Acute Eosinophilic Pneumonia Due to Vaping-Associated Lung Injury

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ABSTRACT

A case is described of a 29-year-old female who presented with acute hypoxic respiratory failure due to acute eosinophilic pneumonia, associated with the use of electronic cigarettes to vape tetrahydrocannabinol (THC), together with the contemporary clinical understanding of the syndrome of electronic-cigarette associated lung injury (EVALI). Attention is drawn to acute eosinophilic pneumonia as a potential consequence of vaping-associated lung injury to understand the diagnostic evaluations and therapeutic interventions for acute eosinophilic pneumonia associated with vaping THC.

Keywords: acute hypoxic respiratory failure, acute eosinophilic pneumonia, tetrahydrocannabinol (THC), electronic-cigarette associated lung injury, EVALI

■ INTRODUCTION

Acute eosinophilic pneumonia (AEP) is a rare clinical disease that has been described in young patients between 20-40 years of age, and more commonly in men [1, 2]. Patients usually present with less than four weeks of symptoms, most commonly including non-productive cough, dyspnea, and fever.

AEP has also been rarely reported as an adverse effect from vaping e-cigarettes [3, 4].

■ CASE REPORT

A previously healthy 29-year-old female was admitted to Beth Israel Hospital in Boston, MA USA. On admission, she reported that she had a current alcohol use disorder, drinking 5-10 drinks per day for the last ten years or so, and excessive tobacco use which she stopped six months before admission.

She started using non-flavoured product THC-containing e-cigarettes ("vape") four weeks before admission. The THC-containing e-cigarette product was purchased from a local licensed marijuana dispensary.

Otherwise, she had been well until one week prior to admission, when she developed profound fatigue. Four days before admission, she developed a sore throat; and one day before admission, she developed subjective fevers and shortness of breath.

On arrival at the hospital, she was afebrile with an oxygen saturation of 71% on a non-rebreather mask. She was in significant respiratory distress, and pulmonary examination revealed diffuse rhonchi bilaterally with bibasilar dullness. Her white blood cell count was 15.3; 88% neutrophils and 5.8% eosinophils. A chest radiograph, taken on the day of admission, demonstrated extensive pulmonary opacities bilaterally (Figure 1). A chest CT scan, on the same day, demonstrated diffuse, bilateral broncho-centric disease including nodular ground-glass opacities coalescing to form consolidation at the bases (Figure 2).

She was immediately admitted to the hospital's ICU and intubated for refractory hypoxemia.

On Day 1 of hospitalization, sputum culture was negative for viral and bacterial pathogens, and a bronchoscopy was performed. The cell count from her bronchoalveolar lavage (BAL) revealed 36% eosinophils, and the cytopathology demonstrated foamy macrophages (Figure 3). Based on these tests, she was diagnosed with acute eosinophilic pneumonia by the critical care physicians, as defined by criteria in Table 1 [1, 2, 5, 6].

Twenty-four hours after admission, she was started on high-dose steroids, 500mg per day of intravenous methylprednisone (Pfizer, New York, US), given intravenously.

By Day 2, chest radiographs showed a reduction of pulmonary infiltrates. There was a rapid improvement

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Fig. 1. Chest radiograph (CXR) demonstrating bilateral peripheral and central opacities with a basilar predominance
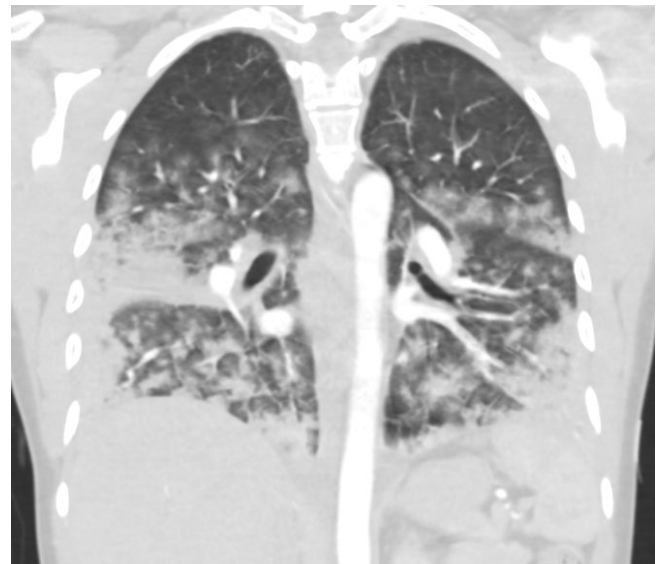

Fig. 2. Chest computerized tomography (CT) demonstrating diffuse, broncho-centric bilateral ground glass opacities with coalescence to consolidation, largely in the lung bases

She was discharged home on Day 7 with exertional oxygen supplementation and plans for a follow-up after two weeks in the hospital's outpatient pulmonary clinic.
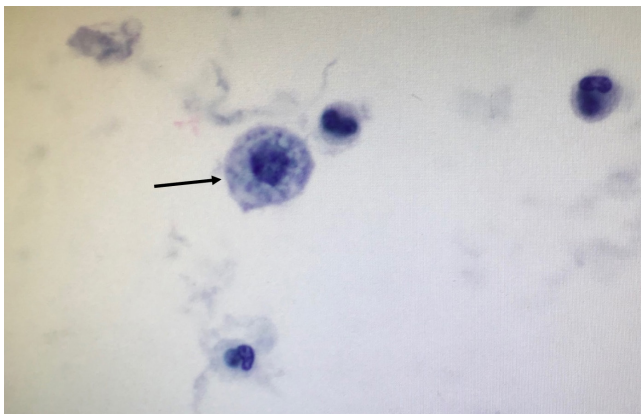
■Discussion

The criteria for making a clinical diagnosis of AEP are listed in Table 1 [1, 2, 5, 6]. This includes a BAL with a cell count demonstrating >25% eosinophilia. These criteria were observed in the present case. They are more commonly described in men [2]. A thorough evaluation should include a review of medications, prior chest irradiation, and travel to areas with endemic parasites. Patients typically have a normal peripheral blood eosinophilia on presentation, although this can rise later.

The differential diagnosis for AEP is delineated in Table 2 [1, 7, 8, 9, 10].

Treatment of AEP includes a high-dose of intravenous systemic glucocorticoids until the respiratory

Fig. 3. Lung cytopathology, demonstrating rare foamy macrophages (black arrow).

in hypoxemia, allowing for extubation on Day 3. Her steroids were tapered to oral prednisone, 1mg/kg per day (American Health Packaging, Columbus, US).

Table 1. Diagnostic criteria for acute eosinophilic pneumonia.

Clinical diagnostic criteria for acute eosinophilic pneumonia
Febrile illness less than four weeks in duration
Hypoxemic respiratory failure
Diffuse pulmonary opacities on chest radiograph
Bronchoalveolar lavage (BAL) with cell count demonstrating >25% eosinophilia
Absence of other known causes for pulmonary eosinophilia

Table 2. Differential diagnosis considerations for acute eosinophilic pneumonia.

Differential diagnosis considerations
Eosinophilic granulomatosis with polyangiitis
Pulmonary fungal infections
Pulmonary parasitic infections
Medication effects
Pulmonary infiltration of eosinophils secondary to overwhelming peripheral eosinophilia

failure has resolved, followed by an oral steroid taper. While the optimal duration of a steroid taper has not been determined, generally a slow taper which extends at least two weeks beyond improvements shown by radiographic and laboratory tests is recommended [1, 11].

Given the rarity of the disease, most experience with AEP is obtained from retrospective case reports. There is a well-described phenomenon of AEP occurring after new inhalational exposures, including case reports from firefighters [12], military service personnel in the Middle East [13], and first-time cigarette smokers [3, 14], and more recently in vaping induced lung disease [3, 4].

In the summer of 2019, national attention in the United States [21] was drawn to the dramatic rise in pulmonary toxicity associated with vaping. This is now termed e-cigarette (or vaping) product use-associated lung injury (EVALI) [21].

Case series of EVALI have described a clinical syndrome (Table 3) with outcomes ranging from mild self-resolving hypoxemia to refractory hypoxemia requiring extracorporeal membrane oxygenation (ECMO) support [15, 16, 17, 18]. There is a broad range of clinical manifestations, including hypersensitivity pneumonitis, diffuse alveolar damage, and organizing pneumonia; however, EVALI manifesting as AEP from THC smoking remains extremely rare. In one of the largest case series of EVALI, a cohort of 98 patients was described, of whom 26 underwent BAL, and none had BAL eosinophilia [15]. In another series of EVALI, all of the forty-three patients underwent BAL. The median eosinophil count was 1% (range 0-18%) [15].

A small case series by Maddock et al. (2019) noted large lipid-laden macrophages with red oil staining on BAL cytology samples [16]. This has been postulated to be due to the carrier oils used to dissolve THC. Vitamin E acetate has been implicated as a potential mechanism for injury due to very high levels found in commercially-available THC vaping products [19]. However, this is difficult to confirm clinically.

Table 3. Characteristics of the clinical syndrome of vaping-associated lung injury.

Differential diagnosis considerations
Recent e-cigarette use
Pulmonary infiltrates on chest imaging
Absence of pulmonary infection
No evidence of an alternative cause

While our patient's cytology showed small lipid-containing vacuoles inside macrophages, these are commonly identified as benign cytologic features in any user of inhaled oils and did not match the large macrophages previously described in previous cases. Other potential toxins include THC or nicotine. The majority of EVALI case reports describe the use of THC-containing products (75-80%), and THC has been found in BAL samples of EVALI patients while it is absent in healthy controls [15, 15, 20, 21]. Fewer EVALI patients report exclusive use of nicotine, and 13-58% of EVALI patients report a history of nicotine-vaping [15, 2, 21]. The patient in this current report did not admit to active nicotine use, so there was a higher suspicion for vitamin E oils or THC as the culprit toxin.

While THC has been legalized in some states, it remains illegal in most of the rest of the USA. Thus, there is a substantial market for street-purchased or home-made THC vaping oils, which confounds the ability of regulatory agencies, such as the CDC and FDA, to study and make recommendations about vaping products.

Beyond the recent attention to acute pulmonary toxicity due to vaping, there are concerns regarding the long term safety of vaping. Common vaping flavourings, including glycerin and benzaldehyde, have caused pulmonary toxicity in food factory workers [22] and may be present in e-cigarettes at levels that exceed OSHA limits. Humectants, including glycerin or propylene glycol, result in increased inflammation *in vitro* human epithelial cells [23]. Furthermore, both flavourings and humectants can undergo pyrolysis or decomposition at high temperatures. Jensen *et al.* (2015) re-

ported that commercially available e-liquids undergo pyrolysis in typical use patterns, creating vapour-phase formaldehyde-releasing agents (FRAs) with potential formaldehyde exposure 5-15x higher than traditional tobacco cigarettes [24]. While the International Agency of Research Center classifies formaldehyde as a possible Group 1 human carcinogen, FRAs are not well understood. If FRAs have the same toxicity as gaseous formaldehyde, then long-term health risks of vaping should be monitored with extreme caution.

■ CONCLUSION

In summary, a case is presented of acute eosinophilic pneumonia associated with daily use of THC-containing e-cigarettes. Increased vigilance about pulmonary toxicity associated with vaping, mainly vaping THC-containing products, is essential for clinicians assessing and caring for patients who use e-cigarettes presenting with shortness of breath and respiratory failure.

■ CONFLICT OF INTEREST

None to declare.

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