Refractory erythrodermic psoriasis in a child with an excellent outcome by using etanercept
Psoriase eritrodérmica refratária em criança com excelente resposta ao etanercept

Naiara Abreu de Azevedo Fraga¹
Ivonise Follador²
Vitória Regina Pedreira de Almeida Rêgo⁴

Maria de Fátima Paim²
Andréia Nogueira Ramos¹

Abstract: Psoriasis affects 0.12% to 0.71% of all children. Erythrodermic psoriasis is an uncommon but serious disorder, occurring in less than 1.5% of cases. Tumor necrosis factor-alpha blockers (TNF-α) are a new class of drugs used to treat moderate to severe psoriasis refractory to conventional therapies. Etanercept is a TNFα receptor fusion protein, approved by the FDA for treating juvenile rheumatoid arthritis. We present the case of a 7-year-old suffering from plaque psoriasis since 8 months old which evolved into erythroderma refractory to cyclosporine and methotrexate. Patient responded excellently to etanercept, with no adverse side effects.

Keywords: Child; Psoriasis; Therapy

Resumo: A psoriase acomete 0,12% a 0,71% da população infantil, sendo que a forma eritrodérmica, grave e rara, ocorre em menos de 1,5% dos casos. Os antagonistas do Fator de Necrose Tumoral-α (TNF-α) constituem nova classe de drogas, utilizada para tratamento da psoriase grave a moderada, refratária às terapias convencionais. O Etanercept é uma proteína de fusão do receptor do TNF-α, aprovada pelo Food and Drug Administration para tratamento da artrite reumatoide juvenil no grupo infantil. Apresentamos um caso de criança com 7 anos de idade, com psoriase em placa desde 8 meses de vida, que evoluiu para eritrodérmia refratária a ciclosporina e metotrexato, com excelente resposta ao etanercepte, sem feitos adversos.

Palavras-chave: Criança; Psoriase; Terapêutica

INTRODUCTION
Psoriasis is a chronic systemic inflammatory disorder which affects 1-3% of the world’s population. A population-based study¹ reveals that the annual incidence of childhood psoriasis is 33.2 cases per 100,000 children. Child psoriasis affects 0.71% of the population under 18 and its prevalence increases linearly with age, from 0.12% in 1 year-olds to 1.2% in 18 year-olds. It is estimated that the disease begins before children reach 16 in 25-45% of cases and before age 2 in 2% of patients.²³

The disease comes in many different clinical forms. In children, most cases are of the plaque variety, followed by the guttata form. In patients under 2 years old the most common form is diaper psoriasis. Less common forms, such as erythrodermic and palmoplantar pustulosis (PPP), occur in fewer than 3% of child cases. The erythrodermic form occurs in about 1.4% of psoriasis cases in children and adolescents.²⁴

No systemic therapy, with proven efficacy and safety, has been approved to date by the FDA for
treatment of moderate to severe psoriasis in children and adolescents. It has however been approved in Brazil and Europe for treating moderate to severe psoriasis in children and adolescents from 8 years of age, in uncontrolled cases and/or cases intolerant to other systemic therapies or phototherapy.

Our case below concerns a 7-year-old girl with plaque psoriasis since 8 months old which evolved into erythroderma refractory to cyclosporine and methotrexate. The patient responded excellently to etanercept, with no adverse side effects to date.

CASE REPORT

7-year-old female patient with a history of scaly erythematous plaques all over the body since 8 months old. Had been treated with coal tar without improvement. No reports of psoriasis in the family. The patient was seen at the Dermatology Department in 2005, with scaly erythematous plaques on the trunk, limbs and scalp, together with meliceric crusts on fingers and toes, buttocks and soles, and subungual hyperkeratosis on the fingers, swollen knee and elbow joints and sporadic episodes of fever.

Admitted to the hospital, the patient was started on cyclosporine 2mg/kg/day. Improvement of general condition and of swollen joints, with maintenance of skin lesions. Secondary gastric intolerance to cyclosporine ruled out an increased dose, and this medication was suspended after 3 months. Patient did not present at the Dermatology Service for 2 years, but returned in 2007 with persistent lesions. Had been receiving systemic corticosteroids and emollients, without improvement. She was referred for phototherapy with narrow-band UVB, evolving with exfoliative erythroderma after three sessions (Figures 1 and 2). Started progressive weaning from steroids, and methotrexate was introduced at a weekly dose of 0.4mg/kg, as well as folic acid. During the 2-year follow-up the patient’s condition remained erythrodermic. Acitretin was indicated, but not used due to the difficulty of acquiring this medication. In 2009 the patient began treatment with etanercept 25mg (0.8 mg/kg), with maintenance of methotrexate (7.5 mg weekly). The patient had no personal or family history of tuberculosis. After three months of therapy, the erythroderma gradually resolved. Put on etanercept and methotrexate (cumulative dose of 1.2 grams) for two years, and the psoriasis stabilized. At present the patient has residual hypochromic macules and small scaly erythematous plaques in the armpit and on the elbow, back and abdomen (Figures 3 and 4). No adverse effects to these drugs. The child’s weight and height development is normal. Finally, the psychosocial impact on the child following treatment was very positive and she is now able to maintain normal school routine and activities.

Pretreatment tests: serology for HIV 1 and 2, HTLV 1 and 2, hepatitis B and C negative; non-reactive ANA; non-reactor PPD; chest X-ray normal; C-reactive protein (CRP) less than 6 mg/L; bone age compatible with chronological age; ultrasound of the abdomen and urinary tract unchanged; blood count and biochemical markers normal.

DISCUSSION

The average age of onset of psoriasis in children...
varies between 7 and 10 years, affecting both sexes equally. Studies have reported increases of incidence in recent years. Approximately 70% of affected children have plaque psoriasis vulgaris, while psoriasis guttata occurs in 28.9% of cases. Other rarer forms are also observed in this group, such as erythroderma (1.4%) and palmar plantar pustulosis (1.1%). Erythrodermic psoriasis is a severe form of the disease, which can lead to high morbidity and mortality rates. Cases of congenital or neonatal erythrodermic psoriasis are even more rare.

Diaper-area psoriasis is a fairly common finding in children under 2 years old. While joint involvement is less prevalent in young patients it should however be considered in the differential diagnosis of arthritis in pediatric patients. Paller et al. (2008), in a phase III study to evaluate the efficacy and safety of etanercept in children and adolescents, reported a 9% incidence of psoriatic arthritis in this age group. The main triggering factors of psoriasis in children are infections, especially beta-hemolytic streptococcal pharyngitis, stress and trauma. Few reports are found in the literature of psoriasis in children under 1 year old (extremely rare).

In the case described here, the diagnosis of plaque psoriasis was justified by the patient’s history and characteristic skin manifestations which began at 8 months old. Note the very unusual (among children) early age of onset and severity of the psoriasis, with joint involvement and erythroderma.

A thorough review of the literature revealed that no systemic therapy had been approved by the FDA to date for the treatment of psoriasis in children.

Although many options are available for treating psoriasis, we found no randomized controlled trials (RCT) to evaluate the efficacy and safety of available drugs for treating the erythrodermic form. Our choice of therapy therefore had to be based on the age, extent and severity of the disease and the comorbidities of the patient. Some case reports in adults have shown good response with the use of biologics, particularly infliximab. In severe and unstable cases, cyclosporine or infliximab are suggested due to their rapid action. In milder cases, or where these drugs are contraindicated, methotrexate or acitretin are the drugs of choice. Given the efficacy of infliximab in treating erythrodermic psoriasis, other anti TNF-α drugs are also considered to be promising. Its use in the treatment of erythrodermic psoriasis is however "off-label". Systemic corticosteroids should be reserved only for exceptional cases.

Psoriasis is a dermatosis mediated by activated T and dendritic cells. These cells secrete proinflammatory cytokines such as Tumor Necrosis Factor Alpha (TNF-α), IL-17 and IL-23 interleukins and interferon gamma (IFN-gamma), activating a cascade of other cytokines, including IL-1, IL-6 and IL-8, resulting in hyperproliferation of the keratinocytes. The serum and lesional levels of TNF-α decrease after effective therapy for psoriasis, correlated with clinical improvement. TNF-α antagonists are a new class of drugs widely used to treat moderate to severe plaque psoriasis in adults and can also be a valuable therapeutic option for managing childhood psoriasis.

Etanercept is a TNFα receptor fusion protein that acts by antagonizing its endogenous effects. It is
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Evidence of good response and safety in the use of etanercept for treating childhood psoriasis has been described in large randomized, placebo-controlled, phase III trials, and also in some reports and articles on isolated or series of cases, including on two patients with erythrodermic psoriasis. In view of this evidence, we decided to proceed with this option in our case, corroborating the results described in the literature. Skin lesions and the patient’s quality of life improved significantly. Despite the high cost, biological agents must be considered in cases which fail to respond to conventional therapies. When deciding to use this class of medication doctors must carefully assess each case and explain fully the risks and benefits of this course of therapy to the parents and/or guardians of the children affected.

REFERENCES