Increased Neutrophils in Bronchoalveolar Lavage Fluids from a Patient with Pulmonary Edema Associated with Pheochromocytoma

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Abstract

Pulmonary edema, both cardiogenic and noncardiogenic, has been reported as a manifestation of pheochromocytoma. We report a patient with pheochromocytoma complicated by acute pulmonary edema that appeared clinically noncardiogenic. The patient had an uncomplicated course and rapid resolution of pulmonary edema. Bronchoalveolar lavage fluids (BALF) showed a marked accumulation of neutrophils, suggesting involvement of neutrophil-mediated lung injury in noncardiogenic pulmonary edema associated with a pheochromocytoma. (Internal Medicine 43: 1194–1197, 2004)

Key words: pheochromocytoma, noncardiogenic pulmonary edema, bronchoalveolar lavage fluid, leukocytosis

Introduction

Pheochromocytoma is usually associated with paroxysmal hypertension, excessive sweating, headache and palpitation (1). We report a patient with pheochromocytoma, who showed acute respiratory distress with no signs of cardiac dysfunction. Although cardiogenic pulmonary edema has been described frequently as a presenting feature of pheochromocytoma, noncardiogenic pulmonary edema is an exceedingly rare manifestation of pheochromocytoma. Only ten cases including the current case have been reported (Table 1) (2–10). The mechanisms underlying the development of noncardiogenic pulmonary edema may include pulmonary capillary membrane damage and catecholamine constriction of capillary venules. To the best of our knowledge, this is the first report of increased neutrophils in the lung of a patient with pheochromocytoma complicated by acute pulmonary edema. Increased neutrophils in the lung may contribute to the pathogenesis of noncardiogenic pulmonary edema in patients with pheochromocytoma.

Case Report

A 63-year-old woman was admitted to the hospital complaining of rapidly progressive dyspnea, nausea and vomiting. The patient did not have previous respiratory disease, symptoms of chronic myocardial dysfunction or hypertension. On arrival, the patient was markedly dyspneic and cyanotic; heart rate was 130 beats/min, respiratory rate was 48 breaths/min, blood pressure was 160/100 mmHg, and temperature was 34.8°C. Respiratory crackles were heard over both lung fields. Initial laboratory findings included the following: leukocyte count, 24,800 cells/µl with 78% polymorphonuclear cells; LDH, 1,084 IU/l (normal, 100 to 450); creatine kinase, 162 IU/l (normal, 30 to 180); urea nitrogen, 43 mg/dl; creatinine, 2.6 mg/dl; C-reactive protein, 0.1 mg/dl. The urine was positive (+) for protein. Room-air arterial blood gas analysis results were as follows: pH, 7.37; Pco₂, 33.0 mmHg; Po₂, 49.6 mmHg; bicarbonate, 19.4 mmol/l. ECG showed sinus tachycardia with no signs of ischemia. Chest radiography (Fig. 1) showed bilateral infiltrates without cardiomegaly. Chest CT scans (Fig. 2) showed bilateral infiltrates with ground-glass opacity mixed with irregular linear opacities and airbronchogram. The patient was treated for presumed severe community-acquired pneumonia, with anti-
biotics and prednisolone (40 mg/day) for 2 days. Neither cardiotonic nor diuretic drugs were administered. On the second hospital day, chest radiography and CT scans showed near complete resolution of the pulmonary infiltrates. Renal dysfunction including elevated levels of urea nitrogen and creatinine, and proteinuria also returned to normal on the third hospital day. Cardiac function tests (echocardiography, 99mTc-cardiac scintigraphy and Holter 24-hour ECG) revealed no signs of cardiac dysfunction. Results of BALF on the third hospital day were as follows: total cells, 3.39×10^5/ml; alveolar macrophages, 19.4%; neutrophils, 70.2%; lymphocytes, 9.3%; eosinophils, 0.2% (Fig. 3). A culture of BALF was sterile. A 24-hour urine collection showed markedly elevated levels of catecholamines including norepinephrine (1,027.3 μg/24 hours; normal, 26 to 121), epinephrine (11.6 μg/24 hours; normal, 3 to 15), dopamine (916.5 μg/24 hours; normal, 190 to 740), metanephrine (0.28 mg/24 hours; normal, 0.05 to 0.23), normetanephrine (15.82 mg/24 hours; normal, 0.07 to 0.26), and vanillylmandelic acid (52.6 mg/24 hours; normal, 1.3 to 5.1). Abdominal CT (Fig. 4) showed an 8.0×4.0-cm left adrenal mass. The diagnosis of pheochromocytoma was confirmed by ^123^I-metaiodobenzylguanidine scintigraphy. The patient underwent an operation, and a pheochromocytoma of 8 cm was removed from the left adrenal gland. The patient has been free of symptoms to date.

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**Table 1. Reported Cases of Pheochromocytoma Manifested as Noncardiogenic Pulmonary Edema**

<table>
<thead>
<tr>
<th>Year</th>
<th>Author</th>
<th>Sex</th>
<th>Age</th>
<th>Hemodynamics</th>
<th>Cathecholamine (Normal)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1975</td>
<td>Scully et al</td>
<td>M</td>
<td>52</td>
<td>PCWP 5 mmHg</td>
<td>U-VMA 30–116 mg/g of CR (0–7)</td>
<td>Death due to pulmonary edema</td>
</tr>
<tr>
<td>1977</td>
<td>Munk et al</td>
<td>F</td>
<td>28</td>
<td>Not done</td>
<td>U-NE 126–210 μg/day (&lt;50)</td>
<td>Discharge after operation</td>
</tr>
<tr>
<td>1978</td>
<td>Naeije et al</td>
<td>F</td>
<td>26</td>
<td>Not done</td>
<td>U-E 61–82 μg/day (&lt;15)</td>
<td>Discharge after operation</td>
</tr>
<tr>
<td>1985</td>
<td>Feldman</td>
<td>F</td>
<td>29</td>
<td>PCWP 5 cmH₂O</td>
<td>U-NE 188–432 μg/day (20–1120)</td>
<td>Discharge after operation</td>
</tr>
<tr>
<td>1986</td>
<td>de Leeuw et al</td>
<td>M</td>
<td>40</td>
<td>PCWP 2 mmHg</td>
<td>U-VMA 2.7 mmol/mmol of CR (&lt;2.5)</td>
<td>Discharge after operation</td>
</tr>
<tr>
<td>1987</td>
<td>O’Hickey et al</td>
<td>M</td>
<td>19</td>
<td>PCWP 5 mmHg</td>
<td>U-MN 30.7 mmol/day (&lt;5.5)</td>
<td>Death due to DIC</td>
</tr>
<tr>
<td>1987</td>
<td>Reuse et al</td>
<td>F</td>
<td>48</td>
<td>PCWP 5 mmHg</td>
<td>U-NE 118–432 μg/day (50–1120)</td>
<td>Operation</td>
</tr>
<tr>
<td>1993</td>
<td>Joshi et al</td>
<td>F</td>
<td>36</td>
<td>PCWP 5 mmHg</td>
<td>U-NE 121 μg/day (&lt;36)</td>
<td>Discharge after operation</td>
</tr>
<tr>
<td>1999</td>
<td>Okada et al</td>
<td>M</td>
<td>30</td>
<td>Not done</td>
<td>U-NE 124 μg/day (&lt;36)</td>
<td>Operation</td>
</tr>
<tr>
<td>2004</td>
<td>Sukoh et al</td>
<td>F</td>
<td>63</td>
<td>Not done</td>
<td>U-NE 1,027.3 μg/day (26.0–121.0)</td>
<td>Discharge after operation</td>
</tr>
</tbody>
</table>


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**Figure 1.** Chest radiography showed bilateral infiltrates without cardiac enlargement.
Here, we report increased neutrophils in the lung of a patient with acute pulmonary edema associated with pheochromocytoma. Although cardiogenic pulmonary edema cannot be excluded without the measurement of pulmonary artery wedge pressure, we speculate that a noncardiogenic form of hydrostatic pulmonary edema developed in the present patient. A hydrostatic cause is supported by the sudden onset with no signs of cardiac dysfunction and the rapid reversal of symptoms.

There have been several reports of a predominant increase of neutrophils in BAL fluids obtained from patients with acute lung injury and acute respiratory distress syndrome (11). Increased neutrophils in the present case suggest that neutrophil-mediated injury was involved in the noncardiogenic pulmonary edema associated with the pheochromocytoma. The importance of endothelial injury and increased vascular permeability in the formation of noncardiogenic pulmonary edema has been well established (11). The main pathogenic mechanism underlying noncardiogenic pulmonary edema associated with pheochromocytoma appears to be increased permeability of pulmonary capillaries, due to injury by sudden pulmonary hypertension and increased pulmonary blood volume (6). Catecholamines can cause leukocytosis (12). Thus, excess catecholamines may be at least partly responsible for increased neutrophils in the lung of the present case. The present findings suggest that increased neutrophils have a toxic effect on pulmonary capillary endothelial cells, increasing permeability.

An association has been demonstrated with acute renal failure and noncardiogenic acute respiratory distress syndrome (13), and the laboratory findings in the present case suggested the presence of renal insufficiency on admission. Therefore, it is important to note that systemic effects of...
renal dysfunction, such as uremic toxins, might play a role in the increased susceptibility of the lung to injury in this case, although these abnormalities were very mild and transient.

In conclusion, significant neutrophil accumulation in the lung was found in the present patient with pheochromocytoma complicated by acute pulmonary edema. Although the pathophysiologic significance of pulmonary neutrophil accumulation remains uncertain, increased neutrophils may contribute to the pathogenesis of respiratory distress associated with pheochromocytoma, by increasing lung vascular protein permeability and promoting lung edema.

References


