

The first case of systemic lupus erythematosus (SLE) triggered by COVID-19 infection

R. BONOMETTI¹, M.C. SACCHI², P. STOBBIONE³, E.C. LAURITANO¹,
S. TAMIAZZO², A. MARCHEGIANI⁴, E. NOVARA⁵, E. MOLINARO⁵,
I. BENEDETTI⁶, L. MASSONE⁴, A. BELLORA⁴, R. BOVERIO¹

¹Department of Emergency Medicine, Santi Antonio e Biagio e Cesare Arrigo Hospital, Alessandria, Italy

²Autoimmunology and Analysis Laboratory Unit, Santi Antonio e Biagio e Cesare Arrigo Hospital, Alessandria, Italy

³Department of Rheumatology, Santi Antonio e Biagio e Cesare Arrigo Hospital, Alessandria, Italy

⁴Geriatric Division, Santi Antonio e Biagio e Cesare Arrigo Hospital, Alessandria, Italy

⁵Department of Emergency Medicine, IRCCS San Matteo Hospital Foundation University of Pavia, Pavia, Italy

⁶Department of Internal Medicine, IRCCS San Matteo Hospital Foundation University of Pavia, Pavia, Italy

Abstract. – Coronavirus disease 2019 (COVID-19) is a respiratory tract infection caused by a newly emergent coronavirus, SARS-CoV-2. The acute phase may be followed by a second phase actually not yet completely understood but probably associated to an autoimmune activation. At the moment is not possible to clearly define an association between immunological findings and pathological symptoms, however, this case report describes the case of a patient who following COVID-19 infection development autoimmune antibodies who persist in time longer than viral phase. Those antibodies can be responsible for the multi pathological clinical picture showed from our patient that, according to EULAR 2019 criteria, could be classified as systemic lupus erythematosus (SLE). SLE is probably one of the possible chronic rheumatologic diseases triggers by COVID-19 and this is the first case of SLE with vasculitis actually described in literature.

Key Words:

COVID-19, Autoimmunity, ESL, Lupus.

Introduction

Coronavirus disease 2019 (COVID-19) is a respiratory tract infection caused by a newly emergent coronavirus, SARS-CoV-2. Genetic sequencing of the virus suggests that SARS-CoV-2 is a beta-coronavirus closely linked to the SARS virus¹.

COVID-19 infection can bring to a different clinical manifestation, from mild or uncomplicated illness, to severe disease with acute respiratory disease syndrome (ARDS), sepsis and septic shock, multi-organ failure and even death².

The acute phase may be followed by a second phase which has not been completely understood so far, but which is probably associated with an autoimmune activation. An autoimmune response has already been reported in some patients affected by COVID-19. Can this infection become a trigger for a chronic autoimmune disease?

Case Presentation

An 85-year-old woman was found lying unconscious at home and taken to the Emergency Unit. No significative medical history or chronic therapy.

Upon arrival she was hemodynamically unstable with severe hypotension and diffuse marbled. Circulatory support with liquids was started. They positioned vesical catheter with detection of hematuria.

The patient was sleepy, but she woke up and reacted to the painful stimulus; she showed diffuse dyscrasic edemas with peripheral cyanosis particularly on her fingers.

Neutrophilic leukocytosis with lymphopenia, elevation of C-reactive protein, thrombocytopenia, severe acute kidney injury with hypokalemia, hypernatremia and elevation of ferritin and LDH resulted on hematochemical tests.

Chest X-ray showed accentuation of the lung design at the basis and pleural effusion. Urine culture was performed and empirical antibiotic therapy with piperacilline/tazobactam was started. A mild respiratory failure at arterial blood gas analysis was detected and oxygen supplementation with non-invasive ventilation (NIV) was started.

A nasal swab for COVID-19 resulted negative but immunoglobulin for COVID-19 resulted positive (IgG positive, IgM negative) as it had happened in a previous infection. She was, therefore, hospitalized to continue analysis and treatment.

They did an autoimmune screening. The result was positivity for ANA with cytoplasmic (1: 160), homogeneous (1: 320) and granular (1: 320) pattern, Ku positivity and atypical ANCA. Steroid therapy was started.

Her clinical condition partially improved with gradual normalization of the renal function and reduction of flogosis; nevertheless, thrombocytopenia and hematuria were still present and dried gangrene developed on her three fingertips (Figure 1, 2).

Clinically, the patient was alert, albeit confused, edematous with eschar on her fingertips and cyanosis of the lower limbs. Blood test showed improvement of the WBC/lymphocytes ratio, persistence of severe thrombocytopenia and proteinuria despite normalization of kidney function.

Autoimmunity was repeated after two months and showed persistence of ANA positivity with cytoplasmic (1:80), homogeneous (1: 640) and granular (1: 640) pattern, as well as Ku positivity and atypical ANCA.



Figure 1. Sign of dry gangrene and vasculitis at III-IV-V fingers of right hand.



Figure 2. Sign of vasculitis at II-III-IV fingers of left hand.

According to EULAR 2019 criteria³ she could be classified as systemic lupus erythematosus (SLE) for the presence, in addition to ANA positivity, of thrombocytopenia, pleural effusion, proteinuria and low complement. Afterwards hydroxychloroquine in association to steroid therapy already in act was started.

Discussion

Currently, there is only one study in which autoimmune characteristic of severe case of SARS-COVID-19 is documented. In this paper, Zhou et al⁴ analyzed 21 patients and came to the conclusion that autoimmune phenomena exist in people affected by COVID-19.

However, the development of rheumatological disease (particularly SLE), following the infection with COVID-19 is not currently described in literature.

SLE is a chronic inflammatory disease that can manifest with different clinical picture and different evolution depending on patients.

Genetic predisposition, environmental triggers, and the hormonal milieu, interplay in the disease development and activity. Clinical manifestations and the pattern of organ involvement are widely heterogenous, reflecting the complex mosaic of disrupted molecular pathways converging into the SLE clinical phenotype^{5,6}.

COVID-19 patients are complex and multivariate patients who need close follow up.

Follow-up becomes even more necessary if unknown autoimmunity alterations have been

detected during COVID-19 infection. It is advisable to look for them in most critical cases or in particularly long diseases. It is also of the utmost importance to re-evaluate them at the resolution of the viral infection to understand if there is an evolution towards a chronic rheumatological pathology.

Conclusions

Systemic lupus erythematosus is one of the possible chronic rheumatologic diseases triggered by COVID-19 and this has been the first full-blown case of SLE with vasculitis described in literature so far.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Funding

No funding.

Statement of Human and Animal Rights

All procedures performed in the study were in accordance with the Ethical Standards of the Institutional and/or National Research Committee and with the 1964 Helsinki declaration and its later amendments or comparable Ethical Standards.

Informed Consent

The patient was informed of the scientific and clinical interest in her disease as well as of this anonymous publication. She gave an informed verbal consent to the anonymous publication.

References

- 1) TEAM NCPERE. Vital surveillances: the epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) China. *China CDC Weekly* 2020; 2: 113-122.
- 2) YANG X, YU Y, XU J, SHU H, XIA J, LIU H, WU Y, ZHANG L, YU Z, FANG M, YU T, WANG Y, PAN S, ZOU X, YUAN S, SHANG Y. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Resp Med* 2020; 8: 475-481.
- 3) ARINGER M, COSTENBADER K, DAIKH D, BRINKS R, MOSCA M, RAMSEY-GOLDMAN R, SMOLEN JS, WOFYSY D, BOUMPAS DT, KAMEN DL, JAYNE D, CERVERA R, COSTEDOAT-CHALUMEAU N, DIAMOND B, GLADMAN DD, HAHN B, HI-EPE F, JACOBSEN S, KHANNA D, LERSTRØM K, MASSAROTTI E, McCUNE J, RUIZ-IRASTORZA G, SANCHEZ-GUERRERO J, SCHNEIDER M, UROWITZ M, BERTSIAS G, HOYER BF, LEUCHTEN N, TANI C, TEDESCHI SK, TOUMA Z, SCHMAJUK G, ANIC B, ASSAN F, CHAN TM, CLARKE AE, CROW MK, CZIRJÁK L, DORIA A, GRANINGER W, HALDA-KISS B, HASNI S, IZMIRLY PM, JUNG M, KUMÁNOVICS G, MARIETTE X, PADJEN I, PEGO-REIGOSA JM, ROMERO-DIAZ J, RÚA-FIGUEROA FERNÁNDEZ Í, SEROR R, STUMMVOLL GH, TANAKA Y, TEKTONIDOU MG, VASCONCELOS C, VITAL EM, WALLACE DJ, YAVUZ S, MERONI PL, FRITZLER MJ, NADEN R, DÖRNER T, JOHNSON SR. 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. *Ann Rheum Dis* 2019; 78: 1151-1159.
- 4) ZHOU Y, HAN T, CHEN J, HOU C, HUA L, HE S, GUO Y, ZHANG S, WANG Y, YUAN J, ZHAO C, ZHANG J, JIA Q, ZUO X, LI J, WANG L, CAO Q, JIA E. Clinical and Autoimmune Characteristics of Severe and Critical Cases of COVID-19. *Clin Transl Sci* 2020 Apr 21:10.1111/cts.12805. doi: 10.1111/cts.12805. Epub ahead of print.
- 5) MATHIAN A, MAHEVAS M, ROHMER J, ROUMIER M, COHEN-AUBART F, AMADOR-BORRERO B, BARRELET A, CHAUVET C, CHAZAL T, DELAHOUSSE M, DEVAUX M, EUVRARD R, FADLALLAH J, FLORENS N, HAROCHE J, HIÉ M, JUILLARD L, LHOE R, MAILLET T, RICHARD-COLMANT G, PALLUY JB, PHA M, PERARD L, REMY P, RIVIÈRE E, SÈNE D, SÈVE P, MORÉLOT-PANZINI C, VIALARD JF, VIROT JS, BENAMEUR N, ZAHR N, YSSEL H, GODEAU B, AMOURA Z. Clinical course of coronavirus disease 2019 (COVID-19) in a series of 17 patients with systemic lupus erythematosus under long-term treatment with hydroxychloroquine. *Ann Rheum Dis* 2020; 79: 837-839.
- 6) FAVA A, PETRI M. SYSTEMIC LUPUS ERYTHEMATOSUS: Diagnosis and clinical management. *J Autoimmun* 2019; 96: 1-13.
- 7) DRENKARD C, VILLA AR, REYES E, ABELLO M, ALARCÓN-SEGOVIA D. Vasculitis in systemic lupus erythematosus. *Lupus* 1997; 6: 235-242.