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Successful Treatment of Rituximab-Associated Palmoplantar Pustulosis With Apremilast in a Patient With Seropositive Rheumatoid Arthritis

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The use of biological therapies for the treatment of rheumatoid arthritis (RA) has significantly improved outcomes in patients with an inadequate response to conventional synthetic disease-modifying antirheumatic drugs. Paradoxically, individual patients may experience worsening of preexisting or new onset of psoriasis, including palmoplantar pustulosis, most often in association with the use of tumor necrosis factor (TNF) inhibitors and less frequently with non-TNF biologics.[1,2]

We here report the case of a 57-year-old woman presenting to our clinic with active rheumatoid factor and anticitrullinated protein antibody–positive RA, diagnosed in 2016. Pretreatment included methotrexate and certolizumab. Under tocilizumab, she developed psoriatic skin lesions. Subsequently, tofacitinib was started but ineffective. Abatacept was initiated, and RA disease activity subsequently improved, but after 5 months, psoriatic skin eruptions were noted, and abatacept was stopped, leading to cutaneous healing. The first course of rituximab (2 infusions of 1000 mg 2 weeks apart) in April 2018 was well tolerated and resulted in a decrease of Disease Activity Score in 28 joints from 6.2 to 3.6. Leflunomide was added at 20 mg/d in August 2018, whereas prednisone was maintained at 10 mg/d. A second course of rituximab was well tolerated. In April 2019, the patient received the first infusion of the third rituximab course, but 3 days later, she started to develop palmoplantar pustulosis, which deteriorated over the course of 1 week. Despite immediate treatment with topical steroids and phototherapy, as well as a temporary increase of oral prednisone, the palmoplantar pustular lesions did not improve (Figure, left side). Six weeks after the last rituximab infusion, apremilast was started and increased up to 30 mg twice daily. It was well tolerated, and significant improvement of palmoplantar pustulosis was observed within 6 weeks (Figure, right side).

Data from the French AIR registry have questioned a causal association of rituximab and new onset or worsening of preexisting psoriasis, showing incidence ratios similar to the general population.[3] In the German RABBIT registry, the use of rituximab was not associated with a significant increase in new-onset psoriasis in comparison to conventional synthetic disease-modifying antirheumatic drug treatment.[1]

Palmoplantar pustulosis has rarely been reported following treatment with rituximab and may present a particular challenge given the pharmacokinetic and pharmacodynamic characteristics of rituximab. As B-cell depletion may persist for at least 6 months following rituximab, we were hesitating to use an alternative biologic within a few weeks after the last rituximab infusion. In contrast, apremilast as a phosphodiesterase type 4 inhibitor has a short half-life that would allow cessation in case of adverse events.

A proposed treatment algorithm for TNF inhibitor–associated psoriasis was recently published.[4] Palmoplantar pustulosis remains difficult to treat. A recent review concludes that phototherapy, topical steroids, and cyclosporine may ameliorate psoriatic skin disease.[2] Few cases reported on the successful use of apremilast in patients with palmoplantar pustulosis, all of them not being associated with the use of biologics.[5]

To our knowledge, our case report is the first that describes the efficacious and safe use of apremilast in palmoplantar pustulosis following the use of rituximab in a patient with seropositive RA and may represent a promising treatment option in affected patients.

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ISSN: 1076-1608
DOI: 10.1097/RHU.0000000000001415

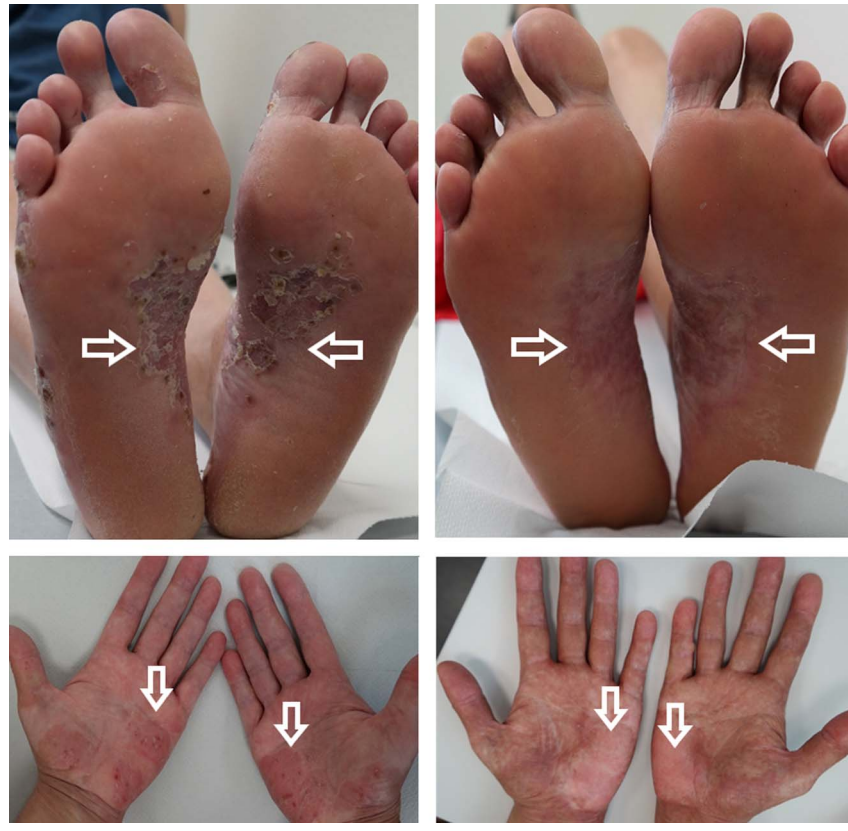

FIGURE. Rituximab-associated palmoplantar pustulosis. Rheumatoid arthritis patient with treatment-associated palmoplantar pustulosis (left side). The patient showed significant improvement after 6 weeks of treatment with apremilast (right side).