

# Mimics of Pneumonia

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# Objectives

- A case presentation from ERS congress.
- An introduction to nonresponding pneumonia & pneumonia mimickers.
- The reasons for delay in diagnosis of mimickers & treatment failure.
- Initial management for alternative Dx of CAP.



On 5<sup>th</sup> August 2020 a **63-year-old woman** presented to the Emergency Department of the University Hospital of Ferrara, **complaining dyspnea, nausea, fever and cough.**

## Vital signs at the time of admission:

- BP: 150/80 mmHg
- Body Temperature: 38°C
- SpO<sub>2</sub>: 85% in ambient air → 95% in FiO<sub>2</sub> 35% with mask → respiratory failure

**Family history:** father affected by rheumatoid arthritis; mother died of heart attack.

**Medical history:** Ex-farmer, non-smoker. Hypertension, previous duodenal ulcer, GERD.

Recent hospitalization for pneumonia (July 2020), with negative investigations for SARS-CoV-2 (both upper nasal swab and BAL) and no other microbiological agents identified. Treated with amoxicillin-clavulanate and clarithromycin. Discharged with methylprednisolone tapering over in 15 days.



## *Blood examination*

- WBC:  $10 \times 10^3$  cells/mm<sup>3</sup>
- **Hb: 11 g/dl**
- PLT  $364 \times 10^3$  cells/mm<sup>3</sup>
- Neutrophils  $8.99 \times 10^3$  cells/mm<sup>3</sup>
- **Lymphocytes:  $0.37 \times 10^3$  cells/mm<sup>3</sup>**
- Monocytes  $0.53 \times 10^3$  cells/mm<sup>3</sup>
- Eosinophils  $0.09 \times 10^3$  cells/mm<sup>3</sup>
- Basophils  $0.02 \times 10^3$  cells/mm<sup>3</sup>
- **Serum D-dimer 1200 ng/mL DDU** (cut off < 250)
- **LDH 404 U/L** (cut off < 247)
- **C- Reactive Protein 14.92 mg/dl** (cut off < 0.50)
- **SARS-CoV-2 RNA on nasopharyngeal swab: NEGATIVE**

## **ABG (FiO<sub>2</sub> 21%):**

- pH 7.42
- pCO<sub>2</sub> 33 mmHg
- pO<sub>2</sub> 49 mmHg
- HCO<sub>3</sub> 24.2 mmol/l
- PaO<sub>2</sub>/FiO<sub>2</sub> 233

## Chest X-Ray

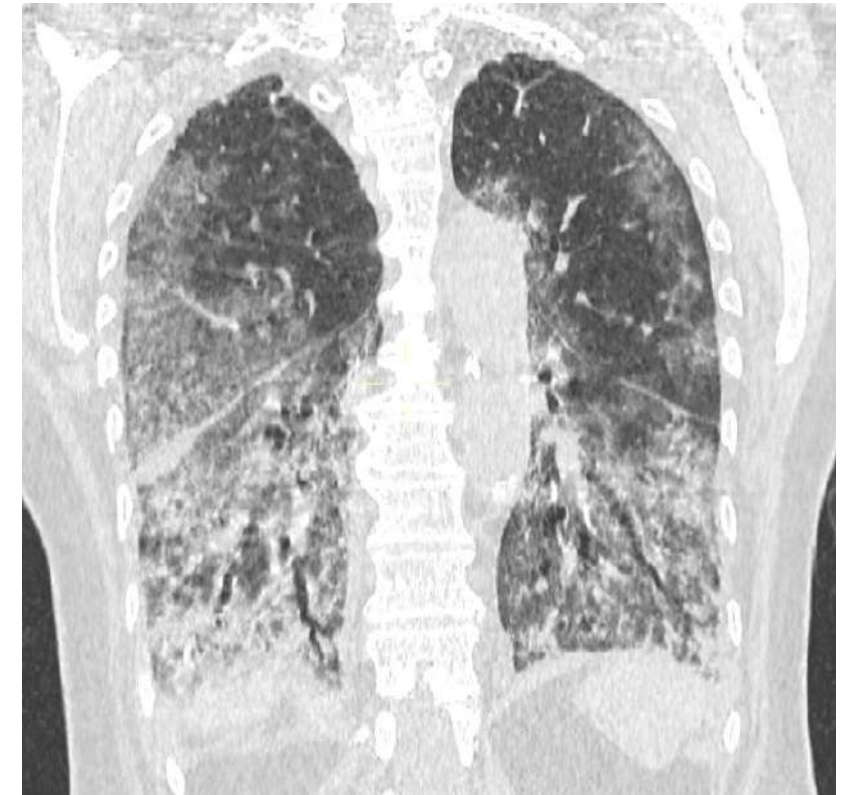
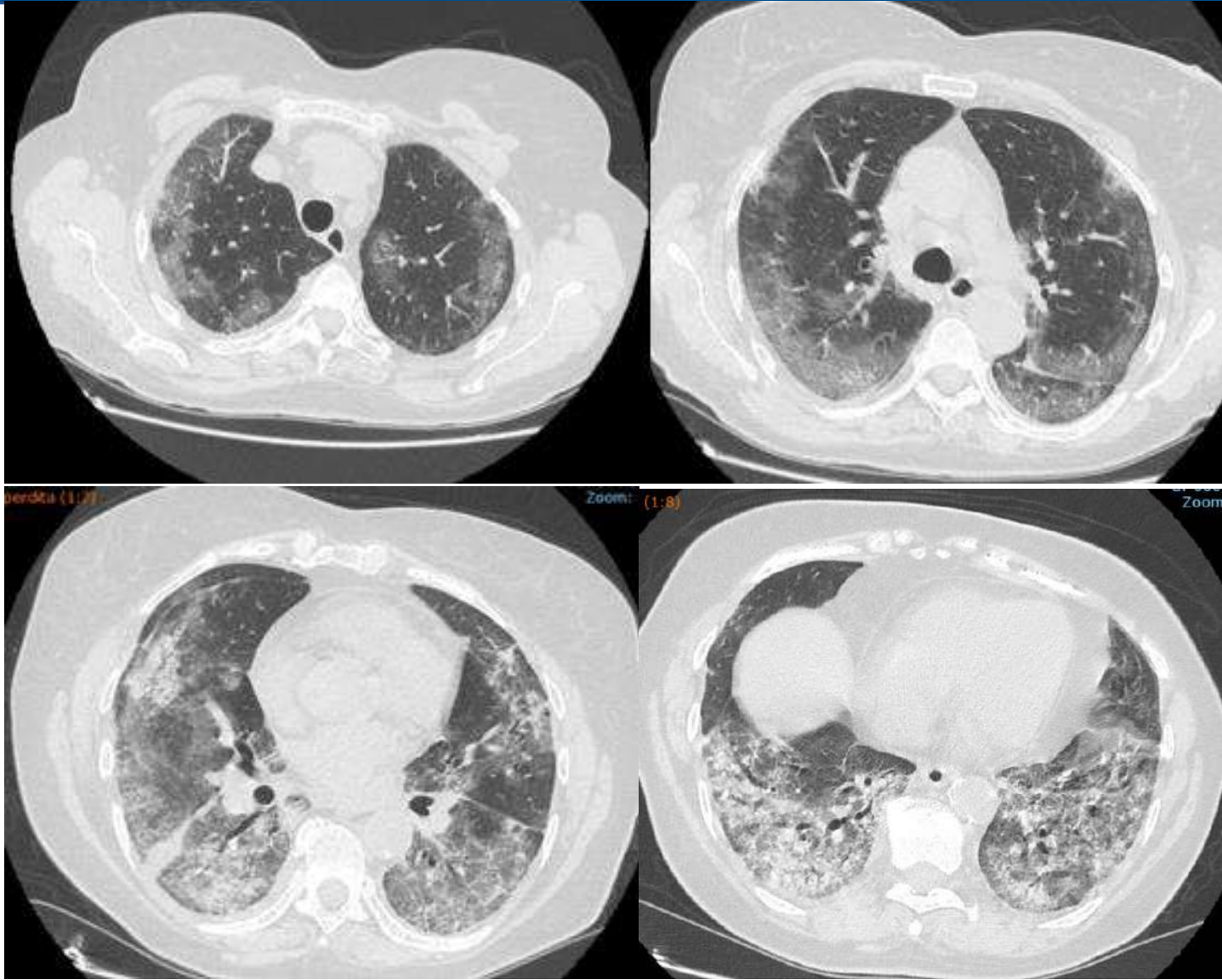


Bilateral medio-basal opacities

# High Resolution CT scan of the chest



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- Bilateral peripheral ground glass opacities
- Bilateral consolidations, prevalent in the lower lobes

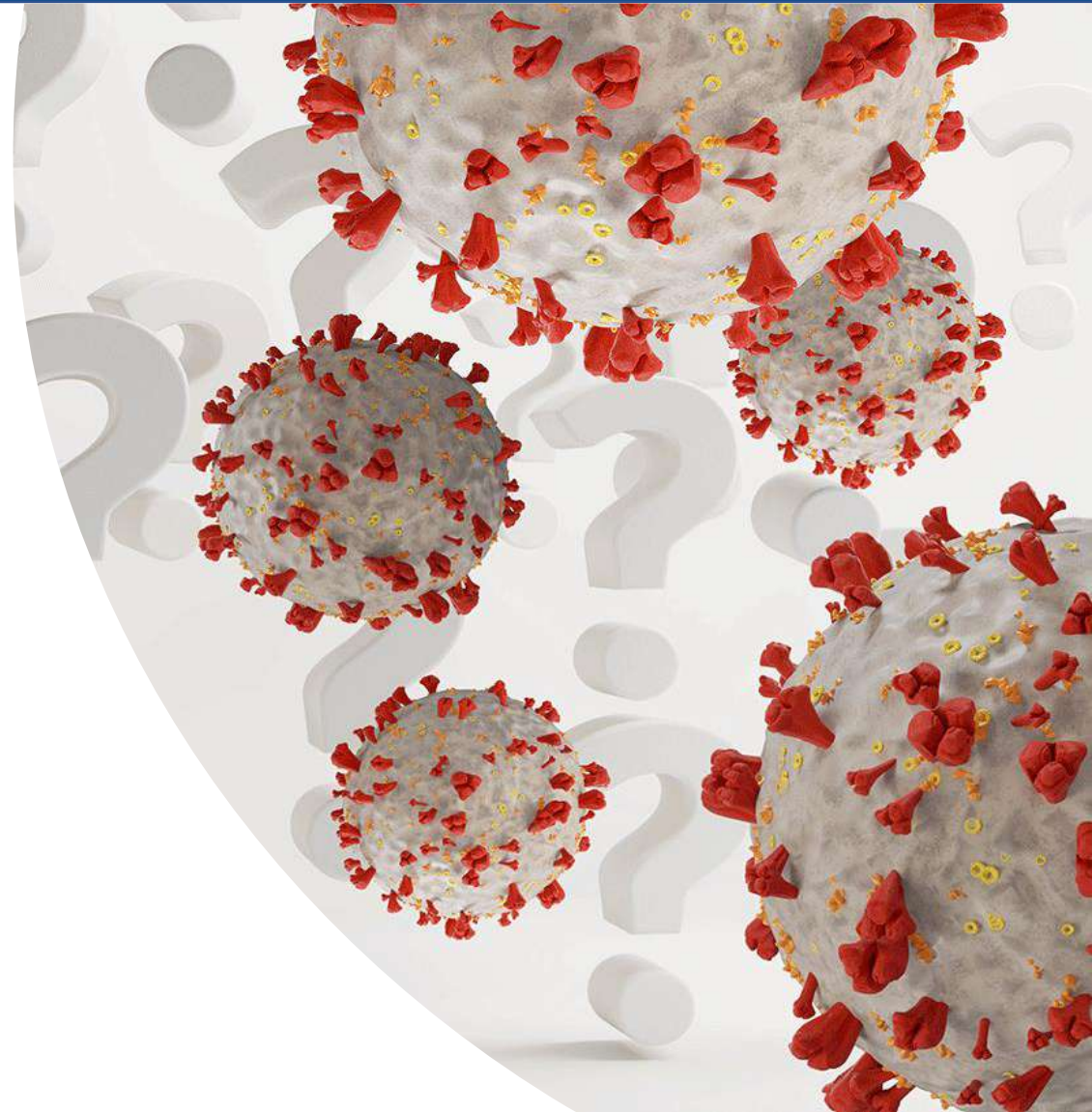
# Multiple Choice Question



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Considering the clinical-radiological presentation, epidemiological data and clinical history, which diagnostic hypothesis is more likely?

- A. Community acquired pneumonia
- B. Interstitial Lung Disease (ILD)
- C. COVID 19, with false negative nasal swab
- D. ARDS related to GERD and aspiration



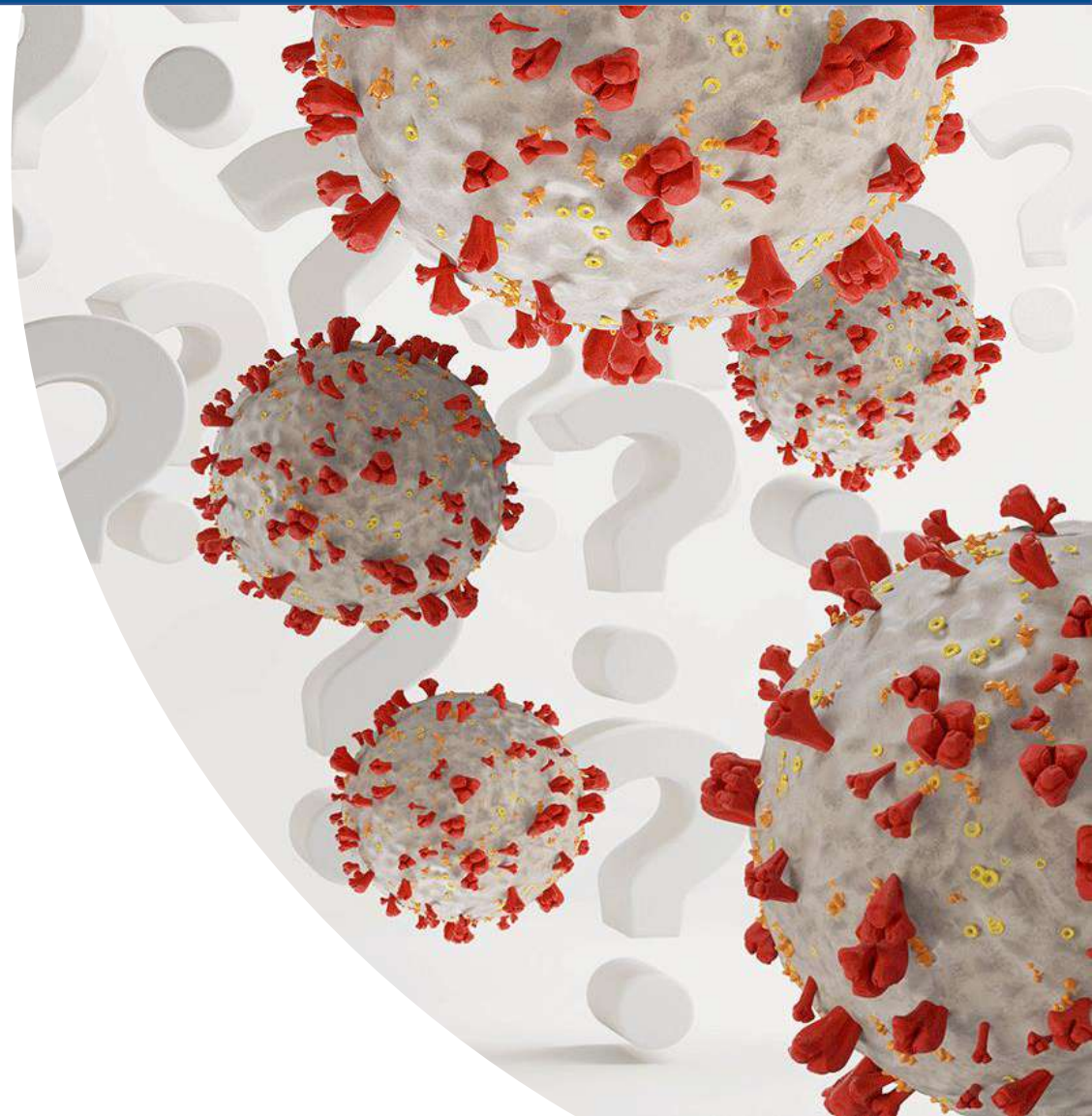
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The patient was considered suspect for COVID-19.

Due to worsening of hypoxemic respiratory failure ( $\text{PaO}_2/\text{FiO}_2$  ratio  $\sim 100$ ), she was admitted to the Respiratory sub-Intensive Unit and treated with:

- High Flow nasal cannulae oxygen (HFNC) alternated with noninvasive ventilation (NIV)
- Empiric antibiotic therapy with Levofloxacin 750 mg/die
- Methylprednisolone 40 mg/die

# Second level investigations



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- Legionella and Pneumococcal urinary antigens;
- Serology for Legionella P., Mycoplasma P., Chlamydia pneumoniae
- HIV test;
- Viral serology (Cytomegalovirus, Coxsackie, HCV, HBV and SARS-CoV-2).
- Bronchoscopy for:
  - Cytology and cytogram assessment;
  - Microbiological assessments on Broncho-alveolar lavage (BAL):
    - SARS-CoV-2 RNA;
    - Pneumocystis jiroveci;
    - Mycobacterium species, bacterial and fungal culture;
    - film Array Pneumonia.
- Autoimmune lab tests:ANA/ENA/MPO-CA/RF/ANCA

**Acinetobacter calc-baumannii compl**

**Enterobacter cloacae complex**

**Escherichia coli**

**Haemophilus influenzae**

**Klebsiella aerogenes**

**Klebsiella oxytoca**

**Klebsiella pneumoniae group**

**Moraxella catarrhalis**

**Proteus spp.**

**Pseudomonas aeruginosa**

**Serratia marcescens**

**Staphylococcus aureus**

**Streptococcus agalactiae**

**Streptococcus pneumoniae**

**Streptococcus pyogenes**

**CTX-M (gene di resistenza)**

**IMP (gene di resistenza)**

**KPC (gene di resistenza)**

**mecA/C (gene di resistenza)**

**NDM (gene di resistenza)**

**OXA-48-like (gene di resistenza)**

**VIM (gene di resistenza)**

**Chlamydia pneumoniae**

**Legionella pneumophila**

**Mycoplasma pneumoniae**

**Adenovirus**

**Coronavir.229E,OC43,HKU1,NL6**

**Human Metapneumovirus**

**Human Rhinovirus/Enterovirus**

**Influenza A**

**Influenza B**

**MERS Coronavirus**

**Parainfluenza Virus**

**Respiratory Syncytial Virus**

# Results



- Negative Legionella and Pneumococcal urinary antigens, HIV test, multiple sierology (Cytomegalovirus, Coxakie, HCV, HBV, Micoplasma and Chlamydia Pn)
- Negative for SARS-CoV-2 (sierology and RNA on BAL)
- All microbiological tests on BAL were negative (bacteria, fungi, P.jirovecii, M. tuberculosis)
- only PCR for Serratia Marcescens was positive => probable contaminant
- Cytogram on BAL: macrophages 79%, lymphocytes 7%, neutrophilis 13%
- Speckled ANA pattern 1:80 and anti-Ro52 antibodies positive

## PANEL OF SPECIFIC MYOSITIS ANTIBODIES

Mi-2 alfa:

Mi-2 beta:

TIF1gamma:

MDA5:

NXP2:

SAE1:

Ku:

PM-Scl 100:

PM-Scl 75:

Jo-1:

SRP:

PL-7:

PL-12:

EJ: +

OJ:

Ro-52: +



**Anti-Synthetase syndrome?**

# Multiple Choice Question



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Which therapeutic strategy/strategies would you consider?

- A. Wide spectrum antibiotics
- B. Systemic corticosteroids/ Immunosuppressor
- C. Plasmapheresis
- D. ICS/LABA/LAMA

# Multiple Choice Question



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- B. Systemic corticosteroids/ Immunosuppressor**
- C. Plasmapheresis
- D. ICS/LABA/LAMA



In the suspicion of an **Anti-Synthetase Syndrome (ASS)** the patient was treated with high systemic corticosteroids dosage (Methylprednisolone 1g/die for 3 days, then 1mg/kg/die)

Physical examination :

- No myopathic features (muscle weakness, cutaneous features, arthralgia);
- Auscultation of the chest: fine inspiratory crackles;
- Xanthelasma palpebrarum.

***Electromyography***: carpal tunnel syndrome

***Nailfold capillaroscopy*** : “non-specific” pattern for mild microvascular lesion.



**Isolated pulmonary involvement of ASS**



- Slow but gradual clinical improvement, and, when clinical stability was achieved, she was transferred to the department of Rheumatology:
  - No fever, eupneic at rest, minimal dyspnea on physical activity
- Respiratory failure resolution
  - ABG in ambient air:  
pH 7.45, pO<sub>2</sub> 70 mmHg, pCO<sub>2</sub> 35 mmHg, HCO<sub>3</sub> 24.3mmol, P/F 333 mmHg
- Blood tests: progressive resolution of lymphopenia, WBC and CRP reduction.

On 18<sup>th</sup> September 2020 the patient was discharged at home with prescription of tapering long term systemic corticosteroid + Azathioprine.

# 3-months Follow up

AUG 2020



DEC 2020



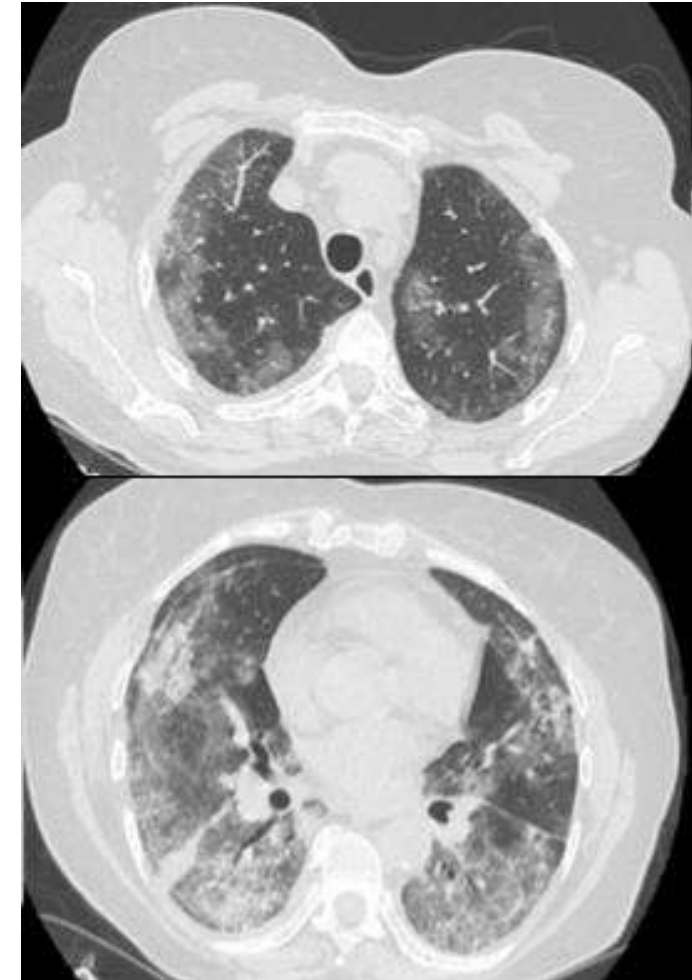
# Multiple Choice Question



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Considering the CT scan at the onset. Which HRTC pattern could be identified?

- A. Non Specific Interstitial Pneumonia (NSIP)
- B. Definite Usual Interstitial Pneumonia (UIP)
- C. UIP in Connective Tissue Disease
- D. Non Specific interstitial Pneumonia(NSIP) + Organizing Pneumonia (OP)



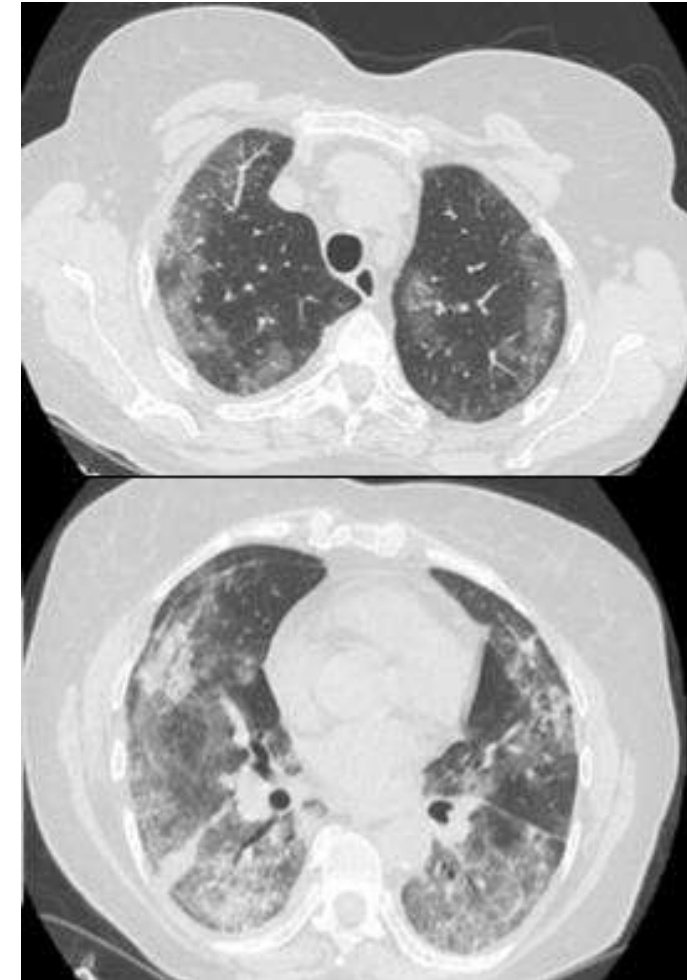
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- B. Definite Usual Interstitial Pneumonia (UIP)
- C. UIP in Connective Tissue Disease
- D. **Non Specific interstitial Pneumonia(NSIP) + Organizing Pneumonia (OP)**



# Conclusions and points of discussion



- ❖ Antisynthetase syndrome (ASS) is a rare autoimmune disease belonging to idiopathic inflammatory myopathies group. It is characterized by antibodies positivity directed against aminoacyl-tRNA synthetase (anti-Jo1, anti-PL7, anti-PL12, anti-Oj, anti-EJ, anti-KS, anti-Zo)<sup>1</sup> ;  
Concomitant positivity of Anti-Ro52 antibodies is related to severe Interstitial Lung disease<sup>1</sup>;
- ❖ Clinical manifestations include: myositis, arthralgia/arthritis, Interstitial Lung Disease (ILD), Raynaud's phenomenon, mechanic's hands<sup>1</sup>;
- ❖ Lung involvement is often the first and dominant manifestation and may present in acute (Rapidly Progressive ILD/RP-ILD) , asymptomatic or chronic form<sup>2</sup>.
- ❖ On HRCT scan of the chest the prevalent pattern is NSIP followed by OP, less commonly UIP and AIP<sup>3</sup>;  
**In a cohort of 46 patients with ASS EJ+, the combination of NIS+OP pattern was more frequent in RP-ILD forms as compared to chronic ILD forms<sup>4</sup>;**
- ❖ Absence of extra-pulmonary manifestation makes the diagnosis more challenging and RP-ILD may mimic ARDS<sup>5</sup>



**Our final diagnosis was Anti-EJ syndrome with dominant lung involvement.**

- The absence of myositis symptoms and the pandemic phase of COVID-19 influenced our diagnostic hypotheses.
- We performed three assays before excluding SARS-CoV-2 Pneumonia.
- Autoimmunity panel should be considered when facing ARDS with unknown etiology.

# References



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- <sup>2</sup> Bajocchi G, Piro R, Lombardini C et al. Acute respiratory distress syndrome-an undercover antisynthetase syndrome: a case report and review of the literature. *Clin Exp Rheumatol*. 2012 May-Jun;30(3):424-8.
- <sup>3</sup> Baratella E, Marrocchio C., Cifaldi R. et al. Interstitial lung disease in patients with antisynthetase syndrome: a retrospective case series study. *Jpn J Radiol* **39**, 40–46 (2021). <https://doi.org/10.1007/s11604-020-01030-3>
- <sup>4</sup> Zhang Y, Ge Y, Yang H. et al. Clinical features and outcomes of the patients with anti-glycyl tRNA synthetase syndrome. *Clinical Rheumatol* **39**, 2417–2424 (2020). <https://doi.org/10.1007/s10067-020-04979-8>
- <sup>5</sup> Vuillard C., Pineton de Chambrun M, de Prost N. et al. Clinical features and outcome of patients with acute respiratory failure revealing anti-synthetase or anti-MDA-5 dermatopulmonary syndrome: a French multicenter retrospective study. *Ann. Intensive Care* **8**, 87 (2018). <https://doi.org/10.1186/s13613-018-0433-3>