

CASE REPORT

Follow-up of two cases of suspected interstitial lung disease following severe COVID-19 infection shows persistent changes in imaging and lung function

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Abstract

Physicians are observing persisting symptoms and unexpected organ dysfunction after severe COVID-19. In this report, we present the follow-up of two cases of suspected interstitial lung disease following the viral infection. Up to the last month of follow-up, both patients presented with persistent changes in imaging and pulmonary function tests.

KEYWORDS

computed tomography, COVID-19, DLCO, follow-up, pulmonary function tests

1 | INTRODUCTION

To date, the COVID-19 pandemic has affected nearly every country, with more than 173 million cases and over 3.7 million deaths and counting.¹ The clinical presentation of COVID-19 is often variable, ranging from mild upper respiratory symptoms to severe acute respiratory distress syndrome.² Despite the spectrum of clinical presentation, most patients present with mild-to-moderate

symptoms and eventually recover.³ However, there is evidence of persisting symptoms among patients who had recovered from the previous SARS outbreak.⁴ This past experience may indicate the potential for long-term effects following COVID-19 infection, which may be particularly relevant among patients with severe disease.⁵ In this report, we describe the follow-up of two cases of suspected interstitial lung disease following severe COVID-19 disease.

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2 | CASE REPORT

2.1 | Case 1

A 72-year-old woman presented to the emergency department (E.R) with a weeklong history of malaise, headache, and dry cough. She had been recently experiencing worsening of her symptoms together with chest pain. Her past medical history was notable for osteoporosis, osteoarthritis, and nonallergic rhinitis. Upon physical examination, fine bilateral velcro-like crackles were heard at the lung bases, together with a low oxygen saturation (60% on room air), which prompted her admission. Her laboratory results were remarkable for elevated inflammatory markers and a positive COVID-19 test. A computed tomography (CT) scan of the chest demonstrated peripheral bilateral ground-glass opacities, areas of consolidation, crazy paving, and fibrous interstitial bands (Figure 1A). These findings were consistent with severe COVID-19 pneumonia. She was treated with a combination of dexamethasone (8 mg daily for 10 days), convalescent plasma (600 ml per day for 2 days), and tocilizumab (400 mg per day for 2 days) and discharged 2 weeks later after her arterial blood gases had returned to normal values.

Two days after the patient was discharged home, the family contacted our office through teleconsultation regarding a persistent shortness of breath. Since arterial blood gases were difficult to obtain at home, the patient was monitored through pulse oximetry with an initial SatO₂ of 93%. Low flow oxygen through nasal cannula was initiated and her oxygenation improved to an average of 97%. After 20 days, the oxygen was discontinued. She also underwent home-based pulmonary rehabilitation for 6 weeks which slightly improved her dyspnea. At her follow-up consultation 1 month after discharge, she had persistent dyspnea, fatigue, and dry cough. Pulmonary function tests (PFTs) were ordered which revealed a severe restrictive pattern and significant oxygen desaturation in the 6-min walk test (6-MWT; Table 1). Pulmonary rehabilitation was continued, and prednisone was initiated at 40 mg/day, which was slowly tapered over 4 months. The follow-up at 8 months since discharge was remarkable for persistent dry cough and slight improvement in her dyspnea. Her PFTs remained abnormal (Table 1), and a subsequent CT scan revealed that more than half of the initial opacities had improved. However, interlobular septal thickening and ground-glass opacities persisted (Figure 1B).

2.2 | Case 2

A 60-year woman presented to the E.R with a week-long history of worsening dyspnea, chest pain, and fatigue. Her past medical history was remarkable only

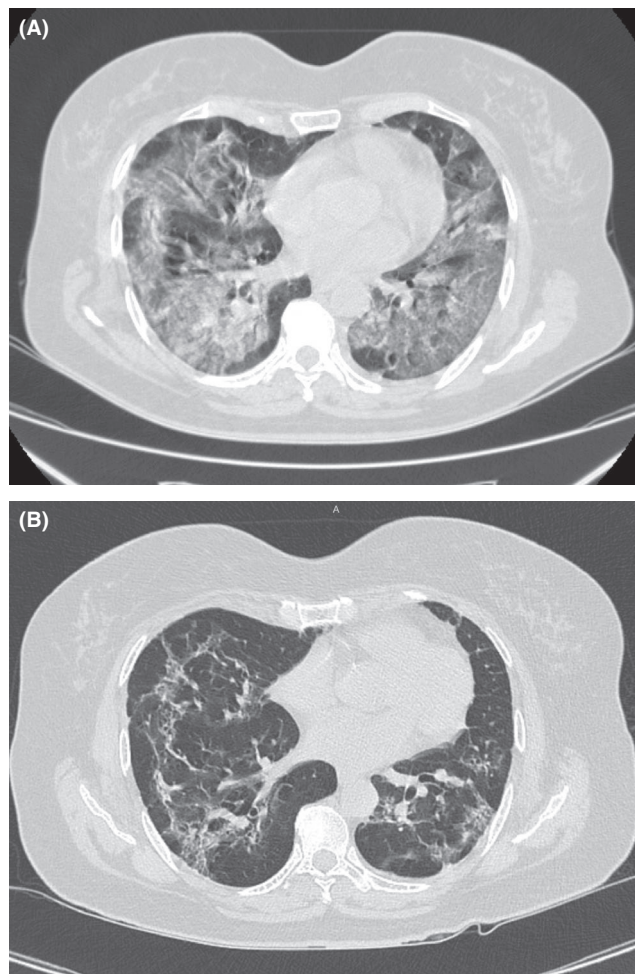


FIGURE 1 A, Initial CT scan of case 1 showing consolidation across both lung bases. B, Follow-up CT after 6 months showing persistent opacities, crazy paving pattern, and traction bronchiectasis

for obesity and a sedentary lifestyle. She had an oxygen saturation of 86% at room air and a respiratory rate of 32/min. Despite the severity of her symptoms, the patient was sent home due to hospital oversaturation, prescribed with symptomatic medication, and advised that a CT scan was needed. Follow-up teleconsultations were conducted to guide her management as best as possible given the circumstances. On her initial CT scan, bilateral ground-glass opacities and consolidations across both lung fields were noticed (Figure 2A). Her laboratory results were consistent with the inflammatory markers seen in severe COVID-19, and a positive PCR test confirmed the diagnosis. She was managed with the help of a registered nurse and received methylprednisolone (250 mg every 24 h for 3 days), followed by prednisone (40 mg for 7 days which was slowly tapered over 3 days), nitazoxanide (500 mg every 8 h for 7 days), colchicine (2 mg loading dose followed by 0.5 mg every 8 h for 12 days), and oxygen through nasal cannula.

TABLE 1 Spirometry, DLCO, and 6-min walk test of the two cases

	Case 1						Case 2					
	2nd mo.		6th mo.		8th mo.		3rd mo.		6th mo.		12th mo.	
	Abs.	Pred.	Abs.	Pred.	Abs.	Pred.	Abs.	Pred.	Abs.	Pred.	Abs.	Pred.
Spirometry												
FEV1/FVC (%)	86.9	115%	81.4	107%	82.9	109%	0.9	111%	81.7	104%	79	105%
FVC (L)	1.08	50%	1.65	82%	1.58	78%	1.1	40%	1.38	52%	1.75	87%
FEV1 (L)	0.94	57%	1.34	90%	1.31	87%	0.9	44%	1.13	54%	1.39	93%
DLCO												
DLCO	5.2	31%	7.8	46%	7.2	43%	8.3	41%	11.7	58%	10.7	63%
TLC sb (L)	1.83	58%	2.47	78%	2.15	68%	2	51%	2.86	72%	2.76	87%
6-MWT												
6-MWD (M)	176	39%	–	–	427	94%	264	55%	359	75%	362	75%
Basal SpO ₂ (%)	94%	N/A	–	–	94%	N/A	93%	N/A	97%	N/A	98%	N/A
Post-ex. SpO ₂ (%)	83%	N/A	–	–	91%	N/A	88%	N/A	96%	N/A	97%	N/A

Abbreviations: 6-MWT, 6-min walk test; DLCO, diffusing capacity of carbon monoxide; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; Post-ex, post expiratory; SpO₂, oxygen saturation; TLC, total lung capacity.

Two weeks later, she presented with marked clinical improvement, which prompted in the discontinuation of medications and oxygen therapy. However, she still reported shortness of breath on exertion and had persistent opacities on her follow-up CT. Due to these findings, the patient was referred for pulmonary rehabilitation and prednisone was initiated, the latter of which was tapered over 4 months. Pulmonary function tests were ordered at subsequent follow-ups and were consistent with a restrictive pattern (Table 1). Also, her diffusing capacity for carbon dioxide (DLCO) remained consistently low until last month of follow-up. On the other hand, the 6-min walk test had slight improvement over time. A CT scan was performed 12 months since the first one was consistent with fibrotic changes across both lung fields (Figure 2A).

3 | DISCUSSION

Although our understanding of the potential long-term effects of COVID-19 might be limited for now, physicians are observing persisting symptoms and unexpected organ dysfunction related to the virus.⁵ A previous study that followed individuals for as long as 9 months after illness found that roughly 30% of patients reported persistent symptoms of which fatigue was the most common. In the same study, authors also found that 29% of patients reported worsened quality of life.⁶ These findings are consistent with existing literature and suggest the possibility of various sequelae among patients who recover.^{7,8}

In addition, new evidence is emerging of changes in the lung function after recovery from COVID-19. A recent systematic review and meta-analysis found that a considerable proportion of post-infection patients had some degree of impairment in their lung function consistent with a restrictive pattern, while the most important parameter affected was the diffusion capacity of the lungs.⁹ Similarly, both of our patients had a restrictive pattern with marked alteration of the DLCO until the 8th and 10th month of follow-up, respectively. Guidelines suggest monitoring patients with severe COVID-19 disease with full PFTs until 12 weeks after discharge.¹⁰ Based on our findings, the alteration in PFTs appears to persist well beyond the suggested timeframe. Whether continued long-term follow-up through PFTs is warranted in selected cases remains to be determined.

Additionally, studies have shown persistent abnormalities in chest imaging following hospital discharge, such as subpleural/peribronchial consolidations, ground-glass opacities, and traction bronchiectasis; these findings may reflect some degree of parenchymal fibrosis which is consistent with the observed changes in the respiratory function.^{11–13} It remains unclear whether these lesions are irreversible since data from long-term follow-up are limited and studies on the subject are still ongoing. In both of our cases, the degree of parenchymal affectation improved over time, but there were some changes that persisted up to the last month of follow-up. Further studies are needed to ascertain the true extent of structural lung changes after COVID-19, and more importantly whether treatment and pulmonary rehabilitation could help in reducing the progression ILD.

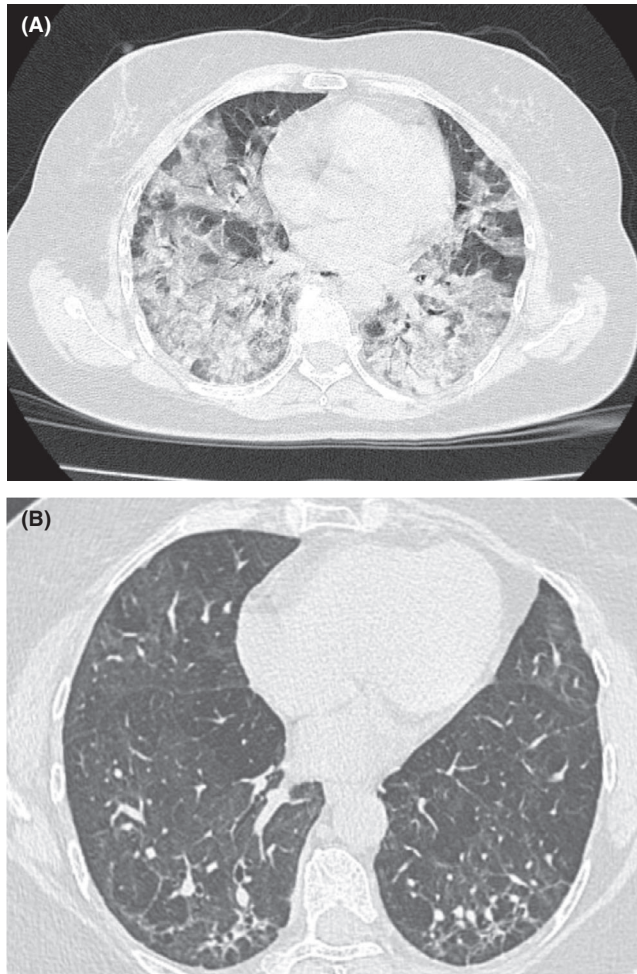


FIGURE 2 A, Initial CT scan of case 2 showing bilateral ground-glass opacities covering most of the lung parenchyma. B, Follow-up CT 12 months later showing marked improvement, with persistence of lesions compatible with interstitial lung disease

To date, there is no specific consensus on how to treat suspected ILD following COVID-19 infection. A previous study suggested that early treatment with corticosteroids was well-tolerated and associated with rapid and significant improvement among patients with persistent inflammatory ILD following COVID-19 infection.¹² Treatment with corticosteroids has been associated with a reduced mortality in the acute setting; however, its role as a therapy for ILD remains unclear. In the case of other agents, antifibrotic therapies may have the potential of preventing patients with severe COVID-19 from developing pulmonary fibrosis and treating those that do occur.² Evidence is limited, but there are some reports on the use of antifibrotic therapies in these patients. A previous case report showed significant clinical improvement in a 78-year-old patient with suspected ILD following severe COVID-19 after 3 months of treatment with nintedanib.¹⁴ Another case-control study analyzing similar patients reported that the nintedanib group had

noticeable improvement in CT volumetry when compared to the control group.¹⁵ These studies offer a cautiously optimistic view on the potential of antifibrotic therapies; however, ongoing clinical trials may soon offer more evidence to justify their use.¹⁶

4 | CONCLUSION

There appear to be persistent abnormalities on pulmonary function tests and imaging following severe COVID-19 disease in some patients. These abnormalities may include a restrictive pattern, a reduced diffusing capacity for carbon monoxide of the lungs, and structural abnormalities compatible with interstitial lung disease.

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CONFLICT OF INTEREST

I declare on behalf of my co-authors and myself that we do not have any conflict of interest to declare related to this work.

AUTHOR CONTRIBUTIONS

ICO, KRV, MFO, and MF developed the research question for the case report. KRV and MFO participated in the data recollection process. KR, MFO, VC, JVC, and MF wrote the final manuscript. All authors read and approved the final version.



CONSENT

Written informed consent was obtained from the patient for the publication of the case report and any accompanying images. A copy of the written consent is available for review by editors if required.

DATA AVAILABILITY STATEMENT

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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