Hypersensitivity Pneumonitis and Acute Respiratory Distress Syndrome From E-Cigarette Use

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abstract

Electronic cigarette (e-cigarette) use, or "vaping," is gaining widespread popularity as an alternative to conventional cigarettes among adolescents. Little is known of the health risks of e-cigarette use, especially in children and adolescents. We present a Case Report of a previously healthy 18-year-old woman who presented with dyspnea, cough, and pleuritic chest pain after e-cigarette use. She developed respiratory failure with hypoxia and was intubated, and ultimately met diagnostic criteria for acute respiratory distress syndrome. Chest tubes were placed to drain worsening pleural effusions. Computed tomography of the chest revealed dependent opacities in both lung bases, superimposed smooth interlobular septal thickening, and pleural effusions. Bronchoalveolar lavage revealed cellular debris and reactive mononuclear cells, and cell counts were remarkable for elevated mononuclear cells and eosinophilia. After the results of a workup for an infectious etiology came back negative, the patient was diagnosed with hypersensitivity pneumonitis and intravenous methylprednisolone therapy was initiated. After this the patient rapidly improved, was weaned off vasopressor support, and was extubated. This is the first reported case of hypersensitivity pneumonitis and acute respiratory distress syndrome as a risk of e-cigarette use in an adolescent, and it should prompt pediatricians to discuss the potential harms of vaping with their patients. Hypersensitivity pneumonitis, lipid pneumonia, and eosinophilic pneumonia should be included in the differential diagnosis of patients who exhibit respiratory symptoms after the use of an e-cigarette.

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Dr Sommerfeld cared for the patient as a resident on the Infectious Disease service, drafted the initial manuscript, and critically reviewed the manuscript; Dr Nowalk was the Infectious Disease attending who was consulted on this patient, and he assisted in the interpretation of data, contributed his expertise toward the patient's care, and critically reviewed and revised the manuscript for important intellectual content; Dr Weiner was the Pulmonology attending who was consulted on this patient, and he assisted in the interpretation of data, contributed his expertise toward the patient's care, and critically reviewed and revised the manuscript for important intellectual content; Dr Larkin was the Allergy and Immunology attending who was consulted on this patient, and she assisted in the interpretation of data, contributed her expertise toward the patient's care, and critically reviewed and revised the manuscript for important intellectual content; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Tobacco use remains a significant public health issue in pediatric patients. The use of electronic cigarettes (e-cigarettes), or "vaping," is gaining widespread popularity as an alternative to conventional cigarettes. Recent data from the National Youth Tobacco survey revealed a threefold increase in e-cigarette use between the years 2011 and 2013 in adolescents without a previous history of smoking.[1]

Currently there are limited data on the health risks of e-cigarettes in pediatric patients because in previous reports researchers have documented respiratory consequences mostly in the adult population. The youngest patient so far described is a 20-year-old man diagnosed with acute eosinophilic pneumonitis immediately after smoking an e-cigarette. Although he presented with respiratory symptoms, his oxygen saturations remained at 100% on room air and he did not require respiratory support during his admission.[2] In another report of a 60-year-old man with a presumptive diagnosis of acute hypersensitivity pneumonitis, this disorder is connected to the

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use of e-cigarettes. This patient required oxygen supplementation for hypoxemia but, again, no further respiratory support.[3] In 2 further reports, researchers describe lipid pneumonia secondary to e-cigarette use, and 1 patient required intubation for acute respiratory distress syndrome.[4,5] There are no case reports in the literature in which researchers describe respiratory failure secondary to hypersensitivity pneumonitis as a consequence of e-cigarette use in the pediatric population.

CASE REPORT

An 18-year-old woman presented to the emergency department with a chief complaint of 2 days of progressive dyspnea, cough, and pleuritic chest pain. She was afebrile during this time and without any upper respiratory symptoms. Her past medical history was significant for mild intermittent exertional asthma, with only rare use of inhaled albuterol. Recently the patient had a reaction (hives and lip swelling) to a Brazil nut that resolved with diphenhydramine. She had not been evaluated for nut allergies, but she had tolerated other nuts without reaction.

The patient lived in a rural town and had no recent bird or farm animal exposure. She had no recent travel, reverse travel, or close contact with incarcerated individuals. The patient recently started to use e-cigarettes over the last 2 to 3 weeks and had been using them 1 to 2 days before the onset of symptoms. She was employed as a hostess in a local restaurant.

On presentation, the patient's vital signs were as follows: temperature of 36.8°C, heart rate of 130 beats per minute, respiratory rate of 32 breaths per minute, and oxygen saturation of 84% on room air. Her cardiac examination did not reveal any rubs, gallops, or murmurs.

Her lung examination was notable for use of accessory muscles and diminished but clear breath sounds bilaterally at the bases. There was no hepatosplenomegaly or digital clubbing.

An initial complete blood cell count revealed an elevated white blood cell count of 35.9 ($\times 10^3$/mL), with 93% neutrophils, 4% bands, 1% lymphocytes, and 2% monocytes. Her hemoglobin level was 13.5 gm/dL, with a platelet count of 309 000/mL. Erythrocyte sedimentation rate was normal, with an elevated C-reactive protein level of 17.4 mg/L. Electrolytes and transaminases were normal. Urinalysis and urine drug screen results were both negative. A chest radiograph revealed patchy bilateral pulmonary infiltrates. Computed tomography (CT) angiography of the chest was negative for pulmonary emboli but did reveal dependent opacities in both lung bases, superimposed smooth interlobular septal thickening in the dependent areas of the lungs, and bilateral, small-to-moderate pleural effusions. Brain natriuretic peptide and cortisol levels were both normal. An echocardiogram revealed normal left ventricle systolic function with no valvular dysfunction.

The patient was admitted to the PICU and started on broad-spectrum antibiotics. Her respiratory distress rapidly worsened, and she was intubated for respiratory failure. She met diagnostic criteria for acute respiratory distress syndrome, requiring a >90% fraction of inspired oxygen with a Pao$_2$ of ~70 mm Hg. She was ventilated with a peak inspiratory pressure of up to 36 cm H$_2$O and positive end-expiratory pressure of 12 cm H$_2$O. Norepinephrine therapy was initiated for poor perfusion, and bilateral chest tubes were placed for worsening pleural effusions. Bronchoscopy revealed normal mucosa of the trachea and mainstem bronchi, with clear frothy secretions.

The results of a respiratory viral panel were negative. Bronchoalveolar lavage (BAL) revealed cellular debris and reactive mononuclear cells. BAL cell counts were notable for a 900 red blood cell count and a 340 white blood cell count (differential of 26% neutrophils, 13% lymphocytes, 14% monocytes, 25% mononuclear cells, and 22% eosinophils). The results of BAL testing for *Mycoplasma* polymerase chain reaction, *Legionella* direct fluorescent antibody, and aerobic and fungal cultures were all negative. BAL cytology revealed no *Pneumocystis* but abundant lipid-laden macrophages on an Oil Red O stain. The patient was started on 40 mg of intravenous methylprednisolone twice daily. After steroid initiation, she was quickly weaned from vasopressor support and was extubated 5 days after initial presentation. She was eventually discharged from the hospital on a prednisone taper with a diagnosis of hypersensitivity pneumonitis, likely secondary to e-cigarette exposure.

DISCUSSION

Hypersensitivity pneumonitis is an inflammatory disease of the lung parenchyma that is the result of an immune response to inhaled antigens. Typically, hypersensitivity pneumonitis is associated with antigens from microbial agents, such as moldy hay or grains (farmer's lung), or with animal proteins in avian droppings (bird fancier's lung). In the acute setting, hypersensitivity pneumonitis can be secondary to chemical exposure, some of which can be found in e-cigarettes.[6]

Hypersensitivity pneumonitis can be categorized by the duration of illness as an acute, subacute, or chronic process. The typical manifestations of acute or subacute hypersensitivity pneumonitis can mimic a viral illness, with symptoms including fever, cough, dyspnea, myalgias, and arthralgias. In an acute presentation,

symptoms will often begin hours after antigen exposure. In a subacute or chronic presentation, the symptoms tend to be prolonged and less severe. With repetitive antigen exposure, patients may develop a progressive chronic respiratory disease secondary to pulmonary fibrosis.

The diagnosis of hypersensitivity pneumonitis is made by a combination of laboratory studies, imaging, BAL, and histologic findings. If possible, serum immunoglobulin G antibodies to specific antigens should be obtained. A positive serology result is suggestive but not diagnostic of hypersensitivity pneumonitis, and the absence of specific antibodies (especially in acute presentations) does not rule out this condition. Chest CT in the acute and subacute setting may reveal nodular, ground glass, or airspace opacities. There may be small nodules present, which represent granulomas.[7] The use of pulmonary function tests can be used to support the diagnosis of hypersensitivity pneumonitis, typically revealing a reduced diffusing capacity of the lung for carbon monoxide. BAL fluid is helpful in diagnosis, in which the leukocyte differential may

reveal lymphocytosis. Neutrophil predominance can also be seen in either the acute phase with recent exposures or with more advanced disease. Increased eosinophil numbers can also be seen in BAL samples.[8]

BAL eosinophilia is also present in acute eosinophilic pneumonia, which may present similarly to hypersensitivity pneumonitis. Typical symptoms include fever, nonproductive cough, dyspnea, myalgias, and malaise.[9] A majority of patients do not have peripheral blood eosinophilia at the time of presentation. A complete blood cell count differential reveals a neutrophilic leukocytosis early in the course, followed by an eosinophil predominance with disease progression.[10] Chest CT will reveal patchy ground glass opacities, usually located along bronchovascular bundles.[11] The diagnosis of acute eosinophilic pneumonia can be made on the basis of clinical features, CT findings, and a BAL sample with >25% eosinophilia.

The treatment of both hypersensitivity pneumonitis and acute eosinophilic pneumonia is centered on avoidance of inciting

agents. In more severely ill patients, intravenous corticosteroids have been shown to accelerate lung recovery.[9,12] Because this is an inflammatory response, antibiotics are not useful unless bacterial superinfection is suspected.

CONCLUSIONS

With this case, we highlight hypersensitivity pneumonitis as a life-threatening health risk of e-cigarette use in an adolescent patient. Although little is known of e-cigarette health risks, especially in children and adolescents, their use in the pediatric population is growing rapidly. This should prompt pediatricians to discuss the potential harms of e-cigarette use with their patients. Hypersensitivity pneumonitis, lipid pneumonia, and eosinophilic pneumonia should be included in the differential diagnosis of patients who exhibit respiratory symptoms after the use of e-cigarettes.

ABBREVIATIONS

BAL: bronchoalveolar lavage
CT: computed tomography
e-cigarette: electronic cigarette

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