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CASE REPORT

Severe Presentation of Acute Eosinophilic Pneumonia Possibly Secondary to Recent E-Cigarette Use

Jae Y. Choi, BS[1]; and Matthew W. Fei, MD[2]

[1]Elson S. Floyd College of Medicine, Washington State University, Spokane, Washington

[2]Kaiser Permanente Bellevue Medical Center, Washington, Bellevue, Washington

Keywords

Bronchoalveolar lavage, Hypoxia, Pulmonary diseases, Pneumonia, Eosinophils, Ventilators, Eosinophilia, Respiratory failure, Fevers, Bronchoscopy, Eosinophilic pneumonia, e-cigarettes, Vaping-associated lung injury (EVALI)

Abstract

A 52-year-old man with type 2 diabetes mellitus presented with fever and hypoxemic respiratory failure requiring intubation. He had no history of pulmonary disease but recently started smoking nicotine-containing electronic cigarettes (e-cigarettes) after 10 years of tobacco abstinence. He had diffuse bilateral ground-glass opacities on chest imaging, 11% peripheral eosinophilia (absolute eosinophil count 1300/μL), and 50% eosinophilia in the bronchoalveolar lavage fluid without evidence of bacterial, viral, fungal, or parasitic infection. Hypoxia and pulmonary infiltrates rapidly resolved after initiation of high-dose corticosteroids after bronchoscopy. A diagnosis of acute eosinophilic pneumonia was made, possibly secondary to recent e-cigarette use.

Background

E-cigarette or vaping-associated lung injury (EVALI) is a well-recognized syndrome of pulmonary disease after a 2019 outbreak that led to hospitalizations of more than 2800 patients in the United States (1). Although cigarette use is a reported risk factor of acute eosinophilic pneumonia (AEP), it appears that AEP is a rare presentation of EVALI because there was no case of AEP described in a recent large case series of EVALI (2, 3). AEP is characterized by an acute febrile illness that typically lasts less than 4 weeks, hypoxemic respiratory failure, diffuse pulmonary infiltrates, and eosinophil count greater than 25% in bronchoalveolar lavage (BAL) fluid (4). Although AEP can be idiopathic, known causes of AEP include various infections, respiratory exposures, and medications such as daptomycin, venlafaxine, and mesalamine (5–8). Because e-cigarette smoking, or vaping, is widely perceived as a safer alternative to conventional smoking by the general public, clinicians need a high clinical index of suspicion for patients presenting with febrile hypoxemic respiratory failure who smoke e-cigarettes.

Objective

We present a severe case of AEP associated with the recent use of e-cigarettes to promote a greater clinical index of suspicion for AEP in the setting of e-cigarette use.

Case Report

A 52-year-old Hispanic man with type 2 diabetes mellitus and no previous history of pulmonary disease presented to the emergency department with chief symptoms of shortness of breath and fever. Shortness of breath had worsened over the past 3 weeks, with the onset of symptoms occurring a few days after smoking a nicotine-containing e-cigarette for the first time after 10 years of tobacco abstinence. His only prescription medication was metformin. He did not report ingestion, inhalation, or injection of any recreational drugs. In the emergency department, he was found to have a blood pressure of 90/50 mm Hg, heart rate of 72 beats/min, temperature of 38.3 °C, and peripheral O_2 saturation of 89% on room air. Findings of a physical examination revealed a well-nourished man with hypotension, labored breathing, dry mucosa, and trace edema in the lower extremities bilaterally. Chest radiograph before intubation showed diffuse

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Corresponding Author
Jae Y. Choi, BS; Elson S. Floyd College of Medicine, Washington State University, 412 E. Spokane Falls Blvd, Spokane, WA 99202; e-mail, jchoi.micro@gmail.com.

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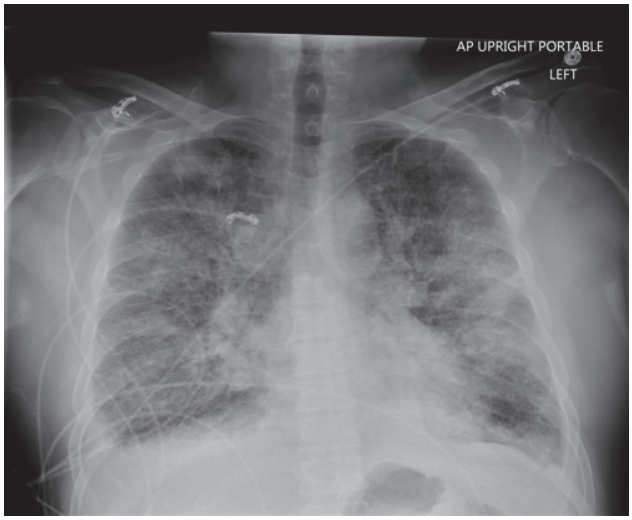

Figure 1. **Chest radiograph demonstrating diffuse bilateral infiltrates.**

bilateral infiltrates that resembled cardiogenic pulmonary edema (Figure 1); however, brain natriuretic peptide was 6.358 pmol/L (reference range 5.78–57.8 pmol/L), and findings of an echocardiogram showed normal cardiac function. Fever and elevated leukocyte count of 20 000 cells/μL with neutrophil predominance was suggestive of infectious cause, although an 11% eosinophilia with absolute eosinophil count of 1300 cells/μL also was noted.

Empiric antibiotics including ceftriaxone and azithromycin were administered. Respiratory virus panel including SARS-CoV-2, influenza, and test results for HIV, legionella, streptococcus pneumonia, *Coccidioides*, and *Strongyloides* infection were negative. Computed tomography scan of the chest showed bilateral ground-glass opacities and interlobular septal thickening, resembling a "crazy paving" appearance (Figure 2). The patient initially maintained peripheral O_2 saturation greater than 90% on a high-flow nasal cannula with fraction of inspired oxygen (FiO_2) of 0.7. However, he progressively worsened and developed hypoxemia less than 88% despite maximal oxygen

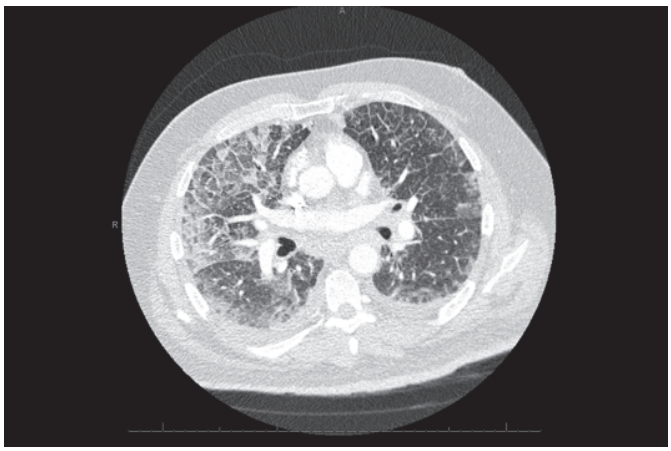

Figure 2. **Chest computed tomography scan demonstrating diffuse bilateral ground-glass opacities, interlobular septal thickening, and "crazy-paving" pattern.**

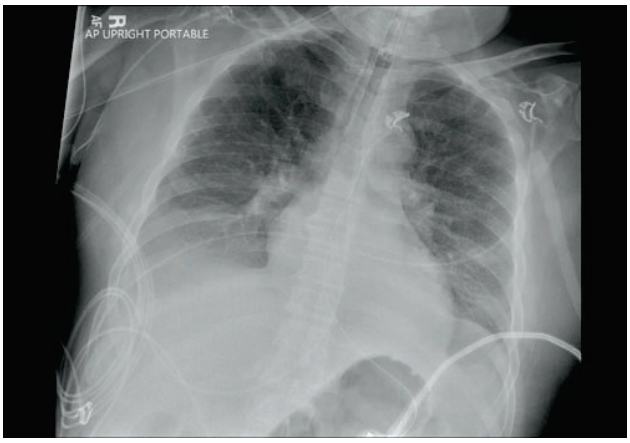

Figure 3. **Chest radiograph on day 3 of mechanical ventilation demonstrating near resolution of diffuse bilateral infiltrates.**

supplementation, which led to intubation and mechanical ventilation using pressure-regulated volume control. Initially, a tidal volume was set at 460 mL (6 mL per kilogram of ideal body weight) with an FiO_2 of 1.0, a positive end-expiratory pressure of 12 cmH_2O, with a peak inspiratory pressure of 28 cmH_2O. Arterial blood gas at the time of intubation revealed a compensated respiratory acidosis with a pH of 7.34 and A-a gradient of 522 mm Hg. Fiberoptic bronchoscopy and BAL were performed, which showed normal endobronchial anatomy with moderate nonpurulent secretions. BAL fluid cell count and differential showed 50% eosinophils. BAL fluid was sent for bacterial, fungal, and AFB cultures, ova and parasite stain, and *Mycobacterium tuberculosis* and fungal polymerase chain reaction, of which all results were negative. Twelve hours after initiation of mechanical ventilation, FiO_2 was titrated to 0.55 with a peak inspiratory pressure of 25 cmH_2O and a plateau pressure between 19 and 23 cmH_2O. Within 24 hours of intubation and initiation of high-dose steroids, a repeat arterial blood gas revealed a normalized pH and an improved A-a gradient of 262 mm Hg. Acute fever, diffuse pulmonary infiltrates, hypoxemic respiratory failure, eosinophilia greater than 25% in the BAL fluid, and negative microbiology suggested the diagnosis of acute eosinophilic pneumonia associated with a recent history of e-cigarette use. Hypoxemia and dyspnea rapidly improved with methylprednisolone, 125 mg twice a day. Over the next 72 hours, FiO_2 was gradually decreased, and the patient was extubated. A chest radiograph on day 3 of mechanical ventilation showed near resolution of diffuse infiltrates previously seen (Figure 3).

Discussion

AEP was first described by Dr. James Allen and colleagues at Ohio State University Hospital in 1989 when a small group of patients presented with acute febrile illness, hypoxemia, diffuse pulmonary infiltrates, eosinophil count greater than 25% in BAL fluid, and no evidence of infection, with rapid resolution of illness after treatment with corticosteroids (4). AEP is an uncommon entity that predominantly affects individuals younger than 50 years of age and is more commonly seen in men than in women. Historically, AEP has been associated with inhalation of toxic fumes among first responders and military

personnel as well as first-time cigarette smokers (9). It should be noted that although EVALI is a well-recognized syndrome of pulmonary disease described after a 2019 outbreak in the United States, EVALI presenting as AEP is uncommon and is limited to a few case reports (2, 3, 10–13). In contrast, there is a more established link between the recent use of conventional cigarette smoking and the development of AEP (5). The mechanism by which cigarette smoke or other inhalants induce AEP is not fully understood, but it is believed that toxins induce an interleukin (IL)-5–mediated inflammatory response in the alveoli, as evidenced by high IL-5 concentrations in BAL fluid in patients with AEP (14). A recent in vitro analysis of BAL fluid from patients with AEP showed that multiple cytokines such as IL-4, IL-5, IL-13, vascular cell adhesion molecule-1, and CC chemokine receptor ligands are involved in migration and accumulation of eosinophils across endothelial cells, suggesting the innate immune system, rather than adaptive immune system, is involved in the pathogenesis of AEP (15).

This case highlights a patient with severe AEP, most likely from nicotine-containing e-cigarette use, who required intubation and mechanical ventilation in the intensive care unit. AEP is a challenging diagnosis to confirm because the initial clinical presentation can resemble bacterial, viral, fungal, or parasitic pulmonary infections and the diagnostic criteria require the exclusion of infectious cause. Laboratory tests to exclude infection may take several days or longer to result while patients continue to clinically worsen. A prompt bronchoscopy and analysis of BAL fluid are essential for the diagnosis of AEP, and clinicians should consider performing bronchoscopy in the setting of an appropriate clinical presentation, as treatment with corticosteroids can achieve a rapid clinical improvement.

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