Are patients with systemic lupus erythematosus more prone to result false-positive for SARS-CoV2 serology?

Sirs,

Infections are a leading cause of hospitalizations and deaths in patients with Systemic Lupus Erythematosus (SLE) (1). To date, there is a lack of data specifically describing the management of COVID-19 in SLE patients.

This document will describe a case highlighting how SLE can represent an additional problem to the diagnostic challenge of COVID-19. We describe the case of a 52-year-old female who was diagnosed with SLE in 1999 for polyarthritis, mucocutaneous manifestations, leukopenia, anti-dsDNA and anti-Ro antibodies.

The patient's comorbidities included: post-ischaemic heart failure, arterial hypertension and latent tuberculosis. In 2011 the patient complained of a persistent dry cough and dyspnea for which she received a diagnosis of a SLE-related BOOP and was subsequently treated with azathioprine.

In October 2019, she developed a biopsy-proven class IV lupus nephritis and received pulse steroids and intravenous cyclophosphamide (total 3 g). In February 2020, she was prescribed mycophenolate mophetile (3 g daily) for persistent renal and serologic activity. On March 18th the patient complained of a productive cough resistant to antibiotics. She was then admitted to the ER due to exertional dyspnea, thoracic pain and persistent cough. On admission, a lung CT scan showed diffuse clustered branching tree-in bud opacities suggestive of a bronchiolar inflammatory process. The laboratory features are reported in Table I.

In accordance with COVID-19 Hospital triage, the SARS-CoV2 serology was tested showing positivity for both IgM and IgG while two consecutive naso-pharyngeal swabs were negative two days apart. Due to the unclear clinical picture, a bronchoalveolar lavage was also performed resulting negative for SARS-CoV2 RNA as well as for other viruses, mycobacteria, fungi and bacteria. The diagnosis of SLE-related BOOP was then confirmed.

This case constituted a significant diagnostic dilemma in the emergency setting; despite the straightforward and positive administering of SARS-CoV2 serology, subsequent analyses failed to confirm the infection. Thus, the patient was initially considered COVID-19+ and managed accordingly, before being switched to a COVID-19- setting. This suggests that although the detection and profile of specific antibodies to SARS-CoV-2 provide valuable information for rapid screening of suspected cases, as well as assisting diagnosis and evaluating the disease course, serology for COVID-19 (2, 3) should be viewed with caution in patients with SLE due to a possible non-specific cross-reaction with autoantibodies. For instance, the possibility of false positive IgM antibody tests for human cytomegalovirus (CMV) in patients with SLE has already been pointed out, especially during the active phases of the disease, and more particularly in patients with lupus nephritis (4, 5). Thus, further studies conducted on a large SLE cohort are needed in order to test the hypothesis that a similar false-positivity could also occur with SARS-CoV-2 serology immunoassay.

Table I. Laboratory data on admission.

	Result	Reference value
ESR (mm/h)	48	<15
CRP (mg/dL)	0.61	<0.5
Procalcitonin (ng/mL)	0.04	<0.05
White blood cells (10^3/μL)	5.54	4.0-11.0
Neutrophils %	61.9	40-75
Lymphocytes %	26	20-50
Eosinophils %	2.7	<7
Monocytes %	9.2	2-13
Basophils %	0.2	<1.5
C3 (mg/dL)	51.9	90-180
C4 (mg/dL)	9.8	10-40
Creatinine (mg/dL)	1.15	0.5-1.1
Proteinuria (mg/24h)	10.556	<150
AST/ALT (U/L)	16/9	<40/<40
Anti-dsDNA	positive	negative

A further point of interest concerning this case study is the possibility of disease-related features (*i.e.* inflammatory lung involvement) mimicking an infectious disease, in this case COVID-19.

Lastly, SLE patients may be more susceptible to infections (6) and the COVID-19 rate risk and disease severity in immunosuppressed hosts for autoimmune diseases is still largely unknown: the infection risk in such patients should therefore be carefully balanced against the need to treat the underlying disease. Moreover, while we must not overlook the fact that, in theory, glucocorticoids and immunosuppressive therapies may promote the spread of COVID-19 infection, it may be hypothesised that the modulation of the immune system induced by chronic immunosuppressive therapy in patients with systemic autoimmune diseases may mitigate the "inflammatory storm" accompanying the most severe cases of COVID-19 (7).

In conclusion, if COVID-19 is suspected in patients with SLE and, more generally with systemic autoimmune diseases, the diagnostic work-up should include a multidisciplinary team evaluating serological as well as microbiological and clinical data in order to avoid a rushed misdiagnosis, incorrect directing of patients and potentially harmful treatments.

E. ELEFANTE[1,2], *MD*
C. TANI[1], *MD, PhD*
D. ZUCCHI[1], *MD*
V. SIGNORINI[1], *MD*
F. FERRO[1], *MD*
M. MOSCA[1], *MD, PhD*

[1]Rheumatology Unit, University of Pisa, Italy;
[2]Department of Medical Biotechnologies, University of Siena, Italy.

Please address correspondence to:
Marta Mosca,
U.O. di Reumatologia,
Dipartimento di Medicina Clinica e Sperimentale,
Università di Pisa,
via Roma 67, Pisa, Italy.
E-mail: marta.mosca@med.unipi.it

Competing interests: none declared.

References

1. ZUCCHI D, ELEFANTE E, CALABRESI E, SIGNORINI V, BORTOLUZZI A, TANI C. One year in review 2019: systemic lupus erythematosus. *Clin Exp Rheumatol* 2019; 37:715-22.
2. GUO L, REN L, YANG S *et al.*: Profiling early humoral response to diagnose novel coronavirus disease (COVID-19). *Clin Infect Dis* 2020 Mar 21 [Epub ahead of print].
3. TO KK, TSANG OT, LEUNG WS *et al.*: Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. *Lancet Infect Dis* 2020 Mar 23 [Epub ahead of print].
4. STRATTA P, COLLA L, SANTI S *et al.*: IgM antibodies against cytomegalovirus in SLE nephritis: viral infection or aspecific autoantibody? *J Nephrol* 2002; 15: 88-92.
5. DE CAROLIS S, SANTUCCI S, BOTTA A *et al.*: False-positive IgM for CMV in pregnant women with autoimmune disease: a novel prognostic factor for poor pregnancy outcome. *Lupus* 2010; 19: 844-9.
6. TSAI C-Y, LI K-J, HSIEH S-C, LIAO H-T, YU C-L: What's wrong with neutrophils in lupus? *Clin Exp Rheumatol* 2019; 37: 684-93.
7. FERRO F, ELEFANTE E, BALDINI C *et al.*: COVID-19: the new challenge for rheumatologists. *Clin Exp Rheumatol* 2020; 38: 175-80.