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New twist to an old problem: COVID-19 and idiopathic pulmonary fibrosis

Dear Editor

Pandemic of COVID-19 has brought a plethora of challenges throughout the world and has opened exposed gaps in already overburdened stressful health system. One of the most important one is diagnosis and monitoring of chronic lung diseases like idiopathic pulmonary fibrosis (IPF). IPF is the commonest type of idiopathic interstitial pneumonia (IIP) which is a spontaneously occurring progressive diffuse parenchymal lung disease. Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) causing COVID-19 clinically manifests itself as mainly atypical pneumonia. Clinical profile of severe COVID-19 and acute exacerbation of IPF are quite similar as both affect the elderly, those with diabetes, ischemic heart disease or cigarette smoke exposure [1]. They are associated with significant hypoxemia, worsening pattern of diffuse lung involvement on high resolution computed tomography (HRCT).

Due to rapid spread of this pandemic, data regarding impact of COVID-19 on IPF disease is scarce, especially regarding the effect of antifibrotic therapy in this setting. COVID-19 has impacted on all the aspects of IPF, including diagnosis, treatment, and monitoring. Ideal multidisciplinary discussion (MDD) approach to the IPF diagnosis requires now several unique modifications. The goal should be to minimize contact with health care workers and at the same time speed up the diagnosis. In this scenario, artificial intelligence and machine learning can prove to be a boon by identifying the ones fitting the criteria to be screened on priority, coupled with final diagnosis on virtual MDD.

This should be complemented with blood work, preferably in an outpatient lab and quick online appointments. As spirometry (with diffusing capacity for carbon monoxide ($T_{L,CO}$) is the cornerstone of assessing lung physiology in these patients, it can be replaced with an easier alternative, 6-minute walk test. Pulmonary function test (PFT) should be avoided as it's an aerosol generating procedure, and previous dictum of starting anti-fibrotic therapy based on patients' forced vital capacity (FVC) % should be more relaxed now since benefit of these drugs have also been seen across various severities of IPF [2]. Diagnosing the ones with indefinite usual interstitial pneumonia (UIP) pattern in chest HRCT can prove to be the hornets' nest as these are the patients who would additionally require histopathological diagnosis. The usefulness of surgical lung biopsy should be weighed against the risks. Risk factors for adverse outcomes post biopsy are likely to get amplified due to COVID-19 [3]. Moreover, the emergence of nintedanib benefit in any progressive fibrotic interstitial lung disease has simplified the dilemma in the current scenario [4].

Acute exacerbations of IPF can also be virus-triggered, which has to be considered too, amplifying the need of COVID-19 Reverse transcription polymerase chain reaction (RT-PCR) in this setting, as early identification can help in better management of these patients [5]. Antifibrotic drugs, pirfenidone and nintedanib are currently being used for IPF treatment and are shown to

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improve life expectancy and increase time to first exacerbation [6]. Both these drugs per se are not immunosuppressive; hence there is no rationale of stopping them during COVID-19 pandemic for the scare of increased exacerbation risk. In the INPULSIS II study, nintedanib has also shown the benefit of reducing exacerbations incidence. The use of these drugs now is restricted to only non-intubated, as only oral form is available, though inhaled form of pirfenidone is under evaluation [7]. Side effects of these medications have considerable overlap with COVID-19 symptoms (like diarrhea) too, and that can interfere with early diagnosis of COVID-19. Renal and hepatic dysfunction during severe illness of COVID-19 should be considered while continuing antifibrotics. Nintedanib is theoretically associated with increased bleeding risk and can be avoided in severe COVID-19 and concomitant coagulopathy, as these patients may be on full therapeutic anticoagulation [8, 9]. Apart from pharmacological therapy in IPF during this pandemic, physical distancing, routine hygiene measures, smoking cessation and virtual social support means should be advised and encouraged in IPF patients.

Conflict of interest

None declared.

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