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Case report

Acute Respiratory Failure Due to Vaping-Induced Lung Injury: A Case Report and Management Review

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Abstract

Awareness of the detrimental effects of vaping on the respiratory system has significantly increased in the last few years. In July 2019 the Wisconsin Department of Health Services and the Illinois Department of Public Health established the definitions for e-cigarette or vaping product use-associated lung injury (EVALI); it was mostly attributed to the flavoring agents containing vitamin E acetate which in the aerosol form causes surfactant dysfunction. The diagnosis and management of severe EVALI still remain a challenge as the presentation can be easily confused with many other respiratory conditions. There are no guidelines regarding the management of those patients and outcomes vary from total resolution to development of chronic lung disease.

We present a patient with EVALI and acute respiratory distress syndrome (ARDS) that was successfully treated with steroids.

Keywords: ***EVALI, ARDS, acute respiratory failure, ICU, vaping, e-cigarette, public health, young adults.***

Introduction

Electronic cigarettes, (e-cigarettes, also called vaping) are battery-powered devices that allow users to inhale aerosolized substances [1]. In the United States, its use was widely commercialized in 2007, and in a 2014 report, it was the most commonly used tobacco product among youths [2]. E-cigarettes and vapes consist of a heating element, which vaporizes the vaping solution or "vape juice" which is delivered through a mouthpiece. This vaping solution consists of many components, mainly nicotine, a flavoring agent, and a carrier like glycerin or propylene glycol. Flavoring agents are particularly notorious for not being regulated by the FDA.

Much debate has surrounded e-cigarette use as an "unstudied" method for smoking cessation that generally contains fewer toxic chemicals than conventional cigarette smoke.

Despite that, e-cigarette aerosol is not harmless. Using gas chromatography–mass spectrometry and mass spectrometry, the Maryland Department of Health Public Health Laboratory analyzed 46 THC-containing e-cigarette or vaping products and found several toxic ingredients alongside nicotine such as glycerin, medium-chain triglyceride, propylene glycol, and vitamin E acetate, cannabidiol (CBD), and tetrahydrocannabinol (THC) [3]. Other harmful ultra-fine particles such as heavy metals, volatile organic compounds, and other harmful ingredients may also be present but not yet identified [3]. Concerns that e-cigarette use enhances rather than helps eliminate psychological behaviors associated with smoking such as dependence and concurrent substance abuse such as THC, CBD, and butane hash oils (also known as dabs) have been raised. E-cigarette use is relatively common among university students, and use is associated with several issues such as poorer academic performance, greater likelihood of using other substances, and greater rates of anxiety, attention-deficit/hyperactivity disorder, and post-traumatic stress disorder [4].

In 2019, the WDH and IDPH reported multiple cases of pulmonary disease of unclear cause possibly associated with the use of e-cigarettes and related products, which prompted a coordinated public health investigation and established case definitions for EVALI [2]. The term EVALI was first used in September 2019 by the CDC to describe a nationwide outbreak of severe lung disease linked to vaping [5]. The 2019 outbreak of EVALI was mostly attributed to the flavoring agents containing vitamin E acetate which in the aerosol form caused surfactant dysfunction. The other components when vaporized also produce toxic substances including but not limited to formaldehyde and hydrocarbons which can lead to airway damage and epithelial cell injury.

The last figures regarding EVALI from the CDC were reported on February 18, 2020, with 2807 cases of hospitalized patients and 68 confirmed deaths in 28 states. The median age in these reported cases was 24 years [5].

The diagnosis of EVALI remains one of exclusion, many factors such as lack of information regarding the source from the devices, the reluctance of users to participate in surveys and studies, and the lack of large studies describing the syndrome, a limitation for the development of guidelines regarding diagnosis and management.

Case presentation

A 25-year-old female with no medical history presented to the emergency department for shortness of breath, subjective fever, dizziness, body aches, abdominal pain, and vomiting for one-week duration. She was not taking any medications, had no allergies, and had no family history. She consumed alcohol on social occasions and vaped daily for more than 3 years.

On initial exam, she was hypertensive and tachycardic, afebrile with normal saturation of oxygen in ambient air. Her cardiopulmonary and the rest of the exam were non-contributory. Initial laboratory revealed hyponatremia, hypochloremia, hypocalcemia, low urine sodium, and low serum osmolality. Admission chest x-ray (CXR) was normal (**Figure 1A**).

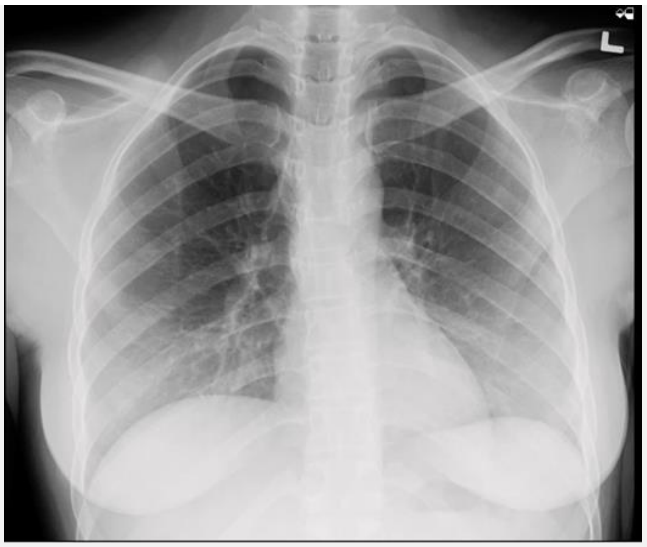

Figure IA: Initial chest X-ray showing no evidence of lung infiltrates

The patient was started on intravenous saline and a workup for a possible infectious process was performed; she clinically improved with the resolution of electrolyte abnormalities.

On day 4 of admission, the patient developed acute shortness of breath and hypoxemia requiring noninvasive ventilation with high-flow oxygen and she was transferred to the intensive care unit (ICU). She was afebrile, tachycardic (131 beats/ min), tachypneic (34 breaths/min). On examination, she was in respiratory distress, and bilateral coarse crackles were elicited on the lung exam. Repeated CXR showed a new infiltrate in the right lung. (**Figure 1B**). She continued to deteriorate and required intubation and mechanical ventilation (MV), for severe ARDS.

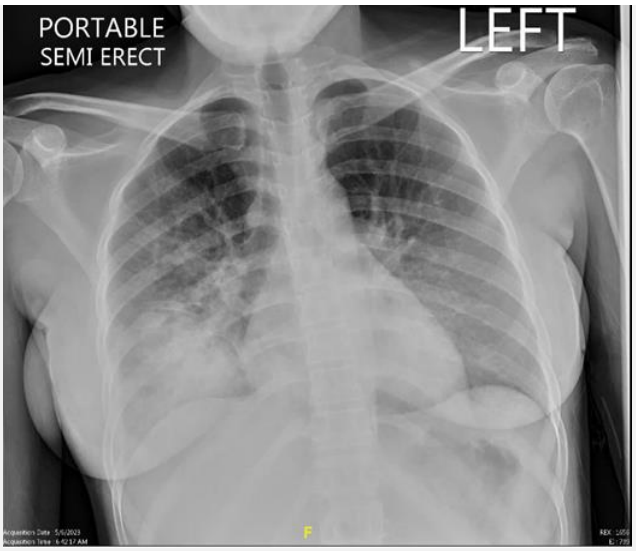

Figure 1B: Chest X-ray on the third day of admission showing dense consolidation in the right lower lobe and increased interstitial infiltrates bilaterally, with a basilar prominence.

Laboratory workup showed anemia (hemoglobin 10 gm/dl units), thrombocytopenia (platelet 137 109 /L units), no leukocytosis, several electrolyte imbalances, and mild transaminitis. She was started on broad-spectrum antibiotics with vancomycin, piperacillin/tazobactam, and doxycycline for presumptive pneumonia while results of infectious work were available. A flexible fiberoptic bronchoscopy (FFB) showed normal airway mucosa, and no secretions or hemoptysis. The bronchoalveolar lavage showed predominant neutrophils, no eosinophils and diffuse alveolar hemorrhage was ruled out. On chest computed tomogram (CT) there were no pulmonary emboli, and extensive bilateral ground glass opacifications with small right-sided pleural effusion were seen (**Figure 2**).

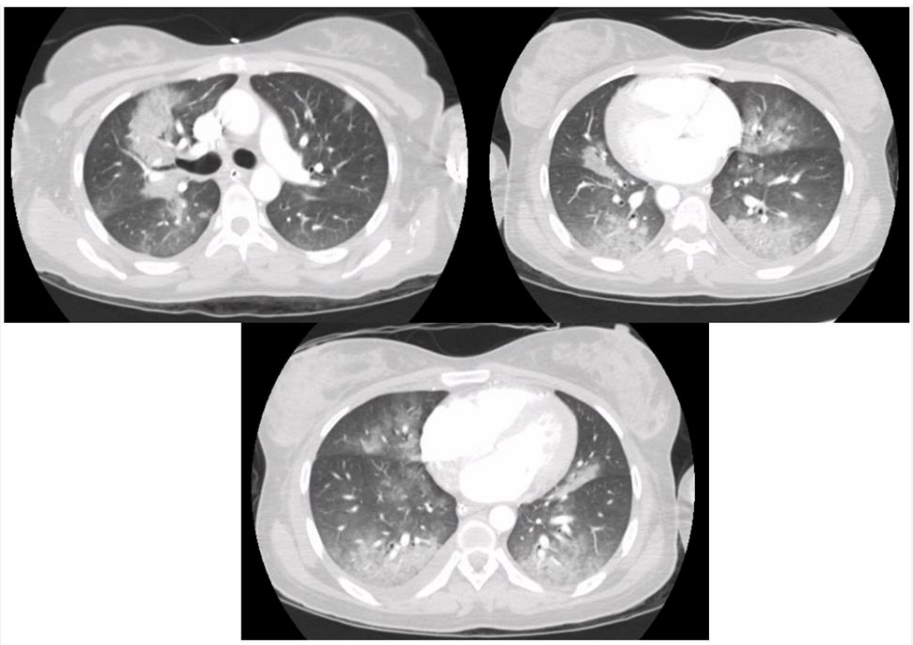

Figure 2: Computed tomography of the chest axial view showing areas of ground glass opacities, dense consolidations with air bronchograms and small left pleural effusion

Infectious workup for bacterial, viral, and mycobacterium pathogens, urine legionella antigen, streptococcus pneumonia antigen, Epstein Barr viral, and Leptospira serology, malaria smear, blood and urine culture, and human immunodeficiency viral screening were all negative. Her autoimmune workup and drug toxicology were negative.

On day 2 of MV, she developed shock requiring vasopressors and stress dose steroids (hydrocortisone 100 every 6 hours). In the next 24 hours, her oxygenation and hemodynamic status started to improve, She was weaned off vasopressors, and stress dose steroids were tapered down to hydrocortisone 50 every 12 hours. The patient was liberated from the ventilator on day 5 of MV to bilevel-positive airway pressure breathing. 24 hours after liberation from MV, she deteriorated again with severe tachypnea, increased oxygen requirements, and no change in CXR findings, she was reintubated.

Given the history of extensive vaping and the negative results from all the workup, a diagnosis of EVALI was considered and her hydrocortisone was changed to methylprednisolone 62.5 every 8 hours.

On day 11 of admission, after 8 days on steroids, she showed clinical and radiological improvement, Antibiotics were discontinued after 7 days and she was liberated from MV. Subsequently, IV steroids were switched to tapering doses of oral prednisone and she was discharged home on day 17 of admission.

On follow-up at the pulmonary clinic 2 weeks after discharge, she was asymptomatic. A repeated CXR and chest CT showed the resolution of abnormalities (**Figure 3A and 3B**). She was slowly tapered off from oral steroids over 6 weeks and remains asymptomatic and free of vaping.

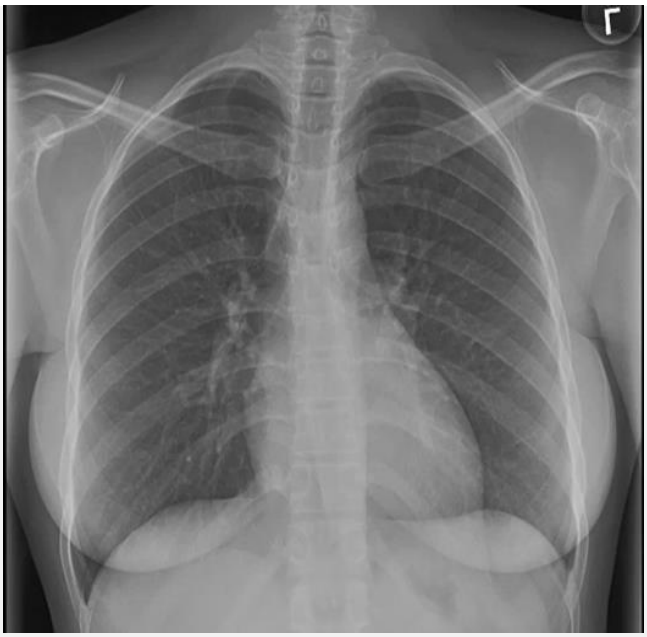

Figure 3A: Chest Xray 2 weeks after discharge showing complete resolution of infiltrates

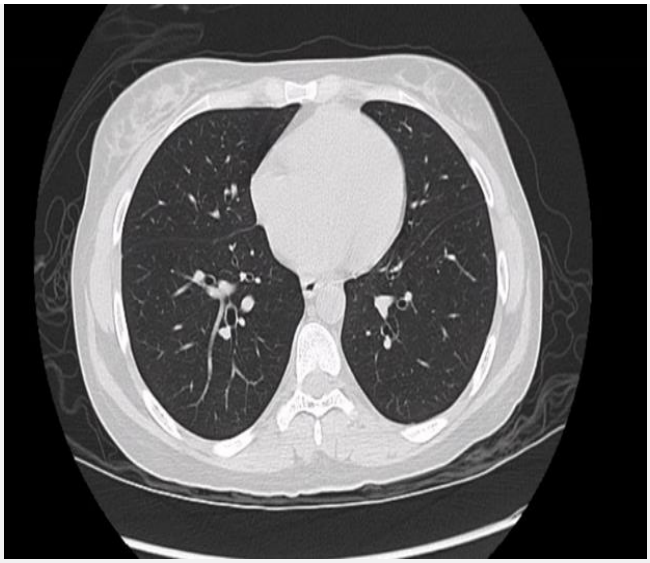

Figure 3B: CT chest 5 weeks after discharge showing complete resolution of infiltrates

Discussion

Our patient highlights the diagnostic and management challenges in critically ill patients with possible EVALI and the potential therapeutic effect of steroids in their management. EVALI is emerging as a respiratory disease affecting youth. The popularity of vaping among youth stems from several factors. The most important contributor is the perceived lost risk [6]. Vaping devices are considered discreet and have a better taste, flavor, and smell than smoked cannabis [7]. Despite that e-cigarette smoking was initially considered an alternative method of smoking cessation, there is enough clinical evidence to suggest the harm of vaping, and the first step in the management, once suspected, is to stop vaping [8].

Clinical presentation of EVALI varies from mild to severe symptoms which can resemble other common conditions like viral or bacterial infections. Similar to our patient, vague constitutional symptoms and respiratory or gastrointestinal symptoms can be present [9]. Key to the suspicion of EVALI is to obtain a detailed history regarding smoking practices.

EVALI is potentially a disease that exhibits sudden rapid and dramatic unpredicted clinical deterioration, as was seen in our case. In recent reports, close to 50% of patients with EVALI, will be admitted to an ICU and 50% of them will need mechanical ventilation [8].

Abnormal laboratory tests found in patients with EVALI include leukocytosis, elevated serum inflammatory markers like C-reactive protein and erythrocyte sedimentation rate, and liver transaminases [10].

Identification of imaging patterns, coupled with the history of vaping is critical in identifying EVALI. CT scan of the chest is more sensitive than Chest X-ray. An array of lung injury patterns has been reported in EVALI. Organizing pneumonia and Diffuse alveolar damage are the most commonly reported patterns of EVALI. CT findings and patterns of vaping-associated lung injury were very elegantly described by Kligerman et al [11]. In their multicenter cohort of 160 cases, common findings in CT imaging include diffuse or lower lobe GGO with subpleural, lobular, or peribronchovascular (PBV) sparing. Septal thickening, lymphadenopathy, and centrilobular nodules are also seen. PBV sparing was associated with younger age. 97% of their patients had one of the six defined patterns (**Table 1**)

Table 1: showing patterns of lung injury on chest CT

Pattern of Injury in 160 cases Kligerman et al. [11]	Percentage
Parenchymal organizing pneumonia pattern	55.6%
Airway centered organizing pneumonia pattern	8.8%
Mixed organizing pneumonia pattern	20%
Acute eosinophilic-like pneumonia pattern	3.8%
Diffuse alveolar damage pattern	5.6%
Diffuse alveolar hemorrhage pattern	3.8%

Although the cause of lung injury associated with e-cigarettes or vaping remains unclear, patterns consistent with toxic inhalational pulmonary injury suggest direct injury rather than an infectious cause [5]. In any case, with suspected EVALI all the other etiologies such as infections must be ruled out. Further investigation including FFB with BAL should be considered to evaluate for other noninfectious conditions like diffuse alveolar damage or eosinophilic pneumonias. Christiani DC et al reported lipid-laden macrophages staining with oil red O on BAL samples [12]. However, due to the lack of a clear understanding of the pathophysiology, the diagnosis of this condition remains one of exclusion as defined by the current case definition [13].

In patients with suspected EVALI specimens sent to pathology include BAL and biopsy. BAL samples usually reveal inflammatory cells most commonly macrophages with distended cytoplasm and fine cytoplasmic vacuoles [14]. A recent case-control study found vitamin E acetate in the bronchoalveolar lavage (BAL) fluid of 94% of 51 EVALI patients and in none of 99 healthy controls in the comparator group [15]. The predominant feature of lung biopsy (transbronchial, cryo, or surgical) is acute lung injury pattern including diffuse alveolar damage, acute fibrinous, and organizing pneumonia [16,17]. It could be airway-centered or diffuse. Careful and detailed evaluation of the histological specimen is necessary to exclude other causes of acute lung injury [18].

The management of critically ill patients with presumptive EVALI starts with stabilization of cardiopulmonary status and evaluation for other diseases that could require specific treatment like autoimmune or infectious conditions. Patients with hypoxic respiratory failure require either noninvasive or invasive mechanical ventilation, few could require extracorporeal membrane oxygenation (ECMO) [8]. There are no randomized studies regarding therapeutics, case reports, or case series that suggest the beneficial effect of high doses of systemic corticosteroids. In one case series, 82% of patients improved on systemic corticosteroids [8]. Co-infections with bacterial or viral pathogens can complicate the diagnosis and management, as corticosteroids may be associated with increased mortality in patients with viral influenza and fungal pneumonia, and increased risk for fungal infections in patients infected with Covid-19. Current evidence for the use of high-dose corticosteroids in patients with EVALI is only based on case series [19]. Concurrent use of antibiotic/antiviral treatment should be considered in EVALI patients, as co-infection with bacterial or viral pathogens is common due to airway cytotoxicity and alteration of cytokines induced by vaping [20]. Vaping was found to increase markers of inflammation in BAL and serum [20]. Patients with milder presentations, who received short courses of moderate doses of steroids had good clinical outcomes [9].

The CDC suggests that selected patients with suspected EVALI who have normal oxygen saturation without respiratory distress or comorbidities might be treated as outpatients initially if they have reliable access to health care and have strong social support systems with a mandatory follow-up within 24-48 hours [5]. Patients with preexisting lung and/or cardiovascular conditions or more than mild symptoms should be hospitalized as the risk of respiratory failure and clinical deterioration is unpredictable, as seen in our patient [21].

There are not many studies reporting on the outcomes of EVALI. Of the 20 cases reported, 50% were admitted to Intensive care units, and no deaths were reported.

The CDC reports EVALI deaths, regardless of hospitalization status. As of February 18, 2020, EVALI deaths were seen in 68 out of 2807 reported cases (2.4%) [5]. Moritz et al. reported that the median age of the patients who survived EVALI was 23 years, as compared with 45 years among those who died; mortality was about 2% in this study [22]. The long-term sequelae of EVALI are not known. We can speculate that some survivors are left with some residual fibrosis. The health effects of tobacco smoke took many decades to manifest and it may take many years for the long-term pulmonary effects of vaping to become apparent.

Conclusions

Patients who engage in vaping are seen by a wide range of specialties from pediatrics to adult medicine. Symptoms of EVALI can be vague and mild and diagnosis can be easily missed or attributed to other conditions. Those patients have the potential for rapid deterioration like our patients. A careful history regarding the use of toxic substances is paramount to establishing the diagnosis. In patients with underlying cardiopulmonary diseases or presenting with more than mild symptoms, consideration of systemic steroids in addition to supportive management should be entertained.

Increased awareness among physicians will probably increase the number of patients with an EVALI diagnosis, and more patients with relatively mild disease may be detected leading to a better understanding of the disease. Further studies are needed to establish the safety and dosing of steroids for the management of EVALI.

Abbreviations

e-cigarette or vaping product use-associated lung injury (EVALI)
Acute respiratory distress syndrome (ARDS)
cannabidiol (CBD),
Tetrahydrocannabinol (THC)
chest x-ray (CXR)
intensive care unit (ICU)
Flexible fiberoptic bronchoscopy (FFB)
Computed tomogram (CT)
Mechanical ventilation (MV)
Bronchoalveolar lavage (BAL)
peribronchovascular (PBV)
extracorporeal membrane oxygenation (ECMO)

Declarations

Conflicts of Interest

The authors declare that they have no competing interests

Ethics approval and consent to participate

Waiver of the Ethical Committee as the identification of subjects was made anonymous according to institutional policy.

Availability of data and materials

The case history and reports used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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Not applicable

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