CASE REPORT

Unilateral lung agenesis, hiatal hernia and atrioventricular septal defect: a rare combination of congenital anomalies

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SUMMARY

Unilateral lung agenesis is a relatively rare congenital anomaly with a reported incidence of 1 in 15 000 births. It is frequently associated with other congenital malformations. Some of the sequelae of lung agenesis are potentially life-threatening. Here, we report a case of left lung agenesis in association with hiatal hernia and atrioventricular septal defect, a rare combination of anomalies which have not been described previously in the literature.

BACKGROUND

Unilateral lung agenesis (ULA), defined as complete absence of pulmonary parenchyma, bronchial tree and pulmonary vasculature on one side, is a rare congenital anomaly.^{1 2} ULA is reported to be associated with other malformations in ~50% of patients, with skeletal, gastrointestinal, genitourinary and cardiovascular systems being the most commonly involved organ systems.³ The morbidity and mortality in these patients are influenced by the degree of tracheobronchial abnormality and other associated anomalies. Here, we describe a neonate with agenesis of left lung associated with a large hiatal hernia and a complex congenital heart disease, a rare combination of anomalies which has not been described previously in the literature. In this scenario, we felt compelled to attempt to elucidate the possible aetiology and contributing factors, as well as the order of events/causality that led to this set of anomalies.

CASE PRESENTATION

A premature baby girl was delivered at 35 weeks of gestation to healthy non-consanguineous parents via caesarean section delivery secondary to severe maternal pre-eclampsia and fetal intrauterine growth restriction. The mother was followed by community obstetrical provider during her pregnancy and was transferred to our centre at ~35 weeks of gestation. The prenatal maternal evaluation for toxoplasmosis, rubella, cytomegalovirus, herpes and other (TORCH) infections was negative. Also, there was no reported history of smoking, alcohol consumption or use of recreational drugs during the pregnancy. There is no family history of genetic syndrome or any major congenital malformations. A comprehensive level 2 prenatal ultrasound performed during the second trimester was

notable for herniation of the abdominal contents into the left hemithorax, along with suspected left lung hypoplasia versus agenesis. A fetal MRI performed at 22 weeks' gestation in view of the above-mentioned findings showed absent left lung with likely absent left bronchial tree, compensatory hypertrophy of the right lung crossing over into the left hemithorax and herniation of bowel into the left hemithorax (figures 1 and 2). Based on the available imaging, the herniated bowel was thought to be congenital diaphragmatic hernia. A fetal echocardiogram performed at our centre at around 35 weeks of gestation was notable for abnormal fetal cardiac axis and position, with the apex of the heart pointing posteriorly. In addition, a primum atrial septal defect along with possible cleft in the anterior mitral valve leaflet were noted, raising concern for a partial atrioventricular septal defect. The newborn was intubated soon after delivery in view of concerning prenatal findings and was transferred to the neonatal intensive care unit. On examination, there was no hypertelorism, prominent epicanthal folds or cleft lip or palate. No triphalangeal thumb or any limb anomalies were noted.

INVESTIGATIONS

A postnatal X-ray (figure 3) and CT scan (figure 4) showed herniated bowel into the left hemithorax, complete agenesis of left lung parenchyma along with ipsilateral absence of bronchial tree and pulmonary vasculature. Postnatal echocardiogram revealed that the heart was shifted leftwards with the apex pointing posteriorly. The intracardiac anatomy revealed a primum type of atrial septal defect, cleft in the anterior mitral valve leaflet and a small inlet ventricular septal defect, classifying her cardiac defect as the transitional form of atrioventricular septal defect. As expected, in view of her pulmonary agenesis, there were no discernible left pulmonary artery and left pulmonary veins in this study. Additional imaging studies, including brain and abdominal ultrasound, did not reveal any brain or renal anomalies. The abdominal ultrasound showed midline liver and an echogenic structure consistent with spleen located in the left suprarenal area. The axis of superior mesenteric vessels was not evaluated in this study. Additional imaging tests such as MRI and upper gastrointestinal contrast study were not performed preoperatively as the available information was thought to be sufficient

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Figure 1 Fetal MRI shows the herniation of the bowel into the thorax (arrow) and a single right lung (star).

by the multidisciplinary team to proceed with the surgical management. A comprehensive infectious disease work-up which included but not limited to cytomegalovirus, Epstein-Barr virus, coronavirus, influenza, parainfluenza, chlamydia, mycoplasma was negative. A chromosomal microarray analysis performed after birth was normal with no identifiable copy number variants. More detailed genetic testing for congenital heart disease panel, and whole exome sequencing could not be performed due to financial limitations related to insurance coverage.

Figure 2 Transverse section of the fetal thorax in MRI showing compensatory hypertrophy of right lung (arrow) and herniation of bowel (star). There was no discernible left lung in this scan.

TREATMENT

On day of life 5, the infant was taken to the operating room for repair of her suspected diaphragmatic hernia. On detailed inspection of the diaphragm during the laparoscopic surgery, she was found to have herniation of the entire stomach into the left hemithorax through the oesophageal hiatus in the diaphragm. The rest of the diaphragm was found to be intact, with no obvious defects in the foramina of Morgagni and Bochdalek. In view of this finding, a diagnosis of hiatal hernia was made. In addition to hiatal hernia, she was also noted to have bowel malrotation. She had reduction of her hiatal hernia, but complete repair was deferred for a later date, given the likelihood of the recurrence at this age. She recovered rapidly from this surgery and was extubated to room air in few days. She was taken to the operating room at 3 months of age and underwent complete repair of her hiatal hernia and intestinal malrotation, along with placement of gastrostomy tube. The infant recovered rapidly from this surgery and tolerated gastrostomy tube feeds.

OUTCOME AND FOLLOW-UP

Following improvement in the clinical status, the infant was discharged home at 4 months of age without any supplemental respiratory support. There is no evidence of pulmonary artery hypertension on the echocardiogram performed during a recent clinic visit at 6 months of age.

She is planned for surgical repair of the large primum atrial septal defect in the second year of life.

DISCUSSION

Underdevelopment of lung is classified into three categories: type 1: complete absence of the lung parenchyma, bronchial tree and pulmonary vasculature; type 2: presence of rudimentary bronchial tree with absence of lung parenchyma; and type 3: presence of variable but diminished amounts of pulmonary parenchyma, bronchus and pulmonary vasculature.⁴ Unilateral agenesis of the lung (type 1) is a rare congenital anomaly with a reported incidence of approximately 1 in 15 000 births.² It is postulated to be multifactorial in origin with complex interplay between genetic, teratogenic and mechanical factors.⁵ Although there have been rare reports of chromosomal abnormalities in patients with lung agenesis, there is currently no consensus on the link between lung agenesis and genetic abnormalities.⁶ In our case, a whole exome sequencing might have yielded additional information on the existence of genetic mutations in this patient. Scimitar syndrome is a rare congenital multisystem malformation where there is partial hypoplasia of the right lung due to sequestration of the pulmonary parenchyma in the right lower lobe.

ULA is typically diagnosed prenatally, mostly during a routine level 2 ultrasound performed in the second trimester of pregnancy.⁷ ULA often leads to other associated intrathoracic abnormalities. The most common sequelae of ULA is abnormal cardiac axis and position as the mediastinum is shifted to the side of lung agenesis due to the ipsilateral emptiness of the hemithorax. Some degree of tension is built in the walls of the great arteries coming out of the heart secondary to the mediastinal shift and twisting of the heart leading to vascular anomalies. Also, right-sided ULA is known to cause tracheal and bronchial stenosis due to the dextroposed heart tugging the vascular pedicle rightward.¹ This rightward shift of the vascular pedicle leads to compression of the lower trachea and left main stem bronchus.

The hiatal hernia diagnosed in our patient is probably a sequela of the ULA. Hiatal hernia is defined as herniation of

Figure 3 Chest X-ray showing absence of left lung and herniation of bowel into the thorax. The orogastric tube is seen curled up in the stomach which was confirmed to be entirely in the chest cavity during initial surgery.

intra-abdominal structures into the thorax through the oesophageal hiatus in the diaphragm. Hiatal hernia frequently involves the herniation of stomach and is classified into four types⁸: type 1, sliding hernia; type 2, rolling hernia; type 3, being a complex mix of the first two types; and type 4, a large hiatal hernia with herniation of the entire stomach and other intra-abdominal organs. As the fetus is not able to generate adequate pressure to dilate the intrathoracic portion of the stomach until the third trimester, hiatal hernia is most often missed prenatally or diagnosed late in the pregnancy. The criteria for prenatal diagnosis of this condition was put forward by Bahado-Singh *et al*⁹ and was later modified by Ruano *et al*.¹⁰ These criteria include presence of hypoechoic mass in the posterior mediastinum between the heart and spine, absence of pericardial or pleural effusion, presence of intra-abdominal midline stomach or complete absence of stomach in the abdomen and dynamic movement of the herniated stomach between the thorax and abdomen. In our patient,

Figure 4 CT scan showing presence of bowel in the thorax (arrow) and mediastinal deviation to left hemothorax (star).

the stomach might have herniated into the thorax through the oesophageal hiatus secondary to lower intrathoracic pressure from ULA. Also, we were able to see the herniated stomach contents as early as 20 weeks of gestation in our patient, probably due to the fact that higher pressures are not needed to distend the herniated contents in this specific scenario.

ULA is also known to be associated with multiple other congenital anomalies in approximately half of the patients.³ Morbidity and mortality in these patients are influenced by the severity of the associated malformations. In comparison with patients with congenital diaphragmatic hernia, patients with hiatal hernia secondary to ULA have less severe respiratory symptoms, possibly due to compensatory hyperplasia of the contralateral lung. In a review on lung agenesis by Cunningham *et al*, the authors demonstrated an association between pulmonary agenesis and ipsilateral facial and/or radial ray abnormalities.¹¹ They hypothesised that disruption in dorsal aortic arch blood flow during the fourth week of gestation could interfere with the development of the lung, limb and derivatives of the first and second branchial arches thus resulting in the ipsilateral limb and facial anomalies. However, in contrary to this hypothesis, our patient did not have any limb or facial anomalies. Another potential long-term developmental problem in ULA is thoracic scoliosis, for which these children should be closely monitored.

In a recent review, Xie *et al* have reported a congenital heart disease incidence of 14% in patients with ULA.⁴ Other common systems effected are: gastrointestinal (14%), skeletal (12%), vascular (9%) and genitourinary (3%). The type of congenital heart defects reported in patients with ULA vary in complexity from simple atrial septal defect to the complex cyanotic defect of double outlet right ventricle. Our patient was diagnosed to have a transitional form of atrioventricular septal defect. In Mardini-Nyhan association, also known as lung agenesis, congenital heart defects, and thumb anomalies (LACHT) syndrome, pulmonary agenesis has been described in association with congenital heart disease. However in those cases there is also ipsilateral thumb anomalies described together. Our patient does not have any thumb or limb anomalies. We do not have a physiological explanation for the atrioventricular septal defect seen in our patient, and therefore it might represent an incidental association.

Learning points

- ▶ An insult during the sensitive early stages of embryological lung development might cause unilateral lung agenesis (ULA).
- ▶ The abnormal cardiac axis and hiatal hernia seen in our case are most likely the sequelae of the ULA and the resultant emptiness of the left hemithorax.
- ▶ The intestinal malrotation and the cardiac anomaly seen in our patient are probably associated incidental findings.
- ▶ Preoperative MRI would have provided additional information on the anatomy of the diaphragm, thereby optimising surgical planning in neonates with suspected diaphragmatic anomalies.
- ▶ Routine evaluation of the vascular axis of the superior mesenteric vessels should be performed in all neonatal abdominal ultrasounds in order to evaluate for malrotation.

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