Refractory endemic pemphigus foliaceous in adolescence successfully treated with intravenous immunoglobulin

Pênfigo foliáceo endêmico refratário na adolescência - sucesso terapêutico com imunoglobulina intravenosa

Talita Alves Teixeira[1]
Marilene Chaves Silvestre[2]
Vanessa Gomes Maciel[3]
Fernanda Coelho Barbosa da Cruz Fiori[1]
Camilla de Barros Borges[2]
Mauricio Barcelos Costa[4]

Abstract: Endemic Pemphigus Foliaceous is a chronic autoimmune bullous skin disease. Treatment with prednisone often produces excellent results, but resistant forms exist, requiring alternative therapy. Alternative treatments have been used in cases of corticosteroid-refractory pemphigus, showing favorable results. This case study focuses on an adolescent male with a clinical-pathological diagnosis of pemphigus foliaceous with a severe clinical form of erythrodermis, unresponsive to multiple therapies, but which showed a satisfactory outcome with intravenous immunoglobulin. In this case we highlight the fact that the patient was a teenager who showed substantial clinical improvement as the result of using intravenous immunoglobulin, followed by complete remission after the fourth cycle of medication, allowing reduced doses of steroids and a consequent reduction of side effects.
Keywords: Skin vesiculobullous; Intravenous immunoglobulins; Pemphigus

Resumo: O Pênfigo Foliáceo Endêmico é doença bolhosa autoimune crônica da pele. Geralmente, o tratamento com prednisona tem excelente resposta, mas existem formas refratárias, sendo necessária terapêutica alternativa. Apresentamos paciente adolescente masculino, com diagnóstico clínico-patológico de pênfigo foliáceo, com forma clínica eritrodérmica grave e refratária a várias terapêuticas, que apresentou evolução satisfatória com imunoglobulina intravenosa. Destaca-se, neste relato, o fato de tratar-se de um paciente adolescente que obteve melhora clínica substancial com imunoglobulina intravenosa e remissão completa da doença, após o quarto ciclo da medicação, possibilitando redução da dose do corticoide e de seus efeitos colaterais.
Palavras-chave: Dermatopatias vesiculobolhosas; Imunoglobulinas intravenosas; Pênfigo

INTRODUCTION

Endemic Pemphigus Foliaceus (EPF) is a chronic autoimmune bullous disease of the skin, also popularly known as *Wild Fire*, a term used by local people to identify the sensation of heat and burning typical of the disease. It is characterized histopathologically by the formation of intraepidermal blisters with acantholysis, and immunologically by antiepithelial autoantibodies directed against the intercellular spaces of the epidermis responsible for the appearance of skin lesions. [1,2]

EPF starts with surface blisters that rupture easily leaving erosions, crusts and thin adherent scales. It usually occurs on the face, neck and upper torso, either localized or fragmented. The disease spreads gradually in the craniocaudal direction over weeks or months and can progress to the generalized form,

Received on 05.12.2010.
Approved by the Advisory Board and accepted for publication on 29.01.2011.
* Study undertaken at the Department of Dermatology, Hospital das Clinicas, Federal University of Goiás (HC-UFG), Goiânia, Brazil .
Conflict of interest: None / *Conflito de interesse: Nenhum*
Financial funding: None / *Suporte financeiro: Nenhum*

[1] Resident doctor at the Prof. Aiçar Chaul Dermatology Department, Hospital das Clinicas, Federal University of Goiás (HC-UFG), Goiânia, Brazil.
[2] MA in Tropical Medicine awarded by the Institute of Tropical Pathology and Public Health, Federal University of Goiás (IPTSP-UFG), Assistant Professor in the Dermatology Service, Hospital das Clinicas, Federal University of Goiás s (HC-UFG), Goiânia, Brazil .
[3] Voluntary Professor, Dermatology Department, Hospital das Clinicas, Federal University of Goiás (HC-UFG), Goiânia, Brazil.
[4] MA in Infectious and Parasitic Diseases, Ph.D. student at the Institute of Tropical Pathology and Public Health, Federal University of Goiás (IPTSP-UFG). Professor of Pathology at the Faculty of Medicine of the Federal University of Goiás (FM-UFG) and Head of the Department of Pathology, Radiology and Image Diagnosis of the Hospital das Clinicas, Federal University of Goiás (HC-UFG), Goiânia, Brazil.

resulting at worst in erythroderma. At this stage several complications with secondary infections are common. [3]

The main drug used in the treatment of EPF is prednisone at a dose of 1 to 2 mg/kg/ day, which normally controls the disease. Other drugs may be used as adjuvants or corticosteroid-sparing agents such as azathioprine, cyclophosphamide, cyclosporine, methotrexate, mycophenolate mofetil, antimalarials and dapsone. [3-6] In more severe cases, treatment can be effected with corticosteroid pulse therapy, with methylprednisolone as the first option, or combinations of drugs such as dexamethasone and cyclophosphamide. [7] In cases that are refractory or unresponsive to corticosteroids and other immunosuppressants, biological and intravenous immunoglobulin (IVIG) is indicated. [8-10]

The authors studied the case of a teenager with typical initial EFP, rapid progression to the severe erythrodermic form, resistant to a number of different therapeutic (including immunobiological) schemes proposed, and which was successfully treated with IVIG.

CASE REPORT

13-year-old male patient from Valparaiso (Goiás), reported the emergence of fragile blisters progressing in the *craniocaudal* direction four months previously. The condition worsened a month after admission and a biopsy was carried out, with histopathological findings revealing acantholytic epidermic blisters, with roofs of keratin and part of the crust and blister floor with a spinous layer containing typical acantholytic cells, confirming the clinical hypothesis of pemphigus foliaceus (Figures 1 and 2). Direct immunofluorescence was performed, which resulted negative. Indirect immunofluorescence was not performed due to local technical difficulties.

The patient was treated with prednisone at a dose of 1mg/kg/day amounting to 2mg/kg / day but with no skin improvement. This was subsequently supplemented with dapsone 100mg/day, suspended after one week on account of hemolytic anemia and increased transaminases. Micophenolate mofetil 1.5 g/day was next tried in conjunction with prednisone, but was discontinued after 1 month due to non-availability of this medication in the Department. No clinical response was observed during this treatment.

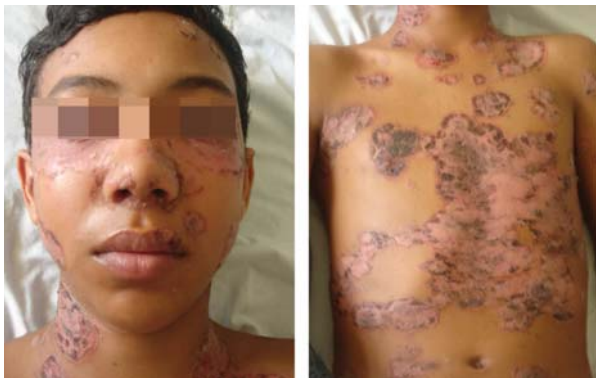

Figure 1: Blisters leaving fragile areas exulcerated

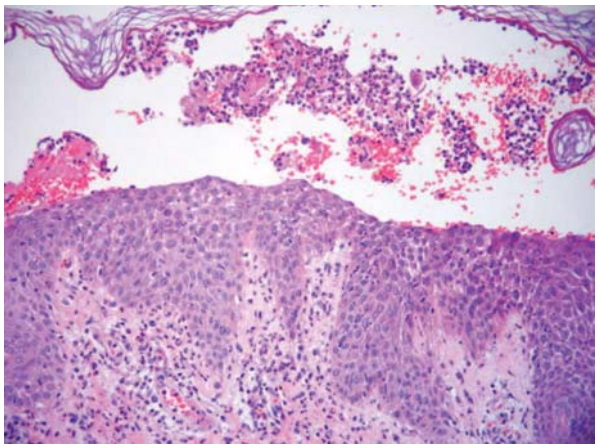

Figure 2: Subcorneal intraepidermal acantholytic dermatitis

Since the onset of symptoms, the patient developed secondary infection, with little response to antibiotic coverage for the skin, which contributed to worsening of the rash. This progressed to the erythrodermic form (Figure 3). 14 blood cultures with antibiograms were performed, all of which showed positive for Staphylococcus *aureus* MR. Therapy was guided by these blood cultures, but erythroderma, fever and tachycardia persisted, despite the patient´s good general condition. Therapeutic treatment for fungal infection (fluconazole 150mg/day orally for 10 days) was also started due to maceration areas in folds suggestive of candidiasis, but with no regression of the condition. Suspecting infection, the infectious disease team next initiated therapy with rituximab 575 mg intravenously in weekly cycles. After the 5th dose the patient persisted with erythroderma and we decided to start IVIG 2g/kg/cycle in monthly doses. During the second cycle we noted significant clinical improvement, with the appearance of several areas of healthy skin and some residual verrucous-like lesions. Four monthly cycles of IVIG were performed and the oral corticosteroid dose was gradually reduced in parallel. The patient is currently off oral corticosteroids, with total improvement of the clinical condition and no signs of recurrence. No use of immunoglobulin for 8 months (Figure 4).

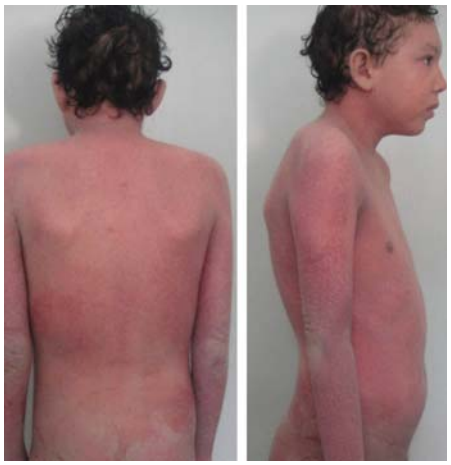

Figure 3: Progression to severe erythrodermic form, with no response to high-dose steroid therapy

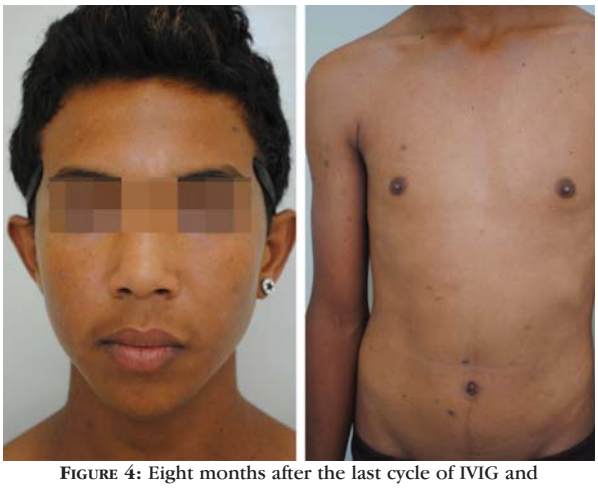

Figure 4: Eight months after the last cycle of IVIG and reduction of corticosteroid dose, total remission of lesions and steroid side effects

DISCUSSION

Before steroids, no effective treatment existed for pemphigus, which often had a fatal outcome. The evolution and prognosis of pemphigus changed significantly after the advent of corticosteroid treatment. [3] Although uncommon, cases of pemphigus resistant to conventional treatment with steroids and associations do exist, but in view of the rarity of this disorder, no large controlled studies or comparative clinical trials have been undertaken (only isolated observations and studies done on a limited number of patients). [9]

Rituximab is an anti-CD20 monoclonal antibody approved by the FDA for treating refractory non-Hodgkin lymphoma and rheumatoid arthritis. Some case reports exist of the use of rituximab in patients with pemphigus, mainly pemphigus vulgaris resistant to steroids and immunosuppressants, with favorable results. The small number of reported cases of pemphigus foliaceus all concerned adults. In the case described above, the patient failed to improve clinically, and persisted with erythroderma despite the use of rituximab. [8]

IVIG is employed in a variety of autoimmune diseases and its use is becoming increasingly frequent in dermatology. In most cases it is used in combination with other immunosuppressants in an average monthly dose cycle of 2g/kg to obtain effective control of the disease. In some sets of cases described in the literature fairly satisfactory clinical results (including reduction of corticosteroid dose) have been reported. [9, 10] In the case reported above, substantial improvement was observed after the first cycles, and virtually complete remission after the fourth cycle, allowing reduction of the corticosteroid dose with consequent reduction of corticosteroid side effects and improved quality of life for our patient.

Few reports exist in the literature of adolescent patients with endemic pemphigus foliaceus. The case described above was an example of the successful use of IVIG. ❑

REFERENCES

1. Cunha PR, Barraviera SRCS. Dermatoses bolhosas autoimunes. An Bras Dermatol. 2009;84:111-24.
2. Campbell I, Reis V, Aoki V, Cunha P, Hans Filho G, Alves G, et al. Pênfigo foliáceo endêmico: fogo selvagem. An Bras Dermatol. 2001;76:13-33.
3. Sampaio SAP, Rivitti EA. Erupções vésico-bolhosas. In: Sampaio SAP, Rivitti EA, editors. Dermatologia. São Paulo: Artes Médicas; 2007. p. 301-14.
4. Empinotti JC. Pênfigo foliáceo endêmico. In: Ramos-e-Silva M, Castro MCR, editors. Fundamentos de dermatologia. Rio de Janeiro: Atheneu; 2009. p. 617-33.
5. Stanley JR. Pênfigos. In: Freedberg IM, Eisen AZ, Wolff K, Austen KF, Goldsmith LA, Katz SI, Fitzpatrick TB, editors. Tratado de Dermatologia. Rio de Janeiro: Revinter; 2005. p. 654-66.
6. Mimouni D, Anhalt GJ, Cummins DL, Kouba DJ, Thorne JE, Nousari HC. Treatment of pemphigus vulgaris and pemphigus foliaceus with mycophenolate mofetil. Arch Dermatol. 2003;139:739-42.
7. Sakthi K, Thappa DM. Outcome of dexamethasone-cyclophosphamide pulse therapy in pemphigus: a case series. Indian J Dermatol Venereol Leprol. 2009;75:373-8.
8. Diaz LA. Rituximab and pemphigus - a therapeutic advance. N Engl J Med. 2007;357:605-7.
9. Caetano M, Amorim I, Selores M. Imunoglobulina intravenosa - uso em dermatologia. Trab Soc Port Ven. 2005;2:177-206.
10. Mydlarski PR, Mittmann N, Shear NH. Intravenous immunoglobulin: use in dermatology. Skin Therapy Lett. 2004;9:1-6.

Mailing Address / Endereço para correspondência:
Talita Alves Teixeira
Primeira Avenida, s/n - Setor Leste Universitário
74.605 020 Goiânia Goiás, Brazil
E-mail: talitateixeira@hotmail.com

How to cite this article/*Como citar este artigo*: Teixeira TA, Fiori FCBC, Silvestre MC, Borges CB, Maciel VG, Costa MB. Refractory endemic pemphigus foliaceous in adolescence successfully treated with intravenous immunoglobulin. An Bras Dermatol. 2011;86(4 Supl 1):S133-3.