EJR European Journal of Rheumatology

DOI:10.5152/eurjrheum.2022.22055

Letter to the Editor

Comment on the Article "Adalimumab-Induced Lupus Nephritis: Case Report and Review of the Literature"

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Dear Sir,

We have recently read with great interest the article by Kazzi et al[1] regarding adalimumab (ADA)-induced lupus nephritis, published in the *European Journal of Rheumatology*.

We would like to comment on this case-based review because, besides the administration of ADA, all tumor necrosis factor-alpha inhibitors (TNFαi) may cause many autoimmune phenomena and paradoxical reactions. More specifically, these phenomena range from an isolated expression in the patients' sera of an autoantibody, such as an antinuclear antibody, or double-stranded DNA, or antiphospholipid antibody, to a full-blown autoimmune organ-specific or systemic disease, including drug-induced lupus (DIL).[2,3] Patients with DIL, due to TNFαi, may present various clinical manifestations like photosensitivity, skin rash (malar rash, psoriasiform, discoid), synovitis, oral ulcers, and myalgias. Still, kidney and central nervous system involvement are uncommon.[3,4] Drug-induced lupus diagnosis requires identifying the temporal relationship between drug administration and symptoms development in patients without pre-existing lupus.[2] Several studies of TNFαi-related DIL have been reported and described in a case-based review published recently by our team.[5] Another issue to be considered is the pathogenetic mechanisms underlying the autoantibodies production and the overall development of DIL in patients treated with TNFαi. One hypothesis relies on the fact that TNFαi block TNFα on the cell membrane and induce cell apoptosis, releasing antigenic material, which leads to the generation of autoantibodies and the clinical manifestations of DIL.[2,6] Another hypothesis is that TNFαi can interfere with the Th1/Th2 response, suppressing the Th1 in favor of the Th2 cell response, leading to the production of interferons, which may contribute to the lupus pathogenesis.[2,7] TNFαi have been extensively used in the last 2 decades to treat predominantly inflammatory arthritides and have proven efficacious with an acceptable toxicity profile.[8] However, their use may alter the normal immune response leading to autoimmune adverse events. Physicians, when using TNFαi, should be aware of possible autoimmune adverse manifestations; thus, close follow-up, minute clinical evaluation, and monitoring are required.

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Cite this article as: Drosos AA, Pelechas E, Venetsanopoulou AI, Voulgari PV. Comment on the article "adalimumab-induced lupus nephritis: Case report and review of the literature". *Eur J Rheumatol.* 2023;10(1):49.

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Received: May 15, 2022
Accepted: August 8, 2022
Publication Date: December 6, 2022

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - A.A.D.; Design - A.A.D.; Supervision - P.V.V.; Materials - E.P.; Literature Review - P.V.V.; Writing - A.I.V.; Critical Review - A.I.V.

Declaration of Interests: The authors have no conflicts of interest to declare.

Funding: The authors declared that this study has received no financial support.

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