Short-Term Outcomes From Pulmonary Rehabilitation In An Adolescent Patient With EVALI

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Abstract

Widespread usage of electronic cigarettes (e-cigarettes) has driven the recent epidemic of e-cigarette, or vaping, product use associated lung injury (EVALI). Recent reports have described a heterogeneous range of pneumonitis-related sequelae from non-regulated tetrahydrocannabinol (THC) oil extract products used through various e-cigarette devices, piloting an ongoing federal investigation into the chemical constituents involved in such cases. However, to the best of our knowledge, no published reports to date have examined the impact of EVALI on post-discharge pulmonary function tests (PFTs), and the role of pulmonary rehabilitation in improving short-term functional outcomes. We describe the clinical course of an adolescent male with EVALI due to the use of an off-label THC based vaping pod. After a prolonged intubation period in the intensive care unit he exhibited exertional dyspnea at the outset of his rehabilitation. His initial PFTs were notable for a mixed obstructive and restrictive lung pattern and mildly decreased diffusion capacity. The patient had a slow and gradual improvement in his PFTs during pulmonary rehabilitation, as well as a stepwise improvement in his activities of daily living and resolution of substance abuse related stressors with continued supportive counseling.

Introduction

The recent escalation of severe pulmonary illnesses from electronic cigarette (e-cigarette) use has centered on several non-specific clinical elements including, but not limited to pulmonary infiltrates, absence of infection, and lack of alternative plausible diagnoses.[1, 2] Description of this phenomenon has been isolated to case reports, primarily in the emergency department (ED) and intensive care settings. A national rise in the incidence of life-threatening complications from e-cigarette, or vaping, product use associated lung injury (EVALI) has spurred a public health investigation to better understand the pathogenesis behind these cases of acute lung injury.

As of February 18th, 2020, a total of 2,807 hospitalized EVALI cases have been reported to the CDC from all 50 states, and two U.S. territories (Puerto Rico and U.S. Virgin Islands). Sixty-eight deaths have been confirmed in 29 states and the District of Columbia, with many events linked to specific tetrahydrocannabinol (THC) based solutions.[3] During this epidemic, several clinical associations of EVALI sequelae in hospitalized patients have been noteworthy.[1-8]

To date, the spectrum of respiratory illnesses in patients with EVALI have mimicked a number of respiratory diseases including hypersensitivity and acute eosinophilic pneumonitis (AEP), lipoid pneumonia, acute respiratory distress syndrome, and organizing pneumonia.[9-13] We present a rare case of an adolescent patient who developed hypoxic respiratory failure and spontaneous pneumomediastinum secondary to an EVALI from vaping off-label THC products and his subsequent outpatient pulmonology management.

A previously healthy 17-year-old male with a history of mild-intermittent asthma presented to the hospital pediatric ED with a 1-week history of worsening pleuritic chest pain and a 3-day history of fever, congestion,

diarrhea and nonproductive cough with dyspnea. Two days prior to admission the patient was prescribed Azithromycin by his pediatrician. A subsequent chest x-ray demonstrated perihilar interstitial prominence with hazy perihilar and basilar opacities suggestive of mycoplasma infection superimposed on mild intermittent asthma (Figure 1). The patient endorsed 18-months of vaping using a JUUL e-cigarette device and dabbing, a process wherein butane hash oils are superheated using vaping devices.[2,14] He later reported an unverified e-cigarette distributor had provided him with THC pods labeled "dank vapes" and "smart cards," two months prior to his illness.

The patient arrived at the ED on a non-rebreather after oxygen saturation at home was noted to be 70% on room air by emergency medical services. Initial vitals were as follows: temperature of 99.8 F, heart rate 110 beats per min, oxygen saturation of 90% on 15 liters with a non-rebreather mask, respiratory rate of 50-60 breaths/min. On exam he was found to be moderately distressed, tachypneic, tachycardic with notable hemoptysis and cough. His lung exam was significant for accessory muscle use and diminished breath sounds bibasilarly with crackles along the right subscapular region.

Laboratory tests revealed leukocytosis of 34 x 10^3/μL, with 95% neutrophils, 2% lymphocytes, 2% monocytes and 1% eosinophils. Electrolytes and transaminases were normal. Erythrocyte sedimentation rate and C-reactive protein levels were elevated at 67 mm/hr and 7.3 mg/dL respectively. Respiratory pathogen panel was negative. Initial sputum gram stain revealed non-significant flora. A portable chest x-ray revealed a pneumomediastinum with air extending into the neck and new bilateral pulmonary parenchymal infiltrates, greatest at the periphery of the lung bases, suggesting possible AEP (Figure 2).

The patient's respiratory status quickly worsened, requiring transfer to the pediatric intensive care unit where he progressed to hypoxic respiratory failure requiring intubation and mechanical ventilation. He was started on steroids due to concern for AEP. Bronchoscopy showed normal mucosa of the airway with clear frothy secretions. Bronchoalveolar lavage (BAL) revealed cellular debris and reactive mononuclear cells. Cell counts were 1250 RBC and 600 WBC (67% segs, 6% lymphocytes, 27% monocytes, 0% eosinophils). BAL cytology showed lipid laden macrophages on an Oil Red O stain and no findings of pneumocystis organisms. BAL cultures as well as a comprehensive infectious work up was negative.

He required paralysis for the first fourteen days due to poorly compliant lungs, initially requiring high inspiratory and positive end expiratory pressures which were slowly weaned off. An echocardiogram demonstrated mildly elevated right heart pressures believed to be related to high airway pressure requirement. High-resolution computed tomography (HRCT) with contrast highlighted extensive bilateral ground glass opacities with subpleural sparing and fine reticulation of intralobular septal thickening (Figure 3). At the bases, there was more dense consolidation and mild traction bronchiectasis (Figure 4). Additionally, there was marked pneumomediastinum and subcutaneous emphysema.

The patient defervesced two weeks into his hospital course during which time he received multiple courses of broad-spectrum antibiotics due to concerns for a superimposed bacterial pneumonia at his lung bases. He was extubated to bilevel positive airway pressure on hospital day 15 due to residual weakness from critical illness myopathy. By hospital day 17, he was weaned to nasal cannula but exhibited moderate dyspnea on exertion. Chest x-rays prior to discharge showed resolution of the pneumomediastinum with residual interstitial prominence and left lower lobe consolidation. A repeat echocardiogram revealed normal left systolic function and normal right sided pressures. He was discharged home on hospital day 22 on a four-week oral corticosteroid taper.

Methods

The patient started pulmonary rehabilitation shortly after his discharge while continuing adjunctive corticosteroid therapy. He participated in routine therapy three times per week, which included progressive endurance and strength training. Serial PFTs were simultaneously conducted during the period of his rehabilitation therapy regimen and bi-monthly afterwards. Verbal consent by the patient and legal guardians for the release of data was provided prior to and upon completion of his PFTs.

Results

His initial PFTs results, including, forced expiratory volume in 1 second (FEV_1) of 1.56 L (40% predicted), forced vital capacity (FVC) of 1.70 L (37% predicted), FEV_1/FVC of 92%, residual volume (RV) of 0.82L (78% predicted), total lung capacity (TLC) 2.55L (50% predicted), RV/TLC of 32%, and a low diffusion capacity (DLCO) 11.2 ml/mmHg/min (37% predicted); were notable for moderate restrictive lung pattern and mild air-trapping.

The gradual improvement in the patient's PFT values was evident during the rehabilitation process (Table 1). Follow-up chest x-ray obtained 4-months after discharge showed residual interstitial thickening with mild pleural thickening and fluid in the left lung base, improved from his prior exam. Significantly, after 6-months, his PFTs had essentially normalized with a stable, but mildly decreased DLCO at 23.4 ml/mmHg/min (72% predicted).

At home the patient demonstrated a slow but steady improvement with his activities of daily living. He initially required physical therapy, however, after completion of his pulmonary rehabilitation he returned to near baseline physical strength with only mild dyspnea on exertion and limitation of activities. The patient has refrained from using e-cigarettes as well as marijuana after hospital discharge through supportive counseling.

Discussion

Colloquially known as "vaping," due to the vaporization of humectant, nicotine and other ingredients, e-cigarettes were advertised to eliminate the irritating and harmful effects of combustible smoking.[14,15] This false pretense has since been dispelled by the Food and Drug Administration (FDA) illustrating unspecified amounts of toxins as well as carcinogens in e-cigarettes.[15] The CDC definition of vaping associated pulmonary illness (VAPI), now termed EVALI, which includes the following criteria: 1) patients who present with respiratory distress in the context of vaping within the past 90 days, 2) bilateral pulmonary infiltrates on imaging, and 3) ground-glass appearance on chest CT imaging with an otherwise unremarkable infectious workup.[2] Our patient met the CDC surveillance definition of EVALI, with mild air-trapping and marked impaired diffusion with a notable acute restrictive lung pattern.

The constitutional symptoms of EVALI seem to parallel those of viral cold-like symptoms with progression to more severe symptoms such as hypoxia, cyanosis, and acute respiratory distress syndrome that may mimic pneumonitis related lung injuries on imaging. A recent case-series study illustrated 80% patients with VAPI who were interviewed with a history of e-cigarette related product use within 90 days of symptom onset reported the use of tetrahydrocannabinol (THC) products.[2] "Dank vapes," a popularized label of vaping cartridges that are filled illegally with THC-containing substances, are the most reported brand used by patients nationwide, specifically in the Northeast.[3] These unregulated markets of e-cigarette products have come under increased scrutiny in recent months by the FDA, recently leading to the ban on most flavored vaping cartridges.

In our report, serial PFTs over a six-month period highlight the progressive improvement in lung function with near normalization, evidenced at 3 months after an EVALI occurrence. We believe the contributions of his pulmonary rehabilitation process are noteworthy in his short-term recovery as long-term pulmonary function analysis of EVALI cases remain unknown. Further research into the timing of post-discharge PFTs, along with the prognostic indicators of EVALI, are needed in the optimization of pulmonary rehabilitation. Equally important, is the need for clarifying the outcomes based on the degree of lung injury and the role of adjunctive corticosteroid therapy.

Current efforts at the state and federal level are investigating the correlation between the use of off-label vaping pods with THC extract products and the pro-inflammatory cascades that potentially lead to the development of EVALI. The most recent CDC reports indicate lung fluid samples tested from a geographically diverse range of patients with EVALI yielded a Vitamin E acetate component. Now regarded to be a common chemical marker in EVALI cases, Vitamin E acetate is an additive in THC-containing e-cigarette products.[3]

However, the contribution of these concerning chemicals in E-cigarette products remain ongoing.

The optimal approach in reducing the economic, psychosocial, and healthcare burdens associated with EVALI cases is multimodal and thus, improving collaboration among healthcare and community leaders is essential. The therapeutic role of pulmonary rehabilitation as a standalone or adjunctive therapy in the current EVALI outbreak, as shown in our case, is promising.

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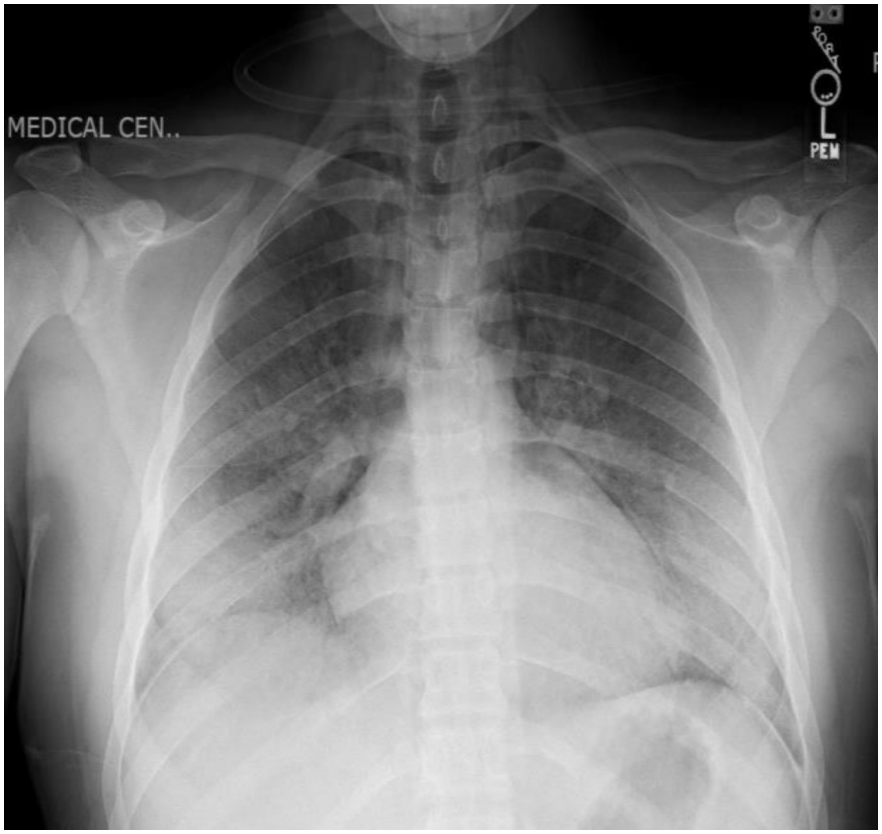

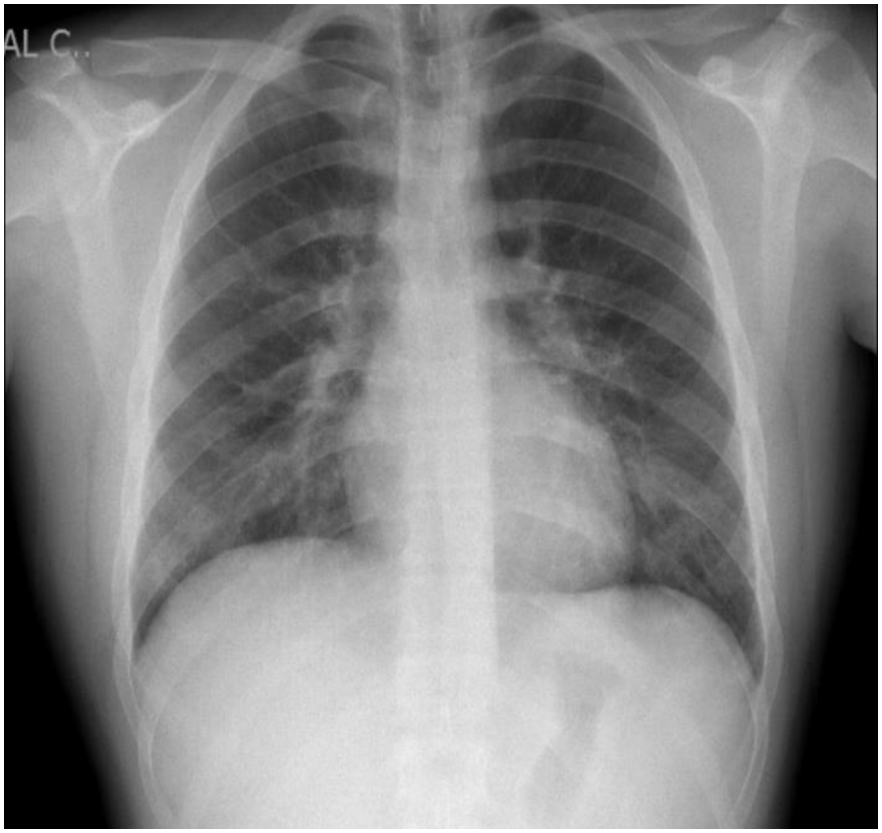

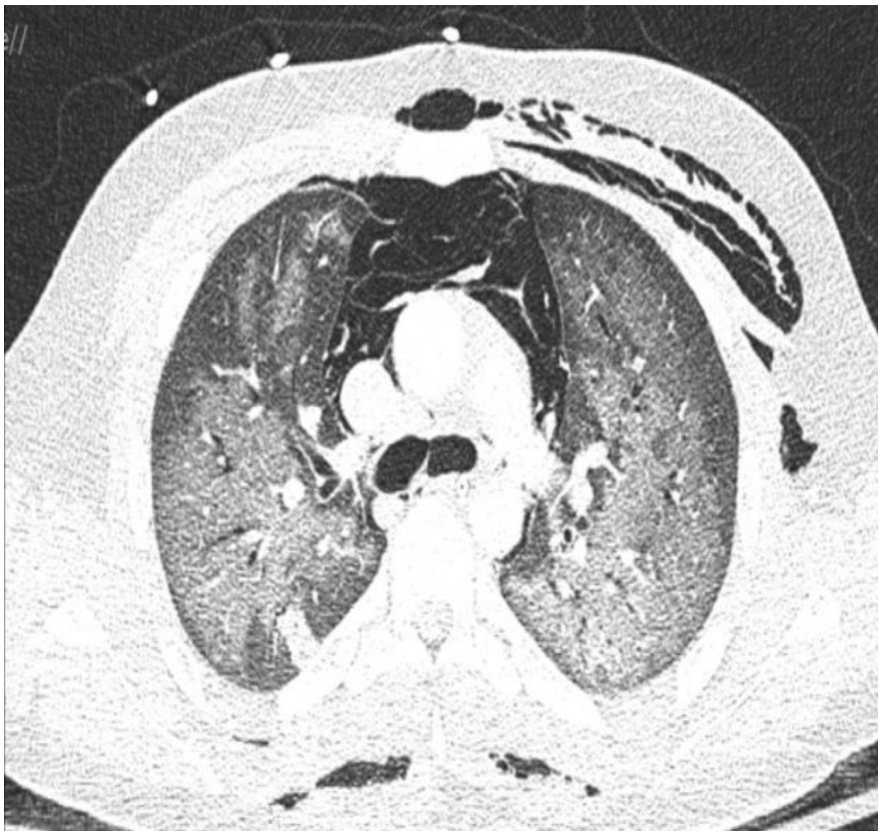

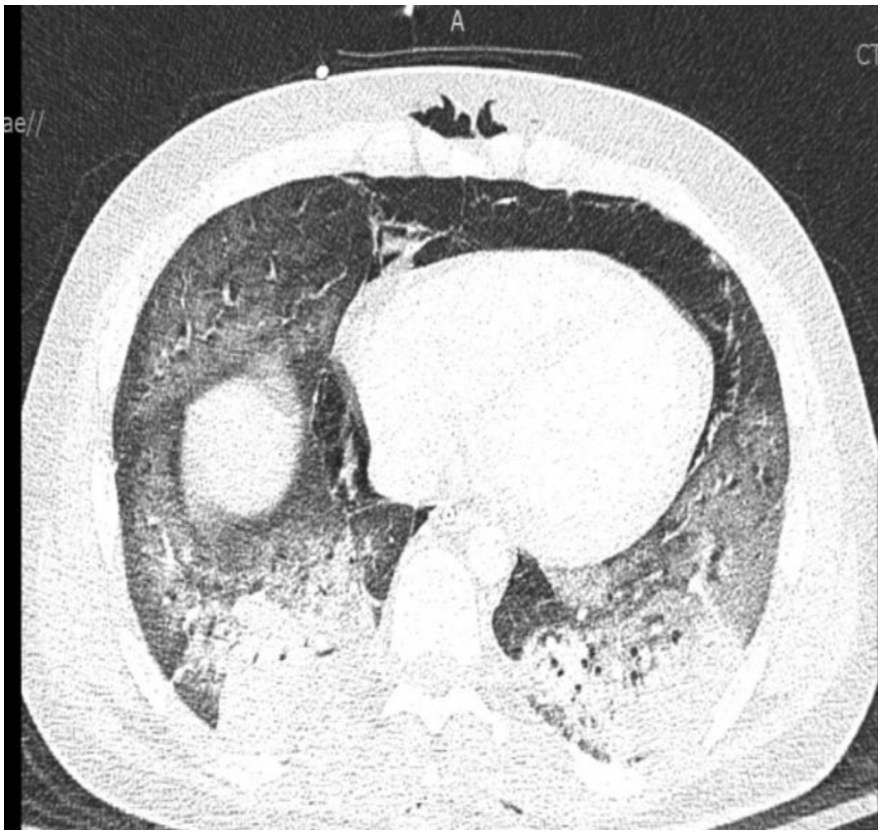

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Table_1_PFT Progression During Pulm Rehab.docx available at https://authorea.com/users/350609/articles/475408-short-term-outcomes-from-pulmonary-rehabilitation-in-an-adolescent-patient-with-evali