

AMSER Case of the Month

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65-year-old female with shortness of breath and cough

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Patient Presentation

- HPI: 65-year-old female presents to the ED with a 2-week history of subjective fever; nausea, vomiting, and diarrhea; fatigue; shortness of breath; and cough.
- ROS: Cough, shortness of breath, and sputum production; nausea and diarrhea.
No fever, chills, or headaches on presentation; no wheezing, chest pain or palpitations.

Patient Presentation - History

- Past Medical Hx: Interstitial lung disease, seasonal allergies. Diabetes mellitus, hypertension, hyperlipidemia.
- Past Hospitalization/Surgical Hx: Bronchoscopy admission for interstitial lung disease in Feb 2017. Hysterectomy in 1984.
- Past Social History: Smoked for several years but has not smoked for at least 40 years.
- Family History: Father – Heart disease, Brother – Cancer (unspecified)

Patient Presentation - Physical

Pertinent Findings:

- General: Awake, alert and not in distress.
- Cardiac: RRR w/normal sounds.
- Pulmonary: Bilateral lower rhonchi w/decreased breath sounds and rales. Not in respiratory distress/no increased effort.
- Psychiatric: Slowed behavior, thoughts are paranoid.

Pertinent Labs

- CBC: Elevated RBCs with decreased platelets. Neutrophilia w/left shift.
- Chem panel: Elevated creatinine/BUN. Hyponatremia, hypochloremia. Serum calcium and phosphate levels - unremarkable.
- LFT: Elevated AST and bilirubin
- Viral PCR – COVID-19 positive

What Imaging Should We Order?

ACR Appropriateness Criteria

| Scenario | Procedure | Adult RRL | Peds RRL | Appropriateness Category |
|---|--|-----------------|------------------------|------------------------------|
| Respiratory illness, acute, abnormal exam, initial exam | Radiography chest | <0.1 mSv ⊕ | <0.03 mSv [ped] ⊕ | Usually appropriate ● |
| | US chest | 0 mSv ○ | 0 mSv [ped] ○ | May be appropriate ● |
| | CT chest without IV contrast | 1-10 mSv ⊕⊕⊕ | 3-10 mSv [ped] ⊕⊕⊕⊕ | Usually not appropriate ● |
| | CT chest with IV contrast | 1-10 mSv ⊕⊕⊕ | 3-10 mSv [ped] ⊕⊕⊕⊕ | Usually not appropriate ● |
| | CT chest without and with IV contrast | 1-10 mSv ⊕⊕⊕ | 3-10 mSv [ped] ⊕⊕⊕⊕ | Usually not appropriate ● |
| | MRI chest without IV contrast | 0 mSv ○ | 0 mSv [ped] ○ | Usually not appropriate ● |
| | MRI chest without and with IV contrast | 0 mSv ○ | 0 mSv [ped] ○ | Usually not appropriate ● |

These imaging modalities were ordered by the ER physician

ACR Appropriateness Criteria – Why Acute Respiratory Illness?

Despite the patient's history of interstitial lung disease, the presentation of pulmonary symptoms coincided with COVID-19 infection and bacterial superinfection as assessed by the attending physician.

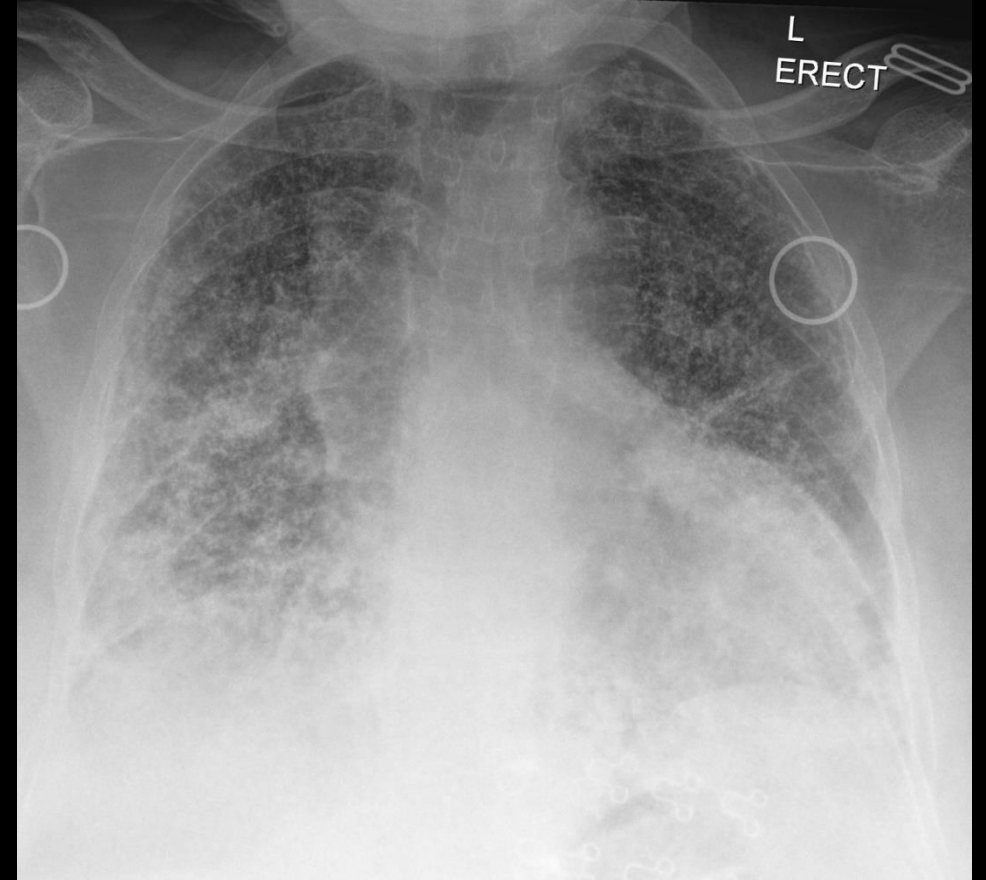
Additionally, prior to this admission, the patient was clinically stable with no symptoms of interstitial lung disease.

XR Findings (unlabeled)

8 mo prior to admission



On admission



XR Findings (labeled)

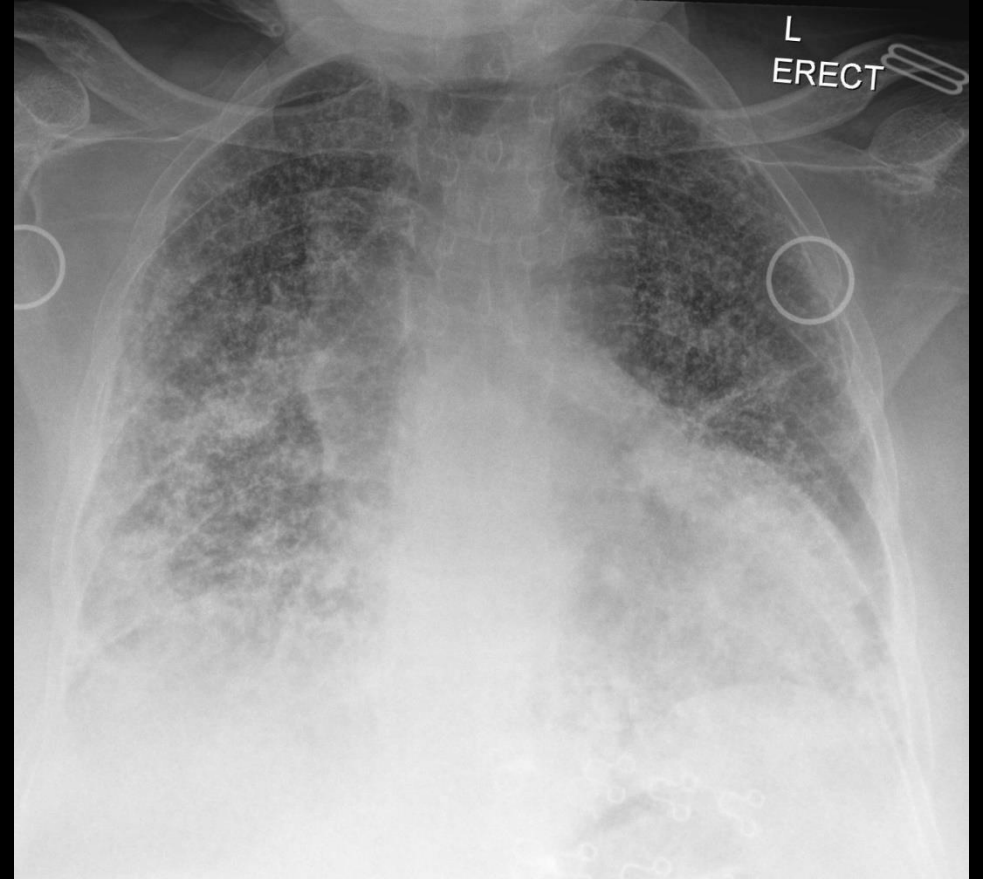
8 mo prior to admission



Both frontal radiographs of the chest show diffuse bilateral reticulonodular opacities.

On admission however, new bilateral scattered ground glass opacities are present in the mid-to-lower lungs.

On admission



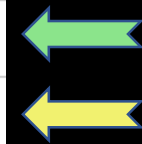
ACR Appropriateness Criteria – What's next?

While the XR provided initial valuable information, some of the finer details are obscured by natural limits of resolution of an XR.

What should we do next? What is ACR appropriate?

ACR Appropriateness Criteria (post-XR)

| Scenario | Procedure | Adult RRL | Peds RRL | Appropriateness Category | |
|---|--|-----------------|------------------------|--------------------------|---|
| Respiratory illness, acute, abnormal exam, xray nondiagnostic | CT chest without IV contrast | 1-10 mSv ⊕⊕⊕ | 3-10 mSv [ped] ⊕⊕⊕⊕ | Usually appropriate | ● |
| | CT chest with IV contrast | 1-10 mSv ⊕⊕⊕ | 3-10 mSv [ped] ⊕⊕⊕⊕ | May be appropriate | ● |
| | US chest | 0 mSv ○ | 0 mSv [ped] ○ | May be appropriate | ● |
| | MRI chest without IV contrast | 0 mSv ○ | 0 mSv [ped] ○ | Usually not appropriate | ● |
| | MRI chest without and with IV contrast | 0 mSv ○ | 0 mSv [ped] ○ | Usually not appropriate | ● |
| | CT chest without and with IV contrast | 1-10 mSv ⊕⊕⊕ | 3-10 mSv [ped] ⊕⊕⊕⊕ | Usually not appropriate | ● |

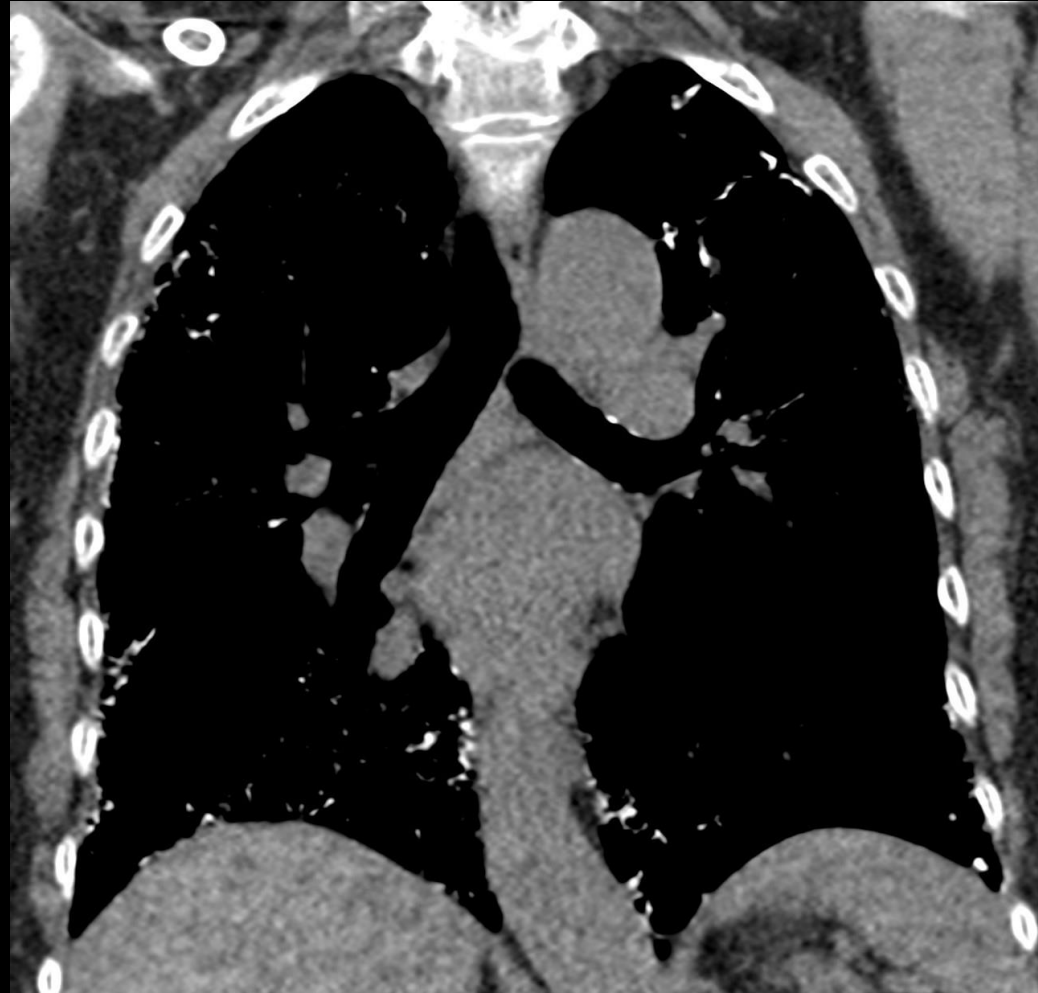


While the CT without contrast is recommended when the XR is non-diagnostic...

The ER physician ordered a CT with IV contrast.

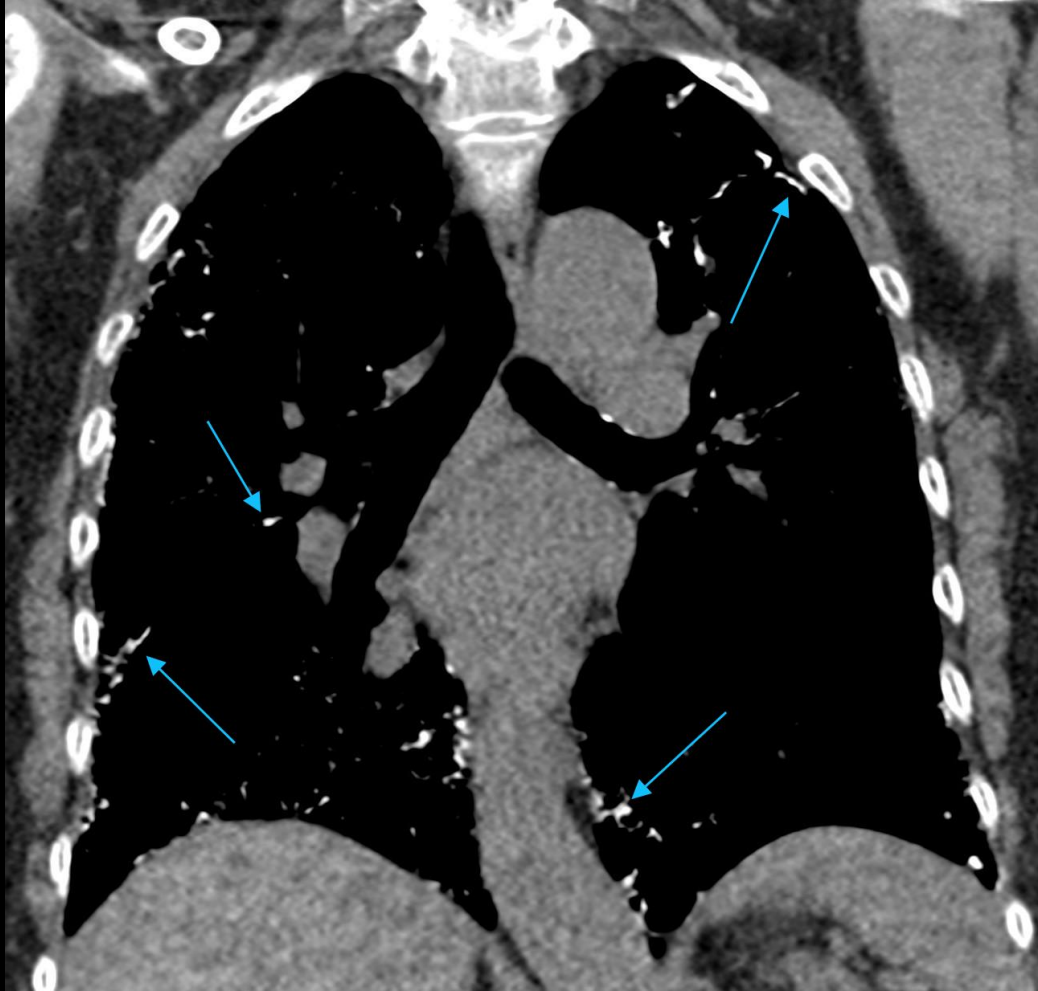
CT Findings (unlabeled)

8 mo prior to admission



CT Findings (labeled)

8 mo prior to admission

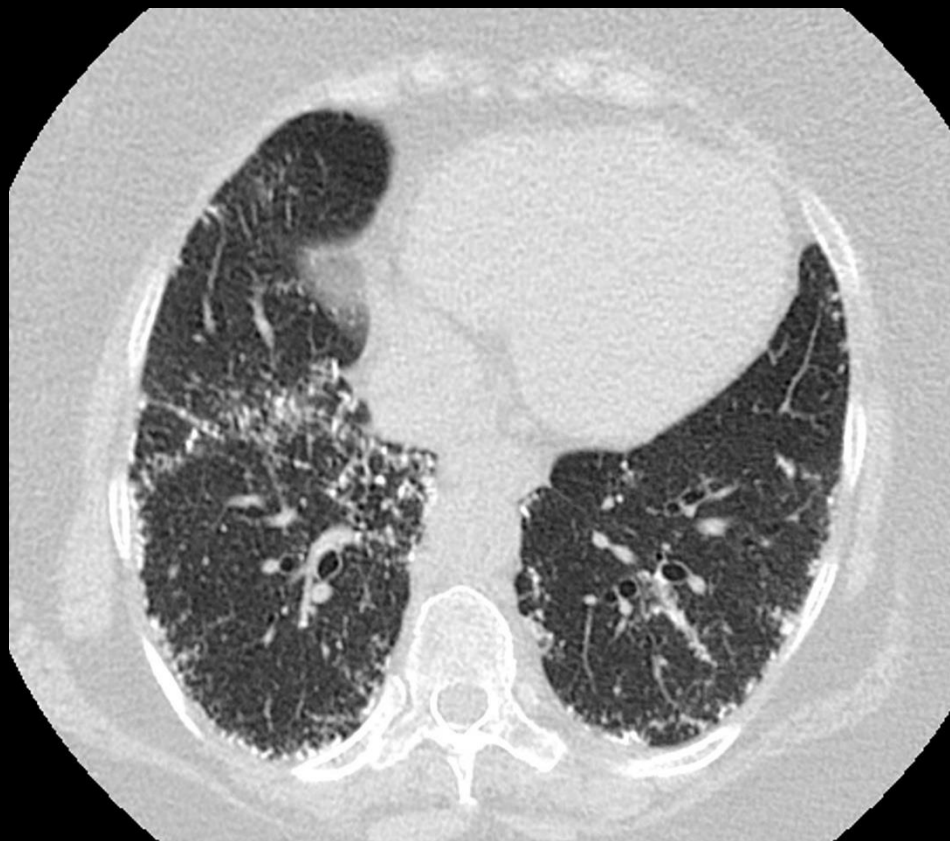


Coronal non-contrast CT soft tissue window shows:

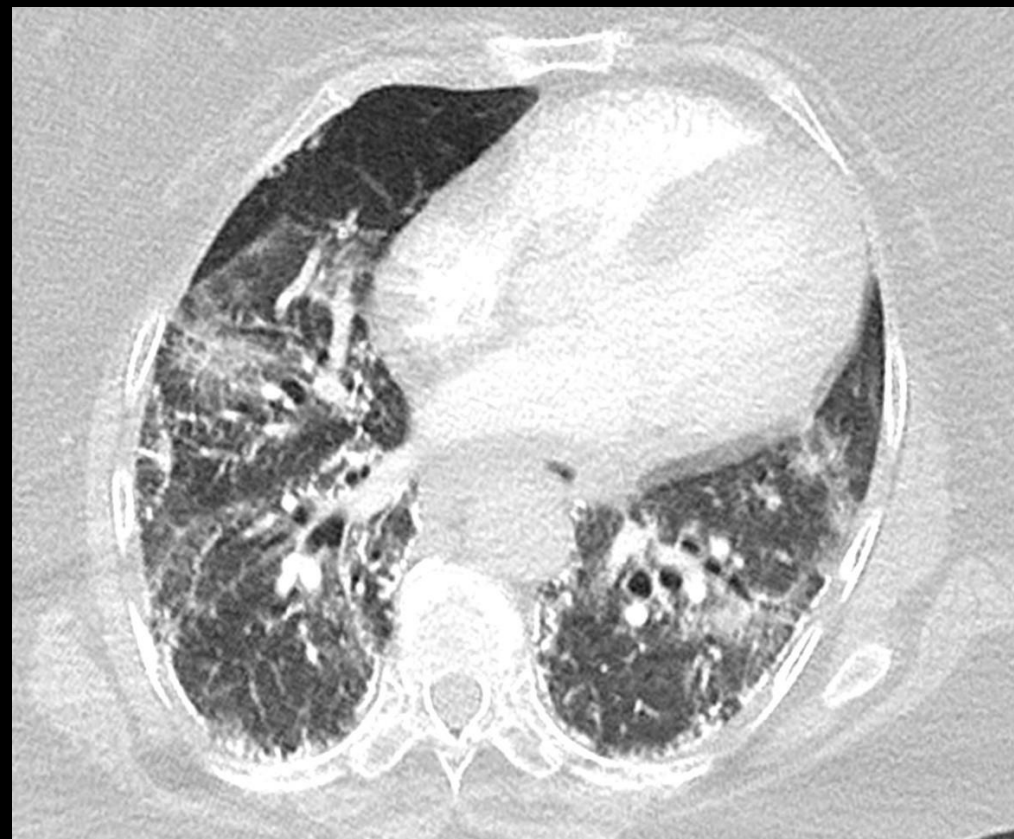
Multiple branching calcific nodules in both lungs

CT Findings (unlabeled)

8 mo prior to admission

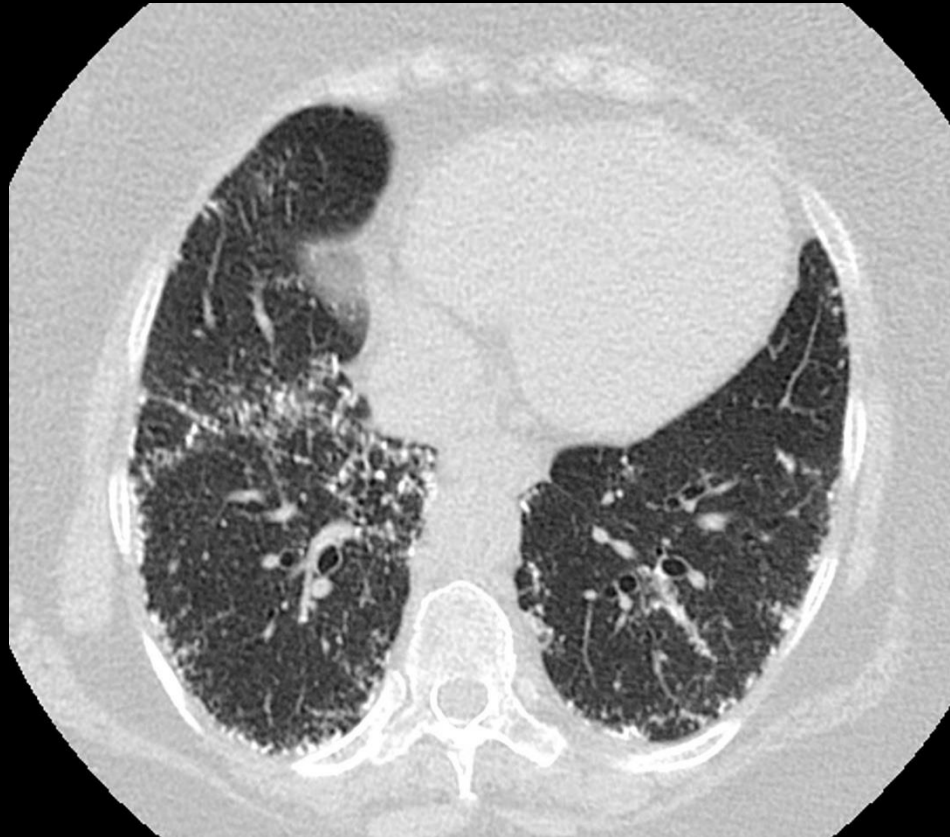


On admission



CT Findings (labeled)

8 mo prior to admission



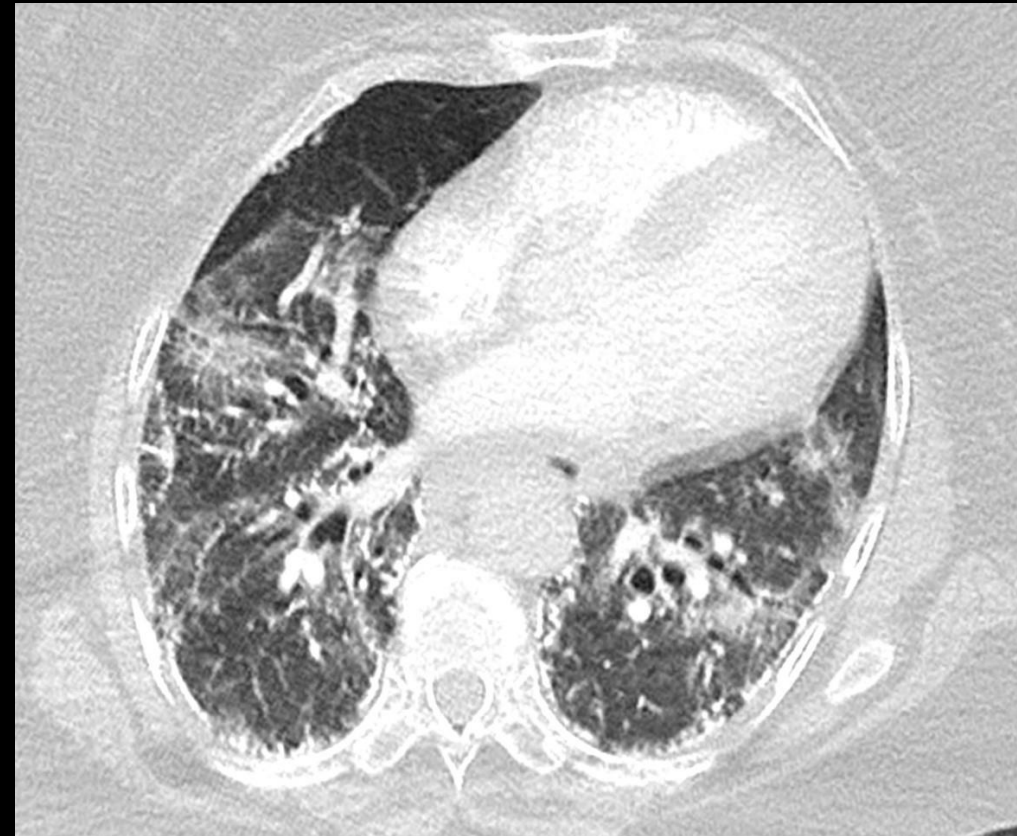
Both axial images on CT show diffuse bilateral reticulonodular opacities.

On admission however, new bilateral scattered ground glass opacities are present.

These finds correlate with the findings seen on the chest radiographs previously mentioned.

Of note, there are no filling defects to suggest pulmonary embolism.

On admission



Final Dx:

Pulmonary heterotopic ossification and concurrent
COVID-19 infection

Case Discussion – Pulmonary Ossification

- Pulmonary ossification (as opposed to calcification) is characterized by presence of mature bone tissue within the lungs.
 - This ossification process involves more than dysregulation of calcium and phosphates and is dependent on other physiological processes.
- When pulmonary ossification is seen several diagnoses can be considered, including:
 - Fibrosing interstitial lung disease, SARS, and acid aspiration
 - Silicosis, pulmonary alveolar microlithiasis, and chicken pox.
 - Rarer diagnoses include idiopathic pulmonary hemosiderosis, lung cancers, osteogenesis imperfecta

Case Discussion – Pulmonary Ossification

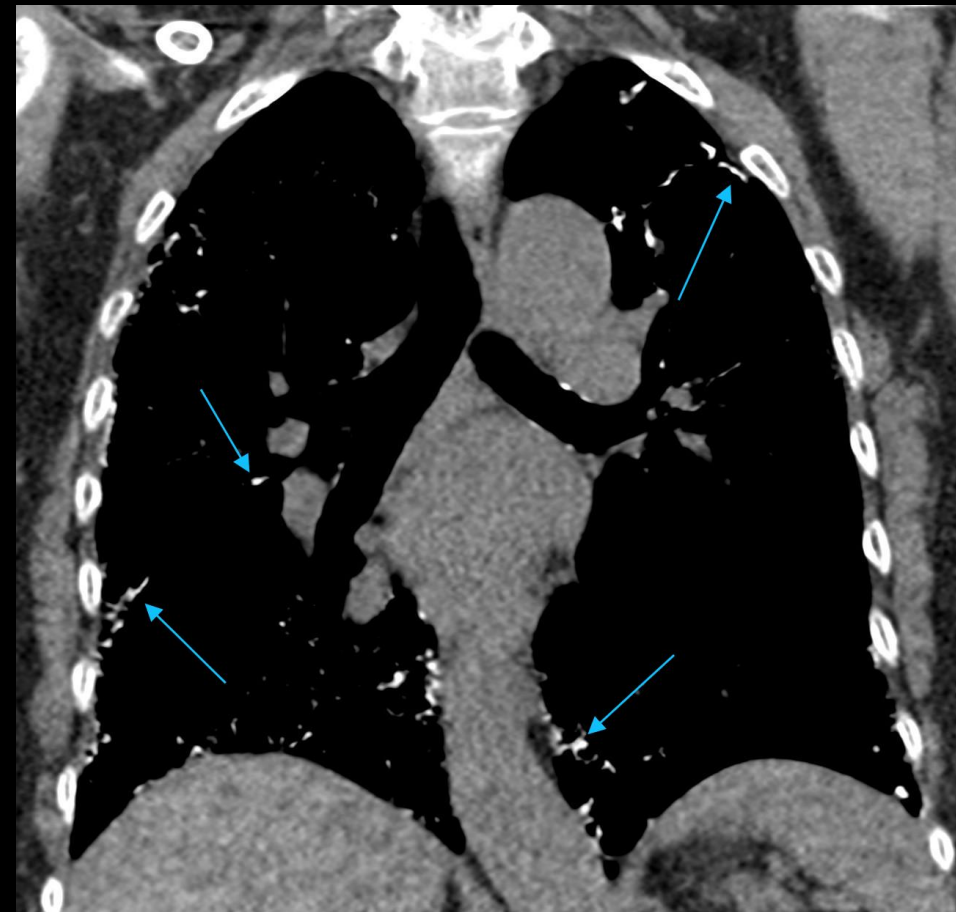
- Etiologies are dependent on histologic form – Nodular vs Dendriform
 - Nodular ossification happens as a result of passive pulmonary congestion and pulmonary edema usually from cardiac pathologies.
 - Dendriform ossification is associated with interstitial lung diseases but can be exacerbated by inflammation and ARDS.
 - Interestingly, SARS-CoV-2 infection is reported as an instigator of dendriform ossification, especially in those with interstitial lung disease.
 - *Given the history, this patient likely has dendriform ossification.*

Case Discussion – Pulmonary Ossification

- Several biochemical factors contribute to the process of ossification.
 - Inflammation and tissue hypoxia can cause a localized availability of calcium and phosphates.
 - Several cytokines implicated in inflammation such as TGF-beta, BMP-2, IL-4, and IL-1 can promote differentiation of macrophages/fibroblasts into osteoclasts and osteoblasts leading to ectopic bone formation.
- Pulmonary ossification is rare. The abnormal functional changes do not tend to cause symptoms themselves – rarely, cases of spontaneous pneumothorax have been seen due to bone spicules causing air leakage.
- Treatment options are limited – glucocorticoids, Ca sequestering drugs, and bisphosphonates are all ineffective.

Case Discussion – Pulmonary Ossification Imaging

- The image shown is of this patient 8 months prior to admission.
- The diagnosis of pulmonary ossification is radiologic, via demonstration of lesion density equivalent to bone.
- This coronal non-contrast soft tissue window CT image shows multiple branching calcific nodules in both lungs (blue arrows).
 - Most commonly, reticular opacities are seen in the lower periphery of the lungs.
- Most cases are asymptomatic without acute exacerbation.



Clinical Course

- Our patient was admitted to the Internal Med floor and followed there through her admission for COVID with suspected community acquired pneumonia.
- She was treated empirically for bacterial pneumonia with ceftriaxone and azithromycin, as well as given supplementary oxygen. Additionally, she was given dexamethasone and remdesivir for COVID infection.
- After a 5-day course, the patient improved and was slowly weaned off oxygen.
- The patient was discharged home with orders that oxygen be tapered down over time until lung function normalized and patient well-saturated.

References:

1. Brodeur, F. J., Jr. and E. A. Kazerooni (1994). "Metastatic pulmonary calcification mimicking air-space disease. Technetium-99m-MDP SPECT imaging." *Chest* 106(2): 620-622.
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3. García Moreno, B., G. Buitrago Weiland, M. L. Sánchez Alegre and J. E. Vanegas Rodríguez (2021). "Accelerated Pulmonary Ossification as a Sequela of SARS-CoV-2 Pneumonia." *Radiol Cardiothorac Imaging* 3(2): e200598.
4. Jamjoom, L., M. Meziane and R. D. Renapurkar (2013). "Dendriform pulmonary ossification: Report of two cases." *Indian J Radiol Imaging* 23(1): 15-18.
5. Lara, J. F., J. F. Catroppo, D. U. Kim and D. da Costa (2005). "Dendriform pulmonary ossification, a form of diffuse pulmonary ossification: report of a 26-year autopsy experience." *Arch Pathol Lab Med* 129(3): 348-353.
6. Peros-Golubicić, T. and J. Tekavec-Trkanjec (2008). "Diffuse pulmonary ossification: an unusual interstitial lung disease." *Curr Opin Pulm Med* 14(5): 488-492.
7. Chan, E. (2021). Calcification and ossification of the lungs, UpToDate. Retrieved January 22, 2022