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CHEST Postgraduate Education Corner
PULMONARY AND CRITICAL CARE PEARLS

An Unexpected Consequence of Electronic Cigarette Use

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A 42-year-old woman was admitted to the hospital with a 7-month history of dyspnea, productive cough, and subjective fevers. She had been seen multiple times in the ED with similar complaints and had received several courses of antibiotics.

The patient had recently started using electronic cigarettes (e-cigarettes), about 7 months prior, which coincided with the onset of her respiratory symptoms. Her past medical history also was significant for asthma, reported rheumatoid arthritis, fibromyalgia, schizoaffective disorder, and hypertension. Her medications included amlodipine, albuterol metered dose inhaler, lovastatin, lisinopril, multiple vitamins, cyclobenzaprine, citalopram, and multiple psychiatric medications.

The patient reported a recent exposure to fumigation chemicals, as the result of a bedbug infestation of her apartment building 2 weeks prior to her hospitalization. She had no pets. There was no other history of significant exposures, illicit drug use, or recent travel. She denied any dysphagia or aspiration.

Physical Examination

On presentation, her vital signs were notable for mild tachycardia and a pulse oximetric saturation of 94% while breathing room air. Her physical examination was normal except for bilateral rales.

Laboratory Tests and Imaging Findings

Laboratory findings showed a WBC count of 18.0 ($\times 10^3$) with a normal differential and hemoglobin level of 11.2 g/dL. The chemistry panel and brain natriuretic peptide levels were normal. Chest radiographic imaging showed new multifocal bilateral opacities. CT images (Fig 1) revealed extensive bilateral upper- and lower-lobe patchy ground glass pulmonary opacities in a "crazy paving" pattern. Results of an HIV test were negative. Results of a nasal *Pertussis* polymerase chain reaction swab were negative. Results of urine *Legionella* antigen and serum *Mycoplasma* IgG and IgM tests were negative. Results of a hypersensitivity pneumonitis panel, extracted nuclear antigen panel, and tests for antinuclear antibody,

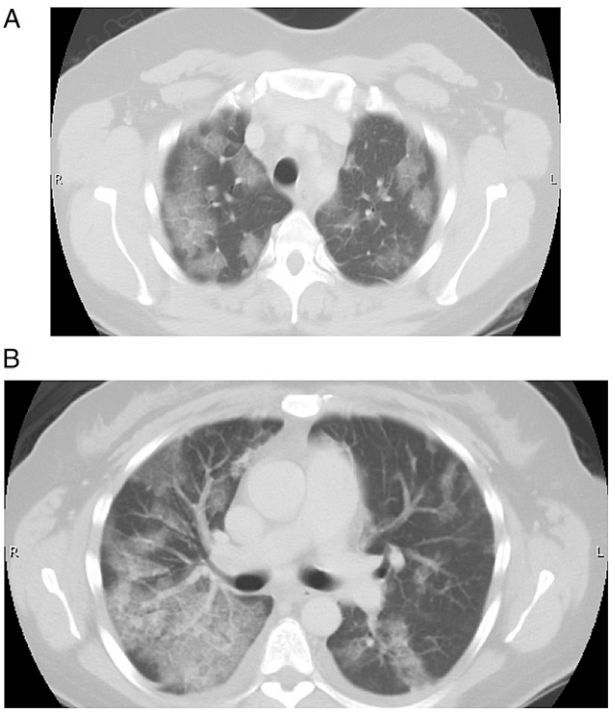

FIGURE 1. Representative CT images show the "crazy paving" pattern of patchy ground glass superimposed on interlobular septal thickening. A, Bilateral upper lobes. B, Bilateral lower lobes.

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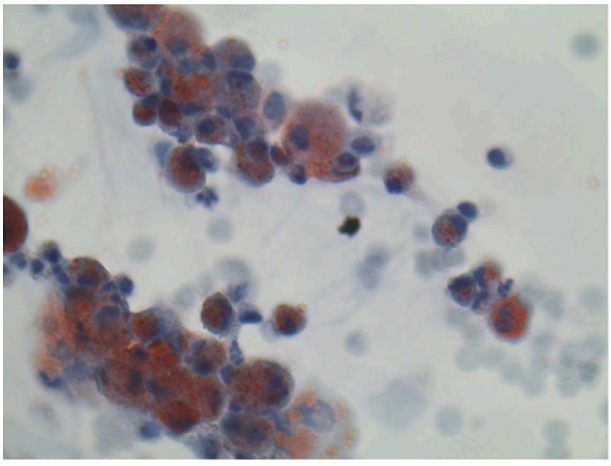

FIGURE 2. Photomicrograph of BAL sample shows lipid-laden macrophages (Oil-Red-O stain, original magnification × 100).

cyclic citrullinated peptide, and rheumatoid factor were negative. A bird fancier's panel showed trace reactivity to pigeon and parrot droppings.

Bronchoscopy and BAL were performed. The cell count showed 48% neutrophils, 8% lymphocytes, 43% monocytes, and 1% eosinophils. Results of all bacterial and viral cultures remained negative; fungal cultures showed light growth of *Candida*. Results of a viral DFA panel, *Pneumocystis jeroveci* DFA, and *Legionella* antigen tests were negative. BAL cytologic examination revealed abundant lipid-laden macrophages (Fig 2).

What is the diagnosis?

Diagnosis: Exogenous lipoid pneumonia due to e-cigarette use

Discussion

Lipoid pneumonia is a rare, primarily chronic inflammatory reaction secondary to the presence of lipid substances in the lungs, with subsequent uptake by alveolar macrophages and accumulation in the interstitium. The endogenous form occurs when fat is deposited into the lung tissue in vivo, typically from proximal obstructive lesions, fat embolism, necrotic tissue, lipid storage disease, or hyperlipidemia. The exogenous form develops from inhaling or aspirating lipids, such as those seen in animal, vegetable, or mineral oil. Classically, exogenous lipoid pneumonia is associated with aspiration of mineral oil-based laxatives in the pediatric population or with occupational exposures. The incidence is also higher in older patients with underlying debility, achalasia, reflux, and other neuromuscular disorders of the pharynx and esophagus.

Most patients are asymptomatic; however, symptoms may include cough, dyspnea, fever, weight loss, chest pain, pleurisy, hemoptysis, chills, and night sweats. Findings on physical examination may be normal or nonspecific, such as tachypnea and adventitious breath sounds. Thus, a high clinical suspicion is required to make the diagnosis of exogenous lipoid pneumonia.

Depending on the severity of the disease, exogenous lipoid pneumonia may present with hypoxia or respiratory alkalosis. Results of pulmonary function tests typically show a restrictive ventilatory defect and/or diffusion impairment, but they may be normal.

The most frequent chest radiographic findings are extensive bilateral alveolar consolidations and ground glass opacities in the dependent portions of the lungs. However, unilateral involvement may be seen, affecting the right and left lungs equally. Adenopathy is rare. Fibrosis may occur and lead to volume loss. Solid lesions may also develop, resembling bronchogenic carcinoma.

High-resolution CT imaging plays an important role in the diagnosis of lipoid pneumonia. The most frequent findings are bilateral posterior and lower-lobe-predominant alveolar consolidation, ground glass opacities, and the "crazy paving" pattern. Consolidated areas are typically hypodense (-30 to -75 HU), with similar attenuation to the surrounding adipose tissue. The use of CT scan angiography may help confirm these findings, with the consolidated lung having a considerably lower attenuation than the enhancing vessels.

A key component to making a true diagnosis of exogenous lipoid pneumonia is the presence of lipid-laden macrophages in the sputum or BAL fluid. These vacuolated macrophages stain orange with Sudan stain or red with Oil-Red-O stain. No clear cytologic profile has been found to be more suggestive of the disease. Histologic examination shows an inflammatory landscape, similar to that seen with a foreign body reaction. In severe disease, a proliferative fibrosis and disorganization of the pulmonary architecture can occur. A biopsy may be necessary to confirm the diagnosis in certain cases.

Once the diagnosis has been identified, all efforts should be made to avoid recurrent oil exposures and stop aspiration. Expectorants and repeat therapeutic BAL have not been shown to offer any benefit. Systemic corticosteroids have been recommended; however, they lack proven efficacy. Therefore, their use should be limited to severe cases.

For this patient, the suspected source of her exogenous lipoid pneumonia was recurrent exposure to glycerin-based oils found in e-cigarette nicotine vapor. Since the 1980s, there has been an ever-increasing development of electronic nicotine-delivery systems. The e-cigarette comprises a plastic tube and a battery-powered electronic heating device that vaporizes a liquid nicotine cartridge. E-cigarettes are advertised as an alternative to smoked tobacco and as a smoking cessation aide.

However, health analysis and empirical research on e-cigarettes is sparse. Recent evaluation of the nicotine solution and vapor content of e-cigarettes found primary components of propylene glycol, glycerin, and nicotine. Other chemicals identified in trace amounts include N-nitrosamines, diethylene glycol, polycyclic aromatic hydrocarbons, anabasine, myosmine, and β-nicotyrine. Many of these compounds are carcinogenic and harmful to humans.

Vegetable glycerin is often added to the nicotine solutions used in e-cigarettes to make the visual smoke when the solution is vaporized. Glycerin is produced by heating palm or coconut oil; however, it can also be produced from animal fat and soap through a fatty-acid splitting operation.

As discussed, most cases of exogenous lipoid pneumonia are associated with aspiration of mineral oil or lipid-based preparations. There is one published case of exogenous lipoid pneumonia due to inhaling vaporized weed oil. Other cases have been reported involving inhalation of crack cocaine mixed with petroleum jelly. To our knowledge, there are no prior published cases of exogenous lipoid pneumonia due to the use of glycerin-based e-cigarettes. Importantly, this case highlights harm caused by the nicotine-solution carrier and the delivery system of the e-cigarette. Prior discussion regarding the safety of e-cigarettes has primarily focused on nicotine and other carcinogenic components. Certainly, the risk of lipoid

pneumonia adds another dimension to the supercharged social, political, and medical debate surrounding the regulation and legality of e-cigarette use.

Clinical Course

The patient was instructed to avoid the use of e-cigarettes, and, subsequently, her symptoms improved. A follow-up chest radiograph was normal, and pulmonary function testing showed mild diffusion impairment but no obstructive or restrictive defects.

Clinical Pearls

1. Exogenous lipoid pneumonia is a chronic inflammatory reaction to the deposition of lipid substances in the lung, typically as a result of aspiration or inhalation of oil-based products.

2. Chest CT imaging typically shows bilateral alveolar consolidation and ground glass opacities, including the "crazy paving" pattern, in the dependent areas of the lungs.

3. The presence of lipid-laden macrophages in sputum or BAL fluid helps to confirm the diagnosis.

4. The symptoms and pathologic changes often completely resolve with the cessation of exposure; however, severe cases can progress to fibrosis and chronic respiratory failure.

5. Many public health authorities, including the US Food and Drug Administration, caution that the risks and benefits of e-cigarettes have not been adequately studied. This case demonstrates an important heretofore unrecognized (as far as we know) health risk of e-cigarette use: exogenous lipoid pneumonia due to glycerin-based e-cigarettes.

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Suggested Readings

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