



## CASE REPORT

# COVID-19 infection triggered juvenile systemic lupus erythematosus-like disease

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## Case Report

A previously healthy 11-year-old girl presented on May 2020, during the first pandemic wave, with a month-long history of bilateral wrist and fingers arthralgia, dry cough, chest pain and orthopnea. After treatment with azithromycin and non-steroidal anti-inflammatory drugs, due to persistent chest pain and non-quantified low-grade fever for 2 days, she was admitted. She denied rash, diarrhoea and taking other medication besides the ones prescribed. Her physical examination revealed bilateral symmetric wrist and second and third metacarpophalangeal and proximal interphalangeal arthritis and decreased right lower vesicular breath sounds.

The initial laboratory results revealed leukocytes 4.500/ $\mu$ L, C-reactive protein 22 mg/L, sedimentation rate 46 mm/h and sterile leukocyturia (74/ $\mu$ L), without proteinuria. The SARS-CoV-2 RT-PCR from nasopharyngeal swab was positive, with a cycle threshold of 32.5 for the targeted gene ORF1ab and 33.1 for the targeted gene E. Plain X-rays of the wrists and hands were normal. A small posterior pericardial effusion with a moderate

right lung pleural exudate effusion was diagnosed and thoracocentesis was performed (Table 1).

Investigations were negative for several infectious agents (Table 1). Autoimmune screening revealed antinuclear antibodies (ANA), 1:640, with a homogenous pattern, and positive anti-double-stranded DNA (anti-dsDNA), anti-nucleosome and anti-histone antibodies. Anti-dsDNA by *Crithidia luciliae* indirect immunofluorescence test was negative. The direct antiglobulin test for IgG was weakly positive. Complement C3 was borderline low (Table 1).

According to EULAR 2019,<sup>1</sup> she gathered systemic lupus erythematosus (SLE) criteria for ANA positivity, joint involvement, pleural and pericardial effusion and positive anti-dsDNA. She started prednisone and hydroxychloroquine, with progressive clinical improvement.

At 2-month follow-up, she had no signs of arthritis, the serositis resolved, the anti-dsDNA turned negative and slowly started tapering steroid dosage. Prednisolone was stopped after 5 months, maintaining hydroxychloroquine and 1 year later she was clinically well, with no relapses, the anti-dsDNA and the anti-nucleosome remained negative and with a normal complement.

## Discussion

Interaction of genes with environmental factors, such as viruses, leads to numerous immunological alterations that can culminate in persistent immune responses against autologous nucleic acids.<sup>2</sup>

SARS-CoV-2 infection can lead to a proinflammatory state with hyperactivation of inflammatory cytokines, setting off aberrant innate and adaptive immune response.<sup>2</sup> Furthermore, some studies documented presence of autoantibodies, including ANA or antiphospholipid autoantibodies in COVID-19 patients, although its significance is still unknown.<sup>3–5</sup> Other case reports of SLE triggered by SARS-CoV-2 in adults<sup>6–8</sup> resemble our case since there are similarities in the immunological and clinical (serosal and musculoskeletal) manifestations.

Although the presented features suggest a COVID-19-induced SLE-like disease, the diagnosis of primary juvenile SLE remains a possibility that only future follow-up will eventually unravel. Given the fact that the adolescent is clinically well, with no complaints or relapses, 9 months after stopping corticosteroids and maintaining hydroxychloroquine, autoimmunity triggered by SARS-CoV-2 is suggested.

### Key Points

- 1 Most children are asymptomatic with SARS-CoV-2 infection or present with mild disease, but associated autoimmune manifestations have been reported.
- 2 SARS-CoV-2 infection can lead to a proinflammatory state with hyperactivation of inflammatory cytokines, setting off aberrant innate and adaptive immune response.
- 3 Systemic lupus erythematosus is considered the great imitator because of its variable clinical features. The findings in this case resemble other adult case reports since there are similar immunological and clinical (serosal and musculoskeletal) features.

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**Table 1** Complementary study: at admission and evolution

	At admission	Peak/Nadir	Relevant results
Haematological tests			
Haemoglobin	18.8	—	—
Leukocytes ( $\times 10^9/L$ )	4.50	4.50 (D1)	5.27 (D18)
Neutrophils ( $\times 10^9/L$ )	2.80	2.80 (D1)	1.90 (D18)
Lymphocytes ( $\times 10^9/L$ )	1.22	1.22 (D1)	2.32 (D18)
Platelets ( $\times 10^9/L$ )	188	—	—
D-dimer ( $\mu g/L$ )	1063	1660 (D2)	191 (1.5 months later)
Inflammatory markers			
CRP (mg/L)	22	22 (D1)	—
ESR (mm/h)	—	<b>46</b>	3 (1.5 months later)
LDH (U/L)	—	310 (D2) (RV 157–272)	224 (D11)
Serum amyloid A protein (mg/L)	—	13.8 (D2) (RV <6.4)	—
Ferritin (ng/mL)	—	93.9 (D2) (RV 13.7–78.8)	58.2 (D11)
Infectious workup			
IGRA	—	—	neg
Acid-fast <i>bacillus</i> smear, NAAT and culture of gastric lavage samples (3)	—	—	neg
Pleural fluid mycobacterial NAAT and culture	—	—	neg
Blood, urine and pleural fluid cultures	neg	—	—
Anti-HIV 1/2	—	—	neg
CMV IgG/IgM	—	—	neg/weak +
CMV viral load	—	—	neg
EBV VCA IgG/IgM/EA IgG/EBNA IgG	—	—	+/neg/+/+
EBV viral load	—	—	neg
Anti-Toxoplasma gondii IgG/IgM	—	—	neg/neg
Anti-Mycoplasma pneumoniae IgG/IgM	—	—	neg/neg
Anti-Chlamydia pneumoniae IgG/IgM	—	—	+/neg
Immunological/autoimmune workup			
ANA	—	<b>1/640</b>	—
Anti-dsDNA (U/mL)	—	<b>423</b> (RV <100)	<b>Neg (2 months later)</b>
Anti-nucleosome (U/mL)	—	<b>215</b> (RV <20)	13.1 (1 year later)
Anti-histones	—	2+	1+
ANCA	—	—	neg
Rheumatoid factor	—	—	neg
HLA-B27	—	—	neg
Anti-citrulline (anti-CCP)	—	—	neg
Anti-DNAse B	—	—	neg
Antistreptolysin O (ASO)	—	—	neg
C3 complement (g/L)	1.21	0.85 (RV 0.9–1.8)	1.13
C4 complement (g/L)	0.32	0.25 (RV 0.1–0.4)	0.32
Direct Coombs test	—	—	Weak +

Note: Bold value represent as compatible with SLE diagnosis (ANA and anti-dsDNA). ANA, antinuclear antibodies; ANCA, antineutrophil cytoplasmic antibodies; CMV, cytomegalovirus; CRP, C-reactive protein; D, day; EBV, Epstein–Barr virus; ESR, erythrocyte sedimentation rate; IGRA, interferon gamma release assay; LDH, lactate dehydrogenase; NAAT, nucleic acid amplification test; neg, negative; RV, reference value; +, positive.

The authors obtained patient's and parents' consent to publish this case report.

## References

- 1 Aringer M, Costenbader K, Daikh D *et al.* 2019 European League Against Rheumatism/American College of Rheumatology Classification
- 2 Fanouriakis A, Tziolos N, Bertsias G, Boumpas DT. Update on the diagnosis and management of systemic lupus erythematosus. *Ann. Rheum. Dis.* 2021; **80**: 14–25.
- 3 Novelli L, Motta F, De Santis M *et al.* The JANUS of chronic inflammatory and autoimmune diseases onset during COVID-19 – A systematic review of the literature. *J. Autoimmun.* 2021; **117**: 102592.

- 4 Sacchi MC, Tamiazzo S, Stobbione P *et al.* SARS-CoV-2 infection as a trigger of autoimmune response. *Clin. Transl. Sci.* 2021; **14**: 898–907.
- 5 Vlachoyiannopoulos PG, Magira E, Alexopoulos H *et al.* Autoantibodies related to systemic autoimmune rheumatic diseases in severely ill patients with COVID-19. *Ann. Rheum. Dis.* 2020; **79**: 1661–3.
- 6 Mantovani-Cardoso E, Hundal J, Feterman D *et al.* Concomitant new diagnosis of systemic lupus erythematosus and COVID-19 with possible antiphospholipid syndrome. Just a coincidence? A case report and review of intertwining pathophysiology. *Clin. Rheumatol.* 2020; **39**: 2811–5.
- 7 Zamani B, Moeini Taba SM, Shayestehpour M. Systemic lupus erythematosus manifestation following COVID-19: A case report. *J. Med. Case Rep.* 2021; **15**: 29.
- 8 Bonometti R, Sacchi MC, Stobbione P *et al.* The first case of systemic lupus erythematosus (SLE) triggered by COVID-19 infection. *Eur. Rev. Med. Pharmacol. Sci.* 2020; **24**: 9695–7.



Sea snail by Ethan Nguyen (aged 8) from “A Pop of Colour” art competition, Youth Arts, Children’s Hospital at Westmead