Permeability Pulmonary Edema following Lung Resection*

Mali Mathru, M.D.; Bradford Blakeman, M.D.; David J. Dries, M.D.; Bruce Kleinman, M.D.; and Runkaj Kumar, M.D.

The etiology of edema associated with pulmonary resection was investigated in five patients during the immediate postoperative period. Three patients received pneumonectomy while two patients had one lobe resected. All patients suffered from severe respiratory distress and had x-ray evidence of diffuse interstitial pulmonary edema within 12 hours of surgery. Hemodynamic data were obtained with radial and pulmonary artery catheters. Edema fluid was obtained along with blood samples for simultaneous determination of protein and albumin content. All patients studied had normal or high cardiac output, normal cardiac filling pressures, and edema fluid protein to serum protein ratio of 0.6 or greater suggestive of permeability changes contributing to edema fluid accumulation. Calculated shunt fraction exceeded 25 percent in all patients. Pulmonary edema has been noted in patients following pulmonary resection in the early postoperative period. In patients reviewed here, two factors appeared to be significant. First is an increase in pulmonary capillary pressure associated with passage of a normal to high cardiac output in a reduced volume pulmonary vascular bed. The second factor, as demonstrated by protein content in the edema fluid, is injury to the alveolar capillary membrane.

(Chest 1990; 98:1216-18)

Pulmonary edema of noncardiac origin following pneumonectomy has been described by Zeldin et al. This has been termed postpneumonectomy pulmonary edema. Surgical manipulation of the lung, excessive intraoperative fluid administration, altered hemodynamics, a restricted pulmonary vascular bed, and reduced lymphatic capacity following lung resection make the remaining pulmonary tissue prone to edema in the immediate postoperative period. Generalized permeability of the alveolar capillary membrane due to microvascular injury accompanying increased flow is believed to play a role in this form of pulmonary edema. To confirm that PPE is, in part, a permeability related pulmonary edema, the protein content of the edema fluid should be measured. Though previous investigators have documented normal filling pressure and normal or high cardiac output in PPE, protein content of the edema fluid, to our knowledge, has not been measured. We report for the first time an increase in the edema fluid protein (EF) to total serum protein (P) ratio (EF/P) in pulmonary edema following lung resection. In addition, we document the occurrence of this syndrome in patients following lobectomy.

**Materials and Methods**

The patients included in this study were in severe respiratory distress following lobectomy or pneumonectomy for carcinoma of the lung. Respiratory distress was defined as a respiratory rate greater than 35 breaths per minute, PaO₂/FI O₂ ratio less than 220, and shunt fraction ≥15 percent within 12 hours following surgery. All patients had chest x-ray evidence of diffuse interstitial pulmonary edema. In addition, all patients had radial artery catheters and pulmonary artery catheters for respiratory care and hemodynamic management. Mean pulmonary artery pressure, mean pulmonary capillary wedge pressure, and cardiac output were measured. Arterial and mixed venous blood samples were drawn for blood gas analysis. Shunt fraction was calculated using a standard shunt equation. Pulmonary capillary pressure was calculated by means of the following formula:

\[ P_{C} = P_{C_{W}} + 0.4 \times (P_{A} - P_{C_{W}}) \]

Samples of blood and edema fluid were obtained simultaneously and analyzed for protein and albumin content using the biuret method. The edema fluid was obtained by aspiration of tracheal contents through the endotracheal tube. There was no roentgenographic evidence of a pneumonic process at the time edema fluid was obtained.

Clinical, spirometric, hemodynamic, and gas exchange data are summarized in Tables 1 and 2 along with EF/P ratio.

**Results**

Clinical data from patients studied are summarized in Table 1 along with fluid administration, urine output, and perioperative complications. The PAP ranged from 18 to 28 mm Hg in hemodynamic, gas exchange, and protein content data as summarized in Table 2. Pulmonary capillary wedge pressure was normal and cardiac output normal or high in all patients coincident with pulmonary edema. Total protein in the tracheal aspirate ranged from 2.5 to 4.3 g/dl and the EF/P ranged between 0.60 to 0.84. Calculated Pc was higher than measured PCW in all patients. Calculated shunt fraction ranged from 25 to 50 percent. All patients ultimately recovered from acute postoperative lung injury.

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Table 1—Clinical Data

<table>
<thead>
<tr>
<th>Type of Surgery</th>
<th>Preoperative Spirometry</th>
<th>Amount of Fluid Intra-op, ml</th>
<th>Fluid 1st Post Op Day, ml</th>
<th>Fluid 2nd Post Op Day, ml</th>
<th>First 24 Hour Urine Output</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonectomy</td>
<td>FEV, 2.44 (77%) FVC 3.12 (79%)</td>
<td>3750</td>
<td>1000</td>
<td>500</td>
<td>1800</td>
<td>Bronchopleural Fistula Nosocomial pneumonia Nosocomial pneumonia Nosocomial pneumonia</td>
</tr>
<tr>
<td>Pneumonectomy</td>
<td>FEV, 1.47 (67%) FVC 2.6 (70%)</td>
<td>2100</td>
<td>1800</td>
<td>800</td>
<td>1000</td>
<td>Nosocomial pneumonia Nosocomial pneumonia Nosocomial pneumonia</td>
</tr>
<tr>
<td>Lobectomy</td>
<td>FEV, 2.4 (77%) FVC 2.9 (76%)</td>
<td>1800</td>
<td>900</td>
<td>500</td>
<td>850</td>
<td>Empyema Nosocomial pneumonia</td>
</tr>
<tr>
<td>Lobectomy</td>
<td>FEV, 2.9 (80%) FVC 3.0 (75%)</td>
<td>1500</td>
<td>800</td>
<td>500</td>
<td>900</td>
<td>Nosocomial pneumonia</td>
</tr>
<tr>
<td>Lobectomy</td>
<td>FEV, 2.67 (75%) FVC 2.12 (69%)</td>
<td>1950</td>
<td>900</td>
<td>600</td>
<td>1150</td>
<td>Nosocomial pneumonia</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Five cases of noncardiogenic pulmonary edema following lung resection are reported here. Noncardiac origin of the pulmonary edema is suggested by the presence of normal filling pressure, normal or high cardiac output, mean EF/P of 0.6 or greater, and roentgenographic evidence of diffuse interstitial pulmonary edema.

In normal lungs, the lymphatics and balance of transcapillary pressures control interstitial fluid accumulation. The sump effect of the pulmonary lymphatics and the favorable balance of hydrostatic and oncotic pressures provide this safety factor. In the postpneumonectomy state, the lymphatic pump capacity is markedly reduced. The magnitude of reduction corresponds to the amount of lung removed. After right pneumonectomy, lymphatic pump capacity is reduced by 50 percent.

Alteration in hemodynamics of the pulmonary circulation associated with lung resection may also play a significant role in the genesis of lung edema. Following pneumonectomy, the entire cardiac output is accommodated in the vascular bed of the remaining lung. The increased flow plus excessive fluid administration results in increases in PAP. The increase in PAP causes a higher upstream pressure at the arterial end of the pulmonary capillary, thus increasing Pc and filtration pressure. The increased flow and the associated increase in linear velocity maintains patency of capillaries. Thus, the increased protein content in the tracheal aspirate may be due to mechanical forces opening the endothelial junction further facilitating protein escape.

Our patients demonstrated higher than normal PAP. This may be due to increased pulmonary flow and pulmonary artery vasoconstriction associated with hypoxia. The calculated Pc was higher than measured PCW in all patients. On the other hand, under normal conditions, when pulmonary vascular resistance is low (and PAP normal), the Pc will be very nearly equal to the PCW. The PCW could be spuriously low due to balloon obstruction of the proximal pulmonary artery. The combination of increased Pc and excessive fluid administration could produce pulmonary edema.

The high EF/P in our patients suggests that the observed pulmonary edema was in part due to altered alveolar capillary membrane permeability. Previous reports have confirmed that determination of EF/P is useful in distinguishing pulmonary edema secondary to increased hydrostatic pressure from that resulting from altered permeability. A EF/P of ≥ 0.6 in the absence of clinical or hemodynamic evidence of cardiovascular disease is suggestive of increased permeability edema.

In conclusion, following lung surgery patients may develop pulmonary edema in the immediate postoperative period. The observed pulmonary edema seems to be the result of a combination of two factors. One factor is hydrostatic, related to increases in pulmonary

Table 2—Hemodynamics/Gas Exchange/Protein Data

<table>
<thead>
<tr>
<th>PAP</th>
<th>PCW</th>
<th>Pc</th>
<th>CO L/min</th>
<th>Fio2</th>
<th>PEEP</th>
<th>Pao2</th>
<th>QS/QT %</th>
<th>EF/P Concent g/dl</th>
<th>EF/P Ratio</th>
<th>Days on Ventilator</th>
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</thead>
<tbody>
<tr>
<td>28</td>
<td>13</td>
<td>19</td>
<td>6.2</td>
<td>0.8</td>
<td>15</td>
<td>112</td>
<td>27</td>
<td>4.3/6.5</td>
<td>0.66</td>
<td>33</td>
</tr>
<tr>
<td>18</td>
<td>5</td>
<td>10.2</td>
<td>9.5</td>
<td>0.6</td>
<td>15</td>
<td>53</td>
<td>52</td>
<td>2.5/4.2</td>
<td>0.60</td>
<td>28</td>
</tr>
<tr>
<td>25</td>
<td>4</td>
<td>12.4</td>
<td>6.1</td>
<td>1.0</td>
<td>20</td>
<td>212</td>
<td>29</td>
<td>3.5/4.3</td>
<td>0.81</td>
<td>15</td>
</tr>
<tr>
<td>18</td>
<td>6</td>
<td>10.8</td>
<td>5.1</td>
<td>0.8</td>
<td>12</td>
<td>206</td>
<td>25</td>
<td>2.7/3.8</td>
<td>0.71</td>
<td>12</td>
</tr>
<tr>
<td>22</td>
<td>8</td>
<td>13.6</td>
<td>5.2</td>
<td>0.8</td>
<td>10</td>
<td>105</td>
<td>37</td>
<td>4.1/4.9</td>
<td>0.64</td>
<td>18</td>
</tr>
</tbody>
</table>

**CHEST / 98 / 5 / NOVEMBER, 1990 / 1217**

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capillary pressure. A contributing element to increased \( P_e \) may be aggressive fluid therapy. The second factor, as demonstrated by an increased \( \Delta F/P \), is injury to the alveolar capillary membrane. An \( \Delta F/P \) \( \approx 0.6 \) in the presence of interstitial pulmonary edema, normal or high cardiac output, and in the absence of elevated filling pressure, strongly suggests that increased permeability of the alveolar capillary membrane plays a central role in the genesis of pulmonary edema following lung resection.

REFERENCES

Permeability Pulmonary Edema after Lung Resection (Mathru et al)