

**IN THE NAME OF GOD**

**COVID-19 DIFFERENTIAL  
DIAGNOSIS**

**PRESENTED BY :**

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# INTRODUCTION

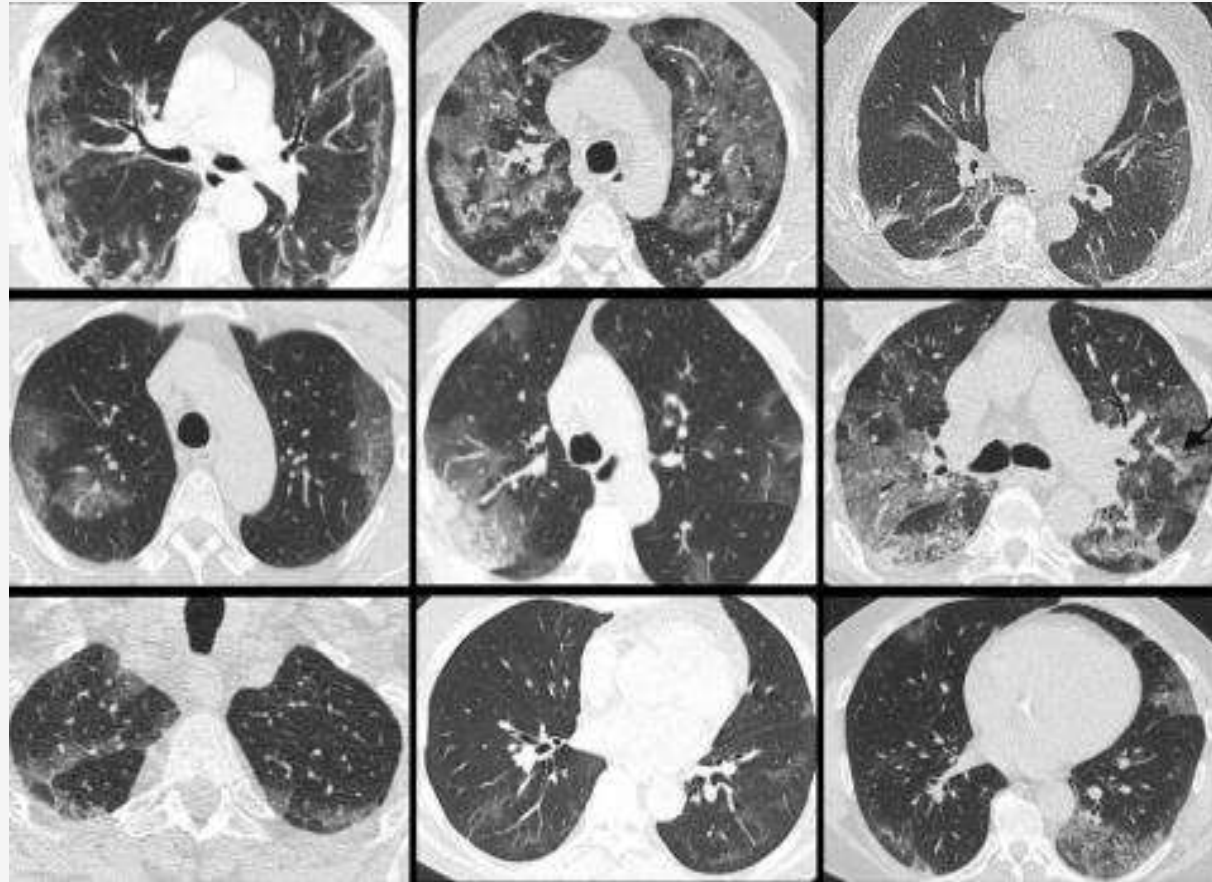
- During the peak of the first wave of COVID-19 the a priori probability that patients, who came to the hospital with
- dyspnea
- coughing
- fever,

# INTRODUCTION

Having COVID-19 was high, **especially if they have an abnormal chest-CT**

- The images are all of patients with **proven COVID-19** infection.
- The CT's were classified as **CO-RADS 5**, which indicates a **very high probability of COVID-19.**

# INTRODUCTION



# INTRODUCTION

- **Chest CT can be helpful in the diagnosis of COVID-19 in hospitalized patients as an adjunct to PCR testing and serology.**
- The **CO-RADS classification** uses **features of COVID-19** on chest CT to indicate the likelihood of COVID-19 pulmonary involvement based on CT imaging

# CO-RADS CLASSIFICATION

- The **CO-RADS classification** is **accurate in the clinical** setting of **hospitalized patients** with high clinical suspicion of COVID-19 and symptom duration of more than 2 days
- The **performance** of the CO-RADS classification ***decreases*** in patients **without typical complaints of COVID-19**
- short symptom duration
- and in patients with overlapping or pre-existing pulmonary disease.

**In those cases we have to consider other diseases in the differential diagnosis**

## CO-RADS

|           | Level of suspicion | CT findings                                                  |
|-----------|--------------------|--------------------------------------------------------------|
| CO-RADS 1 | No                 | normal or non-infectious abnormalities                       |
| CO-RADS 2 | Low                | abnormalities consistent with infections other than COVID-19 |
| CO-RADS 3 | Indeterminate      | unclear whether COVID-19 is present                          |
| CO-RADS 4 | High               | abnormalities suspicious for COVID-19                        |
| CO-RADS 5 | Very high          | typical COVID-19                                             |
| CO-RADS 6 | PCR +              | definite COVID-19                                            |

# DIFFERENTIAL DIAGNOSIS OF COVID-19

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- **Groundglass mimickers**

There is no real ground-glass but high density lung as a result of insufficient inspiration or normal lung looking like ground-glass because it is next to hypoperfused black lung due to vasoconstriction

- **Differential diagnosis**

**Many** diseases that **may look like COVID-19**, but you should be able to find the differences by combining CT and clinical findings

- **Overlapping diseases**

Diseases of the lung that have **the exact pattern as COVID-19**.  
**Distinction** can **only** be made with **clinical parameters**

# DIFFERENTIAL DIAGNOSIS OF COVID-19

| COVID-19 Differential Diagnosis |                                 |                                        |
|---------------------------------|---------------------------------|----------------------------------------|
| Groundglass Mimickers           | Differential diagnosis          | Overlapping diseases                   |
| Insufficient inspiration        | Cardiogenic edema               | Organizing pneumonia                   |
| Asthma                          | Pulmonary infarctions           | Influenza pneumonia                    |
| Bronchiolitis<br>obliterans     | Alveolar hemorrhage             | Pneumocystis<br>pneumonia              |
| Hypersensitivity<br>pneumonitis | Eosinophilic pneumon            | Adult respiratory<br>distress syndrome |
|                                 | Drug-induced<br>pneumonitis     |                                        |
|                                 | Radiation pneumonitis           |                                        |
|                                 | Hypersensitivity<br>pneumonitis |                                        |
|                                 | NSIP                            |                                        |
|                                 | Adenocarcinoma                  |                                        |
|                                 | Alveolar proteinosis            |                                        |

# DIFFERENTIAL DIAGNOSIS OF COVID-19

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- It is therefore important **to take the appropriate clinical setting** into account **when applying CO-RADS**, as a **false positive CT-result** may result in **unnecessary treatment and isolation**
- In addition, framing bias should be avoided by taking the differential diagnoses of COVID-19 CT signs into consideration and to correlate these to the clinical history of the patient

# GROUNDGLASS MIMICKERS

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- Diffuse high density of the lung parenchyma can be caused by inadequate inspiration

# GROUNDGLASS MIMICKERS

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## COVID-19    Ground glass mimickers

**- Inadequate inspiration**

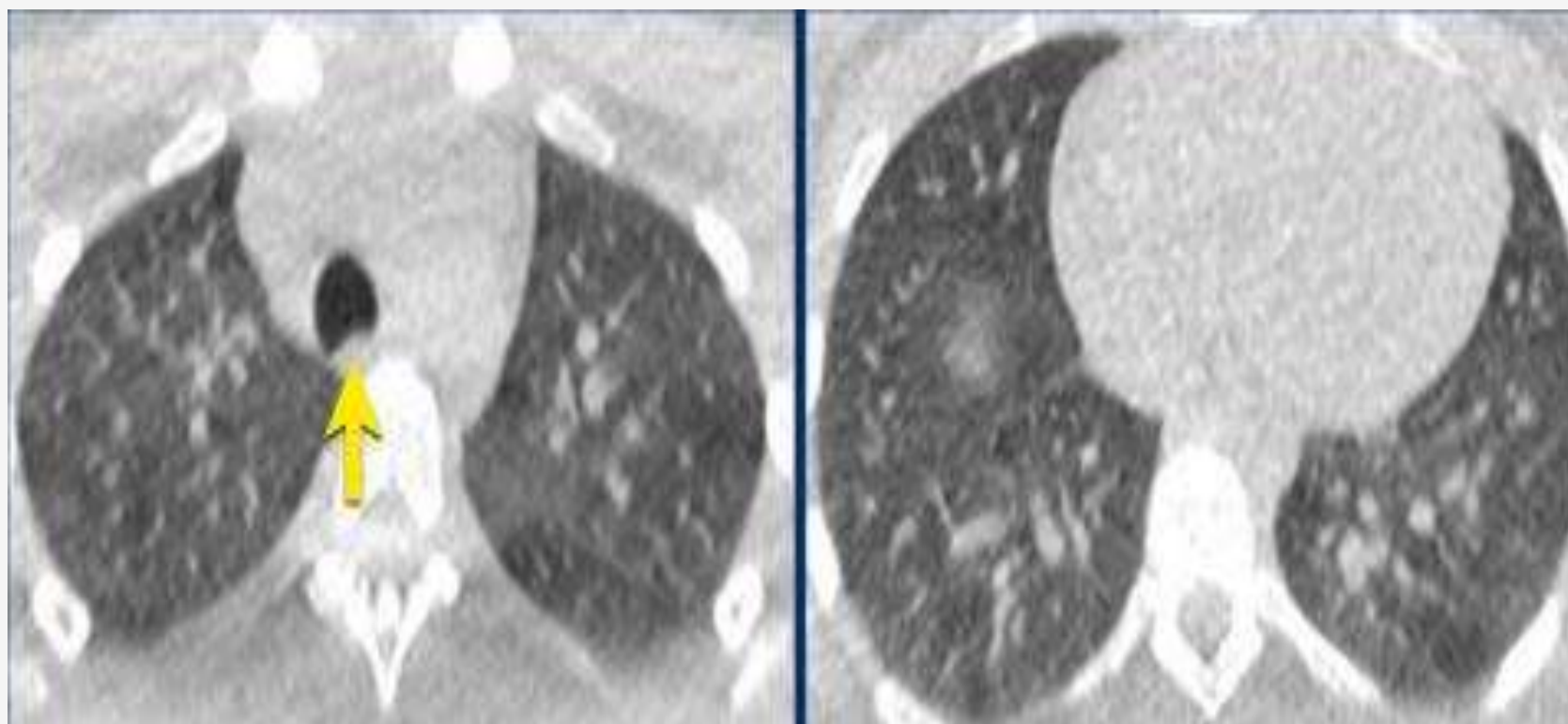
**- Mosaic attenuation**

- hypoperfusion in pulmonary emboli
- bronchopathy with secondary vasoconstriction
  - in:
    - asthma
    - bronchiolitis obliterans
    - hypersensitivity pneumonitis

# INADEQUATE INSPIRATION

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- Notice the presence of inward bowing of the posterior membrane, indicative of inadequate inspiration
- Repeat examination showed normal parenchymal density (not shown)

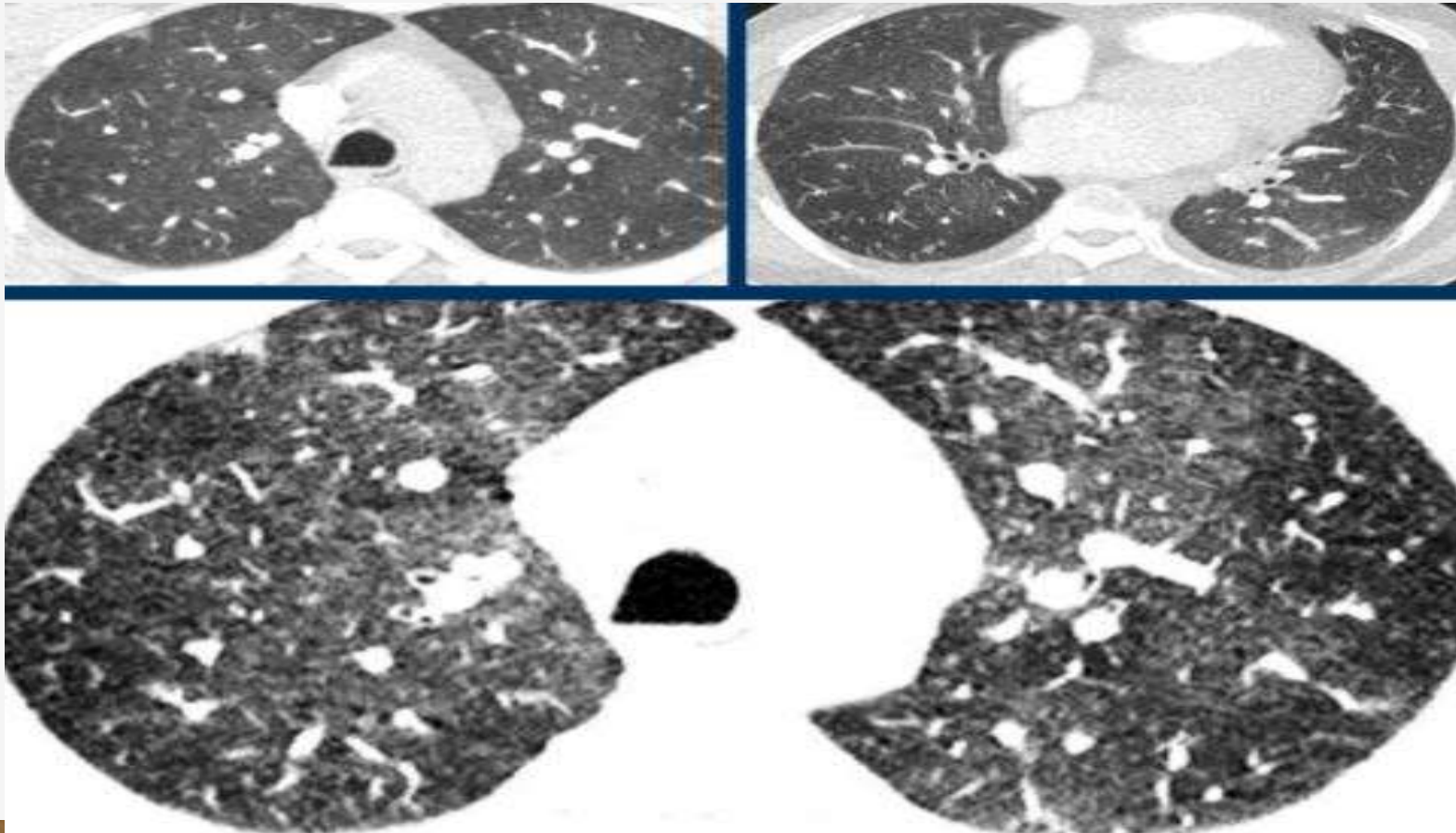


# MOSAIC ATTENUATION

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- based on **multifocal hypoperfusion** or **hypoventilation** can mimic **ground-glass** opacities, but is fundamentally distinct
- Here, it is the **low density pulmonary parenchyma** that is abnormal
- **It is caused by bronchopathy with hypoventilation and secondary hypoxic vasoconstriction**
- The relatively high density parenchyma is normal

# MOSAIC ATTENUATION IN A PATIENT WITH BRONCHOPATHY WITH HYPOXIC VASCONSTRICITION



# DIFFERENTIAL DIAGNOSIS

## PULMONARY CARDIOGENIC EDEMA

- Pulmonary cardiogenic edema presents with bilateral ground-glass opacities reflecting extravascular fluid in the alveolar spaces
- These ground-glass opacities are typically more centrally distributed with sparing of the peripheral parenchyma and do not fulfill the complete obligatory COVID-19 feature of location of ground glass close to the pleural surfaces.

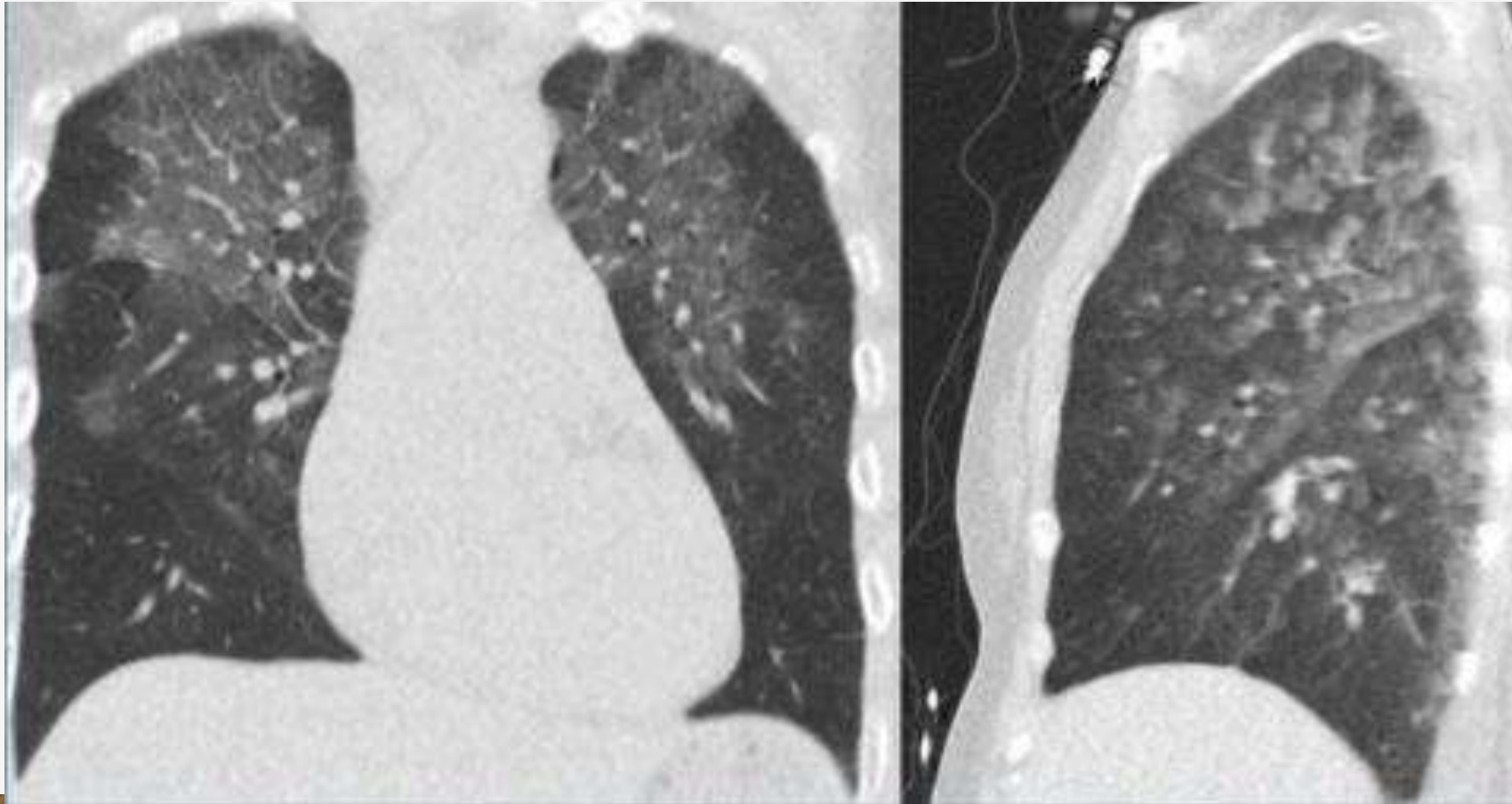
# CENTRALLY DISTRIBUTED GROUNDGLASS WITH INTERLOBULAR THICKENING IN CARDIOGENIC EDEMA



# DIFFERENTIAL DIAGNOSIS

- In addition, distribution of edema can be gravity dependent, which can be appreciated on sagittal reconstructions

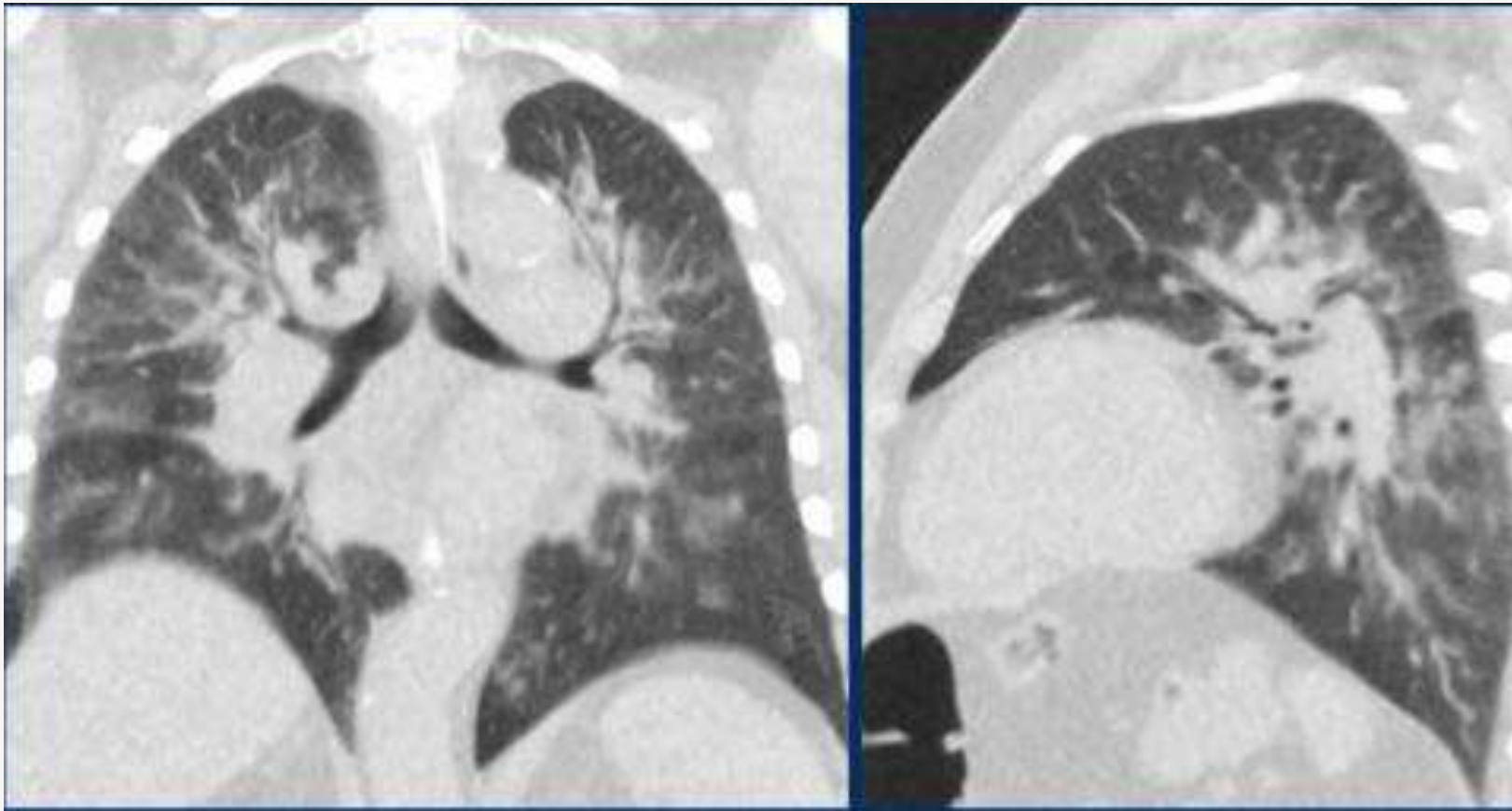
# GRAVITY DEPENDENT GROUNDGLASS WITH INTERLOBULAR THICKENING IN CARDIOGENIC EDEMA



# ACCOMPANYING SIGNS SUGGESTIVE OF CARDIOGENIC EDEMA:

- Interlobular septal thickening
- Diffuse vascular enlargement
- Lymph node enlargement
- Structural cardiac pathology
- Pleural fluid
- Clinical presentation of the patient

# PULMONARY CARDIOGENIC EDEMA WITH CENTRALLY DISTRIBUTED GROUNDGLASS, DIFFUSE VASCULAR ENLARGEMENT, LYMPHNODE ENLARGEMENT AND BRONCHIAL CUFFING



# PULMONARY INFARCTIONS

- Infarctions secondary to pulmonary emboli cause peripheral densities adjacent to the pleural surfaces
- Although these densities in part consist of ground-glass opacities, especially in the early stage, infarctions are frequently more peripheral, triangular and dense

# PULMONARY INFARCTIONS

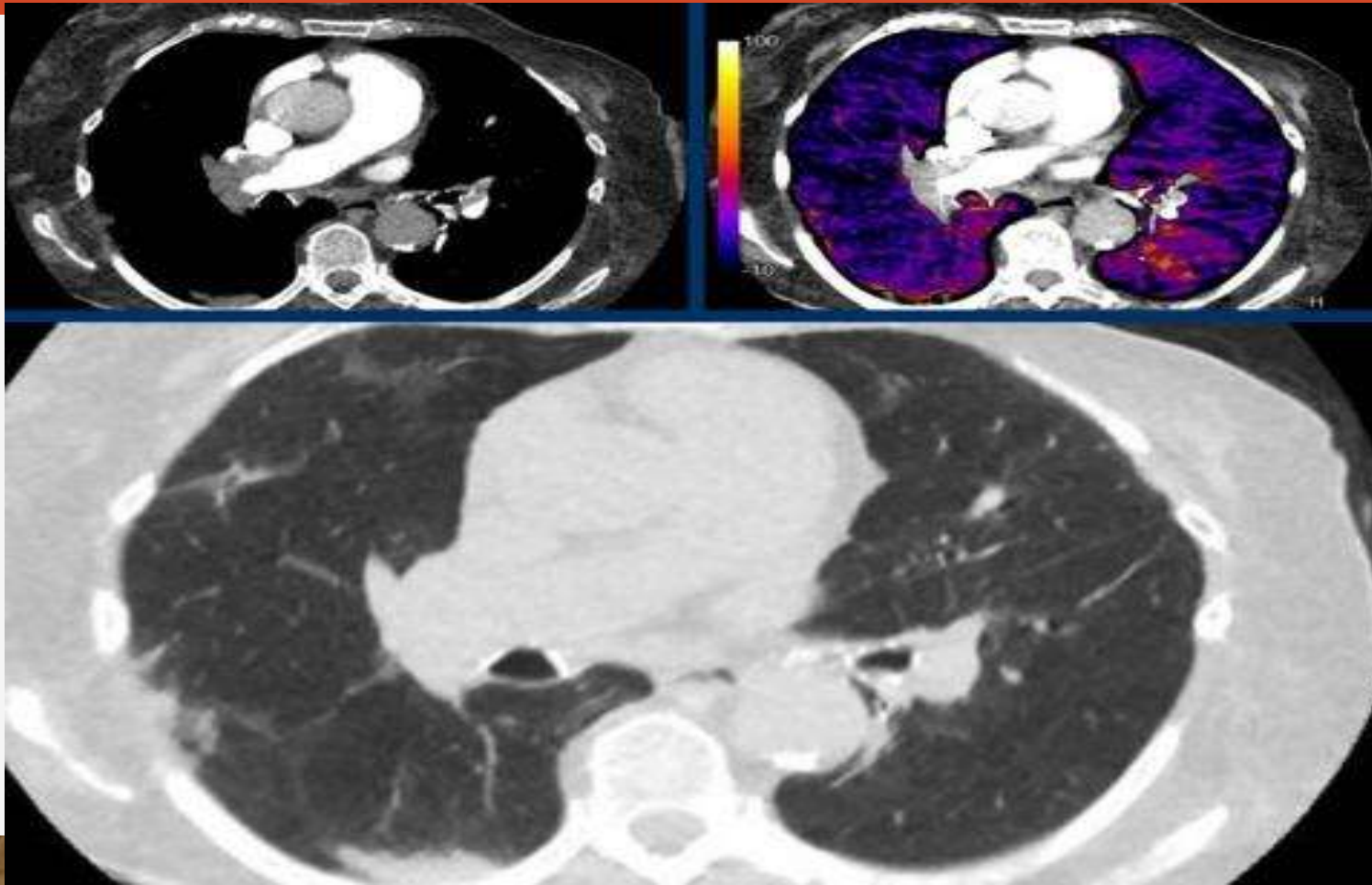
- The images show:

**1. Central pulmonary embolism.**

**2. Corresponding perfusion defects at subtraction iodine mapping**

**3. Peripheral, triangular pulmonary opacities in the vascular territories.**

# PULMONARY INFARCTIONS



# ALVEOLAR HEMORRHAGE

- **Bilateral and confluent airspace opacities** caused by diffuse alveolar hemorrhage such as in e.g. systemic lupus erythomathosus on this image are distributed more along the bronchovascular bundles, and predominantly spare the peripheral pleural surfaces and costophrenic angles
- These opacities should **resolve in weeks** if bleeding **does not recur**
- The image shows alveloar hemorrhage with patchy groundglass along the bronchovascular bundles in a patient with **secondary vasculitis** in **systemic lupus erythemathosus**

# ALVEOLAR HEMORRHAGE

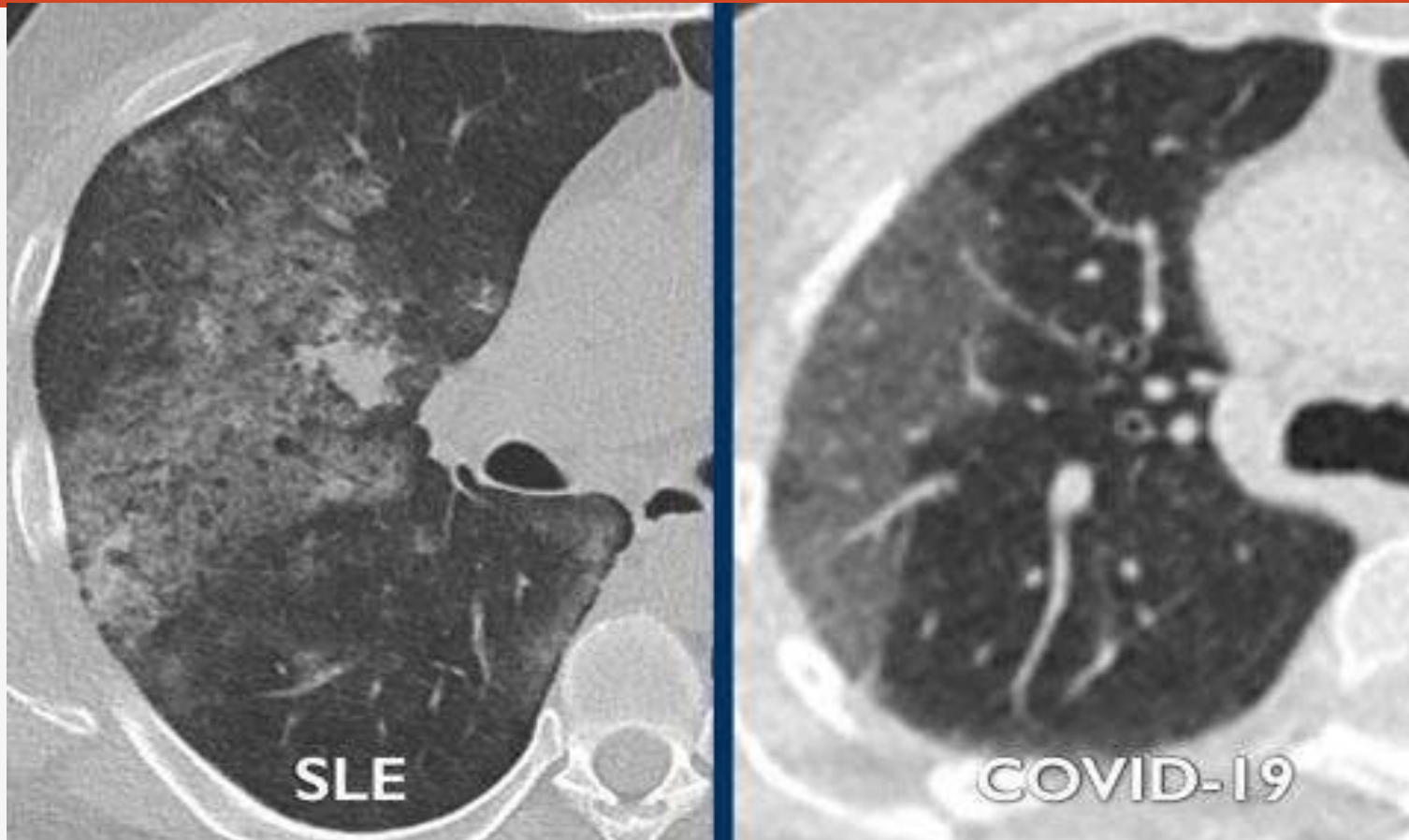
ALVEOLAR HEMORRHAGE IN A PATIENT WITH SLE.



# DIFFERENTIAL DIAGNOSIS

- In COVID-19 the groundglass is more peripheral and diffuse.
- More chronic or subacute hemorrhage causes crazy paving and fibrosis.
- In addition, clinical presentation including fever, cough and leukocytosis are less common in patients with alveolar hemorrhage, although the clinical presentation of diffuse pulmonary hemorrhage remains highly variable.
- Only approximately 2/3 of patients have hemoptysis

# DIFFERENTIAL DIAGNOSIS



# DIFFERENTIAL DIAGNOSIS

## EOSINOPHILIC PNEUMONIA

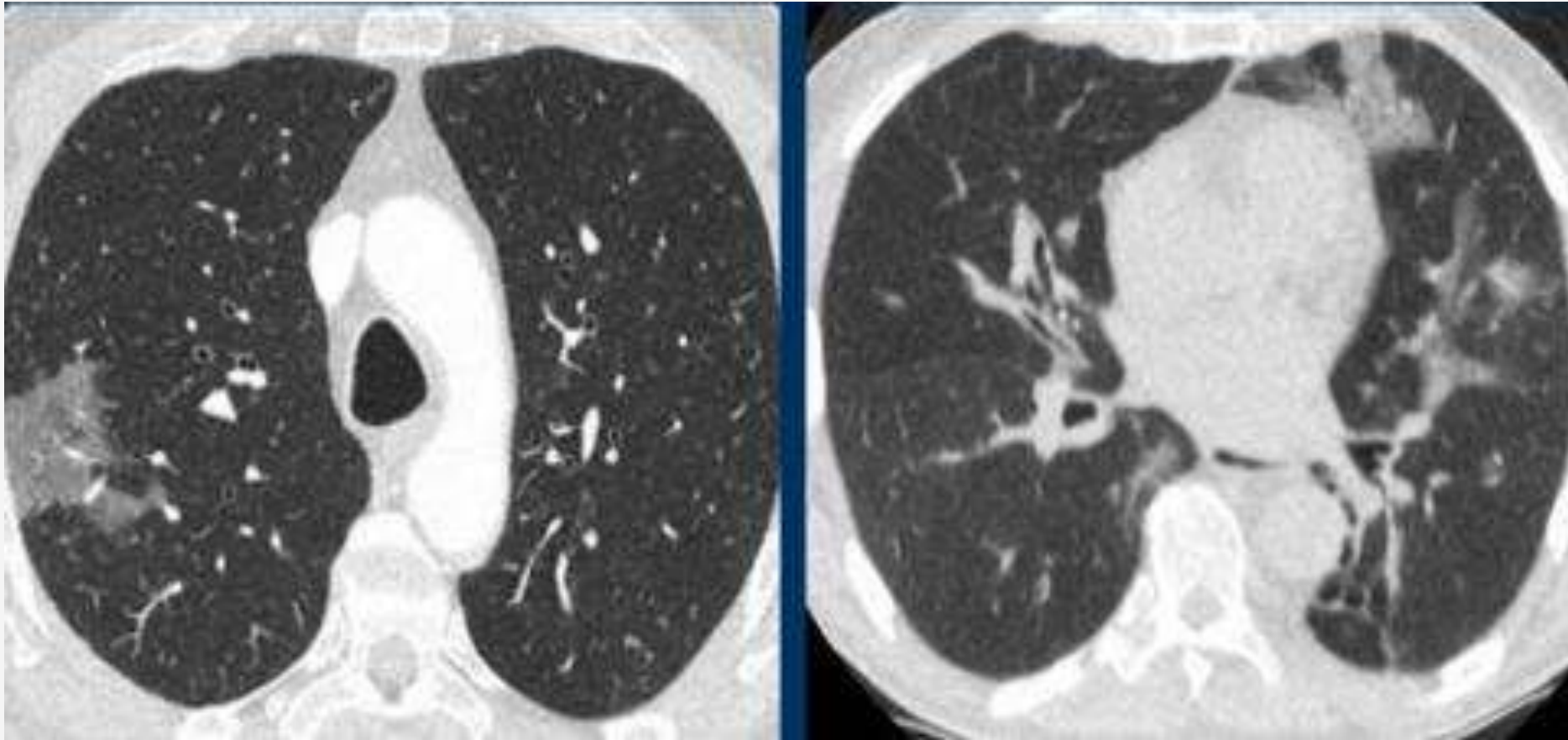
- Eosinophilic pneumonia can also present with fever and cough just like COVID-19
- On CT it presents like COVID-19 with peripheral ground-glass and consolidations, with or without a crazy paving pattern, which makes it very hard to distinguish from COVID-19 on CT alone.
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# DIFFERENTIAL DIAGNOSIS

## EOSINOPHILIC PNEUMONIA

- Differentiation from COVID-19 is possible based on:
- Clinical presentation **with slow onset of symptoms**
- Association with **asthma**
- **Eosinophilia in bronchioalveolar lavage and blood samples**
- Mainly, and more strictly **upper lung zone distribution**

# PERIPHERAL GROUNDGLASS IN CHRONIC EOSINOPHILIC PNEUMONIA

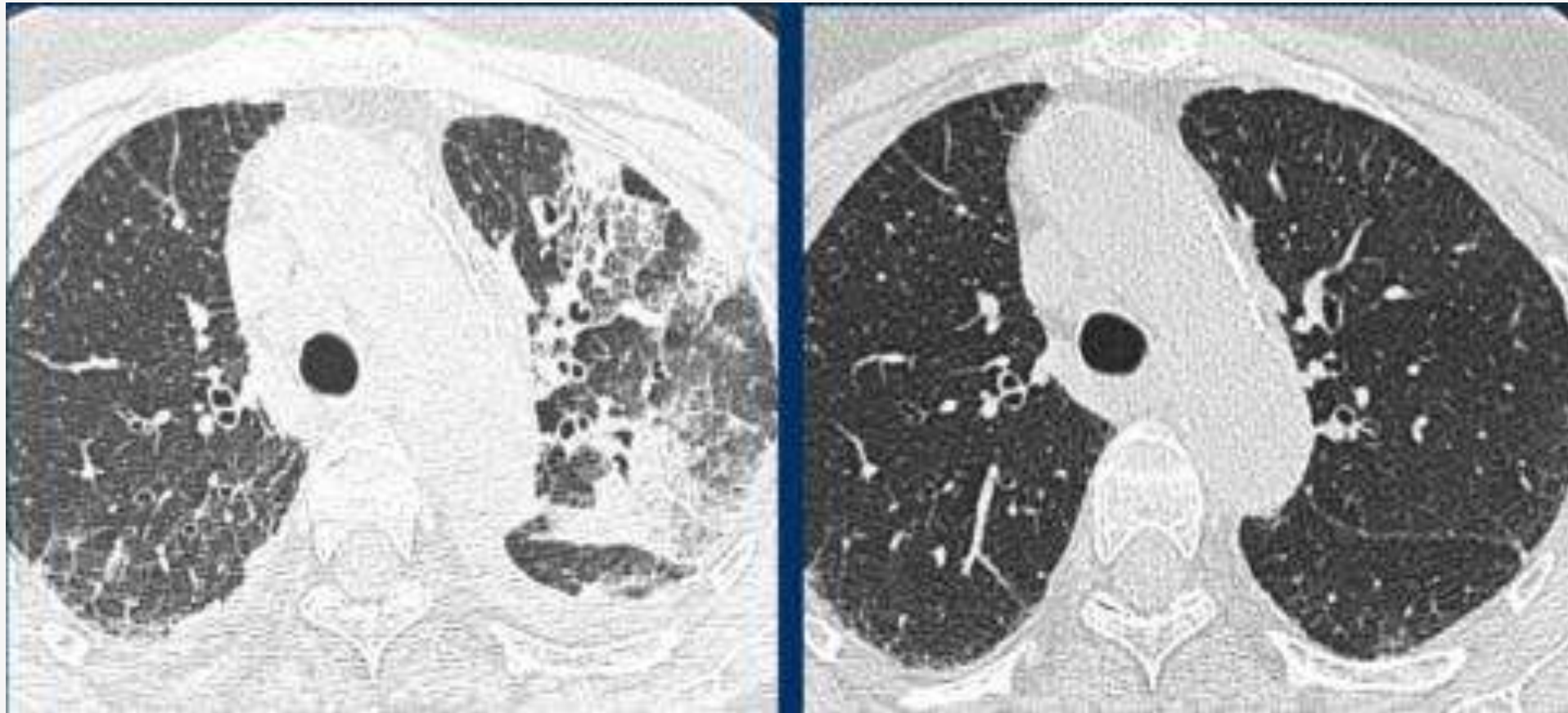


# DIFFERENTIAL DIAGNOSIS

## DRUG-INDUCED PNEUMONITIS

- Drugs can cause CT patterns similar to confirmatory patterns of COVID-19, including ground glass, peripheral consolidations, crazy paving and organizing pneumonia patterns
- The appropriate clinical setting of potentially pneumotoxic drugs and clear improvement after drug withdrawal (right) helps in suggesting this differential diagnosis
- A list of pneumotoxic drugs and the findings on CT is found on

DRUG-INDUCED PNEUMONITIS WITH  
GROUNDGLASS, RETICULATION, CRAZY PAVING AND  
CONSOLIDATIONS (LEFT), WHICH RESOLVED AFTER  
DRUG WITHDRAWAL (RIGHT).

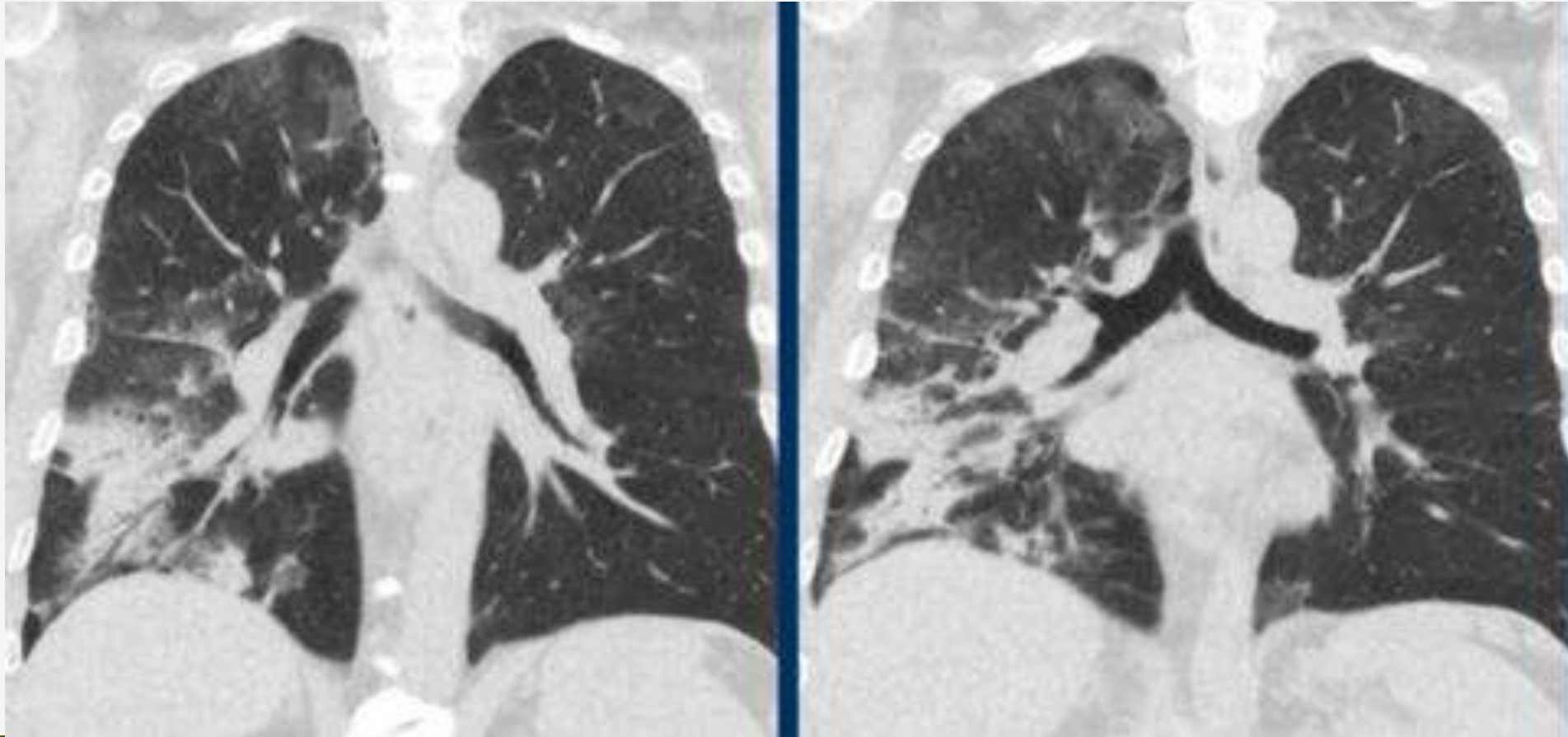


## DIFFERENTIAL DIAGNOSIS

# RADIATION PNEUMONITIS

- Inflammatory and fibrotic changes associated with radiotherapy can cause **peripheral ground-glass and consolidations in the area of the radiation therapy field**
- However, **bilateral organizing pneumonia** outside the radiation field can also occur, mimicking one of the confirmatory feature of COVID-19
- Correlation with the **radiotherapy field** and **stationary location of abnormalities over time** can virtually always confirm radiation pneumonitis

# STATIONARY GROUNDGLASS AND CONSOLIDATIONS IN THE RIGHT LUNG AFTER RADIATION THERAPY



## DIFFERENTIAL DIAGNOSIS

# HYPERSENSITIVITY PNEUMONITIS

- Ground glass opacities in hypersensitivity pneumonitis (HP) are also bilateral, but show a more geographical pattern
- **In addition, HP has other features uncommon in COVID-19:**
  - Centrilobular nodules**
- **Headcheese sign**” with a mixture of lobules with ground glass, normal density parenchyma, and air trapping
- Clinical presentation with a history of exposure to sometimes **unknown antigens**
- HP patients can develop **fibrotic changes** in **a later stage**.

THE IMAGE SHOWS TYPICAL BILATERAL GROUNDGLASS OPACITIES IN HYPERSENSITIVITY PNEUMONITIS WITH HEAD CHEESE SIGN: A MIXTURE OF GROUND GLASS, NORMAL DENSITY PARENCHYMA AND AIR TRAPPING (CIRCLE)



## DIFFERENTIAL DIAGNOSIS

### NSIP

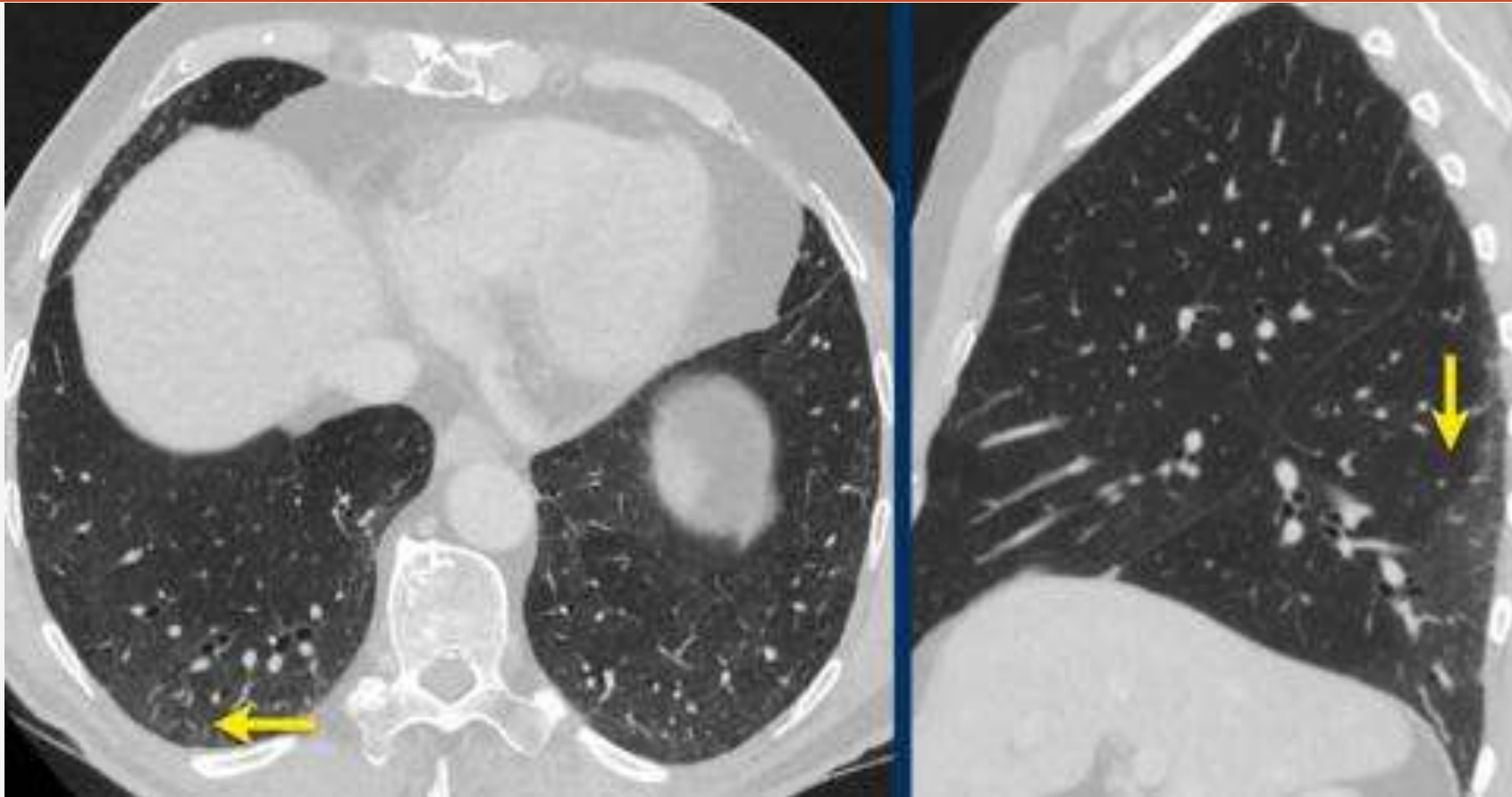
- Other interstitial lung diseases, such as nonspecific interstitial pneumonia can present with **peripheral ground glass opacities, which can simulate COVID-19**
- This patient had **nonspecific interstitial pneumonia** and presented on CT with faint **ground glass resembling** cellular and, to some extent, **fibrotic interstitial disease**

# DIFFERENTIAL DIAGNOSIS

## NSIP

- Differentiation from COVID-19:
- The opacities are not demarcated
- **No vascular** thickening
- **Mostly stable over time**
- **Clinical presentation** is distinct from infection

# PERIPHERAL, FAINT GROUNDGLASS (ARROWS) IN A PATIENT WITH NONSPECIFIC INTERSTITIAL PNEUMONIA

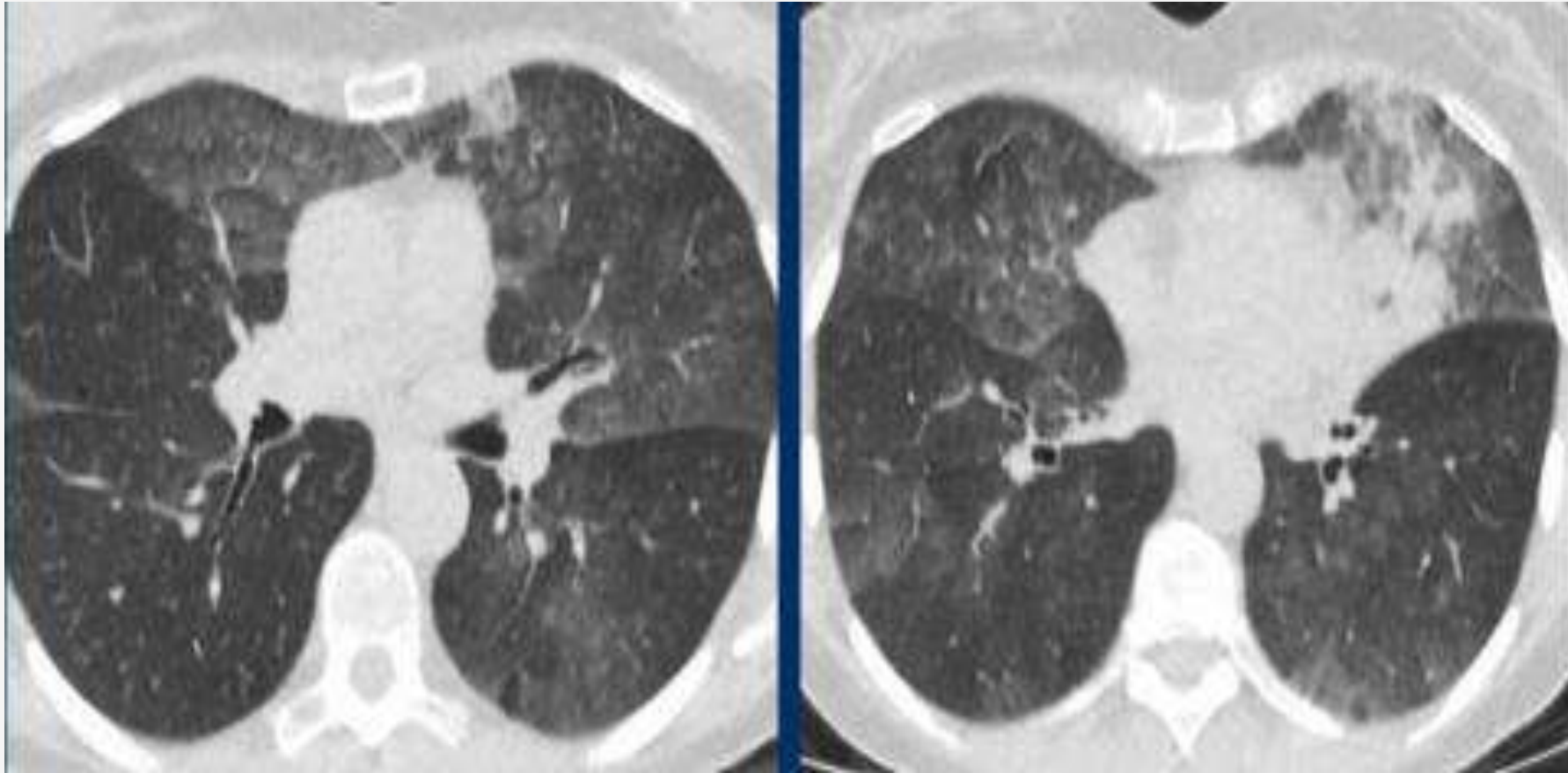


## DIFFERENTIAL DIAGNOSIS

# ADENOCARCINOMA

- Especially adenocarcinoma and its precursors can present with pure ground glass opacities with or without solid components, depending on the degree of invasiveness
- Multifocal adenocarcinoma **in situ** can present as bilateral ground glass opacities, which might look like COVID-19
- Here, distribution is different from COVID-19, with a more geographical and diffuse distribution and no peripheral predominance

# GROUNDGLASS AND CONSOLIDATIONS RESEMBLING EXTENSIVE, BILATERAL NON-MUCINOUS INVASIVE ADENOCARCINOMA AND ADENOCARCINOMA IN SITU

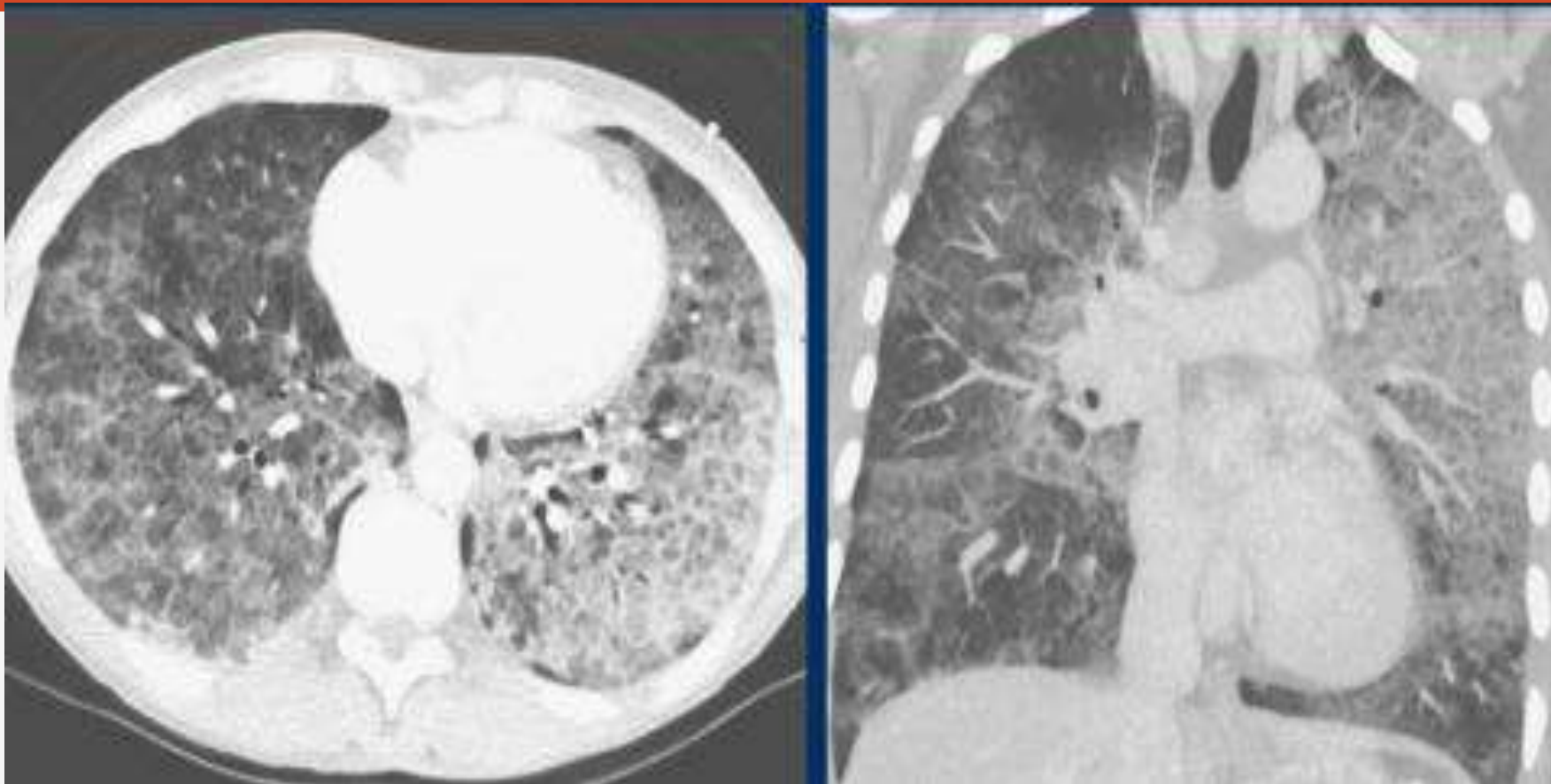


## DIFFERENTIAL DIAGNOSIS

# ALVEOLAR PROTEINOSIS

- **Alveolar proteinosis** is a rare condition, frequently associated with elevated lactate dehydrogenase, antibodies against granulocyte-macrophage colony-stimulating factor and bronchoalveolar fluid findings typical for alveolar proteinosis
- **Crazy paving** in alveolar proteinosis is much more **diffuse than in COVID-19**, with **incidental lobular or geographic sparing**, and is frequently disproportional with **severity of complaints**

# ALVEOLAR PROTEINOSIS WITH DIFFUSE CRAZY PAVING



# OVERLAPPING DISEASES

- With overlapping diseases we mean diseases of the lung that have the **exact pattern** as COVID-19

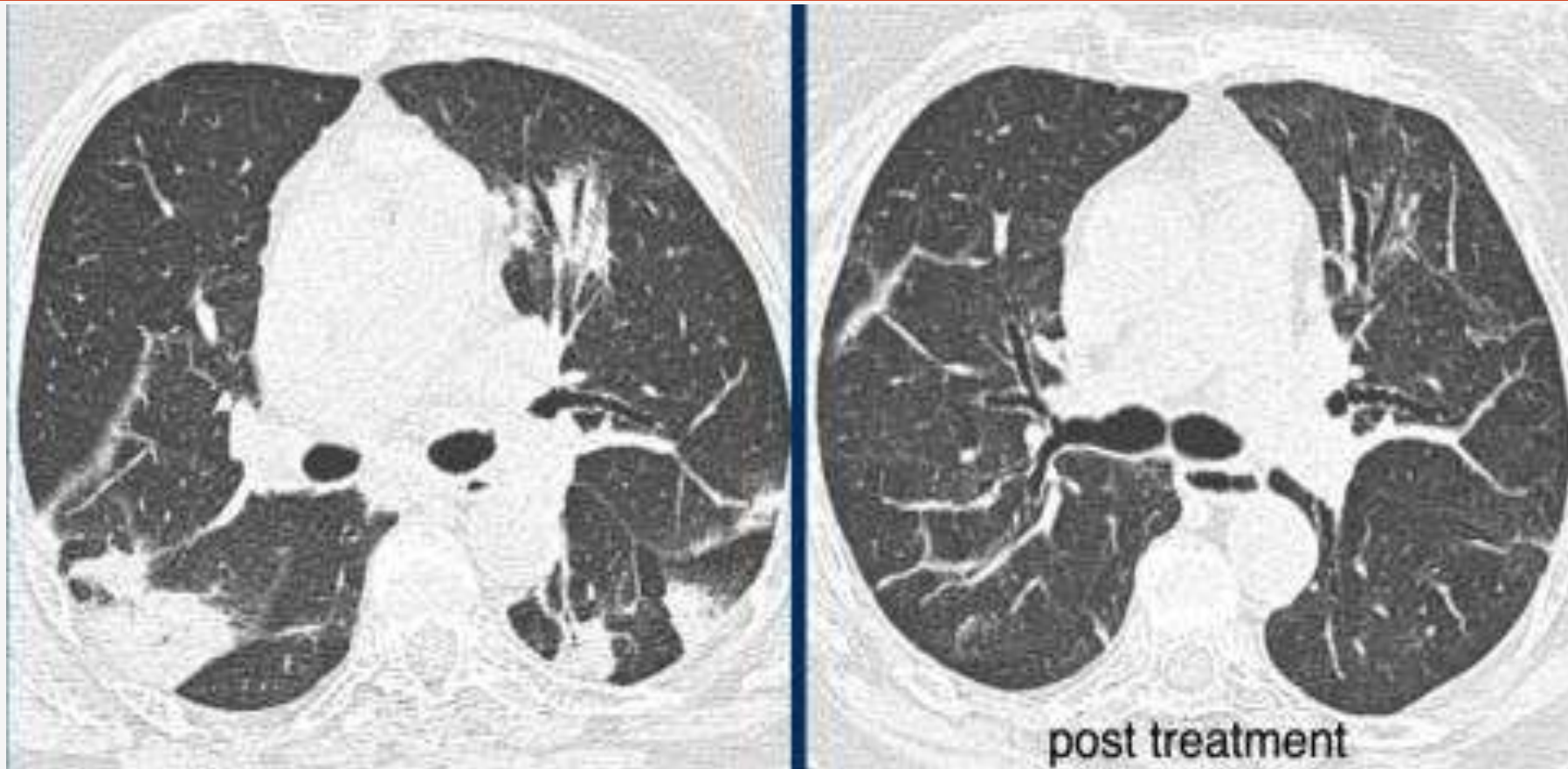
**Distinction** can **only** be made with **clinical parameters**

# OVERLAPPING DISEASES

## ORGANIZING PNEUMONIA

- Patterns compatible with **organizing pneumonia** commonly occur in **COVID-19**
- It is regarded as a confirmatory pattern, reflecting **a later stage in the temporal evolution of the parenchymal abnormalities**
- This pattern in COVID-19 overlaps with organizing pneumonia due to other causes with typical peripheral and central peribronchiolar consolidations and central airway dilatation (figure)
- **The lung abnormalities decreased after treatment with corticosteroids**

ORGANIZING PNEUMONIA. LEFT TYPICAL  
PERIPHERAL AND CENTRAL PERIBRONCHIOLAR  
CONSOLIDATIONS WITH CENTRAL AIRWAY  
DILATATION. RIGHT POST TREATMEN

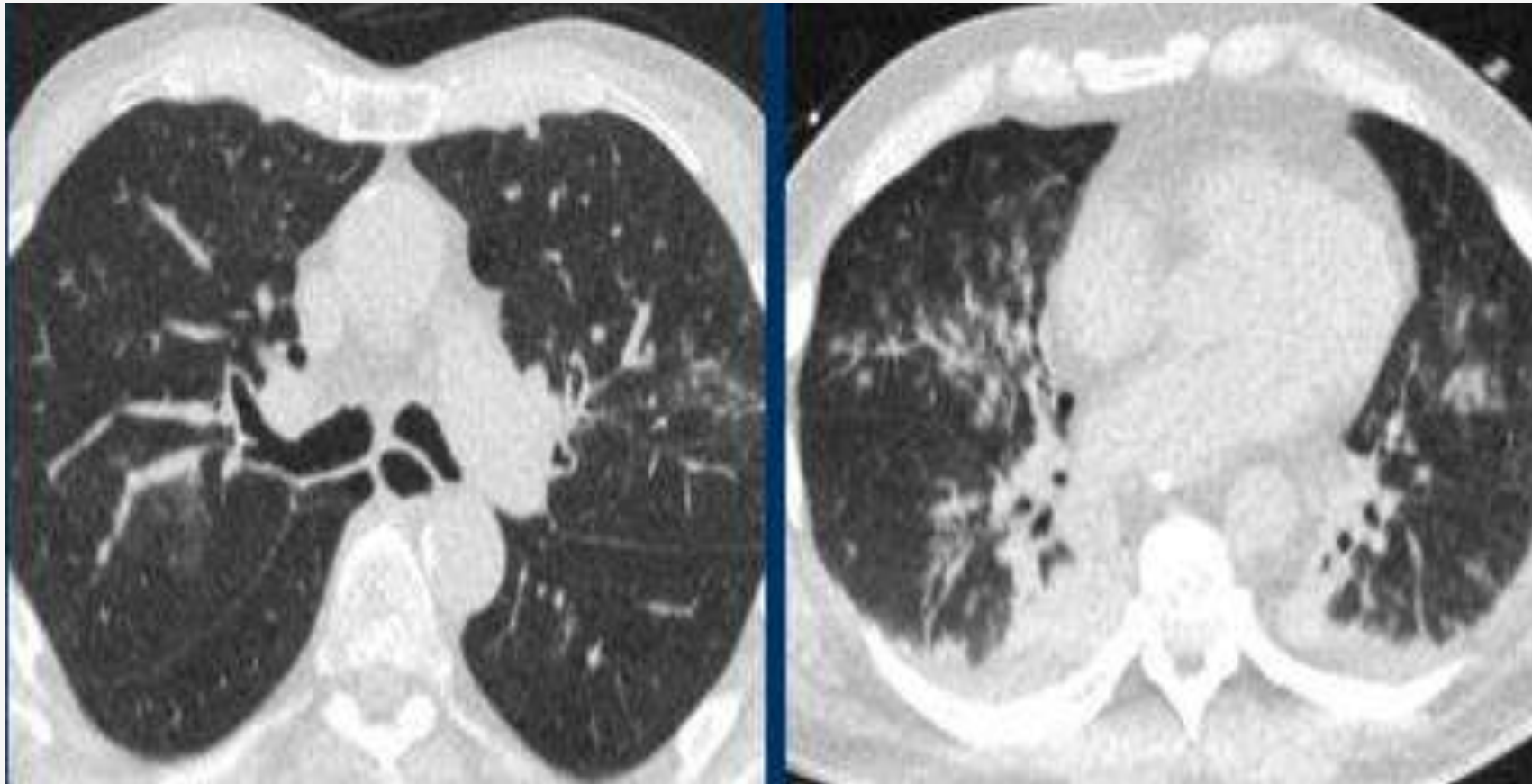


# OVERLAPPING DISEASE

## INFLUENZA PNEUMONIA

- Viral pneumonias show overlapping features on CT.
- Influenza virus infection can result in bilateral ground-glass opacities, consolidations and crazy paving that appear similar to COVID-19.
- **Typical features of influenza** are:
  - Muroid airway impaction
  - Linear opacities
  - Central distribution (as shown in these two cases)
- In addition, **vessel thickening and upper lobe involvement** seem to occur more frequently in the **abnormal COVID-19** parenchyma than in other viral pneumonias.

# INFLUENZA PNEUMONIA. BILATERAL GROUNDGLASS WITH CENTRAL DISTRIBUTION AND CENTRIOLOBULAR GROUNDGLASS NODULES

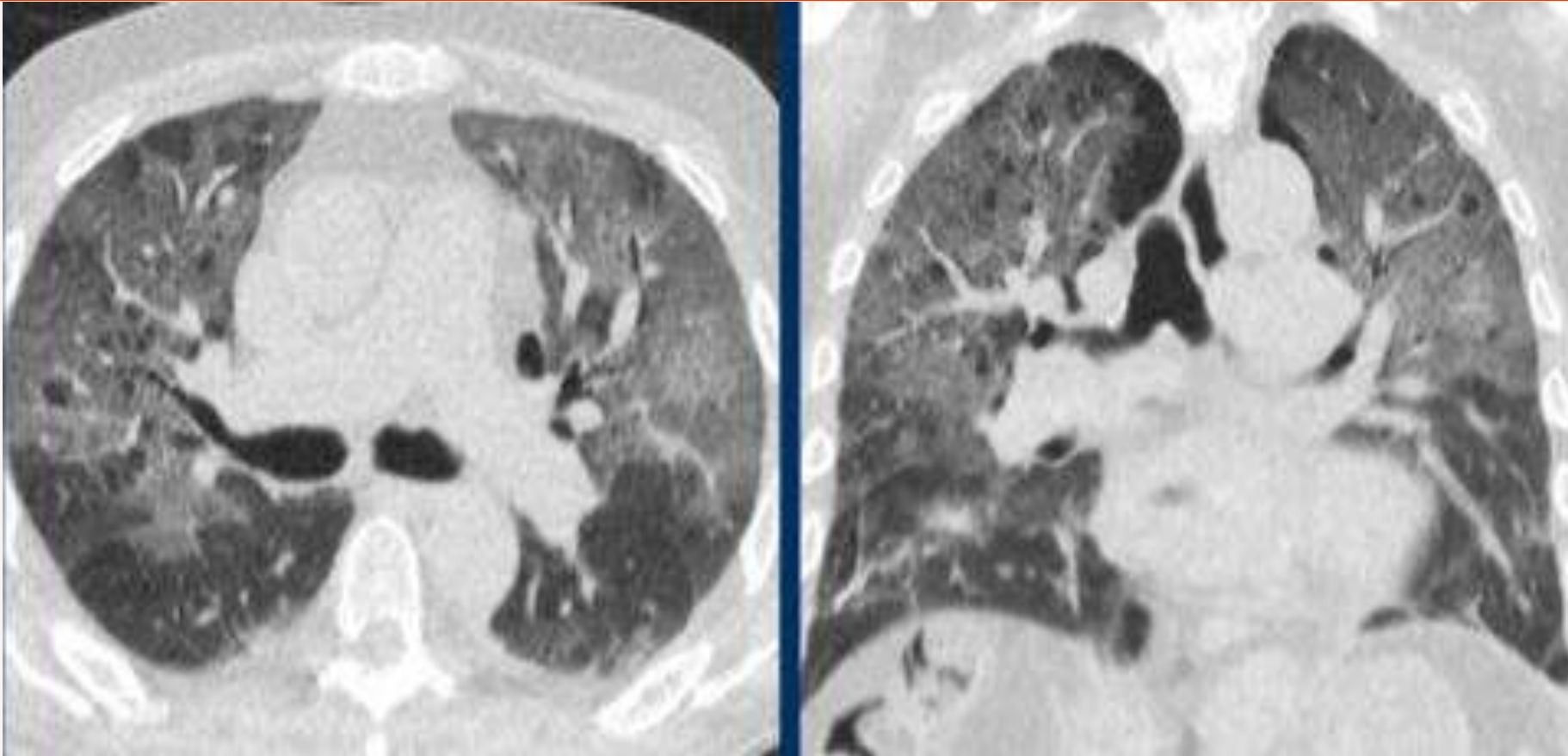


# OVERLAPPING DISEASE

## PNEUMOCYSTIS PNEUMONIA

- **Pneumocystis pneumonia** also causes bilateral ground-glass and in later stages consolidations with or without crazy paving
- However, this frequently occurs in a **more central distribution** **than** in COVID-19, and only in immunocompromised patients
- PCP is furthermore associated with pulmonary cysts and spontaneous pneumothoraces, although pneumothoraces and bullae also present in a small minority of hospitalized COVID-19 patients

# BILATERAL GROUNDGLASS IN PCP IN AN IMMUNOCOMPROMISED PATIENT.



# OVERLAPPING DISEASE

## ADULT RESPIRATORY DISTRESS SYNDROME

- **Diffuse alveolar damage** can also show peripheral ground-glass, consolidations and crazy paving, which can be similar to the alveolar damage in patients with COVID-19 (left), but also **more gravity dependent** reflecting **permeability edema** (right)
- ARDS can only occur in the **appropriate setting**, such as in a **postoperative situation** or in case of **prolonged mechanical ventilation**
- However, ARDS can concomitantly occur with COVID-19 in ICU patients

ARDS. BILATERAL, IN PART GRAVITY DEPENDENT  
GROUNDGLASS WITH ATELECTASIS, AND PLEURAL  
FLUID IN A PATIENT WHO UNDERWENT A GASTRO-  
ESOPHAGEAL RESECTION

