Sarcoidosis and COVID-19: a research letter unveiling our insights

Sirs,

In response to the investigation entitled "Prevalence and Clinical Features of COVID-19 in a Robust Cohort of 199 Sarcoidosis Patients", we present a research letter that looks into the intricate interrelation of these conditions (1).

Sarcoidosis, characterised by granulomatous inflammation of enigmatic origin, primarily targets intrathoracic lymph nodes and lungs while extending its reach to diverse anatomical domains, encompassing ophthalmologic, cardiovascular, cutaneous, musculoskeletal, and extrathoracic lymph nodes, among others. Conversely, COVID-19, an RNA viral infection within the Coronaviridae family, leverages the spike protein to engage ACE 2 receptors on pneumocytes (2). However, both conditions prominently involve Th1 cells and share pivotal inflammatory mediators such as IFN-γ and TNF-α (3, 4). Therefore, noteworthy parallels exist, suggesting that anti-inflammatory modalities targeting one disorder may exert some effects on the trajectory of the other. Therapeutic regimens for sarcoidosis commonly entail immunosuppressants, including glucocorticoids and biologics, while the administration of glucocorticoids during concurrent COVID-19 infection may potentially exacerbate the patient's condition (5).

Despite the generally favourable prognosis of sarcoidosis, with spontaneous remission observed in approximately 60% of cases, a minority (less than 20%) necessitate systemic immunosuppression, thereby heightening the susceptibility to infections. Currently, there is insufficient evidence to affirm that sarcoidosis contributes to an elevated morbidity or severe course of COVID-19.

This study represents a single-institution, retrospective analysis encompassing patients registered in the Outpatient Clinic of the Department of Pneumology at the Medical University of Lodz. Given the prevailing circumstances of the COVID-19 pandemic, most patient visits were conducted through teleconsultations. The primary objective of this investigation is to provide a comprehensive summary of these teleconsultations, specifically focusing on the morbidity of COVID-19 within the sarcoidosis population. During teleconsultations, patients were routinely surveyed to elicit comprehensive data on the manifestations of sarcoidosis, including symptoms, therapeutic interventions, disease activity, comorbidities, smoking history, COVID-19 vaccination status, and extrapulmonary presentations.

Among the 177 patients registered in the Outpatient Clinic, 72 individuals were uncontactable, and 105 successfully underwent teleconsultation. Extrapulmonary manifestations of sarcoidosis encompassed cardiac (4.77%), ophthalmic (4.77%), neural (2.86%), and cutaneous (6.67%) presentations. Noteworthy symptoms observed in COVID-infected individuals comprised diarrhoea (13.33%), headache (59.09%), chest pain (31.11%), conjunctivitis (8.89%), myalgia (64.44%), fatigue (82.22%), anosmia/ageusia (57.78%), rash (11.36%), dyspnea (33.33%), fever (71.11%), and cough (58.7%).

Pulmonary function tests (PFT), obtained within the last available, but not older than 12 months prior to the teleconsultation, were successfully conducted on 72 out of the 105 enrolled patients. Certain factors were identified that may contribute to an elevated risk of COVID-19 morbidity. Our analysis indicated that body mass index (BMI) exerted no significant influence (p=0.55). Spirometry results revealed that individuals with reduced TLCO% exhibited an increased susceptibility to COVID-19 infection (p=0.003), as well as a trend for diminished FVC% (p=0.08) and FEV1% (p=0.08) was observed.

Immunosuppression did not appear to impact COVID-19 susceptibility. Patients undergoing continuous glucocorticosteroid (GCS) therapy (p=0.59) and ongoing non-GCS immunosuppression (p=1.0), as well as those with a history of GCS therapy (p=0.16) and past non-GCS immunosuppression (p=1.0), did not exhibit an increased propensity for COVID-19 morbidity. Within our study cohort, we did not identify a statistically significant association between vaccination status and susceptibility to COVID-19 (p=0.34). Nevertheless, an observable trend emerged, indicating a potential correlation between a higher number of vaccine doses and a reduced incidence of SARS-CoV-2 infections (p=0.06).

Within our cohort, only two patients necessitated hospitalisation, with no recorded fatalities.

Table I presents the differential clinical characteristics between sarcoidosis patients with COVID-19 and those without.

Our research unveils significant clinical implications, shedding light on a potential correlation between reduced TLCO% and heightened vulnerability to COVID-19. Notably, Desbois *et al*. (1) also observed lower TLCO% values in COVID-19 patients, although they did not provide the results of statistical inference for this result. Moreover, our analysis suggests that immunosuppressive treatment in sarcoidosis patients does not seem to affect susceptibility to COVID-19. This aligns with the findings of Desbois *et al*., which similarly found no apparent link between immunosuppressant usage and symptomatic COVID-19 (1).

In conclusion, our study reveals a potential link between heightened COVID-19 susceptibility and sarcoidosis severity measured as reduced TLCO%. On the other hand, immunosuppression does not seem to influence the risk.

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Table I. Differential clinical characteristics between sarcoidosis patients without COVID-19 and those with COVID-19.

	Patients without COVID-19 (n=60)	Patients with COVID-19 (n=45)	Total number of patients (n=105)	*p*-value
Age, years, median [IQR]	49 [42-57.5]	45 [39-54]	47 [40-56]	0.16
Male gender, n (%)	29 (48.33)	22 (48.89)	51 (48,57)	0.74
Active smoking, n (%)	22 (36.67)	16 (35.56)	38 (36.19)	0.72
Neoplasm history, n (%)	3 (5)	4 (8.89)	7 (6.67)	0.46
Diabetes mellitus t.2, n (%)	4 (6.67)	6 (13.33)	10 (9.52)	0.32
Myocardial infarction history, n (%)	1 (1.67)	2 (4.44)	3 (2.86)	0.58
Chronic kidney disease, n (%)	1 (1.67)	0 (0)	1 (0.95)	1.0
Liver failure, n (%)	0 (0)	0 (0)	0 (0)	1.0
Heart failure, n (%)	4 (6.67)	2 (4.44)	6 (5.71)	0.70
Asthma, n (%)	9 (15)	7 (15.56)	16 (15.24)	0.94
COPD, n (%)	2 (3.33)	3 (6.67)	5 (4. 76)	0.65
Arterial hypertension, n (%)	19 (31.67)	13 (28.89)	32 (30.48)	0.76
Stroke history, n (%)	2 (3.33)	1 (2.22)	3 (2.86)	1.0
Actual immunosuppression therapy, n (%)	2 (3.33)	1 (2.22)	3 (2.86)	1
FEV1(%), mean (SD)	88.24 (21.55)	79.91 (19.27)	84.76 (20.91)	0.08
FVC (%), median [IQR]	91 [82.75-105]	83 [74-99]	90 [77.5-102]	0.08
TLCO (%), mean (SD)	105.81 (21.95)	91.22 (22.46)	99.74 (23.19)	0.003
Extrapulmonary manifestation of sarcoidosis, n (%)	10 (16.67)	10 (22.2)	20 (19.0)	0.46
History of Löfgren syndrome, n (%)	4 (6.67)	3 (6,67)	7 (6.67)	1.0
Current systemic GCS therapy, n (%)	8 (13.33)	8 (17.78)	16 (15.24)	0.59
Systemic GCS therapy history*, n (%)	10 (16.67)	13 (28.89)	23 (21.90)	0.16
Immunosuppression history*, n (%)	2 (3.33)	2 (4.44)	4 (3.81)	1
COVID-19 vaccination, n (%)	51 (85)	35 (77.78)	86 (81.90)	0.34

*from March 2020; COPD: chronic obstructive pulmonary disease; FEV1: forced expiratory volume in 1 second; FVC: forced vital capacity; GCS: glucocorticosteroid; TLCO: transfer factor of the lung for carbon monoxide.

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