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Outcomes of fetuses with primary hydrothorax that undergo prenatal intervention (prenatal intervention for hydrothorax)

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ARTICLE INFO

Article history:
Received 6 February 2017
Received in revised form
8 August 2017
Accepted 16 August 2017
Available online xxx

Keywords:
Hydrothorax
Hydrops
Thoracentesis
Thoracoamniotic shunt

ABSTRACT

Background: Primary hydrothorax is a congenital anomaly affecting 1 in 10,000-15,000 pregnancies. The natural history of this condition is variable with some fetuses having spontaneous resolution and others showing progression. The associated pulmonary hypoplasia leads to increased perinatal morbidity and mortality. Optimal prenatal intervention remains controversial.

Methods: After obtaining the Institutional Review Board approval, a retrospective review of all patients evaluated for a fetal pleural effusion in the Fetal Diagnosis and Treatment Center at The University of Michigan, between 2006 and 2016 was performed. Cases with secondary etiologies for an effusion or when families decided to pursue elective termination were excluded.

Results: Pleural effusions were identified in 175 patients. Primary hydrothorax was diagnosed in 15 patients (8%). The effusions were bilateral in 13/15 cases (86%) and 10/15 (66%) had hydrops at presentation. All 15 patients with primary hydrothorax underwent prenatal intervention. Thoracentesis was performed in 14/15 cases (93%). Shunt placement was performed in 10/15 cases (66%). Shunt migration was seen in four patients (40%) and all of these underwent prenatal shunt replacement. Overall survival was 76%. The rates of prematurity and preterm premature rupture of membranes were 69% and 35%, respectively.

Conclusions: Fetal intervention for the treatment of primary hydrothorax is effective, and it appears to confer a survival advantage. Both the fetuses and the mothers tolerated the procedures well. Preterm labor and preterm premature rupture of membranes remain an unsolved problem. Further studies are needed to understand the mechanisms behind the development of fetal hydrothorax.

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http://dx.doi.org/10.1016/j.jss.2017.08.034

Introduction

Primary hydrothorax is a congenital anomaly affecting 1 in 10,000-15,000 pregnancies.[1,2] Fetuses can present with either unilateral of bilateral effusions and males are affected more frequently than females (2:1). This condition is also commonly referred to as "primary chylothorax". It has been argued that because the normal mean percentage of lymphocytes in the fetal blood is >80%, this parameter cannot be used prenatally to characterize an effusion as chyle. Therefore, the term "hydrothorax" is preferred.[3]

The natural history of this condition is variable with some fetuses having spontaneous resolution and others showing progression. A better understanding of this natural history is fundamental, as we try to determine prognosis and develop criteria for fetal intervention. Perinatal mortality in fetuses with pleural effusions has been reported to be between 22% and 53%.[2,4,5] The effusion can behave like a space-occupying lesion with resultant lung growth restriction. In the most severe cases, fetuses may develop large effusions and progress to hydrops. The associated pulmonary hypoplasia leads to increased perinatal morbidity and mortality.[6,7] The prognosis and the effectiveness of prenatal intervention can also vary widely in the presence of secondary causes of hydrothorax. These include chromosomal anomalies, infections, cardiac malformations, and other structural anomalies.[6,8] Therefore, a comprehensive fetal and maternal evaluation is necessary before prenatal intervention is considered.

Since the introduction of prenatal therapy, fetuses with large pleural effusions seem to have an improved outcome.[9,10] The majority of fetuses are treated with drainage or shunting. Shunt placements are associated with shunt dysfunction, prematurity, or other complications. The incidence of these complications in current practice and the outcomes associated with treatment need to be better defined.[11,12] There are reported cases of chemical pleurodesis being used as first-line therapy for this condition, but the role of this therapy is not clear.[13,14] The aim of this study is to review our experience with fetuses diagnosed with primary hydrothorax, which underwent prenatal intervention and describe the clinical outcomes.

Methods

A retrospective review of all patients evaluated for a fetal hydrothorax at the Fetal Diagnosis and Treatment Center at The University of Michigan, between 2006 and 2016 was performed. Institutional Review Board approval was obtained (HUM00091706). Due to the retrospective nature of this approved study, the Institutional Review Board granted a waiver for informed consent of patients included. Cases with other possible etiologies for an effusion such as chromosomal anomalies, infections, cardiac malformations, and other structural anomalies were defined as secondary hydrothorax and were excluded. Cases where the family decided to pursue elective termination of pregnancy were also excluded. Hydrops was defined as the presence of fluid in at least one other compartment in addition to the thorax (peritoneum, pericardium, or integument).[4,6]

Data collected included estimated gestational age (EGA) at diagnosis, the presence or absence of hydrops, the type, side and number of prenatal interventions, the percentage of lymphocytes in the pleural fluid, complications associated with intervention, the EGA at birth, and mortality. Preterm birth was defined as delivery before 36 wk of gestation. Postnatal records were reviewed and interventions were documented. For some patients born at an outside hospital, we had access to electronic records; the rest had telephone or email follow-up. Descriptive statistics were performed using Microsoft Excel 2016 (Microsoft Corporation, Redmond, WA).

All prenatal interventions were performed by maternal-fetal medicine physicians. Thoracentesis and thoracoamniotic shunt placement were done under ultrasound guidance, with the mother receiving intravenous sedation (see Figs. 1–4). For shunt placement, a double pigtail silastic catheter (Rocket Medical, Hingham, MA) was used in all cases. The mothers were discharged home after the procedure and follow-up ultrasound was performed a week later.

Results

Pleural effusions were identified in 175 patients. We excluded patients with cardiac or structural anomalies, chromosomal anomalies, or infections. The specific associated anomalies are described in Table 1. In this study, 80% of the patients had structural or chromosomal abnormalities. We also excluded patients who died before birth with either elective pregnancy termination ($n = 11$) or had intrauterine fetal demise before intervention ($n = 7$).

Primary hydrothorax was therefore diagnosed in 15/175 pleural effusion patients (8%). The effusions were bilateral in 13/15 cases (86%). In this series 10 patients (66%) had hydrops at presentation.

All 15 patients with primary hydrothorax underwent prenatal intervention. A modified version of the algorithm proposed by Yinon *et al.*[15] is used at our institution to determine the timing and type of prenatal intervention (Fig. 5).

Mean EGA at the time of the first intervention was 27w1d (standard deviation [SD] ± 4.1). Thoracentesis was performed in 14/15 patients (93%). One patient had primary shunt placement after the baby showed rapid progression from a small effusion to a large effusion with mediastinal shift and hydrops. Fetal pleural fluid was analyzed in all 15 patients, and the analysis revealed a lymphocyte fraction >80% in 11 patients. The median lymphocyte fraction was 92%.

Shunt placement was performed in 10/13 patients (76%). The mean gestational age at the time of initial shunt placement was 28w1d (SD ± 3.82) (see Table 2). Two patients were excluded from this part of the analysis. The first patient moved out of state after the initial thoracentesis and was lost to follow-up. The second patient had a thoracentesis with subsequent reaccumulation of the effusion. Shunt placement was recommended but the family declined any further intervention. The fetus eventually had intrauterine demise.

When looking only at the patients that presented with hydrops, 7/10 (70%) underwent shunt placement. Three