Severe interstitial lung disease persisting 2 years post-COVID-19 despite anti-fibrotic therapy

Sir,

As of January 2022, at least 60 million people were estimated to have developed post-acute sequelae of SARS CoV-2 (PASC) after infection with this virus.[1] As the number of cases continues to increase globally, post-acute sequelae of SARS CoV-2 is likely to remain a major future public health concern. Pulmonary fibrosis can occur as a serious complication of any viral pneumonia, leading to dyspnea and impaired lung function. It significantly affects the quality of life and is associated with increased mortality in severe cases.[2] Of all the post-COVID problems, post-COVID pulmonary fibrosis or Post COVID - Interstitial Lung Disease (PC-ILD) is one of the most serious problems which are tackled by chest physicians across the globe.[3] In this report, we discuss a patient with severe COVID who 2 years after the onset of COVID has persistent, severely restricted lung function, remains breathless and requiring oxygen on the slightest effort, and has a clinical and radiological picture of severe, established fibrotic ILD.

A 55-year-old male, with no prior history of any respiratory symptoms, was admitted in June 2020 with a short history of fever, breathlessness, and desaturation. He was COVID-19 RTPCR positive and was diagnosed to have severe COVID-19 pneumonia with a high-resolution computed tomography (HRCT) showing multiple patchy confluent areas of ground glass opacification bilaterally. He required prolonged admission and needed oxygen support (Non-rebreathing mask at 15 liter/min). In hospital, he received remdesivir, tocilizumab, steroids, and low molecular weight heparin and was discharged home needing 2 liter/min of oxygen after 1 month of hospital stay.

At his first follow-up visit, 2 months after discharge, since the HRCT scan [Figure 1a] showed multifocal patchy confluent areas of opacification with interspersed reticular interstitial fibrotic changes, pirfenidone 600 mg three times daily was started and pulmonary rehabilitation commenced.

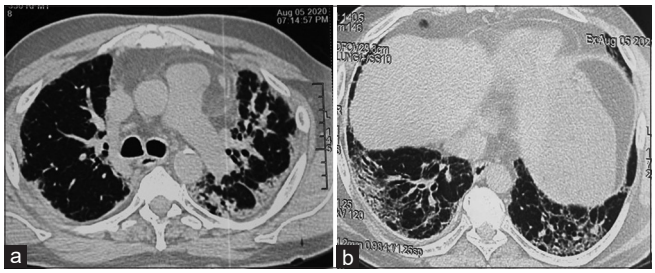

Figure 1: (a) 2 months post-COVID. (b) 2 years follow up

He was followed up at regular intervals at 6, 12, 18, and 24 months post-COVID. At each visit, PFT (pulmonary function test) [Table 1] continued to show severe persistent restriction with desaturation to 83% on a 6-min walk test, while serial computed tomography (CT) scans showed persistent interstitial fibrosis with traction bronchiectasis.

At his recent 2 years post-COVID [Figure 1b] follow-up, his effort capacity has improved marginally, but he still has significant breathlessness on exertion and continues to require oxygen with minimal effort. He is clubbed, has persistent, extensive dry crackles, and his latest HRCT shows the persistence of reticular interstitial fibrosis with traction bronchiectasis, without any improvement over the 2 years of follow-up. His FVC (Forced Vital Capacity) and DLCO (Diffusion Capacity of Lung-Carbon Monoxide) continue to be severely restricted at 46 and 26% of predicted values, respectively. Pirfenidone has been stopped at this stage and he continues to remain on follow-up.

The majority of patients with severe COVID will improve with time.[4] At serial follow-up of such patients, lung shadows resolve leaving a few reticular shadows, and effort tolerance and lung function usually improve over each follow-up visit.[5] Our patient was unusual in that even 2 years post-COVID, he had a picture indistinguishable from advanced fibrotic ILD with clubbing, extensive basal crackles, a severely restricted lung function, and a CT showing persisting fibrotic changes. These changes persisted over four serial follow-up visits without the expected resolution over time that the majority of patients demonstrate post-COVID. Interestingly, these changes occurred despite the patient being on an anti-fibrotic (Pirfenidone) which was started at his initial follow-up visit 2 months post-COVID.

This case is presented to highlight the fact that not all patients with COVID pneumonia resolve over time and persistent fibrosis and established severe ILD may be a long-term sequel in some patients. It emphasizes that careful serial follow-up of all such patients is needed till they reach stable lung function. It also suggests that antifibrotics may not have a specific role and till the results of large trials emerge

Table 1: Shows serial spirometry from 6 months to 2 years post-COVID

Date	FVC	DLCO
6 months follow up	44% (3.51)	27%
1 year follow up	44% (3.51)	27%
2 year follow up	46% (3.49)	26%

their routine use in the anticipation that they will prevent fibrosis may need to be reconsidered. A recent study shed mechanistic insight and suggests pulmonary PASC is driven by inflammatory cytokines produced by activated SARS CoV-2 specific T cells. These patients also demonstrated 6–105 fold increased frequency of interferon-gamma (IFN-γ) and tumor necrosis factor-alpha (TNF-α) producing SARS CoV-2 specific cluster of differentiation-4 (CD4) and CD8 T cells which also co-related with the decline in PFT.[1]

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Submitted: 07-Jul-2022 **Accepted:** 27-Jul-2022

Published: 25-Oct-2022

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Access this article online

Quick Response Code:

Website: www.lungindia.com

DOI: 10.4103/lungindia.lungindia_355_22

How to cite this article: Udwadia ZF, Pawar UP, Nanda VJ. Severe interstitial lung disease persisting 2 years post-COVID-19 despite anti-fibrotic therapy. Lung India. 2022;39:587-8.