Northeast Georgia Medical Center
GRADUATE MEDICAL EDUCATION

# Ground Glass Changes on Chest Imaging: Not another COVID-19 Case

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## Learning Objectives

- Considering broader differential for Ground Glass Opacities (GGO)
- Compare and contrast imaging findings in COVID-19 pneumonia vs common patterns interstitial lung disease (ILD)
- Discuss nonspecific interstitial pneumonia (NSIP) imaging pattern and how it is present in both COVID-19 and mixed connective tissue disease.

## Literature Review

**Introduction:** Ground glass opacity (GGO) imaging findings have become a key diagnostic feature of COVID-19. Yet, it is by far not the only disease process that can present in this way.

**Differentials to consider for GGO:**

| Auto-Immune | Infectious | Other |
|---|---|---|
| Mixed connective tissue disease | COVID-19 | Drug toxicity (eg amiodarone) [2] |
| Systemic Sclerosis | Pneumocystis jirocvecii | Hypersensitivity pneumonitis (inhalation) |
| Rheumatoid Arthritis | Viral and bacterial pneumonias | |
| Dermatomyositis/ Polymyositis | | |

**COVID-19 Pneumonia Imaging Findings**:

Common findings: bilateral, peripheral, and basal with GGO and consolidation ( day 1-6[4])

Less common/later: crazy paving and architectural distortion, these findings can be superimposed on GGO ( day 6-11 or 12-17) can mimic findings of ILD[3,4] Imaging findings peak 9-13 days after infection[4]

**Interstitial Lung Diseases vs COVID-19:**

It is important to highlight that interstitial lung diseases, specifically connective tissue and/or auto-immune, can appear to be very synonymous to COVID-19 on imaging.

1. **Organizing pneumonia:** caused by infection, collagen diseases, and inflammatory myopathies (dermatomyositis/ polymyositis): patchy opacities in peripheral lung fields, uncommonly seen GGO[1,4] **( vs COVID-19 opacities are more migratory, + perilobular thickening, pre-existing condition[3])*

2. **Usual Interstitial Pneumonia** (UIP *exacerbation): Most commonly in rheumatoid arthritis; fibrosis and honeycombing next to GGO, traction bronchiectasis, crazy paving[1] *( vs COVID-19: > fibrotic features, can mimic severe COVID-19/ARDS)*

3. **Nonspecific Interstitial Pneumonia** (NSIP): connective tissue diseases (systemic sclerosis, mixed connective tissue disease) with chronic course (months) diffuse GGO and volume loss in lower lobes and traction bronchiectasis (esp in fibrotic type which also has honeycombing) can be subpleural random or diffuse. Cellular NSIP would be more likely to present as diffuse GGO without fibrosis[1] *(vs COVID-19, more insidious onset although can be exacerbation, pre-existing condition[2])*

## Case Presentation

**Presentation:**
- Patient is a 51-year-old female with a past medical history of hyperlipidemia, hypertension, and migraines who initially presented to the ED with a progressively worsening cough and shortness of breath. CT and X ray imaging at that time were unremarkable.
- COVID-19 PCR test was negative. During the ED visit she was diagnosed with acute bronchitis and went home without antibiotics.

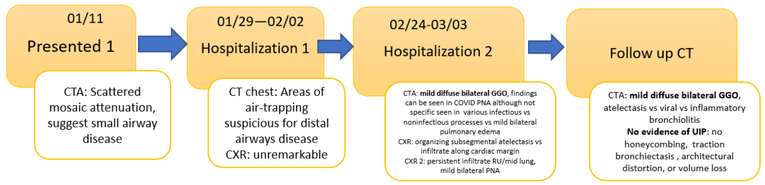
**Hospitalization 1:**
- Admitted for presumedCOVID-19 pneumonia based on clinical picture and imaging findings despite multiple PCR tests revealing a COVID-19 negative result. Her Chest X-ray continued to show no acute process. CT scan 01/11 showed mosaic pattern attenuation suggestive of possible ground glass opacities.

**Hospitalization 2:**
- Patient was readmitted with a similar presentation and respiratory symptoms. She again tested negative for COVID-19. No SARS-CoV-2 Antibody test was done at the time.
- Procalcitonin and WBC were within normal limits. This time she received methylprednisolone and levofloxacin. CXR revealed bilateral pneumonia and CT showed more **ground glass opacities** with mediastinal lymphadenopathy. Although this seemed to support a COVID-19 diagnosis an immunological workup revealed both a **positive ANA and RNP** suggestive of autoimmune interstitial pneumonitis.

**Outpatient Follow up:**
- After being discharged, she had a **negative COVID-19 antibody test**. She also had outpatient follow-up appointments with both pulmonology and rheumatology.

**1. Rheumatology visit:**
- She was found to have some **signs of undifferentiated connective tissue disease** such as alopecia, oral sores and photosensitivity. She also had joint pain which was more degenerative than inflammatory in nature. She lacked any specific findings such as Raynaud's, myositis or sclerodermal skin changes. Her RNP and ANA remained positive. She was diagnosed with **pulmonary predominant mixed connective tissue disease.** Patient continued on systemic steroids and started Mycophenolate.

**2. Pulmonology Visit:**
- **PFT** showing air trapping and decreased DLCO and FVC. She was also diagnosed with OSA.
- A **follow up CT** showed continued **mild ground glass opacities** (improved compared to prior image).



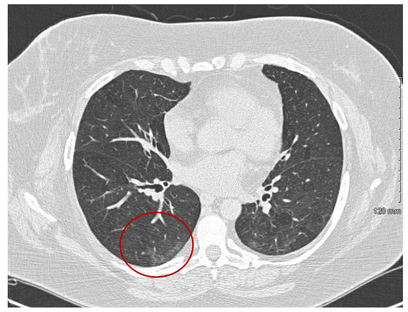



***Figure 1.*** *CT scan of the chest, coronal view, showing ground glass opacities*

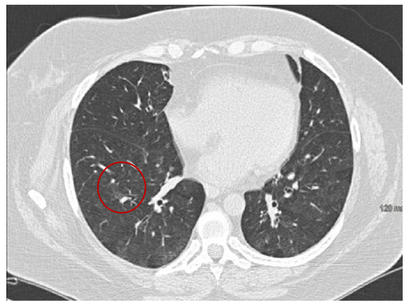


***Figure 2.*** *CT scan of the chest, coronal view, showing mosaic pattern ground glass opacities*

**Images used with permission from Northeast Georgia Hospital System*

| Laboratory | Values | References |
|---|---|---|
| Procalcitonin | 0.03 | 0.00-0.08 ng/mL |
| WBC | 5.50 | 3.5-10.5 10E9/L |
| Anti-Jo | NEGATIVE | |
| Scl-70 antibody | NEGATIVE | |
| CCP | NEGATIVE | |
| Rheumatoid Factor | NEGATIVE | |
| ANCA | NEGATIVE | |
| DNA( DS) Antibody | 3 | < or = 4 IU/mL NEG 5-9 Indeterminate > Or = 10 POS |
| SM Antibody | <1 NEG | <1 NEG AI |
| RNP Antibody | 1.0 POS | <1.0 NEG AI |
| ANA Screen | POSITIVE | |
| CRP | 7.7 | <8.0 mg/L |
| Sed Rate | 14 | < or =30 mm/H |
| Creatinine Kinase, Total | <10 | 29-143 U/L |
| SARS-CoV-2 Antibody test | NEGATIVE | |

## Discussion

It is important to continuously rule out COVID-19 for the safety of both patients and healthcare workers. However, in this particular case, the patient was presumed to be COVID-19 positive ,when in fact she wasn't, further delaying proper care. She had multiple negative tests and it took up to 4 months of repeated hospitalizations and urgent care visits for her to get a proper workup and correct diagnosis. Ground Glass Opacities are very common in respiratory distress syndromes such as COVID-19 but they are not diagnostic. This case shows us the importance of maintaining a broad differential, even in the face of pathognomonic imaging findings.

**Imaging Findings Conclusions:**

Imaging findings in this patient were remarkable for a mosaic pattern of diffuse mild GGO and volume loss or atelectasis. With this consideration the most likely pattern for this case of mixed connective tissue disease is NSIP, specifically cellular type as it does not present with fibrosis/ honeycombing or architectural distortion. NSIP especially can mimic COVID-19 imaging patterns.

## Recommendations

Ground glass opacity imaging findings have become a key diagnostic feature of COVID-19 due it's high sensitivity and specificity. However, this has created a diagnostic bias that can overshadow the relevance of multiple negative PCR tests. It is important that we consider a broader differential for the non-specific finding of GGO to prevent delayed diagnosis. In this case especially the chronicity of presentation should also have been taken into consideration, although this by itself would not have been enough to rule out COVID-19.

## References

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2. Miller W.T. Jr, & Shah R.M. Isolated Diffuse Ground-Glass Opacity in Thoracic CT: Causes and Clinical Presentations American Journal of Roentgenology 2005 184:2, 613-622
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