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Adverse skin reactions to infliximab in the treatment of intraocular inflammation

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Abstract

TNFα inhibitors are more widely used in the treatment of intraocular inflammation, thus ophthalmologists should become aware of possible adverse events, associated with this form of treatment. Herein we report two cases of cutaneous adverse events in uveitis patients treated with infliximab. In one patient, the primary outbreak of pustular psoriasis was observed after her third infusion. A second patient developed impetigo contagiosa induced by Staphylococcus aureus. Thus patients undergoing treatment with infliximab should be monitored carefully since dermal infections and pustular psoriasis, which may be triggered by streptococcal infection, may occur under this regime.

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In the recent past, increasing numbers of patients with various forms of uveitis have been treated with TNF α inhibitors. The more widespread use of these drugs confronts physicians with increased numbers of adverse side effects. Skin reactions as seen in patients treated for Crohn's disease, Behcet's disease, or rheumatoid arthritis with TNF α inhibitors, have however, been described in uveitis patients only once. We present two uveitis patients who developed adverse skin reactions following infliximab treatment.

Case Series

Patient 1

A 55-year-old female patient with a family history of psoriasis and with recurrent episodes

of bilateral idiopathic panuveitis, associated with oral ulcerations unresponsive to standard immunomodulatory treatment consisting of 300 mg cyclosporin in addition to 150 mg azathioprine, was started on infliximab (5 mg/kg body weight) in addition to methotrexate (15 mg/week). After the third infusion at week 6, the patient developed hyperkeratotic erythematous lesions with small white pustules on the palmar/plantar surfaces of her hands (Figure 1a) and feet (Figure 1c), erythematous scaly lesions on the scalp (Figure 1d) and annular erythemato-squamous plaques on the back and lower extremities, which progressed during therapy at weeks 14 and 24. Swabs proved negative for bacteria and fungi. Biopsy of a representative lesion demonstrated psoriasiform dermatitis. (Figure 1b) Cultures of swabs taken from the tonsils grew hemolytic streptococci and haemophilus influenzae. Infliximab was discontinued and the pustules slowly healed over the following 4 months. The patient was then started on adalimumab 20 mg/ weekly with good clinical response, and so far no psoriatic lesion has been seen four months into treatment.

Patient 2

An 18-year-old woman was treated for chronic idiopathic intermediate uveitis, unresponsive to standard immunomodulatory treatment consisting of 20 mg methotrexate combined with 2 g/day mofetil mycophenolate, with infliximab (5 mg/kg body weight) at weeks 0, 2, and 6 and then every 8 weeks, along with methotrexate 12.5 mg/week. Her fourth infusion had to be postponed by 2 weeks due to sinus infection, which she was treated for by her general physician, using 3 g/day of oral penicillin over a period of 10 days. At 5 weeks

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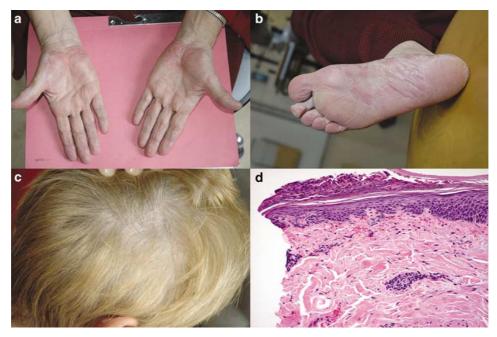


Figure 1 (a) Hyperkeratotic erythematous lesions with small white pustules on the palmar/plantar surfaces of the patient's hands and feet, resembling psoriasis pustulosa. (b) Psoriatic skin lesion on the plantar surface. (c) Erythematous scaly lesions on the scalp. (d) Skin biopsy of palmar changes. Haematoxylin and eosin stained section (magnification \times 200) reveals microabscesses within the cornified layer, slight epidermal hyperplasia and focal hypogranulosis.

after her fifth infusion she developed small red patches, blisters, erosions, and scaly yellowish crusted lesions 4-10 mm in diameter in the inguinal area and the proximal thighs, spreading to the perioral region over the following three days. A dermatologist diagnosed impetigo contagiosa. Skin swabs were positive for penicillin-resistant *Staphylococcus aureus*. Treatment with 3 g/day oral cephalosporine for 1 week promptly resolved these symptoms. The next infliximab infusion given 5 weeks later was well tolerated, and the impetigo remained in remission.

Comment

Various adverse reactions involving the skin, such as rash, pruritus, urticaria, dry skin, fungal dermatitis, onychomycosis, eczema, and bullous eruptions have frequently been described in patients with rheumatoid arthritis or Crohn's disease treated with infliximab.⁵ A far less frequent cutaneous adverse event of anti-TNF-therapy is the induction of psoriatic lesions. It has been described so far only in eight patients. Six off these were treated with infliximab, for Crohn's disease, ^{6,7} seropositive rheumatoid arthritis (RA), Behcets disease, or ankylosing spondylitis.⁴ The other two patients treated for their RA recieved either adalimumab or etanercept.⁴

We describe two patients with skin alterations following infliximab treatment for uveitis. The exact

mechanism leading to the pustular psoriasis in our first patient remains elusive. Psoriasis is a T-cell-mediated disease. Chronic infections with various agents as well as superantigens released from streptococci might activate T cells. Thus, in patients with a family history of psoriasis, infliximab might cause a reactivation of silent streptococcal infection, followed by the induction of psoriatic lesions. In our second patient, the infectious agent causing the prior sinus infection may not have completely cleared, despite penicillin treatment. The isolated staphylococci from the skin were penicillin resistant, and the reinstallation of infliximab might have supported the spreading of the bacterial infection to the skin, leading to impetigo contagiosa.

Our cases stress the importance of subclinical infections in infliximab-treated individuals that might lead to adverse events involving the skin.

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