

## How should we Prepare for Post-COVID-19 ILD

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### DESCRIPTION

Post-COVID-19 ILD is not a rare pathophysiology. Corticosteroid therapy may improve prolonged respiratory symptoms, hypoxemia, and radiographical abnormalities.

Coronavirus disease 2019 (COVID-19) is a global problem. Globally, there have been more than 300 million confirmed COVID-19 cases and more than 5 million deaths [1]. COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). SARS-CoV-2 is known to cause severe acute pneumonia, while the clinical courses vary.

Post COVID-19 Interstitial Lung Disease (ILD) is considered to be “Long COVID” [2], which is of great interest because it causes patients’ disabilities, and the mechanisms, clinical course, and treatments have not been well elucidated.

Generally, post-COVID-19 ILD is characterized by prolonged radiographical abnormalities such as pulmonary fibrosis (consolidation, irregular reticulation, traction bronchiectasis, etc.). Post infectious organized pneumonia is dominant in post-COVID-19 ILD, although other ILD patterns, such as nonspecific interstitial pneumonia and idiopathic pulmonary fibrosis, have also been reported [3-5].

The mechanism of pulmonary fibrosis after COVID-19 has not been elucidated completely. Nevertheless, it is thought that pulmonary fibrosis secondary to COVID-19 is due to an abnormal repair process after pulmonary cell injury induced by SARS CoV-2. The abnormal repair process is thought to be caused by multiple factors, such as mechanical stress, prolonged exposure to hypoxemia or hyperoxia, thromboembolism, and immunological dysregulation (ex. dysregulation of EGFR, IL-6, and TGF- $\beta$ ). To decrease the risk of post-COVID-19 ILD, we may need to avoid ventilator-associated lung injury, inappropriate supplemental oxygen, and thromboembolism [6,7].

Recently, knowledge of post-COVID-19 ILD has been increasing. Valenzuela et al. reported fibrotic-like changes post-COVID-19 in patients without pre-existing ILD of 25 to 63%, and abnormal radiological changes remained in 24% of patients 12 months later. Additionally, patients with post-COVID-19 ILD show

pulmonary function deficits and remain respiratory symptoms [4].

The respiratory symptoms, radiological changes, and pulmonary function deficits caused by post-COVID-19 ILD could be improved without specific treatments, although the abnormalities may be prolonged in some cases [4,8]. Some studies show the efficacy of corticosteroids, immunosuppressive agents, and anti-inflammatory medicine, although further studies are needed to specify the regimen, duration, and adaptation.

Furthermore, in some cases, post-COVID-19 ILD presents rapidly with re-worsening radiological changes and hypoxemia even during the recovery phase of COVID-19 pneumonia [9].

We report three cases of rapid and progressive post-COVID-19 ILD. The three cases showed pulmonary fibrosis without pre-existing ILD and had high KL-6 levels; these characteristics are similar to idiopathic pneumonia [10].

Although it takes a long time to taper corticosteroids, we could treat them with high-dose corticosteroid therapy, and finally, two patients could withdraw corticosteroids. Other case reports also suggested the effect of corticosteroids for patients with progressive or severe post-COVID-19 ILD.

The dose of corticosteroids varied (prednisolone, 0.5 to 1.0 mg/kg/day), and corticosteroid pulse therapy was performed as initial therapy in some cases [11-13]. In these cases, most patients appeared to be able to finally wean oxygen therapy.

We may consider treating with immunosuppressive therapy proactively for progressive post-COVID-19 ILD. It is an important clinical question as to whether post-COVID-19 ILD is exacerbated after the withdrawal of corticosteroids, such as idiopathic interstitial pneumonia. Further observational studies of post-COVID-19 ILD are needed.

### CONCLUSION

Post-COVID-19 ILD is not a rare pathophysiology. The abnormal radiological changes may disappear without specific treatments. Patients with persisting respiratory symptoms and

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pulmonary function deficits would benefit from the immunosuppressive therapy. Although it is a rare case, we may administer corticosteroids proactively for rapid and progressive post-COVID-19 ILD. Further studies on COVID-19 ILD, especially the biological mechanisms, are needed.

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