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Case Report

Use of Adalimumab, a TNF-Alpha Inhibitor, is Associated with Paradoxical Psoriasis: Two Clinical Case Reports

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Abstract: The use of tumor necrosis factor (anti-TNF) antagonists has become a practice applied in the treatment of various inflammatory diseases, such as psoriasis. However, the use of Anti-TNF can, paradoxically, trigger side effects as a form of psoriasiform or worsening of pre-existing symptoms, in patients with or without previously diagnosed psoriasis. In view of this, two case reports were described. First, we described a 21-year-old female patient who used adalimumab for four months due to extensive suppurative hidradenitis. In the second case, we related a 32-year-old male patient diagnosed with severe Crohn's disease, with Adalimumab for three months developed psoriasis.

Keywords: Paradoxical psoriasis; Adalimumab; Crohn disease; Hidradenitis suppurativa.

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1. Introduction

Tumor necrosis factor alpha (anti TNF) inhibitor agents have become an effective therapy and an important advance in the management of chronic inflammatory diseases. The experience accumulated so far demonstrates a good safety profile, low toxicity, and high efficacy [1]. Although safe, this biological therapy option can cause some side effects, especially paradoxical reactions. There is evidence of an increased risk of upper airway infections, reactivation of latent infections, and infusion reactions. It is known that there is a lack of information on specific recommendations for the management of these lesions resulting from the side effect of the use of anti TNF such as infliximabe, etanercept and adalimumab, mainly since the pathophysiology of these reactions is not yet fully understood [1].

The paradoxical reaction may represent an exacerbation of a preexisting condition or the beginning of a new symptomatology, or in patients who were using immunobiological due to other underlying diseases, the appearance of psoriasiform and eczematiform lesions on the skin is often common, called psoriasis. paradoxical [2]. These are rare reactions, but with great potential to impair the patient's quality of life and the ongoing therapeutic course. Although this manifestation is exuberant, it is of great value to medical knowledge, since the rates of paradoxical effects in users of anti-TNF-alpha immunobiological reach 5 cases per 100 patients/year [2].

In this light, we report a series of cases regarding manifestations of paradoxical psoriasis under biological therapy with adalimumab in two different patients being treated for hidradenitis suppurativa and Crohn's disease.

2. Case Report

Case 1

A 21-year-old female patient with hidradenitis suppurativa (HS), using adalimumab 40 mg subcutaneously per week, with control of the underlying disease, but after two months of using the biologic, erythematous squamous plaques appeared in the trunk region and lower limbs (Figure 1).

The histopathological examination of these lesions showed psoriasiform dermatitis with parakeratosis in foci containing neutrophilic clusters, thinning of the suprapapillary epidermis and capillary tortuosity, which confirmed the diagnosis of psoriasis paradoxical to the use of immunobiological medication. Then, treatment with Methotrexate 15mg and folic acid 5mg weekly was started and the use of adalimumab was maintained due to the control of HS and being the last drug of choice in this disease, with regression of the psoriasiform lesions after two months of treatment and maintained until the end of treatment (one year after the exposed image).

Case 2

A 32-year-old male patient diagnosed with Crohn's disease, using adalimumab 40mg every 15 days, after three months of use, he noticed the appearance of lesions in erythematous and scaly plaques in the trunk region and lower members. After the biopsy, the diagnosis of paradoxical psoriasis was confirmed. Due to the worsening of the symptoms of Crohn's disease and the intensification of the skin lesions, it was decided to change the biological medication to ustekinumab, with improvement of the lesions and stability of the gastrointestinal symptoms after one month of the drug change.

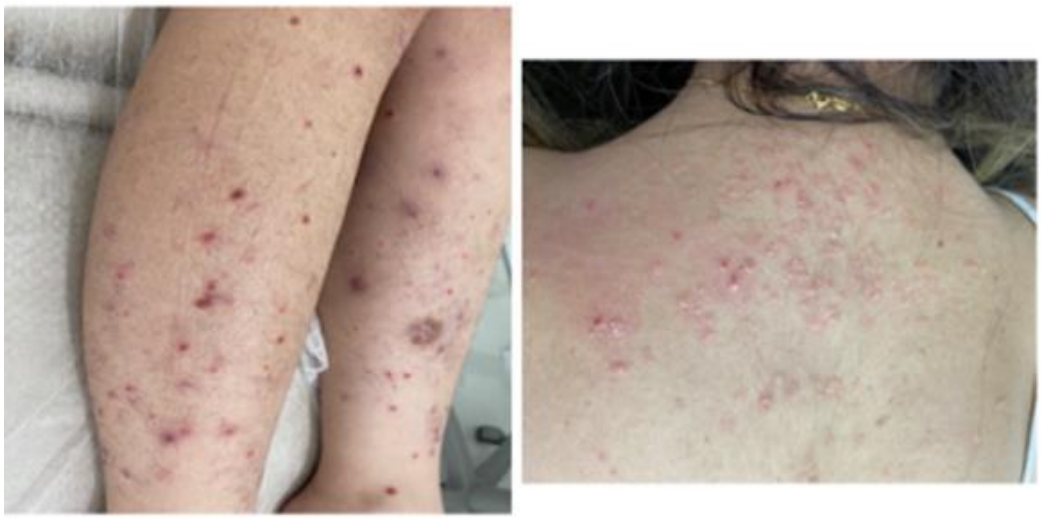

Figure 1. Erythematous, scaly plaques on lower limbs and trunk.

3. Discussion and conclusion

Even though it is rare, Spiegel's hernia is a diagnosis that must be kept in mind when investigating abdominal wall hernias. Predisposing factors include aging, previous surgery, and increased intra-abdominal pressure secondary to obesity, multiparity, ascites, chronic cough, and chronic obstructive pulmonary disease, among others [3,5]. In this report, we describe the case of a patient in her 50th decade of life, obese, multiparous (two cesarean deliveries), and with a previous hysterectomy, which corroborates the literature.

Immunobiological therapy contributes significantly to the treatment of inflammatory diseases such as rheumatoid arthritis, inflammatory bowel disease and psoriasis. Among the therapeutic regimens used are immunobiological that act by inhibiting TNF-alpha, such as infliximab, adalimumab and etanercept [1]. Although therapy with these

medications is highly safe, there are adverse effects that can be found, such as infections, reactivation of latent tuberculosis, demyelinating diseases, and paradoxical skin reactions. These reactions have rare manifestations and can be present in all classes of immunobiological, but mainly in anti TNF-alpha [3]. However, there are no statistics between the rates of paradoxical effect caused by infliximab or adalimumab [4].

In the literature, there are two groups that divide the paradoxical psoriasiform reactions that can be divided into de novo psoriasis in patients who used medication because of another disease, such as Crohn's disease, and never had psoriasis, or preexisting psoriasis exacerbated during treatment with immunobiological such as TNF-alpha inhibitors [4]. Some studies present smoking as the main risk factor for the development of lesions [4,5]. A recent meta-analysis evaluated the incidence and risk factors for Paradoxical Psoriasis or Psoriasiform Lesions in Patients with IBD receiving Anti-TNF Therapy, the factors risk includes patient's female, younger age, smoker, ileocolonic Crohn's disease and the types of anti-TNF were significantly associated with such risk [11].

De novo psoriasis is the most common form, with a higher prevalence in females, in patients who use immunobiological for inflammatory bowel disease and rheumatoid arthritis. Cases in which the patient used infliximab are most reported in the literature, followed by etanercept and adalimumab [4]. The manifestation of lesions has a variable time, which can appear from days to 6 years of treatment.; however, lesions often occur in the first months of medication use. Furthermore, the morphology of the lesions can vary between guttate, inverted, vulgar, pustular and, above all, palmoplantar forms [4]. The data above indicate the rarity of the cases in this report, since both patients had de novo psoriasis due to the use of adalimumab, one for hidradenitis suppurativa and the other for Crohn's disease, both had lesions on the trunk and lower limbs.

The pathophysiology of these reactions is not yet fully understood, but a recent study shows that there is a change in immune homeostasis mediated by Th1 lymphocytes that secrete Interferon – gamma and TNF–alpha and Th17 lymphocytes that secrete IL-17 and IL-22 [6]. In addition, the treatment will depend on the size of the lesions and the damage it may be causing to the patient. First, there is a recommendation from the Brazilian Consensus on psoriasis, which consists of additional topical corticosteroid therapy associated with calcipotriol and/or phototherapy [3].

In most cases, discontinuation of medication use is not necessary, but in the most severe and extensive cases, oral therapy is necessary as an adjunct to treatment, with acitretin, methotrexate and cyclosporine, this occurs around 75% of individuals who present a severe degree of paradoxical psoriasis [7,8]. A therapeutic alternative is the switch from the biological agent to the anti-interleukins class (IL-17-A), (IL-12) and (IL-23), for example, as they have a similar mechanism of action to anti-TNF alpha [2, 9]. In addiction an Italian group presented a similar case of paradoxical psoriasis in a patient with hidradenitis treated with adalimumab. In addition, the authors also presented possible genetic associations that may lead to the immunological disorder characteristic of psoriasis in patients treated with adalimumab [10].

The patient in case 1 had been using adalimumab for 4 months for hidradenitis suppurativa when the lesions were triggered, so it was decided to keep the immunobiological agent and make an association with methotrexate, with improvement of the lesions in two months. In this situation, it was possible to maintain the immunobiological treatment, as the condition of hidradenitis suppurativa was severe and was under clinical control.

In case 2, the patient has severe Crohn's disease, was using adalimumab for three months with partial control of the intestinal disease when the psoriasis lesions appeared. In view of this, it was decided to change the medication for another immunobiological agent, but of another class, an inhibitor of interleukins Il-12 and IL-23, ustekinumab. Therefore, the two reported cases of paradoxical de novo psoriasis due to adalimumab use are rare, as they are described in about one case for every 550 patients treated over 12 months with the immunobiological agent [5].

With the gradual insertion of immunobiological therapy for the treatment of immune mediated inflammatory diseases, more knowledge will be needed about the adverse effects they can cause, which implies greater attention in the early identification of the complications that manifest systemically in the patient.

4. Conclusions

Immunobiological are medications that have revolutionized the treatment of various diseases. Although there is safety in treatments that include the use of anti-TNF, adverse reactions, although rare, do exist. Therefore, it is important for the medical community to be aware of these paradoxical reactions to understand the mechanism and its proper management.

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Supplementary Materials: None.

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