CASE REPORT

Lichen planus secondary complications associated with the use of biologic therapy for rheumatoid arthritis

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Abstract

Objectives: Biologic therapy such as Etanercept, which is a tumor necrosis factor alpha (TNF-α) inhibitor, has been extensively used as election therapy in rheumatoid arthritis. The purpose of this case presentation was to inform about the possibility that lichen planus lesions could potentially become complicated by secondary infections in patients treated with Etanercept. Furthermore, we aimed at analyzing if the complication of the cutaneous lesion was coincidental or it was due to the immunosuppressive systemic therapy, and whether the infected lesion would respond to antibiotic therapy.

Case summary: The patient was a 59-year-old woman with rheumatoid arthritis and that have had lichen planus lesions for approximately 25 years. Only recently, she had been received immunosuppressive therapy (Etanercept and Methotrexate). Further on, the lichen planus flared up with a secondary infection determined by a Methicillin-sensitive Staphylococcus aureus. Uncommon myocardial complications were also characteristic of this case. Results: While a case report described already the appearance of lichen planus following Etanercept therapy (Battistella M et al., 2008), the possibility that the lesion could become secondary complicated following this therapy was never reported before, according to our knowledge. Additionally, we describe in this case the interplay between Etanercept therapy and hypertrophic cardiomyopathy. Conclusions: Our case is not a lichen planus induced by Etanercept, but it is aggravated and secondary infected with Methicillin-sensitive Staphylococcus aureus during the therapy. The additional cardiac complication (hypertrophic cardiomyopathy) may represent solely an evolutive sign of rheumatoid arthritis and therefore not influenced by Etanercept.

Keywords: Etanercept, rheumatoid arthritis, lichen planus, infected lesions.

Introduction

Lichen planus (LP) represents an inflammatory disorder of the skin and mucous membranes of unknown origins, typically characterized by pruritic, purple papules and plaques. Several clinical forms of lichen planus have been described: annular LP, linear LP, hypertrophic LP, atrophic LP, vesiculobullous LP, erosive LP, lichen planopilaris, lichen planus pigmentosus and lichen planus actinicus. In the last years, there were also other clinical variants described such as the eruptive and erythrodermic lesions [2–5].

We present a case of lichen planus in a patient with rheumatoid arthritis and under immunosuppressive therapy (Etanercept and Methotrexate) accompanied by secondary infection with a Methicillin-sensitive Staphylococcus aureus and uncommon myocardial complications.

Patient, Methods and Results

A 59-year-old woman, with a long history of rheumatoid arthritis, under immunosuppressive therapy with Etanercept and Methotrexate referred to the Department of Dermatology for evaluation of a pruritic erythematous infected plaque located on the pretibial areas (Figure 1A).
The patient reported the presence for approximately 25 years of different cutaneous lesions specific to lichen planus (Figure 1B) on the same location on the arm and which had flared over the past three years; she was diagnosed at that time with lichen planus and she continued self-medication with topical steroids. Since she has started the new therapy for rheumatoid arthritis with Etanercept and Methotrexate (one year before admission to our department), the lesions have changed and converted into purple, pruritic, infected plaques.

A culture from the lesion isolated Methicillin-sensitive Staphylococcus aureus, Ciprofloxacin treatment in dose of 500 mg twice daily for two weeks being therefore administered. The antibiotic therapy associated with topical steroids provided excellent results, with alleviation of the pruritus and interruption of the biologic signs.

Clinical exam revealed a systolic murmur; echocardiography identified a suggestive aspect for hypertrophic cardiomyopathy, with mild obstruction into outflow tract of the left ventricle (Figure 2). Because of the cardiac murmur at a patient with infected skin plaques, we had to exclude infective endocarditis: blood cultures were sterile and no vegetation attached to endocardium occurred at echocardiography.

A 4 mm punch-biopsy was performed and the histopathological report provided the following information: perivascular and band-like inflammatory infiltrate predominantly composed of lymphocytes and a few eosinophils (Figure 3D, close view of 3C); vacuolar alteration of the dermoepidermal junction (Figure 3B); irregular epidermal hyperplasia with saw-tooth rete ridges (Figure 3A); frequent necrotic keratinocytes (Figure 3B).

**Discussion**

Our case is a typical lichen planus in a patient diagnosed with rheumatoid arthritis, with secondary infection with Methicillin-sensitive Staphylococcus aureus and hypertrophic cardiomyopathy, which was well balanced and displayed good evolution after administration of
systemic antibiotics. Cardiac complication of the rheumatoid arthritis presented into our patient (hypertrophic cardiomyopathy with mild obstruction into the outflow tract of the left ventricle) is uncommon.

Etanercept is a fully human TNF-α receptor fusion protein that binds TNF-α with greater affinity than natural receptors. The drug is approved for the treatment of adult and juvenile rheumatoid arthritis, ankylosing spondylitis, psoriasis and psoriatic arthritis in the USA, Canada and Europe.

TNF-α therapy is generally well tolerated but various cutaneous manifestations have been encountered as side events (cutaneous vasculitis, lichen planus manifestations, psoriatic palm plantar pustulosis, plaque-type psoriasis localized to the scalp) [4].

On the other hand, the soluble, tumor necrosis factor alpha receptor (Etanercept) is an effective treatment option for LP limited to the nails [6], another study reporting a patient with refractory oral and cutaneous LP who experienced significant improvement after therapy with Efalizumab [7]. Other data on the use of Alefacept in two patients with LP showed a dramatic response of all skin lesions [8].

To our knowledge, there are no reports of lichen planus (hypertrophic) with secondary infection, in female patients with history of rheumatoid arthritis and under immunosuppressive therapy (Etanercept and Methotrexate). Battistella M et al. [1] reported a case of lichen planus occurring secondary Etanercept therapy for rheumatoid arthritis, thereby indicating that anti-TNF-α therapy may also be associated with the paradoxical induction of the inflammatory disease described in this report. Although quite recently, Musumeci ML et al. [4] presented a case of a 24-year-old Caucasian man with psoriasis vulgaris who developed lichen planus after eight months of Etanercept therapy, situations of aggravation of lichen planus and secondary infections following immunosuppressive therapy have not been reported.

Our subject is not a lichen planus induced by Etanercept, but it is aggravated and secondary infected with Methicillin-sensitive Staphylococcus during the therapy, being not clear whether the secondary infection (Methicillin-sensitive Staphylococcus aureus) was due to the scratch and/or related to the immunosuppressive therapy.

The additional cardiac complication (hypertrophic cardiomyopathy) can be regarded as an evolutive sign of rheumatoid arthritis, not influenced by Etanercept. Conflicting evidence has shown that Etanercept had positive effect on diminishing the ventricular hypertrophy in a rat model of the disease, thus potentially diminishing the evolution of cardiomyopathy in patients [9]. A possible explanation for the cardiac complications in this patient is given by a recent study that suggests an association between psoriasis and dilated cardiomyopathy [10]. Tumor necrosis factor alpha may be involved in the pathogenesis of dilated cardiomyopathy and therefore, anti-TNF-α agents may play a role in the treatment of dilated cardiomyopathy.

**Conclusions**

Our case is a typical lichen planus in a patient diagnosed with rheumatoid arthritis, with secondary infection with Methicillin-sensitive *Staphylococcus aureus* and hypertrophic cardiomyopathy, which was well balanced and displayed good evolution after administration of systemic antibiotics. Cardiac complication of the rheumatoid arthritis presented into our patient is uncommon. Whether this represents solely an evolutive sign of rheumatoid disorder and therefore not influenced by Etanercept, or, further monitor of our patient could possibly lead to identification of novel candidate that play roles in TNF-α signaling pathway or the state of extracellular matrix, is still to be debated.

**References**


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