Abstract: Psoriatic arthritis has been recognized as an auto-immune disease in which there is participation of the cytokine-producing T cells (tumor necrosis factor-alpha). Infliximab is a monoclonal antibody that binds to and inactivates tumor necrosis factor-alpha. Reported is a case of severe psoriatic arthritis which was unresponsive to multiple systemic therapies and treated with an intravenous infusion of infliximab, 5mg/Kg in three hours, in weeks 0, 2, 6 and 14, associated with a low dose of methotrexate, with an excellent therapeutic response.

Keywords: Arthritis, psoriatic; Tumor necrosis factor; Psoriasis

Psoriatic arthritis is an inflammatory arthropathy that is associated with psoriasis cutaneous lesions in 5 to 39% of the cases. Its etiopathogenesis is unknown. Recent studies suggest multifactorial heritage, implicating the action of various genes, with external triggering factors.

Progresses in molecular genetics allowed the identification of the genetic loci of susceptibility to psoriasis, named Psors 1, 2, 3 and 4 in chromosomes 6p, 17q, 4q and 1q, respectively. Other loci of minor susceptibility have been found in chromosomes 16q and 20p.

Genetic research suggests that psoriasis is a polygenic disease that is highly influenced by external stimuli, which could explain how genetic variability influences the widely varied therapeutic responses.

Reported is a case of a 20-year-old female patient who had had a diagnosis of psoriatic arthritis for 2 years, having used multiple topic and systemic therapies for disease control. Topic steroids and calcitriol had been used with no efficacy. Oral treatment with acitretin (1 mg/kg/day) combined with PUVA (Re-Puva) was attempted, causing an improvement of lesions, but was discontinued owing to elevation of triglycerides and to absence of articular response. Other treatments, including Methotrexate 15 mg/week, systemic steroids, cyclosporin (5 mg/kg/day) and exclusive use of pentoxiphylline (1200mg/day), were used with little success.

After 12 months of having abandoned therapy, the patient returned to the service with a worsening of the articular picture, unable to walk without support...
and presenting diffuse exacerbation of cutaneous lesions (Figure 1), associated to intense pruritus. Patient reported a worsening of the cutaneous-articular picture after the use of intramuscular steroids for joint pain relief.

The severe articular affection led to the indication of use of infliximab, after a rigorous complementary assessment, administered at the dose of 5 mg/kg, in venous infusion for 3 hours, with reevaluation of patient's vital signs every 30 minutes, up to 2 hours of infusion, in weeks 0, 2, 6 and 14. Methotrexate was associated at the dose of 5 mg/week.

There was an excellent clinical response, with improvement of the cutaneous picture, reduction of erythema, desquamation and infiltration of the lesions, as early as in the 4th treatment week, with absence of pruritus. There was a discrete post-inflammatory residual hyperpigmentation (Figure 2) in the 14th treatment week. Parallelly, there was a resolution of the articular picture, which was assessed through physical examination of joints, with no pain in movements.

The past 10-15 years have seen the greatest advances in the understanding of psoriasis pathogenesis. Discovery of the important role of the immune system has allowed the development of novel therapies. Cytokine-producing T-cells can be divided in type 1 cells, which produce interleukin 2 (IL-2), gamma-interferon and tumor necrosis factor alpha (TNF-alpha); and type 2 cells, which produce IL-4, IL-5, IL-6, IL-9 and IL-13. Type 1 cells re predominant in the psoriatic plaque. TNF-alpha, secreted mainly by macrophages, monocytes and type 1 t-cells, enhances the expression of proinflammatory cytokines, tumor necrosis factor alpha and activates transcription of nuclear factors, such as NF-kb factor, in regions adjacent to keratinocytes, inducing molecular adhesion, leukocyte infiltration with epidermal migration and maturation of Langerhans cells, thus perpetuating the psoriasis inflammatory process. Therefore, its inhibition has proven to be effective for the control of this disease.

Infliximab is a chimeric human-murine monoclonal antibody of the IgG1 class, which binds with high affinity to soluble and transmembrane forms of TNF-alpha in cells that synthesize them. Concurrent use of low dose methotrexate has been employed to prevent the formation of anti-infliximab antibodies. Since TNF-alpha modulates cellular immune response, there is a risk of opportunistic infections because of endogenous TNF-alpha suppression. The risk of latent tuberculosis and other infections should be assessed before the beginning of treatment. Development of lymphomas has been described in the literature.

Reported here is a case of severe vulgar psoriasis with articular affection, which had substantial improvement with treatment with anti-TNF-alpha antibody. The use of infliximab should be reserved only to the severely affected, who are intolerant or refractory to conventional treatments. The role of infliximab in TNF-alpha-mediated diseases seems very promising. The efficacy of the treatment, reported in several studies, corroborates the pathogenesis of the disease. Nevertheless, long-term safety studies are necessary, mainly owing to the fact that the drug is a not fully human monoclonal antibody, and it thus has the potential to induce the formation of antibodies against infliximab itself.
REFERENCES

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