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SARS-CoV-2 lung disease in a patient with pulmonary sarcoidosis — case report

Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the recently identified cause of the current pandemic. In patients with chronic respiratory lung diseases, SARS-CoV-2 may result in significant morbidity and increased mortality. We present a case of a 69-year-old male with stage II pulmonary sarcoidosis who had been under observation for 30 months without immunosuppressive treatment. He then developed severe SARS-CoV-2 disease with typical radiological and laboratory findings. Therapy with oxygen, antibiotics, low-molecular-weight heparin in a prophylactic dose, and dexamethasone resulted in marked clinical improvement. We will discuss the rationale for corticosteroid use in both SARS-CoV-2 disease and in SARS-CoV-2 disease that is complicating comorbid sarcoidosis.

Key words: SARS-CoV-2, sarcoidosis, corticosteroids, anticoagulation, computed tomography

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Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the recently identified cause of the current pandemic. The virus infects type II pneumocytes and endothelial cells via angiotensin converting enzyme (ACE) receptors [1, 2]. SARS-CoV-2 related lung disease has resulted in significant morbidity and mortality worldwide [3]. The risk factors for severe SARS-CoV-2 disease include increasing age and comorbidities, with chronic respiratory diseases being among them [1, 4].

Sarcoidosis is a multi-organ granulomatous disease of unknown aetiology [4]. Respiratory system involvement is observed in 90% of patients and presents as isolated symmetrical hilar lymphadenopathy (stage I), perilymphatic and perivascular nodular infiltrates (stage III), or both (stage II) [5]. In 6% of patients with diagnosed stage II and III of sarcoidosis, lung fibrosis develops (stage IV) [6]. The clinical course of sarcoidosis is difficult to predict in many patients. This is especially true for those who present with stage I seeing as the disease often resolves spontaneously. Thus, treatment should be proposed only to those who present with clear indications such as cardiac sarcoidosis, ocular sarcoidosis, neurosarcoidosis, hypercalcemia, or significant lung involvement with diminished respiratory reserve and decreased exertional capacity [5].

At present, it is not known whether sarcoidosis patients are more prone to SARS-CoV-2 infection and whether immunosuppressive treatment is a risk factor for severe SARS-CoV-2 disease. Therefore, coronavirus infection in sarcoidosis patients is always a diagnostic and therapeutic challenge.

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Table 1. Spirometry, plethysmography, and TLCO results at diagnosis and 30 months post-diagnosis in a 69-year-old male with stage II pulmonary sarcoidosis

Date of plethysmography	TLC [L] (%) SR	VCmax [L] (%) SR	Tiff (%) SR	FEV_1 [L] (%) SR	T_{LCO} mmoL/min/kPA (%) SR
January 2018	7.18 (102) 0.29	4.15 (98)–0.16	0.71 (92)–0.8	2.82 (88)–0.8	6.68 (73)–1.77
September 2020	6.1 (87)–1.26	3.56 (85)–0.97	0.6 (80)–2.07	2.14 (67)–1.96	6,37 (70)–1.89

FEV_1 — forced expiratory volume in one second; T_{LCO} — lung transfer factor for carbon monoxide; TLC — total lung capacity; VCmax — maximal vital capacity

We describe a case of a male with pulmonary sarcoidosis who had a stable course of the disease that did not require treatment during 30 months of observation. This patient presented with sudden disease exacerbation caused by SARS-CoV-2 infection.

Case report

A 69-year-old male diagnosed with pulmonary sarcoidosis (stage II) was admitted on October 22nd, 2020 to the November 2nd, 2020 due to increasing dyspnoea on exertion, non-productive cough, sweating, and marked asthenia of one week duration. He denied experiencing any fevers. This patient's sarcoidosis was previously confirmed by the result of bronchial biopsy in June 2018. The patient was also previously diagnosed with osteoplastic tracheobronchopathy.

For the previous 30 months, he had been observed by pulmonary specialists and did not require any treatment. His last check-up preceding the present episode was in September 2020 and, at the time, his status was stable. During the six-minute walking test (6MWT), he covered 510 meters with no dyspnoea and no desaturation (initial and sixth minute SaO_2 was 97% and 96%, respectively). Spirometry and plethysmography revealed moderate bronchial obstruction [FEV_1/FVC (forced expiratory volume in one second / forced vital capacity) 0.61, FEV_1% pred. 67%, mild lung transfer factor for carbon monoxide (T_{LCO}) decrease to 70% pred.). Lung volumes remained within normal limits [total lung capacity (TLC) — 87% pred., maximal vital capacity (VCmax) — 85% pred.]. The results of plethysmography were comparable to those obtained at diagnosis. However, spirometry revealed moderate bronchial obstruction which was not seen at diagnosis (Table 1).

A chest X-ray performed in September 2020 revealed bilateral, nodular, and patchy parenchymal infiltrates predominantly in the perihilar and middle lung zones, as well as symmetrical hilar lymphadenopathy (Figure 1A).

Chest computed tomography (CT) performed in June 2020 revealed the presence of ill-defined perivascular nodules localized in the middle and lower parts of the lungs with perihilar areas of consolidation (Figures 2A, B) and bilateral hilar lymphadenopathy (Figures 3A, B).

On admission to the hospital, the patient remained in poor condition with profound dyspnoea on exertion. His vitals were as follows: body temperature — 36°C, heart rate — 103 beats/min, respiratory rate — 20 breaths/min, arterial blood pressure — 137/86, and arterial oxygen saturation — 89–91% while breathing room air. On auscultation, diffuse fine crackles and wheezes were noted over both lung fields.

Laboratory analysis revealed a D-dimer concentration of 1600 ng/mL (N — 500 ng/mL), C-reactive protein (CRP) — 49 mg/dL (N — 5 mg/dL), aspartate aminotransferase (AST) — 61 U/L (N — 40 U/L), lactate dehydrogenase (LDH) — 600 U/L (N — 480 U/L), white blood cells (WBC) — 7.81×10^9/L, neutrophils 6.18×10^9/L, lymphocytes 0.8×10^9/L, red blood cells (RBC) — $4{,}76 \times 10^{12}$/L, Hgb — 14,3 g/dL, and platelets (PLT) — 382×10^9/L. The results of arterialised capillary blood gas analysis were as follows: PaO_2 — 58 mm Hg, $PaCO_2$ — 29 mm Hg, and pH — 7,46. The Legionella antigen in urine was negative. A nasopharyngeal swab for SARS-CoV-2 by RT-PCR was negative.

A chest X-ray revealed the presence of new, bilateral consolidations in the middle and lower lung zones (Figure 1B).

Chest CT angiography ruled out pulmonary embolism but revealed the presence of diffuse ground-glass opacities localized mainly in the middle and lower parts of the lungs. These changes were superimposed on previously seen interstitial lung disease and lymphadenopathy (Figures 2C, D and Figures 3C, D). The radio-

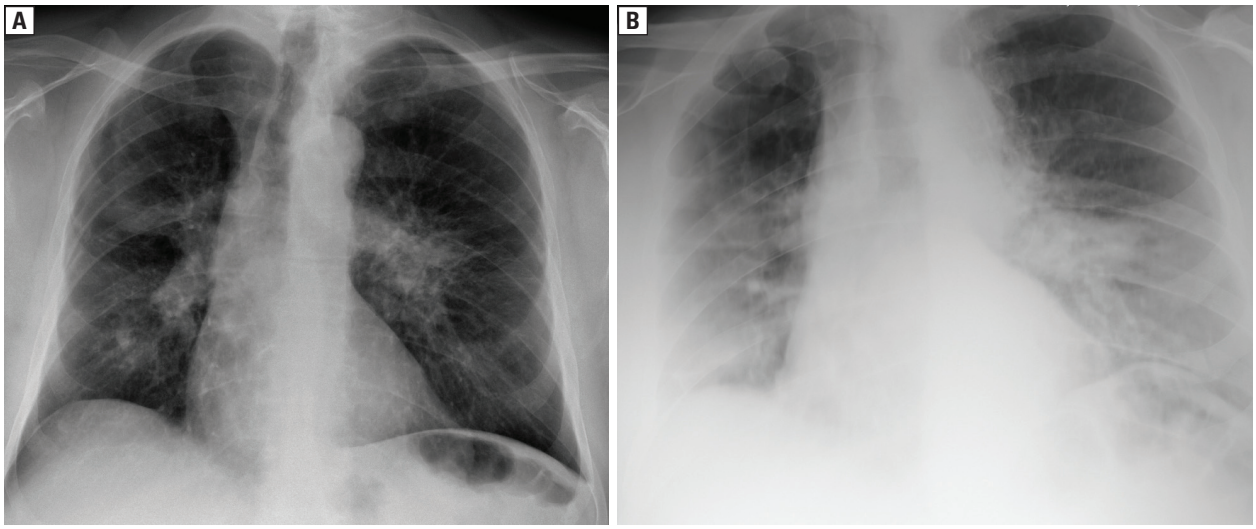

Figure 1A. Posterior-anterior chest radiography before SARS-CoV-2 infection. Bilateral, predominantly perihilar and middle zones nodular and patchy parenchymal infiltrates. Symmetrical hilar lymphadenopathy. **B.** Posterior-anterior chest radiography during SARS-CoV-2 infection. New, bilateral ground-glass consolidations in the middle and lower zones of lungs

logical appearance was suggestive of SARS-CoV-2 infection.

Repeated SARS-CoV-2 RT-PCR (on the third day of hospitalisation) was positive.

The patient was treated with oxygen at 1,5 L/min administered by nasal cannula, low molecular weight heparin (LMWH) in a prophylactic dose (enoxaparin 40 mg/day SC), ceftriaxone 2 g/day IV, levofloxacin 2 × 500 mg/day PO, and dexamethasone 6 mg/day IV. The symptoms gradually diminished. After 10 days of treatment, the patient was released home. The patient's last blood gas analysis performed without oxygen therapy was: PaO_2 — 70 mm Hg, $PaCO_2$ — 36 mm Hg, pH — 7.45, and SaO_2 — 95%. The patient was instructed to continue taking levofloxacin (up to 14 days) and to gradually decrease the dose of dexamethasone.

Discussion

Acute exacerbations of pulmonary sarcoidosis may be caused by infective as well as non-infective factors [7]. Baughman and Lower documented 2–3 acute exacerbations per year in 17% of patients with fibrotic sarcoidosis [8]. As the majority of them had been treated with immunosuppressive therapy, most exacerbations were of an infective origin [8].

In the presented patient, the aetiology of his exacerbation was less clear as he did not receive immunosuppressive treatment and was stable during the previous two years of observation. Furthermore, he complained of increasing dyspnoea, non-productive cough, and asthenia, but with no increase in body temperature. Nevertheless, in the era of the SARS-CoV-2 pandemic, the cause of the exacerbation was most likely to be of an infective origin.

Chest X-ray revealed new infiltrates and chest CT images confirmed the presence of new ground-glass opacities suggestive of SARS-CoV-2 infection.

Recent publications have documented the radiological appearance of SARS-CoV-2 related pulmonary disease [9]. Most often, multiple foci of ground-glass opacities, with or without consolidations, are seen on chest CT images [9–11]. They are distributed in either a peripheral subpleural location or both peripherally and centrally, with a predisposition to the lower lobes [9–11]. In addition, small and widened vessels are often found within the opacities. Other radiological findings such as crazy-paving patterns, interlobular septal thickening, or air-bronchograms, are less frequent [9–11].

The other type of SARS-CoV-2 related lung pathology is thromboembolic disease which, in most cases, is caused by in situ vascular thrombosis [2]. Piazza *et al.* diagnosed venous thromboembolic disease (VTE) despite thromboprophylaxis use in 35% of SARS-CoV-2 patients treated in the ICU [12]. Therefore, CT pulmonary angiogram should be regarded as the procedure of choice in SARS-CoV-2 lung disease because it enables the visualization of both pulmonary vessels and lung parenchyma.

In the presented patient, pulmonary CT angiography ruled out pulmonary embolism. Howev-

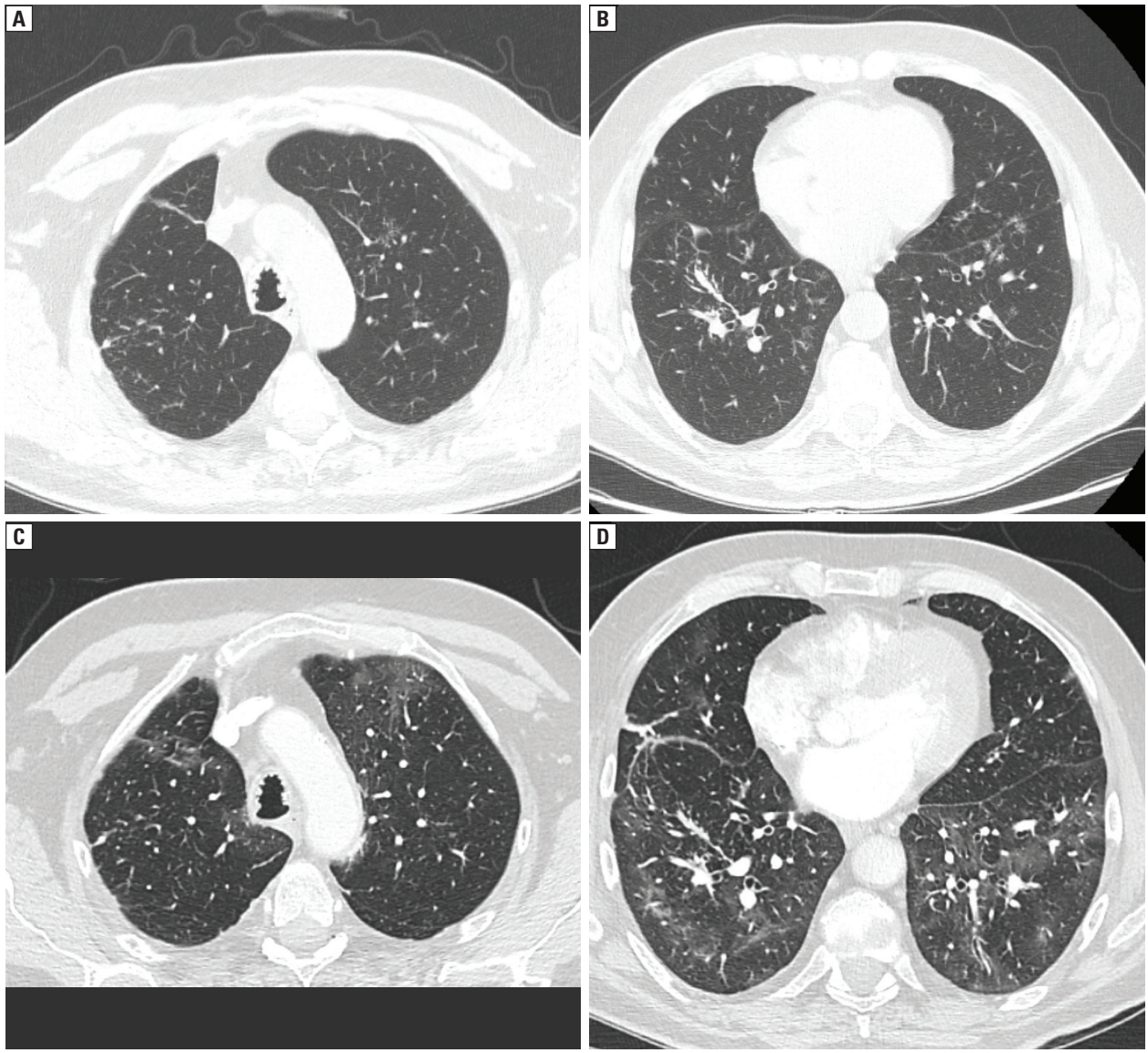

Figure 2. A, B. Axial computed tomography (CT) scans before SARS-CoV-2 infection, lung window. CT images show ill-defined nodules with characteristic perilymphatic distribution. **C, D.** Axial CT scans during SARS-CoV-2 infection, lung window. Comparing to the previous examination, CT images show the presence of diffuse ground-glass opacities

er, it revealed the presence of diffuse ground-glass opacities localized mainly in the middle and lower parts of the lungs. These changes were superimposed on the patient's previously described interstitial lung disease and lymphadenopathy that arose during the course of sarcoidosis.

It is important to differentiate SARS-CoV-2 lung CT findings from other infectious diseases. Bacterial pneumonia produces focal segmental or lobar pulmonary opacities without lower lung predominance, as is seen in the case of SARS-CoV-2 [10, 11].

Viral infections caused by the influenza virus, CMV, and other coronaviruses may show the same radiological features as SARS-CoV-2. Therefore, CT findings alone are not sufficient for a definitive diagnosis of SARS-CoV-2. It is necessary to combine CT scans with epidemiological history, clinical symptoms, and laboratory tests' results.

Increased CRP, D-dimer, and LDH combined with a normal WBC count and a decreased number of lymphocytes were suggestive of SAR-CoV-2 infection in the presented patient. The confirmation of SARS-CoV-2 disease was obtained by the second RT-PCR test performed on the third day of hospitalization.

The patient received therapy according to current recommendations of the Polish Association of Epidemiologists and Infectious Disease Specialists [13]. Such therapy should be com-

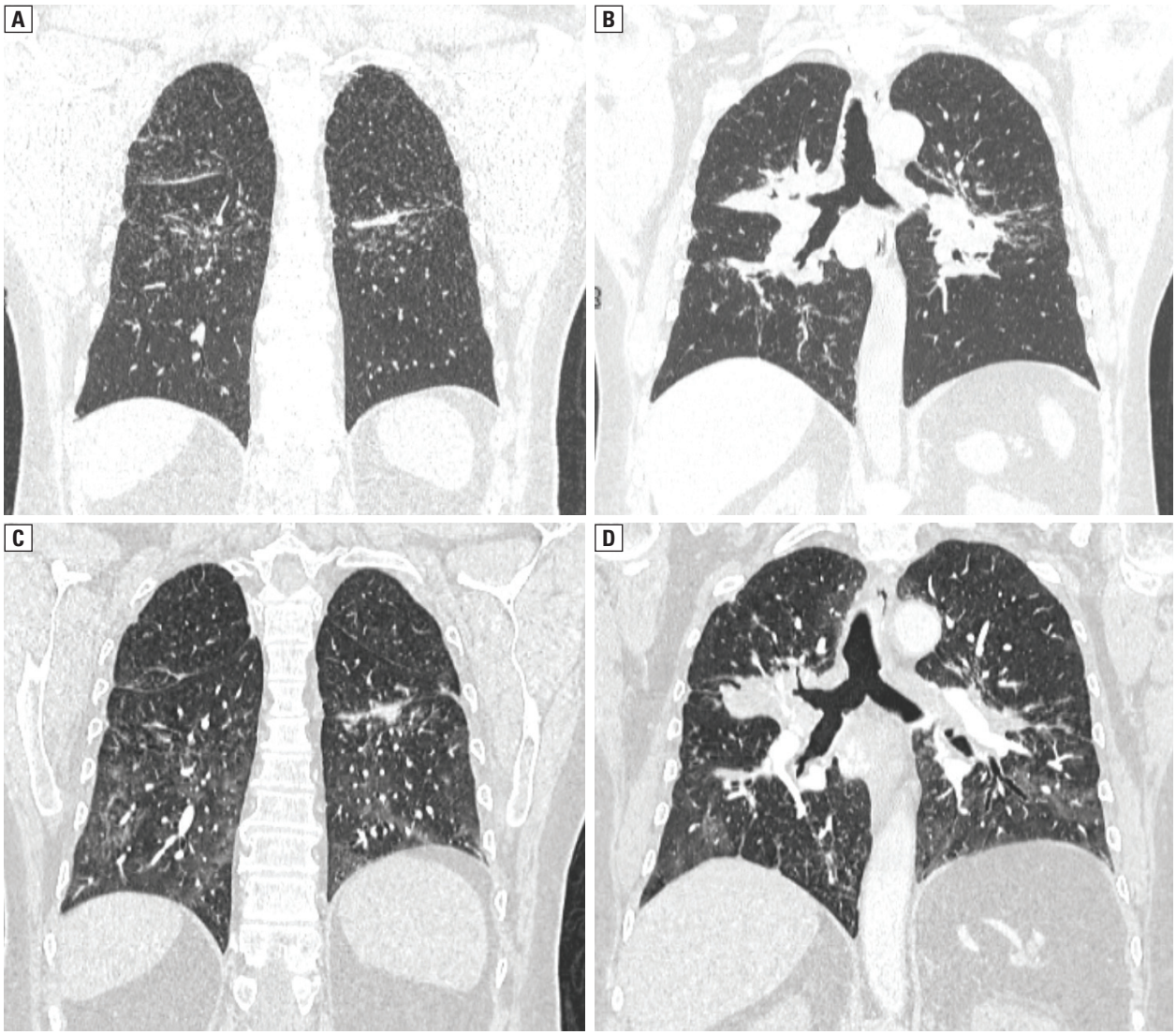

Figure 3. A, B. Coronal reformatted CT images before SARS-CoV-2 infection, lung window. Ill defined nodules and perihilar areas of consolidation. Bilateral hilar lymphadenopathy. **C, D**. Coronal reformatted CT scans during SARS-CoV-2 infection, lung window. Diffuse ground -glass opacities mainly in the middle and lower parts of lungs, superimposed on previously seen interstitial lung disease

posed of oxygen via nasal cannula or ventilation mask, depending on the degree of hypoxemia. In addition, corticosteroids (dexamethasone), antibiotics, and LMWH in a prophylactic or therapeutic dose are recommended [13]. Taccone et al. documented that a high-dose regimen of thromboprophylaxis therapy may decrease the occurrence of venous thromboembolic disease in critically ill SARS-CoV-2 patients [14]. We used LMWH in a prophylactic dose due to previous exclusion of pulmonary embolism and prompt clinical improvement.

The use of corticosteroids (CS) in SARS-CoV-2 lung disease is the most controversial issue in terms of pharmacological therapy. According to Polish guidelines, CS are recommended in standard doses (prednisone 0.5–1 mg/kg body mass per day) in patients with respiratory insufficiency in whom SaO_2 drops below 90% [13]. The first-line CS is dexamethasone, used in an average dose of 8 mg/day. A recent study by Monreal et al. showed that larger doses of CS (≥ 250 mg of methylprednisolone/day) were associated with higher mortality compared to standard doses (up to 1.5 mg/kg/day). It is important to note that the increase in mortality due to higher doses of CS was observed only in elderly patients [15].

According to Polish recommendations, higher doses of CS may be considered in patients who present with a cytokine storm. The preferred treatment in the event of a cytokine storm is an anti-IL 6 drug named tocilizumab [13].

A recently published meta-analysis documented that CS improve life expectancy in severe

SARS-CoV-2 disease but may be harmful for patients who present with mild symptoms [16].

In sarcoidosis complicated by SARS-CoV-2 infection, clinical improvement and viral relapse has been documented after CS treatment [17]. At present, in sarcoidosis patients, the expert guidelines state that CS should be reduced to the minimal effective dose during the coronavirus pandemic to minimize the risk of infection [18]. Nevertheless, in those patients who are already infected with SARS-CoV-2, CS are not harmful and may even be beneficial [3, 17].

In our patient, prompt clinical improvement was observed with no need for further oxygen therapy. He was discharged home and advised to slowly reduce his corticosteroid dose under the supervision of the outpatient clinic.

Sarcoidosis patients infected with SARS-CoV-2 may have a more severe clinical course of viral disease compared to the general population. Jeny et al. documented that among hospitalized patients with sarcoidosis and SARS-CoV-2 disease, 36% required intensive care support. This is in stark contrast to the 5–10% of the general population that required the same type of support [3]. It is suggested that sarcoidosis patients who present with moderate to severe impairment in pulmonary function have an increased mortality rate due to SARS-CoV-2 infection [1, 4].

Thus, high awareness among pulmonary specialists is needed to consider timely hospitalisation and treatment of sarcoidosis patients infected with SARS-CoV-2, especially those who present with lung function impairment and/or multiple comorbidities.

Conflict of interest

None declared.

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