

Acute acneiform eruption induced by interferon beta-1b during treatment for multiple sclerosis*

Erupção acneiforme aguda induzida por interferon beta-1b durante tratamento para esclerose múltipla

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Abstract: Multiple sclerosis is an inflammatory demyelinating disease of presumed autoimmune origin that affects the central nervous system. The main form of therapy is based on the use of immunomodulators such as interferon beta, which are usually well tolerated. Skin manifestations resulting from treatment with interferon beta-1b consist principally of reactions at the site of subcutaneous application of the drug. The present case report describes a female patient who developed an acneiform eruption resulting from treatment with interferon beta-1b.

Keywords: Acneiform eruptions; Interferon-beta; Multiple sclerosis; Therapeutics

Resumo: Esclerose múltipla é uma doença inflamatória desmielinizante, com presumida origem autoimune, que afeta o sistema nervoso central. A principal modalidade terapêutica é baseada no uso de imunomoduladores, como o interferon beta, que são geralmente bem tolerados. As manifestações cutâneas secundárias ao interferon beta-1b são representadas, na maioria das vezes, por reações no local de sua aplicação subcutânea. Descrevemos o caso de uma paciente do sexo feminino que desenvolveu um quadro de erupção acneiforme pelo interferon beta-1b.

Palavras-chave: Erupções acneiformes; Esclerose múltipla; Interferon beta; Terapêutica

INTRODUCTION

Multiple sclerosis (MS) is an inflammatory demyelinating disease that affects the central nervous system (CNS) and is considered one of the most common causes of chronic neurological disability in young adults.¹

The etiology of the disease remains to be fully established but its origin is presumed to be autoimmune. It is characterized by the multifocal infiltration of autoreactive T lymphocytes through the blood-brain barrier, leading to destruction of the myelin layer of the neurons in a genetically susceptible individual.^{2,3}

Currently, the principal therapeutic option available for this disease consists of immunomodulators such as interferon beta, which reduce the frequency of bouts and control the activity and progres-

sion of MS. However, some relatively common side effects occur with the use of this drug, including secondary dermatological manifestations, usually in the form of skin reactions at the site of subcutaneous application.⁴

This case report describes a female patient who developed an acneiform eruption resulting from the use of interferon beta-1b. Her clinical condition improved following suspension of the medication and appropriate treatment.

CASE REPORT

A 32-year old, white, single female patient reported the appearance around seven days previously of erythematous, pruriginous follicular papules with pustules on her face, neck and upper limbs

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FIGURE 1: Follicular papules and pustules on the patient's face



FIGURE 3: Details of the patient's face after she stopped use of interferon beta-1b

(Figures 1 and 2).

She had been diagnosed with the relapsing-remitting form of multiple sclerosis in 2007, at which time she began use of interferon beta-1b and her clinical condition stabilized. She denied any previous history of acne or use of any oral or topical medication.

Laboratory tests performed included full blood count, measurement of electrolyte levels, thyroid function tests and chest x-ray. No abnormalities were found.

Based on a hypothetical diagnosis of an acneiform eruption resulting from the use of interferon beta-1b, the patient was submitted to treatment with antiseptic soap, oral antibiotics (500 mg azithromycin three times weekly for four weeks) and antihistamines. She was advised to stop use of interferon beta-1b.

When the patient returned to the clinic thirty



FIGURE 2: Erythematous follicular papules on the patient's arm

days later, an improvement was found in her skin lesions; however, topical therapy was maintained until full remission was achieved a few days later (Figure 3). Subsequently, treatment for her multiple sclerosis was initiated with glatiramer acetate.

DISCUSSION

Multiple sclerosis (MS) is a chronic demyelinating disease of the central nervous system (CNS). Although the disease is believed to be of autoimmune origin, response to treatment with immunosuppressors is considered disappointing.⁵

The introduction of immunomodulators as a therapeutic option led to a reduction in the frequency and severity of relapses and possibly of the progression of the disease in patients with the relapsing-remitting form of multiple sclerosis for which both interferon beta-1a and interferon beta-1b have been shown to be effective.^{1,6}

Interferon beta is considered a safe and generally well-tolerated drug,^{5,6} and the side effects that have been recorded can be divided into class-specific and agent-specific effects. Class-specific side effects include fever, myalgia, arthralgia and influenza-like symptoms that begin 2-6 hours after injection and abate within 24 hours.⁷ Fatigue, insomnia, leukopenia, alterations in liver enzymes, alopecia, anaphylactic shock, onset or aggravation of depression and onset or aggravation of headache have also been described. Of these, only fatigue and depression are significantly associated with discontinuation of the treatment.⁸ Of the agent-specific side effects associated with the use of interferon beta-1b, reactions at the site of application merit particular mention.⁷ In the present case, the patient developed follicular papules and pustules on her face, neck and upper limbs com-

patible with a clinical diagnosis of drug-induced acneiform eruption while in use of interferon beta-1b, a frequent condition in diverse areas of medicine but one that is not always recognized by professionals who are not specialists in dermatology.

In drug-induced acneiform eruptions, pruritus is a common complaint and represents an important element for differential diagnosis with acne vulgaris. The distribution pattern is similar to that of acne vulgaris, since it also affects the face, although lesions may also be found on the limbs. The characteristic lesions of drug-induced acne are erythematous follicular papules, sometimes with punctiform vesicles in the center, which may develop into small vesicular pustules.⁹ An important clinical feature in the differential diagnosis is the fact that the skin lesions are not preceded by visible comedones.^{10,11}

Drug-induced acneiform eruptions may be caused by topical or systemic drugs.¹² With respect to topical products, the frequent use of cosmetics constitutes the principal cause of acneiform eruption in women, with lesions situated predominantly on the chin or, less commonly, on other areas of the face.

Acneiform eruptions may also be caused by systemic drugs and are dependent on the dose, the duration of administration and the patient's susceptibility. These drugs include glycocorticoids, anabolic steroids, danazol, testosterone, progestogens, thyroid

hormones, halogenated derivatives (iodine, bromine, fluoride and chlorine), vitamin B12, antibiotics (tetracycline and streptomycin), antituberculosis drugs (isoniazid), lithium carbonate, antiepileptic drugs (phenobarbital and hydantoin derivatives), cyclosporin A, antimycotics, gold salts, isotretinoin, clofazimine and epidermal growth factor receptor inhibitors (cetuximab, gefitinib and erlotinib), among others.¹²⁻¹⁵ The patient in question denied having used any other topical or systemic facial medication at that time with the exception of interferon, which she was taking to treat multiple sclerosis.

Treatment consists, whenever possible, in the immediate discontinuation of the drug that is causing the eruption. The use of antihistamines is important when there is associated pruritus, and oral antibiotics should be used in cases of secondary infection with pustules or impetiginization.⁹ The patient refused to allow herself to be re-exposed to interferon beta-1b in a hospital environment for confirmation of diagnosis. Therefore, the severe acute eruption associated with a temporal improvement following suspension of the drug provides proof of this causal association.

A review of the literature failed to identify any other report describing a similar condition caused by interferon beta-1b; therefore, we believe that this is the first report of an acneiform eruption caused by this medication. □

REFERENCES

1. Alemany-Rodríguez MJ, Aladro Y, Amela-Peris R, Pérez-Viéitez MC, Reyes-Yañez MP, Denis-Naranjo MC, et al. Enfermedades autoinmunes y esclerosis múltiple. *Rev Neurol*. 2005;40:594-7.
2. Ferreira MLB, Machado MIM, Vilela ML, Guedes MJ, Ataíde L Jr., Santos S, et al. Epidemiologia de 118 casos de esclerose múltipla com seguimento de 15 anos no centro de referência do hospital da restauração de Pernambuco. *Arq Neuropsiquiatr*. 2004;62:1027-32.
3. Oliveira MR, Santos DF, Fenelon SB, Penha-Silva N. Uso de rosuvastatina em esclerose múltipla. *Rev Neurocienc*. 2007;15:246-50.
4. Walther EU, Hohlfeld R. Multiple sclerosis: side effects of interferon beta therapy and their management. *Neurology*. 1999;53:1622-7.
5. Clerico M, Contessa G, Durelli L. Interferon-beta1a for the treatment of multiple sclerosis. *Expert Opin Biol Ther*. 2007;7:535-42.
6. Kremenchutzky M, Morrow S, Rush C. The safety and efficacy of IFN-beta products for the treatment of multiple sclerosis. *Expert Opin Drug Saf*. 2007;6:279-288.
7. Munschauer FE 3rd, Kinkel RP. Managing side effects of interferon-beta in patients with relapsing-remitting multiple sclerosis. *Clin Ther*. 1997;19:883-93.
8. Neillay LK, Goodin DS, Goodkin DE, Hauser SL. Side effect profile of interferon beta-1b in MS: results of an open label trial. *Neurology*. 1996;46:552-4.
9. Proença NG. Acne medicamentosa. *An Bras Dermatol*. 1987;62:315-319.
10. Segaert S, van Cutsem E. Clinical signs, pathophysiology and management of skin toxicity during therapy with epidermal growth factor receptor inhibitors. *Ann Oncol*. 2005;16:1425-33.
11. Lee JE, Lee SJ, Lee HJ, Lee JH, Lee KH. Severe acneiform eruption induced by cetuximab (Erbix). *Yonsei Med J*. 2008;49:851-2.
12. Medeiros AGC, Carvalho Filho IR, Sobral Filho JF. Erupção acneiforme induzida por gestrinoma. *An Bras Dermatol*. 1996;71:37-9.
13. Martínez de Lagrán Z, Ratón JA, Lasa O, Acebo E, Díaz-Pérez JL. Erupción acneiforme por inhibidores del receptor de crecimiento epidérmico. *Actas Dermosifiliogr*. 2005;96:450-4.
14. Strahan JE, Burch JM. Cyclosporine-induced infantile nodulocystic acne. *Arch Dermatol*. 2009;145:797-9.
15. Wollenberg A, Moosmann N, Klein E, Katzer K. A tool for scoring of acneiform skin eruption induced by EGF receptor inhibition. *Exp Dermatol*. 2008;17:790-2.

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