

New Onset of Psoriasis in a Patient with Rheumatoid Arthritis Treated with Rituximab

To the Editor:

We read with interest reports by Thomas, *et al*¹ and by Hardcastle, *et al*² reporting new onset of psoriasis during rituximab (RTX) therapy for rheumatoid arthritis (RA). We have observed an additional case in a patient who had received several biological agents prior to RTX.

A 44-year-old white woman with a history of erosive peripheral and symmetrical polyarthritis with positive rheumatoid factors and anticyclic citrullinated peptide antibodies had been diagnosed as having RA. She was seen for the first time in 1998. She had no other relevant history, especially no personal or familial psoriasis. Her polyarthritis was successively treated with traditional disease-modifying antirheumatic agents [sulfasalazine, methotrexate (MTX)] in combination with corticosteroids (7.5 to 10 mg/day). Because of progression of structural damage on wrist and hand radiographs, she received tumor necrosis factor- α (TNF- α)-blocking agents (infliximab, followed by etanercept and lastly adalimumab) between 2002 and 2010, with initial clinical improvement followed by secondary loss of efficacy. These treatments were well tolerated without inducing skin disease. No MTX was given in combination with the TNF- α -blocking agents because the patient did not want to continue this medication. In 2010, abatacept was introduced, giving mild results and again with no adverse event. In May 2012, RTX therapy was planned and she received 2 infusions of 1000 mg 2 weeks apart (with paracetamol, methylprednisolone, and chlorpheniramine). The treatment was well tolerated and resulted in substantial improvement (28-joint Disease Activity Score decreased from 5.3 to 4.3). Corticosteroids may be tapered from 5 to 1 mg/day. Five months after this first RTX administration, she developed a psoriatic plaque on the scalp (Figure 1) with no other skin lesion. She was evaluated by a dermatologist who confirmed the diagnosis of psoriasis. Three months later, the psoriatic lesion remained stable without progression or appearance of new plaques. A second course of RTX is planned in 2013.

RTX is a chimeric monoclonal antibody targeting B cells and approved for treatment of lymphoma and RA. Psoriasis is a T cell and macrophage-driven autoimmune disease. We describe a patient with refractory RA who received 3 successive anti-TNF- α agents, abatacept, and RTX. New-onset psoriasis under RTX has been reported in a limited number of cases (n = 6), both in biologic-naïve patients³ and in patients previously treated with TNF- α -blocking agents or anakinra^{1,4}. In all these cases, the patients had no personal or family history of psoriasis and they did not take



Figure 1. A patient received 2 infusions of RTX therapy 1000 mg 2 weeks apart. Five months after this first RTX administration she developed psoriatic plaque on the scalp.

a medication known to induce psoriasis. Our patient had the same clinical profile, but prior to RTX she received 4 biologics for a long period (9 years) without a cutaneous adverse event. It is now admitted that psoriasis (new-onset or reactivation) may be a paradoxical side-effect of TNF- α -blocking agents⁵. Similarly, abatacept has been associated with the development of new-onset psoriasis⁶. RTX has not proved its efficacy in psoriasis. However, some recent reports suggest that this biologic may improve psoriasis⁷ and psoriatic arthritis (PsA)⁸. Alternatively, in a patient without arthritis, RTX has been associated with the development of psoriasis and PsA⁹. All these data were limited, but we would remind readers that the development of psoriasis under TNF- α blockers was not observed during randomized clinical trials but with the use of these drugs in real-life practice. Thomas, *et al* reported 2 cases of new onset of psoriasis from the AIR registry, but these cases were not confirmed (no dermatological diagnosis for 1 case and the second was a patient-reported skin lesion)¹. Their calculated incidence rate of new-onset psoriasis was low (0.52 to 1.04/1000 person-years) and did not argue for a causative role of RTX, a conclusion that must be tempered by the unconfirmed dermatological diagnosis. In the case reported by Hardcastle, *et al*, atypical itchy psoriatic lesions were described involving the sole², while in other cases of psoriasis occurring under RTX, psoriasis was usually limited³. The mechanisms leading to the development of such psoriatic lesions remain hypothetical. An imbalance between B and T cells favored by B cell depletion, a susceptibility to infection, and a T cell immune reaction against murine components of the chimeric monoclonal antibody have been suggested^{3,4}.

Prior to RTX, our patient had received several biologics capable of inducing development of psoriasis, thus we can suggest that the immunological mechanisms involved in the induction of these skin reactions differ between RTX and TNF- α antagonists. In this sense, plasmacytoid dendritic cells, which are believed to play a role in psoriasis induced by TNF- α blockers¹⁰, are probably not involved with RTX. Finally, gathering data for all cases of new-onset psoriasis during RTX therapy from the different registries may probably help us to better understand the mechanisms of such lesions.

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J Rheumatol 2013;40:7; doi:10.3899/jrheum.130050