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A Case of Etanercept Induced Palmoplantar Pustular Psoriasis

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Abstract

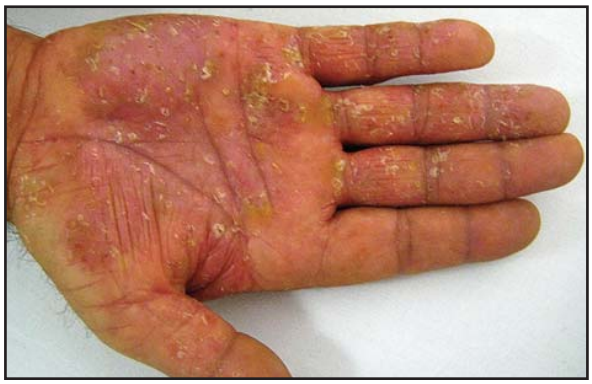
Observations: Etanercept is a human recombinant soluble tumor necrosis factor α (TNF-α) receptor fusion protein. Etanercept has been used successfully to treat a wide range of inflammatory disorders including psoriasis and psoriatic arthritis resistant to classical disease-modifying treatments. The widespread use of TNF-α antagonists led to the recognition of adverse effects. Herein, we report a case of palmoplantar pustular psoriasis in a 37-year-old man during the etanercept therapy.

Introduction

Etanercept, infliximab and adalimumab are the most commonly used anti-tumor necrosis factor-α (TNF-α) biological agents [**1**]. Etanercept is a human recombinant soluble TNF-α receptor fusion protein that has been used for the treatment of inflammatory conditions refractory to classical disease-modifying treatments including rheumatoid arthritis, ankylosing spondylitis, *Crohn*'s disease, psoriasis and psoriatic arthritis [**2**]. In recent years, the increased utilization of TNF-α antagonists has lead to the recognition of paradoxical adverse effects, defined as the onset or exacerbation of disorders [**3**]. The case reports of psoriasiform eruption during TNF-α antagonist therapy have been published increasingly [**1, 2, 3, 4**]. This cutaneous side effect seems to be a class effect as such reaction has been reported regarding patients who are taking each of these 3 TNF-α antagonists [**1, 5**]. We are specifying a case of new-onset psoriasis in a patient with ankylosing spondylitis during etanercept therapy.

Case Report

A 37-year-old man with a 7-year history of ankylosing spondylitis refractory to numerous disease modifying anti-rheumatic drugs (salicylazosulfapyridine, methotrexate), was seen with a 8 months history of a pustular eruption on the palms and soles. Approximately 9 months after the initiation of etanercept therapy (50 mg once-weekly), he gradually developed erythematous papulopustular lesions on the palms and soles (**Figures 1, 2**). The patient had no other comorbidities or was taking any medication other than etanercept. He denied any personal or family history of psoriasis. A skin biopsy sample was taken and neutrophilic pustule in psoriasiform epidermal hyperplasia with hyperkeratosis and confluent parakeratosis, regular acanthosis, loss of granular layer and spongiosis were seen. Dilatation of superficial dermal capilla-



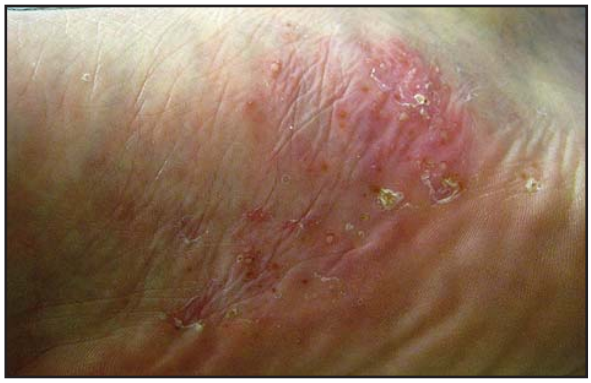


Figure 1 and 2. Erythematous scaly pustular lesions on the palms and soles

ries, perivascular monocytic inflammation was noticed in the upper dermis (**Figure 3**). The findings were consistent with psoriasis. We considered the skin lesions with the clinical and histopathological findings as palmoplantar pustular psoriasis due to etanercept. 0.05% clobetasol 17-propionate cream is used once daily for 3 weeks repeatedly for two months than combined with topical calcipotriol but the treatment benefit was inadequate. Despite the inadequate response to topical therapies, etanercept treatment was continued due to the effective control of joint disease. During the follow-up, at the 20th month of etanercept therapy, psoriasiform eruption development has been observed at his knees and elbows (**Figure 4, 5**).

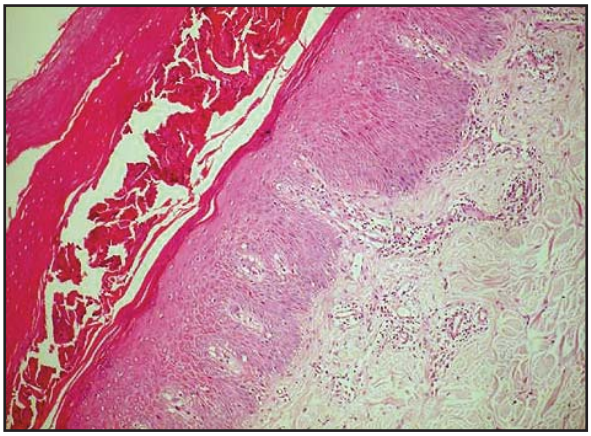
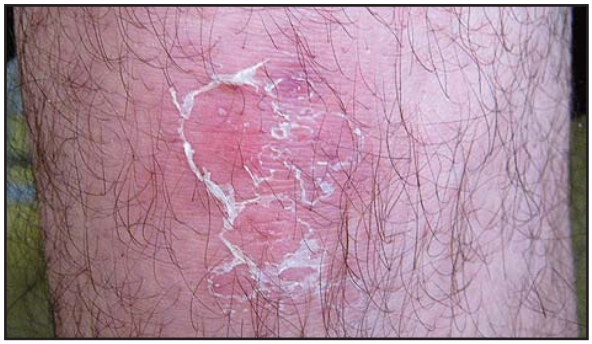


Figure 2. Neutrophilic pustule in psoriasiform epidermal hyperplasia with hyperkeratosis and confluent parakeratosis, dilatation of superficial dermal capillaries and perivascular monocytic inflammation (H&E X 10)

Discussion

TNF-α antagonists have given new insights in the treatment of rheumatic diseases, inflammatory bowel diseases and have had great success in the treatment of psoriasis and psoriatic arthritis [**6**]. Long-term use of systemic immunsuppressive agents in psoriasis management can cause serious side effects like hepatotoxicicity, nephrotoxicity, teratogenicity and myelosuppresion. Therefore, biologic agents promising long term safety in psoriasis treatment are introduced in dermatologic practice [**7**]. Although the treatment effect mechanisms of TNF-α antagonists in psoriasis, are not precisely known, it may involve the reduction of inflammatory cytokines in psoriatic skin and decrease epidermal hyperplasia and cutaneous inflammation [**2,**



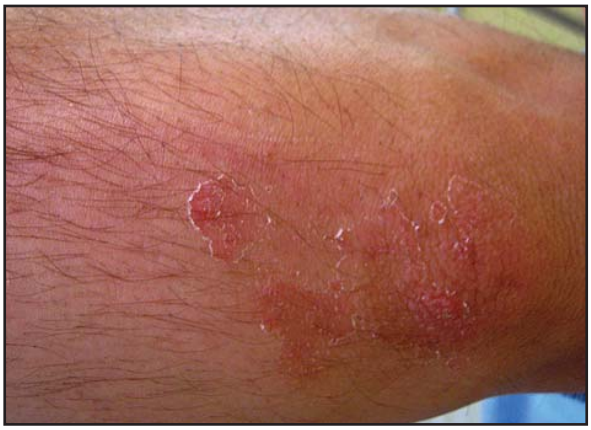


Figure 4 and 5. Erythematous scaly patches on the knees and elbows

8, 9]. Skin reactions during treatment with anti-TNF-α have been described by several researchers. The most common side effects of TNF-α antagonists are itching, pain, swelling and redness at the site of injection. The reported cutaneous adverse events include eczematoid nonspecific rashes, lichenoid eruption, erythema multiforme, lupus erythematosus, bullous skin lesions, vasculitis and cutaneous lymphoma [**2, 4, 8**]. In recent years several cases with psoriasiform eruptions during anti-TNF-α therapy have been described. Approximately half of the psoriasiform eruption cases are palmoplantar pustulosis and not only pustular psoriasis, plaque type of psoriasis, disseminated erythematous squamous eruption and also nail involvement were reported [**1, 9**]. The occurrence of pustular lesions ranges from few days to several years after administration and it is not related with age and gender [**1**]. It is not agreed on the mechanism underlying psoriasis onset or exacerbation during TNF-α antagonist therapy and it suggests a complex role for TNF-α antagonists in psoriasis [**4**]. An increase in the peripheral T cells expressing the chemokine receptor CXR3, that have been found to be upregulated in psoriatic lesions and promotes the infiltration of auto-reactive T cells to the skin, was shown regarding the chronical arthritis patients on such medications [**1, 2**]. The excessive inhibition of TNF-α increases the cutaneous IFN-α release that has recently been implicated in the induction of psoriatic skin lesions [**1, 2**]. It is also considered that TNF-α antagonists promotes infections which may trigger the cutaneous diseases [**4**]. *Michaëlsson* et al suggest that a decrease in TNF-α has been shown to be associated with palmoplantar pustulosis and might therefore be worsened by the treatment [**10**]. The paradoxical effect developed by the complex immune mechanisms suggest an unknown heterogeneity in the physiological properties of psoriasis [**11**]. Further studies are required to identify risk factors for onset or exacerbation of psoriasis during TNF-α antagonist therapy and advanced investigations are required to understand pathophysiologic mechanism of such cases. Although the development of psoriasiform eruption does not always require treatment discontinuation, further studies are necessary to determine the best therapeutic approach.

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