rapidly followed by the onset of a major inflammatory process in the oropharynx, esophagus, and stomach that translates into nausea, vomiting, abdominal pain, and diarrhea, and normally generates toxic hepatitis with centrilobular necrosis and myocarditis, occasionally with a reduced level of consciousness. Very rarely, spontaneous extra-alveolar air appears (pneumothorax, pneumomediastinum, pneumopericardium, subcutaneous emphysema), which has been ascribed to a direct provocation by the toxin of acute lung injury, with the formation of subpleural bullae followed by rupture.

We present a case of massive paraquat poisoning, with the peculiarity that the corrosive effects of the paraquat itself also caused injuries to the trachea and principal bronchi. Although there have been reports that the local corrosive effect of paraquat produces ulcerated lesions in the oropharynx, esophagus, and stomach, the tracheal injuries seen in the present patient have not previously been described. These injuries appeared on the trachea and bronchial tree and ruptured the posterior tracheal wall. They were directly caused by the caustic action of the toxin, probably after its aspiration. The effects at cell level, especially on tracheal epithelial cells, which have shown experimentally a greater sensitivity to paraquat, could be produced by the generation of very-reactive oxygen species, such as superoxide radicals. These radicals have deleterious effects on the cells by attacking the proteins and membranous organelles, inhibiting macromolecular synthesis, and enhancing lipid peroxidation.

The tracheal injuries contributed to the development of extra-alveolar air and to the demise of the patient. Although there has been no previous report of a similar injury, the Toronto Lung Transplant Group described a patient with acute paraquat poisoning who required a lung transplant, with death caused by complications derived from a trachea-innominate artery fistula. The fistula was initially described as a complication of the tracheotomy, although the deleterious effect of the paraquat could also have influenced the genesis of this tracheal injury. There is no efficacious treatment for paraquat poisoning in the clinical setting, but it has been experimentally demonstrated that a reduction in the intracellular nicotinamide adenine dinucleotide phosphate can protect the tracheal cells against paraquat poisoning, which suggests that future studies may show more satisfactory results.

REFERENCES


Severe Pectus Excavatum Associated With Cor Pulmonale and Chronic Respiratory Acidosis in a Young Woman*

Ravichandran Theerthakarai, MD; Walid El-Halees, MD; Seyed Jawadpoor, MD; and M. Anees Khan, MD, FCCP

Pectus excavatum has never been reported to cause hypercapnic respiratory failure. In this report, we describe the first such case in a young woman with severe pectus excavatum who presented with chronic respiratory acidosis, pulmonary hypertension, and chronic cor pulmonale. An extensive diagnostic workup failed to uncover any other cause of respiratory acidosis, which led us to conclude that the severe chest wall deformity and the resulting severe restrictive defect were responsible for the development of chronic respiratory acidosis and cor pulmonale.


Key words: alveolar hypoventilation; cor pulmonale; pectus excavatum; respiratory failure

Abbreviations: TLC = total lung capacity; VC = vital capacity

Unlike deformities of the spine, pectus excavatum rarely results in a measurable impairment of lung function and is said to have never produced hypoventilation and respiratory failure. A MEDLINE search failed to identify a report of a patient who had experienced respiratory failure attributed to pectus excavatum. Congestive cardiac failure also is said to be almost unheard of and has not been observed in extensive hemodynamic studies. Some patients may show a decreased diastolic filling of the right ventricle as a result of compression, but pulmonary arterial and pulmonary wedge pressures have been normal. We describe the case of a young woman with severe

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CHEST / 119 / 6 / JUNE, 2001 1957
pectus excavatum who presented with severe hypercapnic respiratory failure, pulmonary hypertension, and chronic cor pulmonale.

CASE REPORT

A 29-year-old Polish woman was admitted to St. Joseph’s Hospital and Medical Center because of increasing dyspnea of 4 months’ duration followed by the appearance of swelling of both feet of 3 days’ duration.

The patient had been well until 4 months prior to hospital admission when she started noticing dyspnea on moderate exertion such as walking for one block or climbing one flight of stairs. Symptoms worsened over the following months until she started experiencing shortness of breath even at rest. There was no history of protracted cough, sputum production, chest pain, or hemoptysis. A review of her physiologic systems was unremarkable except for easy fatigability during most of her adult life, which she ascribed to a weak constitution. Her history was devoid of incidences of pneumonia, tuberculosis, bronchial asthma, or hospitalization. She had resided in the United States for 8 years and had worked for a garment factory sewing buttons on dresses.

She described her development as normal during her childhood except for being rather frail, which kept her from participating in sports. Only around age 12 years did she become aware of the abnormal funnel-shaped appearance of her chest, which she thought was strikingly different from her friends. She described her siblings and other family members as being devoid of any such deformities.

A physical examination showed a very thinly built, but lively and intelligent, young woman in mild respiratory distress at rest with the following physical characteristics: weight, 33.6 kg; height, 163 cm; pulse, 102 beats/min; BP, 108/58 mm Hg; and respiratory rate, 24 breaths/min. An examination of the chest showed severe pectus excavatum of the entire anterior chest wall with a straight back and mild scoliosis of the thoracic spine. Jugular venous distention at a 45° angle and bilateral pitting pedal edema were noted. Breath sounds were diminished in the left lower lung field posteriorly without any adventitious sounds. Prominent left parasternal heave, enlarged cardiac dullness on percussion, loud P2, and a loud pansystolic murmur at the pulmonic area were noted on cardiac examination. Liver edge was palpable at 2 cm below the right costal margin. Hepatogenous reflux was positive. A neurologic examination failed to show any motor or sensory deficits, with normal deep tendon reflexes.

Laboratory data showed a hemoglobin level of 16.9 g/dL and a WBC count of 5.1 × 10³/μL with a normal differential cell count. Serum chemistry levels were within normal range, except for a serum HCO₃ level of 40 mmol/L, and the results of a urinalysis were within normal limits. Arterial blood gas studies on room air at rest showed the following: pH, 7.38; Paco₂, 70 mm Hg; PaO₂, 44 mm Hg; HCO₃, 42 mmol/L; and arterial oxygen saturation, 76% (alveolar-arterial oxygen gradient, 22 mm Hg). An ECG (Fig 1) showed sinus tachycardia with a rate of 116 beats/min, right-axis deviation, right atrial enlargement, and an rSR’ pattern in V₂ without ST-T segment changes. A chest radiograph (Fig 2) showed the entire heart to be displaced into the left hemithorax, clear visible lung fields, and a severe pectus excavatum with a marked reduction of the anteroposterior diameter of the chest. A CT scan of the chest (Fig 4) confirmed the severity of the pectus excavatum, reducing the space between the sternum and the vertebral bodies to about 2 cm and completely displacing the heart into the left hemithorax, which compressed the left lower lobe and the left mainstem bronchus. A high-resolution CT scan of the chest showed some interstitial changes in the lower lung fields and cystic changes in the left lower lobe with thickened pleura. Gallium scan findings were unremarkable. A quantitative perfusion lung scan showed 72% of the perfusion to the right lung and only 18% perfusion to the left lung. A ventilation/perfusion lung scan showed a matched ventilation defect in the left lower lobe. An echocardiogram and a transesophageal echocardiogram showed severe pulmonary hypertension with no evidence of atrial or ventricular septal defect. The right atrium and right ventricle were dilated with reduced right ventricle systolic function and moderate tricuspid regurgitation. The left ventricle showed a normal ejection fraction with normal wall motion. Both the mitral and aortic valves were normal. Pulmonary function studies (Table 1) showed evidence of a severe
restrictive defect (total lung capacity [TLC], 35% of predicted). Volume-adjusted diffusing capacity was mildly impaired (71% of predicted).

Cardiac catheterization showed both the right atrium and right ventricle to be dilated with increased filling pressure of the right ventricle, decreased right ventricular systolic performance, and severe tricuspid regurgitation, severe pulmonary hypertension, increased pulmonary vascular resistance, and significant pulmonary venous desaturation. No intracardiac shunt was evident. The left atrium was normal in size with normal pulmonary venous return. Mitral valve prolapse was noted. Left ventricular systolic function was normal. No branch pulmonary artery stenosis or pulmonary venous stenosis was discovered. These findings are consistent with the diagnosis of cor pulmonale. A workup for collagen vascular disease, including antinuclear antibody, anti-DNA, complement level, and rheumatoid factor, was negative. Thyroid studies (triiodothyronine, levorotatory thyroxine, thyroid-stimulating hormone) were within normal limits. The results of a fluoroscopic examination of the diaphragm and a sniff test were normal, excluding a significant diaphragmatic dysfunction.

The patient was treated with diuretics, salt restriction, low-flow oxygen, and bilevel pressure ventilation, which resulted in improvement in dyspnea, pedal edema, and arterial blood gas levels. The patient was discharged to be observed in the pulmonary and cardiac clinics. She later underwent polysomnography and a shunt study as an outpatient. Polysomnography failed to show evidence of obstructive sleep apnea or central apnea. A shunt study was performed by sampling the patient’s arterial blood after having her breathe 100% oxygen for 20 min, and the results showed a shunt fraction of 11%. Surgery was not offered as there was a concern that there was a prohibitive risk and that the procedure would not enhance her pulmonary function.

**Table 1—Pulmonary Function Studies**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Results</th>
<th>% Predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC, L</td>
<td>0.72</td>
<td>19</td>
</tr>
<tr>
<td>FEV₁, L</td>
<td>0.72</td>
<td>24</td>
</tr>
<tr>
<td>FEV₁/FVC, %</td>
<td>100</td>
<td>had to be adjusted due to increased lung volume.</td>
</tr>
<tr>
<td>FEF₂₅₋₇₅, L/s</td>
<td>1.26</td>
<td>36</td>
</tr>
<tr>
<td>TLC, L</td>
<td>1.76</td>
<td>35</td>
</tr>
<tr>
<td>RV, L</td>
<td>1.04</td>
<td>76</td>
</tr>
<tr>
<td>FRC, L</td>
<td>1.34</td>
<td>48</td>
</tr>
<tr>
<td>ERV, L</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td>IC, L</td>
<td>0.43</td>
<td></td>
</tr>
<tr>
<td>DLCO, mL/min/mm Hg</td>
<td>4.8</td>
<td>28</td>
</tr>
<tr>
<td>DLCO/VA</td>
<td>4.14</td>
<td>71</td>
</tr>
</tbody>
</table>

*FEF₂₅₋₇₅ = forced expiratory flow, midexpiratory phase; RV = residual volume; FRC = functional residual capacity; ERV = expiratory reserve volume; IC = inspiratory capacity; DLCO = diffusing capacity of the lung for carbon monoxide; VA = alveolar volume.*

**DISCUSSION**

Clinical features of this case consist of a young woman with the physical findings of a severe pectus excavatum deformity of her chest wall and right-sided heart failure. Laboratory and other investigational data indicate the presence of chronic hypercapnia, hypoxemia with a significantly widened alveolar-arterial oxygen gradient (22 mm Hg), an increased hemoglobin level, severe pulmonary hypertension, and right atrial and right ventricular enlargement without evidence for an intrinsic cardiac disease or an intracardiac shunt. Lung fields were essentially clear.

**FIGURE 3.** Lateral chest radiograph showing severe pectus excavatum and the complete displacement of the heart into the left hemithorax.

**FIGURE 4.** CT scan of the chest showing marked reduction of the sternovertebral space and the complete displacement of the heart into the left hemithorax.
except for some interstitial changes in the left lower lobe seen on a high-resolution CT scan. Is this a ‘zebra or a cobra on high heels,’” to paraphrase Dr. Eugene Robins’ colorful description of the dilemma of separating an esoteric case from the mundane? To answer this question, a systematic approach considering all relevant diagnoses is essential.

The absence of a left ventricular disorder, valvular heart disease, or an intracardiac shunt as a cause of severe pulmonary hypertension and the presence of hypercapnia in this case would point to lung disease, chest wall disorder, diaphragmatic dysfunction, neuromuscular disease, obstructive apnea, or obesity-hypoventilation as possible causes of cor pulmonale with secondary pulmonary hypertension. An intrinsic (ie, diffuse infiltrative/interstitial) lung disease causing chronic hypoxemia resulting in cor pulmonale can be excluded on the basis of its absence on a chest radiograph and a CT scan of the chest. A low TLC and a normal FEV1/FVC ratio exclude an obstructive lung disease. Clinical features, polysomnography, and the studies of diaphragmatic function exclude obesity-hypoventilation, obstructive apnea, central apnea, neuromuscular disease, or diaphragmatic dysfunction as possible causes of alveolar hypoventilation. By process of elimination, chest wall deformity seems the only logical cause of hypercapnic respiratory failure and cor pulmonale in this case. Severe impairment of vital capacity (VC) [0.72 L; 19% of predicted] and TLC (1.76 L; 35% of predicted) are clearly the consequences of the severe restraint imposed by pectus excavatum deformity.

Prolonged gas exchange abnormalities, in this case, are the combined results of venous admixture, ventilation/perfusion mismatch, and alveolar hypoventilation. Evidence of a widened alveolar-arterial oxygen gradient of 22 mm Hg and a shunt fraction of 11% suggest significant contributions to hypoxemia from both ventilation-perfusion mismatch and venous admixture. Hypercapnia, the result of alveolar hypoventilation, is an additional contributing factor. Similar mechanisms for gas exchange abnormalities are operative in patients with other disorders of the chest wall, including kyphoscoliosis, neuromuscular disease, or obesity-hypoventilation, as a consequence of the compression of otherwise normal lung parenchyma. Compression of the left lower lobe by the displaced heart alone could account for the widened alveolar-arterial oxygen gradient in our patient.

The most significant abnormality in this case is a severe pectus excavatum (funnel chest) deformity, with only 2 cm of space between the vertebral bodies and the sternum, displacing the entire heart into the left hemithorax. Severe impairment of VC and TLC with a normal FEV1/FVC ratio and a near-normal, volume-adjusted diffusing capacity of the lung (Table 1) appear to be the consequences of the displacement and compression of lung parenchyma by an extreme degree of pectus excavatum, resulting in severe chronic hypercapnia, hypoxemia, and cor pulmonale. Pectus excavatum was first described by Bauhinus in 1566 and later exhaustively studied by Ebstein.3 Anatomic changes of pectus excavatum and the approaches for its correction were first described comprehensively by Brown.4 Pectus excavatum is the result of a developmental abnormality of the anterior portion of the diaphragm. Often familial in nature, the deformity affects about 2.2% of the population. Clinical manifestations are mainly cosmetic and orthopedic in nature, with frequent psychological effects on children and their parents. Cardiac manifestations are said to be limited mostly to auscultation findings in one half of the patients and consist of a loud parasternal systolic murmur with a thrill and a split second sound. ECG changes (Fig 1) occur because of the displacement of the heart toward the left. Subjective symptoms of easy fatigability, exercise intolerance, dyspnea, precordial pain, and palpitations have been attributed to cardiac displacement, rotation, and angulation of great vessels. Congestive cardiac failure is almost unheard of and has not been observed in a number of extensive hemodynamic studies.3–4 In a few cases, right ventricular pressure patterns showed a postystolic dip with elevated end-diastolic pressure much like that seen in patients with mild constrictive pericarditis, which suggested disturbed right ventricular diastolic filling as a result of compression, which has been demonstrated by angiography in some cases.5

Similarly, the lung volume profile generally has been found to be within the normal range except for an occasional slight increase in the residual volume or mild reductions in TLC and VC.5,8,9 Pectus excavatum, unlike deformities of the spine, rarely causes measurable functional impairment and has never resulted in hypoventilation and respiratory failure.1

A comparison with other reported surgical series10–15 indicates that our patient has the most severe degree of pectus excavatum deformity based on the criteria in Table 2. An exhaustive review by Gaensler4 and our review of the

### Table 2—Indexes of Severity*

<table>
<thead>
<tr>
<th>Indexes</th>
<th>Normal</th>
<th>Patient</th>
<th>Worst Reported/Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sternotransverse distance on chest radiograph, cm</td>
<td>8</td>
<td>2</td>
<td>2/Gaensler⁴</td>
</tr>
<tr>
<td>Sternotransverse distance/radius of chest on CT scan, cm</td>
<td>0.6</td>
<td>0.06</td>
<td>0.05/Kagura et al¹⁰</td>
</tr>
<tr>
<td>Maximum distance between anterior and posterior chest walls on the right/sisternovertebral distance on CT scan, cm</td>
<td>1.68 ± 0.12⁴</td>
<td>4.66</td>
<td>3.84/Nakahara et al¹¹</td>
</tr>
<tr>
<td>Transverse diameter of chest/maximum distance between anterior and posterior chest walls on the right on CT scan, cm</td>
<td>1.49 ± 0.12⁴</td>
<td>3.07</td>
<td>2.08/Nakahara et al¹¹</td>
</tr>
</tbody>
</table>

*Data are presented as No. unless otherwise indicated.

†Values given as mean ± SD.
Severe Immune Hemolytic Anemia in Disseminated Tuberculosis With Response to Antituberculosis Therapy*

Ping-Hung Kuo, MD; Pan-Chyr Yang, MD; Shoo-Shown Kuo, MD, FCCP, and Kwen-Tay Luh, MD, FCCP

Many reports have associated mycobacterial diseases with hematologic abnormalities. Minor degrees of anemia are commonly found in patients with disseminated tuberculosis, but hemolytic anemia is exceedingly rare. We describe an episode of severe immune hemolytic anemia due to miliary tuberculosis in a previously healthy young man.

CASE REPORT

A 26-year-old man presented to the emergency department of our hospital in January 1997 with a 2-week history of intermittent fever and exertional dyspnea. He also complained of malaise, fatigue, and weight loss of 4 kg over the preceding 3 weeks. There was no history of hematologic disorders or blood transfusions, and he was not receiving any drugs. The family history was noncontributory. On examination, the patient’s temperature was 38.4°C, the pulse was 100 beats/min, and the respirations were 28 breaths/min. The BP was 110/60 mm Hg. Several lymph nodes were palpated in the left neck and in both axillary regions. The patient’s chest radiograph showed a widened mediastinum and miliary lesions over both lung fields. A CT scan of the chest revealed heterogeneous hepatic echogenicity but noncontributory findings. On laboratory examination, the patient’s laboratory tests revealed the following: hemoglobin level, 5.0 g/dL; hematocrit, 16.7%; mean corpuscular volume, 107 femtoliters; mean corpuscular hemoglobin, 29.9 g/L. Laboratory tests for malaria, human immunodeficiency virus, and hepatitis were negative. Tests for Coombs’ test, haptoglobin, immune hemolytic anemia, and miliary tuberculosis were negative. Further evaluations, including hemoglobin content, serum iron, red cell distribution width, and reticulocyte count, were normal. The direct and indirect Coombs’ tests were negative. The patient’s liver function tests were normal. The urine analysis showed no abnormalities.

The patient was admitted to the hospital for further evaluation and treatment. He was started on antituberculosis therapy, and the results of the laboratory investigations were as follows: hemoglobin level, 5.0 g/dL; hematocrit, 16.7%; mean corpuscular volume, 107 femtoliters; mean corpuscular hemoglobin, 27.5 pg/cell; mean corpuscular hemoglobin concentration, 29.9 g hemoglobin per deciliter RBCs; total leukocyte count, 109/L (43% neutrophils; 3.0% lymphocytes; 10% monocytes); platelet count, 478 x 10^9/L; reticulocyte count, 21.4%; albumin level, 3.8 g/dL; globulin level, 3.6 g/dL; total bilirubin level, 2.5 mg/dL (with a direct component of 0.6 mg/dL); aspartate aminotransferase 2478 U/L; asparagine aminotransferase 673 U/L; creatine phosphokinase 226 U/L; alkaline phosphatase 202 U/L; total cholesterol level, 6.0 mmol/L; triglyceride level, 2.2 mmol/L; albumin level, 3.8 g/dL; globulin level, 3.6 g/dL; total bilirubin level, 2.5 mg/dL (with a direct component of 0.6 mg/dL); and aspartate aminotransferase 2478 U/L.

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