Clinical response to brodalumab in a patient affected by refractory SAPHO syndrome

Sirs,

Synovitis-acne-pustulosis-hyperostosis-osteitis (SAPHO) syndrome is a rare disease of unknown origin, characterised by different clinical manifestations, *i.e.* peripheral synovitis, sternoclavicular inflammatory involvement, acne, palmoplantar pustular psoriasis, hyperostosis, osteitis, and sacroiliitis. The complexity and severity of its symptoms make the treatment of SAPHO particularly challenging. In these patients a multidisciplinary approach is needed.

We present a case of SAPHO syndrome featuring severe palmoplantar pustulosis (PPP) unresponsive to multiple biotechnological treatments but successfully managed with brodalumab.

In 2016, a 38-year-old male patient with HLAB27-negative spondyloarthritis and recurrent anterior uveitis came to our attention. Latent tuberculosis was detected during routine biochemical assessment, prompting initiation of prophylactic isoniazid treatment. Subsequently, adalimumab and methotrexate were introduced, leading to complete control of arthritis symptoms.

After 36 months of substantial remission, the patient developed inflammatory sternoclavicular and costosternal joint involvement (finding confirmed by total-body scintigraphy), trunk and facial acne, and severe PPP (Fig. 1). A diagnosis of SAPHO syndrome was made. Initial treatment with infliximab at 5 mg/kg intravenously every 8 weeks partially improved joint symptoms but had no effect on skin. We then adjusted the infliximab dosage to 8 mg/kg and co-administered apremilast. This approach, based on one efficacy report in SAPHO syndrome (1), yielded no improvement, especially concerning skin involvement. Due to persistence of disease activity, especially PPP, the patient was switched to secukinumab at 300 mg every 28 days, maintaining joint remission but minimally impacting skin lesions. Secukinumab was then discontinued after 12 months due to inefficacy on PPP. After a multidisciplinary consultation involving rheumatologists and dermatologists, we transitioned the patient to brodalumab at 210 mg every 14 days.

Within 3 months, the patient experienced complete resolution of acne and PPP (Fig. 1), along with sustained joint remission. After 15 months of brodalumab therapy, the patient remains in complete remission. As of today, the therapeutic approach to SAPHO syndrome essentially consists of off-label treatments, which typically have empirical effectiveness data. Therefore, we based our therapeutic choices on the available literature data. The effectiveness of secukinumab as a treatment for SAPHO syndrome is described in a case series conducted by Wang *et al*. (2). This study describes a series of 4 patients affected by SAPHO syndrome showing an improvement of skin lesions and arthritis after secukinumab treatment. Notably, these improvements were observed without the concomitant use of any supplementary treatments. These results could be justified by the pivotal role of IL-17 in the pathogenesis of PPP in SAPHO syndrome (3). Brodalumab, a monoclonal antibody targeting interleukin-17 receptor (IL-17RA), was then considered due to its efficacy in psoriasis and psoriatic arthritis (4-6). Furthermore, as reported in a single case report, authored by Masahide *et al*. (7), brodalumab showed efficacy in a patient affected by SAPHO syndrome refractory to IL-17A inhibition. This additional effect may be attributable to the inhibition of multiple IL-17 isoforms (A,C,E,F) achieved by IL-17RA blockade (8). However, data on brodalumab efficacy in SAPHO syndrome and PPP are currently scarce and controversial (9). A case series by Pinter *et al*. evaluated brodalumab in four PPP patients demonstrating either no improvement or minimal improvement (10). Our decision to shift to brodalumab to treat our patient was based on the fact that the cases in which this drug revealed limited efficacy exclusively involved patients affected by PPP, with no additional manifestations of SAPHO syndrome.

On these premises, IL-17RA inhibitor brodalumab revealed to be a viable treatment choice for patients with SAPHO not responsive to TNF-alpha and IL-17A inhibitors. Additionally, given its complex nature and heterogeneity, SAPHO syndrome requires a multidisciplinary approach involving both rheumatologists and dermatologists.

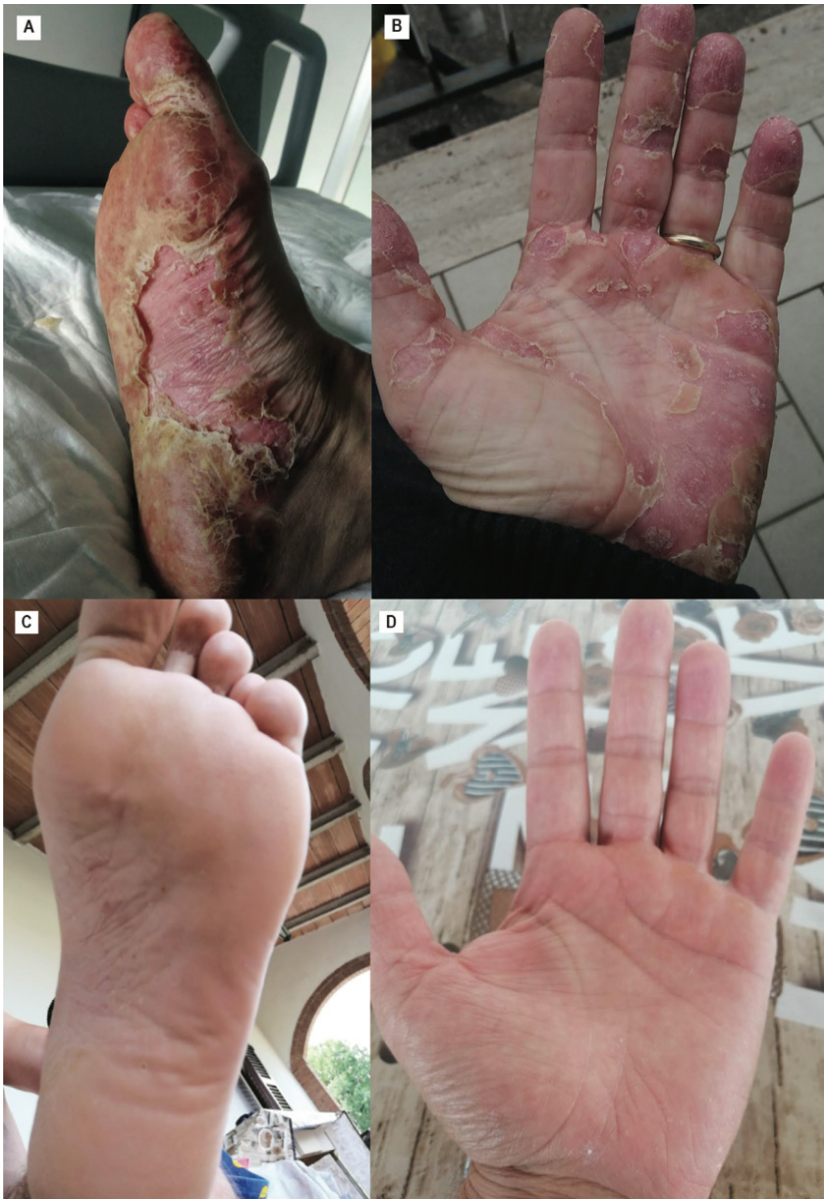

Fig. 1. Palmoplantar pustulosis at SAPHO syndrome onset (**A**, **B**) and its evolution after 3 months of treatment with brodalumab (**C**, **D**).

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