CASE REPORT

Ex utero intrapartum treatment (EXIT) of severe fetal hydrothorax

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Ex utero intrapartum treatment (EXIT) of a fetus with severe bilateral hydrothorax is described. EXIT allows therapeutic interventions on the neonate while maintaining fetoplacental circulation. Thus it may be useful for fetuses presenting with severe pleural effusion towards the end of gestation and in whom in utero drainage is technically not possible or available and drainage post partum would result in profound and prolonged hypoxia until sufficient drainage of pleural fluid allowed lung expansion.

Congenital hydrothorax is a rare disorder (1:10 000–15 000 births) with various causes (Noonan's syndrome, chromosomal anomalies, immunological, heart failure, idiopathic),^{1,2} defined by the accumulation of fluid in the pleural cavity. The availability of prenatal diagnosis by ultrasound scan and the emergence of various intrauterine treatment options have potentially improved its outcome. The choice of prenatal therapeutic options depends primarily on the severity of the intrathoracic liquid accumulation and the gestational age of the fetus at diagnosis. Spontaneous resolution of the pleural effusion has been described.³ However, isolated fetal pleural effusions or hydrothorax generally have a poor outcome, with neonatal death rates varying from 55% when diagnosis is made before 32 weeks gestation to 30% when the diagnosis is made later.⁴ Mortality may rise close to 100% when hydrops is associated.⁵ Interventions on the fetus aim to drain the intrathoracic fluid by either pleuroamniotic shunt, where one or several shunt devices are left in place, or thoracocentesis, where liquid is evacuated after single or multiple transthoracic punctures.

If the diagnosis is made in early pregnancy, pleuroamniotic shunting is considered to be the treatment of choice, as thoracocentesis is often followed by rapid restitution of the hydrothorax.⁵ The persistence of pleural effusions particularly in the first or second trimester impedes normal development of the lungs, resulting in a significant risk of lung hypoplasia.^{6–9} In contrast, if hydrothorax is diagnosed close to term, the favoured therapeutic approach is by either ultrasound guided fetal thoracocentesis or neonatal transthoracic puncture immediately after birth.¹⁰ However, mortality reported for both fetal intervention and conservative management followed by neonatal intervention remains high at 33% and 37% respectively⁴ depending on the cause, associated heart failure, and lung hypoplasia.

Ex utero intrapartum treatment (EXIT) is a management strategy that allows interventions on a neonate delivered from the uterus with the fetoplacental circulation preserved. The aim is to maintain oxygenation in the neonate who has short lived respiratory insufficiency. So far, EXIT has mainly been used for the perinatal management of prenatally diagnosed extrinsic (teratomas, lymphangiomas) or intrinsic (laryngeal atresia, congenital high airway obstruction syndrome) obstructive malformations of the upper airways.^{11–13} Various

interventions have been performed with EXIT support including tracheotomy, tracheoplasty, bronchoscopy, intratracheal intubation, surfactant instillation, and, more rarely, ablative surgery of compressive tumours. Most recently, surgical occlusion of the trachea has been advocated for the treatment of fetuses with severe pulmonary hypoplasia secondary to congenital diaphragmatic hernia in order to attempt catch up growth of the hypoplastic lungs and to improve the outcome. In this situation, rapid repermeabilisation of the voluntarily occluded trachea may be undertaken safely during short lived maintenance of the fetoplacental circulation at birth.¹⁴

We report our experience with EXIT in a fetus presenting in late gestation with severe bilateral pleural effusion.

CASE REPORT

After an initially uneventful pregnancy, this 32 year old woman with type II diabetes was referred to our centre for further assessment of polyhydramnios and suspected macrosomia. Obstetric ultrasound scans up until 32 weeks gestation had been normal.

On the patient's admission at 38 weeks gestation, the fetal scan showed severe polyhydramnios, as well as a moderately macrosomic fetus with isolated bilateral pleural effusions (fig 1). Echocardiographic assessment excluded cardiac malformation, but showed that the umbilical cord vein and inferior vena cava were dilated to internal diameters of 1 cm and 0.65 cm respectively. An additional sign of increased central venous pressure was the reduced peak flow velocity measured by pulsed Doppler within the ductus venosus (0.55 cm/s; normal at term: 0.75 cm/s). No cardiac anomalies were detected, and systolic ventricular function appeared to be preserved. However, the Doppler flow velocity pattern through the atrio-ventricular valves suggested impaired diastolic ventricular filling (fig 2), probably caused by extrinsic compression of the fetal heart by the extensive fluid accumulation, which occupied the whole intrathoracic space (tamponade effect). On two dimensional ultrasound examination, the lungs appeared to be completely collapsed and echo dense (fig 1). The biophysical profile and cardiotocography were normal.

Three options for management were discussed: thoracocentesis (a) in utero, (b) ex utero intrapartum (EXIT), and (c) postnatally after complete delivery.

Ultrasound guided thoracocentesis before delivery of the fetus is the most commonly used approach in similar fetal pathologies. The right hemithorax is usually drained first to minimise compression of the central veins by the opposite side. In this case, polyhydramnios and the fetal position in cephalic presentation with its back low in the maternal left flank restricted low risk access in utero to the right hemithorax.

Abbreviations: EXIT, ex utero intrapartum treatment.

Figure 1 Fetal thoracic scan. Transverse view of the fetal thorax and heart at 38 weeks gestation. A massive effusion (*) is evident in both pleural cavities. The left lung lobes appear completely collapsed or compressed (arrows). The right lung is not seen in this view. On the four chamber view, the fetal heart is normal in size and shape.

Figure 2 Fetal cardiac scan. Abnormal fetal Doppler flow velocity pattern through the mitral valve. Unlike in the normal late gestational fetus, the flow velocity during early diastole (E wave) is higher than during atrial contraction (A wave). This indicates impaired diastolic ventricular filling, probably as a consequence of external compression of the fetal heart by the accumulated pleural fluid producing an external tamponade effect.

Delivery of the fetus followed by immediate postnatal drainage of a very large volume of bilaterally accumulated pleural fluid was considered to pose a high risk of prolonged and, possibly severe, hypoxia. Despite immediate intubation and ventilation of the newborn, insufficient lung expansion had to be expected until at least part of the effusion had been withdrawn.

Thus EXIT supported thoracocentesis appeared to be the lowest risk procedure. Incomplete delivery of the fetus by caesarean section was planned. Temporary preservation of the fetoplacental circulation was to allow sufficient time for both thoracic cavities to be drained and the lungs to distend before the newborn had to rely on its own lung function.

A detailed therapeutic plan was set up to minimise time lost during perinatal management. Rachi anaesthesia was chosen for minimal maternal risk, and fentanyl was added during the intervention to provide fetal analgesia. Caesarean section was performed by the obstetric team in the presence of two neonatologists dressed in sterile surgical clothing. Avoiding the inferior margin of the anteriorly placed placenta, uterotomy was performed leaving the uteroplacental and placentofetal circulations intact. A normally developed slightly oedematous baby girl (weight 3670 g (P90); length 52 cm (P90)) was extracted and positioned on a flat sterile surface that had been prepared on the maternal legs. Avoiding stretching of the umbilical cord, the newborn was positioned about level with the placenta so as to avoid hydrostatic

Figure 3 Neonatal chest radiograph taken on the patient's arrival at the neonatal intensive care unit, at 1 hour of life and high frequency oscillation ventilation at a mean pressure of 14.5 cm H₂O. Gauge 16 catheters used for bilateral drainage of 400 ml liquid at birth are still in place. Note the persistence of considerable effusion at this early stage.

pressure on the placentofetal circulation and to allow the neonatologists on either side of the maternal legs easy access to the thorax of the newborn. The obstetricians achieved accurate maternal haemostasis and verified persistence of pulsatility of the umbilical cord. Uterine relaxation was not necessary. Bilateral thoracocenteses were simultaneously performed using 16G intravenous catheters inserted through the 4th intercostal spaces. Overall, more than 400 ml liquid was evacuated, transparent and citrin on the right side, initially haemorrhagic but progressively clear on the left side. During the procedure, which lasted four minutes, pulsatility of the cord confirmed that the neonatal heart rate remained above 100 beats/min. The newborn started to cry faintly after one or two minutes (about 100 ml of fluid had been withdrawn) followed progressively by larger respiratory movements and more vigorous crying. When no more liquid was easily drained, the cord was cross clamped and sectioned, and resuscitation measures were continued under a radiant warmer and conventional cardiorespiratory monitoring. The girl underwent elective intubation and ventilation initially with 100% inspired oxygen, which was reduced to 50% within 15 minutes. Analysis of capillary blood gas taken at 10 minutes of life showed mixed acidosis with a pH of 7.04, Pco₂ 96 mm Hg, and base excess -9.9, which prompted volume expansion with 10 ml/kg 0.9% NaCl. Central venous gases 35 minutes later were largely improved, with pH 7.33, Pco₂ 46 mm Hg, and base excess -2.1, and when transferred to the neonatal intensive care unit, the patient was in a stable condition (fig 3). Ventilation was continued by high frequency oscillations with maximal pressures of 15 cm H₂O and Fio₂ of 50%. Permanent bilateral chest drains were inserted to drain the persisting bilateral effusion.

Besides respiratory anomalies, physical examination of the girl was normal. Postnatal echocardiography showed a small, haemodynamically insignificant pericardial effusion, abdominal ultrasound examination showed minimal ascites, and the brain scan was normal. Serology for cytomegalovirus, Epstein-Barr virus, parvovirus B19, and toxoplasmosis remained negative. The karyotype was normal (XX). Placental pathology remained inconclusive. Examination of pleural fluid showed a pattern typical for chylus (150 erythrocytes/mm³, 1700 nucleated cells/mm³ composed of 97% lymphocytes; protein 35 g/l). During the first 3–4 days of life, about 150 ml fluid was drained daily, with a progressive reduction in the quantity during the following days. The infant was started on total parenteral nutrition, and maternal milk was introduced from day three onwards without adverse effect on chylus secretion. The right and left sided chest drains

were withdrawn after 5 and 10 days respectively. Weaned to room air by day 3, the infant was easily extubated directly from high frequency oscillation ventilation on day 5. After uneventful progression of enteric feeding, the girl was finally discharged home at 25 days of age, fully breastfed, with a normal physical examination and a normalised chest radiograph.

DISCUSSION

We report our experience in the management of severe bilateral hydrothorax diagnosed in late gestation. A rapidly developing polyhydramnios called for prenatal assessment. Polyhydramnios may occur secondarily because of extrinsic oesophageal compression by extensive bilateral pleural effusions.¹⁵

When hydrothorax develops before 27 weeks, normal fetal lung development is often compromised. Furthermore, cardiac and central vein compression may lead to heart failure and intrauterine demise. When diagnosed in mid-trimester, hydrothorax requires a detailed fetal investigation including morphology scans for associated cardiac and extracardiac anomalies, karyotyping, and maternal serological assessment for detection of treatable conditions. Thoracoamniotic shunting with placement of a permanent device should be considered, particularly if there is evidence of compromised lung development and fetal wellbeing—for example, mediastinal shift in unilateral hydrothorax, signs of cardiac tamponade in bilateral hydrothorax, fetal hydrops.

So far, fetal hydrothorax detected in late gestation has been classically managed by thoracocentesis in utero or immediately after delivery. This represents to our knowledge the first report of perinatal management of severe congenital hydrothorax or chylothorax by EXIT. Maintenance of the fetoplacental circulation ex utero as the sole or main source of oxygenation of a critically affected newborn for a prolonged time requires close and efficient collaboration between anaesthetists, obstetricians, neonatologists, and sometimes surgeons, and the procedure should be carefully planned. Two hardly predictable complications may hamper the success of EXIT. Firstly, intraoperative uterine haemorrhage may need immediate placental delivery; secondly, uterine contraction after delivery of the newborn may restrict uteroplacental perfusion and require halothane administration. Our experience shows that EXIT may be a useful approach especially for the fetus presenting with severe pleural effusions towards the end of gestation and in whom either accurate in utero drainage is technically impossible or unavailable or drainage post partum would result in profound and prolonged hypoxia until sufficient drainage of pleural fluid allowed lung expansion.

Because of the risks of permanent hypoxaemic brain damage if the postnatal drainage fails to establish rapid lung expansion and alveolar gas exchange, intrapartum thoracocentesis is usually preferred.¹⁰ However, ultrasound guided intrauterine thoracocentesis carries a risk for both the mother and fetus, and lung puncture and withdrawal of large quantities of pleural fluid may induce considerable fetal distress. In

addition, the success of the fetal procedure may be limited by the fetal position, as in our case. Thus perinatal evacuation of large pleural effusions during preserved placental circulation may represent a valid and safe treatment option. The technique provides the same advantages as postnatal drainage with the benefit of preserved oxygenation during the intervention. With regard to the intrapartum approach, the EXIT technique facilitates the invasive approach and enables accurate monitoring of the newborn during and after the procedure. Nevertheless, at present, its use should be limited to late gestational interventions in potentially viable neonates.

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