

Lung Agenesis: An Embryological Perspective

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Abstract - Lung agenesis or aplasia is a very rare congenital anomaly. It is estimated at 34 per million live births. The etiology of this disorder has not been clearly known. Failure of development of the primitive lung bud leads to the cause of this condition. In half of these cases, it has been reported in association with other congenital defects such as congenital malformation of the cardio-vascular, skeletal, gastrointestinal or genitor-urinary system. This condition is usually diagnosed during childhood. Some patients with lung agenesis may suffer from recurrent respiratory distress, dyspnea, and lung infections. We report a case of a 1-month 28-day-old male infant with right-sided lung agenesis associated with spina bifida as other congenital defects presented to us with recurrent severe respiratory distress. The purpose of writing this case report is to explore a case of pulmonary agenesis in terms of its embryological aspects.

Keywords:

Lung agenesis; lung aplasia; congenital malformation

I. Introduction

Pulmonary agenesis is a very rare congenital disorder in which there is an absence of pulmonary parenchyma, bronchus, and pulmonary vascular. [1,2,3] This is a rare type of deformity that occurs due to failure of the development of primitive pulmonary buds. This abnormality was first discovered incidentally by De Pozze (1673) when performing an autopsy on the body of an adult woman. [3]

The prevalence of pulmonary agenesis is estimated at 23-24 per 1,000,000 live births, and 1 per 10,000-15,000 autopsies with a slightly more female proportion than male. More common cases are unilateral agenesis, aplasia and hypoplasia, of which only one third of cases are diagnosed throughout their lives. The etiology of this disorder is not known yet, but its pathogenesis may be related to genetic factors, such as duplication of the distal part of the arm over chromosome 2, deficit of vitamin A or viral infections. [4]

Pulmonary agenesis is often associated with cardiovascular, gastrointestinal, genitourinary or musculoskeletal disorders. Both lungs are equally likely to experience this disorder, but patients with right lung agenesis have a worse prognosis. [6] If no other malformation occurs, the patient with unilateral pulmonary agenesis can live normally, but will often experience recurrent respiratory tract infections at childhood which are often associated with severe conditions and high mortality. [4,5]

Physical examination of patients with pulmonary agenesis shows asymmetrical chest wall movements with no

or reduced breathing sounds in the unilateral hemithorax. Chest X-ray shows opacity throughout the hemithorax, while further examinations such as thoracic CT scan, bronchoscopy, bronchography and pulmonary angiography are needed for definitive diagnosis. Management of these cases is more often medical, but surgical intervention is sometimes needed in some cases, especially when accompanied by other congenital anomalies. [6]

II. Case report

A 1-month and 28-day-old boy was admitted to Sardjito Hospital Yogyakarta with a diagnosis of severe bronchopneumonia accompanied by distress respiratory syndrome. This patient began to have symptoms of fever, coughing and shortness of breath 3 days before being admitted to hospital. In the previous hospital patients had been treated with analgesics and antibiotics.

This baby was born quite a month, spontaneously, with a birth weight of 3,600 g, no complication in labor, strong crying and no cyanosis. The patient experienced normal growth and development until the age of 1.5 months. At the time of admission, the patient had fever, cough and dyspnea. Physical examination showed tachypnea with subcostal and intercostal retraction. On auscultation, no breath sounds in the right hemithorax were found. Chest X-ray showed homogeneous opacity throughout the right hemithorax with a shift of the mediastinal structures to the right and hyperinflation of the left lung. Laboratory tests showed hemoglobin level of 9.3 gr/dl, white blood count 12,000/mm³, and oxygen saturation 87%. The patient was then treated for pneumonia (Figure 1).

The patient suffered from recurrent respiratory distress and right hemithorax opacity with a mediastinal shift and the hyperinflation of the left lung was very impressive with suspicion of right lung agenesis with a differential diagnosis of right lung aplasia. To get clearer information, thoracic CT scan was performed. The thoracic CT scan showed there were no right lung, right pulmonary artery and vein, no right main bronchial branching and left lung hyperinflation and a deviation of the mediastinal structure to the right.

Based on history, physical examination, laboratory and thoracic imaging, it was concluded that the patient had left lung pneumonia and right pulmonary agenesis accompanied by spinal bifida.



Figure 1. Chest X-ray shows right hemithorax opacity and hyperinflation of the left lung. There are deviation of the mediastinal structures to the right.

In the musculoskeletal system, spina bifida 1-10 thoracic vertebrae are present.



Figure 2. Thoracic CT shows the absence of the right lung, right pulmonary artery and vein. The tracheal appearance continues as the main left bronchus.

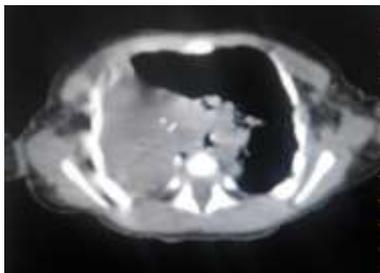


Figure 3. Thoracic CT shows no right lung, right pulmonary artery and vein. There is hyperinflation of the left lung.

III. Discussion

Unilateral pulmonary agenesis is a very rare congenital pulmonary malformation and is included in the pulmonary underdevelopment group or pulmonary development disorder. There are 3 groups of pulmonary development disorders according to the Schneider and Schwalbe classification: Type 1 - agenesis: there is no lung,

bronchus and vascularization of the affected lung; Type 2 - Aplasia: there is a rudimentary bronchus, but there are no lungs and vascularization; Type 3 - Hypoplasia: Lung is still present with vascularization and rudimentary bronchus in varying volumes.^[2,3,4] Functionally, unilateral agenesis and aplasia are the same. "Normal" lungs become larger than normal size, and this enlargement is pure hypertrophy, not an emphysema.^[7]

Embryologically, this abnormality is associated with the failure of the development of the respiratory system from the foregut. In the normal development, the embryonic phase begins during the 4th week or the 22nd day of gestation with the formation of a respiratorial diverticulum from the ventral wall of the primitive foregut. Respiratory buds that develop at the caudal laryngotracheal diverticulum during the fourth week are immediately divided into two sacs, namely primary bronchial buds. These buds grow laterally into the pericardioperitoneal canal, the primordial pleural cavity. Secondary and tertiary bronchialis buds develop immediately. Along with the surrounding splanchnic mesenchyma, bronchial buds differentiate into bronchi and branch them into the lungs. At the beginning of the fifth week, the connection of each bronchial bud with the trachea enlarges to form the primary primordial bronchus. The embryonic right main bronchus is slightly larger than the left bronchus and more vertically oriented. This embryonic relationship continues into adulthood; as a result, foreign bodies are more easily entered into the right main bronchus than the left bronchus. The major bronchus splits the secondary bronchi which form lobar, segmental, and intrasegmental branches. On the right, the superior bronchus will supply the upper lobe of the lungs, while the inferior bronchus is divided into two bronchi, one to the medius lobe of the right lung and the other to the lower lobe (inferior). On the left, two secondary bronchi supply the upper and lower lobes of the lungs. Each lobar bronchus undergoes progressive branching. The segmental bronchi, 10 in the right lung and 8 or 9 in the left lung, begin to form in the seventh week. When this happens, the surrounding mesenchyme also divides. Each segmental bronchus with surrounding mesenchymal accumulation is a primordium bronchopulmonary segment. At the 24th week, about 17 bronchial branches have formed and respiratory bronchioles have developed. Seven additional airways develop after the baby is born.

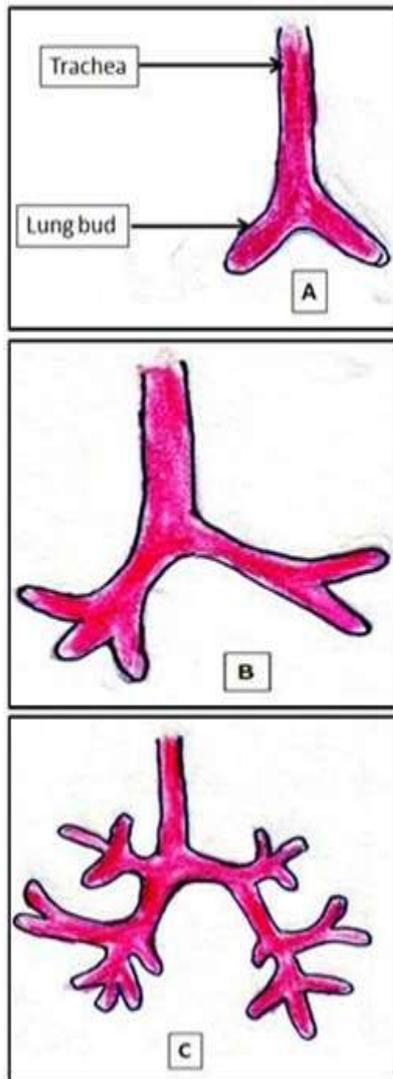


Figure 4: Development of lung buds. (A) The right and left buds begin to appear. (B) They are divided into lobar bronchi (three on the right side and two on the left side). (C) A segmental bronchus is formed.^[1]

Lung agenesis is likely caused by the failure of the bronchial analog to divide and develop equally between two pulmonary buds. If the balance does not occur, one side will grow and develop normally, and the other side will not develop and lung agenesis/aplasia or pulmonary hypoplasia will occur. The type of defect and its severity depend on the time of cessation of development, in the embryo or fetal phase.^[6,7] In theory, the cause of lung agenesis is due to irregular blood flow in the dorsal aortic arch during the 4th week of pregnancy (embryonic phase).

The absence of a fissure that normally exists causes a reduction in the number of lobes, for example, the absence of a transverse fissure in the right lung produces the right lung with only two lobes. Transverse fissures are present on the left side with the result that the left lung has three lobes (A), and the medial basal segment of the left lung can be separated by a fissure from the rest of the lower lobe (B). The superior segment of the inferior lobe may be equally separated (C) and also, the part of the superior lobe of the right lung may be

located medially from v. azygos (D). This section is called the azygos lobe. The accessory lobe is usually connected to the bronchi which are not part of the normal bronchial tree. Such bronchi can rise from the trachea above the bifurcation and esophagus. Sometimes, lobes may not have bronchi. The embryonic area of the lung tissue can be separated from the tracheobronchial tree.^[6,7]

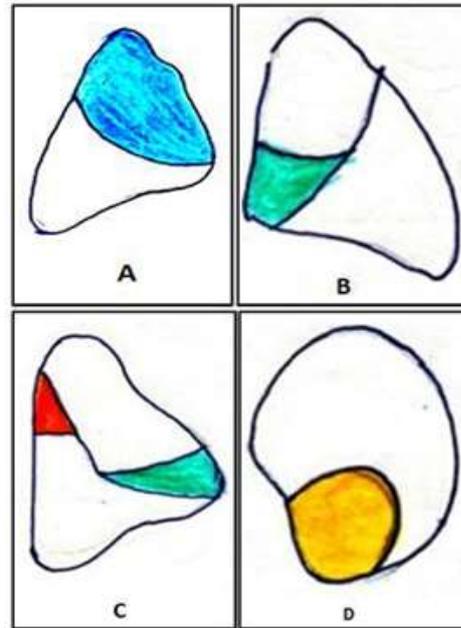


Figure 5: The abnormal lobe of the lungs: (A) The right lung with only two lobes; (B) The left lung with three lobes; (C) The apical segment of the lower lobe is separate; (D) Separate medial segments.^[1]

Lung agenesis occurs with one and the same event on the left and right. However, the right-sided agenesis is associated with a much worse prognosis due to the greater anatomical deformation of the airway and large vessels, intermittent infections and tracheobronchomalacia. Associated anomalies are regularly found, in more than 50% of fetuses involved, and that includes congenital heart disease, spinal abnormalities, imperforate anus, renal agenesis, and tracheo-esophageal fistulas.^[6,7]

The cases reported in this paper can be classified as type 1 - lung agenesis because these patients did not have pulmonary parenchyma, bronchus or right lung vascularization. The patients were identified as having experienced agenesis pulmo dextra at the age of 2 months because of a pulmonary infection accompanied by distress respiration. In addition to agenesis pulmo dextra, patients also experienced other congenital abnormalities, namely spina bifida.^[6,7]

The clinical presentation of this disease varies among different patients. In some cases, symptoms appear immediately after birth as a distress respiration syndrome. While other patients can be asymptomatic until adulthood, lung agenesis is detected by chance on routine examinations. Patients also often experience other congenital abnormalities, which include cardiovascular, gastrointestinal and musculoskeletal system malformations. Cardiovascular

system abnormalities that often occur are patent ductus arteriosus and patent foramen ovale. Frequent gastrointestinal tract abnormalities are tracheoesophageal fistula and duodenal atresia. Musculoskeletal malformations include hemivertebrae, no cost and changes in extremities (absence of radius). Facial and renal abnormalities, including horseshoe kidney are also common.^[4]

Patients with unilateral lung agenesis can experience repeated pulmonary infections.^[6] In most cases patients are examined for recurrent pulmonary infection. More often, the main complaint in unilateral lung agenesis patients is an attack of recurrent lower respiratory tract infections, in the form of bronchiolitis, asthmatic bronchitis or pneumonia. Severe respiratory tract infections during infancy are one of the main signs of this disorder and can cause death. In case of unilateral lung agenesis, the trachea continues as bronchus directly from the normal developing lung, and respiratory tract disorders usually occurs due to inflammation and retention of bronchial secretions.^[7]

The physical examination shows some typical signs. The affected hemithorax is usually slightly flat, and there is usually a slight difference in size between the two sides. On the affected side, the percussion is found to be faint from top to bottom, front and back. However, there is a sonor sound in the upper chest on chest percussion. This is because some "normal" lungs experience emphysema and herniation towards the affected hemithorax. The heart and mediastinum can be found by percussion or auscultation, and by inspection and palpation can be found ictus cordis which shifts towards the side of the agenesis. Above normal hemithorax percussion can be sonor or hipersonor, and breath sounds are stronger and do not hear additional breath sounds.^[7]

Imaging tests are very necessary to diagnose lung agenesis. Chest X-ray and CT show pulmonary hyperinflation that is present and mediastinal shift towards the affected side. Echocardiography is needed to rule out possible heart abnormalities. Other supporting checks that can be done are bronchoscopy to confirm the diagnosis and MRI to detect vascular malformations.

Diagnosis of lung agenesis can be established if there are respiratory difficulties with tracheal deviation, clinically symmetrical thorax, and chest X-ray suspicious of massive atelectasis with mediastinal deviation. Diagnosis is usually sufficient to be confirmed by chest X-ray and thoracic CT scan and invasive procedures, such as bronchography, bronchoscopy, and angiography can be avoided. Typical CT findings are hemithoracic opacity with mediastinal deviation towards the affected part with no lung parenchyma, pulmonary vascular and bronchial branching found as in the reported cases. This condition can also be diagnosed in the antenatal period using prenatal ultrasound and fetal MRI. Although the sensitivity and specificity of fetal ultrasonography have increased, the diagnosis of unilateral lung agenesis without other congenital abnormalities is often not detected during routine antenatal examination.^[6,7]

In regards to the management of unilateral lung agenesis, asymptomatic patients do not need intervention, especially if not accompanied by other congenital abnormalities. However, pulmonary infections or other lung diseases should be treated earlier. Pulmonary hypertension,

which is more common in some patients, is a complication that requires special attention because a reduction in the pulmonary vascular bed, if associated with congenital heart disease (left to right shunt), can develop into an irreversible vascular disease. Patients who experience respiratory tract obstruction may need surgery to remove the blockage if postural drainage and antibiotics have not managed to cure the infection. If signs of respiratory distress occur due to twisting and tracheal compression by rotation of the heart, mediastinum and shift in the location of the aortic arc, this is an indication for diaphragm and aortopexy translocation.^[6] Corrective surgery can be done for the treatment of other congenital abnormalities if at all possible.^[4]

The prognosis of unilateral lung agenesis is influenced by 2 factors: first, the severity of the accompanying congenital anomalies, and second, normal pulmonary involvement in various disease processes. More than 50% of patient with lung agenesis pass away within the first 5 years of birth. Respiratory tract inflammations are the biggest risk for these children.^[6] If patients can survive in the first 5 years of life, usually these patients have normal life expectancy.^[7]

Patients with right lung agenesis usually have a higher mortality than the left lung agenesis. This is because the right lung agenesis is usually associated with a shift in the location of the mediastinal structure and heart to the right and by distortion of vascular and bronchial structures which can cause bronchial suppression.^[7]

Conclusion

A 1 month 28 day old male baby with recurrent lung infection was reported with the right lung agenesis accompanied by congenital spina bifida abnormalities. Lung agenesis is very rare, but it is a severe condition that must be diagnosed early and followed up. Diagnosis of lung development disorders is often challenging for doctors. The prognosis, regardless of abnormal formation, is because the patient only has a functional lung. Right lung agenesis, without any other congenital abnormalities, is very rare.

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