While it is widely recognized that patients with a major medical illness often have psychiatric symptoms, it is less commonly appreciated that psychiatric symptoms may be the first presentation of the illness. This has been documented by several authors who report that 9 percent to 40 percent of patients undergoing treatment for presumed psychiatric disease may actually have a medical illness accounting for their symptoms. We present the case of a woman who was given the diagnoses of panic disorder, psychogenic hyperventilation, and endogenous depression. Following medical and physiologic evaluations, however, it was apparent that her hyperventilation and symptoms of panic most likely resulted from the physiologic derangements consequent to pulmonary vascular disease. The purpose of this report is to describe how these derangements could precipitate such symptoms.

CASE REPORT

A 61-year-old woman presented to the emergency room with the chief complaint of suicidal ideation. Eight months prior to admission, she had noted exertional dyspnea and pedal edema. She saw a physician who prescribed a diuretic, following which she had resolution of the edema. Two months prior to admission, she had an episode of "flu" and was treated with metoclopramide for abdominal discomfort. At about the same time, she began experiencing episodes of severe anxiety, chest discomfort, and breathlessness. One month prior to admission, she was hospitalized at another facility for four days with these symptoms and was told that she had no evidence of heart disease, but that she was hyperventilating. She was treated with alprazolam and discharged with instructions to breathe into a paper bag if breathlessness occurred.

She was referred to our psychiatric clinic where she was described as having severe depression. She reported anorexia and insomnia, only sleeping about two hours per night. She also described episodes of anxiety, reaching a state of panic, recently accompanied by frightening impulses to stab her husband or herself with a knife. She had dreamt of her own death and stated that when she closed her eyes she saw an image of billowing sheets with a baby waving to her. She was agitated and feared that she was losing her mind.

She had no prior history of depression or other psychiatric disorder and was described by her family as a strong and capable woman. Her medical history was remarkable only for mild hypertension, treated with atenolol and a diuretic. Examination of her mental status revealed no evidence of a thought disorder nor abnormalities of perception, memory, or orientation. Metoclopramide was discontinued because of concern about its potential psychiatric side effects, and she was treated with amoxapine.

She did not improve, and presented several days later to the psychiatric emergency room requesting admission. Because she appeared tachyphneic, she was referred for medical evaluation.

Physical examination revealed a well-developed woman who was intermittently tremulous and anxious. She was afebrile with a blood pressure of 162/106 mm Hg, pulse rate of 110, and respiratory rate of 30. The thorax was clear to percussion and auscultation. Cardiac examination revealed a regular rhythm, a loud S1 and no murmur. One of three examiners reported that P2 was louder than A2. Results of the remainder of the examination were normal.

The electrocardiogram showed sinus tachycardia and was consistent with right ventricular hypertrophy. A chest radiograph revealed mild cardiomegaly with a prominent right ventricle and pulmonary arteries. The lung fields were clear, but peripheral vascular shadows were sparse. An arterial blood sample, drawn while breathing room air, showed: PO2 of 59 mm Hg, PCO2 of 32 mm Hg, and pH, 7.47.

The patient was admitted to the medical service with the diagnoses of suicidal depression and possible pulmonary embolism. She was treated with intravenous heparin and supplemental oxygen. Result of a ventilation-perfusion scan of the lungs obtained the following day was reported as indicating a "low probability of pulmonary embolism." Heparin was discontinued, and, as her suicidal thoughts abated, she was discharged with referrals to the psychiatric and chest clinics.

Pulmonary function test results obtained through the chest clinic revealed mild airflow obstruction, with normal lung volumes and diffusing capacity. To further define the etiology of her dyspnea and hypoxemia, exercise testing was performed on a cycle ergometer using work rates incremented by 5 watts every minute. The patient stopped exercise because of dyspnea at a work rate of only 20 watts, achieving 67 percent of her predicted maximum oxygen uptake. The pattern of her gas exchange response to exercise indicated impaired perfusion to ventilated lung units, in that her calculated physiologic dead space/tidal volume ratio (Vd/Vt) became abnormal with exercise, and the arterial-end tidal PCO2 difference was abnormally elevated (Table I). Her PaO2 level decreased from 71 mm Hg at rest to…

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Table 1—Data from Exercise Study Performed while Breathing Room Air

<table>
<thead>
<tr>
<th>Time (minutes)</th>
<th>Work rate (watts)</th>
<th>Heart rate (min-1)</th>
<th>V̇E (L/min)</th>
<th>V̇O₂ (L/min)</th>
<th>P(A-a)CO₂ (mm Hg)</th>
<th>R* V̇D/V̇Tt</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest</td>
<td>61</td>
<td>6.4</td>
<td>2.10</td>
<td>0.71</td>
<td>0.31</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>12</td>
<td>14.9</td>
<td>0.350</td>
<td>0.77</td>
<td>0.35</td>
<td>7</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>25.3</td>
<td>0.530</td>
<td>0.88</td>
<td>0.42</td>
<td>10</td>
</tr>
<tr>
<td>6</td>
<td>20</td>
<td>37.7</td>
<td>0.630</td>
<td>0.95</td>
<td>0.47</td>
<td>12</td>
</tr>
</tbody>
</table>

*Respiratory gas exchange ratio (V̇E/V̇O₂).
†V̇D/V̇Tt is calculated from the modified Bohr equation using arterial Pco₂ and corrected for breathing valve dead space; normal <.30.
‡Arterial to end-tidal Pco₂ difference; normal exercise value = -1 or less.

40 mm Hg at a work rate of 20 watts (Fig 1). Repeating the same exercise protocol with breathing 100 percent oxygen, the PaO₂ decreased from 550 mm Hg at rest to 70 mm Hg at the 20-watt work rate. Such an increase in venous admixture is indicative of development of right-to-left shunt during exercise as ventilation-perfusion mismatching or diffusion abnormality alone could not account for this great an increase in P(A-a)O₂.

On the basis of these studies, a diagnosis was made of pulmonary vascular disease and probable patent foramen ovale, allowing intracardiac right-to-left shunting during exercise. Cardiac catheterization was subsequently performed and confirmed the presence of pulmonary hypertension (pulmonary artery systolic pressure of 140 mm Hg) and a patent foramen ovale. The patient continues to use supplemental oxygen and remains dyspneic with minimal exertion. She has had no recurrence of anxiety or depression, however, and dates resolution of these symptoms to the institution of oxygen therapy.

**DISCUSSION**

The frequent occurrence of apprehension and anxiety in patients with pulmonary vascular disease is well recognized. The Urokinase Pulmonary Embolism Trial reported apprehension as the third most common symptom in patients with documented thromboembolism, with an incidence of 59 percent. The relationship of these symptoms to pulmonary vascular pressures per se, or to the presence of hypoxemia is not reported, however, and the pathogenesis of these symptoms is not evident from review of the literature.

Approximately 20-25 percent of individuals have potential patency of the foramen ovale, but because pressure is normally lower in the right atrium than the left, it is not a functional communication. If pulmonary hypertension develops in the presence of a large enough potential defect, however, right atrial pressure may become great enough to result in a right-to-left shunt, especially under conditions of increased venous return, as occurs during exercise. This will abruptly divert venous blood into the arterial circulation, possibly resulting in acute symptoms of hypercapnea and hypoxemia (breathlessness and anxiety). The shunting of CO₂ away from the lungs results in an elevation of the effective V̇D/V̇T (as calculated by the modified Bohr equation using arterial Pco₂ values) and requires that ventilation increase to maintain arterial eucapnea. We speculate that this patient's shortness of breath was due, in part, to the right-to-left shunt and increased effective V̇D/V̇T which was demonstrated to occur even during minimal exercise. The associated abrupt fall in PaO₂ may well have precipitated her acute anxiety attacks.

Multiple factors, including underlying personality traits, fluctuating hypoxemia, and concomitant drug therapy may have contributed to the disturbed mental status of this patient at the time of presentation. Her pulmonary vascular disease, if recognized, was initially overlooked on first hospitalization, in the presence of her dramatic psychiatric complaints. Her later psychiatric evaluation concluded that the lack of medical recognition of her problem may have compounded the initial symptoms of anxiety, which progressed to the threat of psychologic anhilation (manifest as panic) and regression (illustrated by the image of the baby waving to her). The ensuing feelings of helplessness and rage may have then led to the impulses to attack the person closest to her, and because this was unacceptable to her, to attack herself as well.

This case illustrates again that psychiatric complaints need not arise from a primary psychiatric disorder. In addition, it demonstrates the utility of making physiologic measurements during the stress of exercise. In this patient, venoarterial shunting and the resultant alterations in arterial blood gas levels were not evident from resting studies. The response to exercise, however, reflected both the presence of pulmonary hypertension and the unsuspected finding of a variable right-to-left shunt.

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