E-cigarette or vaping product use-associated lung injury (EVALI) masquerading as COVID-19

Nandita Ganne,[1] Raj Palraj ,[2] Elizabeth Husted,[1] Ishan Shah[1]

[1]Family Medicine, Mayo Clinic Health System, La Crosse, Wisconsin, USA
[2]Infectious Disease, Mayo Clinic College of Medicine and Science, Rochester, Minnesota, USA

Correspondence to
Dr Nandita Ganne;
ganne.nandita@mayo.edu

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SUMMARY

SARS-CoV-2, the novel coronavirus causing COVID-19, has caused a global pandemic resulting in over 4 million deaths globally (data current as of 14 July 2021). E-cigarette or vaping product use-associated lung injury (EVALI) is a type of acute lung injury of unclear pathogenesis. The two pathologies present with overlapping clinical symptoms, laboratory values and imaging, making them difficult to distinguish, especially in the setting of a global COVID-19 pandemic. We present the case of a 32-year-old woman treated for COVID-19 despite multiple negative SARS CoV-2 PCR tests and nucleocapsid antibody test. On further investigation, she endorsed use of E-cigarettes and was subsequently diagnosed with EVALI. The patient was treated with oral and intravenous steroids, resulting in significant improvement in her symptoms. This case highlights the challenge of diagnosing rarer aetiologies of respiratory distress during the COVID-19 pandemic.

BACKGROUND

Novel COVID-19 was first identified in Wuhan, China in December 2019 and has resulted in 187 million total reported cases and 4 million deaths globally as of 14 July 2021.[1 2] As of 14 July 2021, there have been 33 million cases and 605 551 deaths in the United States (data current as of 14 July 2021). Similar to COVID-19, E-cigarette or vaping product use-associated lung injury (EVALI) is a recently discovered cause of respiratory illness and was first described in August 2019. As of February 2020, 2807 cases and 68 deaths secondary to EVALI have been reported (Centers for Disease Control and Prevention).[3] EVALI is a form of acute lung injury with pathologic findings of acute fibrinous pneumonitis, diffuse alveolar damage or organising pneumonia.[4] Due to overlapping clinical symptoms with COVID-19—including fever, cough, shortness of breath and fatigue—differentiating between COVID-19 and EVALI has its diagnostic challenges. This may lead to delay in diagnosis and providing improper treatment.[3] We share our experience with a young woman who presented with respiratory symptoms and the challenges of diagnosing rarer causes of pneumonia/pneumonitis in the era of COVID-19.

CASE PRESENTATION

A 32-year-old woman with a history of opioid use, generalised anxiety disorder and latent tuberculosis presented with an 8-day history of relapsing fevers, shortness of breath, cough, myalgias and fatigue. She also reported of pain with inspiration, lower abdominal pain, nausea/vomiting and headaches, but denied haematuria, skin lesions or rashes, pain or swelling in her extremities or history of coagulopathy. The patient had no sick contacts and denied recent travel. Social history was most notable for E-cigarette use.

She had a negative COVID-19 nasopharyngeal (NP) PCR test on day 6 of her illness. Her vital signs at admission were temperature 37.3 °C, heart rate 122 bpm, respirations 20/min, blood pressure 123/74 mm Hg. While the patient reported of fevers at home, her temperature was not elevated during either hospitalisation. She was initially saturating at 88% on room air and required 2 L supplemental oxygen to maintain saturations greater than 94%. On physical examination, the patient was noted to be tachycardic, tachypneic, anxious and diaphoretic. The patient's pulmonary examination was significant for decreased air movement in all lobes with scant rhonchi and wheezes. Chest X-ray revealed significant bilateral opacities and the patient was hospitalised for 2 days. The patient was treated under the presumptive diagnosis of COVID-19 pneumonitis despite two negative NP COVID-19 PCR tests and a subsequent negative SARS-Cov-2 total antibody.

Eleven weeks later, the patient presented with similar reports but now had worsening cough, shortness of breath, nausea, vomiting, diarrhoea and fevers. She required 1 L supplemental oxygen and was hospitalised for further management. Labs were significant for an elevated C reactive protein (CRP), D-dimer, ferritin, lactate dehydrogenase. The patient's ANA, DNA double-stranded antibody, cyclic citrullinated peptide antibodies, complement C4, vasculitis panel were negative and there was no peripheral eosinophilia. She had increasing oxygen requirements throughout her hospitalisation. She was able to saturate well on 2 L nasal cannula but desaturated when lying flat on her back despite continued oxygen support. Despite her desaturation episodes, the patient continued to breathe comfortably on 2 L. CT chest angiogram showed mild progression of bilateral pulmonary infiltrates suspicious for COVID-19 pneumonitis. On further questioning, the patient admitted to using an E-cigarette approximately five times per week. Due to the CT findings and negative infectious workup, the patient was thought to have vaping-induced lung injury. The patient was started on oral prednisone 40 mg/day and subsequently transitioned to intravenous Solu-Medrol due to persistent hypoxia. Remdesivir was discontinued at this time. She improved significantly over the next 24–48 hours after intravenous steroid initiation and was eventually weaned off oxygen.

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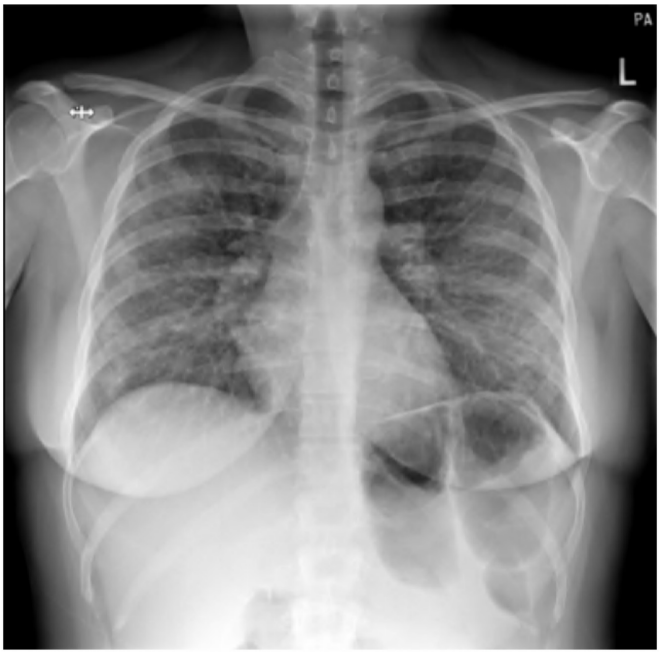

Figure 1 Chest x-ray on admission; new diffuse bilateral pulmonary infiltrates in both upper and lower lungs.

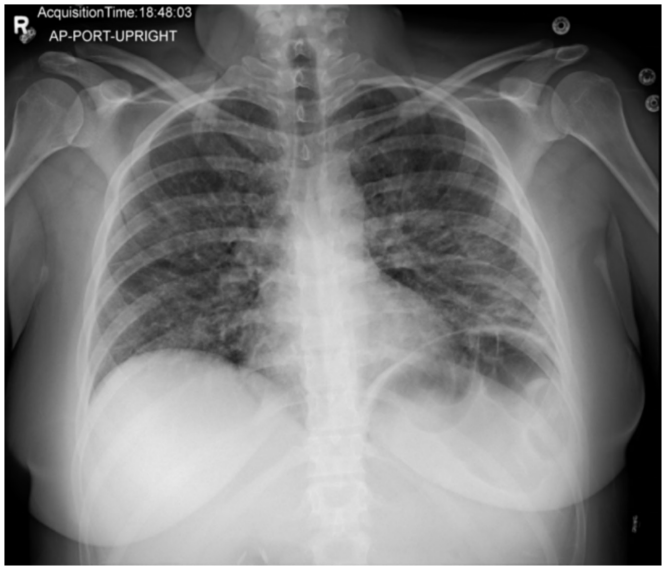

Figure 2 Progression of disease with significantly increased bilateral patchy hazy airspace opacities.

INVESTIGATIONS

The patient was hospitalised two times and received a similar workup each visit. On initial presentation, a urinalysis was ordered due to her flank pain and history of nephrolithiasis; it showed mixed flora. Urine culture subsequently showed white blood cells, red blood cells and bacteria. The following laboratory values were within normal limits: haemoglobin 12.7, haematocrit 37.8, leucocytes 7.7, lymphocytes level ranging from 0.94 to 1.34 with an upward trend during hospitalisation, platelet count 384, sodium 137, potassium 3.7, chloride 98, bicarbonate 22, blood urea nitrogen 11, creatinine 0.76, glucose 102, albumin 3.7, alkaline phosphatase 100, bilirubin 0.4. Abnormal labs included an anion gap of 17, aspartate aminotransferase (AST) 83, alanine aminotransferase (ALT) 53, D-dimer 871, lactate 2.4, procalcitonin 0.21, CRP >400, ferritin 706. Streptococcus pneumoniae antigen and legionella antigen were negative. Histoplasma, blastomyces and cryptococcus antigen and antibody were also negative. Her chest X-ray showed new diffuse bilateral pulmonary infiltrates in upper and lower lungs (figure 1). Her CT chest angiogram and pulmonary arteries showed diffuse bilateral pulmonary interstitial and ground-glass opacities but was negative for a pulmonary embolism (figure 2). Her rheumatoid factor was mildly elevated at 18 and her ANCA vasculitis panel was negative. She was tested for COVID-19 NP PCR two times with negative results and her SARS-CoV-2 nucleocapsid total antibody was negative on discharge.

On readmission, the patient's liver function tests and D-dimer were normalised. Her troponin and thyroid-stimulating hormone were within normal limits. Her urinalysis continued to show trace leucocyte esterase and bacteria and her blood cultures continued to remain negative. Her influenza A and B PCR and SARS CoV-2 PCR were negative. Her chest X-ray during this admission shows significantly increased bilateral patchy hazy airspace opacities (figure 3). Her CT chest angiogram and pulmonary arteries showed mild progression of bilateral pulmonary infiltrates, further raising suspicion for COVID-19 pneumonitis and was negative for acute pulmonary embolism (figure 4). The following laboratory values were within normal limits: haemoglobin 12.5, haematocrit 37.3, leucocytes 9.2, lymphocyte level ranging from 0.44 to 1.04, platelets 232, sodium 137, potassium 3.5, chloride 101, bicarbonate 23, anion gap 13, blood urea nitrogen 8, creatinine 0.72, calcium 9.2, glucose 108, AST 18, ALT 9, alkaline phosphatase 71, bilirubin 0.7. Other pertinent labs included lactate dehydrogenase 357, ferritin 379, D-dimer 604, CRP >400. The patient's urine drug screen was positive for tetrahydrocannabinol (THC).

DIFFERENTIAL DIAGNOSIS

The patient was initially suspected to have COVID-19 pneumonitis. Nonetheless, a broad differential was maintained including bacterial, viral pneumonia and acute eosinophilic pneumonitis as the patient had multiple negative COVID-19 NP PCR tests and a negative SARS COVID-19 total antibody. On further questioning, the patient also admitted to E-cigarette use, prompting suspicion for EVALI and had continued to use E-cigarettes between hospitalisations. Our case highlights the difficulties in diagnosing rarer aetiologies of respiratory distress during the

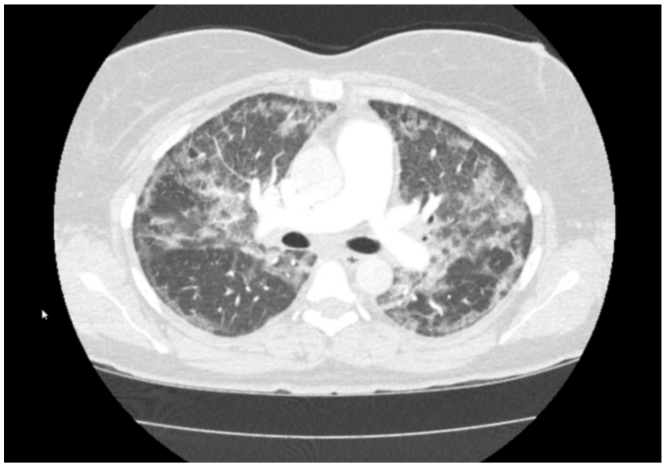

Figure 3 CT chest on admission. Diffuse bilateral pulmonary interstitial and ground-glass opacities.

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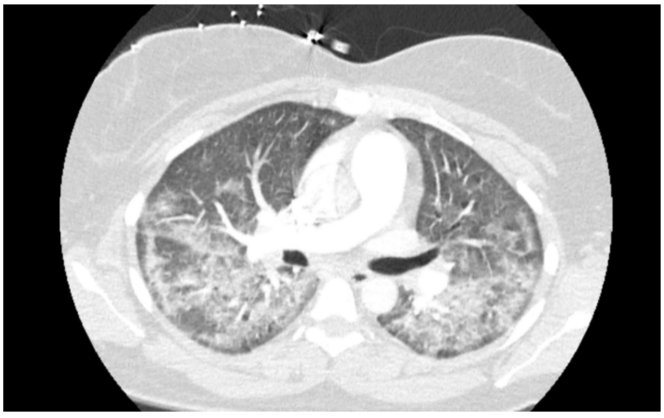

Figure 4 CT chest on readmission. Mild progression of bilateral pulmonary infiltrates, suspicious for COVID-19 pneumonitis.

COVID-19 pandemic. Due to the heightened sense of awareness and concern with SARS-CoV-2 infections, the patient was presumed to be positive even though PCR testing was negative two times. It was known that she was a smoker at the initial admission, but the significantly higher incidence of COVID-19 in smokers as well as rare diagnosis of EVALI led us to treat the patient with antivirals.

TREATMENT

During the patient's first admission, she was treated with dexamethasone, ceftriaxone, azithromycin and intravenous fluids. The patient was noted to have a significantly improved condition on hospital day 2. She was weaned off the oxygen and steroids were held. Due to suspicion of an atypical or bacterial pneumonia, antibiotics were continued. During her rehospitalisation, intravenous remdesivir was used to empirically treat for COVID-19 despite negative tests. Infectious disease and pulmonary were consulted and she was initially started on oral prednisone 40 mg/day. This was transitioned to intravenous Solu-Medrol due to the patient's persistent hypoxia. She improved significantly in the next 24–48 hours after intravenous steroids and was weaned off oxygen.

OUTCOME AND FOLLOW-UP

The patient was discharged in stable condition and counselled regarding the importance of eliminating tobacco and E-cigarettes use. Chest X-ray following discharge showed hazy bilateral infiltrates that appeared to have improved from the last examination. Due to this improvement, we plan to repeat her CT chest in 3 months to confirm improvement of her lung pathology.

DISCUSSION

EVALI is thought to be a type of acute lung injury with an unknown pathogenesis. E-cigarette use, especially those containing THC and/or vitamin E acetate, is a key risk factor for developing the disease process.[4] Similarities in clinical presentation, laboratory studies and imaging studies make distinguishing between COVID-19 infection and EVALI challenging. Both disease processes present with similar initial symptoms, including cough, dyspnoea, fevers, vomiting, diarrhoea and headache.[4] Similarly, laboratory studies including inflammatory markers (CRP, erythrocyte sedimentation rate, procalcitonin) and markers of coagulation may be unremarkable or elevated in both presentations and do not help distinguish between them. Furthermore, chest X-ray and CT have very similar findings in both presentations, including diffuse hazy or consolidative opacities and ground-glass opacities, respectively.[4] As well, both COVID-19 and EVALI are associated with worse outcomes in older adults or those with underlying chronic conditions, including cardiac and pulmonary disease. A national cross-sectional online survey has found that COVID-19 diagnosis was five times more likely in E-cigarettes users, making finalising a diagnosis challenging.[5] However, there are a few key differences that can be used to distinguish the two pathologies. EVALI can present with leucocytosis while COVID-19 often presents with lymphopenia. This trend was not observed in our patient, as she had normal white cell counts with normal and low lymphocyte counts, inconsistent with EVALI.[6]

Additionally, E-cigarettes are used more commonly by younger adults, so EVALI often affects this population, rather than the older population seen in more severe cases of COVID-19.[6]

COVID-19 diagnosis relies on SARS-Cov-2 by PCR and previous infections can be confirmed with SARS-CoV-2 total antibody; however, EVALI remains a diagnosis of exclusion. Despite multiple negative COVID-19 tests in our patient, she was treated for COVID-19 pneumonitis over the course of two hospitalisations due to high suspicion in the setting of the current pandemic and lack of definitive tests for EVALI. In the setting of pandemic, pretest probability of COVID-19 was considered high clinically. Though COVID-19 NP PCR has high analytical sensitivity and specificity, the clinical performance depends on the quality of specimen and time of testing in the course of illness. In the setting of high clinical suspicion, if initial NP COVID-19 PCR is negative, it is recommended to repeat it in 48–72 hours to reduce rate of false-negative results. However, two negative COVID-19 PCR tests prompted evaluation for alternative diagnoses. This highlights the importance of understanding the sensitivity and specificity of COVID-19 tests being ordered. As well, earlier diagnosis can be made by including questions regarding E-cigarette use in the initial admission history and physical in patients with respiratory failure.

Delayed diagnosis results in delayed treatment in the setting of EVALI and subjects patients to other treatments of unknown efficacy. In general, COVID-19 infections in hospitalised patients are treated with remdesevir to reduce recovery time and dexamethasone if supplemental oxygen or ventilatory support is required. The utility of convalescent plasma and IL-6 pathway inhibitors in the treatment of COVID-19 is not well established at this time. Alternatively, the optimal treatment for EVALI is currently unknown. Patients are initially treated with empiric antibiotics to cover for possible community-acquired pneumonia.

Learning points

- E-cigarette or vaping product use-associated lung injury (EVALI) and COVID-19 present with similar signs/symptoms and radiologic imaging. In patients with one or more negative COVID-19 tests, the differential should remain broad and EVALI should be considered.
- In patients suspected of having COVID-19 infection, a thorough history should be obtained, especially in the setting of negative COVID-19 tests.
- The optimal treatment for EVALI is currently unknown. Antibiotics are recommended to cover for possible community-acquired pneumonia and glucocorticoids are recommended in patients with worsening symptoms and hypoxemia, despite unknown efficacy.

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The efficacy of glucocorticoids in EVALI is unknown, but their use is recommended in patients with EVALI that have progressively worsening symptoms and hypoxemia. In less severe cases, current recommendations advise holding glucocorticoids due to potential adverse effects, the possibility of an infectious aetiology causing the presentation or resolution of symptoms without treatment.[4] Due to our patient's symptoms and hypoxemia, she was started on glucocorticoids and improved significantly.

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ORCID iD

Raj Palraj http://orcid.org/0000-0003-3319-9565

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