Pulmonary Edema following Intracranial Hemorrhage

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Hemodynamic changes and samples of fluid from pulmonary edema were studied in a 50-year-old woman who developed florid pulmonary edema following intracranial hemorrhage. Marked systemic and pulmonary arterial hypertension were associated with the rapid production of edema fluid that contained red blood cells, but had a lower protein content than plasma. After restoration of pulmonary vascular pressures to a normal range, the production of fluid ceased, and clinical signs of edema resolved. These findings point to the sudden increase in pulmonary microvascular pressure as the cause of pulmonary edema in this patient. Our findings contrast with those of previous reports and with speculations on the extent of a defect in permeability accounting for pulmonary edema following injury to the brain.

A acute injury to the central nervous system is a well-recognized cause of pulmonary edema (neurogenic pulmonary edema); however, studies on the development and subsequent resolution of this form of edema in man have been meager. The present report documents the clinical course of edema in a patient following massive intracranial hemorrhage.

CASE REPORT

A 50-year-old woman with a history of mild hypertension (160/100 mm Hg) but with no previous heart disease complained of sudden generalized headache. Within a few minutes, she became lethargic, experienced a grand mal seizure, and became apneic. She was immediately ventilated with a mask and valved bag, followed by intubation of the trachea, as the respiratory arrest occurred in the hospital’s operating suite. No evidence of aspiration was observed. Measurements of arterial blood gas levels obtained five minutes after the arrest revealed an arterial oxygen pressure of 245 mm Hg, an arterial carbon dioxide tension of 36 mm Hg, and a pH of 7.41 (fractional concentration of oxygen in the inspired gas, 1.0). The patient was comatose and unresponsive to pain.

Within 15 minutes, significant findings included sinus

\[ \text{Figure 1. Sequential changes in hemodynamics and fluid of pulmonary edema (PE) following respiratory arrest (at \(-120 \text{ minutes}). Pulmonary arterial wedge pressure and colloid osmotic (oncotic) pressure of plasma and edematous fluid are depicted, as well as volume of edematous fluid suctioned from endotracheal tube. ATRIAL FIB, Atrial fibrillation; RIHSA, radioactive iodinated I 125 human serum albumin; and NITROPRUSS, nitroprusside.} \]
tachycardia to 130 beats per minute and elevation of arterial pressure to 260/155 mm Hg, together with pulmonary hypertension of 77/44 mm Hg, with an occluded pulmonary arterial (wedge) pressure of 40 mm Hg. Marked arterial hypertension persisted. A 15-minute interval of atrial fibrillation with a ventricular response of 150 beats per minute occurred. The subsequent rhythm was sinus.

By 20 minutes after the arrest, frothy pink fluid of pulmonary edema began to well up in the endotracheal tube. The chest roentgenogram revealed bilateral alveolar infiltrates and pulmonary vascular congestion. Therapy with furosemide and digoxin was given. Urinary output increased to 200 ml over 60 minutes, but the mean pulmonary arterial and wedge pressure remained high (Fig 1). Nitroprusside was infused at 50 μg/min for 35 minutes, resulting in a reduction of systemic and pulmonary pressure (wedge, 7 to 10 mm Hg). The infusion of nitroprusside was stopped, and there were no subsequent episodes of pulmonary or systemic hypertension.

During the initial 120 minutes, approximately 300 ml of fluid were suctioned from the endotracheal tube. At this time (+120 minutes), 2 ml of radioactive iodinated 125I human serum albumin (R125 IHSA) containing 1μCl/ml were given intravenously. Samples of arterial blood and edematous fluid were collected at ten-minute intervals. Radioactivity, the hematocrit reading, osmolality, colloid osmotic pressure (oncotic pressure), and the concentration of protein were measured.3 Albumin and globulin were fractionated by cellulose acetate strip electrophoresis on selected samples. Sampling of fluid from pulmonary edema was discontinued 150 minutes later, when less than 3 ml could be obtained during a ten-minute interval. Only scant amounts of fluid could be recovered for the next 15 minutes and none subsequently.

The radioactivity of successive samples of fluid increased progressively; however, the radioactivity of fluid was substantially less than that of corresponding samples of blood (Fig 2).

The colloid osmotic pressure and the concentration of protein in the fluid were less than those of corresponding samples of plasma (Table 1); however, osmolalities of the two fluids were essentially identical. Since we sampled fluid during florid edema and since the edematous fluid was isoosmolar to plasma, we assumed that the fluid was representative of alveolar and, in turn, interstitial fluid; however, absorption or secretion by the bronchial circulation or in the larger airways cannot be excluded. The ratio of the concentration of albumin in fluid to that in plasma was greater than the ratio of the concentrations of globulin in the two fluids. The edematous fluid was pink; the average hematocrit reading was 1.6 percent.

Only 370 ml of a 5 percent solution of dextrose in water were given intravenously during the first three hours. The blood volume was calculated using a standard formula.2 The plasma volume was reduced in this patient, similar to the findings observed in other patients with hemodynamic pulmonary edema.3 Cardiac output measured at +120 min thermal dilution. Cardiac output after injection of radioactive medium was reduced to 3.4 L/min. Measurements of arterial blood gas levels obtained during the initial three hours

Table 1—Data from Simultaneous Samples of Fluid from Pulmonary Edema and Plasma

<table>
<thead>
<tr>
<th>Time</th>
<th>Colloid Osmotic Pressure, mm Hg</th>
<th>Protein Level, gm/100 ml</th>
<th>Albumin Level, gm/100 ml</th>
<th>Globulin Level, gm/100 ml</th>
<th>Osmolality, mOsm/kg</th>
<th>Hematocrit Reading, percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>12.4/18.7 (0.66)</td>
<td>4.4/6.3 (0.70)</td>
<td>2.5/2.9 (0.86)</td>
<td>1.9/3.4 (0.56)</td>
<td>330/298</td>
<td>2/55</td>
</tr>
<tr>
<td>+20 min</td>
<td>13.0/19.0 (0.68)</td>
<td>4.7/6.4 (0.73)</td>
<td>2.9/3.3 (0.88)</td>
<td>1.8/3.1 (0.58)</td>
<td>305/305</td>
<td>2/54</td>
</tr>
<tr>
<td>+40 min</td>
<td>13.0/19.3 (0.67)</td>
<td>5.4/6.3 (0.85)</td>
<td>3.2/3.3 (0.97)</td>
<td>2.2/3.3 (0.63)</td>
<td>301/301</td>
<td>1/54</td>
</tr>
<tr>
<td>+60 min</td>
<td>12.9/19.2 (0.67)</td>
<td>4.6/6.3 (0.73)</td>
<td>2.6/3.1 (0.84)</td>
<td>2.0/3.2 (0.63)</td>
<td>289/292</td>
<td>1/52</td>
</tr>
<tr>
<td>+120 min</td>
<td>13.7/18.9 (0.72)</td>
<td>5.0/6.5 (0.77)</td>
<td>2.9/3.3 (0.88)</td>
<td>2.9/3.2 (0.97)</td>
<td>293/294</td>
<td>2/53</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>13.7 (0.72)</td>
<td>5.0 (0.77)</td>
<td>2.9 (0.88)</td>
<td>2.9 (0.97)</td>
<td>304/301</td>
<td>2/54</td>
</tr>
</tbody>
</table>

*Times represent samples obtained at onset of pulmonary edema and after injection of radioactive iodinated 125I human serum albumin.

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revealed no hypoxemia or acidemia, although there was an increase in the alveolar to arterial oxygen tension gradient.

The patient remained comatose and flaccid. Bilateral retinal hemorrhages were observed; the pupils were dilated and unresponsive to light. Successive roentgenograms showed partial clearing of pulmonary congestion and edema within 24 hours and complete resolution of edema at 75 hours. The patient died on the fifth day of hospitalization.

At autopsy, minimal atherosclerosis of the vascular system was found. The heart weighed 420 gm; no occlusive coronary vascular lesions were found. The right and left lungs weighed 800 and 700 gm, respectively. A large hematoma occupied the region of the pons, midbrain, and cerebral hemispheres.

**DISCUSSION**

The mechanisms that account for pulmonary edema following catastrophic injuries to the brain are unclear. Following the landmark observations of Cushing, several investigators have attributed the onset of neurogenic pulmonary edema to a transient, centrally mediated, massive sympathetic discharge that leads to systemic and pulmonary hypertension. Therefore, a direct increase in pulmonary microvascular pressure would result. In addition, microvascular pressure could also be elevated by the development of acute left ventricular failure induced by marked changes in arterial impedance. In either case, at the onset, pulmonary edema would be due to a hemodynamic mechanism; that is, an increase in microvascular hydrostatic pressure. Accordingly, the edematous fluid would contain less protein than plasma, corresponding to previous studies of hemodynamic (cardiogenic) pulmonary edema; however, it has been suggested that following the interval of intense sympathetic discharge, pulmonary edema may persist, mediated by alterations in pulmonary microvascular permeability. This hypothesis is supported by an experimental study of injury to the central nervous system, in which edematous fluid with high protein content was recovered. In addition, one clinical report has documented similar findings.

We were able to pinpoint the onset of injury to the central nervous system in this patient and to measure vascular pressures and sample fluid very early in the course of the development of pulmonary edema. The findings point to a hemodynamic mechanism as the cause of edema. We documented extreme elevations of pulmonary arterial wedge pressure, similar to experimental studies. Also, the fluid contained a lower protein content and colloid osmotic pressure than plasma, and the edema resolved relatively rapidly, consistent with a hemodynamic mechanism. Furthermore, the presence of red blood cells in edematous fluid suggests a hemodynamic process. The ratios of the levels of albumin and globulin in edematous fluid over those in plasma are consistent with molecular sieving, similar to findings in experimental studies of cardiogenic pulmonary edema. We made no correction for the contamination of hemoglobin on the electrophoretic fractionation of albumin and globulin; however, the hemoglobin present in edematous fluid would be expected to reduce the size of the albumin peak and to increase the globulin peak on electrophoresis. Therefore, the reduced globulin ratio that we report may actually underestimate molecular sieving. Although the protein concentration of edematous fluid was slightly higher than that typically associated with cardiogenic edema, the protein content was substantially less than values reported for pulmonary edema due to altered permeability. Hypoxia or acidemia do not appear to be likely contributing factors in this patient.

Therefore, we believe that the major factor in the genesis of pulmonary edema in this patient was an unbalancing of the Starling forces across the pulmonary vasculature and especially to an increase in pulmonary vascular hydrostatic pressure. Since we did not measure left ventricular filling pressure directly, we cannot separate the relative contributions of left ventricular failure and direct increases in pulmonary vascular resistance that may have accounted for the increases in pulmonary arterial wedge pressure.

We believe that neurogenic pulmonary edema may be due to a spectrum of hemodynamic and permeability mechanisms. All reports have documented that the early changes in neurogenic pulmonary edema are of hemodynamic origin; however, in some studies a subsequent defect in permeability has been observed. Our findings are not consistent with a defect in pulmonary vascular permeability. The primary cause of pulmonary edema in this patient was a hemodynamic mechanism induced by the injury to the brain.

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**REFERENCES**

Superior Vena Cava Syndrome due to a Retained Central Venous Pressure Catheter*

Daniel J. Kanada, M.D.;**, Ralph C. Jung, M.D.;†
and Stanford Ishihara, M.D.‡

A 70-year-old man had the superior vena cava syndrome. At thoracotomy a retained central venous pressure line was found to be the cause of venous thrombosis at the outlet of the superior vena cava into the right atrium. A retained central venous pressure catheter and catheter-induced venous thrombosis should be added to the list of causes of the benign form of the superior vena cava syndrome.

Obstruction of the superior vena cava usually implies the presence of malignant disease and requires ur-

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Figure 1. Posteroanterior chest roentgenogram taken on admission, showing superior mediastinal widening and enlargedazygos vein.