CASE REPORT

Right Lung Agenesis Associated with Dextrocardia in Adulthood

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ABSTRACT

Introduction: Pulmonary agenesis is a rare lung disease, occurring in approximately 1 out of every 100,000 births. Most cases of pulmonary agenesis result in death during the neonatal period. Although survival in cases of pulmonary agenesis is rare, it is possible to encounter lung agenesis in adults.
Case: A 26-year-old female patient presented with progressive dyspnea. On physical examination, retraction of the breathing muscles, reduced chest excursions, and decreased breath sounds on the right side were observed. A chest X-ray raised suspicion of pulmonary agenesis. A computed tomography (CT) scan showed hypoplasia of the right lung, accompanied by mediastinal shift, hyperinflation of the left lung, and retraction of the diaphragm and liver to the right. Spirometry showed moderate obstruction.
Conclusion: Pulmonary agenesis in adult patients is extremely rare. Chest X-rays and CT scans are the main diagnostic modalities for pulmonary agenesis. There is no specific treatment for asymptomatic cases. Management focuses on conservative and symptomatic care.

INTRODUCTION

Agenesis refers to the failure of a partial or complete organ to develop during the embryonic stages. Organ formation and development begin during the first trimester of pregnancy.[1] Lung agenesis occurs due to a disruption in the division of bronchial buds. When this failure occurs, one side develops normally, while the other, which fails to divide, develops into lung agenesis.[2]

Pulmonary agenesis was first discovered in 1673. Since then, only a few cases have been reported, with a very rare prevalence of 24-34 per million births.[3] A study stated that the prevalence rate is 1 per 100,000 births.[4] In Indonesia, there have been no reported cases of adult pulmonary agenesis. This may be due to many cases of patients not surviving the early years of life before a diagnosis can be confirmed.[5]

The etiology of lung agenesis is not definitive, but it is suspected to be multifactorial, involving genetics, teratogenic, or environmental factors.[6] Lung agenesis found in adulthood is usually asymptomatic or presents with varying symptoms. These symptoms are closely related to another lung disease due to volume loss.[7] Hence, they are often misdiagnosed with other lung disorders.[7]

A precise diagnostic approach is essential, as patients with unilateral lung agenesis will experience volume loss. This loss will lead to limitations in activities and affect daily function. Additionally, retention of bronchial secretions often leads to infections and various complications.[7]

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CASE

A 26-year-old female presented to the pulmonary department for a monthly follow-up. Her main complaint was shortness of breath, which occurred consistently and worsened with strenuous activities such as running and heavy lifting. Other complaints, such as fever, cough, and cold, were denied by the patient. Her past medical history included a diagnosis of pulmonary agenesis in 2022. The patient also had a history of pulmonary tuberculosis (TB) with complete treatment in 2015. The patient had no family history of the same illness.

On physical examination, vital signs were within normal limits, blood pressure 100/60 mmHg, pulse rate 80 bpm, respiratory rate 24 breaths/min, and oxygen saturation was 95%. The patient's nutritional status was normal, with a weight of 45 kg and a height of 150 cm.

Chest inspection revealed asymmetrical chest movement, reduced excursion on the right side, and retraction in the suprasternal and supraclavicular regions. Palpation showed increased vocal fremitus in the right chest. Percussion revealed dullness in the right hemithorax. Auscultation revealed decreased breath sounds, stridor, and regular heartbeats in the 4th intercostal space of the right hemithorax. Other physical examinations were normal.

Chest X-ray showed tracheal deviation to the right, infiltrates in the lower left lung field, increased bronchovascular patterns, and closure of the right phrenic costal angle, suggesting right pulmonary agenesis and left pulmonary edema, with a differential diagnosis of pneumonia.

A computed tomography (CT) scan confirmed the absence of the right main bronchus, right lung hypoplasia, hyperinflation of the left lung extending into the right hemithorax, multiple ground-glass opacities, parenchymal fibrotic bands, traction bronchiectasis dominant in the periphery and posterior lobe, right diaphragm and liver pulled in the cranial direction, with the conclusion of pneumonia, suggestive of right lung hypoplasia with volume loss in the right hemithorax which causes the mediastinal shift, withdrawal of the right side of the liver and diaphragm and hyperinflation of the left lung and intratracheal mucus. Spirometry showed moderate obstruction and restriction, with a percentage of the forced expiratory volume within 1 second/forced vital capacity (FEV1/FVC) being 41% and a percentage of vital capacity (VC) being 56%.

DISCUSSION

Lung agenesis is part of a group of developmental lung anomalies (DLA) characterized by varying clinical and radiological manifestations. DLAs are divided into several categories based on the location of the abnormality. The three main categories known are bronchopulmonary anomalies, vascular anomalies, and combined lung and vascular anomalies.[1,8]

Congenital bronchial atresia, bronchogenic cysts, congenital lobar emphysema, and congenital pulmonary airway malformations are included in bronchopulmonary anomalies. Unilateral absence of the pulmonary artery, pulmonary agenesis-aplasia-hypoplasia complex, partial anomalous pulmonary venous return, pulmonary artery sling, pulmonary arteriovenous malformations, and pulmonary venous varix belong to vascular anomalies. The combination of lung parenchymal-vascular anomalies of the lung then involves bronchopulmonary sequestration and hypo genetic lung (scimitar) syndrome.[9]

Developmental lung anomalies are rarely detected in adulthood, as they are typically diagnosed during the prenatal and childhood periods. According to Kumbasar, *et al*. (2024), DLA cases reached 30 to 42 cases per 100,000 births.[10] Meanwhile, Cherian, *et al*. (2019) mentioned that lung agenesis was less common than DLA cases.[1] The exact incidence of lung agenesis is unknown. Parry, *et al*. (2021) revealed that the prevalence of lung agenesis was 1 per 100,000 in all births in the general population.[3] Other studies mentioned that the prevalence reached 24-34 per million births.[1,11]

However, it is estimated that these numbers are falsely underestimated. The rare hypoplasia cases cause differentiation in data incidence. Hence, they are rarely reported, and mortality caused by lung hypoplasia is often undiagnosed. Most cases of lung hypoplasia are found outside Indonesia, and until now, no data states the discovery of lung hypoplasia cases in Indonesia.[1,11]

Schneider and Schwalbe, as cited by Hayati, *et al*. (2019), classified lung agenesis into three types: agenesis, aplasia, and hypoplasia.[6] Type 1 (agenesis) is the non-development of lung tissue, bronchi, and blood vessels. Type 2 (aplasia) means there is no lung parenchymal tissue, but there is bronchial and tracheal tissue. Type 3 (hypoplasia) involves underdeveloped lung tissue, bronchial tissue, and vascularization.[11] In this case, the patient had unilateral pulmonary agenesis with type 3 lung hypoplasia. Most cases of pulmonary agenesis found in adulthood are unilateral pulmonary agenesis. Unilateral pulmonary agenesis has a better prognosis because the healthy lung will compensate for oxygen exchange. Additionally, adult cases of pulmonary agenesis rarely present with other congenital abnormalities because if there are other congenital abnormalities, mortality often occurs at the first start of life and in the prenatal period, making it impossible to survive into adulthood.[7]

The exact etiology of pulmonary hypoplasia is unknown. In theory, lung hypoplasia can be either primary or secondary, but it is usually caused by secondary lung hypoplasia.[7] The cause of primary pulmonary hypoplasia has not been identified. Hypoplastic lung conditions associated with genetic disorders, such as trisomy 21 and congenital acinar dysplasia, are examples of primary pulmonary hypoplasia. Underlying anomalies affecting the thoracic cavity or amniotic fluid volume can cause fetal lung compression, ultimately leading to pulmonary hypoplasia.[12]

The pathophysiology of lung agenesis is closely tied to the embryological development of the lung organs. The fourth week of intrauterine life is crucial, as this is when lung development begins. The groove of the laryngotracheal tube emerges from the wall of the primitive pharynx. Both lung buds develop from the laryngotracheal bud on the ventral wall of the foregut. Each lung bud then undergoes repeated branching and elongation.[2] Therefore, the conductive airways develop during the 16 weeks of organogenesis.[2]

The gaseous exchange system forms between 16 and 26 weeks as the acini develops during the canalicular phase. From 26 weeks to birth, lung maturation continues through the terminal sac stage, which persists into childhood. Lung maturation is determined by fluid movement in and out of the fetal lungs, regulated by airway contractions and fetal respiratory movements.[12]

Several theories attempt to explain abnormalities in lung development, including genetic traits, airway obstruction, defective foregut development, or vascular obstructions due to different causes. The failure of the laryngotracheal bud to divide during the embryonic period results in lung agenesis. The cause of this division failure remains unknown. It is theorized to be linked to factors such as folic acid or vitamin A deficiency, genetic traits (such as autosomal recessive chromosomal aberration, particularly in consanguineous marriages), viral infections, the use of salicylates during pregnancy, or intrauterine infections.[12,13]

The clinical symptoms associated with lung agenesis often vary depending on the severity of the disease and whether organ abnormalities are present.[13] Most cases of lung agenesis occur in early childhood. However, if the patient survives, they often experience mild to severe respiratory abnormalities. Severe cases are frequently associated with complications like pulmonary hypertension, bronchopulmonary dysplasia, or alveolar hemorrhage. In contrast, milder cases are rarely diagnosed until adulthood and are often diagnosed incidentally during chest X-rays or recurrent lung infections.[14]

In cases of unilateral lung hypoplasia, the affected side typically exhibits diminished breath sounds, restricted chest wall expansion, and an asymmetrical appearance of the thoracic cage during examination. Signs of obstruction may include tachypnea, shallow breathing, chest retraction, and respiratory distress. Vocal fremitus may also worsen on the affected side. Bilateral pulmonary hypoplasia typically presents as a bell-shaped thoracic cage deformity. Initial suspicion of other congenital anomalies should be raised if symptoms similar to lung hypoplasia are observed.[2,14]

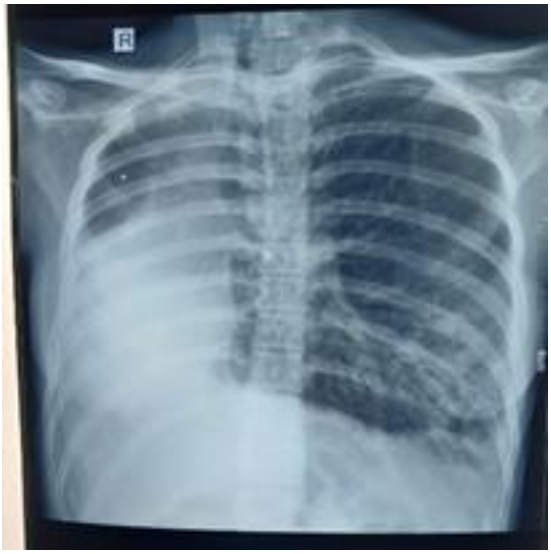

Figure 1. Chest X-ray showed radiopaque in the right hemithorax

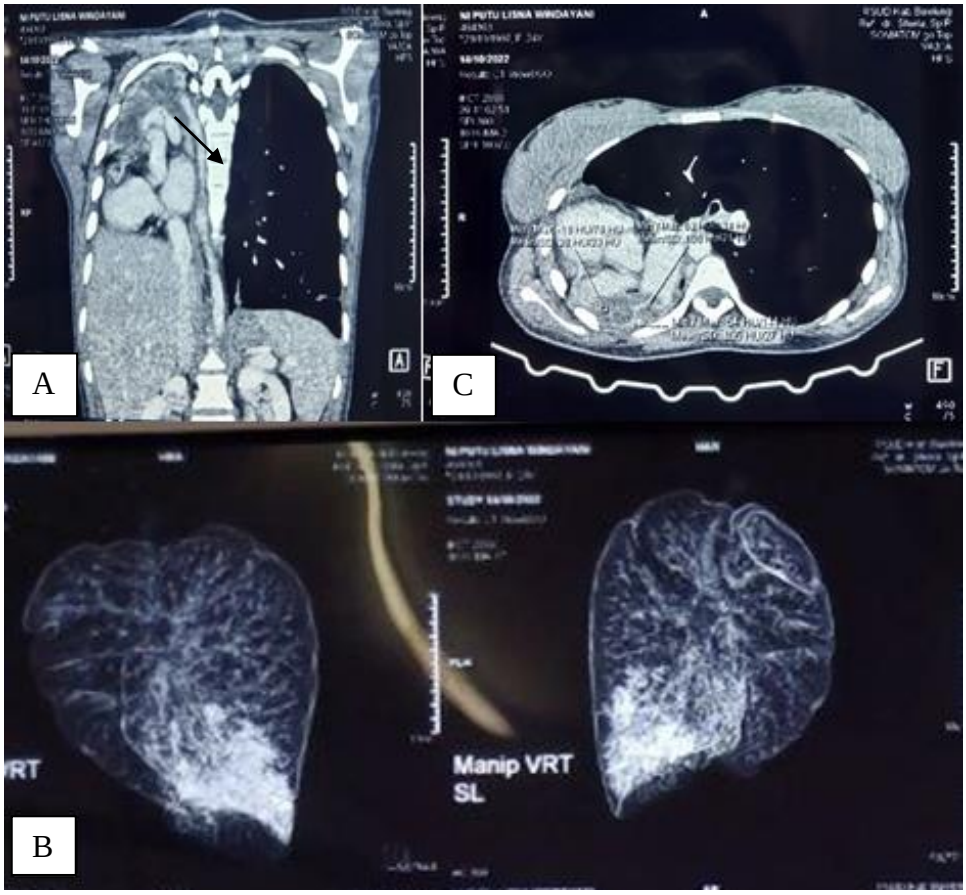

Figure 2. A) Coronal CT scan image shows lung hypoplasia; B) Hyperinflation in the left lung and images of pulmonary agenesis and heart deviation; C) CT scan showed ground glass opacity in the periphery and posterior lung lobes, indicating signs of infection.

Developmental abnormalities in the skeletal, gastrointestinal, genitourinary, and cardiovascular systems may coexist with pulmonary hypoplasia. At birth, infants with congenital diaphragmatic hernias (CDH) exhibit a scaphoid abdomen and respiratory insufficiency. In addition to hernias, congenital kidney defects, neural tube defects, or heart abnormalities may also be present. Numerous distinctive physical manifestations are present at birth in cases of Potter syndrome. Hypoplastic lungs caused by oligohydramnios coexist with the non-renal characteristics of Potter syndrome, such as flexion contractures, huge floppy ears, flat nose, spade-like hands, and facial deformities.[2,14]

In this case, the patient was diagnosed with suspected pulmonary agenesis accidentally. The diagnosis was made when the patient was 26 years old when she was pregnant with her second child. She was admitted to the hospital with shortness of breath. A chest X-ray was performed, and pulmonary agenesis with secondary lung infection was suspected. The diagnosis was confirmed using a CT scan, which revealed pneumonia, hypoplasia of the right lung with volume loss of the right hemithorax, causing a mediastinal shift, withdrawal of the right side of the liver and diaphragm, and hyperinflation of the left lung.

The underlying etiology of pulmonary hypoplasia, in this case, remains unknown. Lung hypoplasia can result from various factors, including genetics, environmental influences, maternal factors, and antenatal nutritional factors. The patient is the fifth of six children, and her mother had dietary deficiencies during pregnancy due to low socioeconomic status. However, nutrition is not the only factor. Genetics, environmental, and maternal factors may also contribute, though their involvement in this patient is unclear.[15]

Radiographic examination remains the primary method for identifying developmental lung abnormalities. Thoracic asymmetry without a history of trauma or surgery typically raises suspicion of lung anomalies. Other indicators include hyperlucency on hemithorax, focal cystic or solid pulmonary or mediastinal masses, and relevant clinical presentations.[15]

Radiological examination is one of the main modalities for confirming lung agenesis. Radiological examinations such as CT scans and chest X-rays can see lung abnormalities. CT scan images can show pulmonary hypoplasia and the presence or absence of main bronchial branches. Meanwhile, a chest X-ray can show a radiopaque image of the hemithorax

experiencing agenesis or hypoplasia, ipsilateral mediastinal shift, and compensatory hyperinflation in normal lungs. Moreover, pneumothorax or pneumomediastinum can occur if there are complications.[16] In this case, a chest X-ray revealed a tracheal deviation to the right, indicating lung volume loss, a finding also seen in conditions like fibrosis, atelectasis, or lung collapse. The CT scan confirmed the presence of lung agenesis in this patient, which was the absence of the right main bronchus and hypoplasia of the right lung.[17]

Supporting examinations, such as laboratory tests for serum creatinine, blood urea nitrogen, and electrolytes, are used to evaluate oligohydramnios. An electrocardiogram (ECG) is performed to detect dextrocardia and dextroversion. If present, all waves in Lead-I are inverted, there is a positive QRS complex in aVR, and there is a right axis deviation. Congenital heart defects can be ruled out via two-dimensional echocardiography (2D Echo). Pulmonary function testing in late childhood or adulthood reveals reduced diffusion capacity due to restrictive or obstructive lung abnormalities.[17]

Prenatal ultrasonography (USG) can predict pulmonary hypoplasia development by assessing factors such as lung area, the lung-to-chest area ratio, the thorax-to-abdomen circumference ratio, and lung volume. Three-dimensional USG is particularly useful for this.[17] USG can also detect masses in the thorax and abdomen, diaphragmatic hernia, pleural effusion, renal dysplasia, renal agenesis, oligohydramnios, renal cysts, renal obstruction, and other congenital abnormalities associated with pulmonary.[17]

The following conditions are included in the differential diagnosis for unilateral low lung volume on thoracic imaging: (1) Scimitar syndrome, characterized by hypoplasia of the right lung with anomalous venous drainage of the right lung to the inferior vena cava; (2) Congenital pulmonary airway malformation, characterized by cystic structure arising from the trachea or bronchi with mediastinal shift to the opposite side; (3) Bronchopulmonary sequestration, characterized by the absence of connection of the sequestrated segment to the tracheobronchial tree; (4) Congenital lobar emphysema, characterized by hyperinflation of the involved pulmonary lobe with mediastinal shift to the affected side; (5) Swyer-James syndrome, also known as Macleod syndrome, characterized by hyperlucent lung caused by post-infectious bronchiolitis; and (6) Persistent pulmonary hypertension of the newborn (PPHN).[18]

There is no specific treatment for asymptomatic lung hypoplasia. Management focuses on alleviating symptoms. Survivors of pulmonary hypoplasia often experience chronic lung conditions. Recurrent infections are treated with antibiotics. Bronchodilators for symptoms of shortness of breath and obstruction-related, chest physiotherapy, vaccine prophylaxis, and treatment of bronchiectasis can be surgically resected.[16]

Antenatal management involves multidisciplinary care. In the antenatal period, management of lung hypoplasia starts with the prevention of preterm labor. Before 24 weeks of gestation, corticosteroids are administered to promote fetal lung maturation. Amnio-patch procedures, involving the intraamniotic injection of platelets and cryoprecipitate, can prevent oligohydramnios and preterm labor.[19]

Infants may need breathing support in the immediate postpartum period. This period should be followed by oxygen supplemental support in immediate response. This can be supplemental oxygen for mechanical ventilation and extracorporeal membrane oxygenation.[19]

After birth, a pediatric pulmonologist should monitor individuals with lung agenesis. Therefore, the necessary diagnostic procedures can be performed and regularly followed. Close patient monitoring is required if early surgery is not performed during infancy. As previously mentioned, certain cystic lung abnormalities can resolve on their own over several months or years. On postnatal chest CT, newborns who have been referred for a cystic lesion seen on prenatal USG may show complete clearance. Furthermore, patients treated conservatively may require surgery for recurrent respiratory infections or pneumonia.[20]

Interdisciplinary fields are required to provide optimal lung agenesis care and treatment. For CDH, complementary and alternative medicine (CAM), or any other lesion needing surgery, consult a pediatric surgeon. Furthermore, speak with a pediatric surgeon in situations involving pulmonary hypertension or respiratory failure necessitating extracorporeal membrane oxygenation (ECMO). If the origin of the pulmonary hypoplasia is a renal obstructive, cystic, or agentic disease, then a nephrologist and a urologist are required. If the patient has an abnormal pulmonary venous connection or another causal or concomitant heart defect, a cardiologist and cardiothoracic surgeon may be involved. In addition, if the patient has a congenital neuromuscular disorder, the patient should be consulted with a neurologist.[20]

The prognosis for pulmonary hypoplasia is generally poor, with approximately 70% of causes resulting in perinatal death. However, those who survive into adulthood may experience various complications due to pulmonary hypoplasia. Complications that may occur are recurrent lung infections, shortness of breath, limited activity capacity, or chronic obstructive disease. This complication also happened in the patient of this

study, where the patient experienced pneumonia accompanied by pulmonary edema. Moreover, the patient also often experienced recurrent respiratory infections and activity limitations. The patient also experienced symptoms of chronic lung disease resulting from recurrent infections or sputum retention due to lung hypoplasia. Diseases related to pulmonary obstruction are also indicated by pulmonary function test results, which show obstruction and restriction.[20]

Patients with pulmonary hypoplasia require long-term follow-up and care to monitor for any abnormalities, particularly related to the initial lesion. To approach this patient, pulmonologists, nephrologists, pediatricians, cardiovascular surgeons, and intensivists must join a multi-disciplinary team. The caregiver and mother should have been fully educated as early as possible about prenatal conditions, especially nutrition, complications, prognosis, and decision-making.[21]

The prognosis for unilateral pulmonary hypoplasia is associated with nutritional, musculoskeletal, gastrointestinal, or neurological comorbidities involved. Chronic lung conditions such as low exercise capacity and higher susceptibility to infection are common in infants who survive until adulthood.[21]

Patients with unilateral pulmonary hypoplasia may undergo normal growth and development without associated lesions. The underlying cause of secondary hypoplasia may involve a wide variety of phenotypes. Mortality can rise to 50% in CDH cases during the perinatal period.

Other complications frequently associated with pulmonary hypoplasia include pneumothorax (spontaneous or secondary to mechanical ventilation), acute respiratory failure, persistent pulmonary hypertension, and tracheomalacia, which are common complications of pulmonary hypoplasia in the neonatal period. Chronic lung disease, growth retardation, low exercise capacity, recurrent respiratory infections, and chest wall deformity like scoliosis are the long-term complications of pulmonary hypoplasia in adults.[21]

CONCLUSION

Lung agenesis is a rare condition, and finding cases in adults is rare because most cases have a high mortality rate in the early years of life. In this case, unilateral pulmonary agenesis is found asymptomatic until diagnosed when symptoms and complications appear in adulthood. Radiological examinations, such as a CT scan and chest X-rays, are essential for confirming a diagnosis of pulmonary agenesis. There is no specific treatment for cases of adult lung agenesis. Management focuses on addressing the symptoms that arise.

Consent

Written informed consent was obtained from the patient.

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Conflict of Interest

The authors declared there is no conflict of interest.

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Authors' Contributions

Conception: MYK, SGD. Data collection: MYK. Writing the manuscript: MYK, LPFS. Review and revision: SGD, LPFS, GNRS. All authors contributed and approved the final version of the manuscript.

REFERENCES

1. Cherian SV, Kumar A, Ocazionez D, *et al*. Developmental Lung Anomalies in Adults: A Pictorial Review. *Respir Med* 2019; 155: 86–96. [PubMed]
2. Tisekar OR, AK AK. Hypoplastic Lung Disease. Treasure Island (FL), 2024. [PubMed]
3. Parry AH, Raheem M, Ismail H, *et al*. Late Presentation of Unilateral Lung Agenesis in Adulthood. *Egypt J Radiol Nucl Med* 2021; 52: 153. [Springer]
4. Vincent M, Karolak JA, Deutsch G, *et al*. Clinical, Histopathological, and Molecular Diagnostics in Lethal Lung Developmental Disorders. *Am J Respir Crit Care Med* 2019; 200: 1093–1101. [PubMed]
5. Pimenta DA, Aguiar FL, Fernandes BC, *et al*. Late Diagnosis of Pulmonary Agenesis. *BMJ Case Rep*; 14. Epub ahead of print October 2021. [PubMed]
6. Hayati N, Susyanto M. *Lung Agenesis: An Embryological Perspective*. 2019. Epub ahead of print 1 January 2019. [Proceeding]
7. Bush A, Chitty L, Harcourt J, *et al*. Congenital Lung Disease. In: Wilmott RW, Deterding R, Li A, *et al*. (eds). Philadelphia: Elsevier, pp. 289-337.e8. 2019. [ScienceDirect]
8. Khankan H. Pulmonary Agenesis Type 3 (Hypoplasia) - A Report of Two Cases in Children. *Acta Sci Paediatr*; 2. Epub ahead of print 10 July 2019. [ResearchGate]
9. Kunisaki SM. Narrative Review of Congenital Lung Lesions. *Transl Pediatr* 2021; 10: 1418–1431. [PubMed]
10. Kumbasar U, Uysal S, Doğan R. Congenital Pulmonary Malformations. *Turk Gogus Kalp Damar Cerrahisi Derg* 2024; 32: S60–S72. [PubMed]
11. Durhan G, Duzgun SA, Akpınar MG, *et al*. Imaging of Congenital Lung Diseases Presenting in the Adulthood: A Pictorial Review. *Insights Imaging* 2021; 12: 153. [PubMed]

12. Caldeira I, Fernandes-Silva H, Machado-Costa D, *et al*. Developmental Pathways Underlying Lung Development and Congenital Lung Disorders. *Cells*; 10. Epub ahead of print November 2021. [PubMed]
13. Rehman S, Bacha D. Embryology, Pulmonary. Treasure Island (FL), 2024. [PubMed]
14. Alwan A, Mohammoud S, Assefa AZ. Incidental Pulmonary Agenesis with Multiple Associated Anomalies: A Case Report. *Radiology Case Reports* 2023; 18: 3724–3728. [PubMed]
15. Weber J, Sati SK, Karody VR. Unilateral Lung Agenesis: A Case Series and Review of Literature. *AJP Reports* 2023; 13: e40–e43. [PubMed]
16. Speier R, Cotten CM. Pulmonary Hypoplasia BT - Manual of Neonatal Respiratory Care. In: Donn SM, Mammel MC, van Kaam AHLC (eds). Cham: Springer International Publishing, pp. 699–703. 2022. [Springer]
17. Avena-Zampieri CL, Hutter J, Rutherford M, *et al*. Assessment of the Fetal Lungs in Utero. *Am J Obstet Gynecol MFM* 2022; 4: 100693. [PubMed]
18. Mamat TAR, Sayuti KA, Nadarajan C, *et al*. Unilateral Opaque Chest Radiograph in Paediatrics: A Case Series. *SA Journal of Radiology* 2021; 25: 2164. [PubMed]
19. Hallman M, Ronkainen E, Saarela TV, *et al*. Management Practices during Perinatal Respiratory Transition of Very Premature Infants. *Front Pediatr* 2022; 10: 862038. [PubMed]
20. Kumar MK, Kalyana H, Yogaraj S. Congenital Primary Right Lung Agenesis in A Child – MDCT Imaging Features. *Curr Trends Clin Med Imaging* 2019; 2: 81–85. [Journal]
21. O'Hare EM, Jelin AC, Miller JL, *et al*. Amnioinfusions to Treat Early Onset Anhydramnios Caused by Renal Anomalies: Background and Rationale for the Renal Anhydramnios Fetal Therapy Trial. *Fetal Diagn Ther* 2019; 45: 365–372. [PubMed]