Polish Annals of Medicine

Journal homepage: https://www.paom.pl

Case Report

A case of successful treatment of diffuse post-coronavirus pulmonary fibrosis with pirfenidone

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Article info

Article history
Received: February 9, 2023
Accepted: May 7, 2023
Available online: November 17, 2023

Keywords
Pulmonary fibrosis
COVID-19
Severe acute respiratory syndrome
Antifibrotic agents

Doi
https://doi.org/10.29089/paom/165960

Abstract

Introduction: Accumulated evidence suggests that pulmonary fibrosis is a common complication of COVID-19. Fibrotic post-coronavirus lung changes are similar to the changes found in patients with idiopathic pulmonary fibrosis.

Aim: The paper describes the outcomes of pirfenidone usage in treatment of patients with post-coronavirus pulmonary fibrosis.

Case study: The paper presents a case study about a 51-year-old male patient, who had diffuse post-coronavirus pulmonary fibrosis with significant impairment of external respiratory function. The patient had experienced severe COVID-19 bilateral polysegmental pneumonia. In the 3rd week of the disease, multislice computed tomography detected signs of fibrosis that affected 80% of lung tissue. It was decided to start antifibrotic treatment with pirfenidone, which is usually used to treat idiopathic pulmonary fibrosis.

Results and discussion: Pirfenidone was prescribed for 3 months according to the conventional scheme in combination with methylprednisolone. This therapy resulted in significant decrease of fibrosis scope , normalization of respiratory function and improvement of patient's quality of life. A key feature of the presented clinical case is a significant positive effect of pirfenidone in treating coronavirus-associated pulmonary fibrosis, which affected 80% of lung tissue of the patient.

Conclusions: Post-coronavirus pulmonary fibrosis is characterized by the severe oxygen insufficiency and requires a constant oxygen support. The treatment that included pirfenidone in combination with steroids has demonstrated convincing positive effect. It reduces post-coronavirus pulmonary fibrosis and improves lung function.

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1. INTRODUCTION

The coronavirus disease 2019 (COVID-19) was a global pandemic for more than 2 years and it still influences our daily lifestyle.[1,2] COVID-19 infection may cause many complications including pulmonary fibrosis.[2] According to the computed tomography (CT) data, large areas of reduced transparency in the lung tissue are discovered even if patients have relatively moderate forms of the disease.[3] Affected areas may be replaced by connective tissue during the course of the disease, resulting in lung fibrosis formation.[3,4] Patients with coronavirus disease have changes in the lung tissue that are almost identical to the changes observed in patients with idiopathic pulmonary fibrosis. Thus, antifibrotic agent pirfenidone and tyrosine kinase inhibitor nintedanib can be considered for treatment of post-coronavirus pulmonary fibrosis.[5,6] Pirfenidone modulates fibrogenic growth factors, thereby attenuating fibroblast proliferation, myofibroblast differentiation, collagen and fibronectin synthesis as well as deposition of the latter in the extracellular matrix, its effects are mediated predominantly by suppression of transforming growth factor (TGF)-β1 as well as other growth factors.[7,8]

2. AIM

The paper presents the results of the effective use of pirfenidone in treatment of patients with post-coronavirus pulmonary fibrosis.

3. CASE STUDY

A 51-year-old male patient was admitted to the Intensive Care Unit with a diagnosis of COVID-19 complicated by severe bilateral polysegmental pneumonia. Patient was admitted on the 5th day of disease manifestation. Patient's condition worsened sharply, general weakness was growing. Moreover, the patient had shortness of breath, malaise, fever, the temperature of 38.5°C, general weakness, and nausea. The oropharyngeal swab sample tested for SARS-CoV-2 PCR was positive, it was done during hospitalization. Multislice CT (MSCT) revealed bilateral polysegmental pneumonia with up to 70% of lung tissue damage. Patient had the following concomitant diseases: coronary heart disease, hypertension, and diabetes mellitus. There were high marker levels of COVID-19 severity and pro-inflammatory status: serum levels of C-reactive protein (197.85 mg/mL; normal range <6 mg/mL), blood lactate dehydrogenase levels (587.6 U/L; normal range 100–250 U/L), and interleukin (IL)-6 (145 ng/mL, normal range <50 ng/mL). As it was vital to manage cytokine storm in the patient, the following treatment was given: tocilizumab – 800 mg on the 1st day followed by 200 mg on the 2nd day, dexamethasone 8 mg for 14 days, enoxaparin sodium 0.6 mL (6000 anti-Xa IU) daily. Patient was transferred to the pulmonology clinic on the 14th day after admission. At this time, his condition stabilized and SARS-CoV-2 PCR test was negative. Results of the patient's chest MSCT showed the post-coronavirus pulmonary fibrosis that affected 80% of lung tissue. The patient constantly required oxygen support using high flow nasal cannula (HFNC), due to which his oxygen saturation level ranged 90%–93%.

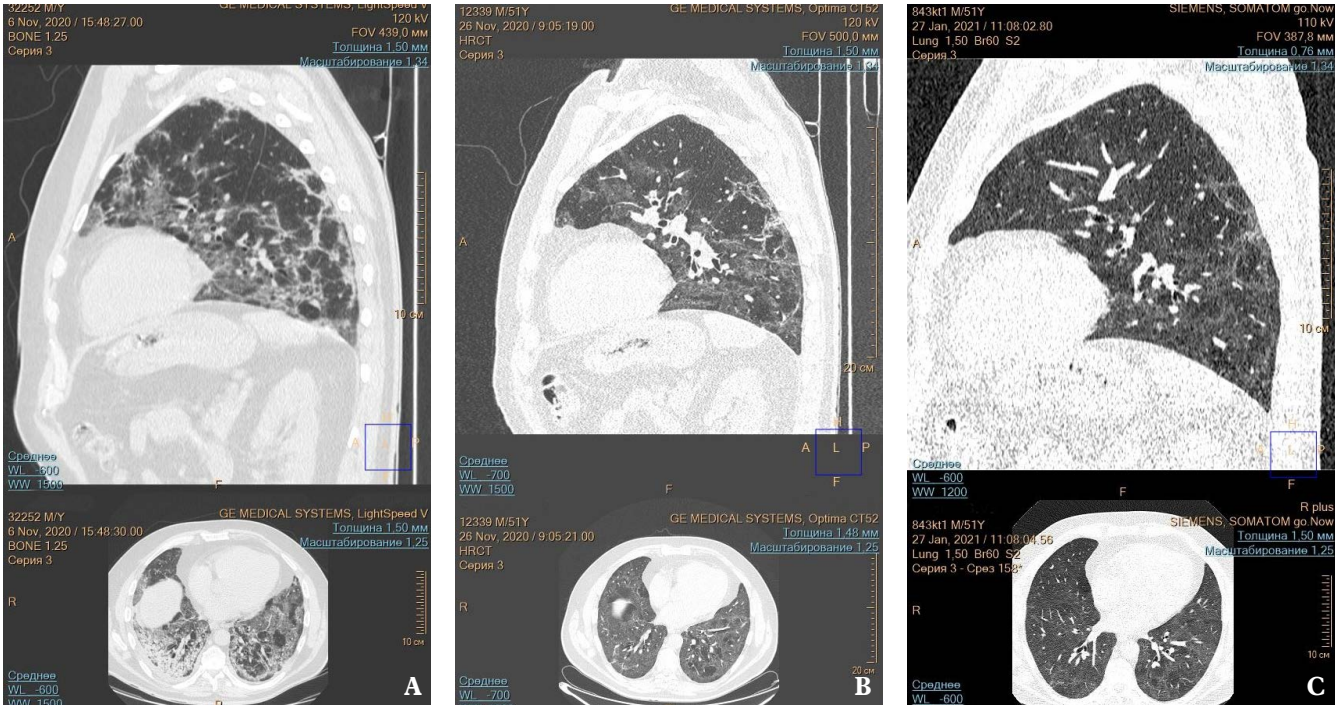

Figure 1. Series of the chest MSCT images illustrate dynamics of lung tissue fibrosis on treatment with pirfenidone and methylprednisolone: (A) before treatment; (B) two weeks after the start of treatment; (C) 2.5 months after the start of treatment.

4. RESULTS AND DISCUSSION

Considering insufficient efficacy of the therapy and pulmonary fibrosis formation, experts decided during Multidisciplinary Team Council to use pirfenidone as antifibrotic agent from the 4th day of patient's stay at the pulmonology clinic with a total duration of 3 month. Methylprednisolone was also prescribed starting with the dosage of 24 mg a day with a gradual decrease to 4 mg a day within 2 months, and pantoprazole was prescribed at the dosage of 40 mg daily.

Figure 1 demonstrates great positive dynamics, as by according to MSCT, with significant reduction in the manifestation of pulmonary fibrosis after 2 weeks of treatment with pirfenidone and methylprednisolone. It should be noted that since that time patient didn't need oxygen support as his oxygen saturation level ranged between 95% and 96%. Hospitalization in pulmonology clinic lasted 20 days.

After 2.5 months of therapy, MSCT images of the patient's lung tissue were close to normal. The dynamics of lung function, which was determined by spiromertry, was impressive (Table 1). The treatment with pirfenidone and steroids improved parameters of vital capacity and forced vital capacity more than twice during 2.5 months.

Pulmonary fibrosis is a frequently reported COVID-19 complication. Apart from the complications mentioned in scientific literature, our patient had many other risk factors of pulmonary fibrosis formation: diabetes mellitus, hypertension, gender (male), age, smoking history. All these factors are crucial for cytokine storm progression.[2,5] The combination of increased inflammatory response, bacterial co-infections, thromboembolic events, microvascular damage, and endothelial dysfunction leads to rapid formation of pulmonary fibrosis in patients after COVID-19.[1] Till now, there is no proven treatment for post-coronavirus pulmonary fibrosis, which causes certain concerns.. However, antifibrotic agents may be used to decrease pulmonary injury in cases with severe COVID-19.[3] Our patient had pulmonary fibrosis that affected 80% of lung tissue, accompanied by cough and dyspnea which meant that he required oxygen support all time. The presence of diabetes mellitus was taken into consideration when pirfenidone was prescribed to that patient instead of the long-term steroid treatment as monotherapy.[10,11] According to results of relevant trials, steroids should be considered as a standard of care for hypoxic patients for no longer than 10 days; moreover, steroids alone do not seem to be sufficient to prevent development of fibrosis.[12] Pirfenidone has demonstrated good effects in patients with idiopathic pulmonary fibrosis, as it inhibits experimental lung injury, IL-1, IL-1B, IL-6, and especially TGF-β levels – the main profibrotic cytokine.[13,14] An increased TGF-β serum concentration is the specific marker of bronchial remodeling and irreversible bronchial obstruction formation in patients with chronic obstructive pulmonary disease and all types of pulmonary fibrosis.[13] That is why we offered this pathogenetic treatment to that patient, and it turned out to be effective, as the patient demonstrated significant decrease of the fibrotic changes in the lungs, normalization of respiratory function and improvement of quality of life.

Table 1. Dynamics of spirometric indicators during the treatment of the patient.

Parameter of external respiratory function	The term of spirometry			
	First examination	2 weeks after	1 month after	2.5 months after
VC, % of predicted value	30	46	51	66
FEV1, % of predicted value	34	51	56	68
FVC, % of predicted value	32	48	52	71

Comments: VC – vital capacity; FEV1 – forced expiratory volume in the first second; FVC – forced vital capacity.

5. CONCLUSIONS

(1) Post-coronavirus pulmonary fibrosis is characterized by the severe oxygen insufficiency and requires a constant oxygen support.
(2) The treatment that included pirfenidone in combination with steroids has demonstrated convincing positive effect. It reduces post-coronavirus pulmonary fibrosis and improves lung function.
(3) It is essential to conduct stringent carefully-planned clinical trials to study the efficacy and safety of pirfenidone in treating patients with post-coronavirus pulmonary fibrosis.

Conflict of interest
None to declare.

Funding
None.

Ethics
The patient was informed that the medicine was labeled and used for idiopathic pulmonary fibrosis treatment only, not for COVID-19-associated one, so before the therapy started, the patient had given his written consent to obtain treatment and prepare the paper manuscript. The decision to prescribe pirfenidone was made by the Multidisciplinary Team Council, and the patient was treated at the specialized clinical center under the robust supervision of specialists and scientists. It must be mentioned that while we were working on the manuscript, the patient's personal data were securely protected in accordance with the rules and regulations of the medical institution.

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