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Severe acute respiratory distress syndrome secondary to concomitant influenza A and rhinovirus infection complicated by methicillin-resistant Staphylococcus aureus pneumonia in an early pregnancy patient with vaping-induced lung injury

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CASE REPORT

Severe Acute Respiratory Distress Syndrome Secondary to Concomitant Influenza A and Rhinovirus Infection Complicated by Methicillin-resistant *Staphylococcus aureus* Pneumonia in an Early Pregnancy Patient With Vaping-induced Lung Injury

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Abstract

Acute respiratory distress syndrome (ARDS) is a life-threatening lung injury characterized by rapid onset of widespread inflammation in the lungs. Multiple risk factors, including pneumonia, non-pulmonary sepsis, aspiration of gastric contents or inhalation injury, have been reported, to cause ARDS. We present a case of a healthy young woman in her first trimester with vaping-induced lung injury who presented with spontaneous pneumothorax and acute respiratory distress syndrome with concomitant influenza A and rhinovirus infection followed by methicillin-resistant *Staphylococcus aureus* pneumonia.

Keywords: Acute respiratory distress syndrome, Vaping-induced lung injury, Upper respiratory tract infection, Influenza, Rhinovirus, MRSA pneumonia

1. Background

Acute respiratory distress syndrome (ARDS) presents with progressive arterial hypoxemia, dyspnea, and decreased lung compliance requiring positive pressure ventilation. Multiple risk factors have been described; these include pneumonia, non-pulmonary sepsis, and chemical or inhalation injury.[1] Electronic-cigarette smoking or vaping is commonly used by adolescents and can affect lung defense mechanisms and increase susceptibility to respiratory infections.[2] Influenza A is the predominant viral cause of ARDS in adults and can occur with other viruses, especially rhinovirus.[3-6] Human rhinoviruses (HRV) are a common cause of upper respiratory tract infection but usually do not cause serious lower respiratory tract infections.[7] Methicillin-resistant *Staphylococcus aureus* (MRSA) is a common cause of community- and hospital-acquired bacterial superinfection after viral infection and has a 55% of ICU fatality rate. Here, we report an interesting case with severe pulmonary sequelae associated with vaping and pregnancy.

2. Case presentation

An 18-year-old woman in her 10th week of pregnancy presented with a three-day history of fever, productive cough, and dyspnea and a one-day history of left-sided chest pain. She initially experienced fatigue, nausea, and vomiting 10 days before her presentation. She had an uneventful course during her first pregnancy at age 16. Her social history was positive for vaping and cannabinoid use. On

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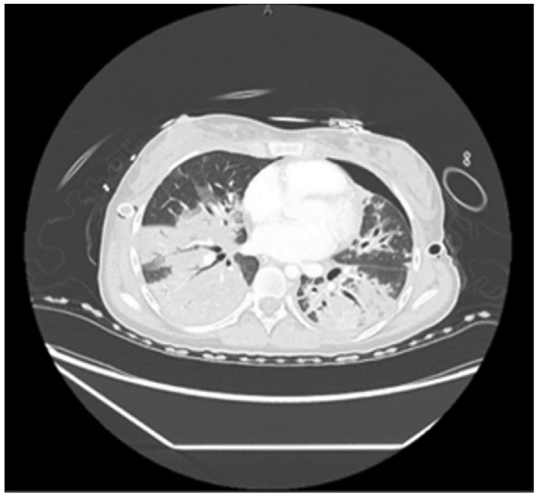

Fig. 1. Coronal view of CT chest revealing multifocal bilateral infiltrates more on the right side with subpleural sparing, suggestive of vaping use.

examination, she was in acute distress with oxygen saturation of 83% on room air and had a respiratory rate of 34 breaths per minute. Her heart rate was 168 beats per minute, blood pressure was 101/65 mm Hg, and the temperature was 98.7 °F. On chest auscultation, she had decreased air entry in the left upper and middle lung zone. Lab results were unremarkable except for elevated C-reactive protein, erythrocyte sedimentation rate, and lactic acid. An electrocardiogram showed sinus tachycardia at 170 beats per minute. Initial nasal swabs for influenza and SARS-CoV2 were negative. An autoimmune panel was unremarkable. Chest radiography revealed a moderately sized left-sided pneumothorax with a rightward shift of the mediastinum and multifocal alveolar opacities. A left chest tube was placed. Further imaging with chest tomography revealed multifocal bilateral infiltrates on the right side with subpleural sparing (Fig. 1), suggesting vaping lung injury.

Her respiratory and hemodynamic status continued to decline, and she required mechanical ventilation and vasopressor support. She was started on broad-spectrum antibiotics. During her early admission, she was found to have a complete abortion. Initial sputum was positive for MRSA. Bronchoscopic inspection revealed multiple vesicular, scabbing lesions throughout her tracheobronchial mucosa and dry bloody secretions, suggestive of chronic vaping use (Fig. 2). A respiratory PCR panel from bronchoalveolar lavage was positive for influenza A/H1 2009 and rhinovirus. She was started on 5-days of oseltamivir along with vancomycin and 5-days of methylprednisolone (1.2 mg/kg/day) for suspected E-cigarette or Vaping Product Use Associated Lung Injury (EVALI). Her respiratory condition persistently declined despite low tidal volume ventilation, paralytics, and prone positioning. A repeat bronchoscopy was done on day 9 and revealed partial healing of the mucosa with less friability and fewer scabbing lesions and copious mucopurulent dry secretions with persistent positive MRSA on BAL. Her hospital course was complicated by a right upper pulmonary artery embolism, despite prophylactic anticoagulation. Eventually, she was transferred to another hospital for extracorporeal membrane oxygenation on the 14th day of admission.

3. Discussion

This present case had multiple severe pulmonary infections leading to pneumothorax and subsequent ARDS in a relatively young and healthy woman. Two main risk factors could contribute to this presentation.

E-cigarettes and vaping affect immune function, especially innate immune response, and increase the susceptibility to infection. These aerosols cause sloughing of epithelial cells and disrupts epithelial

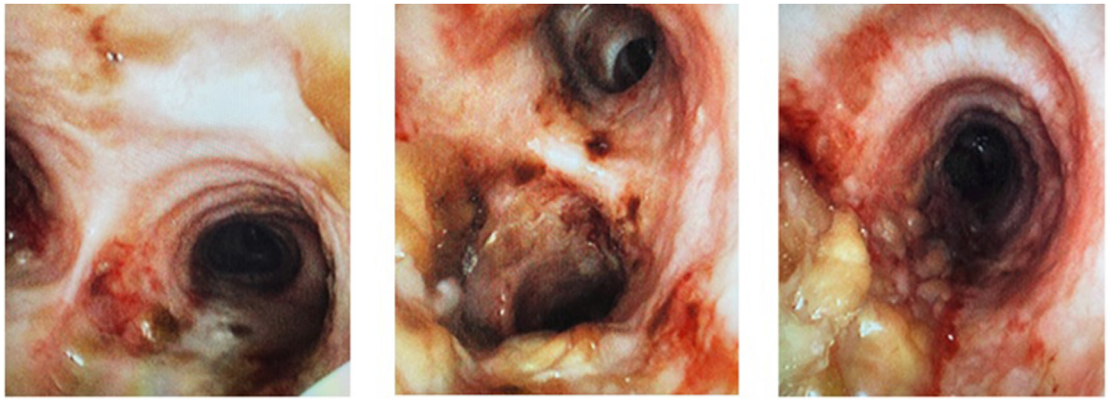

Fig. 2. Bronchoscopy images showed multiple vesicular, scabbing lesions throughout her tracheobronchial mucosa and dry bloody secretions, suggestive of chronic vaping use.

Table 1. Representative cases of EVALI associated with bacterial and viral infections.

	Age (year old), Gender	Comorbidities	Duration form onset to hospitalization	Imaging	Microbiology investigations	Bronchoscopy reports	Treatment	Outcome
Akkanti et al., 2020[20]	20, Male	None	2 weeks	CXR: patchy infiltrates of the right upper and bilateral lower lobes	A respiratory pathogen panel was positive for Influenza A. Sputum was positive for methicillin-sensitive *staphylococcus aureus* (MSSA).	Copious airway secretions and a thick, sloughing, erythematous mucosa	Intubation, hydrocortisone, multiple antibiotics (vancomycin, cefepime, azithromycin and doxycycline), oseltamivir, extracorporeal membrane oxygenation (ECMO) and intra-aortic balloon pump (IAPB)	Deceased
El Chebib et al., 2020[21]	15, Female	None	1 week	CXR: infiltrates in the lower lobes of both lungs and a right-sided parapneumonic effusion. CT chest: extensive multilobar necrotizing pneumonia with early cavity formation and right-sided parapneumonic effusion	Blood cultures were positive for *fusobacterium necrophorum*	N/A	Supplemental oxygen and intravenous piperacillin plus tazobactam.	Improved
Alam et al., 2021[22]	22, Male	None	6 days	CXR: pneumomediastinum with subcutaneous emphysema extending into the cervical region with bilateral pneumonia CT chest: severe pneumomediastinum with diffuse pneumonitis	Tested positive for influenza B prior	N/A	Supplemental oxygen and oseltamivir	Improved
Patil et al., 2021[23]	38, Female	Asthma during childhood, obesity	5 days	CXR: left lower lobe opacification with a trace left pleural effusion. CT chest: significant left lung consolidation with a partially loculated left-sided pleural effusion	Sputum and pleural fluid culture were positive for methicillin-sensitive *staphylococcus aureus* (MSSA)	N/A	Supplemental oxygen, a left chest tube placement and intrapleural fibrinolytic therapy with tissue plasminogen activator and dornase alpha, vancomycin	Improved

(*continued on next page*)

Table 1. (continued)

	Age (year old), Gender	Comorbidities	Duration form onset to hospitalization	Imaging	Microbiology investigations	Bronchoscopy reports	Treatment	Outcome
Choudhry et al., 2022[24]	27, Female	Anxiety disorder	Not mentioned	CXR: bilateral interstitial infiltrates more extensive on the right concerning for atypical pneumonia and pneumonitis. CT chest: remarkable for bilateral airspace opacities concerning EVALI	Elevated *mycoplasma pneumonia* IgM titer	N/A	Noninvasive mechanical ventilation, high dose steroid, ceftriaxone and azithromycin	Improved

CXR, Chest x-ray; CT, Computed tomography; EVALI, E-cigarette or Vaping Use-Associated Lung Injury; IgM, Immunoglobulin M; N/A, Not applicable.

barrier integrity leading to necrosis. Vitamin E acetate (VEA) in vaping products causes alveolar edema and perivascular inflammation. This patient had extensive airway damage which was evident on bronchoscopic inspection.[8] Airway epithelial cells from subjects who vape have decreased expression of Toll-like receptor 3, and this may reduce host defense responses to viral infection. Recent experimental studies have shown mice exposed to e-cigarettes had higher levels of rhinovirus viral loads and that mice with influenza virus infection have higher mortality rates.[2] Mucociliary clearance is also impaired, and this can increase pathogenic bacterial colonization and growth. E-cigarette vapor exposure inhibits antibacterial function of epithelial cells, macrophages and neutrophils, eventually reducing bacterial clearance.[8] After the appearance of EVALI, many cases of associated pulmonary infections have been reported, including bacterial and viral infections (see Table 1 for representative cases).

Progesterone and glucocorticoids increase during pregnancy, can have anti-inflammatory effects leading to increased severity of infections, such as influenza, which require prompt inflammatory responses for the initial control and clearance of pathogens.[9] Estrogen appears to have both anti- and pro-inflammatory effects depending on the level expressed. Influenza infection seems to induce a hypoestrogenic state resulting in decreased clearance of alveolar fluid through sodium channels, and thereby increasing susceptibility to pneumonia.[10] Reports indicate that pregnant women with severe influenza infection are also at increased risk of having pregnancy-related complications, possibly contributing to the spontaneous abortion in this case. Pregnant women in all 3 trimesters were at increased risk of influenza-associated complications, especially with delayed antiviral treatment beyond 48 h after symptom onset, namely ARDS in this case. Among deaths associated with influenza infection, 7.1% occurred in the first trimester, 26.8% in the second, and a remarkable 64.3% in the third.[11]

Influenza A virus is the most frequently reported cause of viral pneumonia and ARDS in adult patients. Some patients with influenza (13.1%) have other viral coinfections; human rhinovirus (HRV) was the most frequent infection, but this virus seems to cause less severe disease than other non-rhinovirus co-infections.[12] Human rhinovirus is one of the most commonly identified viruses in adults admitted to hospital but is rarely the sole cause of pneumonia.[13]

Influenza infection is substantially worsened by the onset of secondary pneumonia caused by bacteria, such as MRSA. The influenza-injured lung

microenvironment causes MRSA infections to increase cytotoxin expression.[14] The pathogenesis of viral-induced ARDS includes increased capillary permeability with alveolar damage, stimulation of cytokines and chemokines, and recruitment of both innate and adaptive immune cells.[15] Superinfection with MRSA also reduces expression of IL-1β, and decreased expression of IL-1β impairs host immunity and leads to more severe inflammation in the lungs.[16]

This patient presented with a secondary spontaneous pneumothorax which was more likely caused by vaping rather than influenza infection. Vaping has not yet been established as a risk factor for pneumothorax, and more cases are needed to establish any association.[17] Possible mechanisms include cell injury from inhalation compounds and airway barotrauma from repeated inhalation through a resistive device that generates large negative intrathoracic pressure.[18]

Spontaneous pneumothorax from influenza is very rare unless it is co-existent with other respiratory disorders.

This patient was treated with antibiotics and antivirals drugs and was started on corticosteroids for EVALI. There is no consensus on the corticosteroid treatment for EVALI on a specific dose, duration, or taper plan, and these factors usually depend on the patient's response to the treatment, while there have been reports where patients recovered with conservative/supportive measures alone.[19] This patient showed improvement in her airways on her second in bronchoscopy after starting the corticosteroid, but her parenchymal lung injury persisted.

This case exemplifies the deleterious effect of vaping induced lung injuries in association with pregnancy and multiple subsequent viral and bacterial infections in a young and healthy woman.

Conflict of interest

All the authors declare no conflict of interest.

Author contribution

PY, JT, SS contributed on data acquisition and manuscript drafting. All of the authors have contribution on manuscript revision and final approval.

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