Received: 1 September 2021 | Revised: 2 October 2021 | Accepted: 18 October 2021

DOI: 10.1111/jocd.14572

JCD Journal of Cosmetic Dermatology WILEY

LETTERS TO THE EDITOR

Letter to the editor regarding the article "Patil S, Patil A. Systemic lupus erythematosus after COVID-19 vaccination: A case report. J Cosmet Dermatol. 2021 Aug 21. 10.1111/jocd.14386"

Dear *Editor*.

We read with interest the report titled "Systemic lupus erythematosus after COVID-19 vaccination: A case report" by Patil et al.[1] The authors report on a 22-year-old woman who developed systemic lupus erythematosus (SLE) following coronavirus disease-19 (COVID-19) vaccination with COVISHIELD. However, they do not expand on possible underlying immunological pathways that may explain the relationship.[1] Similar additional cases of LE developing after COVID-19 vaccination or in association with COVID-19 infection have been described.[1–3] Given this association, we here intend to complement the authors in highlighting the possible role that type I interferons (IFN-Is) and their main cellular source, the plasmacytoid dendritic cell (pDC), may play in elucidating how COVID-19 vaccination may trigger SLE.

While the vital role IFN-Is and pDCs play in SLE pathogenesis is well-established, it has recently been demonstrated that IFN-Is, and pDCs play a significant role during COVID-19 infection or vaccination.[4] Characterized by plasma cell morphology and by expressing HLA-DR, CD4, BDCA-2, CD123, and Toll-like receptor (TLR)9 and TLR7 in endosomal compartments, pDCs are peculiar DC subset that play a vital role in innate immunity through their ability to sense nucleic acids via their TLRs.[4–6] Upon TLR7/9 activation, pDCs produce substantial amounts of IFN-Is that is chiefly involved in antiviral immunity. Actually, pDCs are the most potent producers of IFN-Is, which, in turn, are crucial cytokines in controlling viral replication by inducing the expression of numerous genes leading mostly to an antiviral state.[5,6] pDCs also contribute to the adaptive immunity regulating the function of other immune cells. Coronaviruses, including COVID-19, have been shown to be effective stimulators of pDCs leading to strong IFN-I induction.[4] Similarly, COVID-19 vaccines, including mRNA (such as Pfizer and Moderna) and AdV (DNA delivered within non-replicating recombinant adenovirus vector systems such as AstraZeneca, Sputnik V, COVISHIELD, and Johnson and Johnson) vaccines, provoke immunity to COVID-19 by producing high levels of spike proteins.[7,8] While mRNA vaccines interact with various endosomal (especially TLR7) and cytosolic cellular innate sensors (inflammasome components), AdV vaccines interact with multiple pattern-recognition receptors, particularly TLR9.[7] Despite these differences, both vaccine types converge on IFN-I production which partly occurs through pDC-mediated innate immune response. [5–8]

Upon activation and increased production, IFN-Is and pDCs may then play a significant pathologic role in the development of various autoimmune diseases including SLE after COVID-19 vaccination.[5,9] In SLE, the main IFN-I producers have been identified as the pDCs and immune complexes composed of autoantibodies and nuclear antigens are capable of activating pDCs in a TLR-dependent way. In SLE, circulating pDCs diminish as they tend to migrate infiltrating target tissues. In an experimental mouse model, early transient ablation of pDCs before disease initiation has been shown to ameliorate LE. In addition, several studies have consistently confirmed large numbers of IFN-I-producing pDCs in cutaneous lesions of LE. As for IFN-Is, SLE patients with active disease have strong upregulation of IFN-inducible genes in their peripheral blood. In experimental mouse models of SLE, IFN-Is were shown to control the onset and severity of autoimmune manifestations.

In summary, the IFN-I-mediated protective immune response activated post-COVID-19 vaccination (or infection), may trigger IFN-driven autoimmune disorders such as SLE in genetically predisposed people.

KEYWORDS

COVID-19 vaccine, interferon, lupus, plasmacytoid dendritic cell

FUNDING INFORMATION

There is no funding source.

CONFLICT OF INTEREST

None of the authors have any conflict of interest to disclose.

ETHICAL STATEMENT

We, the authors, assure that this paper is our original work, which has not been previously published elsewhere and is not being considered for publication elsewhere.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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