Psoriasis induced by infliximab in a Saudi patient with ankylosing spondylitis

Iehab B. Alabed, MD, *Khalid A. Qushmaq,* MD, FACP, *Muhammad A. Khan,* MD, MACP.

ABSTRACT

يترتب على العلاج بالأدوية المضادة لعامل تنخر الأورام ألفا (TNF–alfa) العديد من الآثار الجانبية وذلك بالرغم من فعاليتها العالية في علاج التهاب الفقار المقسط وما يُصاحب ذلك من حالات اعتلال المفاصل الفقرية.

نستعرض في هذا المقال حالة مريض سعودي يشكو من التهاب الفقار المقسط وأُصيب فيما بعد بمرض الصدفية من الدرجة الحادة وذلك بعد علاجه بعقار إنفليكسيماب (infliximab). لم يشكوا المريض من الصدفية سابقاً وليس لديه أي تاريخ بالمرض في العائلة، كما أن ليس لديه أياً من العوامل التي تزيد من خطر الإصابة بالصدفية. لقد طرحنا هذه الحالة من أجل إلقاء الضوء على هذا الأثر الجانبي الذي ظهر في المريض.

Although the therapeutic uses of tumor necrosis factor alpha antagonists have added a highly effective treatment of ankylosing spondylitis and associated spondyloarthropathies, they are associated with many untoward effects. We describe a Saudi patient with ankylosing spondylitis who developed severe psoriatic lesions in treatment with infliximab. He had no personal, or family history of psoriasis, and no other triggering factors known to induce psoriasis.

Saudi Med J 2010; Vol. 31 (9): 1054-1056

From the Department of Internal Medicine (Alabed, Qushmaq), Rheumatology Division, King Fahad Medical City, Riyadh, Kingdom of Saudi Arabia, and the Department of Medicine (Khan), Case Western Reserve University, MetroHealth Campus, Cleveland, United States.

Received 27th April 2010. Accepted 9th August 2010.

Address correspondence and reprint request to: Dr. Iehab Alabed, Department of Internal Medicine, Rheumatology Division, King Fahad Medical City, PO Box 4756, Riyadh, Kingdom of Saudi Arabia. Tel. +966 553460470. Fax. +966 (1) 2889999 Ext. 1395. E-mail: aba1974@hotmail.com

Ankylosing spondylitis (AS) is chronic inflammatory disorder of uncertain etiology that primarily affects the axial skeleton (sacroiliac [SI] joints and spine); SI joint involvement (sacroiliitis) is one of its hallmarks.[1] The disease usually starts in the late teens and early twenties, and belongs to a group of rheumatic diseases known as the spondyloarthropathies.[1,2] It can lead to progressive bony fusion of the SI joints and the vertebral column, and some patients may also show involvement of the hip and/or shoulder joints, and extra-articular structures such as eyes, and rarely the ascending aorta and aortic valve.[1,2] The disease is associated with HLA-B27 although the strength of this association is weaker among Arabs, particularly in Saudi Arabia and adjacent countries in the gulf.[1-3] Tumor necrosis factor (TNF)-alpha antagonists, such as infliximab, belong to a newer group of drugs called the biologicals, which stop inflammation by blocking TNF-alpha, a pro-inflammatory cytokine. Anti-TNF therapy is dramatically effective in AS and related spondyloarthropathies, but has many potential untoward effects.[1,4,5] A rare side effect is the occurrence of new-onset psoriasiform eruptions after initiation of TNF antagonist therapy in many inflammatory diseases, reported primarily from Europe and North America.[5-8] The major reported clinical presentation is palmoplantar pustulosis, sometimes accompanied with plaque-like psoriasis.[6,7] This is an unusual side effect, as TNF inhibitors have documented benefit in the treatment of psoriasis. Herein, we describe a Saudi patient with AS who developed severe psoriasis, including nail involvement, on treatment with infliximab for his AS that was non-responsive to conventional treatment. He had no personal or family history of psoriasis. This case is intended to highlight the occurrence of this side effect in a Saudi patient.

Case Report. This is a case of a 30-year-old male patient that was seen in the cardiology unit with left-sided chest pain along with ECG changes and cardiac enzymes elevation. Cardiac catheterization showed severe ostial narrowing of his left main and right main

coronary arteries for which he underwent a bypass graft. During the operation, the surgeon noticed that the wall of the ascending aorta was inflamed, and so a consultant rheumatology was requested. On obtaining a detailed clinical history, we found that he had a longstanding history of chronic back pain and stiffness for the last 15 years. His symptoms were worse in the morning, improved on exercise, but not with rest. He had seen many physicians and visited many medical centers and did not get a clear well-established diagnosis for his symptoms. He had been treated intermittently with many different analgesics. He was diagnosed with AS, and he had radiographic evidence of bilateral sacroiliitis (**Figures 1 & 2**), with no evidence of peripheral arthritis, psoriasis, or inflammatory bowel disease. His AS was clinically active with a Bath AS Disease Activity Index (BASDAI) score of 6, and his erythrocyte sedimentation rate (ESR) was 45 mm/first hour. He was HLA-B27-negative. His symptoms had not adequately responded to various non-steroidal anti-inflammatory drugs (NSAIDs) in the past, and we treated him with meloxicam 15 mg orally once daily. Due to lack of adequate response, he was started on infliximab by intravenous infusion at the usual dose of 5 mg/kg at 0, 2, and 6 weeks, and then every 8 weeks. He showed an excellent response with a BASDAI score of 2. After the fifth dose infusion of infliximab, he developed symmetric erythematous desquamating large plaques located on the palms and soles, with multiple pustules overlying erythematous pruritic skin, with typical psoriatic nail involvement with nail discoloration, thickening, onycholysis, and subungual keratosis (**Figures 3 & 4**). He had no peripheral arthritis or inflammation of his fingers or toes. He had not taken any drug known to induce psoriasis and his

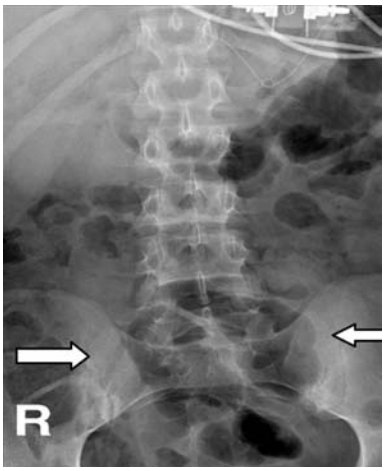

Figure 1 - Frontal radiograph shows bilateral sacroiliac joint erosions and iliac side subchondral sclerosis (arrows).

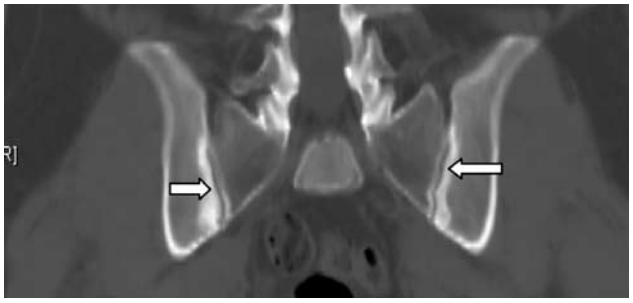

Figure 2 - Axial CT scan shows erosions and iliac side subchondral sclerosis of both sacroiliac joints (arrows).

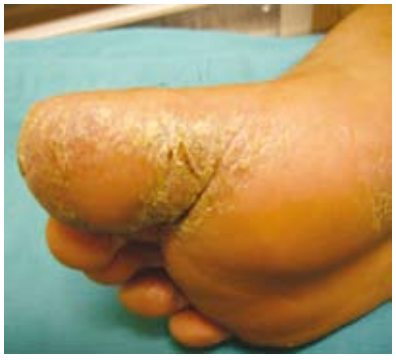

Figure 3 - Sharply demarcated and red scaling plaque at the right foot sole

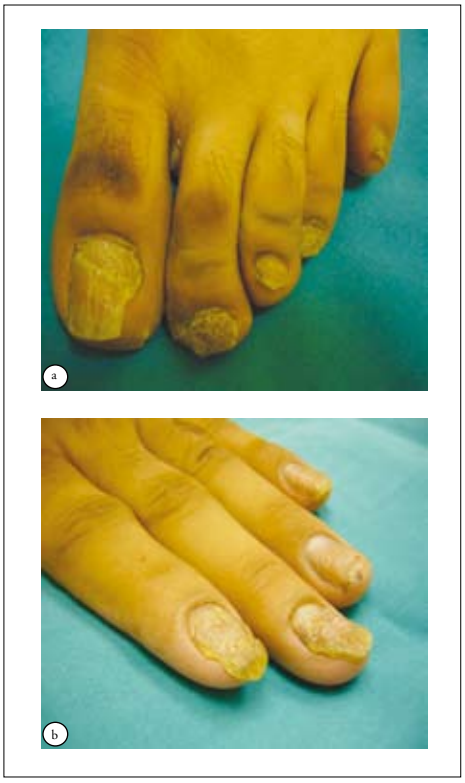

Figure 4 - Typical psoriatic nail involvement with onycholysis, pitting, leukonychia, and subungual hyperkeratosis of **a)** nails of the feet and **b)** nails of the hand.

family and personal history was negative for psoriasis. A skin biopsy of the lesions on the hands showed typical histology of psoriasis, with mild to moderate hyperkeratosis, hypergranulosis, psoriasiform epidermal hyperplasia with lymphocytic perivascular infiltrates in the dermis. His psoriasis was treated with topical therapy (calcipotriene and betamethasone topical ointment once daily) and infliximab infusions were continued. There was only mild improvement of the skin lesions, and therefore infliximab was discontinued and treatment was switched to etanercept, which resulted in partial resolution of the psoriasis.

Discussion. Several adverse reactions have been associated with the use of TNF-alpha blocking therapy, such as allergic reaction, skin abnormalities, upper respiratory and opportunistic infections, activation of latent tuberculosis, neutropenia, interstitial lung disease and peripheral demyelinating disorders.[5] The adverse effects affecting the skin include injection-site reactions and infusion-related urticaria, skin infections, eczema, flushing, pruritus, erythema multiforme, Stevens-Johnson syndrome or toxic epidermal necrolysis.[5] The TNF antagonist-induced psoriasis is a newly recognized, but uncommon adverse effect of TNF antagonists, not restricted to any single TNF-antagonist, but seems to be a class effect of TNF-blockade itself, since they have been reported with use of each of the 3 TNF-antagonists: infliximab, adalimumab, and etanercept.[6-9] The psoriasis vulgaris form is the most common form in the general population, whereas the palmoplantar pustulous pattern, as seen in our patient, is the most common presentation of psoriasis induced by TNF-antagonists. These skin lesions may not require cessation of therapy with TNF-antagonists, but there may be a need to change the TNF antagonist if the lesions are unresponsive to conventional psoriasis treatment. The skin lesions usually resolve on discontinuation of the treatment with TNF antagonists. The underlying pathophysiologic mechanisms responsible for this paradoxical clinical response remain elusive.[5-10] Recent comprehensive reviews have explored possible immunologic mechanisms of action, and it appears to involve a disruption in cytokine imbalance following TNF inhibition that results in an increased expression of type I interferons.[6] Patients with palmoplantar pustulosis have been reported to have lower expression of TNF-alpha in the eccrine palmar sweat gland and in the skin, when compared with healthy patients.[9]

In conclusion, we described a Saudi patient with AS who developed severe psoriatic lesions on treatment with infliximab. He had no personal or family history of psoriasis and no other triggering factors known to induce psoriasis. This case is intended to highlight the occurrence of this rare side effect. A large prospective observational cohort study is needed to further investigate the prevalence and reason for an apparent relationship between anti-TNF therapy and new onset psoriasis suggested by published case reports.

References

1. Khan MA. Ankylosing Spondylitis. New York: Oxford University Press; 2009.
2. Khan MA. Update on spondyloarthropathies. ***Ann Intern Med*** 2002; 136: 896-907.
3. Khan MA. HLA and spondyloarthropathies. In: Mehra N, editor. The HLA Complex in Biology and Medicine. New Delhi (India): Jaypee Brothers Medical Publishers; 2010. p. 422–446.
4. Baraliakos X, Braun J. Anti-TNF-alpha therapy with infliximab in spondyloarthritides. ***Expert Rev Clin Immunol*** 2010; 6: 9-19. Review.
5. Sfikakis PP. The first decade of biologic TNF antagonists in clinical practice: lessons learned, unresolved issues and future directions. ***Curr Dir Autoimmun*** 2010; 11: 180-210.
6. Seneschal J, Milpied B, Vergier B, Lepreux S, Schaeverbeke T, Taïeb A. Cytokine imbalance with increased production of interferon-alpha in psoriasiform eruptions associated with antitumour necrosis factor-alpha treatments. ***Br J Dermatol*** 2009; 161: 1081-1088.
7. Wollina U, Hansel G, Koch A, Schönlebe J, Köstler E, Haroske G. Tumor necrosis factor-alpha inhibitor-induced psoriasis or psoriasiform exanthemata: first 120 cases from the literature including a series of six new patients. ***Am J Clin Dermatol*** 2008; 9: 1-14. Review. Erratum in: Am J Clin Dermatol 2008; 9: 347.
8. Moustou AE, Stratigos AJ, Vergou T, Gregoriou S, Georgala S, Danopoulou I. Arthralgia as an adverse event to infliximab: a reactive arthritis or triggering of psoriatic arthritis? Successful management by switching to etanercept. ***J Eur Acad Dermatol Venereol*** 2009; 23: 968-969.
9. Michaëlsson G, Kajermo U, Michaëlsson A, Hagforsen E. Infliximab can precipitate as well as worsen palmoplantar pustulosis: possible linkage to the expression of tumour necrosis factor-alpha in the normal palmar eccrine sweat duct? ***Br J Dermatol*** 2005; 153: 1243-1244
10. Nestle FO, Conrad C, Tun-Kyi A, Homey B, Gombert M, Boyman O, et al. Plasmacytoid predendritic cells initiate psoriasis through interferon-alpha production. ***J Exp Med*** 2005; 202: 135-143.