North Clin Istanb 2023;10(1):127–129

Letter to the Editor

New-onset of juvenile systemic lupus erythematosus following COVID-19 vaccination: First case report

Jozélio Freire de Carvalho

Núcleo de Pesquisa em Doenças Crônicas não Transmissíveis (NUPEN), School of Nutrition from the Federal University of Bahia, Salvador, Bahia, Brazil

To the Editor,

Coronavirus disease 2019 (COVID-19) is a pandemic infection initiated in 2019 in Wuhan, China, and spread worldwide. Nowadays, about 5 million deaths occurred after COVID-19, and the most important weapon against this disease is the vaccination process. In July 2022, there were 565.207.160 cases confirmed, 6.373.739 deaths, and 12.219.375.500 vaccine doses as registered by the World Health Organization [1].

There are presently eight case reports on systemic lupus erythematosus (SLE)-induced by COVID-19 vaccination in the literature [2–9], although no juvenile lupus was reported. Herein, we described the first juvenile SLE patient following the COVID-19 vaccine and reviewed the adult cases of lupus onset after COVID vaccination.

A 10-year-old girl previously healthy received her first dosage of the COVID-19 vaccine (Comirnaty, Pfizer-BioNTech, US) in January 2022. She felt nausea, vomiting, and cephalalgia on the same day of vaccination. After 4 days, she started symmetrical bilateral arthralgia on her shoulders, metacarpal phalangeal, proximal interphalangeal, and wrists joints. She was treated with nimesulide with improvement. After 30 days from the vaccine, she returned to feel polyarthralgia. She went to a rheumatologist, and polyarthritis of wrists and proximal interphalangeal was detected. Her laboratory tests revealed positive antinuclear (1:320 speckled pattern) and anti-dsDNA (1:80) antibodies, with CH50 32 U/mL [normal range (nr): 60–350 U/mL], C3 66 ng/dL (nr: 90–180 mg/dL) and C4 6 ng/dL (nr: 16–38 mg/dL). Antibodies to Ro/SS-A, La/SS-B, RNP, Sm, and histone were all negative. Her urinary sediment showed proteinuria and hematuria of 91 erythrocytes per field (nr: <3). Twenty-four hours of proteinuria showed 730 mg, with normal creatinine and blood pressure levels. A renal biopsy was refused by patient's family. A diagnosis of juvenile SLE was then determined. Prednisone 50 mg/day, azathioprine 100 mg/day, and hydroxychloroquine 300 mg/day were started. After 3 months, a reduction of hematuria to 23 erythrocytes per field and proteinuria to 200 mg was achieved. We continue following the patient.

This case illustrates the first case of juvenile lupus induced by the COVID-19 vaccination. About eight cases were previously described in the literature, although all patients were adults.

Analyzing these eight cases, we see that age varied from 24 to 70 years old; female gender was predominant in 5/8 (63%), signs and symptoms appeared from 2 weeks to 2 and 1/2 months of vaccine application; Pfizer-BioNTech was the leading applied vaccine in 5/8 cases (63%), followed by Astra-Zeneza 2/8 (25%), and Moderna 1/8 (12,5%). Lupus onset was more common after the second vaccine dose 6/8 (75%), and 2/8 (25%) appeared after the first dose. As observed in our case, nephritis was seen in 4/8 (50%) of the published cases. ANA was detected in all cases, followed by anti-dsDNA antibodies in 6/8 (75%) of the cases, low complement levels in 6/8 (75%), anti-Ro/SS-A in 4/8 (50%), anti-La/SS-B in 3/8 (38%), and anti-Sm in 2/8 (25%) of the cases. Glucocorticoid was done in all patients, followed by hydroxychloroquine in 4/8 (50%), mycophenolate in 2/8 (25%), azathioprine in 1/8 (13%), and cyclophosphamide in 1/8 (13%) (Appendix 1).

The close temporal context, the normalization of the laboratory parameters related to SLE, and the absence of other trigger factors support the possibility that the COVID-19 vaccination caused lupus in our case.

It is important to emphasize the SLE developed after other vaccines such as hepatitis B, anthrax, typhoid, hepatitis A, influenza, meningococcal, tetanus, mumps, measles, and rubella, diphtheria, polio, and others [10, 11].

SARS-CoV-2 vaccines are generally deemed safe, but concerns have been raised about developing autoimmunity in subjects undergoing vaccination with the production of SARS-CoV-2 spike glycoproteins antibodies [11]. Various mechanisms such as molecular mimicry, epitope spreading, polyclonal activation of B cells, vaccine-triggered auto-immunity in a genetically susceptible individual, and even immune cross-reaction to vaccine preservatives have been suggested to be the basis of these adverse events following immunization [12].

Cite this article as: *de Carvalho JF. New-onset of juvenile systemic lupus erythematosus following COVID-19 vaccination: First case report. North Clin Istanb 2023;10(1):127–129.*

Conflict of Interest: No conflict of interest was declared by the author.

Financial Disclosure: The author declared that this study has received no financial support.

REFERENCES

1. World Health Organization. WHO Coronavirus (COVID-19) Dashboard. Available at: https://covid19.who.int. Accessed Feb 6, 2023.
2. Gamonal SBL, Marques NCV, Pereira HMB, Gamonal ACC. New-onset systemic lupus erythematosus after ChAdOX1 nCoV-19 and alopecia areata after BNT162b2 vaccination against SARS-CoV-2. Dermatol Ther 2022;35:e15677. [CrossRef]
3. Liu V, Messenger NB. New-onset cutaneous lupus erythematosus after the COVID-19 vaccine. Dermatol Online J 2021;27:9. [CrossRef]
4. Kaur I, Zafar S, Capitle E, Khianey R. COVID-19 vaccination as a potential trigger for new-onset systemic lupus erythematosus. Cureus 2022;14:e21917. [CrossRef]
5. Molina-Rios S, Rojas-Martinez R, Estévez-Ramirez GM, Medina YF. Systemic lupus erythematosus and antiphospholipid syndrome after COVID-19 vaccination. A case report. Mod Rheumatol Case Rep 2023;7:43–6. [CrossRef]
6. Kim HJ, Jung M, Lim BJ, Han SH. New-onset class III lupus nephritis with multi-organ involvement after COVID-19 vaccination. Kidney Int 2022;101:826–8. [CrossRef]
7. Hidaka D, Ogasawara R, Sugimura S, Fujii F, Kojima K, Nagai J, et al. New-onset Evans syndrome associated with systemic lupus erythematosus after BNT162b2 mRNA COVID-19 vaccination. Int J Hematol 2022;115:424–7. [CrossRef]
8. Zavala-Miranda MF, González-Ibarra SG, Pérez-Arias AA, Uribe-Uribe NO, Mejia-Vilet JM. New-onset systemic lupus erythematosus beginning as class V lupus nephritis after COVID-19 vaccination. Kidney Int 2021;100:1340–1. [CrossRef]
9. Nune A, Iyengar KP, Ish P, Varupula B, Musat CA, Sapkota HR. The emergence of new-onset SLE following SARS-CoV-2 vaccination. QJM 2021;114:739–40. [CrossRef]
10. Aron-Maor A, Shoenfeld Y. Vaccination and systemic lupus erythematosus: the bidirectional dilemmas. Lupus 2001;10:237–40. [CrossRef]
11. Agmon-Levin N, Zafrir Y, Paz Z, Shilton T, Zandman-Goddard G, Shoenfeld Y. Ten cases of systemic lupus erythematosus related to hepatitis B vaccine. Lupus 2009;18:1192–7. [CrossRef]
12. Vojdani A, Vojdani E, Kharrazian D. Reaction of human monoclonal antibodies to SARS-CoV-2 proteins with tissue antigens: implications for autoimmune diseases. Front Immunol 2021;11:617089. [CrossRef]

Received: August 26, 2022 *Accepted:* September 28, 2022
Online: February 15, 2023

Correspondence: Jozélio Freire DE CARVALHO, MD.
Núcleo de Pesquisa em Doenças Crônicas não Transmissíveis (NUPEN), School of Nutrition from the Federal University of Bahia, Salvador, Bahia, Brazil.
Tel: +5571-99187-1169 e-mail: jotafc@gmail.com

doi: 10.14744/nci.2022.93899

Appendix 1. Adult cases of lupus onset after COVID-19 vaccination

Author, year	Age, gender	Time between COVID vaccine and SLE onset	COVID-19 vaccine type	Vaccine dose that SLE appeared	Clinical manifestations	Autoantibodies and compleme	Treatment	Outcome
Liu and Messenger, 2021 [3]	70, M	2 ½ m	Pfizer-BioNTech	2nd dose	Subacute cutaneous lupus	ANA, anti-Ro/SS-A	Glucocorticoid	Improvement after 1 month
Garmonal et al., 2022 [2]	27, F	3 w	Astra-Zeneca	2nd dose	Skin lesions, fever, fatigue, anemia, leucopenia, lymphopenia, altered urine protein/creatinine ratio, alopecia areata	ANA, anti-Sm, anti-Ro/SS-A, anti-La/SS-B, anti-dsDNA, low C3 and C4	Prednisone 80 mg/day, hydroxychloroquine 400 mg/day	ND
Kaur et al., 2022 [4]	54, M	2 w	Pfizer/BioNTech®	2nd dose	Fever, rash, lymphadenopathy, pancytopenia, nephritis, mental confusion, and amnesia	ANA, anti-dsDNA, anti-Ro/SS-A, anti-La/SS-B, low C3 and C4	Prednisone 60 mg/day and mycophenolate mofetil 1,000 mg/day	Good
Molina-Rios et al., 2022 [5]	42, F	2 w	Pfizer/BioNTech®	1st dose	Arthralgia, dyspnea, pulmonary thromboembolism (APS), cardiac tamponade	ANA, anti-dsDNA, low C4, anti-beta-2-glycoprotein IgG 90 U/mL and IgM 46 U/mL	Hydroxychloroquine 200 mg/day, intravenous methylprednisolone 250 mg/day for 3 days, followed by prednisolone 0.5 mg/kg/day, azathioprine 100 mg/day, anticoagulation	Good
Zavala-Miranda, 2021 [8]	23, F	1 w	Astra-Zeneca	1st dose	Anasarca, hair loss, lymphopenia,ritis	ANA, anti-dsDNA, antibodies and low C3 and C4 levels	Prednisone, hydroxychloroquine, mycophenolate mofetil	Good
Hidaka et al. 2022 [7]	53, F	2 w	Pfizer/BioNTech®	1st dose	Evans' syndrome	ANA, lupus anticoagulant, low C3 and C4, Coombs test	Prednisone 60 mg/day	Good
Nune et al., 2021 [9]	24, M	2 w	Pfizer/BioNTech®	2nd dose	Polyarthralgia, polyarthritis, joint stiffness, fever and fatigue, leucopenia, lymphopenia	ANA, anti-dsDNA, low C3 and C4	Prednisone 60 mg/day, methotrexate 15mg/week	Good
Kim et al., 2022 [6]	60, F	2 m		2nd dose	Proteinuria, fever, anemia, thrombocytopenia, lymphopenia, hematuria, increased creatinine levels, class III lupus nephritis	ANA, anti-dsDNA, anti-Sm, low C3 and C4	Prednisone, glucocorticoid pulse, cyclophosphamide, hydroxychloroquine 200 mg/day	Good

ANA: Antinuclear antibodies; APS: Antiphospholipid syndrome; ND: Not described; F: Female; M: Male; m: Months; w: Weeks.