Treatment of anti-TNF-related paradoxic palmoplantar psoriasis in Behçet's disease with azathioprine

Sirs,

Anti-TNF agents, especially infliximab (IFX), adalimumab (ADA) and etanercept are used in the treatment of aggressive manifestations of Behçet's disease (BD). However, multiple adverse effects including psoriasis, cytopenia, infection, and demyelinating disorders may be observed after the initiation of anti-TNF treatment. Sometimes these adverse effects result in discontinuation or switching of therapy. Herein, we describe a patient with BD who developed palmoplantar pustular psoriasis (PPP) after initiation of ADA and treated with azathioprine (AZA) without discontinuation of ADA.

A 34-year-old male patient with a diagnosis of BD admitted to our outpatient clinic with skin lesions. He had had a diagnosis of BD with recurrent oral aphthous and genital ulcers, positive pathergy test and bilateral posterior uveitis according to the International Study Group Criteria for Behçet's disease since 2013 and was on AZA and methylprednisolone (MP) treatment. Recurrence of posterior uveitis was observed with AZA and MP and then treatment was switched to interferon alpha (IFN-α). IFN-α was discontinued due to fever and mood changes like adverse effects. Then AZA and cyclosporine combination was prescribed. During the patient's follow-up, bilateral sensorineural hearing loss was observed. He was treated with intravenous pulse methylprednisolone 1000 mg for three consecutive days and ADA 40 mg every two weeks. An improvement in hearing loss was observed. At the 6th week of ADA treatment the patient was admitted to our outpatient clinic with skin lesions. On physical examination, papulopustular lesions in the palms and soles were observed (Fig. 1A). ESR and CRP levels were 18 (N: 0–20) mm/h and 3 (N: 0–5) mg/L, respectively. He was referred to the dermatology department and a punch biopsy was performed. The pathology of skin lesions was consistent with palmoplantar pustular psoriasis. The pathological findings; there is increased neutrophil and neutrophilic microabscess in the epidermis, parakeratosis on the epidermal layer. Also, perivascular lymphocyte infiltration, tortuous capillary, suprapapillary thinning and dermal oedema were detected. He had no history of smoking and a recent infection. Topical steroid, calcipotriene and methotrexate 15 mg/week were added to ADA by dermatology, the respectively.No improvement was observed in psoriatic lesions and then ADA was discontinued. With the cessation of ADA, worsening in hearing loss was observed. So, ADA was again prescribed to the patient and AZA was added to ADA treatment. At the 6th week of treatment with AZA and ADA combination an improvement both in hearing loss and PPP was observed (Fig. 1 B-C). Then we continued AZA treatment without cessation of ADA. In the literature, there are a few case reports of patients with BD who developed PPP after the initiation of IFX (1-3). In these case reports, IFX was discontinued to treat PPP. This was the first case of BD who developed PPP with adalimumab and treated with AZA. Although anti-TNF drugs are used in the treatment of psoriasis, psoriasis due to anti-TNF drugs also has been observed as a paradoxical effect. The definite mechanism of this paradoxical effect is unknown. Overproduction of IFN-α increased infiltration of autoreactive T lymphocytes to the skin and increased keratinocyte proliferation are proposed mechanisms in the pathogenesis of anti-TNF related PPP (4). Azathioprine is a steroid-sparing, purine antagonist which has an important role in inducing apoptosis of lamina propria T lymphocytes and monocytes which contribute to pustular psoriasis development (5). By these mechanisms, concomitant use of AZA may decrease the development of anti-TNF therapy-related PPP (6).

In conclusion, AZA can be used in patients who developed anti-TNF agents related to PPP, without interrupting anti-TNF treatment, which is generally mandatory in organ involvement of BD.

H. KARADENIZ, *MD*
N. ATAS, *MD*
A. AVANOĞLU GÜLER, *MD*
A. TUFAN, *MD*

Division of Rheumatology, Department of Internal Medicine, Gazi University Faculty of Medicine, Ankara, Turkey.

Please address correspondence to:
Dr Hazan Karadeniz,
Gazi University Faculty of Medicine,
Department of Internal Medicine,
Division of Rheumatology,
06100 Ankara, Turkey.
E-mail: drhazankaradeniz@hotmail.com

Competing interests: none declared.

References

1. ADLER S, BAUMGARTNER I, VILLIGER PM: Behçet's disease:successful treatment with infliximab in 7 patients with severe vascular manifestations. A retrospective analysis. *Arthritis Care Res* 2012; 64: 607-11.
2. KO JM, GOTTLIEB AB, KERBLESKI JF: Induction and exacerbation of psoriasis with TNF-blockade therapy: a review and analysis of 127 cases. *J Dermatolog Treat* 2009; 20: 100-8.
3. ROUX CH, BROCQ O, LECCIA N *et al*.: New-onset psoriatic palmoplantaris pustulosis following infliximab therapy: A class effect? *J Rheumatol* 2007; 34: 434-37.
4. COLLAMER AN, GUERRERO KT, HENNING JS, BATTAFARANO DF: Psoriatic skin lesions induced by tumor necrosis factor antagonist therapy: a literature review and potential mechanisms of action. *Arthritis Rheum* 2008; 59: 996-1001.
5. SHEN C, ASSCHE GV, COLPAERT S *et al*.: Adalimumab induces apoptosis of human monocytes: a comparative study with infliximab and etanercept. *Aliment Pharmacol Ther* 2005; 21: 251-58.
6. VERMA P, VERMA KK, KHANNA N, GUPTA S, BHARI N: Effectiveness of weekly azathioprine pulse in the treatment of chronic plaque psoriasis: an open-label study. *Clin Exp Dermatol* 2016; 41: 717-22.

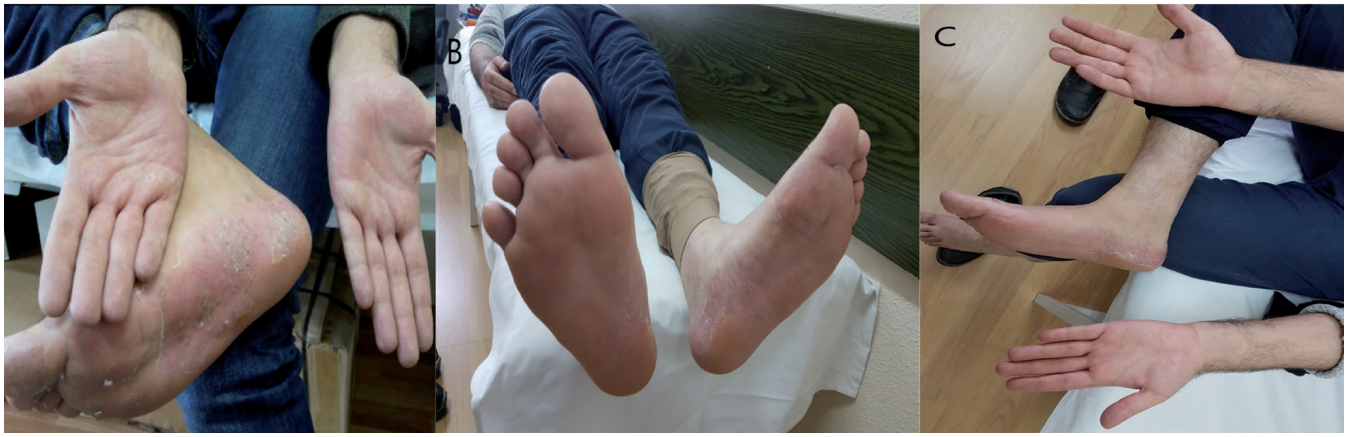

Fig. 1. A: Papulopustular lesions were present on the palms and soles of the patient at the 6th week of ADA therapy. **B-C**: Improvement in papulopustular lesions after addition of AZA to ADA treatment.