Agenesis of the Lung
Report of Four Patients with Unusual Anomalies

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Four patients had pulmonary agenesis. All were symptomatic in infancy. In three, symptoms improved during two to six years of follow-up. One, who died at one month, had a unique combination of agenesis of the right upper and middle lobes and a hypoplastic right lower lobe supplied by systemic arteries from below the diaphragm, total anomalous pulmonary venous drainage to the left superior vena cava, tricuspid regurgitation with severe right atrial dilatation, patent ductus arteriosus, and reduplication of the right thumb. Abnormalities of the thumb were encountered in three patients. Parental consanguinity in all four patients suggests an autosomal recessive mode of inheritance. Cardiac catheterization and angiography are essential procedures for diagnosis and elucidation of the anatomic abnormalities and identification of associated cardiac defects.

Agenesis of the lung is a rare developmental defect in which there is complete absence or hypoplasia of one or both lungs.1-11 The majority of reported cases had associated congenital anomalies involving the cardiovascular, musculoskeletal, or gastrointestinal systems. Infrequently there was involvement of the genitourinary or central nervous systems. The incidence of this condition is not known. The report of four patients among 114,569 admissions1 suggests a prevalence of 0.0034 percent among hospital admissions. In a six-year period, four patients with this condition were found among 41,403 admissions to the King Faisal Specialist Hospital and Research Centre, which would represent a prevalence of 0.097 percent, or about one in 10,000 admissions, or 0.67 percent of the 596 patients who underwent cardiac catheterization. Certainly, it is not possible to calculate the incidence of rare anomalies with accuracy, but the data do suggest that this anomaly may be more frequently encountered in Saudi Arabia.

This report describes the four infants (Tables 1 and 2; Fig 1 to 4). All four had associated atrial septal defects (ASD), and three had other congenital heart defects. One had a unique combination of defects including total anomalous pulmonary venous drainage of the left lung into the left superior vena cava, tricuspid regurgitation with marked dilatation of the right atrium, a large ASD, a patent ductus arteriosus, and reduplication of the right thumb. Three of the four patients had ipsilateral abnormalities of the thumbs.

DISCUSSION

Ipsilateral malformation of the thumb was a striking feature in three of these four patients (Table 1), which could serve as an alerting feature to pulmonary agenesis, especially in an infant with respiratory manifestations. Each of these radial defects was different. They included a triphalangeal, angulated thumb, in which the middle phalanx was hypoplastic; a preaxial polydactyly; and an abnormal thumb with a short first metacarpal. Ipsilateral hemivertebrae also were seen in two patients. Thumb abnormalities, including duplication and digital positioning, have been infrequently reported in previous patients.2,10,11 Others have been reported with malformation of ulna, carpus, or absence of the radius or first phalanx.10-12 Vertebral and costal defects have been observed.10,11

The coexistence of these malformations suggests an interference with embryologic development in the fourth week of fetal life. The coexistence of total anomalous pulmonary venous drainage seen in one of these patients has been previously observed.1,11 The primitive lung buds are forming at the fourth week of embryonic life11,12 when the pulmonary venous system is changing from its early association with the systemic venous circulation to make connection with the left atrium. An insult occurring at this time along the laryngotracheal groove on the ventral surface of the foregut could interrupt lung bud development and interfere with the creation of normal pulmonary venous return. The close parental consanguinity in all four patients suggests that the embryologic insult was genetically determined and autosomally recessive. Consanguinity has previously been reported.4 Three of the four patients were girls, but there appears to be no sex predilection in this condition.14 Two of the four patients were delivered by cesarean section because of fetal distress.

It is possible that several syndromes lead to pulmonary agenesis. The patient reported by Say et al.15 had ears and facial characteristics similar to our case 3. Both patients had flexion contractures and no abnor-
<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Presentation</th>
<th>Sex</th>
<th>Initial Respiratory Symptoms</th>
<th>C-section for Fetal Distress</th>
<th>Parental Consanguinity</th>
<th>Admission Physical Examination</th>
<th>Location of Agenesis</th>
<th>ASD</th>
<th>PA</th>
<th>Systemic Blood Supply</th>
<th>Other</th>
<th>Systolic Ejection Murmur</th>
<th>Both Lungs</th>
<th>Follow-up Respiratory Symptoms</th>
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<tbody>
<tr>
<td>1</td>
<td>2 wk</td>
<td>Frequent attacks of respiratory infection and wheezing</td>
<td>F</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>RUL &amp; RML</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td></td>
<td>+</td>
<td>-</td>
<td>3 Phalanges Hypoplastic Middle Hypoplastic Middle Phalanx</td>
</tr>
<tr>
<td>2</td>
<td>24 hr</td>
<td>Dyspnea, tachypnea, cyanosis</td>
<td>F</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>RUL &amp; RML</td>
<td>+</td>
<td>+</td>
<td>+ to RLL</td>
<td></td>
<td>+</td>
<td>+</td>
<td>Replication thumb</td>
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<tr>
<td>3</td>
<td>3 wk</td>
<td>Dyspnea, cyanosis, irritability</td>
<td>M</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>Left</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td></td>
<td>+</td>
<td>+</td>
<td>Flexion contractures of limbs</td>
</tr>
<tr>
<td>4</td>
<td>2 wk</td>
<td>Tachypnea, dyspnea, cyanosis when crying</td>
<td>F</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>Left</td>
<td>+</td>
<td>+</td>
<td>+ Anomalous Interventricular septum</td>
<td></td>
<td>+ Abnormal proximally placed thumb, dimple or depression of metacarpophalangeal joint, flexion contracture at second interphalangeal joint preventing full extension of the thumb Spina bifida</td>
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</table>

*Abbreviations: +, present; and -, absent; TAPVD, total anomalous pulmonary venous drainage; TR, tricuspid regurgitation.*
Table 2—Hemodynamic and Other Data in Four Patients With Pulmonary Agenesis*

<table>
<thead>
<tr>
<th>Patient</th>
<th>PQ/SQ</th>
<th>P_{O_2}, mm/Hg</th>
<th>P_{CO_2}, mm/Hg</th>
<th>PA Pressures, mm/Hg (S/D/M)</th>
<th>ECG</th>
<th>Bronchography</th>
<th>Pulmonary Scan</th>
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<tr>
<td>1</td>
<td>1.2/1</td>
<td>56†</td>
<td>87</td>
<td>34</td>
<td>30/12/19</td>
<td>Deep Q, leads 2, 3, aVF</td>
<td>No perfusion RUL &amp; RML; decreased perfusion RLL</td>
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<tr>
<td>2</td>
<td>4.2/1</td>
<td>50</td>
<td>84</td>
<td>41</td>
<td>117/86/101†</td>
<td>RAD, RVH</td>
<td>—</td>
</tr>
<tr>
<td>3</td>
<td>1.2/1</td>
<td>39</td>
<td>77</td>
<td>48</td>
<td>60/5/26†</td>
<td>RVH</td>
<td>Absent left bronchus</td>
</tr>
<tr>
<td>4</td>
<td>1.3/1</td>
<td>55</td>
<td>86</td>
<td>40</td>
<td>38/8/16</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

*PQ/SQ = pulmonary flow/systemic flow; RUL = right upper lobe; RML = right middle lobe; RLL = right lower lobe; S = systolic; D = diastolic; M = mean; PA = pulmonary artery; RAD = right axis deviation; and RVH = right ventricular hypertrophy.
†This slight oxygen desaturation was noted early in infancy in association with respiratory difficulties. Repeat arterial P_{O_2} was normal later.
‡Equal to systemic pressure.

Anomalies of the thumbs. This combination of malformations has been called the ankylosis, facial anomalies, pulmonary hypoplasia syndrome.

The association of pulmonary agenesis with total anomalous pulmonary drainage into the superior vena cava, tricuspid regurgitation with marked dilatation of the right atrium, patent ductus arteriosus, and preaxial polydactyly, or reduplicated thumbs, has not previously been reported. Total anomalous pulmonary drainage into the azygos vein or the right atrium has been described. In case 1, a hypoplastic right lower lobe was supplied by an anomalous pulmonary artery branch arising from the left pulmonary artery. A similar situation has been observed on the opposite side in a patient in whom a small branch from the right pulmonary artery supplied the hypoplastic remaining lung on the side of the agenesis on the left.14 Pulmonary agenesis has been categorized according to the classification of Schneider and Schwalbe.18 In group 1 the entire lung and its pulmonary artery are

![Figure 1. Case 1: A, Malformed right thumb angulated in an ulnar direction, and its roentgenogram to show the three phalanges, of which the middle phalanx was hypoplastic. B, Chest roentgenogram illustrates a homogeneous opacity in the area of the right middle lobe (RML) and upper lobe (RUL), with mediastinal shift and herniation of the left upper lobe (LUL) toward the right hemithorax. C, Bronchogram documented the absence of the RUL and RML, the dysplastic changes in the right lower lobe (RLL), and the tracheal shift to the right hemithorax. D, Pulmonary angiogram shows total absence of the right pulmonary artery (open arrow). The RLL was supplied by a small arterial branch (closed arrow) originating from the normal-sized left pulmonary artery. (Roentgenogram of the chest after 4 years showed hyperexpansion of the RLL to occupy almost the entire right chest.)](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21462/)
FIGURE 2. Case 2: A, Right hand illustrating the reduplication of thumb (right axial polydactyly). B, Roentgenogram of the chest illustrating the homogeneous opacity of a major portion of the right chest. There was a marked shift to the right of the mediastinum and trachea and a herniation of the LUL across the mediastinum into the right hemithorax (arrow). The RLL appeared poorly aerated and hypoplastic. The left hemi-diaphragm was flattened, whereas the right was elevated. C, Right ventricular (RV) angiogram in the AP projection revealing a dilated main pulmonary artery (PA) and left PA. The right PA was absent (open arrow). There was severe tricuspid regurgitation; its degree was much greater than expected from catheter placement. Further, the right atrium (RA) was markedly dilated (small arrow), and following RV injection there was massive filling of the IVC. D, During levophase, anomalous left pulmonary veins (APV) were seen to be confluent and to drain into the innominate vein (curved arrow), then to the left superior vena cava (SVC). (A left ventricular angiogram showed that the descending aorta gave rise to the systemic arteries below the diaphragm that supplied the hypoplastic RLL.)

FIGURE 3. Case 3: A, Chest roentgenogram showing total opacity of the left hemithorax; the right lung was hyperexpanded and the ribs separated, and there was a marked herniation of the right lung across the mediastinum (arrow). Mediastinal structures were shifted into the homogeneous opacity of the left hemithorax. The lower arrows point to the hemivertebrae at T₉ and L₁. There was secondary scoliosis. There were 11 ribs on the left and 12 on the right. B, Pulmonary (PA) angiogram in the left anterior projection showing absence of the left pulmonary artery. C, Massive pneumothorax and pneumomediastinum, a complication of mechanical ventilation during a period of respiratory distress the first year. D, Three-year follow-up roentgenogram of the chest showing less herniation of the right lung, but more flattening of the right diaphragm.
absent. In group 2 the lung and pulmonary artery are absent, but there is a rudimentary bronchus coming off the trachea. In group 3 there is hypoplastic lung and a fully formed bronchus. This classification is most useful for autopsy purposes or for cataloguing the results of bronchography, but considerably more data are now regularly obtained with angiography.14 Groups 1 and 2 are, for practical and developmental purposes, the same; there is no lung tissue, and the ipsilateral pulmonary artery is always absent, and the main pulmonary artery sends its only branch to the existing lung. It appears that the existence of embryonic pulmonary tissue is important for the growth and vascularization of the pulmonary artery.15 When angiography demonstrates pulmonary artery or systemic arterial blood supply, some lung must exist. Supply to the hypoplastic lung could be from a small branch directly from the pulmonary artery, or from the contralateral pulmonary artery, as in case 1, or from the systemic circulation, as in case 2. Pulmonary and left ventricular or aortic angiography provides information of value in management. A complete absence of the pulmonary artery is consistent with the presence of a normal-sized lung on that side if there is ipsilateral bronchial supply, but in the absence of a systemic arterial supply, if there is no pulmonary artery, there is no lung on that side and thus never an indication for pulmonary surgery.

On the other hand, hypoplastic lung, when present, is subject to atelectasis and infection. Two patients in this series had been examined by bronchography, but we do not believe that this procedure is indicated, and it may carry substantial morbidity. Bronchoscopy may be indicated in a patient with repeated infections in a hypoplastic lung who may be a candidate for surgery. Cardiac catheterization and angiography are also required to evaluate the presence and nature of associated congenital heart disease. If surgery is required for correction of congenital heart disease, it may be prudent to resect the hypoplastic lung, especially when it is sequestered and has a systemic blood supply. Thus, a more useful clinical classification based on angiographic data would be to divide the patients first into two groups: one in which there is total absence of pulmonary parenchyma and the ipsilateral pulmonary artery in the absence of any systemic arterial supply; and the other in which there is hypoplastic pulmonary tissue. This group can be subdivided into two subgroups: one in which the affected lung receives its blood supply from the pulmonary artery, and the other in which the affected lung is sequestered and receives a large amount of systemic arterial blood supply. Pneumonectomy or lobectomy is required in the first subgroup only when recurrent respiratory infection results from abnormal bronchopulmonary tissues. Surgery may be indicated in the second group when the systemic blood flow causes congestive heart failure or recurrent respiratory infections. Our patients 3 and 4

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**FIGURE 4.** Case 4: A, Chest roentgenogram showing a homogeneous opacity of the left chest, a hyperinflated right lung, and a mediastinal shift, as well as herniation of the right lung into the left hemithorax (solid arrows). The heart shadow was not well delineated because of the opacity on the left. Open arrows point toward the hemivertebra and the incomplete vertebral fusion. B, Pulmonary angiogram showing the absence of the left PA (open arrow). C, Left ventricular (LV) angiogram showing the aneurysm of the muscular interventricular septum (arrows). D, Hand roentgenogram showing the short first metacarpal.
fell into the first group (group 1 or 2 of Schneider and Schwalbe) according to this classification, although they presented with respiratory symptoms, both improved significantly during the two- and three-year periods of observation and growth. Patients 1 and 2 would fall into the second group, or into class 3 of Schneider and Schwalbe. Case 1 would fit into the first subgroup in which one would usually predict that surgery would not be required. The patient was, in fact, asymptomatic except for a single respiratory infection throughout a six-year period of follow-up. Case 2, on the other hand, fell into the second subgroup, but she did not survive long enough to know whether surgery would have been required for removal of the right lower lobe.

Patients with pulmonary agenesis may be asymptomatic, and the diagnosis may not be made until adulthood. However, there are usually some pulmonary manifestations, as in all of our patients. The cyanosis and respiratory difficulties that were observed in early infancy in cases 1 and 4 improved, and the P\textsubscript{a}O\textsubscript{2} returned toward normal during the two- to six-year period of growth. This may reflect a decrease in the degree of tracheobronchial shift (case 1), intrapulmonary shunting, or a drop in pulmonary hypertension, causing less right-to-left shunting at the atrial level (case 4).

In patients with complete pulmonary agenesis and absent pulmonary artery in whom the prognosis for further pulmonary manifestations should be good, acute respiratory symptoms could result from extrinsic compression of the airways by enlarged pulmonary arteries or cardiac chamber or from pulmonary vascular engorgement and edema. Pulmonary hypertension and congestive heart failure can result from changes in the pulmonary arteriolar system in the contralateral lung. Tracheal compression has been reported to be caused by a normal but deviated aorta associated with right-sided pulmonary agenesis.

Right-sided pulmonary agenesis has been thought to have a prognosis graver than that of the left, with death occurring earlier and with greater frequency. This would be consistent with our case 2, who died early. A worse prognosis for the right-sided defect could be due to a higher incidence of associated cardiac abnormalities or to the greater mediastinal shift produced by right-sided agenesis, leading to more significant distortion of the bronchial and vascular structures. Left-sided agenesis has been reported to occur more frequently than right.

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REFERENCES
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