Treatment of psoriasis with etanercept in immunocompromised patients: Two case reports

Clara De Simone, Francesca Perino, Giacomo Caldarola, Magda D’Agostino and Ketty Peris

Abstract
Tumour necrosis factor (TNF)-α blocking agents have revolutionized the treatment of psoriasis and psoriatic arthritis. Concerns remain about increased susceptibility to infection and onset of malignancies, and the use of TNF-α agents in patients with HIV infection or undergoing immunosuppressant treatment is debated. We report cases of severe plaque psoriasis in a patient with HIV infection and in a liver transplant recipient who were successfully treated with etanercept, an anti-TNF-α agent, without notable side-effects.

Keywords
Antitumour necrosis factor-α agents, comorbidities, etanercept, psoriasis, psoriatic arthritis

Introduction
Tumour necrosis factor (TNF)-α blocking agents have good efficacy and safety profiles, and have revolutionized the treatment of psoriasis and psoriatic arthritis. The main concerns related to these therapies are the increased susceptibility to infectious diseases and the onset of malignancies in treated patients. The use of anti-TNF-α agents in people with HIV infection or those undergoing immunosuppressive therapy (e.g. transplant recipients) is debated, because such treatment could represent an adjunctive risk in those whose immunological status renders them susceptible to infection and malignancy.

Data regarding the use of anti-TNF-α agents in immunocompromised patients are scarce, since such patients are excluded from clinical trials and few cases are reported in the literature. Case reports, however, indicate that biological treatments appear to have minimal impact on HIV viral load and CD4 count, and also on allograft function.
Case reports

We report two cases of severe plaque psoriasis that were successfully treated with an anti-TNF-ω agent (etanercept) without notable side-effects. Case 1 was a patient with HIV infection; Case 2 was a liver transplant recipient.

Case 1 was a 50-year-old man with a history of psoriasis since the 1980s, treated with standard regimens of topical therapies and a 3-month course of acitretin (25 mg/day, orally) in 2003, without consistent results. The patient had a history of drug addiction and began highly active antiretroviral therapy with lamivudine, zidovudine and efavirenz following a positive HIV test in 2000. In 2010 he was referred for severe psoriasis with a Psoriasis Area and Severity Index (PASI) score of 24.2.\textsuperscript{13} Serological tests confirmed HIV infection, and revealed previous hepatitis B virus (HBV) infection (absence of HBV surface antigen and HBV DNA), active hepatitis C virus (HCV) infection (genotype 2a/2c; viral load 1 200 000 IU/ml). His CD4\textsuperscript{+} T lymphocyte count was 445 cells/µL, representing 21\% of total lymphocyte count. The infectious disease consultant agreed to etanercept treatment (50 mg twice weekly for 12 weeks, then 50 mg once weekly; treatments were administered subcutaneously). After 6 months’ treatment the patient’s PASI score was 1.8 without any significant change in total and CD4\textsuperscript{+} lymphocyte counts, HCV viral load or liver function tests (Figures 1 and 2); these parameters were assessed monthly. No reactivation of HBV infection or opportunistic infection was observed. At the time of writing the patient is still being followed up through clinical and laboratory assessment at 3-month intervals. During this time, mild relapses of psoriasis have occurred, which have been controlled with topical therapy.

Figure 1. Lymphocyte and CD4\textsuperscript{+} cell counts during etanercept treatment in a 50-year-old man with HIV infection and a 30-year history of psoriasis.
liver function tests have not shown substantial changes over the follow-up period.

Case 2 was a 56-year-old man with history of psoriasis since 2009 and liver transplantation in 2010 for alcoholic cirrhosis. Antirejection therapy comprised of standard regimens of prednisone, tacrolimus and mycophenolate mofetil. The patient presented in June 2013 with severe psoriasis (PASI 26.2) that was nonresponsive to standard therapy with topical steroids and acitretin. Treatment with 50 mg etanercept twice weekly, subcutaneously, for 12 weeks was initiated, resulting in a reduction in his PASI score (to 3.5). The dosage was then changed to 50 mg weekly and PASI improvement was maintained throughout the 6-month treatment period. Monthly liver function tests showed normal results during treatment. There were no infective complications or dysfunction of the transplanted organ during etanercept treatment. A new therapeutic cycle with etanercept (ongoing at the time of writing) started in September 2014 following a relapse of psoriasis. Efficacy was again confirmed without notable side-effects.

**Discussion**

The onset or exacerbation of psoriasis, a T-helper (Th)-1 cell-mediated disease, may appear paradoxical in an immunosuppressed patient with depletion of T lymphocytes (due to HIV or drug addiction). HIV infection can both trigger and exacerbate psoriasis. In psoriasis, the presence of CD8+ T cells in the epidermis and dermis is associated with active disease. HIV infection induces a change in the T-cell balance, with a decrease in CD4+ cells and an increase in CD8+ cells that produce increased quantities of interferon-γ. The expansion in CD8+ cell numbers may explain the...
paradoxical exacerbation of psoriasis in a setting of immunosuppression. An alternative hypothesis is that the T-cell imbalance is associated with a depletion of CD4\(^+\) suppressor T cells, which results in uncontrolled proinflammatory pathways.\(^{15}\)

In a transplanted patient, immunological status is influenced by the immunosuppressive agents of the antirejection regimen, which act on different T-cell subsets. For example, mycophenolic acid and sirolimus have an inhibitory effect on Th1 and also on Th17; sirolimus can also induce proliferation of regulatory T lymphocytes.\(^{16,17}\)

**Conclusions**

In patients with HIV infection or pharmacological immunosuppression and severe psoriasis, the use of anti-TNF-\(\alpha\) agents should be limited to those unresponsive to standard therapeutic regimens. We chose etanercept to treat both patients reported here because of its good efficacy and safety profiles, and its convenient dose regimens.

**Declaration of conflicting interest**

The authors declare that there are no conflicts of interest.

**Funding**

Editorial assistance was provided by Ray Hill on behalf of HPS–Health Publishing and Services Srl and funded by Pfizer Italia.

**References**

1. Ryan C, Abramson A, Patel M, et al. Current investigational drugs in psoriasis. *Expert Opin Investig Drugs* 2012; 21: 473–487.
2. Semble AL, Davis SA and Feldman SR. Safety and tolerability of tumor necrosis factor-\(\alpha\) inhibitors in psoriasis: a narrative review. *Am J Clin Dermatol* 2014; 15: 37–43.
3. Menon K, Van Voorhees AS, Bebo BF Jr, et al. Psoriasis in patients with HIV infection: from the medical board of the National Psoriasis Foundation. *J Am Acad Dermatol* 2010; 62: 291–299.
4. Cepeda EJ, Williams FM, Ishimori ML, et al. The use of anti-tumour necrosis factor therapy in HIV-positive individuals with rheumatic disease. *Ann Rheum Dis* 2008; 67: 710–712.
5. Lindsey SF, Weiss J, Lee ES, et al. Treatment of severe psoriasis and psoriatic arthritis with adalimumab in an HIV-positive patient. *J Drugs Dermatol* 2014; 13: 869–871.
6. Sellam J, Bouvard B, Masson C, et al. Use of infliximab to treat psoriatic arthritis in HIV-positive patients. *Joint Bone Spine* 2007; 74: 197–200.
7. Lee ES, Heller MM, Kamangar F, et al. Long-term etanercept use for severe generalized psoriasis in an HIV-infected individual: a case study. *J Drugs Dermatol* 2012; 11: 413–414.
8. Brokalaki EI, Voshege N, Witzke O, et al. Treatment of severe psoriasis with etanercept in a pancreas-kidney transplant recipient. *Transplant Proc* 2012; 44: 2776–2777.
9. Collazo MH, González JR and Torres EA. Etanercept therapy for psoriasis in a patient with concomitant hepatitis C and liver transplant. *P R Health Sci J* 2008; 27: 346–347.
10. Hoover WD. Etanercept therapy for severe plaque psoriasis in a patient who underwent a liver transplant. *Cutis* 2007; 80: 211–214.
11. Mansouri B, Patel M and Menter A. Tumour necrosis factor-\(\alpha\) inhibitor use in patients with psoriasis with organ transplantation. *Br J Dermatol* 2013; 169: 481–483.
12. Ting PT and Koo JY. Use of etanercept in human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) patients. *Int J Dermatol* 2006; 45: 689–692.
13. Fredriksson T and Pettersson U. Severe psoriasis – oral therapy with a new retinoid. *Dermatologica* 1978; 157: 238–244.
14. Patel RV and Weinberg JM. Psoriasis in the patient with human immunodeficiency virus,
part 1: review of pathogenesis. *Cutis* 2008; 82: 117–122.

15. Morar N, Willis-Owen SA, Maurer T, et al. HIV-associated psoriasis: pathogenesis, clinical features, and management. *Lancet Infect Dis* 2010; 10: 470–478.

16. Abadja F, Atemkeng S, Alamartine E, et al. Impact of mycophenolic acid and tacrolimus on Th17-related immune response. *Transplantation* 2011; 92: 396–403.

17. Chung BH, Kim KW, Kim BM, et al. Dysregulation of Th17 cells during the early post-transplant period in patients under calcineurin inhibitor based immunosuppression. *PLoS One* 2012; 7: e42011.