doi: 10.1093/qjmed/hcab229 Advance Access Publication Date: 27 August 2021 Case report

CASE REPORT

OXFORD

The Emergence of new-onset SLE following SARS-CoV-2 vaccination

A. Nune lo ^{1,*}, K.P. Iyengar², P. Ish lo ³, B. Varupula⁴, C.A. Musat⁵ and H.R. Sapkota⁶

¹From the Department of Rheumatology, Southport and Ormskirk NHS Trust, Southport, UK. PR8 6PN, ²Department of Trauma and Orthopaedics, Southport and Ormskirk NHS Trust, UK, PR8 6PN, ³Department of Pulmonary and Critical Care Medicine, VMMC and Safdarjung Hospital, Delhi 110029, India, ⁴Department of Endocrinology, Southport and Ormskirk NHS Trust, Southport, UK, PR8 6PN, ⁵Department of Medicine, Southport and Ormskirk NHS Trust, Southport, UK. PR8 6PN and ⁶Department of Rheumatology, The Royal Wolverhampton NHS Trust, UK, WV10 0QP

*Address correspondence to A. Nune, Consultant Rheumatologist & General Physician. Department of Rheumatology, Southport and Ormskirk NHS Trust, Southport, UK. PR8 6PN. email: arvind.nune@nhs.net

Learning points for clinicians

- Rheumatic-Immune-Mediated Inflammatory Disease (R-IMD) following severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination has been described recently.
- We report a rare case of a patient with a new diagnosis of systemic lupus erythematosus following SARS-CoV-2 vaccination.
- Molecular mimicry, epitope spreading, polyclonal activation of B cells and vaccine triggered autoimmunity in a genetically susceptible individual can be the underlying etiology.
- Early recognition of clinical features and histopathological analysis minimizes diagnostic delay, ensuring timely and appropriate treatment for a favorable outcome.

Case report

Systemic lupus erythematosus (SLE) is uncommon in the young male population.¹ Recent case reports have described the clinical course of Rheumatic-Immune-Mediated Inflammatory Disease (R-IMD) following severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccinations.² Herein, we highlight probably the first case of a patient with a new diagnosis of SLE following SARS-CoV-2 vaccination.

A 24-year-old, previously fit and a healthy Caucasian gentleman was admitted to a United Kingdom (UK) hospital in May 2021 with a 4-week history of polyarthralgia, joint stiffness, fever and fatigue; 2 weeks after receiving the second dose of Pfizer-BioNTech SARS-CoV-2 vaccine. On admission, he was febrile and maintaining oxygen saturation at 97%. He had multiple tender joints with synovitis in metacarpophalangeal joints. The patient tested negative for a SARS-CoV-2 reverse transcriptase-polymerase chain reaction (RT-PCR) test. His Creactive protein was elevated -54 mg/L (normal range 0-5). Subsequent investigations revealed normal creatinine kinase, anti-cyclic citrullinated peptide antibodies and rheumatoid factor, leukopenia with 2.8 \times 10 9 cells/L (3.7–9.5 \times 10 $^9)$ and lymphopenia at 0.6 \times 10⁹ cells/L (1.0–2.5 \times 10⁹). The kidney function was normal without proteinuria. He had negative blood cultures, transthoracic echocardiogram and viral screen for HIV, hepatitis, cytomegalovirus and Epstein-Barr viral infections.

Further immunology workup confirmed positive antinuclear antibodies (ANA) of 1:2560 with a raised double-stranded DNA levels (ds-DNA) at 379 units (0–1.9), a low serum complements C3 level at 0.76 g/l (0.80–1.7) and C4 of 0.05 g/l (0.12–0.36). A

Submitted: 20 August 2021

[©] The Author(s) 2021. Published by Oxford University Press on behalf of the Association of Physicians. All rights reserved. For permissions, please email: journals.permissions@oup.com

contrast computed tomography scan of the thorax, abdomen and pelvis showed reactive lymphadenopathy in the left axilla and both groins. Core biopsy of the left groin lymph node revealed features of lymphoid tissue with necrosis and histiocytes without granulomata. Histopathology report confirmed necrotizing lymphadenitis.

The patient met the SLE diagnostic criteria according to the SLICC (Systemic Lupus International Collaborating Clinics) and ACR (American College of Rheumatology) classification³ based on the presence of polyarthritis, oral ulcers, leukopenia, lymphopenia and strongly positive ANA, anti-dsDNA and low complements; C4 and C3. A multidisciplinary team discussion concluded that he had a diagnosis of SLE with necrotizing lymphadenitis based on the clinico-histopathology features.

The patient had a remarkable improvement of his symptoms with 60 mg oral prednisolone (1 mg/kg body weight). However, as prednisolone was being weaned, the patient noticed worsening of arthralgia and subsequently was commenced on oral Methotrexate 15 mg weekly. The patient made a slow but steady recovery and has had no recurrence of fever on review at 2 months.

Discussion

SLE following SARS-CoV-2 vaccination has not been reported so far to the best of our knowledge. The patient did not have any clinical features of underlying SLE preceding the vaccination. This unusual presentation reminds clinicians to keep a high index of suspicion and utilize immunological and histopathological investigations to confirm the diagnosis of SLE in a patient with non-specific symptoms.

This association may not necessarily imply causation and may merely be temporal and coincidental. However, SLE is relatively uncommon in men and thus raises the possibility of vaccine triggered autoimmunity.¹ SARS-CoV-2 vaccines are generally deemed safe, but concerns have been raised about developing an auto-immune response in individuals undergoing vaccination with the production of antibodies to SARS-CoV-2 spike glycoproteins.⁴ Various mechanisms such as molecular mimicry, epitope spreading, polyclonal activation of B cells and 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. $^{\rm 5}$

Conclusion

Although R-IMD such as SLE following SARS-CoV-2 vaccination appears rare, our case helps raise awareness of such an uncommon association. Early recognition of clinical features and histopathological analysis minimizes diagnostic delay, ensuring timely and appropriate treatment for a favorable outcome.

Conflict of interest. None declared.

Patient consent for publication: Written informed consent taken from the patient.

Statement of ethics: The current submitted article is not a clinical study and does not involve any patients.

References

- 1. do Socorro Teixeira Moreira Almeida M, da Costa Arcoverde J, Barros Jacobino MN, Coimbra Neto AR. Male systemic lupus erythematosus, an overlooked diagnosis. *Clin Pract* 2011; 1: e103.
- Watad A, De Marco G, Mahajna H, Druyan A, Eltity M, Hijazi N, et al. Immune-mediated disease flares or new-onset disease in 27 subjects following mRNA/DNA SARS-CoV-2 vaccination. Vaccines (Basel) 2021; 9:435.
- 3. Petri M, Orbai AM, Alarcón GS, Gordon C, Merrill JT, Fortin PR, *et al.* Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. *Arthritis Rheum* 2012; **64**:2677–86.
- 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 2020; 11: 617089.
- 5. Caso F, Costa L, Ruscitti P, Navarini L, Del Puente A, Giacomelli R, et al. Could Sars-coronavirus-2 trigger autoimmune and/or autoinflammatory mechanisms in genetically predisposed subjects? *Autoimmun Rev* 2020; **19**:102524.