CASE REPORT

Fetal bronchoscopy: its successful use in a case of extralobar pulmonary sequestration
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Objective: To report the performance of fetal bronchoscopy in a case of pulmonary sequestration. Materials and Methods: A 24 year-old female, Gravida 2, Para 1, was referred at 27.5 weeks with a large fetal left lung mass with marked right mediastinal shift and no visible normal left lung. Differential diagnosis included possible bronchial atresia. Results: The patient underwent fetal laryngoscopy and fetal bronchoscopy at 31.5 weeks. The right lung and a portion of the left lung expanded during surgery as a result of bronchial lavage. Bronchial atresia or bronchogenic cyst were not found. The patient delivered uneventfully, with continuous growth of the right lung and a small amount of left lung. The patient delivered vaginally at term. The baby underwent thoracoscopic resection of a pulmonary sequestration at 10.5 months of age and did well. Conclusion: Fetal bronchoscopy is feasible. The procedure may prove useful in the differential diagnosis and in the potential treatment of different fetal lung lesions, as well as aid in the understanding of the role of bronchial obstruction as a common pathophysiologic mechanism for different fetal lung masses. Risks and benefits of fetal bronchoscopy warrant further experience.

Keywords: fetal laryngoscopy, fetal therapy, fetoscopy, pulmonary sequestration, ultrasound

Introduction

Pulmonary hypoplasia and subsequent neonatal death may result from various space occupying lesions including congenital diaphragmatic hernia, cystic adenomatoid or congenital pulmonary airway malformation (CCAM/CPAM), lobar or extralobar pulmonary sequestration, pulmonary emphysema, bronchial atresia and hydrothorax among others [1–3]. The mechanism by which space occupying lesions result in pulmonary hypoplasia is thought to be due to arrest of normal embryological lung development. Fetal therapy may be considered in selected cases to counter the effect of the lesion and avoid the development of pulmonary hypoplasia [1,4–6]. The fundamental steps required to offer fetal therapy include an accurate as possible prenatal differential diagnosis, knowledge of the natural history of each condition, development of antenatal criteria for intervention and the proper form of treatment. Prenatal differential diagnosis can be undertaken using ultrasound, color and pulsed Doppler, as well as fetal MRI. In particular, the differential diagnosis between CCAM/CPAM, pulmonary sequestration and pulmonary emphysema may be difficult, especially if an obvious feeding vessel stemming from the aorta cannot be distinctly identified with ultrasound [7]. The differential diagnosis is important because as many as 60% of CCAM/CPAM lesions regress spontaneously [1], as well as for devising the appropriate fetal therapeutic approach [8,9].

In the year 2000, Quintero et al. [10] described for the first time the technique of direct fetal laryngoscopy, which consists of minimally-invasive percutaneous access to the fetal trachea with the combined use of ultrasound and endoscopy. This approach has been used for fetal intraluminal tracheal occlusion (FITO) for congenital diaphragmatic hernia [11], as well as for fetal lung biopsy in the differential diagnosis of CCAM/CPAM [9]. Thus far, endoscopic access had been limited to the level of the carina. We hereby report the performance of fetal bronchoscopy in a case of extralobar pulmonary sequestration which resulted in expansion of the normal lung parenchyma, avoidance of pulmonary hypoplasia and postnatal survival.

Case report

A 24-year-old, Gravida 2, Para 1 was referred at 27 5/7 weeks with the possible diagnosis of fetal congenital cystic adenomatoid malformation (CCAM/CPAM) of the lung in the left hemithorax. Ultrasound at our institution showed a hyperechogenic left lung mass measuring 6.1 x 4 x 3.7 cm, with marked right mediastinal deviation and downward displacement of the diaphragm (Figure 1). There was no visible normal left lung. The right lung was significantly compressed, with a right Quantitative Lung Index (QLI) of 0.4 (<0.01st percentile) and a lung-to-head ratio (LHR) of 0.1. A small eucalyptus area near the left hilar region was noted, measuring 5 mm. Color Doppler failed to show blood flow within this eucalyptus area, as well as any obvious feeding vessel from the aorta. Differential diagnosis included type III CCAM/CPAM, bronchogenic cyst or lobal bronchial atresia, and pulmonary sequestration. Fetal MRI suggested the possibility of left lobal bronchial atresia [12] (Figure 2) The amniotic fluid volume was increased with an amniotic fluid index of 24 cm. Fetal echocardiogram showed no obvious structural congenital heart disease and a Tei index of 0.41. Estimated fetal weight was at the 22nd percentile.
for growth. The cervix measured 3.4 cm via transvaginal ultrasound. Prior workup had shown negative TORCH titers and a normal 46, XY karyotype from amniocentesis. Follow up ultrasound at 30 5/7 weeks showed the mass at 5.8 × 5.3 × 3.1 cm, with a QLI of 0.5, an LHR of 0.14, an amniotic fluid index of 22 and a Tei index of 0.41. The trachea measured 3.4 mm in diameter.

The patient was counseled about the poor prognosis for the fetus, with a high risk for pulmonary hypoplasia. Management alternatives included expectant management, with the risk of pulmonary hypoplasia and neonatal death, or termination of pregnancy outside the State of Florida, given the advanced gestational age beyond the legal limit (24 weeks). Percutaneous fetal sclerosis was not offered as the primary differential diagnosis was left bronchial atresia or bronchogenic cyst. Consideration was given to the possibility of offering fetal lung biopsy to aid in the differential diagnosis [9]. Direct fetal laryngoscopy was also considered, with the potential use of a flexible endoscope to perform fetal bronchoscopy and surgically eliminate the presumed bronchial obstruction. If an obstruction were not to be found, we considered occluding the trachea with an intraluminal device to promote lung growth, similar to the approach used in fetuses with severe congenital diaphragmatic hernia [10]. To our knowledge, neither diagnostic nor operative bronchoscopy had been previously performed.

After listening to all possible alternatives, the patient elected to undergo an attempt at direct fetal laryngoscopy and possible fetal bronchoscopy. The surgical approach was discussed in multidisciplinary meetings involving maternal-fetal medicine, fetal therapy, pediatric surgery, pediatric radiology, neonatology and pediatric pulmonology. Surgery was approved by the University of Miami and Jackson Memorial Hospital as per the innovative fetal therapy pathway. The patient gave written informed consent.

The patient was taken to the operating room at 31 5/7 weeks. Under local anesthesia, a 3.8 mm trocar (Richard Wolf, Inc., Vernon Hills, IL, USA) was inserted into the amniotic cavity. The fetus was paralyzed, using 0.15 cc of vecuronium bromide. Fetal laryngoscopy was performed as previously described [10], using a 3.3 mm, 30° rigid diagnostic endoscope (Richard Wolf, Inc., Vernon Hills, IL, USA). No obvious airway obstruction was noted up to the level of the carina. The diagnostic endoscope was removed. Fetal bronchoscopy was then performed using a 2.8 mm flexible pediatric endoscope (Olympus Corp, Center Valley, PA, USA). The right and left bronchi were assessed. To improve visualization, extensive bronchial lavage was performed with normal saline infused through the operating channel of the endoscope. Altogether 200 ml of fluid was injected. The continuous clear fluid injection also showed floating whitish particles. Both right and left bronchial trees were inspected to the segmental level and showed a normal anatomic branching pattern, ruling out the possibility of a left main bronchus atresia or a proximal obstructive bronchogenic cyst (Figure 3).

On ultrasound, bronchial lavage resulted in small hypercho- genic images corresponding to air bubbles admixed with the bronchial lavage fluid. As the bronchoscopy was being performed, we noted delineation of a small portion of the left lower lung with the bronchial lavage fluid that had not been previously seen either with ultrasound or with MRI. Most importantly, there was a remarkable expansion of the right lung, presumably as a result of increased airway pressure from the bronchial lavage (Figure 4). The lavage fluid did not enter the hyperechogenic lung mass, suggesting lack of communication of the mass with the airway and normal lung parenchyma. The left main bronchus and branches were reassessed endoscopically,

![Figure 1. Transverse (a) and sagittal views (b) of the fetal thorax at 27.5 weeks. A large hyperechogenic mass (M) occupies the entire left hemithorax with large mediastinal shift and extremely compressed right lung. D, diaphragm; RL, right lung; H, heart; R, right; L, left.](image1)

![Figure 2. Fetal MRI showing left lung replaced by large mass (M) with downward displacement of the diaphragm (D).](image2)
confirming patency of all bronchi up to three generations. At this point, no further diagnostic or therapeutic maneuvers were considered necessary. The operating time was 73 min.

Postoperative ultrasound examination, 24-h later, showed persistent expansion of the right lung, with a QLI of 0.89, which was a significant increase from 0.5 preoperative. Weekly ultrasounds showed progressive expansion of the right lung (Figure 5). The left lung also showed progressive increase, with concomitant regression of the hyperechogenic mass. By 38 5/7 weeks, the right lung was virtually completely expanded, the left lung was virtually normal, no mediastinal shift and the hyperechogenic mass was hardly discernible. The patient was induced at 40 3/7 weeks, and delivered a male fetus who weighed 3585 g, with Apgar scores of 9, 9 and 9 at 1, 5 and 10 min, respectively. He had an uneventful course and remained stable with no respiratory distress, and an oxygen saturation of 100% on room air. Chest X-ray (CXR) after delivery revealed diffuse even haziness throughout the left hemithorax. A chest CT scan on the first day of life showed a large mass in the posterior aspect of the left lung, possible CCAM/CPAM versus pulmonary sequestration. CT with contrast showed an anomalous vessel stemming from the left side of the descending aorta and another vessel, defining the lesion as extralobar sequestration (ELS) (Figure 6). There was no evidence of cystic lesions within this mass. No intervention was undertaken and the infant was discharged to home. The mass was resected thoracoscopically at the age 10.5 months without complications. Surgical pathology showed a 5 × 3 × 2 cm mass consistent with extralobar sequestration and CCAM/CPAM type III. The baby is asymptomatic and doing well at 1 year of age.
Discussion

Our case demonstrates the feasibility of performing percutaneous fetal bronchoscopy for diagnostic or therapeutic purposes. This is an important expansion of our development of direct fetal laryngoscopy and intraluminal tracheal occlusion for the \textit{in utero} treatment of congenital diaphragmatic hernia \cite{10}. The findings and postoperative course in our case may also further the understanding of the etiology and pathophysiology of fetal lung lesions. The successful outcome of this case supports the rationale for late second-trimester and early-third trimester fetal therapeutic interventions aimed at avoiding pulmonary hypoplasia.

Untreated, the fetus was likely to die in the neonatal period from pulmonary hypoplasia, given the sonographic findings of no normal left lung, severe right mediastinal shift and an extremely small right lung with a QLI $<0.01$st percentile at 27.5 weeks. Bronchoscopy was undertaken with the expectation that either a left main bronchial atresia \cite{13,14} or an obstructing bronchogenic cyst \cite{15} would be present and would need to be surgically treated. If we had found either of these two lesions, we would have considered the possibility of reestablishing bronchial patency \textit{in utero}. Fortunately, this was not necessary and we only needed to advance the endoscope through the bronchi under continuous manual irrigation. Bronchoscopy was able to assess all bronchi up to three generations. During the procedure, small debris floated proximally as a result of the continuous lavage, clearing the way for more distal endoscopic assessment. We surmise that the therapeutic effect of the procedure, i.e., expansion of the right lung and a segment of normal left lung, resulted from establishing luminal patency in bronchi that may have been occluded by inspissated material or collapsed from the pressure of the large contralateral lung lesion. This bronchial lavage resulted in permanent expansion of the normal lung parenchyma for the rest of the pregnancy and subsequent normal fetal lung growth, avoidance of pulmonary hypoplasia and neonatal survival. The proposed therapeutic mechanism is in line with the observation that some lesions identified \textit{in utero} by ultrasound, spontaneously regress or improve during gestation, presumably from reestablishment of bronchial patency \cite{16}.

Our case may underpin the suggested etiologic paradigm of bronchial obstruction as the unifying pathway for different pulmonary congenital anomalies, including cystic adenoid malformation (CCAM/CPAM), intralobar (ILS) and extralobar (ELS) sequestration and lobar emphysema (LE). This suggestion is based on the fact that many of these anomalies share similar CT findings and histopathology \cite{17}, and may be present simultaneously in a single individual \cite{16,18,19}. The term “bronchial atresia sequence” has been proposed to include the degree of bronchial obstruction, the level of obstruction, and the timing within gestation as potential factors responsible for the different abnormal lung patterns \cite{16}.

Our case was a combination of ELS and CCAM/CPAM. The aberrant systemic blood supply to the mass could not be detected antenatally with ultrasound or fetal MRI, given its location in proximity to the main arteries. This points to the difficulty in establishing an accurate prenatal diagnosis in some cases. Ironically, the inability to identify the feeding vessel antenatally allowed consideration for the innovative procedure. Had we identified the feeding vessel, we would have offered instead percutaneous fetal sclerosis of the vessel with 5% ethanolamide \cite{5,6}.

\begin{figure}[h]
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\includegraphics[width=\textwidth]{figure4.png}
\caption{Intraoperative ultrasound. Bronchial lavage resulted in dramatic intraoperative expansion of the right lung and delineation of left lower lobe not previously detectable.}
\end{figure}

\begin{figure}[h]
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\includegraphics[width=\textwidth]{figure5.png}
\caption{Assessment of right lung growth before and after fetal bronchoscopy with the Quantitative Lung Index (QLI). The QLI was at $<0.1$st percentile ($<0.6$) before surgery (red line). The intraoperative expansion of the right lung resulted in a QLI of 0.89 (arrow) and normalization ($=1.0$) within 3 weeks of surgery. The 50th percentile of the QLI from 16–32 weeks is 1.0. Beyond 32 weeks, the value of the 50th percentile of the QLI is unknown, but it is not higher than 1.0.}
\end{figure}

\begin{figure}[h]
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\includegraphics[width=\textwidth]{figure6.png}
\caption{Computed tomography with contrast on day 1 of life. The systemic vessel can be seen feeding the extralobar sequestration (arrow). A, aorta. ELS, extralobar sequestration.}
\end{figure}
Fetal bronchoscopy has limitations. First, it is an invasive procedure that could result in premature rupture of membranes, preterm labor, maternal or fetal injury. Placental location and fetal position may also hinder performance of the procedure, as with any other fetal intervention. For example, we would not advocate its use in cases of pulmonary sequestration with a prenatally identified feeding vessel, or in type III CCAM/CPAM with hydrops, where percutaneous fetal sclerosis is both less invasive and very effective [5,6]. However, once access to the fetal trachea has been achieved, fetal bronchoscopy is actually less stressful than bronchoscopy in the postnatal period, as it is performed without concern of hindering oxygenation, since fetal oxygenation derives from the placenta and not from the airway. It is quite conceivable that fetal bronchoscopy could be indicated in cases suspected of having main bronchial stenosis or atresia [14] or obstructing bronchogenic cysts [15], where patency of the bronchi could be attempted. We do not know whether diagnostic fetal bronchoscopy would be enough to revert the effects of lung compression from other fetal lung entities, such as lobar emphysema. Further experience with this novel approach to fetal lung lesions seems warranted.

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Declaration of Interest: The authors report no conflict of interest.

References


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