DOI: https://doi.org/10.5114/ceji.2025.151738

Sustained remission of rheumatoid arthritis following COVID-19 vaccination

ANGELO NIGRO

Department of Rheumatology of Lucania – UOSD of Rheumatology, "Madonna delle Grazie" Hospital, Matera, Italy

Abstract

Introduction: *Rheumatoid arthritis (RA) is a chronic autoimmune disease that, if uncontrolled, leads to progressive joint damage. The potential immunomodulatory effects of COVID-19 vaccination on autoimmune disease activity remain an area of investigation.*

Case report: *We describe a 79-year-old woman with a 40-year history of RA, initially treated with methotrexate and, since 2008, with leflunomide (20 mg/day) in combination with corticosteroids (Urbason 8 mg/day) and non-steroidal anti-inflammatory drugs (NSAIDs). During the COVID-19 pandemic, after receiving three doses of the Pfizer vaccine, she discontinued leflunomide due to concerns about infection risk. Upon evaluation in 2021, despite residual joint damage in the hands, clinical and radiographic assessments confirmed inactive RA. Over a three-year follow-up, radiographs demonstrated stable erosions and osteopenic changes, corticosteroid therapy was progressively reduced, and anti-citrullinated protein antibody (ACPA) titers declined by approximately 50% compared to pre-vaccination levels.*

Discussion and Conclusions: *This case suggests a potential immunologic "reset" following COVID-19 vaccination, contributing to sustained RA remission despite discontinuation of a conventional disease-modifying antirheumatic drug (DMARD). Although the precise mechanisms remain unclear, this observation aligns with emerging evidence that vaccine-induced immunomodulation may influence autoimmune disease activity. Further research, including larger controlled studies, is warranted to explore the potential benefits of COVID-19 vaccination in RA management.*

Key words: *immunomodulation, remission, rheumatoid arthritis, COVID-19 vaccination, leflunomide discontinuation.*

(Cent Eur J Immunol 2025; 50 (2): 188-189)

The advent of COVID-19 and the subsequent implementation of global vaccination campaigns have catalyzed substantial discourse regarding the immunomodulatory implications of SARS-CoV-2 vaccination, particularly in the context of autoimmune disorders such as rheumatoid arthritis (RA). Accumulating evidence suggests that SARS-CoV-2 infection and vaccination may disrupt immune homeostasis, potentially triggering disease exacerbation [1, 2] or, conversely, facilitating sustained remission *via* complex immunoregulatory pathways [3]. Moreover, numerous case reports and observational studies within the international literature have documented RA and other rheumatic disease flares following SARS-CoV-2 infection and vaccination [4], underscoring the intricate interplay between viral immunity and autoimmunity.

We report a rare case of a 79-year-old female with a four-decade history of RA who achieved prolonged remission following COVID-19 vaccination and the autonomous discontinuation of leflunomide. No identifiable confounding variables, including modifications in lifestyle, dietary habits, or concomitant pharmacotherapy, were noted throughout the follow-up period. The diagnosis adhered to the 2010 ACR/EULAR classification criteria, characterized by symmetric bilateral arthritis of the wrists and metacarpophalangeal joints, persistently elevated inflammatory markers, seropositivity for anti-cyclic citrullinated peptide antibodies (ACPA), and bilateral erosive changes in the affected joints. Initial management consisted of methotrexate (15 mg/week), with a subsequent transition to leflunomide (20 mg/day) in 2008 due to loss of efficacy. Corticosteroids (methylprednisolone, starting at 16 mg/day and gradually tapered to 8 mg/day) were also administered, along with non-steroidal anti-inflammatory drugs (NSAIDs; diclofenac 100-150 mg/day).

Following the administration of three doses of the Pfizer COVID-19 vaccine, initiated in 2020, the patient independently discontinued leflunomide due to concerns regarding an increased susceptibility to infection linked to immunosuppression. During the subsequent four years of follow-up, the patient exhibited a persistent state of remission of rheumatoid arthritis, with no evidence of active synovitis, radiographic progression, or resurgence of systemic

Correspondence: Angelo Nigro, Department of Rheumatology of Lucania – UOSD of Rheumatology, "Madonna delle Grazie" Hospital, Matera, Italy, e-mails: angelonigro13@gmail.com; angelo.nigro@asmbasilicata.it
Submitted: 18.02.2025, Accepted: 03.04.2025

inflammation, despite preexisting structural joint deformities. ACPA titers exhibited a significant reduction, decreasing by approximately 50% compared to pre-vaccination levels.

While this clinical course may appear temporally related to COVID-19 vaccination, it remains uncertain whether such remission is causally linked to it. In clinical practice, sustained remission in elderly patients with RA receiving low-dose corticosteroids alone is uncommon but not unprecedented. Notably, the patient continued treatment with low-dose methylprednisolone (4 mg/day) throughout the follow-up period, raising the possibility that the prolonged disease control may be at least partially attributable to the continued corticosteroid therapy.

According to the 2022 EULAR recommendations, glucocorticoids are considered part of initial therapy in combination with conventional or biological DMARDs, with the overarching goal of achieving clinical remission or low disease activity using the lowest possible steroid dose and withdrawing them as soon as clinically feasible [5]. In the present case, remission occurred following discontinuation of leflunomide, while maintaining low-dose corticosteroids. This represents a rare and unusual clinical course, particularly in the absence of any other immunosuppressive therapy.

Given the patient's long-standing disease, structural joint damage, and age-related fragility, complete steroid withdrawal could carry a substantial risk of disease flare, potentially leading to functional deterioration and reduced quality of life. For this reason, continuation of a minimal effective steroid dose was deemed clinically justified.

This case represents a rare and exceptional observation of sustained remission of rheumatoid arthritis following SARS-CoV-2 vaccination, a phenomenon scarcely reported in the current medical literature [3]. Nonetheless, the temporal relationship alone does not establish causality, and the remission might have occurred independently of the vaccination event. The underlying mechanisms remain speculative but may involve vaccine-induced reprogramming of immune homeostasis [6]. Possible explanations include the activation of regulatory immune pathways, such as enhanced T-regulatory cell function, suppression of pathogenic Th17-mediated inflammation, and shifts in cytokine signaling profiles (e.g., IL-10, TGF-β). Additionally, modifications in autoantibody kinetics, altered antigen presentation, and transient immune reprogramming via type I interferon signaling may contribute to this unexpected outcome [7]. While molecular mimicry and bystander activation have been historically considered as drivers of vaccine-induced autoimmunity, an alternative hypothesis posits that these mechanisms might paradoxically induce immune tolerance. Further rigorous investigation is necessary to delineate the precise pathways involved and assess the broader implications of SARS-CoV-2 vaccination in modulating autoimmune disease trajectories.

Although similar cases have occasionally been reported in patients not exposed to SARS-CoV-2 infection or vaccination, the rarity of such events precludes definitive conclusions. Given the ongoing paradigm shift toward precision medicine in rheumatology, well-designed, controlled investigations are essential to elucidate whether SARS-CoV-2 vaccination can durably modify immune responses in RA and influence long-term disease trajectories.

Funding

This research received no external funding.

Disclosures

Approval of the Bioethics Committee was not required. The authors declare no conflict of interest.

References

1. Jung SW, Jeon JJ, Kim YH, et al. (2024): Long-term risk of autoimmune diseases after mRNA-based SARS-CoV2 vaccination in a Korean, nationwide, population-based cohort study. Nat Commun 15: 6181.
2. Terracina KA, Tan FK (2021): Flare of rheumatoid arthritis after COVID-19 vaccination. Lancet Rheumatol 3: e469-e470.
3. Barman B, Nune A, Ish P, et al. (2022): Complete persistent remission of rheumatoid arthritis after COVID-19 infection: A rare case and literature review. Monaldi Arch Chest Dis 93.
4. Rai A, Aashish, Priya, et al. (2022): Prevalence of rheumatoid arthritis following COVID-19 vaccine: An autoimmune disorder. Ann Med Surg (Lond) 82: 104628.
5. Smolen JS, Landewé RBM, Bergstra SA, et al. (2023): EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2022 update. Ann Rheum Dis 82: 3-18.
6. Dhanasekaran P, Thirunavuc Karasu B, Mak A (2024): Safety, efficacy, and immunogenicity of SARS-CoV-2 mRNA vaccination in children and adult patients with rheumatic diseases: a comprehensive literature review. Rheumatol Int 44: 2757-2794.
7. Provine NM, Klenerman P (2023): Adenovirus vector and mRNA vaccines: Mechanisms regulating their immunogenicity. Eur J Immunol 53: e2250022.