Systemic sclerosis and COVID-19: what's new in the literature

Sirs,

During the current pandemic, identifying patients most at risk for COVID-19 is crucial. Older age and underlying health disorders have been identified as risk factors for severe disease (1). Systemic sclerosis (SSc) is a rare chronic autoimmune disease characterised by inflammation and fibrosis of the skin and internal organs. Infections are more common among SSc patients, especially in those with respiratory and oesophageal disease, and contribute to morbidity and excess mortality (2). Moreover, immunosuppressive medications increase vulnerability of the patients so that, if infected, may develop a more severe and prolonged disease course (2). However, little is known about the clinical course of COVID-19 in patients with systemic sclerosis (SSc).

We conducted a systematic literature review on Medline, Embase, and Web of Science (WoS) from December 1st 2019 up to and including June 22nd 2020. All types of papers reporting cases of SSc infected with SARS-CoV-2 were included.

The literature search resulted in 350 hits, after duplicates were eliminated. Following the screening of titles and abstracts, seven articles were found to be relevant. An eighth relevant study was retrieved by screening references of included papers, and added manually.

The eligible articles include 2 case reports (3, 4), one case series (5), two retrospective studies (6, 7), two surveys (8, 9), and one paper summarising the findings of a large registry (10). A total of 25 SSc patients were identified. Gender was provided for 9 patients of which 7 (78%) were female. Among the same 9 patients, age was listed, with a median of 65±16.5 years (range 32–84) (Table I). COVID-19 infection was severe in 7 of 9 cases providing information on disease course, with 3 recorded deaths. Among the 3 patients with interstitial lung disease, one developed a mild disease, one required intensive care unit level care and one died. Treatment at diagnosis (available for 7) included rituximab (n=4, severe), tocilizumab (n=1, mild), mycophenolate mofetil (n=1, severe), and methylprednisolone (n=1, severe).

Our study shows a significant heterogeneity in the information provided about SSc and the clinical course of COVID-19. Symptoms at onset of SARS-CoV-2 infection in SSc are in line with those described in the general population. HRCT features seem to be shared by the two diseases. In some SSc

Table I. Included studies with features of underlying systemic sclerosis and COVID-19 clinical course.

Study	Study type	Country	Population	No. of SSc COVID-19+ pts	Age	Sex	SSc-related Rx	Subset	Extra-skin organ involvement	Auto-Ab's	Comorbidities	COVID-19 severity	Hospitalisation	COVID-19 Rx	Outcome
Mihai *et al*. (3)	Case report	Switzerland	n/a	1	57	F	TCZ	u/a	ILD, polyarthritis	ATA	DM, obesity	Mild	No	TCZ	R
Cheng *et al*.(4)	Case report	China	568 COVID-19 hospitalised pts	1	79	M	MTP	u/a	u/a	u/a	COPD	Critical	Yes	arbidol ribavirin IFN-γ TCZ IVIg HFNC	R
Avouac *et al*. (5)	Case series	France/ Italy	n/a	3	71	M	PDN MTX RTX	dcSSc	none	RNA pol III	HTN, HLD	Severe	Yes (ICU)	ABX NIV	R
					84	F	PDN RTX	lcSSc	polyarthritis	u/a	CKD, PE	Severe	Yes	lopinavir anakinra TCZ pulse GCs HFNC	improved O2 requirements, still hospitalised
					44	F	PDN MTX RTX	lcSSc	polyarthritis	RNA pol III	Thyroidectomy for goiter	Severe	Yes (ICU)	ABX NIV	improved O2 requirements, still hospitalised
Moiseev *et al*. (6)	Retrospective	Russia	902 ICU pts with COVID-19	2	65	F	u/a	dcSSc	ILD, GI system	u/a	MM	Severe	Yes (ICU)	NIV or IV	D
					66	F	u/a	u/a	none	u/a	AF, CKD	Severe	Yes (ICU)	u/a	D
Favalli *et al*. (8)	Survey	Italy	123 pts with CTD	1	32	F	RTX HCQ	u/a	ILD	u/a	u/a	Severe	Yes (ICU)	TCZ IV	D
Zen *et al*. (9)	Survey	Italy	916 pts with rheumatic disease, 176 with SSc	1	54	F	MMF	u/a	u/a	u/a	u/a	u/a	Yes (ICU)	AZ HCQ Low Flow O2	R
Gianfrancesco *et al*. (10)	Registry	40 countries	600 rheumatic pts with COVID-19	16	u/a	u/a	u/a	u/a	u/a	u/a	u/a	u/a	u/a (40% of overall cohort hospitalised)	u/a	9% overall cohort D
Pablos *et al*. (7)	Retrospective	Spain	26,131 pts with rheumatic disease	1.14% of those with SSc	u/a	u/a	u/a	u/a	u/a	u/a	u/a	u/a	u/a	u/a	u/a

AF: atrial fibrillation; autoAb: autoantibodies; ATA: anti-topoisomerase; AZ: azithromycin; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; CTD: connective tissue disease; D: death; dcSSc: diffuse SSc; DM: diabetes mellitus; GC: glucocorticoids; GI: gastrointestinal; HCQ: hydroxychloroquine; HFNC: high flow nasal cannula; HLD: hyperlipidemia; HTN: hypertension; ICU: intensive care unit; IFN: interferon; ILD: interstitial lung disease; IVIg: intravenous immunoglobulins; lcSSc: limited SSc; MMF: mycophenolate mofetil; MTP: methylprednisolone; MTX: methotrexate; n/a: not applicable; NIV: non-invasive ventilation; O2: oxygen; PE: pulmonary embolism; pts: patients; PDN: prednisone; R: recovered; RNA pol III: ribonucleic acid polymerase III; RTX: rituximab; Rx: treatment; SSc: systemic sclerosis; TCZ: tocilizumab; u/a: unavailable.

patients, COVID-19 had a fatal outcome. The small number of patients, heterogeneity of data and tendency to report severe cases limit our understanding of how underlying disease or treatment influence prognosis. More robust data gathering derived from the databases (ACR, EULAR, EUSTAR) will allow for a more systematic view of the main signs and symptoms characterising SARS-CoV-2 infection in SSc. In particular, for the better understanding of the intersection of SSc and COVID-19, the launch of the EUSTAR COVID-19 registry will provide a much more detailed picture.

B. Russo*[1,2], *MD, PhD*
J. Ben Shimol*[3]
M. Matucci-Cerinic§[4,5], *MD, PhD*
C. Bruni§[4], *MD*

**Equal contribution as first author.*
§Equal contribution as senior author.

[1]Department of Pathology and Immunology, School of Medicine, University of Geneva, Switzerland;
[2]Division of Dermatology and Venereology, Geneva University Hospitals, Switzerland;
[3]Department of Rheumatology, E. Wolfson Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel;
[4]Department of Experimental and Clinical Medicine, Division of Rheumatology, University of Firenze, Italy;
[5]Department of Geriatric Medicine, Division of Rheumatology AOUC, Firenze, Italy.

Please address correspondence to:
Barbara Russo,
Centre Médical Universitaire (CMU),
Rue Michel-Servet,
Genève 1206, Switzerland.
E-mail: barbara.russo@unige.ch

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