Successful treatment of refractory palmoplantar psoriasis in a psoriatic arthritis patient with the JAK inhibitor tofacitinib

Sirs,

Palmoplantar psoriasis (PP) is an incapacitating condition that significantly impairs quality of life. PP prevalence is between 2–40% among psoriasis and psoriatic arthritis (PsA) patients (1). It tends to be refractory to conventional therapies and may last for several years causing significant impairment in mobility and agility. (2). One study reported that just 27.4% of PP patients showed improvement with topical agents, whereas the remaining patients required systemic therapies (3).

This report presents details on a 55-year-old male Caucasian patient with refractory PP, diagnosed with psoriasis vulgaris at the age of 15, while PsA started at the age of 52.

The initial treatment targeting psoriasis vulgaris was oral methotrexate from 2011 to 2016 with success. Suddenly he presented a persistent psoriasis flare, resistant to an increase in the methotrexate dosage. A switch to apremilast was decided, with improvement of the skin lesions; however, the patient developed joint involvement, in accordance with clinical features resembling psoriatic arthritis with morning stiffness, joint pain and swelling of the hand joints and inflammatory back pain in July 2017. Laboratory parameters were normal, including ESR and CRP.

Ustekinumab was introduced at 90 mg improving peripheral and axial symptoms. The skin was in complete remission. At this time, a supplementary MR examination of the lumbar spine showed sacroileitis. After 17 months and because of lower back pain worsening, we decided to switch to infliximab 500 mg. Clinical symptoms resolved progressively and lower back pain disappeared. At month 4 of treatment, the patient suddenly relapsed, by not known trigger, with generalised psoriatic lesions including *de novo* PP, with hyperkeratotic plaques symmetrically distributed, thenar, hypothenar and at the central region of palms and soles, with intense erythema, scaling and deep fissuring (Fig. 1A). In contrast, peripheral and axial joint symptoms were still well controlled. CRP was discretely elevated at 6.2 mg/L.

Infliximab was withdrawn and secukinumab was started at 150mg/month, after 3 months increased to 300mg/month, and stopped due to lack of efficacy after 5 months. Consequently, based on an initial response to ustekinumab, 90 mg ustekinumab /12 weeks was started again. Due to the persistent activity of PP with increased scaling and fissuring, functional disability and substantial impairment in quality of life, ustekinumab had to be withdrawn after 5 months. In January 2020 a switch to the JAK inhibitor tofacitinib at standard dosages (5 mg/BID) was decided. Rapid, clinically significant and sustained improvement of PP lesions was observed upon tofacitinib (Fig. 1B). The patient is now in remission for the last six months without signs of PP, psoriasis vulgaris or musculoskeletal symptoms.

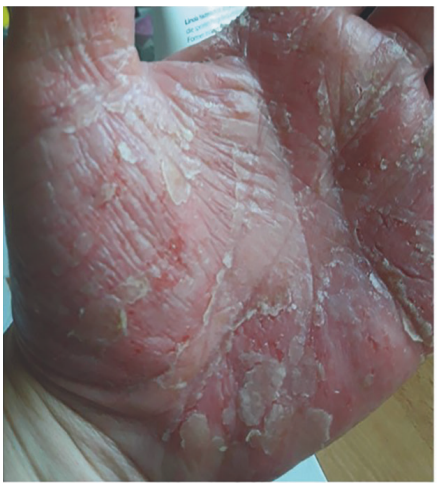

Fig. 1. Palmar lesions appeared under infliximab therapy.

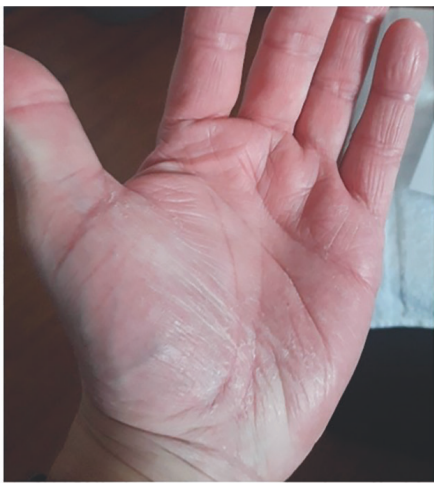

Fig. 2. Five days after starting tofacitinib.

Various factors including smoking, stress and trauma can trigger PP in genetically susceptible individuals leading to excessive cytokine production and keratinocyte proliferation. Inducible IL-23 expression can trigger a TH17 response with local production of TNF-α, IL-17, and IL-22 that induce keratinocytes stimulation and recruitment of neutrophils. Neutralisation of TNF-α, IL-23 and IL-17A has demonstrated to be effective in patients presenting with PP who do not respond to topical or other systemic medications (3-7). In our patient, targeting these cytokines one by one, turned out to be insufficient, and TNF inhibition even triggered PPP lesions, as previously described (4).

Tofacitinib inhibits Janus kinases JAK1, JAK2 and JAK3, involved in the signalling of a variety of cytokines present in psoriasis (IL-23, IL-22 and IFN-gamma), hence, the complete remission observed in this refractory PP patient indicates that downregulation of the signalling of more than one individual cytokine by tofacitinib prevents potential escape mechanisms of inflammation during single cytokine targeting. To the best of our knowledge, this is the first case report of a successful therapy of a patient with PP using tofacitinib.

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