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Introduction

- Electronic-cigarettes or “vapes” consist of a liquid material that can deliver tobacco or marijuana products. The liquid is heated up to create an aerosol, which is inhaled. Although these products are marketed to be safer than tobacco cigarettes, e-cigarettes also contain harmful chemicals.¹
- A Centers for Disease Control and Prevention (CDC) study estimates 2.7% of adults in the United States (US) were regular e-cigarette users in 2017.¹
- E-cigarette or vaping-associated lung injury (EVALI) emerged in the US in the summer of 2019.²
- CDC reports 2,807 documented cases of EVALI and 68 confirmed deaths in the US as of February 18, 2020.
- Marijuana-containing vapes have been associated with an estimated 82 percent of cases.³
- EVALI has been characterized by respiratory, gastrointestinal, and/or constitutional symptoms in e-cigarette users.²
- Imaging consistent with this clinical syndrome most commonly shows diffuse basilar infiltrates and “ground-glass” opacities.^{4,5}
- Diagnosis can be made from an otherwise negative laboratory workup and history of e-cigarette use. Further testing may reveal lipid-laden macrophages from bronchoalveolar lavage samples.²
- Some patients documented in a case series required intubation and mechanical ventilation due to deteriorating clinical status and hypoxemia. Most patients improved within 72-hours of parenteral steroid therapy and were subsequently discharged on an oral steroid taper with clinical improvement.²
- CDC investigations of vaping products have identified vitamin E acetate, a component of e-cigarettes, as a common factor isolated from cellular components of individuals with EVALI.³

Case Description

History

HPI: 38-year-old female with a history of asthma, HTN, obesity, GAD, PTSD presented to the ED with high-grade fever, nausea, and vomiting. She was sent home from the ED with ibuprofen and PO ondansetron but returned two days later with continued high fevers/chills with a reported Tmax of 104°F. She also complained of worsening nausea/vomiting with non-bloody diarrhea for three days. She endorsed associated weakness, generalized body aches, chest tightness, and a productive cough.

Pertinent negatives: No history of DVT or PE. No recent travel.

ROS: One sick contact one month prior to admission with a friend who had spent a few weeks in East Asia. The friend allegedly had a two- to three-day, self-limited respiratory illness at the time of contact with the patient.

PMH: asthma, HTN, obesity, PCOS, endometriosis, stress urinary incontinence, uterine fibroids, ADHD, GAD, PTSD, insomnia.

PSH: cholecystectomy.

Medications: albuterol MDI 1-2 puffs q4-6hrs prn cough/wheeze, clonidine 0.2 mg PO qHS, medical marijuana prn PTSD/anxiety, trazodone 50 mg PO qHS, vilazodone 40 mg PO qDay, lisdexamfetamine 40 mg PO qAM

Allergies: penicillin (hives).

Social history:

- Reported daily use of a marijuana vape. Denied use of tobacco cigarettes or tobacco vape products. Denied ETOH consumption or any other drug use.
- Reported she was currently sexually active with two trans-female partners. She was previously on emtricitabine/tenofovir for pre-exposure prophylaxis up until 3 months prior to admission; reported she and her partners all recently tested negative for HIV.
- Reported having one dog and two ferrets at home, one of which was newly adopted. She reported they did not prophylactically treat their animals for ticks.

Family history: breast and lung cancer.

Physical Exam

- General: Alert, awake, in mild distress, moving around in discomfort.
- HEENT: EOM intact, PERRLA, oral mucosa pink and moist, conjunctiva pink.
- Skin: No cyanosis or pallor, normal capillary refill.
- CV: Tachycardic, normal rhythm, no murmurs/rubs/gallops. Peripheral pulses symmetrical.
- Respiratory: Diminished respiratory effort, clear lung sounds in all fields with no wheezes/rales/rhonchi. Patient coughs with deep inspiration.
- GI: Abdomen mildly distended, normoactive bowel sounds, bilateral adnexal tenderness.
- Neurologic: Alert and oriented to person, place, time, and situation. Normal motor and sensory function.
- Psychiatric: Anxious mood, normal speech and thought content.

VITALS:

- BP: 156/88 mmHg • SaO2: 97% on RA
- HR: 126 bpm • Temp: 101.4°F
- RR: 18 breaths/min

Diagnostic Results

ON ADMISSION:

11.5	136	98	6	122
12.6	4.0	26	0.70	
35.5				

- LFTs: ALT 27 IntUnits/L, AST 37 IntUnits/L, alk phos 83 IntUnits/L, total protein 7 g/dL, albumin 3.6 g/dL, total bilirubin 0.9 mg/dL
- Calcium 9 mg/dL, lactate 1.7 mmol/L
- Negative influenza antigen
- UA: specific gravity 1.022, pH 5.5, protein 30, ketones 40, trace blood, moderate epithelial cells, few bacteria, few mucus, few amorphous crystals
- Urine pregnancy test negative
- EKG: normal sinus rhythm

FURTHER WORKUP:

- Negative tests: influenza PCR, Legionella urine antigen, respiratory viral panel, Cryptococcal antigen, Aspergillus galactomannin, ANA, Q fever antibody, HIV antibody, Leptospira, Coccidioides, Histoplasma, VZV.
- Blood cultures negative, sputum cultures grew normal flora.
- Bronchoalveolar lavage culture grew normal flora.
- Acid-fast bacilli and fungal cultures were negative.

Table 1. Differential Diagnosis

Community-acquired pneumonia (CAP)
Legionella pneumonia
Pneumocystis jirovecii pneumonia
Fungal pneumonia: Aspergillus, Coccidioides, Histoplasma, Blastomycosis
Q fever secondary to Coxiella species
Autoimmune: vasculitis, granulomatosis with polyangiitis
Tuberculosis
Cannabinoid hyperemesis syndrome
Chemical irritant from daily vaping

Hospital Course

- Patient was admitted for sepsis secondary to CAP.
- The patient was started on IV levofloxacin 750 mg, continued once daily for seven days. She was given three liters of fluid and a one-time dose of IV methylprednisolone 125 mg in the ED, followed by five-day taper of PO prednisone. She was also receiving nebulized albuterol q4hr with a q2hr dose as needed.
- Leukocytosis resolved soon after admission.
- Continued to spike daily high fevers up to Tmax of 102-103°F and had a persistent non-productive cough despite treatment.
- Infectious disease and pulmonology were consulted.
- Antibiotic therapy was switched to PO doxycycline 100 mg BID after one week of levofloxacin without clinical improvement.
- On serial physicals, pulmonary exam continued to be overall normal with clear lung sounds accompanied by a dry cough.
- Completed multiple repeat chest x-rays during hospital stay that showed worsening infiltrates (Images 1 and 2).
- Underwent a bronchoscopy with bronchoalveolar lavage (BAL); cultures grew normal flora. BAL cytology revealed foamy macrophages with scattered small lymphocytes consistent with EVALI.
- A final chest x-ray showed partial clearing of lung infiltrates (Image 3), however she continued to spike fevers until she was restarted on PO prednisone a few days prior to discharge.
- She was discharged on a PO prednisone taper to complete two weeks of therapy and PO doxycycline to complete two weeks of treatment.
- She was strongly urged to avoid use of vape products or e-cigarettes in the future to prevent recurrence of EVALI.

Conclusions

- EVALI is a clinical syndrome characterized by respiratory, gastrointestinal, and systemic symptoms, diffuse basilar infiltrates on chest radiographs, and foamy macrophages with scattered small lymphocytes on pathology.
- EVALI should be considered in individuals with a clinical picture consistent with pneumonia in the setting of a negative laboratory workup and a history of e-cigarette use.
- Parenteral steroid therapy until clinical improvement followed by PO steroids is the current recommendation for treatment of EVALI. As it applies to this case, the patient began improving clinically with the use of steroids, however improvement may have been seen earlier had she received more than an initial one-time dose of IV methylprednisolone.
- Vitamin E acetate has implications in this disease process, however further studies are required to determine the exact mechanism of damage and in turn determine the best treatment regimen.

References

- ¹Electronic cigarettes: What's the bottom line? CDC. https://www.cdc.gov/tobacco/basic_information/e-cigarettes/pdfs/Electronic-Cigarettes-Infographic-p.pdf. Updated Feb 25, 2020. Accessed Nov 30, 2019.
- ²Layden JE, Ghinai I, Pray I, et al. Pulmonary illness related to e-cigarette use in Illinois and Wisconsin – final report. *NEJM*. 2020; 382:903-916. doi:10.1056/NEJMoa1911614
- ³Outbreak of lung injury associated with e-cigarette use, or vaping. CDC. https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html. Updated Feb 25, 2020. Accessed May 4, 2020.
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- ⁵Schier JG, Meiman JG, Layden J, et al. Severe pulmonary disease associated with electronic-cigarette-product Use — Interim Guidance. *MMWR Morb Mortal Wkly Rep*. 2019;68:787–790. doi: <http://dx.doi.org/10.15585/mmwr.mm6836e2>

Image 1.

Chest x-ray on admission:

Bilateral perihilar infiltrates

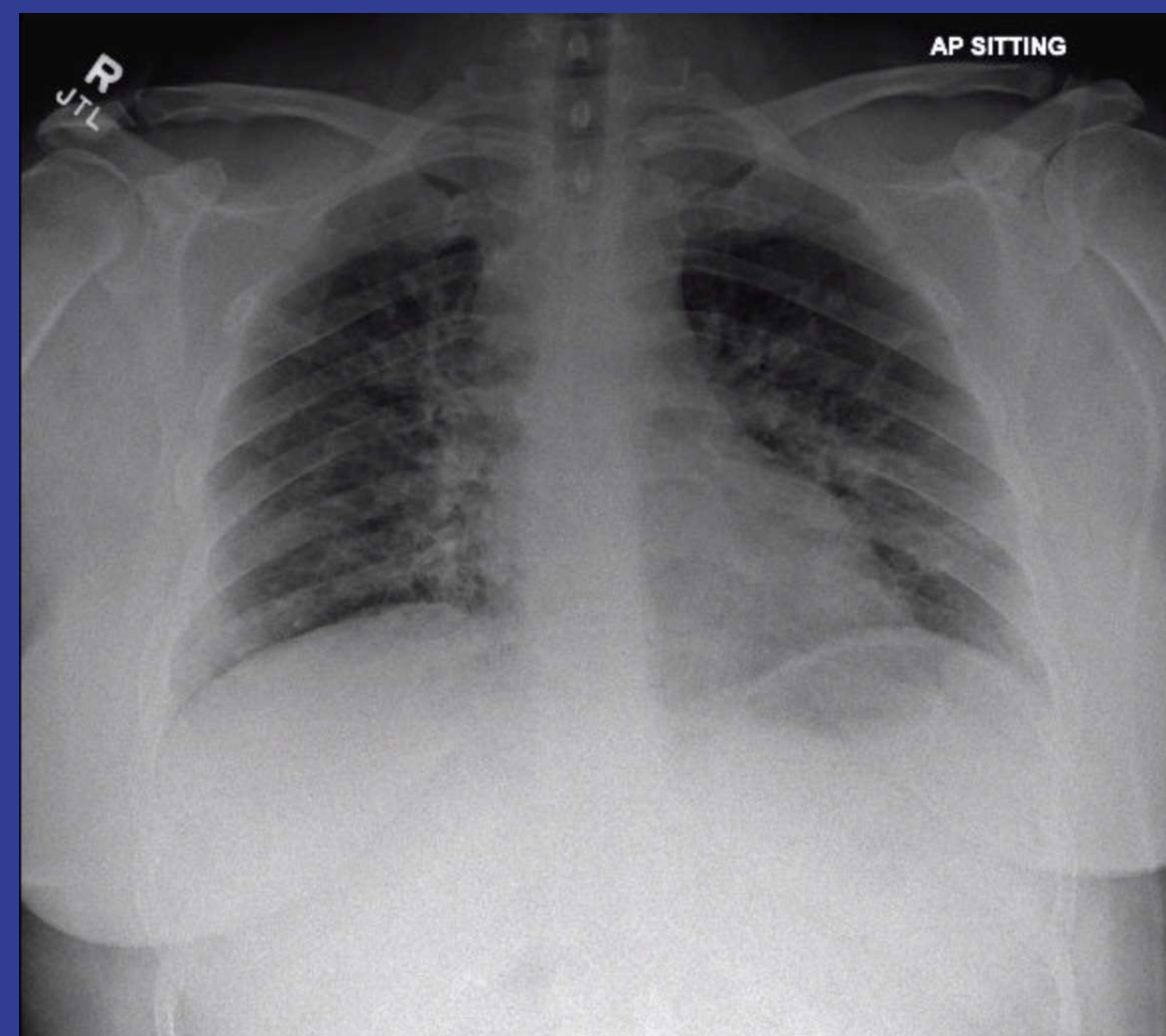


Image 2.

Repeat chest x-ray:

Worsening lung infiltrates

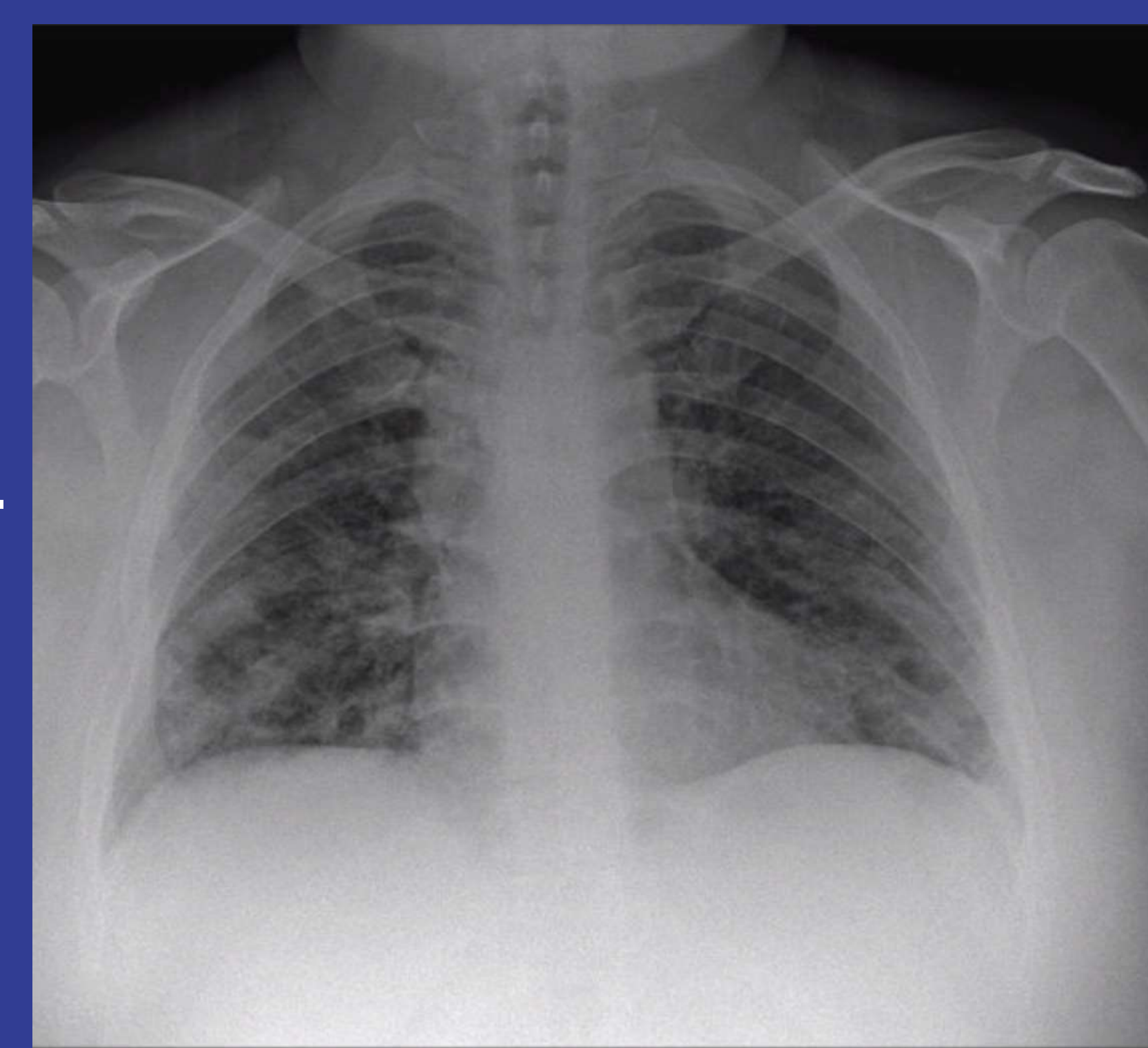


Image 3.

Final chest x-ray:

Partial clearing of infiltrates

