

Psoriasis, lymphoma and etanercept: is there a correlation? *

Psoríase, linfoma e etanercepte: existe correlação?

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Abstract: Psoriasis is a chronic inflammatory disease that can affect skin and joints. Their treatment varies depending on the severity and includes topical and systemic. Among the latter are the immunobiological that target the T cell. We report a case that demonstrates the close relationship between psoriasis, lymphoma and biologic therapies.

Keywords: Lymphoma; Psoriasis; Tumor necrosis factor-alpha

Resumo: A psoríase é uma doença inflamatória crônica que pode afetar a pele e as articulações. Seu tratamento varia conforme a gravidade e inclui medicamentos tópicos e sistêmicos. Dentre os últimos estão os imunobiológicos, que têm como alvo a célula T. Relatamos um caso que demonstra a estreita relação entre a psoríase, o linfoma e os imunobiológicos.

Palavras-chave: Fator de necrose tumoral alfa; Linfoma; Psoríase

INTRODUCTION

Psoriasis is a chronic inflammatory disease that may affect the skin and articulations in mild, moderate or severe form. Systemic therapy is usually prescribed for the two last ones, either with conventional drugs (PUVA, cyclosporine, methotrexate, acitretin) or with biological therapy, that targets the T cell (anti-TNF α), modifying the immune response.^{1,2}

The physiopathology of psoriasis involves abnormal immune activation, characterized by increased activity of T cells, which present antigens and B lymphocytes. Several studies have been carried out to elucidate how this activation is related to greater risk of neoplasias. Furthermore, the therapies used in psoriasis and genetic predisposition also may be associated with the development of malignancies.^{3,4} In patients with moderate to severe psoriasis, a greater prevalence of non melanoma skin cancer and lymph proliferative disorders are observed.²

Lymphomas constitute an heterogeneous group of neoplasias, originated in T and B lympho-

cytes. Although its etiology remains unexplained, immunosuppression is a widely known risk factor. Associations with autoimmune skin conditions are normally limited to cutaneous T lymphomas. An increased risk for cutaneous T lymphomas is observed in psoriasis, mainly Mycosis fungoides / Sezary Syndrome.⁵ Although the literature shows that association with autoimmune skin diseases are normally limited to cutaneous T lymphomas, this case reports the development of lineage B lymphoma.

Investigating the lymphoma risk in psoriasis patients is a challenge, as lymphomas are statistically rare and large samples should be analyzed to obtain significant results.⁶ A clear causal relationship between exposure to anti-TNF and risk for lymphoproliferative disease has still not been established, but the known predisposition to lymphoma of patients with rheumatoid arthritis or Crohn's disease, information about a large number of lymphoma cases with the use of other immunosuppressors, and the anti-TNF

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effects on the immune system are biologic bases that warrant the need for additional epidemiological studies to formalize this possible association.

CASE REPORT

A 33-year-old female patient, white, had had psoriasis vulgaris since 2004. She refers the onset of asymptomatic mass with progressive growth in the right thigh proximal region, that had progressed for 04 months (Figures 1 and 2). She underwent several systemic treatments for psoriasis, and had not taken any medication for 02 months before the onset of the symptom complex (Table 1). The physical examination showed diffuse erythematous desquamative plaques on her body and a hard mass, painless on palpation, with local hyperthermia, measuring 6 x 10 cm at the right thigh proximal region. The tests requested during hospitalization for diagnostic clarification are listed in Table 2. An incisional lesion biopsy was performed and the histopathological report was large B-cell lymphoma rich in T lymphocytes and histiocytes, with positive immunohistochemistry for LCA and CD 20 in neoplastic cells, negative for CD 15 and positive for CD 30 in rare immunoblasts. An opinion was requested from Hematology, which programmed a chemotherapeutic schedule with CHOP every 21 days.

After the first chemotherapy session there was reduction in tumor size and consistency, but the cutaneous picture of psoriasis worsened, with dissemination and darkening of lesions and the onset of pustules (Figure 3). In view of this, we restarted methotrexate in an attempt to avoid progression, but the clinical response was not satisfactory. Two months later acitretin was introduced and the clinical picture stabilized.

TABLE 1: Treatments prescribed to the patient

Medication	Time of use	Motive for discontinuance
PUVA phototherapy	03 months (24 sessions)	not effective
Sulfasalazine	01 month	clinical worsening
Cyclosporine	36 months	time of use
Methotrexate (oral)	04 months	not effective
Methotrexate IM	06 months	not effective
Etanercept	31 months	lack of compliance

DISCUSSION

Psoriasis is historically related to the development of lymphomas, mainly those of the T lineage (non Hodgkin), be it for its autoimmune nature, be it for the drugs used in its treatment, even though there are few studies available. While psoriasis patients have an increased relative risk for lymphoma, the absolute risk is low, since it is a rare neoplasia and the magnitude of its association with psoriasis is modest.

Psoriasis is the only dermatological disease with immunobiological drugs approved by Food and Drug Administration (FDA) for its treatment.⁷ The biological agents became one more confounding factor in the genesis of lymphomas in psoriasis patients. A prospective cohort study carried out by Wolfe F. *et al* in 2004, suggested increased risk of lymphomas in patients treated with anti-TNF when compared with those treated with methotrexate.⁸ On the other hand, Chong and Wong reported the case of a patient with prior history of B lymphoma, with psoriatic arthritis and psoriasis (non responsive to conventional medications) that was treated with etanercept, with no adverse effect.⁹



FIGURE 1: Anterior view of tumor in the proximal region of right thigh and psoriatic lesions



FIGURE 2: Lateral tumor view

TABLE 2: Supplementary tests requested during hospital stay

Tests	Results
Hemogram	no alterations
LDH	769 UI/L (VR < 460 UI/L)
VHS	22 mm
B2-microglobulin	1.8 mg/mL (VR < 2.7 mg/mL)
βHCG	negative
Serologies (EBV, CMV, hepatitis, mononucleosis, toxoplasmosis, rubella and syphilis, HIV, HTLV)	negative
Echocardiogram	normal
US of soft parts	lymph node conglomerate
CT of thorax and neck	no alterations
CT of abdomen and pelvis	nodules in the spleen and lymph node enlargement in the internal iliac chain and external iliac chain on the right

In most of the cases where there was development of lymphoma after use of etanercept, it was the non Hodgkin of the B lineage type and occurred in average 8 weeks after the beginning of therapy, with neoplasia regression observed after suspension of the immunobiological agent.⁴ One of the studies also identified a greater incidence of lymphoma with the use of monoclonal antibodies (infliximab and adalimumab), when compared with the use of protein fusion agent (etanercept).¹⁰ In this case, we report the development of non Hodgkin lymphoma of the B-cell type (CD20+), in patient that underwent several

**FIGURE 3:** Psoriasis exacerbation after the first chemotherapy session

immunosuppressive treatments, including etanercept, which she used for 1 year and had discontinued in the 2 months preceding onset of the symptom complex. Is there a correlation between psoriasis, immunobiological agents and lymphoma? The answer has not been totally clarified in the literature.⁴

The proposal of this case report was to alert dermatologists that prescribe immunobiological agents about the possibility of association with the increased risk for lymphoma development; encourage notification of similar case reports to the medical population and medication vigilance of laboratories; and especially motivate further studies on the subject. □

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