

Case Report

Paradoxical pustular psoriasis flare after infliximab therapy

抗腫瘤壞死因子誘發反常式牛皮癬復發的病例

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While tumour necrosis factor (TNF)- α blockers have proven efficacy for the treatment of both arthritis and psoriasis, new appearance or exacerbation of psoriasis after TNF- α blockers has been increasingly reported. We report the first local case of psoriasis flare after infliximab treatment and review the literature on the topic.

抗腫瘤壞死因子對牛皮癬及牛皮癬關節炎的療效顯著，但抗腫瘤壞死因子誘發反常式牛皮癬復發或新發病例卻時有報告。我們現報告一本地首例，並檢討報導相關的醫學文獻以作參考。

Keywords: Adverse event, psoriatic arthritis, psoriasis flare, tumour necrosis factor- α blockers

關鍵詞：不良事件，牛皮癬關節炎，牛皮癬復發，抗腫瘤壞死因子

Introduction

Tumour necrosis factor (TNF)- α blockers offered great excitement and advances in the treatment of psoriatic arthritis and psoriasis. However, there have been case reports of new-onset psoriasis or worsening of existing psoriasis after the

administration of TNF- α blockers. We hereby report the first local case of this phenomenon and review the literature.

Case report

A 33-year-old gentleman was started on intravenous infliximab treatment for active psoriatic arthritis from August 2008. He had no family history of psoriasis or chronic arthritis. He had active arthritis over the elbows, wrists, metacarpophalangeal joints, proximal and distal interphalangeal joints, knees and toes. Tender and swollen joint counts were 16 and 11, active and tender dactylitis were present in two digits, with enthesitis over both Achilles tendons. Extensive psoriasis was present with a psoriasis area and severity index (PASI) of 19.5. The pain severity and

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patient global health assessment on a 100 mm visual analogue scale were 70 and 100. He had chronic hepatitis B infection and had a history of hepatitis in 2007 after taking herbal medications. He received entecavir prophylaxis during infliximab treatment.

The patient experienced rapid improvement in skin and joint conditions since week 2 after infliximab and the improvement was maintained till week 18 (Figure 1). Around week 19, just one week before scheduled infliximab infusion, he was admitted for cellulitis of both shins. He experienced worsening psoriasis with thick plaques reappearing on the shins. He stretched the lesions and peeled off the scaling skin. There was diffuse redness and hotness over both shins. Patient had

a fever of 38°C and serum WBC was $14 \times 10^9/L$. Erythema of the shin improved with a course of ampicillin and cloxacillin. However, plaque lesions persisted and new pustular lesions arose on palms and soles (Figure 2). The patient also experienced mild joint symptoms including three tender joints, one swollen joint and three dactylitis. Differential diagnoses were either inadequate dosing of anti-TNF therapy or a paradoxical flare of psoriasis due to anti-TNF therapy.

Infliximab infusion was stopped and the patient was put on topical steroid treatment with partial resolution of skin lesions. He was then given cyclosporine, which he could not tolerate. His skin lesions were later controlled by acitretin and the joint symptoms were controlled by sulphasalazine.

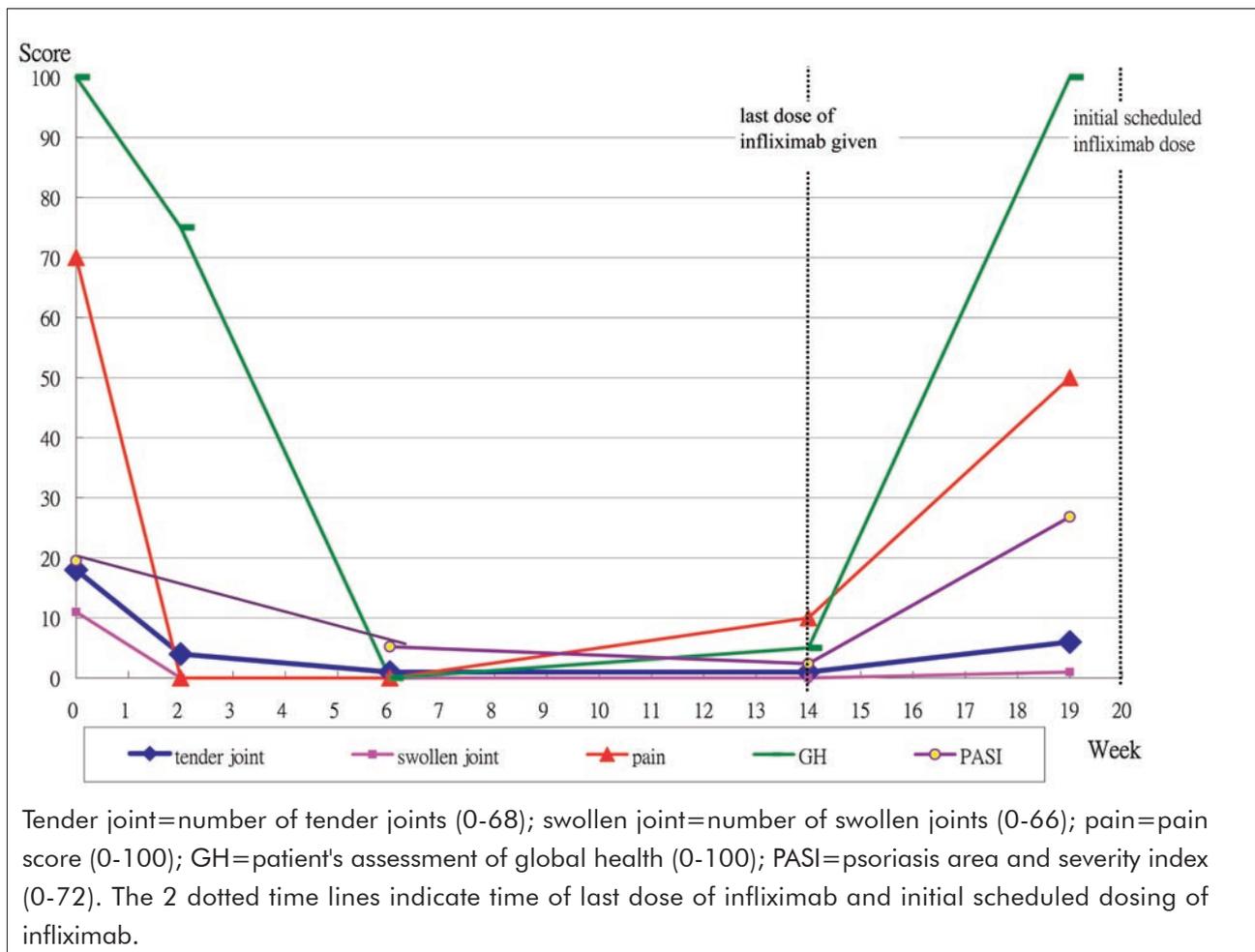


Figure 1. Disease activity after infliximab treatment.



Figure 2. Flare of psoriasis and pustular eruptions after infliximab.

Discussion

TNF- α blockers have been very effective in the control of both joint and skin manifestations of psoriatic arthritis. However, the sudden appearance or exacerbation of psoriasis during anti-TNF- α treatment has been increasingly described in case reports and series. We present the first local case of paradoxical pustular psoriasis eruption related to TNF- α blockers. The presentation of pustular psoriasis can mimic cellulitis.

Goiriz et al reported eight cases of psoriasis receiving anti-TNF treatment in a dermatology unit.¹ Two had unexpected appearance of psoriasis while 6 had exacerbations and changes in morphology of existing psoriasis. The fact that one case had a flare-up of pustular psoriasis on

adalimumab re-challenge suggested a causal role by TNF- α blockers. The authors emphasised the change in morphology of psoriatic lesions. Six patients developed guttate psoriasis between 15 days and 18 months after anti-TNF- α treatment, and lesions appeared in areas of the body that were free of psoriasis at baseline. The same group reviewed another 14 cases in the literature and found that 13 cases had new-onset psoriasis while one had exacerbation during anti-TNF- α treatment. All three TNF- α blockers in the market including etanercept, infliximab and adalimumab were involved. The clinical type of psoriasis was another matter of interest. Nine out of the 14 reported cases had pustular psoriasis with or without plaque lesions.

Wollina et al reviewed 120 cases of TNF- α blocker induced psoriasis or psoriasiform exanthemata in

2008.² Again, all three TNF- α blockers in the market were implicated. TNF- α blockers were given to patients with rheumatoid arthritis (n=61) followed by ankylosing spondylitis (n=21), psoriasis (n=10) and other diagnoses. Psoriasis (excluding palmoplantar pustular type) was the commonest type of skin lesion (n=73), followed by palmoplantar pustular psoriasis (n=37) and nail psoriasis (n=6). Seventy-four cases had newly induced psoriasis and 25 had aggravation of pre-existing psoriasis. The mean time from the first administration of TNF- α blocker to the onset of psoriasis flare was 9.5 months. The psoriasis flare might occur after a single dose of TNF- α blocker, or the flare might be delayed up to 63 months after the first administration of drug. Variable outcomes were reported. Forty-seven patients discontinued TNF- α blockers with or without adjunct anti-psoriatic therapy. Twenty-one, twenty and three patients achieved complete, partial remission and stable disease respectively. Fifty-three patients continued TNF- α blockers with anti-psoriatic therapy despite cutaneous adverse effects; complete, partial remission and stable disease were achieved in 24, 27 and 2 patients respectively. These results were not different from those who discontinued TNF- α blockers. In six patients with an immediate switch to another TNF- α blockers, 5 patients improved.

In a study using data from the British National Registry from 2001 to 2007, there were 25 incident cases of new-onset psoriasis out of 9826 rheumatoid arthritis patients treated with TNF- α blockers. The incidence of psoriasis was 1.04 (95% CI 0.67-1.54) per 1000 person years. Patients treated with adalimumab had a higher rate of incident psoriasis when compared with etanercept (IRR 4.6, 95% CI 1.7-12.1) and infliximab (IRR 3.5, 95% CI 1.3-9.3).³

It is an interesting paradox that while TNF- α blockers are on one hand efficacious for psoriasis, they may also trigger the occurrence of psoriasis. The underlying pathomechanisms for the induction of psoriasis remains elusive. A number of

possibilities have been proposed. Firstly, it could be a misdiagnosis of primary rheumatic disease, where psoriatic arthritis could precede psoriasis in 15% of cases. Others have suggested drug hypersensitivity reaction or a bacterial infection due to TNF- α suppression.⁴ However, these are not likely. The pattern of the psoriatic adverse events did not match the rapid time to onset of allergic reaction and biopsies of selected cases have confirmed typical psoriasis instead of infection.^{1,5} It is possible that TNF- α blockers disrupt the balance between various cytokines. TNF- α blockers may have a role in triggering cross-reactivity implicated in psoriasis.⁶ One hypothesis is on the balance of TNF- α and type 1 interferon (IFN)- α . Dermal plasmacytoid dendritic cells (PDC) which produce IFN- α have been implicated in playing a key role in the early phase of induction of psoriasis, and TNF- α downregulates PDC and thus IFN- α .^{7,8} TNF inhibition may produce locally sustained IFN- α production leading to the outbreak of psoriasis.⁹ Raised lesional type I IFN- α activity has been demonstrated in TNF induced psoriasis as compared to psoriasis vulgaris.¹⁰ Although not a common side effect, the clinician should be alerted to new eruptions or aggravation of pre-existing psoriasis during TNF- α blocker treatment. There is no easy answer as to whether to continue anti-TNF- α therapy if a psoriatic eruption occurs. Variable courses have been observed in the literature. Many physicians would stop the treatment. There are however, some reports on improvement of psoriasis despite continuation of anti-TNF- α with or without anti-psoriasis treatment. If re-challenge of anti-TNF- α therapy is considered, a second TNF inhibitor may be a better choice.

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