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Letter to the Editor

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Letter to the Editor (Case report)

Re-exposure with a TNF inhibitor bio-similar was well tolerated and led to sustained control of psoriatic arthritis after allergic reaction to the TNF inhibitor bio-originator

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Rheumatology key message

- A TNF bio-similar might be a therapeutic option after a reaction to a TNF bio-originator.

Dear Editor, Infliximab, a chimeric mAb against TNF-α, is approved for PsA treatment. Infliximab is available as an originator (Remicade) and as biosimilars (CT-P13, Remsima, Inflectra; SB2, Flixabi) [1–4]. We present the case of a 38-year-old Caucasian female physician, who was diagnosed with PsA in 2009, with skin and peripheral joint involvement. She received treatment with MTX, which was not tolerated, before receiving adalimumab, ultimately controlling her disease. In 2010, she developed lymph node tuberculosis and was treated successfully with standard tuberculostatic treatment. After her tuberculosis was treated, she started on etanercept, which was maintained until 2013. Treatment with etanercept was stopped owing to sustained absence of symptoms related to psoriatic arthritis (PsA).

In 2018, after a long drug-free phase because of sustained minimal disease activity, the patient presented with a relapse of PsA, with severe arthritis and dactylitis involving the hand, feet and knee joints, in addition to exacerbation of skin disease. Sequential attempts at treatment of PsA with etanercept, certolizumab pegol and secukinumab failed. The patient was therefore started on infliximab (Flixabi), which led to a status of minimal disease activity. However, after 6 months the symptoms recurred and the patient was switched to infliximab (Remsima), which worsened skin and joint symptoms. Therefore, treatment with infliximab (Remicade) was started, but led to an allergic reaction, with flushing, dizziness, shortness of breath, nausea and shivering. The infusion was stopped, and prednisolone controlled the symptoms. Based on the initial response to infliximab (Flixabi) and after discussion with the patient, who was well aware of the potential harms and benefits, treatment with infliximab (Flixabi) was reintroduced. Other therapeutic options, such as apremilast, ustekinumab or a Janus kinase inhibitor, were rejected because of possible side effects. The patient did not develop any allergic reaction and responded in an excellent manner, reaching controlled disease after 8 weeks, with ongoing improvement of symptoms thereafter. Our patient has been treated based on her preferences and experiences, which she brought to the decision-making process, which goes against normal clinical advice to switch back to an agent that had previously been ineffective or had caused an adverse reaction. She had no concomitant MTX treatment because it was not well tolerated. Infliximab levels were found to be sub-therapeutic before the infusions/injections (<3 μg/ml) and supra-therapeutic (>60 μg/ml) after the infusions/injections, while anti-infliximab antibodies were persistently positive from the commencement of the infliximab therapies. To date, our patient has been treated with Flixabi for 24 months at 4-week intervals, achieving minimal disease activity, occasionally presenting with recurrent hand and finger joint tenosynovitis. Subjectively, she is satisfied with her status quo and therapy.

This case is interesting for two reasons. First, the patient developed an allergic reaction to one of the three different infliximab products and tolerated re-exposure with another infliximab product. Allergic reactions occur in ∼5–20% of patients treated with infliximab. Those occurring during administration and within 24 h of infusion are categorized as acute. Their symptoms include headache, hypotension/hypertension, dizziness, shortness of breath, shivering, sweating, increase in temperature and rash/urticaria [5]. The explanations for the differential response to different infliximab products are unclear and might not necessarily be related to the antibody itself. Although switching between bio-originator and bio-similar is

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widely practised [6, 7], we could not find another documented case of an allergic reaction to one infliximab product, with subsequent exposure to another infliximab product.

The second interesting finding is that the patient became responsive to infliximab (Flixabi), once again, after the allergic reaction against infliximab (Remicade). Hence, the patient experienced a good response, although the first course of infliximab (Flixabi) before the allergic reaction resulted in only a spurious response with rather rapid secondary failure. The reason for this is also unclear. However, a possible explanation is the fact that allergic reaction is associated with type 2 immunity, and recently, eosinophils have been shown to be important for resolution of arthritis [8]. Hypothetically, the combined activation of pro-resolving pathways in conjunction with eosinophils and TNF inhibition might have shown added efficacy in controlling PsA. Further work is planned to evaluate this possible mechanism of action.

Data availability statement

Derived data supporting the findings of this case report are available from the corresponding author on request.

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