A dilemma in the management of fetal pleural effusion: A case report of two cases*

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ABSTRACT

Fetal Pleural Effusion is a rare case whose management is still a matter of debate.

Its course may spontaneously resolve or lead to pulmonary hypoplasia and result in death in utero or poor neonatal outcome. This paper is a report of 2 cases and their course, from prenatal diagnosis of Pleural Effusion to delivery. This report includes sonographic scans, description of the laboratory work – up and other imaging tests that were done. The 1st case report was successfully managed with Thoraco-amniotic shunting, while the 2nd case was seen late and had an adverse neonatal outcome.

This case report was done to increase awareness among obstetricians and sonologists in offering counsel to patients and their families, especially in our low resource set-up, where in in utero interventions are not available.

INTRODUCTION

Fetal Pleural Effusion, a nonspecific accumulation of fluid in the pleural space is a rare condition, whose incidence has been estimated to occur in 1 in 15,000 pregnancies.[1]

Prenatally, the condition may be an isolated finding (primary pleural effusion) or may occur in association with other conditions (secondary pleural effusion). The clinical course varies from spontaneous resolution to a progressive increase leading to development of hydrops and polyhydramnios.[2]

The optimal approach to prenatal management is still a matter of debate given that the natural course of the disease can vary. Spontaneous resolution have been reported in the literature. There is, however, general consensus that pleural effusion is a serious condition with a high rate of perinatal morbidity and mortality, making it advisable in selected cases to offer in-utero intervention for fetuses with persistent effusion which may improve the chances of survival.[3]

We report herein 2 cases with pleural effusion. The 1st case with primary pleural effusion was seen early and successfully managed. The 2nd case with secondary pleural effusion was seen late with adverse neonatal outcome.

The objective of presenting these cases is to increase the awareness among sonologists and obstetricians about fetal pleural effusion. Awareness regarding the management of this condition would help in counseling the parents and early referral of the mother to tertiary perinatal centers.

CASE 1

R.C., 37 years old, G5P2 (2022), on her 21 weeks AOG, with TORCH test positive for CMV IgG, who was admitted for IVIG administration.

Patient delivered to two children with her 1st partner via normal spontaneous delivery. The last two pregnancies with her 2nd partner were spontaneous miscarriages for which completion curettages were done.

Patient denies febrile episodes. She had exposure at around 6-8 weeks AOG to pre-school children, who had flu-like symptoms described as generalized body malaise and headaches.

History started at 18 weeks AOG, when patient during her routine prenatal check-up had Fetal Biometry with Congenital Anomaly Scan done. The result was Pleural Effusion, (Volume = 2.61ml), (Figure 1) with cardiac displacement to the right. No other Gross Fetal Anatomical Anomalies seen in scan. A TORCH Panel (Table 1) was done which tested positive for CMV IgG. A repeat scan done at 21 weeks revealed persistence of Pleural Effusion (Volume= 27.68ml), with cardiac displacement to the right, consider Left Pulmonary Hypoplasia. No cardiovascular structural defects seen. Maternal peripheral blood sample was extracted for cell-free Fetal DNA Microassay Genetic Studies (Panorama™) which showed patient at Low Risk for Chromosomal Anomalies (Table 2). The patient was advised about possible spontaneous resolution of the pulmonary effusion.

The patient was referred to an Infectious Specialist, thus the present admission for Empiric Immunoglobulin therapy for CMV infection.

Pertinent physical Examination showed normal vital signs. Abdomen was gravid, soft and non-tender. Fetal heart tones were reassuring with good fetal movements.

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The patient was given 100u/kg/BW of IVIG. Patient had an unremarkable hospital stay after 1 hospital stay.

The patient had repeat ultrasound scans (Table 3) to monitor progression of effusion or development of other complications. Fetal 2D echo was done with no gross cardiac anomalies seen. A repeat ultrasound at 28 weeks AOG showed the fetal heart was deviated to the right of the chest. Outflow tract with normal crossover seen. There was minimal fluid within the right pleural cavity, right, (Volume= 13.27 ml), Pleural effusion on the left lung (volume = 40.30ml), Scalp thickness measured 0.49cm. There is minimal fluid within the scrotum. The impression was Unilateral Fetal Hydrothorax (Pleural Effusion), Left, with fluid accumulation on the Right. Consider Early Scalp and Nuchal Fold Edema. Findings may evolve to Pulmonary Hypoplasia with changes compatible with Fetal Hydrops (Figures 2-5).

The patient was then referred to a Perinatologist whose working impression was Primary Pleural Effusion due to it unilaterality and pattern of occurence. The perinatologist advised the patient that the fetus was a good candidate for *in utero* intervention (fetal thoracentesis or in utero shunting). Since the procedure was not being done locally, the patient was advised to seek medical treatment overseas and was subsequently admitted at a tertiary perinatal center in Texas, USA at 30 wks AOG. The patient

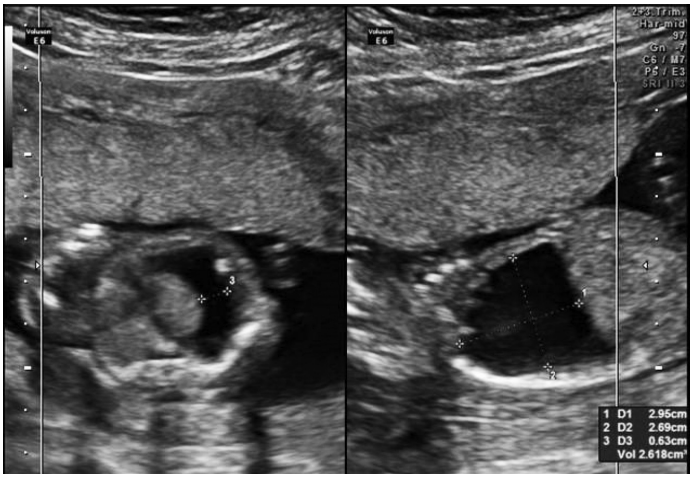

Figure 1. Congenital Anomaly Scan at 18 wks AOG; Pleural Effusion, left lung measuring 2.96 x 2.69 x 0.63 ml (Vol 2.61 cm).

relayed that corticosteroids were given for lung maturity and further work-up done to identify exact pathology included amniocentesis for culture and genetic studies which revealed normal results. The patient was then managed as a case of Primary Isolated Pleural Effusion. Thoraco-amniotic shunting was done under ultrasound guidance. The 1st shunt was noted to be free-floating in the amniotic fluid after a few days and the procedure had to be repeated. After the 2nd shunt, there was note

Table 1. Pertinent Laboratory Exams

CBC	Hgb 9.7	Hct 28	WBC 12.9	Segmenters 65	Lymphocytes 25	Platelet 266
Urinalysis	WBC 1/hpf	RBC 2/hpf	Epithelial Cells 1/hpf	Bacteria 4/hpf	Blood trace	
FBS	91.89 mg/dl					
TORCH ASSAY	CMV IgG (+) CMV IgM (-)	Rubella IgG (+) Rubella IgM (-)	HS 1 IGG (-) HS 1 IgM (equivocal)	HS 2 IgG (-) HS 2 IgM (-)	Toxoplasmosis IgG (NR) Toxoplasmosis IgM (-)	

Table 2. Report Summary: LOW RISK
Sex of Fetus: Male Fetal Fraction: 18.1%

Condition tested	Prior Risk	Panorama Risk Score	Result
Trisomy 21	1/218	<1/10,000	Low Risk
Trisomy 18	1/25,689	<1/10,000	Low Risk
Trisomy 13	1/6,050	<1/10,000	Low Risk
Monosomy X	<1/10,000	<1/10,000	Low Risk
Triploidy/Vanishing Twin			Low Risk
22q11.2 deletion syndrome	1/2,000	1/13,000	Low Risk
1p36 deletion syndrome	1/5,000	1/12,400	Low Risk
Angelman syndrome	1/12,000	1/16,000	Low Risk
Cri-du-chat syndrome	1/20,000	1/57,000	Low Risk
Prader-Will syndrome	1/10,000	1/13,800	Low Risk

Table 3.

7 wks AOG	TVS	Single live intrauterine pregnancy 7 1/7 wks gestation by CRL with good cardiac activity (158 bpm). Normal ovaries with corpus luteum on the right. Long and closed cervix.
12 wks AOG	TVS	Single live intrauterine pregnancy 12 3/7 wks AOG by CRL, with good cardiac activity (170bpm) and somatic activities. No adnexal mass seen. Long and closed cervix.
18 wks AOG	FB + TIFFA	Pregnancy uterine 20 wks AOG by biometry, breech, live, singleton, male, with good somatic and cardiac activity (161bpm). EFW 333g (12oz) is large for gestational age (90th percentile for menstrual age). Biometric ratios within normal. Normohydramnios (SVP 5.14cm) Placenta anterior, high lying, grade II. Pleural effusion, left (4.7x3.5x3.2cm), volume 27.68ml, with cardiac displacement to the right, consider left pulmonary hypoplasia. No other gross fetal anatomical anomalies seen in this scan. Suggest ff up scan after 2 weeks.
21 wks AOG	FB + TIFFA	Pregnancy uterine 25 5/7 wks gestation by biometry, in cephalic, presentation, live, singleton, male fetus with good somatic and cardiac activities. EFW 600g (1lb 5oz). Normohydramnios (SVP 4.56cm). Placenta anterior, high lying, grade II. Pleural effusion, left (4.7x3.5x3.2cm), volume 27.68ml, with cardiac displacement to the right, consider left pulmonary hypoplasia. No other gross fetal anatomical anomalies seen in this scan. Suggest ff up scan after 2 weeks.
25 wks AOG	FB + TIFFA	Pregnancy uterine 25 5/7 wks gestation by biometry, in cephalic presentation, live, singleton, male fetus with good somatic and cardiac activities. EFW is large for age (93rd percentile). Biometric ratios within normal. Normohydramnios. Placenta anterior, high lying, grade I. Unilateral Fetal Hydrothorax (Pleural Effusion), left, essentially same volume on previous scan. Consider early scalp and nuchal fold edema. Rest of fetal anatomy is normal. Sonologic findings may evolve to pulmonary hypoplasia with changes compatible with fetal hydrops.
28 wks AOG	FB	Pregnancy uterine 30 wks gestation by biometry, in breech presentation, live, singleton, male fetus with good somatic and cardiac activities. EFW is 93rd percentile. Normohydramnios. Placenta posterior, high liying, grade II. The fetal heart is deviated to the right of the chest. Outflow tracts with normal crossover seen. There is minimal fluid within the right pleural cavity, volume 13.27 ml. Left chest fluid (7.86x2.41x4.06cm), volume 40.30ml. Scalp thickness 0.49cm. There is minimal fluid within the scrotum. Rest of fetal anatomy is normal. Sonologic findings may evolve to pulmonary hypoplasia with changes compatible with fetal hydrops.

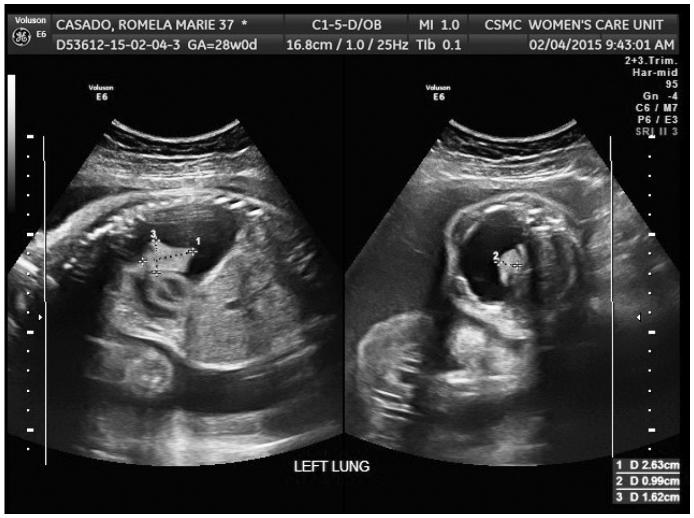

Figure 2. Congenital Anomaly Scan at 28 wks AOG; Left Lung measures 2.63 x 0.99 x 1.62 cm

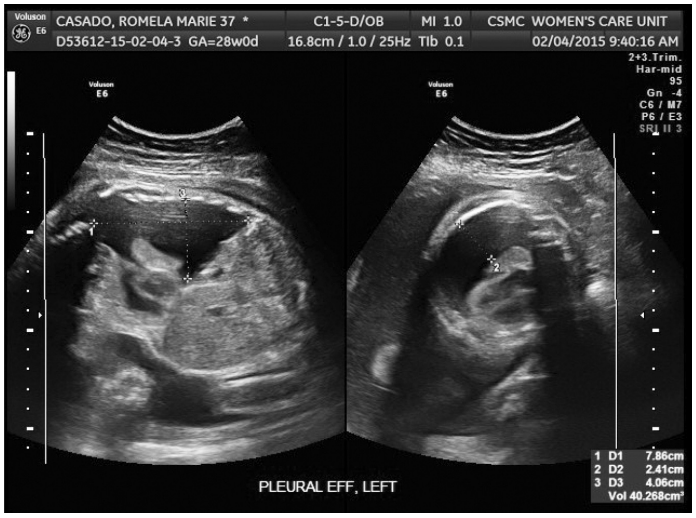

Figure 3. Congenital Anomaly Scan at 28 wks AOG; Pleural Effusion, left, measuring 7.86 x 2.41 x 4.6 cm (Volume 40.26 cm)

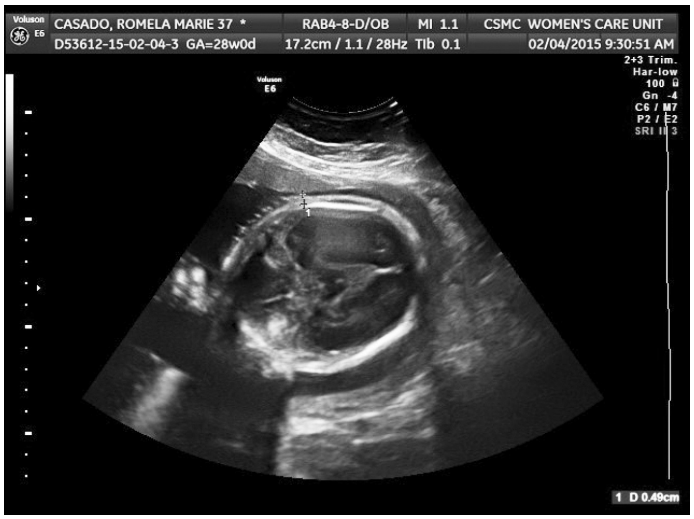

Figure 4. Congenital Anomaly Scan at 28 wks AOG; Scalp Edema 0.49 cm

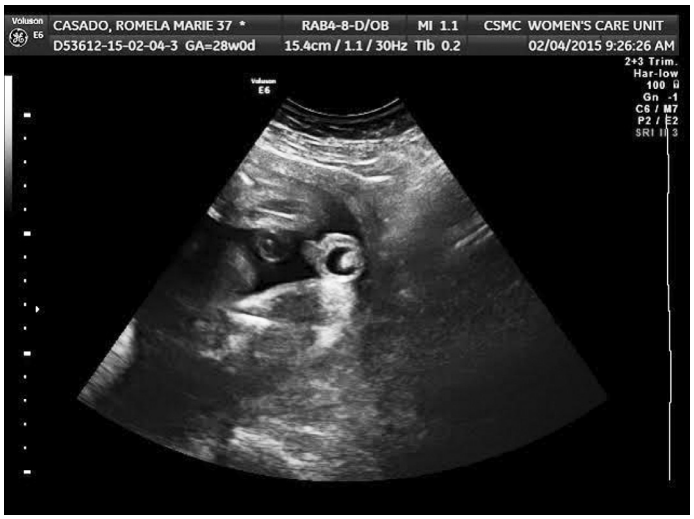

Figure 5. Congenital Anomaly Scan at 28 wks AOG; (L) Right Lung measures 1.92 x 0.82 cm. (R) Left Lung measures 1.76 x 0.90 cm

of slight resolution of the fluid but was dislodged again, no re-insertion followed until after 10 days wherein serial monitoring revealed recurrence and *in utero* shunting was repeated a third time.

At 36 6/7 weeks AOG, patient went into early labor. A Primary Caesarian Section was done and she delivered to a live baby boy. The newborn was immediately intubated and underwent chest tube insertion to allow further expansion of the lungs. Aspirated fluid was screened for possible pathologies with no clear etiology identified. The baby was then transferred to neonatal ICU for observation. The mother was discharged after 3 days with an unremarkable hospital stay. Presently, infant is contraption-free with an unremarkable neonatal course.

CASE 2

A 17-year-old, primigravida, 28 weeks gestation, was referred to the Out-Patient Department with an ultrasound diagnosis of Fetal Hydrops.

The patient had prenatal check-up at 16 weeks AOG and 20 weeks aog in a local health center. An ultrasound requested showed the following: Polyhydramnios, Bilateral Pleural Effusion, Pericardial Effusion and Ascites prompting referral to a tertiary center. At the hospital, a repeat ultrasound confirmed the diagnosis. The ultrasound showed single, live, intrauterine pregnancy, 28 weeks age of gestation. There were changes suggestive of hydrops fetalis with bilateral pleural effusion, pericardial effusion, ascites, bilateral hydrocele, scalp edema and polyhydramnios. Lungs were very small with small cardio-thoracic ratio of 15.6%. Placenta was thin. Color Doppler studies showed high velocity in the fetal umbilical vein and ductus venosus. Uterine arteries had low resistance index without notching (Figure 6).

During ultrasound examination, uterine contractions were noted. The patient was subsequently admitted with normal vital signs. The abdomen was gravid with fundic height of 28 cm, fetal heart tone of 140 and regular uterine contractions. Internal examination showed cervix at 2cm dilated, 50% effaced, intact BOW, floating, in cephalic presentation

The patient's blood group was O Rh (+) and her VDRL test and TORCH screen were negative. Premature uterine contractions were controlled with Isoxuprine and antenatal steroids were started. Fetal 2D Echo was also contemplated but was not done due to financial constraints. The plan was to do amniocentesis and test the amniotic fluid for karyotyping and fetal lung maturity. However, on the 3rd day after admission, patient had spontaneous rupture of water and she delivered to a live baby boy, 28-29 weeks gestation, 1500 gms, Extreme prematurity, Hydrops fetalis. Abnormal examination findings were micrognathia, small mouth, short broad flat nose, low set ears, and rocker bottom feet. The baby expired on the 6th hour of life.

DISCUSSION

Fetal Pleural Effusion refers to a nonspecific accumulation of fluid in the pleural space. In newborn infants, pleural effusion is defined as chylothorax. Prenatally, it is more pertinent to define any accumulation of fluid in the fetal thorax as hydrothorax.[4]

In normal condition, the minute spaces (stomata) between the mesothelial cells of the parietal pleura allow free movement of fluid from and to the pleural space. These stomata communicate directly with lymphatic lacunae, which empty into lymphatic channels and in turn drain into the mediastinal lymph nodes. If there is a

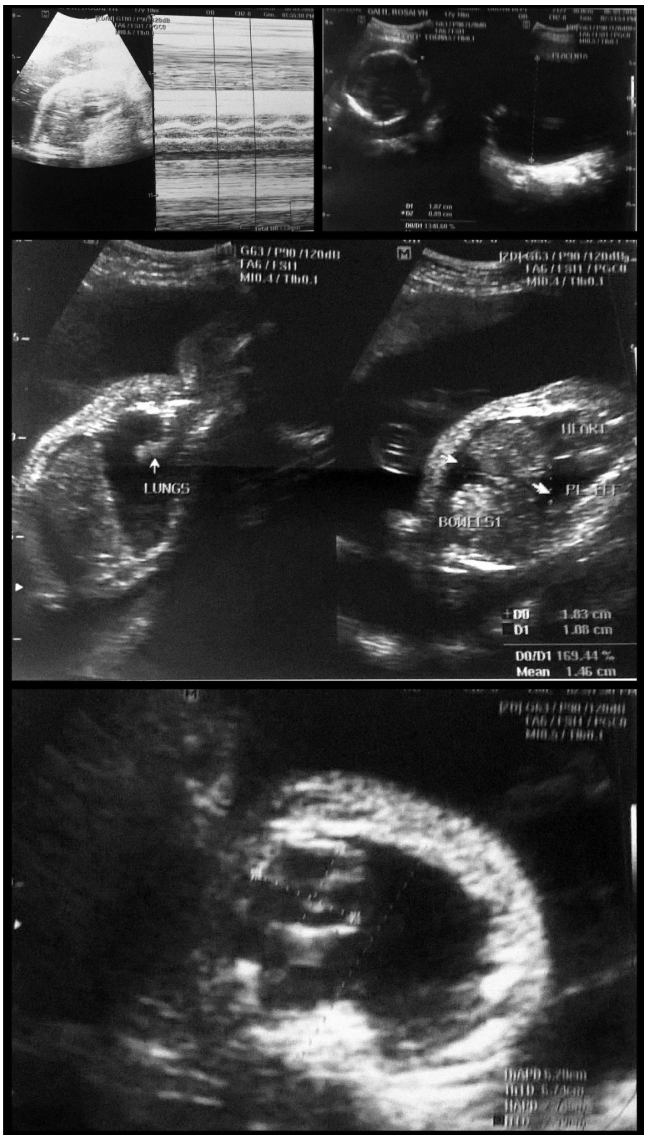

Figure 6. Single live intrauterine pregnancy in cephalic presentation, with good cardiac and somatic activity. Average sonologic age of 28 wks (hadlock), possible over estimation secondary to ascites and skin edema. Placenta anterior grade 2. Polyhydramnios (AFI 34.71). Possible bilateral renal agenesis. Venous Doppler studies consistent with beginning decompensation.

Remarks:

(+) scalp edema, thick echogenic skin
(+) pericardial effusion
(+) pleural effusion
(+) ascites, hydrocele, bilateral
Binocular distance 4.40 cm equivalent to 27 5/7 wks gestation.
Cardiothoracic ratio: 15.67% (small). Lungs are very small and highly echogenic or compact.
Polyhydramnios.
Both kidneys not seen, fetal urinary bladder not seen.
Minimal gross body movement. Placenta is thin.
Kidney shadows and urinary bladder could not be identified.
Unremarkable findings bilateral extremities.
Color Doppler studies, shows high velocity of umbilical vein and ductus venosus consistent with hydrops fetalis and compensating hemodynamics. Uterine arteries have low resistance index without notching.

disruption to this drainage pathway, lymphatic fluid collects in the pleural space. At prenatal ultrasonography, pleural effusion appears as a unilateral or bilateral anechoic space in the thorax, surrounding the lungs [2].

Prenatally, the condition may be an isolated finding (primary pleural effusion) or may occur in association with other conditions (secondary pleural effusion). Fetal pleural effusion may occur as a primary abnormality after excluding structural abnormalities, chromosomal anomalies and other conditions that causes hydrops fetalis. Pleural effusion is thought to be one of the earliest signs of hydrops fetalis. The causes of pleural effusions with hydrops include those of immune hydrops fetalis and non-immune hydrops fetalis (Table 4). Primary effusion is usually unilateral and can rapidly progress or spontaneously regress. Secondary effusion is usually bilateral and symmetric with high association with Fetal Hydrops[10].

Case 1 presented with unilateral pleural effusion and TORCH test positive for CMV IgG. Following primary infection, CMV becomes latent, and there is periodic reactivation with viral shedding. One test that could verify if patient was having a recurrent or reactivated infection is an IgG avidity index which was not done in our patient. Patient was given Empiric Treatment with Immunoglobulin during the 2nd trimester.

At the perinatal center in Texas, amniocentesis was done. The amniotic fluid tested negative for CMV infection. The single best test for the diagnosis of congenital infection is detection of virus in the amniotic fluid by culture or PCR. Lipitz and associates noted that amniocentesis was 100% sensitive in diagnosing congenital CMV infection. In a more recent investigation, Azam and associates showed that amniocentesis was 77% sensitive in detecting congenital CMV infection with specificity of 100%. (reference - Diagnosis and Management of CMV Infection in Pregnancy Patrick Duff, M.D. Perinatology 2010; 1:1-6). Other tests done in Case 1 were all negative, thus the fetus was managed as a case of isolated primary pleural effusion.[10]

Case 2 is an example of fetus with secondary pleural effusion. It was a diagnosed case of Pleural Effusion which developed Hydrops with multiple morphological anomalies suggestive of chromosomal aberrations, making Immune Hydrops unlikely. While the underlying cause of a secondary fetal pleural effusion may be evident from detailed ultrasound examination and karyotype analysis, in many instances, the etiology remains obscure even after a postmortem examination[10].

Irrespective of the etiology, morbidity and mortality may result from the fetal pleural effusion acting as a space occupying lesion, impending normal lung development with the risk of pulmonary hypoplasia and neonatal death. Histological studies have shown that when pleural

Table 4. List of Associated Disease Entities with Pleural Effusion

Cardiovascular	Malformation, Anemia secondary to Immune Hydrops
Chromosomal	Trisomy 21, Trisomy 13, Monosomy XO
Genetic	Noonan's, Opitz-Frias hypertelorism hypospasdias syndrome
Hematologic	Fetomaternal hemorrhage, Fetal Hemorrhage, Hemoglobinopathies (a-thalassemia)
Infectious	Adenovirus, Parvovirus B19, Herpes Simplex Type 1, Cytomegalovirus
Thoracic	Congenital Cystic Adenomatoid Malformation, Bronchopulmonary Sequestration, Mediastinal Tumors
Lymphatic Dysplasia	Localized Intrathoracic lymphatic dysplasia

effusion is persistent, normal pulmonary development is compromised due to a decrease in the number of lung cells, airways and alveoli, resulting in reduced organ size and weight. The associated respiratory dysfunction together with prematurity, are the main causes of death postnatally.[3]

The clinical course varies from spontaneous resolution to a progressive increase and the development of Hydrops and polyhydramnios, The mechanism by which Hydrops develops is thought to be the increased intrathoracic pressure, which reduces cardiac ventricular dimensions and stroke volume, without impairment in contractility (tamponade effect), resulting in reduced cardiac output. The polyhydramnios frequently observed with pleural effusion is probably related to obstruction of the physiological fetal swallowing due to esophageal compression.

At prenatal ultrasonography, pleural effusion appears as a unilateral or bilateral anechoic space in the thorax, surrounding the lungs. One of the most important contributions of sonography is determining whether the hydrothorax is primary or secondary abnormality. Sonographic features suggestive of primary pleural effusion include the following: (1) The hydrothorax is unilateral, or bilateral, very asymmetric; (2) The unilateral hydrothorax occurs as an isolated finding with no other abnormalities; (3) There is considerable mediastinal shift implying mass effect from the hydrothorax. If there are other serous effusion such as in ascites, the pleural fluid is disproportionately large compared with other effusions.[8]

For a long-time, the rarity of this condition and its unpredictable clinical course prevented a uniform approach to management, and indeed, gave rise to a great deal of uncertainty about the usefulness of any intervention.[8] Therefore, it has been advisable in selected cases to offer prenatal therapy such as thoracentesis, pleuro-amniotic shunting and pleurodesis.

Thoracocentesis is performed under the ultrasound control generally using a 20-gauge spinal needle to aspirate the pleural fluid. After multiple aspirations, a small number of pleural effusions can resolve in utero.

Because fluid reaccumulates rapidly after aspiration, long-term drainage as in thoraco-amniotic shunting has been proposed as a more appropriate procedure for treating pleural effusion. This technique (Figure 6) employs a metal cannula with trocar inserted transabdominally into the fetal chest, under ultrasound control. The trocar is then withdrawn into the amniotic cavity to position the other end of the catheter outside the chest wall. Thoraco-amniotic shunting was done in Case 1 because of progressive increase in pleural fluid.

The fetus benefits from shunting by allowing the pleural fluid to decompress to the pressure of the amniotic fluid, allowing the lungs to expand potentially reducing the risk of pulmonary hypoplasia[10]. The most common complications arising with shunting seem to be premature rupture of the membranes, preterm labor and chorioamniotis[9].

Pleurodesis was based on the experience in adult patients. Fetal intrapleural injection of OK-432 causes the pleura to become infiltrated by inflammatory cells and adhere to the surface of the lung. Data on this new procedure are very limited.

In countries with low resources such as in the Philippines, in utero interventions are not available. What then can we offer our patients?

1. Expectant management

We can explain to the patient that conservative management may lead to spontaneous *in utero* resolution resulting to an uncomplicated neonatal course. When the hydrothorax is small and well tolerated, frequent ultrasound surveillance maybe most prudent. If it increases over time with signs of fetal decompensation, intervention may be needed.

2. Early delivery

Traditional management of fetal hydrothorax has been based on the knowledge that the condition has a high perinatal mortality and morbidity. Reasons for neonatal death are related to the length of time and effect of the pleural fluid as a space occupying lesion to normal lung growth and development.

In our low resource setting, early delivery can be

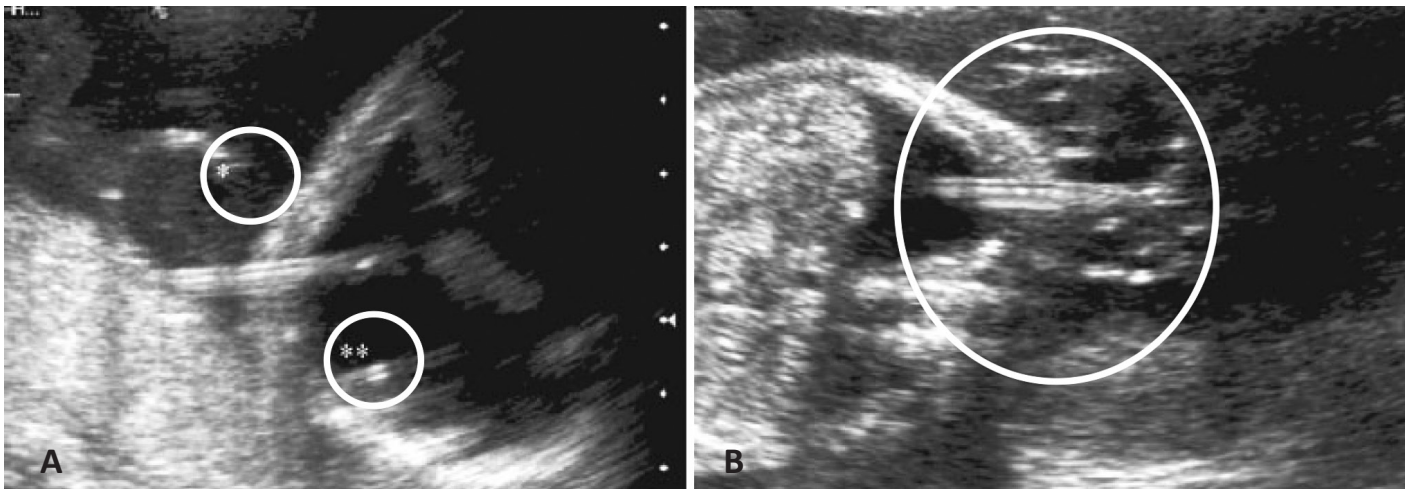

Figure 7. A: Left Pleural Effusion with Pleuroamniotic shunting (pig tail) (Images courtesy of *Romina Castagno et al*., 2007. Fetal Pleural Effusion). One of the ends is within the amniotic activity (*) the other (**) in the pleural cavity. It allows to drain the effusion, decompress the lung and prevent pulmonary hypoplasia; B: Pleural Effusion with Thoracoamniotic shunting. (Images courtesy of *Romina Castagno et al*., 2007. Fetal Pleural Effusion).

offered in order to stop the space occupying effect of the pleural fluid. Steroids can be given to induce fetal lung maturation. Amniocentesis or amnioreduction in cases with polyhydramnios can be done to test the amniotic fluid for chromosome analysis and fetal lung maturity. When there is evidence of fetal lung maturity, the fetus can be delivered and managed immediately with neonatal thoracentesis. This was the plan for Case 2 but was not done when the patient who delivered a fetus with congenital anomalies suggestive of chromosomal abnormalities decided not to pursue further treatment on her baby.

The presence of hydrothorax does not influence the mode of delivery. Cesarean delivery should be reserved for obstetrical indications[10]. In the delivery room, the neonatal team should anticipate the needs of severely affected fetus and be prepared to provide respiratory support that includes intubation, positive pressure ventilation, and removal of fluid by needle aspiration.

CONCLUSION

Fetal Pleural Effusion is an uncommon clinical entity. It can be an isolated finding or can be associated with a wide range of congenital anomalies and structural malformations which in many cases may be evident only after delivery and postnatal examination.

This report is intended to put emphasis on developing management options in pregnancies complicated by pleural effusion. A thorough perinatal evaluation (detailed prenatal records, laboratory analysis, and ultrasound evaluation) is recommended before considering any type of in utero intervention. In low resource setting, expectant management that can result to spontaneous resolution may be offered. In cases with progressive increase in pleural fluid, early delivery in fetus with proven lung maturity can be done followed by neonatal thoracentesis. ■

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