Ginekol Pol. 2014, 85, 708-712

Successful treatment of fetal bilateral primary chylothorax – report of the two cases

Udane leczenie obustronnego, pierwotnego wysięku opłucnowego (chylothorax) u płodu – opis dwóch przypadków

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Abstract

Primary fetal chylothorax is an uncommon complication, associated with high perinatal morbidity and mortality. In our report, we describe two cases of fetal bilateral primary chylothorax successfully treated with pleuro-amniotic shunting.

In both cases, ultrasound scans showed bilateral, hypoechoic fluid in the pleural space without any associated structural malformations and features of infection and aneuploidy. Laboratory analysis of pleural fluids revealed 79% and 92% of lymphocytes, respectively, confirming chylothorax in both fetuses. In the first case, pleuro-amniotic shunts were successfully inserted at 31 weeks and 6 days of gestation. Ultrasound scan after two weeks showed expansion of the left lung and lack of fluid in both pleural cavities. At 39 weeks of gestation, a 2660 g baby boy was delivered by cesarean section (Apgar score: 9). The child did not require surgical intervention and was discharged home on day 16 of life. In the second case, the insertion of shunts (at 24 weeks and 6 days of gestation) also significantly reduced the amount of the fluid in the pleural cavities, but one shunt had to be surgically removed after birth. At 30 weeks and 2 days of gestation, a cesarean section was performed due to maternal cholestasis. A female weighing 1400 g was delivered (Apgar score: 7). The chest X-ray revealed only a small amount of fluid in the left pleural cavity. The infant was discharged on postnatal day 26, in good condition and with body weight of 2150g.

Pleuro-amniotic shunt insertion is a method of choice in the treatment of confirmed primary fetal chylothorax.

Key words: **primary fetal chylothorax** / **pleural effusion** / **pleuro-amniotic shunts** / / **pregnancy** /

Streszczenie

Pierwotny wysięk w jamie opłucnowej (chylothorax) to rzadkie powikłanie u płodu o trudnym do przewidzenia przebiegu klinicznym. Przedstawiony artykuł opisuje dwa przypadki skutecznego leczenia pierwotnego, obustronnego chylothoraxu u płodu.

W obu przypadkach badanie USG wykazało obecność obustronnego, hipoechogennego płynu w jamach opłucnej po wykluczeniu występowania wad wrodzonych, cech zakażenia wewnątrzmacicznego i zaburzeń chromosomalnych. U płodów stwierdzono dodatkowo cechy akumulacji płynu w tkance podskórnej górnej połowy ciała. Pobrany płyn z jamy opłucnowej zawierał odpowiednio 79% oraz 92% limfocytów, co potwierdziło chylothorax u obu płodów.

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Otrzymano: **26.09.2014**
Zaakceptowano do druku: **31.03.2014**

W pierwszym przypadku dreny opłucnowo-owodniowe umieszczone zostały w obu jamach opłucnej i działy skutecznie do zakończenia ciąży. Wyniki badań USG po założeniu drenów wykazały rozprężenie lewego płuca i tylko śladowe ilości płynu w obu jamach opłucnej. W 39. tygodniu ciąży, metodą cięcia cesarskiego urodzono chłopca o wadze 2660 g (punktacja 9 w skali Apgar). Noworodek nie wymagał interwencji chirurgicznej i został wypisany do domu w 16. dniu życia, w dobrym stanie ogólnym.

W drugim przypadku po wprowadzeniu drenów opłucnowo-owodniowych również uzyskano znaczące zmniejszenie ilości płynu w jamach opłucnej, ale jeden z drenów musiał być usunięty chirurgicznie po porodzie. Z powodu objawów cholestazy u matki, ciąża została zakończona w 30. tygodniu ciąży drogą cięcia cesarskiego. Urodzono dziewczynkę o wadze 1400g (Apgar 7), która z powodu problemów z oddychaniem musiała zostać zaintubowana. Po usunięciu zastawki i zakończeniu antybiotykoterapii dziecko zostało wypisane do domu w 26. dniu życia z wagą 2150g, w dobrym stanie ogólnym.

Zastosowanie zastawek opłucnowo-owodniowych jest metodą leczenia z wyboru w przypadku potwierdzonego pierwotnego chylothoraxu u płodu.

Słowa kluczowe: **pierwotny wrodzony chylothorax** / **pierwotny wysięk opłucnowy** / / **zastawka opłucnowo-owodniowa** / **ciąża** /

Introduction

Chylothorax, the accumulation of chyle in the pleural space, is the most common cause of pleural effusion in fetuses and newborns. In prenatal ultrasonography, it appears as a unilateral or bilateral anechoic space in the thorax surrounding the lungs. The incidence of chylothorax is reported at 1/10000 – 15000 pregnancies. It occurs twice as often in males as compared to females, and in 90% of cases it involves the right side of the chest [1-4]. Chylothorax can be an isolated manifestation or may be associated with malformations or various syndromes (e.g. Down, Noonan and Turner), but in many cases it has no clear underlying etiology. The cause of the effusion may remain unclear even after a detailed postnatal evaluation [3-4].

Primary fetal chylothorax can be diagnosed only by cytological and biochemical analysis of the pleural fluid, with identification of high triglyceride concentrations and abundance of T lymphocytes. Lymphocyte count of the pleural fluid could be a useful marker of chylothorax in cases when the diagnosis is uncertain. Rarity and variable clinical course of the disease are the reasons why there is no consensus in the literature on the optimal antenatal management of chylothorax. According to our observations, pleuro-amniotic shunting is an appropriate method of treatment in case of confirmed primary fetal chylothorax. In this report we present two cases of congenital fetal chylothorax, managed successfully at the DFMMG, Polish Mother's Memorial Hospital Research Institute.

Case report I

A 27 year-old primigravida was admitted to our department at 31 weeks of gestation due to fetal pleural effusion and polyhydramnios. Ultrasonographic scanning demonstrated a 30-week-old fetus with bilateral, hypoechogenic fluid in the pleural space and edema of the upper body (Fig. 1A). No structural malformations, features of infection or aneuploidy were detected. The mother did not consent to genetic testing. Amniocentesis and thoracentesis were performed at 31 weeks and 5 days and 6mL of the pleural fluid and 440mL of the amniotic fluid were collected and sent for laboratory analysis. Pleural fluid contained 79% lymphocytes, 4% monocytes, 8% eosinophils and 4% macrophages. The next day, having obtained an informed consent from the parents, two (because one of them malfunctioned) pleuro-amniotic shunts on the right and one on the left side were successfully installed under ultrasound guidance. The patient remained in hospital, what ensured proper positioning of the pleuro-amniotic shunts. Consecutive fetal ultrasound examinations after two weeks (33 weeks of gestation) revealed an expansion of the left lung, lack of fluid in the left pleural cavity and about 7 mm in the right one (confirmed by MRI scan), and significantly reduced amount of fluid in the subcutaneous tissue of the upper part of the body (Fig. 1B). AFI was 13 cm (26.8 cm at the previous examination). At 37 weeks of gestation, a cesarean section was performed and a baby boy with birth body weight of 2660 g was born (Apgar score: 9), in good general condition. No signs of maternal or fetal infection were observed. Swabs taken from the skin and blood cultures were negative. Serological test examinations for cytomegalovirus, parvovirus B19, toxoplasmosis, rubella, adenovirus infection and herpes simplex virus type 1 and 2 were also negative. The chest radiogram demonstrated a small amount of fluid in both pleural cavities, i.e. 3 mm on the left and 5 mm on the right. Ultrasonographic scanning showed evenly aerated and symmetrical lungs, without focal solid lesions and parenchymal densities. A fat-free diet including MCT (medium chain triglycerides) diet was administered. The child did not require surgical intervention and was discharged home on day 16 of life, in good and stable condition. Follow-up visits at 2 and 3 months of age revealed trace amounts of fluid in both pleural cavities. At present, at 8 months of life, the baby boy is developing normally, with no signs of fluid on ultrasound scan.

Case report II

A 29-year-old nullipara was referred to DFMMG at 24 weeks of gestation. The mother had earlier been diagnosed with hereditary hyperbilirubinemia but until then her pregnancy had developed normally. An ultrasound examination showed bilateral fluid in the pleural space, but fetal anatomy, growth parameters, fluid volume, and umbilical artery Doppler findings were

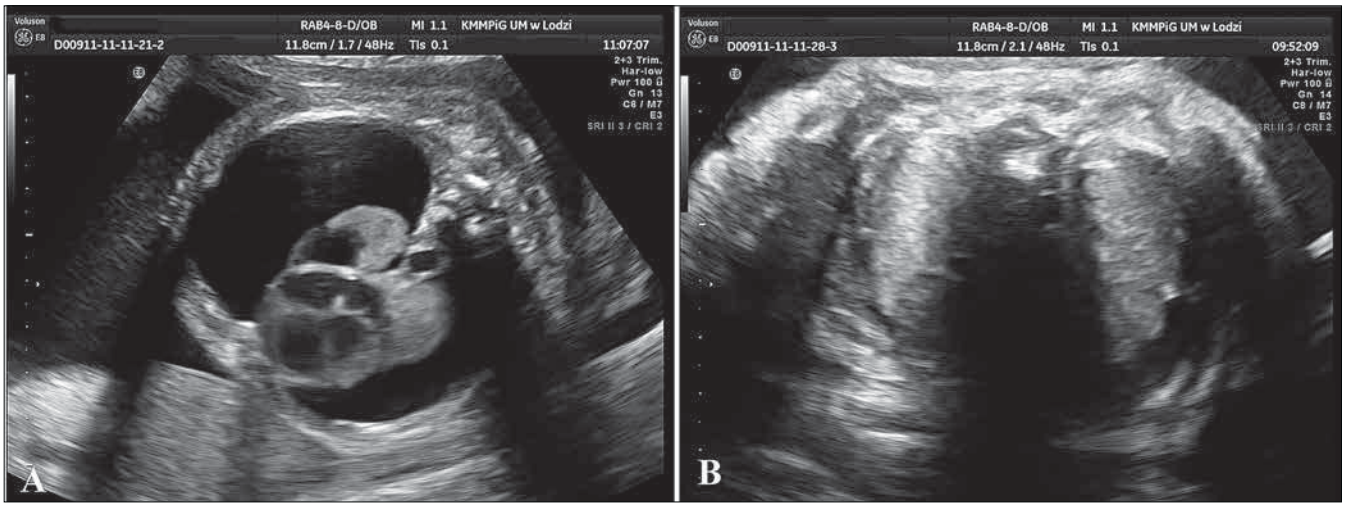

Figure 1. Case I. Ultrasonographic scan of bilateral, hypoechoic fluid in the pleural space at 30 weeks of gestation (A) Expansion of the left lung, lack of fluid in the left pleural cavity and small amounts in the right one at 31 weeks of gestation (B).

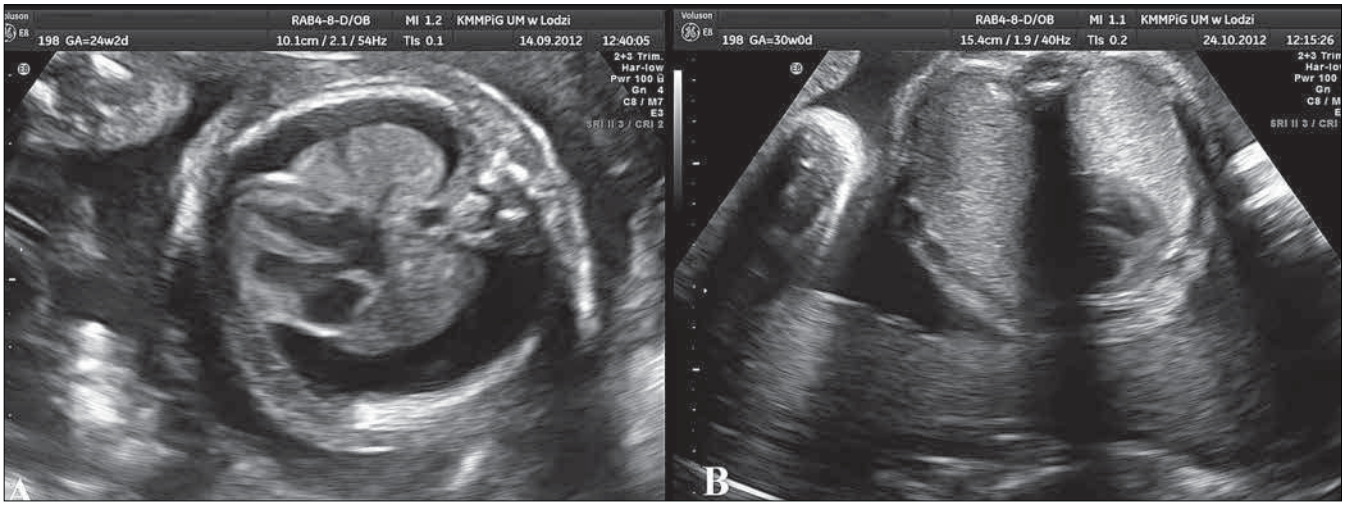

Figure 2. Case II. Primary fetal chylothorax diagnosed at 24 weeks of gestation (A) Significantly reduced amount of fluid in both pleural cavities observed at 30 weeks of gestation (B).

otherwise normal (Fig. 2A). There was no ascites in the fetus but accumulation of the fluid in the subcutaneous tissue of the upper part of the body was observed. After an informed consent was obtained from the parents, amniocentesis and thoracentesis were performed at 24 weeks and 5 days of gestation. Pleural and amniotic fluids were sent for laboratory and genetic analyses. Serological tests for infections, including Toxoplasma gondii, cytomegalovirus and parvovirus B19, excluded the presence of a current infection caused by these agents. Fetal karyotype was also normal (46, XX).

Pleural fluid contained 92% lymphocytes, 6% monocytes and 2% polymorphonuclear leukocytes, what confirmed the diagnosis of primary fetal chylothorax. On the following day, an attempt to place two shunts in the left pleural cavity was made. Unfortunately, the position of the fetus did not allow for insertion of the shunt on the right side. An ultrasound scan 3 days later (25 weeks and 2 days) revealed lack of fluid in the right pleural cavity and about 8 mm in the left one. The next ultrasound scan performed one week later demonstrated only minimal residual pleural effusion in the right pleural cavity and about 4 mm in the left one (Fig. 2B). At 30 weeks and 2 days of gestation, the mother was hospitalized again. Due to very high levels of bile acids in serum (29.6 umol/l) and amniotic fluid (22.3 umol/l), as well as elevated liver enzymes in serum (ALAT up to 334IU/l, ASPAT up to 163IU/l), she was scheduled for a cesarean section on the following day. A female newborn with a birth body weight of 1400g was delivered (Apgar score: 7). One pleuro-amniotic shunt was removed during the delivery. The neonate developed respiratory problems, which were initially treated with nasal continuous positive airway pressure (nCPAP) but because of deteriorating respiratory problems, at 9 hours of life, the child required mechanical support. Exogenous surfactant therapy was initiated due to increased demand for oxygen, which allowed for decreasing ventilation parameters. The baby was examined

with ultrasound and X-ray which revealed the presence of inflammatory changes in the lungs and small amount of fluid in the left pleural cavity. Antibiotic therapy was administered. The newborn was extubated on day 7 of life. Consecutive X-ray examinations revealed no re-accumulation of pleural fluid. The second shunt was surgically removed by thoracoscopy on day 26 of life. The baby required blood transfusion on days 2 and 25 of life due to primary and secondary anemization. Oral feeding was initiated on day 2 of life (milk enriched with medium-chain triglyceride), parenteral nutrition was administered between day 1 and 21 day of life. The infant was discharged on postnatal day 26, in good general condition and body weight of 2150g.

Discussion

Congenital pleural effusion can occur as a result of damage to the thoracic duct by rupture, laceration or compression and may be produced by congenital chylothorax, anemia, cardiac defects, aneuploidy, viral infections or lung malformations (diaphragmatic hernia, congenital cystic adenomatoid malformation and bronchopulmonary sequestration) [2-4]. In most cases, primary congenital effusions are chylous and in 90% of cases congenital chylothorax occurs in the right pleural space [2]. The most serious consequences include pulmonary hypoplasia, congestive heart failure and hydrops through disruption of venous return [5]. Polyhydramnios, frequently accompanying pleural effusion, is most likely related to obstruction of physiological fetal swallowing due to esophageal compression, and is associated with a high risk of preterm delivery [6]. Management of chylothorax ranges from waiting and monitoring by ultrasound scans (in the cases of small and temporary effusions) to therapeutic interventions [4, 7-8]. Spontaneous regression of unilateral pleural effusion in the second trimester has been reported, but there is a general consensus that pleural effusion is a serious condition with a high rate of perinatal morbidity and mortality (ranging from 57 to 100%), making it advisable in selected cases to offer prenatal treatment [7]. Rustico et al., reviewed 54 cases of primary pleural effusion which did not receive treatment in utero and the overall survival rate was 59%, but only 35% in hydropic fetuses [3].

Thoracentesis with pleuro-amniotic shunting is an acceptable therapy for in utero bilateral pleural effusion. The success of prenatal intervention through thoracentesis and/or pleuro-amniotic fluid drainage depends on early diagnosis, volume and reappearance of the effusion, degree of pulmonary compression and the existence of hydrops, all of which are factors that worsen the prognosis [6-7]. Fetal thoracentesis is often ineffective due to rapid re-accumulation of the fluid. Shunts provide long-term drainage and are therefore preferred [6, 8]. Shunting is also indicated if the pleural effusion is complicated by hydrops and/or polyhydramnios. However, it should be noted that according to our observations this prenatal treatment is helpful only in case of hydrops caused by accumulation of chyle when compression on the great vessels of the chest, induced by increased intrathoracic pressure, disrupts venous return [3]. Therefore, shunting should not be used in case of hydrops caused by other factors such as anemia, circulatory insufficiency or other diseases of unknown etiologies. Although some studies have reported that around 20% of the shunts can migrate or obstruct, in most cases the shunt is effective in achieving permanent decompression of pleural effusion [3, 9-10]. Apart from isolated reports of fetal bleeding and scarring, fetal hypoproteinemia and placental edema, the most common complications associated with shunts are chorioamnionitis, premature rupture of the membranes and preterm labor [11]. In our case, there were no complications in the first case. The second child had to undergo thoracoscopy because one shunt could not be removed after birth. Regardless, the baby was also discharged home in good general condition without re-accumulation of pleural fluid in the lungs. Picone et al., conducted a retrospective study evaluating the policy of emergency pleuro-amniotic shunting in hydropic fetuses with suspected chylothorax, and reported that shunting was performed in 60 cases. There were 10 in utero deaths, 7 pregnancy terminations, and 43 live births (7 children died in the neonatal period and 36 survived). All 36 survivors (60%) had chylothorax, of which 33 primary and 3 secondary (congenital diaphragmatic hernia, pulmonary sequestration and Noonan syndrome) [12].

Although a randomized study regarding pleuro-amniotic shunting in cases of confirmed chylothorax has not been performed, the accumulated literature suggests that this procedure improves the outcome. The procedure of shunting requires experience, thus cases with pleural effusion should be immediately referred to a center where confirmation of chylothorax and successful insertion of the shunt can be performed without delay to avoid development of hydrops.

Acknowledgement:

This research was supported by grant from The National Science Centre "Assessing the importance of ultrasonography and magnetic resonance imaging in the diagnosis of cytomegalovirus infection in the fetus" (N407 547138).

Oświadczenie autorów

1. Dorota Nowakowska – autor koncepcji i założeń pracy, analiza i interpretacja wyników badań ultrasonograficznych, wdrożenie leczenia wewnątrzmacicznego, korekta i akceptacja ostatecznego kształtu manuskryptu – autor zgłaszający i odpowiedzialny za manuskrypt.
2. Zuzanna Gaj – współautor tekstu pracy, aktualizacja piśmiennictwa, przygotowanie, korekta i akceptacja ostatecznego kształtu manuskryptu.
3. Mariusz Grzesiak- ocena badań ulreasonograficznych i wdrożenie leczenia wewnątrzmacicznego.
4. Ewa Gulczyńska – analiza i interpretacja wyników z części neonatologicznej artykułu, korekta i akceptacja ostatecznego kształtu manuskryptu.
5. Jan Wilczyński – autor koncepcji i założeń pracy, uzyskanie funduszy na realizację badań, koordynacja działań klinicznych, osteteczna weryfikacja i akceptacja manuskryptu.

Źródło finansowania:

Praca częściowo finansowana z grantu Narodowego Centrum Nauki nr N407 547138.

Konflikt interesów:

Autorzy nie zgłaszają konfliktu interesów oraz nie otrzymali żadnego wynagrodzenia związanego z powstawaniem pracy.

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