Unilateral Absence of a Pulmonary Artery*

Data from Cardiopulmonary Exercise Testing

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A case of congenital, unilateral absence of a left pulmonary artery is described in a patient presenting with exertional dyspnea. Data from cardiopulmonary exercise testing suggest that the mechanism of dyspnea is secondary to a paradoxical elevation of the physiologic dead space to tidal volume ratio (Vd/Vt) during exercise.

(Chest 1993; 103:293-95)

Unilateral absence of a pulmonary artery (UAPA) or pulmonary artery agenesis is a rare congenital malformation first reported by Faerentzel in 1868. Initial angiographic findings in the syndrome were described in 1962 by Pool et al.1 Although these patients may remain asymptomatic, many present with dyspnea.2,3 Mechanisms proposed to explain the dyspnea include cardiac shunting, pulmonary vascular overperfusion with edema, an increase in resting and/or exercise physiologic dead space, or pulmonary hypertension.1,4 However, little information on the etiology of exercise limitation and dyspnea is available. We report a patient with UAPA presenting with dyspnea and evaluated by right-heart catheterization and cardiopulmonary exercise testing.

CASE REPORT

A 23-year-old man was admitted to the hospital for evaluation of increasing shortness of breath. The patient described the onset of exertional dyspnea at age 12 years and at presentation was unable to run 2 miles within the US Army age-standards despite appropriate training efforts. Medical history was unremarkable, and the patient denied tobacco use.

Physical examination at the time of hospital admission revealed a muscular man with a temperature of 37.1°C, pulse rate of 67/min, blood pressure of 126/70 mm Hg, respiratory rate of 14/min, weight of 81.6 kg, and height of 172.7 cm. Chest examination revealed diminished breath sounds at the left base. Results of cardiovascular examination were normal. Hospital admission chemistry profile, complete blood cell count, ECG, and room air arterial blood gas values were normal. An inspiratory chest roentgenogram revealed right lung hyperinflation and a right-sided aortic arch (Fig 1). An expiratory roentgenogram showed proportional emptying of both lungs.

Pulmonary function values revealed FVC of 4.54 L (95 percent predicted), FEV, of 2.95 L (71 percent), FEV/FVC of 65 percent, unchanged following bronchodilator administration with normal lung volumes and diffusing capacity of carbon monoxide. An echocardiogram and flexible fiberoptic bronchoscopy were also normal. Contrast-enhanced chest computed tomographic (CT) scan confirmed mediastinal herniation and the right-sided aortic arch with no left pulmonary artery visualized. A 133Xe/99mTc ventilation-perfusion scan showed mild reduction in left lung ventilation with absent left perfusion (Fig 2). Pulmonary angiography demonstrated a large right pulmonary arterial trunk with normal branching and complete absence of the left main pulmonary artery.

The patient underwent right-heart catheterization. Central venous pressure, pulmonary capillary wedge pressure, and mean pulmonary artery pressure at rest and with exercise at 50 W (Table 1) were within normal limits for young men previously exercised in our laboratory.6 There was no increase in oxygen saturation from the vena cava to the pulmonary artery to suggest a left to right shunt.

Finally, a full cardiopulmonary exercise test (CPX) with bicycle ergometry and exhaled gas analysis (SensorMedics MMC 4400 tc, SensorsMedics Corporation, Anaheim, Calif) was obtained, using an incremental protocol beginning with 0 W and increasing the workload by 25 W/min. An arterial blood gas determination was obtained at rest and at maximum exercise to calculate physiologic dead space to tidal volume ratio (Vd/Vt) using the Bohr equation, with correction for apparatus dead space. The patient exercised 9.0 min to a maximum workload of 200 W (76 percent predicted). The maximum VO, was 2.275 L/min (65.7 percent predicted) and the ventilatory anaerobic threshold was 1.25 L/min (36.1 percent of the maximum predicted VO). The resting VO/Vt of 30.0 percent was normal; however, a paradoxic increase to 31.3 percent occurred with exercise. Other measured and calculated parameters are listed in Table 2.6

DISCUSSION

Congenital UAPA is a rare syndrome; patients often present with an abnormal chest roentgenogram in the absence of clinical findings.7 In the case described, the patient presented with exertional dyspnea with studies confirming left UAPA associated with a right-sided aortic arch. This represents a developmental abnormality of the left fourth and proximal sixth aortic arches.2 Although

FIGURE 1. Inspiratory chest roentgenogram showing mediastinal herniation with displaced anterior junction line (small arrowheads) and right-sided aortic arch (large arrowhead).
patients with thromboembolic disease or pulmonary artery stenosis may present with similar symptoms and ventilation-perfusion abnormalities, the lack of an acute medical event along with the roentgenographic and angiographic findings were considered conclusive for UAPA.¹

Table 1 — Cardiac Catheterization*  

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Rest</th>
<th>Exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAP, mm Hg</td>
<td>18.3 (&lt;19.3)</td>
<td>25 (&lt;31.8)</td>
</tr>
<tr>
<td>CVP, mm Hg</td>
<td>7 (&lt;9.0)</td>
<td>6 (&lt;11.6)</td>
</tr>
<tr>
<td>PCWP, mm Hg</td>
<td>10 (&lt;13.6)</td>
<td>7 (&lt;16.4)</td>
</tr>
<tr>
<td>PAsat, %</td>
<td>78.2</td>
<td>45.9</td>
</tr>
</tbody>
</table>

*PAP = mean pulmonary artery pressure; CVP = central venous pressure; PCWP = mean pulmonary capillary wedge pressure; and PAsat = percent hemoglobin saturation in pulmonary arterial blood. The figures in parentheses are the upper limit of the 95 percent confidence intervals for 13 normal young men studied in our laboratory.⁸

Figure 2. ¹³³Xe–¹⁵O₂ ventilation-perfusion scan, posterior views. (a) Upper: mild reduction in left lung ventilation; (b) Lower: absent left lung perfusion.

Despite his vascular anomalies and reduced ventilatory anaerobic threshold, the patient did not appear to have a cardiac limitation given his normal heart rate reserve, echocardiogram, and findings at exercise right-heart catheterization. Instead, his limitation appeared to be ventilatory. The patient stopped secondary to dyspnea occurring at a reduced maximum VO₂ (66 percent predicted), maximum work rate (76 percent predicted), and maximum heart rate (81 percent predicted). However, his maximum exercise ventilation (VE) was greater than 80 percent of his calculated maximal voluntary ventilation (MVV) and therefore probably limited his ability to continue to exercise. This large ventilatory expenditure most likely is due to the rise in percentage of dead space ventilation (VD/VT) compared with the substantial reduction normally seen with exercise.

This paradoxic response of the VD/VT to exercise has not, to our knowledge, been demonstrated in patients with UAPA, but it has been described previously by Nadel et al.² in patients with other diseases. They reported normal resting and elevated exercise VD/VT ratios in four patients with chronic pulmonary vascular obstruction from fibromuscular hyperplasia or thromboemboli presenting with dyspnea. These patients were shown to have normal pulmonary vascular pressures. They proposed that the mechanism for this paradoxic response involves a compensatory reduction in ventilation to the nonperfused area of the lung at rest. However, with exercise, this autoregulation is reversed as deep breathing increases ventilation to the nonperfused alveoli. The result is an abnormally increased dead space ventilation compared with perfused alveolar ventilation reflected by an elevated VD/VT.

In our patient, evidence of ventilatory compensation with reduced left lung resting tidal volumes was demonstrated by right lung hyperinflation per chest roentgenogram and by decreased left lung radiosotope uptake with ¹³³Xe lung scanning. The VD/VT is normal at rest because the affected lung commonly receives collateral perfusion via the bronchial circulation or directly from vessels off the ascending or descending thoracic aorta. A substantial Pco₂ gradient exists between this systemic blood and alveoli allowing for a

Table 2 — Selected Cardiopulmonary Exercise Data*  

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Rest</th>
<th>Maximum Exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Workload, W</td>
<td>0</td>
<td>200 (76%)</td>
</tr>
<tr>
<td>HR, min⁻¹</td>
<td>67</td>
<td>160 (81%)</td>
</tr>
<tr>
<td>Blood pressure, mm Hg</td>
<td>140/90</td>
<td>200/96 (66%)</td>
</tr>
<tr>
<td>VO₂, L/min</td>
<td>0.300</td>
<td>2.275 (66%)</td>
</tr>
<tr>
<td>VE, L/min</td>
<td>10</td>
<td>91 (81%)†</td>
</tr>
<tr>
<td>RF, min⁻¹</td>
<td>15</td>
<td>39 (&lt;50)</td>
</tr>
<tr>
<td>ABG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pH</td>
<td>7.408</td>
<td>7.311</td>
</tr>
<tr>
<td>PaO₂</td>
<td>91.7</td>
<td>94.8</td>
</tr>
<tr>
<td>PaCO₂</td>
<td>41.9</td>
<td>41.8</td>
</tr>
<tr>
<td>SaO₂</td>
<td>97.0</td>
<td>96.6</td>
</tr>
<tr>
<td>VD/VT</td>
<td>30.0 (&lt;40)</td>
<td>31.1 (&lt;21)</td>
</tr>
</tbody>
</table>

*HR = heart rate; VO₂ = oxygen consumption; VE = expired minute ventilation; RF = respiratory frequency; and VO₂/VT = ratio of dead space to tidal volume ventilation. The figures in parentheses are the predicted or percent predicted values based on Wasserman et al.¹
†Percentage of calculated maximal voluntary ventilation (MVV = 40 × FEV₁).

Unilateral Absence of Pulmonary Artery (Brassard, Johnson)
contribution to gas exchange by the abnormal lung. However, with exercise, one would expect ventilation-perfusion matching to worsen. The unaffected lung will receive an increase in perfusion appropriate or high relative to the rise in ventilation as all of the right-sided cardiac output goes through the single pulmonary artery. The affected lung will also receive an increase in ventilation, but it is doubtful that perfusion will increase appropriately since it is supplied by the left-sided circulation and most of the augmented left-sided cardiac output goes to the exercising muscles. The net result of this would be an inappropriate reduction or rise in V̇o2/V̇t as was seen in our patient.

In summary, a patient with UAPA and dyspnea on exertion was studied. In the absence of associated cardiac disease or pulmonary hypertension, exercise limitation appeared to be due to increasing percent dead space ventilation.

REFERENCES
3 Sherrick DW, Owings WK, DuShane JW. Agnensis of a main branch of the pulmonary artery. AJR 1962; 87:917-28

Occupational Asthma in a Pesticides Manufacturing Worker

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A 34-year-old male chemical manufacturing worker had new onset of work-related asthma after several years of exposure to the fungicide, captafol. On specific bronchial challenge testing, he demonstrated a marked and persistent fall in FEV1. Cessation of exposure resulted in improved symptoms and pulmonary function. The delay in symptoms after several years of workplace exposure and the dual reaction demonstrated on specific bronchial challenge testing suggest sensitization to some component of technical-grade captafol, but an IgE response was not detected.

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Captafol (Difolatan) is a chlorinated thiocarboximide fungicide extensively used in the United States until the Environmental Protection Agency designated it as a "probable human carcinogen," and the sole US manufacturer cancelled its registration in 1987. Its manufacture and distribution in the United States was prohibited after May 1988, but use of existing stocks is allowed. Active suppliers of captafol include companies based in the United States, India, Italy, Taiwan, Brazil, the Netherlands, Germany, Canada, and Singapore.

There have been numerous reports of skin rashes associated with captafol manufacture and use14 and several authors have reported positive patch testing that they interpreted to represent allergic contact dermatitis.5-7 Captafol's respiratory effects are less well studied. Two unpublished epidemiologic studies in the US manufacturing plant where this patient worked both showed a significant prevalence of work-related respiratory tract symptoms. Eight cases of captafol-associated wheezing have also been reported.8,9

The captafol manufactured at this plant consists of respirable particles, 1.5 to 5.0 μm in diameter. The technical-grade product consists of 97 percent captafol, 0.5 percent dye, <0.5 percent solvents, and several captafol metabolites. Two of captafol's precursors, tetrahydrophthalic acid and maleic anhydride, have been documented to cause occupational asthma via immunologic mechanisms.4-7

CASE REPORT

A 34-year-old male chemical manufacturing worker was examined at the Occupational Health Clinic at San Francisco General Hospital because of recurrent attacks of chest tightness, wheezing, and shortness of breath for the prior three years. He was a nonsmoker with no personal history of asthma, hay fever, hives, or eczema. Twelve years before presentation, the patient started work without respiratory protection in the captafol bag room where there was visible dust in the air. (Three personal air samples in the bag room in 1986 exceeded the current threshold limit value of 0.1 mg/m3 set by the American Conference of Governmental Industrial Hygienists.) Within two years, he developed sneezing and rhinitis at work. He was then transferred to the captafol production line, during which time he had a facial splash of a precursor called 1,1,2,2-tetrachloroethylysufenyl chloride (TES) caused pleuritic chest pain followed by several weeks of morning sputum production.

Three years prior to presentation, the patient noted burning eyes, rhinitis, and rash on his wrists between his coveralls and his gloves precipitated by entering the bagroom. Three to 4 h after leaving the area, he would notice chest tightness followed by wheezing awakening him from sleep. During a two-week vacation, his chest symptoms disappeared, but recently they had begun to recur upon exercise.

Physical examination at presentation to the clinic revealed clear lungs and no skin rash. Pulmonary function testing included an FEV1 of 3.62 L (100 percent of predicted), with an FVC of 4.70 L (98 percent of predicted), and an FEV1/FVC ratio of 0.76. His forced expiratory flow-volume curve demonstrated decreased flow rates at low lung volumes. The concentration of methacholine that produced a 100 percent increase in airway resistance (SRaw) from baseline (PC100) was 0.7 mg methacholine per milliliter. (A value of 4 mg/ml is the lower limit of normal for PC100 in the laboratory where the test was performed.) After returning to intermittent