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Herpes zoster seven days after SARS-CoV-2 vaccination in a patient with ankylosing spondylitis under adalimumab

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We enjoyed reading the article by Maranini et al. about a 41-year old female with ankylosing spondylitis (Bechterew disease) under adalimumab, who developed a cutaneous herpes zoster (VZV) infection seven days after the first dose of an mRNA-based SARS-CoV-2 vaccine (1). She recovered with acyclovir, discontinuation of adalimumab, and postponement of the second vaccine dose (1). A causal relation was assumed based on the close temporal occurrence of VZV after vaccination and previous reports about a suspected causal relation between SARS-CoV-2 vaccinations and VZV infections (1). The study is interesting, but it elicits some concerns and comments.

According to the data provided, a causal relation between vaccination and the development of herpes zoster is unproven. The authors did not exclude a subclinical SARS-CoV-2 infection, the role of adalimumab as the triggering agent, any malignancy or infections other than SARS-CoV-2.

Herpes zoster following a SARS-CoV-2 infection has been repeatedly reported (2). As of the end of October 2021, this association was already published in at least 29 patients (2). Therefore, it is crucial to exclude that the patient had subclinical or mild SARS-CoV-2 infection. Results of the PCR swab tests should be provided.

The authors did not consider immunosuppression with adalimumab as a possible trigger of the viral infection. In a study of 92,374 patients with psoriasis, adalimumab was associated with an increased risk of herpes zoster [hazard ratio 5.52, 95% confidence interval (CI) (1.72-17.71)] (3). The TNF-alpha blocker adalimumab also increased the risk of tuberculosis. In a study of 5317 person-years exposure to adalimumab, the adjusted hazard ratio for tuberculosis was 3.06, 95% CI 2.09-4.49 (4). Adalimumab treatment can also be complicated by herpes zoster meningitis (5).

A comprehensive previous history is also missing. It is important to know in particular whether the patient had any previous herpes zoster infection. Can the current herpes zoster infection be regarded as an exacerbation? We should be also informed whether the history was positive or negative for malignancy. In patients undergoing TNF-alpha treatment, the odds ratio for cancer was 1.36, 95% CI: 1.20-1.53, P<0.00001) in an extensive literature review (6).

No findings from the blood tests were shown for C-reactive protein, leukocyte count, blood cultures, and PCR tests and antibody titres for viruses other than VZV and SARS-CoV-2 to exclude a concomitant infection as the trigger of the herpes zoster superinfection.

Overall, the elegant report has several limitations which make the results and their interpretation challenging. As long as alternative triggers of the herpes zoster infection are not thoroughly excluded, a causal relation between zoster and SARS-CoV-2 vaccination remains unproven.

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Conflict of interest
The author declares no potential conflict of interest.

Contribution
JF: design, literature search, discussion, first draft, critical comments.

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