Eosinophilic Pneumonia and Lymphadenopathy Associated With Vaping and Tetrahydrocannabinol Use

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Idiopathic acute eosinophilic pneumonia is a rare and potentially life-threatening condition that is defined by bilateral pulmonary infiltrates and fever in the presence of pulmonary eosinophilia. It often presents acutely in previously healthy individuals and can be difficult to distinguish from infectious pneumonia. Although the exact etiology of idiopathic acute eosinophilic pneumonia remains unknown, an acute hypersensitivity reaction to an inhaled antigen is suggested, which is further supported by recent public health risks of vaping (electronic cigarette) use and the development of lung disease. In this case, a patient with a year-long history of vaping in conjunction with tetrahydrocannabinol cartridge use who was diagnosed with idiopathic acute eosinophilic pneumonia with associated bilateral hilar lymphadenopathy is described.

CASE REPORT

A 16-year-old white girl who resides on a farm in Ohio where corn is grown and animals are raised, including pigs, horses, and dairy cattle, took 5-mg levocetirizine daily because of a medical history of seasonal allergies. Her farmhand work was limited to moving hay and feeding the animals in the mornings. She had a one-year history of vaping from a Juul device with nonbranded mint-flavored cartridges that she had purchased from friends at school. The patient reported recent cessation immediately after her brief admission for pneumonia 3 months before this reported admission, but she continued to have secondhand exposure to vaping through her boyfriend. She was prescribed albuterol and inhaled mometasone by her pediatrician after her initial discharge from the hospital.

She presented to the emergency department (ED) with complaints that included a 3-month history of cough and shortness of breath and a one-week history of abdominal discomfort, diarrhea, fever, and chest pain. Four days before her ED encounter, she was seen at a local urgent care facility, where a chest radiograph was obtained. She was diagnosed with left lower lobe pneumonia and was started on a 5-day course of azithromycin from the urgent care facility. She reported compliance with administering her prescription of inhaled mometasone while using albuterol 4 to 5 times a day, with no reported improvement since beginning the treatment.

In the ED, the patient was afebrile, with a peripheral oxygen saturation of 92% and a respiratory rate of 32 breaths per minute. The physical examination revealed a distressed girl with tachypnea, labored breathing, wheezing, and rales in both lower lung fields. Because of her distressed appearance and complaints of shortness of breath with chest pain, a urine toxicology test,

abstract

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Dr Mull was the consulting pulmonary fellow who evaluated the patient and performed a bronchoscopy, and he was the primary author of this case report; Dr Erdem was the infectious disease attending who managed the patient through her primary service, and she contributed references and revisions to the manuscript; Dr Adler provided radiologic figures and corresponding interpretations for the manuscript; Dr Nicol performed a cytologic review of the bronchioalveolar lavage sample, provided corresponding figures with descriptions for this manuscript, and contributed revisions to the manuscript; Dr Shell, section chief of pulmonary medicine, was the precepting physician for Dr Mull, and he contributed revisions to the manuscript; and all authors approved the final manuscript as submitted.

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electrocardiogram, and computed tomography (CT) chest angiogram were obtained. The results of the urine toxicology test were positive for tetrahydrocannabinol, which she admitted to using in conjunction with vaping one month before. Her acknowledgment was questionable given the time line of tetrahydrocannabinol in the urine test and her reports of vaping cessation 3 months before. Although her CT chest angiogram proved unremarkable for a pulmonary embolism, it revealed multifocal airspace ground-glass opacities in all lobes and hilar lymphadenopathy (Fig 1). These pulmonary findings were observed on her chest radiograph obtained during this hospital course. On her past admission, similar findings were observed on her chest radiograph (Fig 2A). Because of her history of previous pneumonia and the completion of the ED workup, the patient was admitted to the infectious disease service for hypoxia secondary to suspected recurrent bacterial pneumonia.

Further laboratory evaluation during the initial 24 hours of her hospitalization included a comprehensive infectious and immunologic workup. The obtained test results included the following inflammatory markers: an erythrocyte sedimentation rate of 34 mm/hour, a C-reactive protein level of 1.6 mg/L, a quantitative immunoglobulin G level of 584 mg/dL (reference range for age 16–19 years: 549–1584 mg/dL), an immunoglobulin M level of 257 mg/dL (reference range for age 16–19 years: 23–259 mg/dL), an immunoglobulin A level of 69 mg/dL (reference range for age 16–19 years: 61–348 mg/dL), an immunoglobulin E level of 413 mg/dL (reference range for age 16–19 years: 150–1000 UI/mL), and a CD4/CD8 ratio of 1.5 (reference range: 1–2). The *Legionella*, *Strongyloides*, and

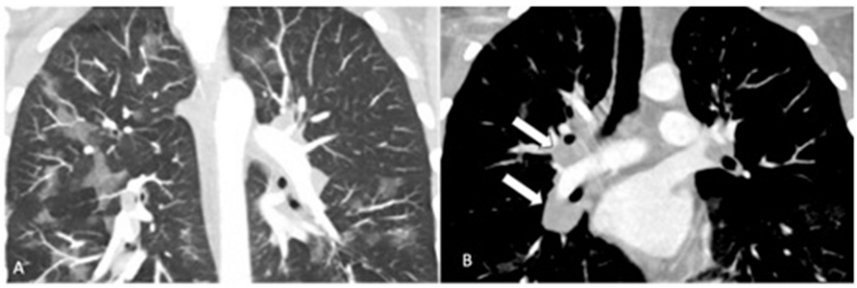

FIGURE 1
A, CT image at presentation revealing subsegmental ground-glass nodules without centrilobular thickening or cavitation. The image is slightly asymmetric but diffuse and both peripheral and central. B, Enlarged lymph nodes in the right hilum (arrows); similar lymph nodes were found on the left.

histoplasmosis serology results were negative. The results of the sputum acid-fast bacillus smear, fungal polymerase chain reaction, blood cultures, purified protein derivative for tuberculosis, and QuantiFERON assay were also negative. Her complete blood count was within normal limits, although her complete blood count 3 months before indicated considerable peripheral eosinophilia (33.3% [reference range: 1%–4%]), which was not evaluated and resolved by this reported admission to 1.5%.

Because of the negative infectious workup and persistent radiologic findings, paired with a history of vaping that was similar to cases reported in a recent public health announcement from the Centers for Disease Control and Prevention, the pulmonary service was consulted. The patient required 2 L of low-flow nasal cannula supplemental oxygen for respiratory support. It was determined that a bronchoscopy with bronchioalveolar lavage (BAL) was warranted as a result of persistent radiologic findings and no clear etiology. The procedure was uncomplicated, and no significant clinical findings were observed. A BAL sample was obtained and then sent for a cytology review, where the sample was noted to have considerable pulmonary eosinophilia of 62% (normal >10%), and Charcot-Leyden crystals were present (Fig 3) with no signs of parasitic larvae or eggs. These findings were consistent with the findings of hypersensitivity pneumonitis or acute eosinophilic pneumonia.

With these cytologic findings and the comprehensive evaluation that ruled out infectious etiologies, the patient was started on systemic corticosteroids. Within 24 hours of treatment, the patient was

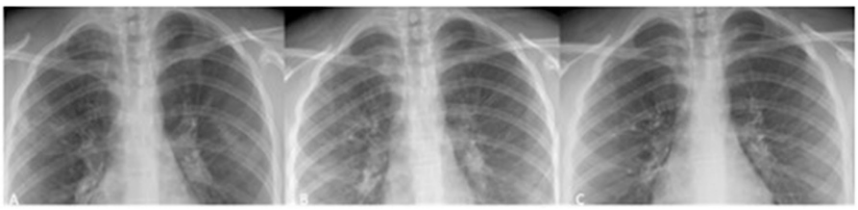

FIGURE 2
A, Initial image 3 months before presentation revealing upper lobe patchy alveolar disease and hilar lymph node enlargement. B, More right-upper lobe disease with similar hilar lymph node enlargement at the time of admission. C, Resolution of alveolar opacities and lymph node enlargement 1 week into corticosteroid therapy.

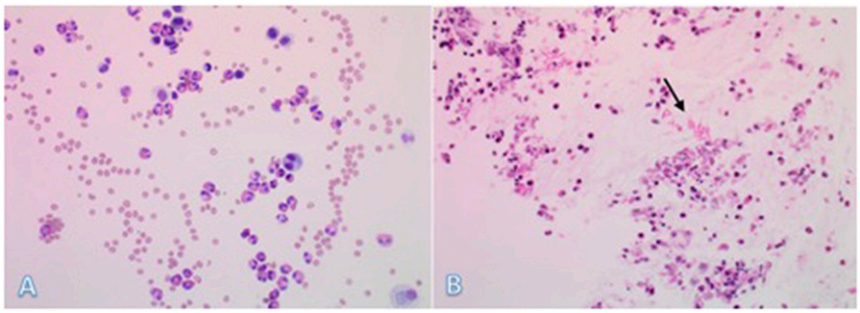

FIGURE 3

A, Cytospin preparation (Wright-Giemsa stain, original magnification ×100) revealing eosinophilia. B, Image of a cell block section (hematoxylin and eosin, original magnification ×100) revealing eosinophilia with the Charcot-Leyden crystals.

successfully weaned off supplemental oxygen. She was discharged from the hospital and prescribed a 2-week course of corticosteroids, followed by a prolonged steroid taper of an additional 4 weeks. Although there was no concern for an infectious disease, the patient was seen in the infectious disease clinic one week after discharge to follow-up on the serologies from her hospitalization. Radiologic findings revealed the resolution of opacities and the lymphadenopathy while on corticosteroid therapy (Fig 2). Long-term follow-up with her pediatrician and pulmonary clinic was established. She reported the complete resolution of symptoms within 2 weeks of initiating therapy. Her physical examination findings were unremarkable, with no adventitious lung sounds.

DISCUSSION

Idiopathic acute eosinophilic pneumonia is a relatively rare condition with an unclear etiology, and it is even rarer with the presence of associated bilateral hilar lymphadenopathy.[1] Although the etiology is not always straightforward, the differential diagnosis for this condition should be inclusive of fungal infections, such as *Coccidioides immitis* and less commonly *Histoplasma capsulatum*, while encompassing potential parasitic infections, such as *Strongyloides*. Despite potential environmental exposure from residing on a farm, the workup results for these infections were negative in our patient. Other potential causes, including eosinophilic granulomatosis with polyangiitis, were ruled out during this workup. Through the diagnosis of exclusion, a potential pulmonary irritant via drug or inhaled toxins was determined.[2] It is worth noting that in a previous case series, 32 of 33 patients were active smokers of tobacco at disease onset, with 21 patients having started 1 month before disease onset, suggesting a strong association between the two.[3]

This disease process that is generally characterized by infiltration of eosinophils into the lungs and associated with acute onset of dyspnea, and fever can progress to significant respiratory failure that requires the use of invasive mechanical ventilation or even extracorporeal membrane oxygenation. Radiologic imaging may be useful for diagnostic purposes, with chest radiographs typically revealing reticular opacities bilaterally and CT scans revealing ground-glass opacification in association with septal thickening. Ultimately, bronchoscopy with BAL is necessary for confirming the diagnosis, and for the cytologic examination, an eosinophilic percentage must be >25%.

Because eosinophilic pneumonia frequently mimics infectious pneumonia at presentation, it often leads to an inappropriate use of antibiotics in a disease process during which the mainstay of therapy consists of systemic corticosteroids. After appropriate therapy is initiated, there is often rapid resolution of symptoms, as observed in the patient presented in this case.[3]

Through the example in this case, we intend to convey the potential risk of the unstudied and unregulated vaping and illicit tetrahydrocannabinol use that is currently popular among teenagers and young adults. For the first time after several decades of steady decline of cigarette smoking among 15- to 19-year-old adolescents, the statistics have not changed significantly between 2015 and 2017. The proportion of adolescents who vaped at least 20 days within a month increased from 20% in 2017 to 28% in 2018.[4] As of October 1, 2019, the Centers for Disease Control and Prevention released a statement on nearly 1100 cases reported from 48 different states and 18 confirmed death from 15 states that suggested a potential connection with the use of vaping (electronic cigarettes) in conjunction with tetrahydrocannabinol use. Each case exhibited the associated symptoms and radiologic findings consistent with this presented patient.[5,6]

After the negative result of the workup with the patient's symptoms of chest pain, dyspnea, and diarrhea, coupled with the pertinent history of vaping and tetrahydrocannabinol use, the necessity of a bronchoscopy with BAL was indicated. A delay in an accurate diagnosis, compounded by ineffective therapy of antibiotics, can pose the serious risk of a potential progression of a life-threatening

hypoxic respiratory failure, which was avoided in this patient.[7]

ABBREVIATIONS

BAL: bronchioalveolar lavage
CT: computed tomography
ED: emergency department

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