Atypical Psoriasis Following Rituximab for Rheumatoid Arthritis

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Atypical Psoriasis Following Rituximab for Rheumatoid Arthritis

To the Editor:

Rituximab (RTX) is a chimeric B cell-depleting monoclonal antibody used in the treatment of non-Hodgkin’s lymphoma and rheumatoid arthritis (RA), and with an emerging role in connective tissue disease therapy. Its use has rarely been associated with skin reactions, in particular psoriasiform skin lesions. We report a case of atypical psoriasis reactivation in a patient with RA following RTX, and we review the literature.

A 49-year-old woman presented in 1999 with a seronegative polyarthritis affecting the hands, elbows, feet, hips, and knees. At the time she gave no history of psoriasis. Over the next 10 years she received several disease-modifying antirheumatic drugs (DMARD) sequentially and in combination including sulfasalazine, hydroxychloroquine, methotrexate, azathioprine, gold, and leflunomide. Disease activity persisted, although radiographs remained nonerosive. Her 28-joint Disease Activity Score (DAS28) in September 2010 was 6.45 despite triple DMARD therapy, and she was assessed for a biologic. RTX was chosen in preference to anti-tumor necrosis factor (TNF) treatment because of recurrent shingles and a previous positive Heaf test (chest radiograph normal, quantiferon test negative).

In November 2010 she received 2 intravenous infusions of 1 g RTX 2 weeks apart with paracetamol, chlorpheniramine, and methylprednisolone premedications. Ten weeks posttreatment her DAS28 score was 4.32, but she had developed skin lesions (present for 6 weeks) on the sole of her right foot plus some nail changes suggestive of psoriasis. Two months later, further red, itchy, scaly patches around the ankles and heels were seen, including some well-defined plaques (Figure 1). She was given methylpred

Figure 1. A. Right medial ankle showing well-defined patches of scaly erythema, in keeping with psoriasis. B. Right heel with erythema, scaling, and resolving pustular changes, more in keeping with plantar pustular psoriasis.
nisolone acetate intramuscular injection 120 mg and assessed by a dermato-
ologist (SG) who confirmed the clinical diagnosis of acral psoriasis. Onset of
the rash 1 month post-RTX treatment suggested causation. Topical treat-
ments containing steroid, salicylic acid, and coal tar proved effective, with
improvement over several weeks. On reviewing the notes it was estab-
lished that she had had a single episode of guttate psoriasis in her teens;
however, she had never developed extrarticular manifestations suggestive
of psoriatic arthropathy; her pattern of joint disease (predominantly
metacarpophalangeal, proximal interphalangeal joints, and knees) was
more in keeping with RA. The patient’s brother has psoriasis.

There are conflicting reports about the relationship between psoriasis
and RTX therapy. In oncology, Mielke, et al reported a case of a patient
with non-Hodgkin’s lymphoma treated with RTX and cyclophosphamide,
donorubicin, vincristine, and prednisone (CHOP) who developed psoriasis
and arthritis within 6-8 weeks of exposure\(^1\). In the rheumatology setting,
Markatseli, et al\(^2\) reported a patient with seropositive RA developing de
novo psoriatic skin lesions of the arms and thighs 10 days after a second
course of RTX treatment. Dass, et al\(^3\) published a case series of 3 patients
with inflammatory arthritis (1 seronegative, 1 seropositive, and 1 with sys-
temic lupus erythematosus) developing skin psoriasis following RTX treat-
ment, but the interval between treatment and the development of the psori-
atic skin lesions was longer in each case (4-6 months) than in our case.
There has been 1 case of RTX used specifically to treat skin psoriasis\(^4\)
because R-CHOP chemotherapy had previously improved psoriasis in the
same patient: this resulted in worsening of the skin psoriasis within weeks.
However, Cohen\(^5\) reported a patient with psoriatic arthritis and a history of
skin psoriasis 15 years previously who received RTX for his joint disease,
with no adverse skin effects.

The particularly noteworthy features of our case are the atypical distri-
bution of the skin lesions (confined to the legs and feet, asymmetrically)
and their quality, which around the ankles resembled chronic plaque psori-
asis and on the soles plantar pustular psoriasis. The interval between RTX
treatment and psoriasis development was relatively short (1 month).
Although in our patient there was a history of psoriasis and rheumatoid fac-
tor and anticitrullinated protein antibodies were negative (raising the pos-
sibility of underlying psoriatic arthropathy), this problem has also been
seen in seropositive RA and those with no prior history of psoriasis\(^2,3\).
As our patient had an initial good clinical response to RTX, we do not consid-
er this event to be an absolute contraindication to retreatment in the future.

The mechanism by which RTX may cause or worsen skin disease is
unclear, as psoriasis is thought of as a T cell-mediated disease. Potential
mechanisms proposed by other authors include disruption of regulatory
actions of B cells on T cells\(^2,3\), increased susceptibility to infections, which
may trigger plaque development\(^2,3\), and T cell reactivity against the murine
component of the chimeric molecule\(^1,2\). Interestingly, there have also been
several case reports of the induction of psoriasis following anti-TNF treat-
ment\(^6\), especially infliximab\(^7\), despite the fact that anti-TNF is an estab-
lished treatment for psoriatic arthritis.

Clinicians should be aware of the possible link between B cell deple-
tion with RTX and development or worsening of psoriasis. This is a con-
sideration when planning treatment, in the same way as with hydroxy-
chloroquine, corticosteroids, and anti-TNF agents, which can exacerbate or
unmask psoriasis in an unpredictable way. As use of biologic agents
becomes more widespread in rheumatology it is likely that further such
phenomena will emerge.

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