Pulmonary Fibrosis Caused by Severe COVID-19 Infection: Discharge May Not Be The End of Treatment

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Since December 2019, COVID-19 caused by SARS-CoV-2 infection has been spread rapidly in the world. Beside acute respiratory distress syndrome found in acute phase of infection, there is also pulmonary fibrosis as a chronic complication due to COVID-19. With the global pandemic of COVID-19, more and more autopsy and puncture histopathological results have been published.[1] Liu et al.[2] reported the world's first case of gross anatomy of COVID-19 in elderly male, suggesting that most of the left lung showed gray-white patchy changes. There was also severe congestion of the right lung, showing dark red patchy. In the marginal area of lung, a large amount of gray-white mucus overflows and fibrotic cords can be seen after incision. Subsequently, Yao et al. reported three cases of puncture pathology. The pathological description was that the alveolar structure was destroyed in varying degrees and a small amount of serous and fibrin exudate were found in the alveolar cavity. The exudative cells are mainly monocytes and macrophages, with a few multinucleated giant cells, lymphocytes, eosinophils and neutrophils. The lymphocytes were mainly CD4 positive T cells. Type II alveolar epithelial cells proliferated significantly and some of these cells exfoliated to the alveolar cavity. There were also focal pulmonary hemorrhage, partial alveolar exudation and pulmonary interstitial fibrosis. Different degree of pulmonary fibrosis was found in pathological examination from all cases.[3]

Several studies have also found that cytokines (mainly transforming growth factor-β [TGF-β], IL-6 and TNF-α) involved in pulmonary fibrosis are increased, which indirectly suggest pulmonary fibrosis as a crucial component in the development of the disease. Up to 15% of COVID-19 patients developed acute respiratory distress syndrome (ARDS), and ARDS itself is one of the most important risk factors for developing of pulmonary fibrosis.[4] The factors mediating for profibrotic response to SARS-CoV-2 virus are not fully known, but from some studies suggest that age, severity of illness, use of mechanical ventilation, smoking and chronic alcoholism may contribute. Furthermore, the mechanisms by which SARS-CoV-2 infection may cause pulmonary fibrosis are also not fully understood. Although ARDS seems to be the main predictor of pulmonary fibrosis in COVID-19, several studies showed that COVID induced ARDS is different from the classical ARDS. Lung CT scan finding in many cases of are also not suggestive for classical ARDS. Therefore, mechanism of pulmonary fibrosis in COVID-19 is different from that of idiopathic pulmonary fibrosis (IPF), especially with pathological findings pointing to alveolar epithelial cells being the site of injury and not the endothelial cells. Most of study suggest that cytokine (especially TGF-β), fibroblast, angiotensin converting enzyme-2, ventilator induced-lung injury (VILI) and oxygen toxicity have an important role for developing of pulmonary fibrosis in COVID-19.[5,6]

The diagnosis of pulmonary fibrosis can be made based on clinical symptoms, radiologic information and history of severe ARDS due to COVID-19. Clinical symptoms of pulmonary fibrosis consisting of dry cough, fatique and dyspnea.[7] Lung CT scan finding from pulmonary fibrosis consisting of parenchymal bands, architectural distorsion and traction bronchiectasis.[8]

Until now there is no specific therapy to handle post-inflammatory pulmonary fibrosis due to COVID-19 infection. Several studies are ongoing to determine an effective treatment for this chronic complication. While ARDS appears to be the main cause of pulmonary fibrosis in COVID-19, the pathogenesis of ARDS caused by SARS-CoV-2 is different from the typical ARDS. Some therapies may be considered for reducing the fibrosis process in lung after COVI-19 infection namely pirfenidone, nintedanib and mesenchymal stem cells.[9-17] Many patients are still recovering spontaneously in the first six weeks after acute COVID-19 infection and do not generally require fast-track entry into a pulmonary rehabilitation programme. However, those who have significantly persistent respiratory illness may need to be supported by pulmonary rehabilitation. Multidisciplinary intervention based on personalized evaluation and treatment which includes exercise training, education and behavioral modification can be given to improve the physical and psychological condition of patients with post-COVID pulmonary fibrosis.[18]

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