-up reported that 4 of the 15 survivors were diagnosed as having asthma in early infancy, placing the hypothesis that even the cases with no neonatal relapse can have subsequent pulmonary function impairment⁹. However, all of those patients were also born prematurely and had recurrent respiratory infections. In our case, the subsequent diagnostic investigation reported normal pulmonary function tests. Long-term follow-up studies also suggested that most of the survivors diagnosed with primary chylothorax

remain asymptomatic, with an age-appropriate development. Neurocognitive impairment seems to be related to associated anomalies or extreme prematurity^{8,9}.

In conclusion, prenatal diagnosis of fetal pleural effusion implies a thorough etiological research and serial ultrasounds to assess its evolution and possible associated anomalies. Although this condition is still often associated with poor outcomes, advances in prenatal medicine are improving the prognosis of these patients and nowadays most of them are likely to survive. The optimal strategy for fetal intervention has not been fully elucidated. According to the actual evidence, a case-by-case evaluation based on time of diagnosis, effusion severity and prognostic factors seems to be the most reasonable approach.

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