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Case Report:

Infliximab treatment in two Chinese patients with psoriatic arthritis

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Abstract: Psoriatic arthritis (PsA) is a rheumatoid factor (RF)-seronegative systemic inflammatory disorder associated with psoriasis. Current treatment for PsA in China is still focused on disease modifying anti-rheumatic drugs (DMARDs). In this paper, we report two Chinese patients with active longstanding PsA treated with infliximab, a human-mouse chimeric monoclonal antibody against tumor necrosis factor alpha (TNF-α). The results show that infliximab acted quickly and effectively in relieving peripheral and axial symptoms and refractory skin lesions, even in recombinant human TNF-α receptor (rhTNFR)-resistant case. The take-home message from our cases is that infliximab is a useful therapeutic option for refractory PsA, especially when a patient has a combination of psoriasis and psoriatic arthritis. Further local evidence and experience must be accumulated in order to make anti-TNF-α therapy more accessible to PsA patients in China.

Key words: Refractory psoriatic arthritis, Skin lesions, Infliximab, Anti-tumor necrosis factor alpha (TNF-α) treatment
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1 Introduction

Psoriatic arthritis (PsA) is a rheumatoid factor (RF)-seronegative inflammatory disorder associated with psoriasis. In China it affects 1.23‰ of the population and can lead to disability. Presently, in China, drug therapy for PsA is still focused on disease modifying anti-rheumatic drugs (DMARDs), such as methotrexate, sulfasalazine, leflunomide, and cyclosporine (Chinese Rheumatology Association, 2004). For those with severe and refractory PsA, however, these agents are insufficient. According to the lastest "treatment recommendations for psoriatic arthritis" released by the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) (Ritchlin *et al*., 2009), tumor necrosis factor alpha (TNF-α) inhibitors, such as recombinant human TNF-α receptor (rhTNFR), adalimumab, and infliximab, are recommended in moderate to severe PsA, a recommendation supported by large scale randomized controlled trials (Antoni *et al*., 2002; 2005a; 2005b; van der Heijde *et al*., 2007; Voulgari *et al*., 2008). Anti-TNF-α agents play an increasing role in PsA treatment. There has been little literature about the applications of anti-TNF-α agents in PsA in China. Thus, we present these cases of PsA treated with infliximab, a useful therapeutic option for refractory PsA.

2 Case reports

2.1 Patient 1

A 29-year-old female was diagnosed with psoriasis in 1990. Although her psoriasis skin lesions were under control, she began to develop severe joint symptoms in 1999. Her symptoms included swollen and painful distal and proximal interphalangeal joints, as well as wrist joints. She also experienced prolonged morning stiffness. Despite receiving treatments with

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methotrexate, sulfasalazine, leflunomide, and non-steroid anti-inflammatory drugs (NSAIDs) at various points, her joint symptoms continued to evolve. Gradually, the patient's knee and ankle joints also became affected. X-ray studies of the hands revealed bone erosions. Treatment with infliximab (5 mg/kg given by an intravenous infusion at Weeks 0, 2, 6, and 14) was started in June 2009, combined with weekly oral doses of methotrexate (10 mg, once a week). We assessed morning stiffness duration (min), patient pain assessment with visual analogue scale (VAS, 0–100 mm), the disease activity score 28 (DAS28), and the health assessment questionnaire disability index (HAQ-DI, 0–3) to evaluate the disease progression before and after the infliximab treatment. The assessments were conducted 7 d after each administration (Fig. 1). After the first administration, the patient's morning stiffness and pain dramatically decreased from 180 min and 85 mm to 60 min and 52 mm, respectively. There was also a significant reduction in the DAS28 from 8.02 to 5.86 and in the HAQ-DI from 2.25 to 1.75. After the second use of infliximab, the patient's DAS28 and HAQ-DI levels gradually decreased, dropping to 2.6 and 0.5, respectively, when last measured. The patient's assessment indices also improved remarkably from her previous evaluations, a good indication that the disease was being stablilized. As a result, we planed to prolong the administration interval to more than eight weeks in her follow-up treatments.

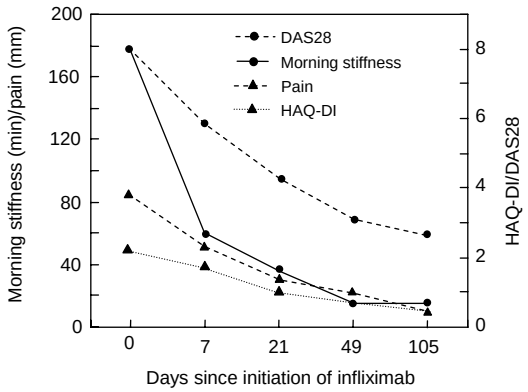

Fig. 1 Changes in different assessment indices since beginning the use of infliximab

2.2 Patient 2

A 43-year-old man presented to the rheumatology clinic with lower back pain and stiffness in March 2008. He was diagnosed with psoriasis 11 years prior and received topical steroid ointment, methotrexate, and etretinate with little effect. In the previous three years, the patient had developed lower back pain and stiffness, also complicated with right hip pain. Physical examination showed that the patient had large areas of a squamous rash on his limbs and trunk. There was also mild limitation in the forward flexion of the patient's lumber spine and his right hip motion. The maximal anteflexion value in Schober test measured less than 15 cm. Computed tomography (CT) of the sacroiliac joints demonstrated fuzziness of the articular surface and magnetic resonance imaging of right hip revealed synovitis. RF was negative. The patient was subsequently diagnosed with PsA and was treated with methotrexate and rhTNFR (25 mg, twice one week, given by subcutaneous injection). Two weeks later, the patient's pain and stiffness in the lower back and right hip were relieved dramatically, with the bath ankylosing spondylitis disease activity index (BASDAI) score decreasing from 6.4 to 3.0, and the bath ankylosing spondylitis functional index (BASFI) score from 93 to 48. Psoriatic lesions also partially dissipated. He continued rhTNFR treatment with gradually decreased dosages (to 12.5 mg once a week one year later). In September 2009, his back pain and psoriasis skin lesions deteriorated, and he was not capable of turning over or getting out of the bed by himself. The rhTNFR dose was switched to 25 mg twice one week again, but the patient still did not experience improvement. The BASDAI and BASFI increased to 7 and 95, respectively. He was subsequently treated with infliximab (5 mg/kg). Two days after his first dose, his back pain was relieved, he could get out of the bed by himself, and the rash started to resolve. Two weeks later, the patient's back pain was markedly relieved with BASDAI and BASFI decreasing to 2 and 30, respectively, and the psoriasis rash was also assuaged notably (Fig. 2).

3 Discussion

PsA is an inflammatory arthropathy associated with psoriasis. It involves peripheral and axial joints, dactylitis, as well as enthesitis. Although this disorder varies considerably in its clinical manifestations,

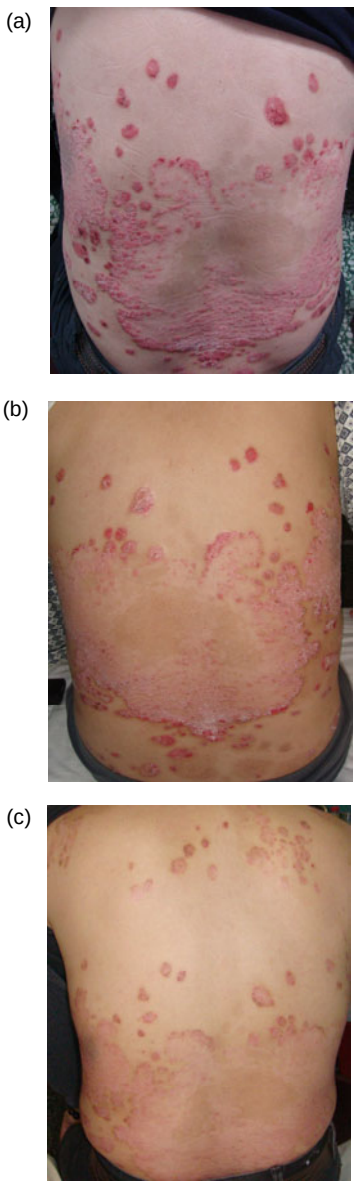

Fig. 2 Psoriasis rash before and after infliximab therapy
(a) Before therapy; (b) 2 d after first use; (c) 14 d after first use

some cases can be debilitating and destructive, causing erosive joint damage, functional impairment, and premature death (Wong *et al*., 1997; Sokoll and Helliwell, 2001). In China, PsA affects 1.23‰ of the population and approximately 15% of PsA patients have symmetric polyarticular joint involvement, a marker of a poor outcome. About 5% of PsA patients manifest as spondylitis, which resembles ankylosing spondylitis (Chinese Rheumatology Association, 2004). Traditional treatment agents for PsA include NSAIDs and DMARDs such as methotrexate, leflunomid, cyclosporine, and azathioprine. Traditional agents, however, are sometimes not enough to control the disease. With the development of anti-TNF-α biological therapies, treatments of PsA patients have more options.

Infliximab is a human-mouse chimeric immunoglobulin G_1 (IgG_1) monoclonal antibody that specifically targets TNF-α, a proinflammatory factor that plays a pivotal role in many autoimmune diseases. Anti-TNF-α therapy has proven to have superior efficacy and better prevention of erosive joint damage than traditional DMARDs therapy (Gratacos *et al*., 2007; van der Heijde *et al*., 2007; Haugeberg *et al*., 2009). In addition, infliximab was approved by the European Union (EU) and by the Food and Drug Administration (FDA) for the treatment of psoriasis and active PsA. Although anti-TNF-α therapy has become an important option in developed countries, in China, PsA treatment is still mainly focused on DMARDs therapy, and few anti-TNF-α therapies have been tried.

In this report, we present two Chinese patients with active longstanding PsA who responded well to infliximab after failing to achieve satisfactory benefit from long-term and adequate DMARDs therapy. The patients represented two important clinical patterns of PsA: symmetric polyarthritis and predominant spondyloarthritis (Moll and Wright, 1973). The PsA polyarthritis in Patient 1 was rapidly and efficaciously controlled after infliximab use. Patient 2 had rhTNFR as his first biological therapy and had a good response, but as the disease relapsed, he developed resistance to adequate doses of rhTNFR, and then was switched to infliximab. Patient 2 also had a satisfactory response to infliximab, suggesting this may be a better drug than rhTNFR for PsA. Smith *et al*. (2007) also reported similar experiences. Moreover, the refractory psoriasis skin lesions in Patient 2 also showed marked remission after infliximab therapy. And therefore, when a patient has a combination of psoriasis and psoriatic arthritis, a systemic agent is reasonable (Boehncke *et al*., 2010).

The successful experience in these two patients suggests that infliximab acts quickly and effectively in relieving peripheral and axial symptoms and skin lesions, even in rhTNFR-resistant case. Interestingly, local databases have no reports of infliximab use in Chinese PsA patients. Further local evidence and

experience must be accumulated in order to revise the current domestic guidelines as well as to make anti-TNF-α therapy more accessible to PsA patients in China.

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