Profound pulmonary shunting without edema following stereotaxic biopsy of hypothalamic germinoma

Case report

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Hypoxemia is a nearly constant accompaniment of head injury. Diverse theories have been proposed to explain this relationship. The authors report the case of a patient who suffered an episode of severe, transient, arterial oxygen desaturation during "controlled" brain trauma: an otherwise uneventful stereotaxic biopsy of a small germinoma of the hypothalamus. Evidence is provided that pure ventilation-perfusion mismatching, without pulmonary edema, underlay the hypoxemia. The hypothalamus is intimately involved in matching pulmonary ventilation to perfusion; the hypoxemia of various brain injuries may be mediated by perturbation of this structure.

KEY WORDS □9 brain neoplasm □9 germinoma □9 pulmonary edema □9 stereotaxic biopsy

VARIOUS degrees of arterial oxygen desaturation are regularly encountered in cases of brain injury. Progressive microscopic atelectasis is often invoked, and is ascribed to a variety of disordered breathing patterns that follow injury of the central nervous system (CNS), including transient apnea. Impaired pharyngeal reflexes have also been incriminated; the resultant bacterial and acid aspirates provoke further loss of air space. Beyond this, a substantial body of literature, both clinical and experimental, has addressed the subject of neurogenic pulmonary edema. Varying degrees of extravascular collections of water in the lung have been demonstrated in acute brain injury. Nevertheless, clinical experience and laboratory models have provided compelling evidence of centrally mediated hypoxemia in the absence of significant loss of lung volume or extravascular pulmonary water accumulation. These observations have suggested to some investigators that the matching of pulmonary perfusion and ventilation, upon which adequate oxygenation is dependent, is in part mediated by the CNS. In circumstances where the CNS servomechanisms are abruptly impaired, profound arterial desaturation may be a direct consequence.

We have recently encountered a case of sudden, severe hypoxemia occasioned by the stereotaxic biopsy of a hypothalamic germinoma. In a controlled operative setting, we could reliably eliminate apnea, aspiration, and, in particular, pulmonary edema as the responsible mechanism for this event. The circumstances appear to substantiate the direct mediation of ventilation-perfusion matching in the lung by the CNS.

Case Report

This 14-year-old boy was brought for medical consultation because of increasing polyuria and polydipsia associated with a 15-kg weight gain over the preceding 3 months. There had been no headache or visual alteration, nor had a personality change been observed at home or at school, where he had continued his customary good work. There was no personal or family history of diabetes or asthma.

Examination. The patient weighed 69.3 kg (95th percentile), his height was 164 cm (50th to 75th percentile), and his blood pressure was 110/70 mm Hg. He was an alert, cooperative youngster with a generally normal neurological and systemic examination save for a rather characteristic pasty obesity and a lack of pub-
ertal changes in the genitalia. The lungs were clear, the fundi normal, and the visual fields full.

Urinalysis was normal, and revealed a specific gravity of 1.002. The hemogram was unremarkable. The serum sodium level was 163 mEq/liter, and the serum potassium content was 2.6 mEq/liter; the remainder of the blood chemistries, including the blood glucose level, were normal. Following intravenous hydration, the patient’s potassium concentration entered the normal range but the serum sodium level remained above 155 mEq/liter. Urine volumes remained in the range of 4 to 6 liters a day, with near-zero specific gravity associated with the increase in serum sodium and osmolarity. Although the patient drank substantial amounts of water, he subjectively experienced little or no thirst. Water deprivation resulted in a rising serum sodium level and an increase in osmolarity in conjunction with undiminished urinary volumes and low specific gravity levels. Parenteral vasopressin reversed these abnormalities.

A chest x-ray film and a conjunctival biopsy gave no evidence of sarcoidosis. A skull film and bone series displayed neither intracranial calcification nor evidence of diffuse histiocytosis. A computerized tomography (CT) scan demonstrated a small globular enhancing lesion in the region of the median eminence (Fig. 1).

Extensive pituitary-hypothalamic axis endocrine studies were performed. The patient exhibited panhypopituitarism: in addition to the central diabetes insipidus, he had hypogonadotrophy and displayed inadequate adrenal and thyroid reserve. He was treated with thyroxin, cortisol acetate, desmopressin acetate, and testosterone. A stereotaxic biopsy was arranged.

Operation. A CT-guided stereotaxic biopsy was performed in the operating room using a Brown-Roberts-Wells stereotaxic system.* The biopsy trajectory was aimed at the enhancing lesion noted on the CT scan, which was at the floor of the third ventricle in the region of the median eminence. Two specimens were obtained via a right frontal twist-drill hole with the Nashold side-cutting biopsy needle. A No. 5 French polyethylene catheter was then inserted stereotaxically into the third ventricle via the right foramen of Monro for monitoring intracranial pressure (ICP). The ventricular fluid remained crystal clear in the subsequent 24 hours and the ICP remained between 4 and 12 mm Hg. The pathological diagnosis from the biopsy material was germinoma.

Because of the patient’s apprehension, the biopsy was performed under general anesthesia. There were no discernible effects on his vital signs or clinical course during or immediately following the biopsy (Table 1). However, a routine arterial blood gas measurement taken 5 minutes after the biopsy on an inspired oxygen concentration of 0.4 revealed: $pO_2$ 68 mm Hg and $pCO_2$ 45 mm Hg; the pH was 7.29. Breathing sounds were clear and symmetrical. Endotracheal tube suctioning produced no secretions or fluid. The inspired oxygen concentration was increased to 0.5, and an immediate intraoperative portable chest x-ray film was normal. With the higher fractionated inspired oxygen ($FIO_2$) level and an increased minute ventilation, the blood gas values were: $pO_2$ 68 mm Hg and $pCO_2$ 32 mm Hg; the pH was 7.4. Upon ventilation with 100% oxygen, the $pO_2$ rose to 164 mm Hg and the $pCO_2$ was 32 mm Hg; the pH was 7.42. These reflect shunt fractions of 26% to 31%. At this point 1 hour had elapsed from the time of the biopsy. Another blood gas measurement obtained 1½ hours following biopsy, with the same parameters, yielded a $pO_2$ of 468 mm Hg and a $pCO_2$ of 29 mm Hg; the pH was 7.47.

Postoperative Course. With cessation of anesthesia, the patient awoke rapidly; he was alert and able to follow commands readily. He was extubated and given 60% oxygen by mask; on transfer to the pediatric intensive care unit, his blood gas levels were: $pO_2$ 125 mm Hg and $pCO_2$ 41 mm Hg; pH was 7.35. At this point the patient remained alert and conversed readily with staff and his parents; his vital signs and ICP were normal. Throughout the course of the day, whenever he removed the mask, he was noted by the staff to become cyanotic, although asymptomatic. He was maintained on 50% oxygen by mask throughout the evening and night. The blood gas levels showed adequate oxygenation, although a significant shunt was still noted. Over the course of the next 2 days he was weaned from the supplemental oxygen and remained well despite the persistent hypoxemic shunt (Table 1).

After discharge, the patient continued stable on the endocrine supplement regimen mentioned above and returned for outpatient pulmonary function studies.

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* Brown-Roberts-Wells stereotaxic system manufactured by Radionics, Inc., Burlington, Massachusetts.
TABLE 1
Physiological parameters during and after biopsy*

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control Levels</th>
<th>Preinjection 8 a.m.</th>
<th>Biopsy 9:05 a.m.</th>
<th>9:35 a.m.</th>
<th>9:50 a.m.</th>
<th>10:30 a.m.</th>
<th>Operating Room 2:47 p.m.</th>
<th>6:28 p.m.</th>
<th>Intensive Care Unit 11:37 a.m.</th>
<th>Ward 4:36 p.m.</th>
<th>Pulmonary Lab Tests 8:00 a.m.</th>
<th>POD 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>blood pressure (mm Hg)</td>
<td>100–110/140/60–70</td>
<td>130/100</td>
<td>130/85</td>
<td>130/85</td>
<td>110/70</td>
<td>125/75</td>
<td>130/80</td>
<td>124/76</td>
<td>114/70</td>
<td>126/76</td>
<td>116/68</td>
<td></td>
</tr>
<tr>
<td>pulse (/min)</td>
<td>60</td>
<td>100</td>
<td>80</td>
<td>90</td>
<td>85</td>
<td>85</td>
<td>80</td>
<td>86</td>
<td>76</td>
<td>72</td>
<td>70</td>
<td>70</td>
</tr>
<tr>
<td>ICP (mm Hg)</td>
<td>RA</td>
<td>RA</td>
<td>0.4</td>
<td>0.4</td>
<td>0.5</td>
<td>1.0</td>
<td>1.0</td>
<td>0.6</td>
<td>0.5</td>
<td>0.24</td>
<td>RA</td>
<td>RA</td>
</tr>
<tr>
<td>FIO₂</td>
<td>RA</td>
<td>RA</td>
<td>&gt; endotracheal tube</td>
<td>&gt; mask</td>
<td>&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>peak inspiratory pressure (mm Hg)</td>
<td>RA</td>
<td>RA</td>
<td>10 × 650</td>
<td>10 × 650</td>
<td>12 × 650</td>
<td>12 × 650</td>
<td>12 × 650</td>
<td>12 × 650</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pO₂ (mm Hg)</td>
<td>68</td>
<td>68</td>
<td>164</td>
<td>468</td>
<td>125</td>
<td>89</td>
<td>55</td>
<td>68</td>
<td>63</td>
<td>540</td>
<td>84</td>
<td>86</td>
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<tr>
<td>pCO₂ (mm Hg)</td>
<td>45</td>
<td>32</td>
<td>32</td>
<td>29</td>
<td>41</td>
<td>35</td>
<td>41</td>
<td>35</td>
<td>39</td>
<td>37</td>
<td>42</td>
<td>41</td>
</tr>
<tr>
<td>pH</td>
<td>7.29</td>
<td>7.40</td>
<td>7.42</td>
<td>7.47</td>
<td>7.35</td>
<td>7.45</td>
<td>7.45</td>
<td>7.45</td>
<td>7.45</td>
<td>7.44</td>
<td>7.43</td>
<td>7.37</td>
</tr>
<tr>
<td>shunt fraction</td>
<td>0.30</td>
<td>0.31</td>
<td>0.26</td>
<td>0.11</td>
<td>0.17</td>
<td>0.18</td>
<td>0.24</td>
<td>0.09</td>
<td>0.15</td>
<td>0.07</td>
<td>0.04</td>
<td>0.04</td>
</tr>
</tbody>
</table>

* Abbreviations: POD = postoperative day; ICP = intracranial pressure; FIO₂ = fractionated inspired oxygen; RA = room air; RR × vol = respiratory rate × tidal volume.

The results are shown in Table 1. At that time, he demonstrated a shunt fraction of 0.07, which can be assumed to represent a good reflection of his prebiopsy status. In addition, his carbon monoxide diffusion capacity was normal. Thus, no fixed underlying anatomical or physiological shunting could be demonstrated.

Discussion

This report demonstrates that a needle biopsy of the hypothalamus, which was invaded by a germinoma, was sufficient stimulus to provoke an abrupt, profound, and reversible hypoxemia. The disturbance in pulmonary oxygenation evolved without concomitant cerebral hemorrhage or intracranial hypertension. It was not associated with apnea, aspiration, disordered ventilatory patterns, or manifest pulmonary edema. That is to say, relatively mild traumatic stimulation of the region of the hypothalamus can induce a notable (albeit reversible) pulmonary shunt.

It has been recognized for some time that some degree of hypoxemia is an almost invariable concomitant of CNS trauma, whether ischemic, inflammatory, or percussive. Itinerant clinical and laboratory observation initially ascribed the hypoxia to progressive atelectasis provoked by either posttraumatic apnea, disturbed and inadequate ventilatory patterns (such as lack of sighing or shallow and irregular breathing), or aspiration-induced surfactant damage. Although in some circumstances these may play a major role in the hypoxemia accompanying acute CNS injury, it is clear that a substantial proportion of cases lack sufficient grounds to incriminate these mechanisms alone.

The rare but striking case of florid pulmonary edema in association with an acutely injured brain seemed to provide a unifying mechanism for all the hypoxic states associated with CNS injury. A substantial body of experimental evidence was adduced to conclude that increased extravascular lung water accounted for the oxygen desaturation accompanying acute CNS pathology. In general, profuse edema was associated with the severest injuries, whether ischemic, inflammatory, or percussive, although this was by no means always the case either clinically or in animal models.

Two mechanisms were invoked to explain neurogenic pulmonary edema. Perturbation of the CNS produced a massive sympatho-adrenal response, and the resulting severe hypertension precipitated acute left-sided heart failure and its attendant pulmonary edema. Later work stressed the role of a low-pressure capillary leak edema. Microvascular injury was mediated directly by the CNS insult, without the contribution of severe hypertension or heart failure. However, further experience has shown that relatively mild CNS insults are frequently accompanied by arterial oxygen desaturation, and 2) that hypoxemia may be manifest without clinical or physiological evidence of interstitial or alveolar edema.

The foregoing observations have led to the proposal that diverse CNS injuries manifest hypoxemia because of a disruption in the normally ongoing matching of ventilation to perfusion in the lung. In this view, aspiration, apnea, patchy pulmonary contusions, and diffuse lung edema are additional and inconstant accompaniments to, rather than underlying mecha-
nisms of, this hypoxemia. Furthermore, widespread brain damage may not be necessary; the salient pathophysiology may lie in small abrupt perturbations in the region of the hypothalamus.13,14,36

Our case seems to corroborate this conclusion. In a setting where the airway was controlled, minute ventilation fixed, blood pressure stable, inspiratory pressure and tidal volume (compliance) nearly invariant, and the customary indicators of alveolar closure or edema (such as chest x-ray film, auscultation, and endotracheal tube suctioning) unexceptionable, this patient abruptly developed a shunt fraction of 30% after an otherwise uncomplicated biopsy of a hypothalamic germinoma.

The post-biopsy CT scan and the stereotactically implanted third ventricular catheter gave no evidence of intracranial bleeding or elevated ICP. Although baseline preoperative arterial blood gas levels were not obtained, the patient's asymptomatic preoperative state and his subsequent pulmonary function studies support the claim that this was an abruptly evolving and transient (perhaps lasting a few days) physiological state.

There are two alternative explanations for the events described here, both unlikely for the reasons to be presented. On the one hand, it is known that general anesthesia and muscle paralysis alters diaphragmatic mechanics, diminishing basal lung ventilation sufficiently to produce a surprisingly high shunt fraction.10 Restoration of spontaneous ventilation should rapidly reverse this condition, yet the shunting lasted over 2 days in our case although the patient was awake and talking shortly after anesthesia ceased. The second possible explanation is that immobility in the supine position can lead to progressive microatelectasis which, although invisible on routine chest radiographs, leads to progressive shunting hypoxemia. However, the time course in this case was uncharacteristic, inasmuch as maximum hypoxemia due to microatelectasis usually makes its appearance several hours after the induction of anesthesia. Our patient had a shunt fraction of 0.30 within an hour of the onset of anesthesia.

With the increasing resort to CT-guided stereotactic biopsy of suprasellar lesions,12,17 this report mandates some caution. Biopsy in this region, perhaps in the setting of prior pathology, may provoke profound hypoxemia at the customary levels of inspired oxygen (FIO2 = 0.3 to 0.4) employed in low-risk surgical cases.

Of course, the more general implication of this report is that the hypothalamus and adjacent diencephalic structures are intimately concerned with ventilation-perfusion matching in the lung. This may be mediated by circulating hormone release or (which is more likely) by direct innervation of the lung bronchovascular units via sympathetic and parasympathetic outputs to the pulmonary hilum and parenchyma. To what extent this relation is operant in the normal physiological setting remains an open question.

References

F. M. Epstein, K. R. Cooper, and J. D. Ward

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Pulmonary shunting after hypothalamic tumor biopsy


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