

Correspondence on 'Glucocorticoid-induced relapse of COVID-19 in a patient with sarcoidosis'

Patients with interstitial lung disease have been considered at high risk of complications of COVID-19 because of their underlying lung disease and use of immunosuppressive agents.¹ However, data on COVID-19 in patients with sarcoidosis are scarce.²⁻⁴ Several reasons for an increased risk of severe forms of COVID-19 among sarcoidosis patients have been hypothesised: the involvement of the lung in almost 90% of patients with COVID-19, some of whom have reduced pulmonary function and comorbidities such as diabetes or hypertension, which are largely associated with the use of glucocorticosteroids for treating sarcoidosis; and the use of immunosuppressive agents in a subset of these patients.⁵ Recently, Gyorfı *et al*⁶ described the case of a patient with sarcoidosis who experienced a symptomatic SARS-CoV-2 infection with spontaneous clinical improvement, and a virological relapse after steroids treatment. This case illustrated the fact that immunosuppression with glucocorticoids may induce relapse of COVID-19 in patients with sarcoidosis. However, we lack data on the outcomes of patients with sarcoidosis affected by COVID-19. We retrospectively collected data for all patients with sarcoidosis and SARS-CoV-2 infection seen among 15 French centres between 1 March and 20 May 2020. The inclusion criteria were a sarcoidosis diagnosis based on the American Thoracic Society/European Respiratory Society/World Association for Sarcoidosis and other granulomatous diseases criteria⁷ and SARS-CoV-2 infection based on at least one of the following: nasopharyngeal or tracheal swab reverse transcription (RT)-PCR positive for SARS-CoV-2; SARS-CoV-2-positive serology; or typical clinical and radiological findings.

Thirty-six patients were included. Among them, 34 patients had a confirmed SARS-CoV-2 infection: 3 were not tested with SARS-CoV-2 RT-PCR but had positive serology; 31 were tested with SARS-CoV-2 RT-PCR, which was positive in 29 patients. The two remaining patients had typical clinical and radiological findings despite negative RT-PCR results and were admitted to the hospital, with one patient being admitted to the intensive care unit (ICU). These two patients were not tested with serology. The demographic data and clinical features of the patients are detailed in table 1. Among the patients, 33% had lung fibrosis. The presenting symptoms of COVID-19 were classical and included fever in most of the patients (67%), despite the use of glucocorticosteroids. Twenty-five (69%) patients were receiving long-term treatment with glucocorticosteroids at the time of COVID-19 diagnosis. The steroids were stopped in only one patient at the time of COVID-19 diagnosis (this patient initially received a daily dose of 7.5 mg). The daily dose of steroids was increased in five patients because of COVID-19 diagnosis. Corticosteroids were introduced in two patients who did not previously receive this treatment for sarcoidosis. In comparison with steroids, methotrexate was more frequently stopped at the time of COVID-19 diagnosis, in 4/8 (50%) patients. Among the six patients under tumour necrosis factor (TNF)-alpha antagonist treatment, the treatment was temporarily suspended in all. All patients were admitted to ICUs when needed.

Five patients died during the SARS-CoV-2 infection: four patients died from acute respiratory failure due to SARS-CoV-2 infection. Of note, two patients had chronic renal failure, one

Table 1 Demographic and clinical characteristics and outcomes of 36 patients with sarcoidosis and COVID-19

Characteristics	All (n=36) n (%)	Admitted in ICU (n=13) n (%)	Not admitted in ICU (n=23) n (%)
Age at sarcoidosis diagnosis (years), median (range)	38.5 (21-74)	39 (30-61)	38 (21-74)
Age at COVID-19 diagnosis (years), median (range)	54.5 (26-100)	55 (36-100)	51 (26-90)
Sex (female/male)	10/26	03/10/20	7/16
BMI, kg/m ² , median (range)	26.4 (12.6-38.4)	25.0 (12.6-38.4)	26.1 (19.5-35.2)
Active smoker	4 (11)	2 (15)	2 (9)
Past smoker	9 (25)	4 (31)	5 (22)
Overweight	13 (36)	3 (23)	10 (43)
Obesity	7 (19)	3 (23)	4 (17)
Chronic comorbidities			
COPD	2 (6)	1 (8)	1 (4)
Diabetes	12 (33)	8 (62)	4 (17)
With insulin	5 (14)	4 (31)	1 (4)
Hypertension	14 (39)	6 (46)	8 (35)
Malignant tumour	2 (6)	1 (8)	1 (4)
Chronic kidney disease	5 (14)	3 (23)	2 (9)
Dialysis	1 (3)	1 (8)	0
Cardiovascular disease	3 (8)	2 (15)	1 (4)
ACE inhibitor or ARB	3 (8)	0	3 (13)
History of thrombosis	1 (3)	1 (8)	0
Organ transplantation	2 (6)	0	2 (9)
Sarcoidosis involvement			
Pulmonary	35 (97)	13 (100)	22 (96)
Intrathoracic lymph nodes	32 (89)	11 (85)	21 (91)
ILD	26 (72)	10 (77)	16 (70)
Lung fibrosis	12 (33)	5 (38)	7 (30)
Skin	6 (17)	2 (15)	4 (17)
Peripheral lymph nodes	5 (14)	2 (15)	3 (13)
Liver	7 (19)	5 (38)	2 (9)
Heart	4 (11)	2 (15)	2 (9)
CNS	7 (19)	3 (23)	4 (17)
PNS	3 (8)	2 (15)	1 (4)
Kidney	3 (8)	2 (15)	1 (4)
Löfgren syndrome	1 (3)	0	1 (4)
Treatments at the time of COVID-19			
Corticosteroids	25 (69)	11 (85)	14 (61)
Daily dose, median (range)	7.8 (5-50)	7.5 (5-50)	8 (5-35)
Hydroxychloroquine	3 (8)	0	3 (13)
Methotrexate*	8 (22)	4 (31)	4 (17)
MMF*	3 (8)	1 (8)	2 (9)
Azathioprine*	3 (8)	1 (8)	2 (9)
TNF-alpha antagonist*	6 (17)	1 (8)	5 (22)
Signs and symptoms at diagnosis			
Fever	24 (67)	12 (92)	12 (52)
Cough	29 (81)	11 (85)	18 (78)
Shortness of breath	24 (67)	11 (85)	13 (57)
Anosmia	9 (25)	0	9 (39)
Dysgeusia	7 (19)	0	7 (30)
Diarrhoea, nausea or vomiting	10 (28)	2 (15)	8 (35)
RT-PCR positive	31/33 (94)	12/13 (92)	19/20 (95)
Serology positive	3/3 (100)	0/0 (0)	3/3 (100)
Chest CT findings: extension of GGO and/or consolidation			
Chest CT performed	27 (75)	11 (85)	16 (70)
None	0 (0)	0	0
Minor	5 (19)	0	5 (22)
Moderate	9 (33)	5 (45)	4 (17)

Continued

Table 1 Continued

Characteristics	All (n=36) n (%)	Admitted in ICU (n=13) n (%)	Not admitted in ICU (n=23) n (%)
Severe	11 (41)	5 (45)	6 (23)
Missing data	1 (4)	1 (9)	0 (0)
Treatments for COVID-19			
Antiviral	4 (11)	4 (31)	0
Hydroxychloroquine	5 (14)	3 (23)	2 (9)
Steroids	7 (19)	4 (31)	3 (13)
Management			
Admission to hospital	28 (78)	13 (100)	15 (65)
Admission in ICU	13 (36)	13 (100)	0
Mechanical ventilation	4 (11)	4 (31)	0
Outcomes			
Deaths	5 (14)	4 (31)	1 (4)
Thrombosis	3 (8)	2 (15)	1 (4)
Acute kidney injury	3 (8)	2 (15)	1 (4)
Bacterial infection	5 (14)	3 (23)	2 (9)

*All patients with methotrexate, MMF, azathioprine and/or TNF-alpha antagonists also received corticosteroids.

ARB, angiotensin receptor blockade; BMI, body mass index; CNS, central nervous system; COPD, chronic obstructive pulmonary disease; GGO, ground glass opacity; ICU, intensive care unit; ILD, interstitial lung disease; MMF, mycophenolate mofetil; PNS, peripheral nervous system; RT, reverse transcription; TNF, tumour necrosis factor.

was undergoing haemodialysis and the last patient had an acute kidney injury complicating the chronic renal disease and required renal replacement therapy during the COVID-19 course. One patient also had an active thromboembolic disease. The fifth patient, who was receiving a TNF-alpha antagonist treatment for sarcoidosis, died from acute and uncontrollable hypercapnia in the context of chronic obstructive pulmonary disease and obesity. Thirteen patients (36%) were admitted in ICU (table 1). The admission in ICU was always possible, when decided by the treating physician.

Our findings support previous data obtained on COVID-19 in autoimmune diseases.^{8,9} Although it is estimated that 15%–20% of people infected with COVID-19 develop severe pneumonia and that 5%–10% require critical care in the general population, we found a higher percentage of patients requiring intensive care support (36%) among the sarcoidosis population, probably because the study population was recruited from hospital-based centres. The percentage of patients with lung fibrosis was similar in patients admitted in ICU and those who were not.

The role of immunosuppressive agents in the course and severity of COVID-19 is still debated.¹⁰ Our results share similarities with those of previous studies about COVID-19 in patients with immune-mediated inflammatory diseases.^{11–13} In a previous study, the use of oral glucocorticosteroids and methotrexate was higher among patients for whom hospitalisation was warranted.¹¹ We found that TNF-alpha antagonist treatment was not associated with more severe forms of the disease, even if this should be considered with caution in this small sample. This is in accordance with the results of previous studies that supported the safety of chronic use of TNF-alpha antagonist treatment.^{9,11}

With this study of 36 patients with sarcoidosis and COVID-19 from a French multicenter registry, we provide a better understanding of the implications of COVID-19 in the sarcoidosis population.

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Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval This study was approved by the ethics committee 'Comité d'éthique de la recherche de Sorbonne Université' and was conducted in accordance with the Declaration of Helsinki.

Provenance and peer review Not commissioned; internally peer reviewed.

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To cite Jeny F, Lhote R, Lorillon G, et al. *Ann Rheum Dis* 2022;**81**:e241.

Received 23 August 2020

Accepted 26 August 2020

Published Online First 1 October 2020



► <https://doi.org/10.1136/annrheumdis-2020-218983>

Ann Rheum Dis 2022;**81**:e241. doi:10.1136/annrheumdis-2020-218957

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