

# Cocaine-induced Fatal Acute Eosinophilic Pneumonia: A Case Report

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## ABSTRACT

We present a case of fatal acute eosinophilic pneumonia clinically simulating acute respiratory distress syndrome in a 32-year-old man. Clinical, radiographic, and histologic features of this entity are discussed along with a review of the literature.

## INTRODUCTION

Acute eosinophilic pneumonia (AEP) is an uncommon inflammatory condition of the lung that is considered part of a heterogeneous group of diseases known as 'eosinophilic lung disease.'<sup>1,2</sup> These diseases can affect the airways, vasculature, or lung parenchyma. Eosinophilic pneumonia specifically affects the lung parenchyma. Three clinical subtypes of eosinophilic pneumonia have been described, including acute eosinophilic pneumonia (AEP), chronic eosinophilic pneumonia (CEP), and drug-induced eosinophilic pneumonia (drug-EP).<sup>1</sup> AEP, first described by Badesch et al,<sup>3</sup> has a variable clinical presentation that ranges from mild respiratory symptoms often associated with fever to acute life-threatening respiratory failure.<sup>4</sup> Its etiology remains unknown. A strong correlation to recent onset of cigarette smoking and concurrent 'crack' cocaine abuse has been identified.<sup>4,5</sup> We present a case of fatal acute respiratory failure in a 32-year-old man with acute exposure to cocaine. The clinical presentation was consistent with acute respiratory distress syndrome. Subsequent autopsy findings were conclusive for AEP.

## CASE HISTORY

The deceased was a 32-year-old male laborer at a local industrial machinery manufacturing plant who, by family history, was in his usual state of good health. In addition to his occupation, family members reported

that his health-risk factors also included smoking and alcohol consumption. On the day prior to his death he was reported to have been out late drinking; family members admitted that on at least 1 occasion during the evening he used cocaine. After returning home with his girlfriend in the early morning hours on the day of death, the girlfriend reported him to be awake, conversant, and with no complaints. Soon thereafter, at approximately 2:30 AM, she stated that he passed out while sitting at the computer. At this point she remembered him to be breathing without difficulty and simply appeared intoxicated. He was repositioned to his side and left to sleep it off.

At approximately 8:00 AM the girlfriend found him 'unresponsive, blue, and barely breathing.' Basic life support was started and an ambulance was summoned. Within 6 minutes he was being attended by Manitowoc Fire Department paramedics. The initial advance life support found the patient to be in a bradycardic rhythm with small pupils and with a labored respiratory effort. A peripheral line was established, supplemental oxygen was administered and he received 2 doses of Narcan. This resulted in an increase in pulse rate and an increase in the spontaneous respiratory effort. No elevation in temperature was noted and no rhonchi were identified on auscultation of the lungs.

During transport, his condition deteriorated, requiring ACLS protocol with intubation and the use of atropine and epinephrine for treatment of bradycardia and hypotension. Immediately on arrival to the emergency department, the patient received aggressive resuscitation efforts. An arterial line was placed to monitor accurate blood pressures. An arterial blood gas determination at this time while on 100% oxygen delivered via endotracheal tube showed a pH of 6.95,  $\text{paO}_2$  of 40mm Hg, and a  $\text{paCO}_2$  of 80mm Hg. A portable chest radiograph (see Figures 1 and 2) showed the endotracheal tube tip to be just above the level of the carina. The lung parenchyma showed bilateral alveolar-interstitial infiltrates suggestive of pulmonary edema.

Multiple fluid boluses of normal saline were ad-

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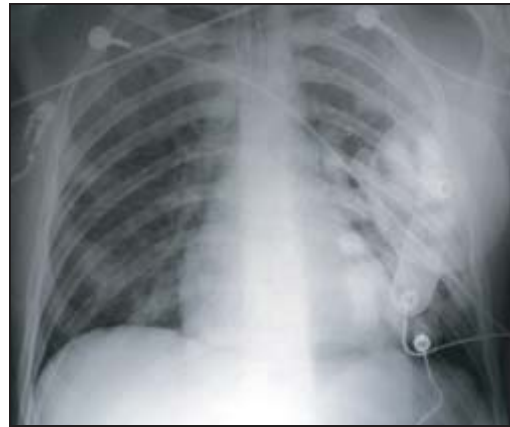
ministered and an ampule of sodium bicarbonate was given once the profound acidosis was identified. A Dopamine infusion was also begun but the patient remained hypotensive. Despite aggressive resuscitative efforts, within 15 minutes a repeat blood gas assessment showed the patient deteriorating to a pH of 6.84 with a  $paO_2$  of 28mm Hg and a  $paCO_2$  of 87.5mm Hg. The patient subsequently deteriorated into ventricular fibrillation requiring multiple defibrillation attempts and the administration of antiarrhythmic medication. Spontaneous circulation was obtained during the course of the resuscitation effort but the patient remained profoundly hypoxemic and acidotic. Additional lab values showed a Troponin I within reference range, a complete blood cell count that showed a white blood cell count of 11.4 with a normal differential, a hemoglobin of 15.6 g/DL and a hematocrit of 45.2%. Serum electrolytes displayed a marginal elevation in blood sugar at 149 with the other values within reference range. A blood alcohol level was 0.088 and a urine drug screen was positive only for cocaine. The electrocardiogram displayed sinus bradycardia with widened QRS complexes and diffuse acute ischemic changes. A bedside ultrasound showed no evidence of pericardial effusion. The perfusing rhythm was short lived and the patient progressed to asystole. Despite over an hour of intensive resuscitative efforts, the patient progressed to refractory ventricular fibrillation and subsequent asystole. Approximately 1 hour and 15 minutes after arrival in the emergency department, he was pronounced dead with the presumed clinical diagnosis of diffuse alveolar damage (ARDS). The Manitowoc County Coroner requested an autopsy.

### *Radiographic Correlation*

A portable AP chest radiograph (Figures 1 and 2) obtained at the time of presentation to the emergency department displayed significant bilateral alveolar-interstitial densities with an unremarkable cardiac silhouette.

### *Gross Autopsy and Microscopic Tissue Correlation*

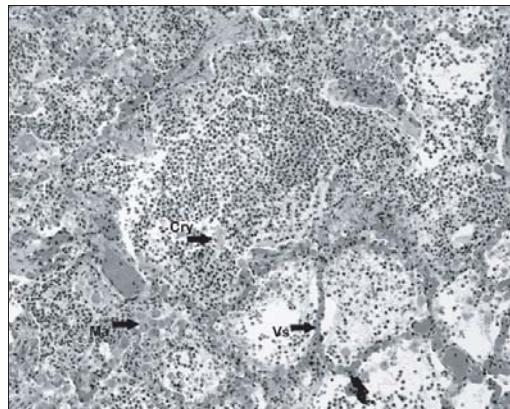
The autopsy revealed an in situ anatomy that was unremarkable. The organs by systematic evaluation were negative for significant gross pathology with the exception of the pulmonary system. No airway obstruction indicative of vomitus was present but the lungs were heavy (right lung 1430 grams; left lung 1220 grams) and showed moist frothy to firm cut surfaces. Histologic evaluation of tissue sections from both the right and left lungs (Figures 3, 4, and 5) in all lung lobes showed no evidence for ARDS. Instead the sections showed pulmonary vascular congestion (Vs) with alveolar spaces distended by a mixed in-



**Figure 1.** AP portable chest radiograph with bilateral increased interstitial densities.

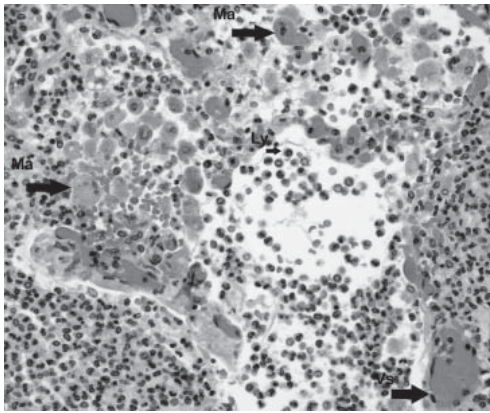


**Figure 2.** AP portable chest radiograph detail.

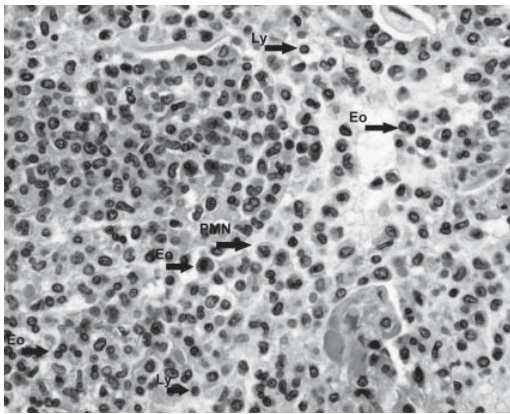


**Figure 3.** Low power of lung tissue showing alveolar capillary congestion (Vs), mixed alveolar inflammation, and birefringent material (Cry).

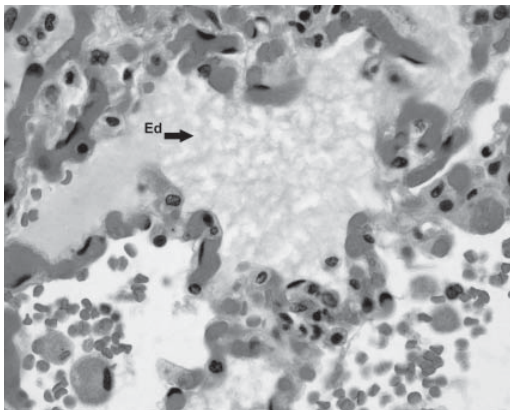
flammatory infiltrate and occasional birefringent foreign material (Cry). The predominant inflammatory cells were eosinophils (Eo) in varying stages of degranulation and degradation on a background of occasional macrophages (Ma), polymorphonuclear leukocytes (PMN), and small lymphocytes (Ly).



**Figure 4.** Medium power showing ectatic alveolar capillaries (Vs) and alveolar spaces with hemosiderin-laden macrophages (Ma), eosinophils, and lymphocytes.



**Figure 5.** High power of distended alveolar space containing eosinophils (Eo) in various stages of degranulation and occasional polymorphonuclear leukocytes (PMN) and lymphocytes (Ly).



**Figure 6.** Other alveolar spaces displayed vascular congestion with edema (Ed).

**DISCUSSION**

Acute eosinophilic pneumonia is an illness with a variable prodrome of hours to several days. Individuals may exhibit fever, cough, and pleuritic chest pain and many have hypoxemia often requiring mechanical ventilation for support.<sup>1</sup> The alveolar space to arterial blood oxygen gradient (A-a) is commonly greater than 40 mm Hg.<sup>4</sup> Peripheral blood counts may or may not show a concurrent leukocytosis and peripheral eosinophilia.<sup>4</sup> Chest radiographs show alveolar-interstitial infiltrates affecting the entire lung parenchyma. Pleural effusions are common. Chest computed tomography scan may show diffuse areas of ground-glass attenuation sometimes with well-defined nodular changes. Published diagnostic criteria<sup>4</sup> include the following:

- Acute onset of symptoms of less than 7 days before presentation.
- Fever (greater than 99° F.
- Bilateral chest infiltrates on chest radiographs.
- Severe hypoxemia: PaO<sub>2</sub> on room air of <60 mm Hg and oxygen saturation on room air of <90% or A-a gradient of greater than 40 mm Hg.
- Lung eosinophils: bronchoalveolar lavage differential with >25% eosinophils or predominance of eosinophils on open lung biopsy.
- No history of hypersensitivity to drugs, no historical or laboratory evidence of infection, and no other known cause of acute eosinophilic lung disease.

Even with this constellation of features the diagnosis is difficult unless AEP is considered in the differential diagnosis. Bronchoalveolar lavage is perhaps the most clinically useful diagnostic test, frequently showing >25% eosinophils.<sup>4,8,9</sup>

The exact cause of AEP remains unknown but a positive correlation with the use of crack cocaine has been identified.<sup>4,6-9</sup> Initiation of AEP is thought to be a type I hypersensitivity reaction with the acute phase consisting of antigen exposure, mast cell activation with the release from mast cells of VEGF, IL-5, IL-6, and IL-8. Elaboration of these cytokines results in immediate vascular dilation with an increase in the permeability of the pulmonary capillaries. Bronchial smooth muscle contraction and alveolar space edema ensue. Four to 20 hours after initiation of the hypersensitivity reaction during the so-called ‘late phase,’ eosinophils, neutrophils, macrophages, and lymphocytes are recruited into bronchial airways and alveolar spaces. IL-5 activates eosinophils causing degranulation with further tissue damage but without the formation of hyaline membranes characteristic of ARDS. In many cases

of AEP the alveolar spaces show Prussian blue staining macrophages (hemosiderin) that some investigators feel is evidence for microvasculature damage and perhaps evidence of remote damage.<sup>6</sup> Indeed our case displayed Prussian blue positive macrophages within the alveolar spaces associated with a predominance of eosinophils admixed with occasional lymphocytes, polymorphonuclear leukocytes and recently extravasated red blood cells. As in cases of ARDS, the treatment of AEP is directed toward the correction of emergent acid/base abnormalities in conjunction with respiratory and cardiac support as indicated by clinical and laboratory parameters. Initial treatment in patients suspected of AEP should also include interrupting the hypersensitivity reaction with parenteral steroids. While there is some evidence that aggressive therapy with extracorporeal membrane oxygenation (ECMO) in patients with acute respiratory failure may be beneficial, the use of ECMO is still controversial.<sup>10</sup>

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## REFERENCES

1. Ribeiro J, Fischer G. Eosinophilic lung diseases. *Paediatr Respir Rev.* 2000;3:278-284.
2. Alberts WM. Eosinophilic interstitial lung disease. *Curr Opin Pulm Med.* 2004;10:419-442.
3. Badesch DB, et al. Acute eosinophilic pneumonia: a hypersensitivity phenomenon? *Am Rev Respir Dis.* 1989;139:249-252.
4. Pope-Harmon, et al. Acute eosinophilic pneumonia: a summary of 15 cases and review of the literature. *Medicine.* 1996;75:334-342.
5. Shorr AF, et al. Acute eosinophilic pneumonia among us military personnel deployed in or near Iraq. *JAMA.* 2004;292(24):2997-3005.
6. Haim DY, et al. Pulmonary complications of crack cocaine: a comprehensive review. *Chest.* 1995;107:233-240.
7. Baldwin G, et al. Evidence of chronic damage to the pulmonary microcirculation in habitual users of alkaloidal ("crack") cocaine. *Chest.* 2002;121:1231-1238.
8. Oh PI, Balter MS. Cocaine induced eosinophilic lung disease. *Thorax.* 1992;47(6):478-479.
9. Strong DH, et al. Eosinophilic "empyema" associated with crack cocaine. *Thorax.* 2003;58:823-824.
10. Hemmila MR, Napolitano LM. *Crit Care Med.* 2006;34(9Suppl):S278-290.

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