Progressive Pulmonary Fibrosis After Non-Critical COVID-19: A Case Report

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Patient: Male, 42-year-old
Final Diagnosis: Pulmonary fibrosis
Symptoms: Dyspnea
Medication: —
Clinical Procedure: —
Specialty: General and Internal Medicine • Pulmonology

Objective: Unusual clinical course
Background: The COVID-19 global pandemic is ongoing, and despite vaccination efforts, SARS-CoV-2 continues to circulate worldwide. The spectrum of COVID-19 illness is broad, from asymptomatic infection to respiratory failure and acute respiratory distress syndrome (ARDS), and the long-term sequelae of infection are unclear. COVID-19-related pulmonary fibrosis has been previously described in the setting of critical illness and ARDS but has not been well described in cases requiring minimal supplemental oxygen.

Case Report: We present the case of a 42-year-old man hospitalized with coronavirus disease 2019 (COVID-19) who initially required minimal supplemental oxygen but weeks later developed progressive pulmonary fibrosis requiring high-flow nasal cannula and ICU admission. Using novel computed tomography (CT) imaging processing techniques, we demonstrate progression from initial ground-glass opacities to pulmonary fibrosis and traction bronchiectasis over several months. Additionally, we describe clinical responsiveness to an extended course of corticosteroids.

Conclusions: Although pulmonary fibrosis is a known complication of severe COVID-19-related ARDS requiring mechanical ventilation, our report suggests that patients with milder forms of COVID-19 infection may develop post-acute pulmonary fibrosis.

Keywords: Case Reports • COVID-19 • Idiopathic Pulmonary Fibrosis

Abbreviations: COVID-19 – coronavirus disease 2019; ACE2 – angiotensin-converting enzyme 2; ARDS – acute respiratory distress syndrome

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/933458
**Background**

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the viral pathogen that causes COVID-19. Hundreds of millions of people have developed COVID-19 [1], ranging from asymptomatic infection to respiratory failure and ARDS requiring intubation and mechanical ventilation [1-3]. Pulmonary fibrosis is one known sequela of severe COVID-19 [4-6], and imaging studies describe residual pulmonary abnormalities in a subset of patients after recovery from COVID-19 [7,8]. Known risk factors for development of pulmonary fibrosis after COVID-19 include age, development of ARDS, and need for mechanical ventilation [5]. Pulmonary fibrosis is not well described as a complication of less severe COVID-19. Some small-scale prospective studies have not shown development of fibrosis in mild-to-moderate cases [7] but larger studies are needed to capture rare but significant long-term sequelae of COVID-19. In an ongoing global pandemic, rare outcomes may have far-reaching impacts.

We present a case of a patient with COVID-19 pneumonia who initially required only supplemental oxygen with nasal cannula. He subsequently developed progressive pulmonary fibrosis requiring prolonged hospitalization for high oxygen requirement and severe dyspnea on exertion.

**Case Report**

A 42-year-old man with a history of hypertension and previously treated latent tuberculosis developed fever and shortness of breath and tested positive for COVID-19. He subsequently developed worsening dyspnea and presented to an outside hospital 2 days after diagnosis, where he was febrile and hypoxic to 84% on ambient air. He received supplemental oxygen by nasal cannula, remdesivir for 5 doses, and dexamethasone for 10 doses. Only intermittent oxygen requirement data were available from the outside hospital (Figure 1), but his maximum supplemental oxygen requirement during admission was 5-L by nasal cannula. A chest CT obtained 7 days after diagnosis (Figure 2) showed diffuse focal ground-glass opacities consistent with viral pneumonia. He was weaned from supplemental oxygen to air and was discharged 15 days after diagnosis.

On the sixteenth day after diagnosis, he re-presented to the outside hospital with continued dyspnea on exertion and chest discomfort. He was afebrile, found to be hypoxic, and was treated with oxygen by nasal cannula. Repeat COVID-19 PCR testing and other infectious workup was negative, and he did not receive further glucocorticoid treatment. A CT pulmonary angiogram revealed no evidence of a pulmonary embolus, but showed extensive and increased bilateral ground-glass opacities and consolidation compared with his previous CT. He was discharged after 8 days (24 days after diagnosis).

He presented again 27 days after diagnosis to this hospital with isolated dyspnea limiting his ability to walk more than a few feet or perform activities of daily living. Oxygen saturation was 100% on 3-L nasal cannula on admission. A chest CT showed extensive peripheral reticulation replacing the prior ground-glass opacities, with no focal consolidation. He was discharged to home after 4 days (31 days after diagnosis) with home supplemental oxygen by nasal cannula.

He re-presented 56 days after diagnosis to this hospital with continued dyspnea. On admission, vitals were significant for

![Figure 1. Patient’s oxygen requirement throughout COVID-19-associated pulmonary fibrosis progression. Day 1 represents time at which a SARS-CoV-2 nasopharyngeal PCR test was positive. Oxygen requirement quantified by liters per minute on either nasal cannula or high-flow nasal cannula. Data not shown include pressures during noninvasive positive-pressure ventilation and percent of oxygen delivered.](image-url)
a respiratory rate of 52 breaths per minute and oxygen saturation of 88% on 5-L nasal cannula. He was placed on non-invasive positive-pressure ventilation and later was transitioned to high-flow nasal cannula.

An extensive workup for other causes of idiopathic pulmonary fibrosis, including repeat infectious workup and auto-antibody testing, was uneventful. The patient was unable to tolerate pulmonary function testing. Bronchoscopy was offered but declined by the patient. Methylprednisolone 1 mg/kg was initiated 63 days after diagnosis, when a chest CT showed substantially increased ground-glass opacities, peripheral reticulation, and traction bronchiectasis. He was trialed on mycophenolate mofetil but was unable to tolerate its adverse effects. He continued on a prolonged taper of corticosteroids and showed clinical improvement, subsequently transitioning to nasal cannula 106 days after diagnosis, on hospital day 50. Chest CTs were obtained 127 and 151 days after diagnosis and showed persistent pulmonary fibrosis and mild progression. He was discharged with 4-L home oxygen.

Figure 2. Flattened curved planar reformat images extracted from high-resolution CT chest images, and high-resolution CT axial chest images, at day 7 (A, D, G), day 66 (B, E, H), and day 151 (C, F, I) after diagnosis demonstrate progressive pulmonary fibrosis. Images A-C show sub-pleural ground-glass opacity and reticulation along a curved plane 1 mm below the posterior lung surface. Images D-F illustrate progressive traction bronchiectasis with an airway-optimized curved plane. Images G-I are standard axial CT images.
by nasal cannula and nighttime biventricular positive airway pressure (BiPAP), which was initiated in the setting of suspected obstructive sleep apnea.

### Discussion

We describe a case of subacute progressive pulmonary fibrosis occurring after mild COVID-19 pneumonia in a patient with no history of pulmonary disease. The patient’s acute phase of illness lasted approximately 2 weeks, requiring only supplemental oxygen by nasal cannula. A subsequent negative SARS-CoV-2 PCR result suggested successful viral clearance, but the patient developed hypoxemic respiratory failure requiring months of ICU-level care. Serial CT studies demonstrated a progressive fibrotic change characterized by traction bronchiectasis and a pattern of usual interstitial pneumonia. Treatment with corticosteroids was associated with an improvement in symptoms, hypoxemia, and trajectory of fibrosis progression on chest CT. This is an unusual case of COVID-19 complicated by progressive lung fibrosis long after clearance of the initial viral insult, and represents an infrequent but important sequela of non-critical COVID-19.

Knowledge of post-acute complications of COVID-19 infection continues to evolve as new clinical data become available. Although the majority of post-COVID-19 pulmonary fibrosis is thought to occur in individuals with COVID-19 requiring mechanical ventilation and diagnosed with ARDS [5], this case highlights the post-acute disease that can occur with less severe acute infection. Long-term outcomes following diagnosis of post-COVID-19 pulmonary fibrosis are not yet reported, but complications such as pneumothorax are already described [10].

With the ongoing pandemic and continued emergence of new SARS-CoV-2 variants, mild cases of COVID-19 are likely to continue for years to come. Development of pulmonary fibrosis in even a small fraction of mild cases could result in a significant global morbidity and mortality burden [11].

The mechanisms underlying SARS-CoV-2-related fibrosis remain unclear. Other coronavirus, such as SARS-CoV-1 and Middle East Respiratory Syndrome-CoV, have been linked to the development of pulmonary fibrosis [12-16]. Proposed mechanisms include viral activation of pro-fibrotic pathways, direct cellular injury, cytokine-induced injury, mechanical injury, likely modified by age, genetic, and metabolic factors, but more research is needed [17,18].

### Conclusions

This case suggests that some patients may be susceptible to significant pulmonary fibrotic changes without prior development of ARDS or requirement for mechanical ventilation during the acute phase of COVID-19. Our patient’s clinical improvement after initiation of corticosteroids raises the possibility that persistent, but potentially reversible, inflammation after clearance of SARS-CoV-2 contributes to fibrosis. This case highlights the importance of further research into the pathophysiologic underpinnings of post-infectious pulmonary fibrosis in COVID-19.

### Acknowledgements

We thank the patient and his family for allowing us to participate in his care and share his case for the greater good.

### Declaration of Figures’ Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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