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CLINICAL VIGNETTE

Oil Red O Staining for the Diagnosis of E-Cigarette or Vaping Use-Associated Lung Injury

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Introduction

E-cigarette or vaping use-associated lung injury (EVALI) peaked in September 2019. From September 2019 through February 2020 there were a total of 2,807 hospitalized EVALI cases or deaths and 68 confirmed deaths reported to the CDC across the United States.¹ We present a case that occurred during the peak of the EVALI outbreak in which Oil Red O staining of bronchoalveolar lavage (BAL) fluid supported the diagnosis of EVALI.

Case Presentation

A 37-year-old male developed three weeks of drenching night sweats and two weeks of shortness of breath, cough, fatigue, headaches and diarrhea without fevers or chills. Imaging showed diffuse ground glass and consolidative opacities with lymph node enlargement (Figure 1 left). He completed a course

of azithromycin without improvement. Social history included tetrahydrocannabinol (THC) vaping with last use two weeks prior to symptom onset. He was afebrile with a heart rate of 123, blood pressure 123/88, oxygen saturation 96%. He appeared pale and sweating. Lungs were clear to auscultation bilaterally. Repeat chest imaging done one week later showed improvement (Figure 1 right) although the patient had no clinical improvement. EVALI was suspected and steroids were recommended. However, the patient requested a more definitive diagnosis prior to start of steroids and flexible bronchoscopy with BAL was performed. All BAL microbiology was negative. Cytology was negative for malignant cells and flow cytometry was negative. Cell count showed 87% alveolar macrophages and 13% lymphocytes. Oil Red O stain was positive for lipid-laden macrophages (Figure 2). This supported the diagnosis of EVALI. The patient abstained from vaping without symptom improvement, and steroids were started. He completed a two-week prednisone taper with complete resolution of symptoms.

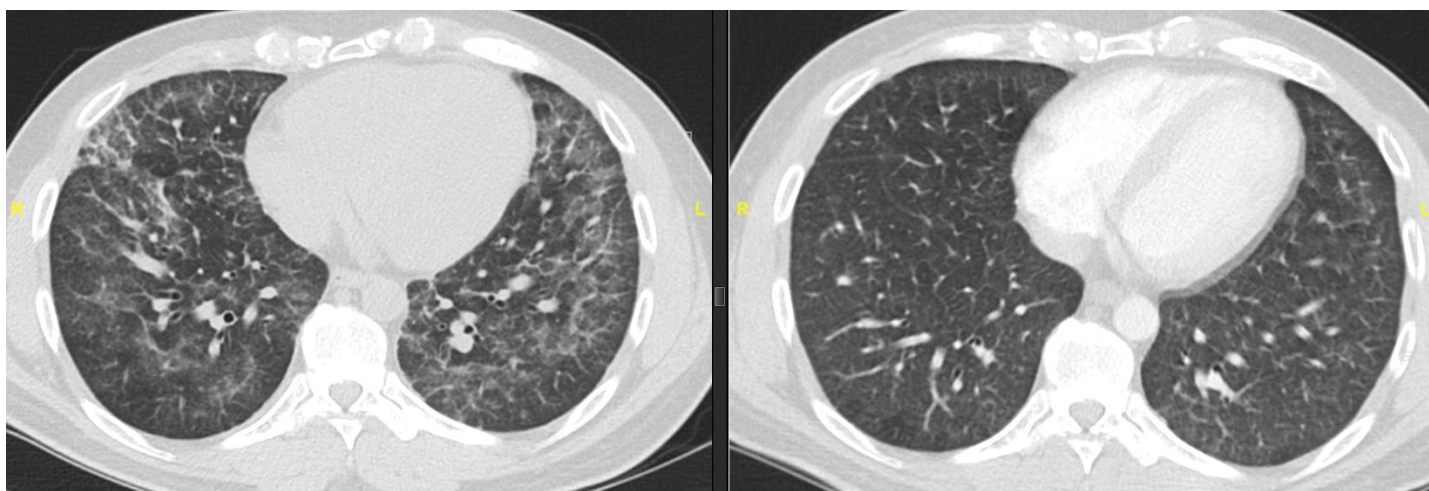


Figure 1. Left – CT chest image with diffuse ground glass and consolidative opacities. Right – CT chest image performed one week later with improvement to diffuse ground glass and consolidative opacities

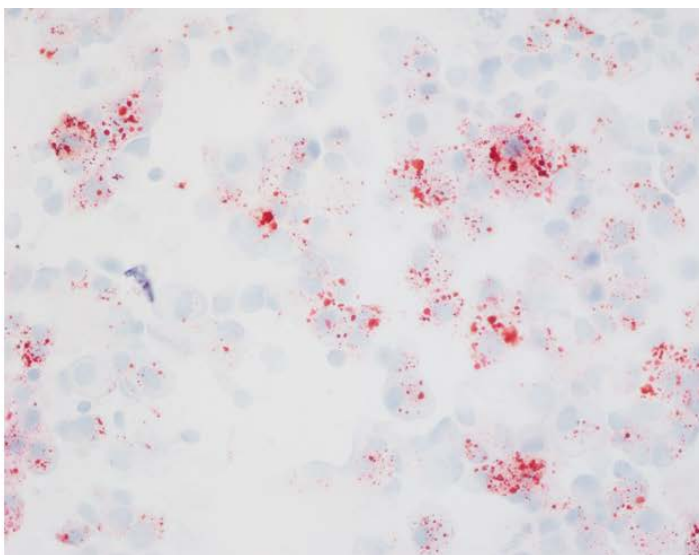
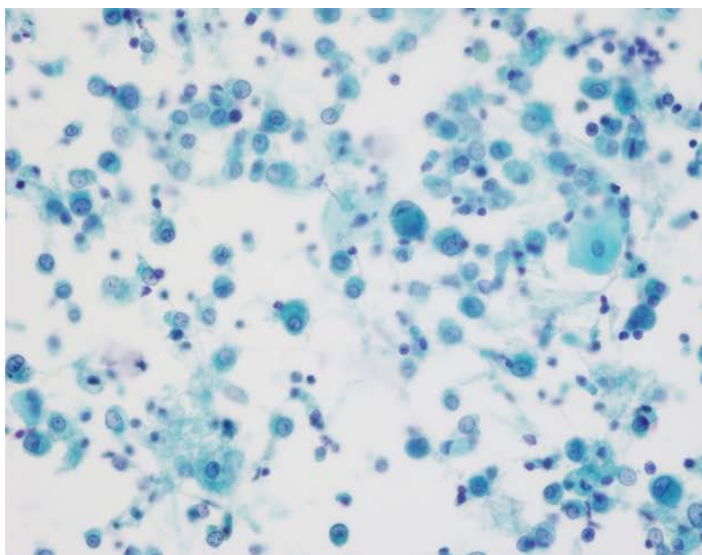


Figure 2. Left – Pap stain showing macrophages at 400x magnification. Right – Oil Red O stain showing scattered lipid laden macrophages at 400x magnification

Discussion

Emergency visits related to e-cigarette or vaping products peaked in September 2019. Tetrahydrocannabinol (THC)-containing e-cigarette, or vaping, products, particularly from informal sources like friends, family, or in-person or online dealers, are linked to most EVALI cases. Vitamin E acetate is strongly linked to the EVALI outbreak. Vitamin E acetate has been found in product samples tested by FDA and state laboratories and in patient lung fluid samples tested by the CDC from geographically diverse states. Vitamin E acetate has not been found in the lung fluid of people that do not have EVALI. Vitamin E acetate usually does not cause harm when ingested as a vitamin supplement or applied to the skin. However, when inhaled, it interferes with normal lung function. Cases of EVALI have steadily declined since 2019 due to increased public awareness, removal of vitamin E acetate containing products and law enforcement efforts.¹

The diagnosis of EVALI is largely one of exclusion. The CDC guidelines suggested that a patient with a vaping history within 90 days prior to illness, pulmonary infiltrates on imaging, and no other alternative etiology (infectious or otherwise) should be diagnosed with EVALI. BAL is one of the least invasive procedures to obtain diagnostic specimen in patients with pneumonia or other forms of lung injury. Microbiologic studies can be performed to exclude alternative infectious etiologies. Ancillary studies such as Oil Red O staining can be performed to detect lipid material.²

An animal model was developed in which mice were exposed to aerosols generated from vitamin E acetate at a dose equivalent to the amount that an adult e-cigarette user would inhale daily and matched the findings of vitamin E acetate in BAL fluid from patients with EVALI. Numerous markers indicated that pulmonary injury was present after inhalation of vitamin E acetate aerosols. Cells isolated from the BAL fluid of vitamin

E acetate-exposed mice contained numerous lipid-laden macrophages. Examination of lung-tissue sections from mice exposed to vitamin E acetate revealed alveolar macrophages containing abundant Oil Red O stained lipid, often in clusters, residing with pneumocytes lining the alveoli.³

Several studies have shown that many patients with EVALI had positive oil red O staining in BAL specimens. One study performed Oil Red O staining on 6 confirmed EVALI and 36 non-EVALI patients. All EVALI specimens showed a high percentage of oil red O positive macrophages and large lipid droplets, while the majority of non-EVALI specimens showed a low percentage of Oil Red O positive macrophages and small lipid droplets. The differences between the two groups in both high Oil Red O positive macrophages and large lipid droplet rates was statistically significant ($P < .0001$ for both comparisons). The combined sensitivity and specificity of high Oil Red O positive macrophages and large lipid droplets for diagnosing EVALI were 100% and 94%, respectively.²

Conclusion

Oil Red O staining on BAL specimen is a minimally invasive diagnostic test that can add to the diagnostic certainty of EVALI in the appropriate patient.

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