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Interferon beta 1a anaphylaxis, a case report. Standardization of non-irritating concentration for allergy skin tests

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Key words

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Summary

Multiple sclerosis is a disease with a potentially severe prognosis and epidemiologically increasing. Interferon beta 1a is a very useful maintenance therapy widely used by neurologists. In the literature, there are several case reports of hypersensitivity reactions. In this case report we describe an anaphylactic IgE mediated reaction to interferon beta 1a. We also describe, for the first time in the medical literature, the non-irritating concentration (NIC) to be used for skin tests.

Introduction

Multiple sclerosis (MS) is a chronic autoimmune demyelinating disease that critically affects the central nervous system (brain and spinal cord). A personalized treatment for each person affected by MS must be sought on the basis of clinical criteria. There are 3 main drug treatments:
1) basic therapies, disease modifying drugs (DMD),
2) treatment of recurrences,
3) symptomatic therapy.
DMDs are the maintenance treatments of MS with the main clinical outcome of preventing or delaying the progression of the disease and the occurrence of relapses as much as possible and, therefore, modifying the natural history of MS. The Target of DMD therapies is the modulation of immunological inflammation which is mainly related to T-lymphocytes and causes the multifocal demyelination and axonal damage. There are 3 main classes of DMD: Immunomodulatory drugs (IFN β), Immunosuppressive drugs (mitoxantrone), new biological drugs (natalizumab).

Common Interferon β 1a and β 1b side effects are: flu-like symptoms (myalgia, fatigue, general malaise, headache and fever); skin reactions after injection can occur after a few minutes or up to a few days (erythema, pain, swelling, and damage to the skin). Uncommon side effects are: behavioural disorders (depression) and suicide attempts and/or autoimmune diseases, appearance of neutralizing antibodies (Nabs).
In the literature, there are 3 case reports of urticaria [2] [3] due to administration of interferon beta 1a, 1 case report of anaphylaxis, without clear demonstration of IgE mediated mechanism [4] and 2 case reports of non-urticarial skin reactions.
In addition, we find also local skin reactions caused by hypersensitivity to the drug [5].
Finally, another case report describes the procedure of desensitization to the drug [6]. Anyway, this case report do not demonstrate IgE mediated reaction through control skin tests in non allergic subjects. At present, in the literature we do not have Non-irritating Concentration (NIC) for skin tests for beta 1a interferon.

Clinical case

A 34 year old woman received Multiple Sclerosis therapy for three months with interferon beta 1a injections every other day: R. ® (Merck-Serono). This patient experienced an anaphylactic reaction a few days after she developed a local reaction on her skin where she had the injection.
Last injection was performed 2 h after a meal in a restaurant (sausages, beer, alcohol). Fifteen minutes after the injection, the patient presented symptoms of pruritus, urticarial rash, sickness, dyspnea, hypotension. For these reasons, the patient was immediately hospitalized in the Emergency Department of the hospital and treated with 0,5 ml intramuscular adrenalin, corticosteroids, and antihistamines. In her history she had never had food allergies.
Anyway, food allergies were excluded with allergological investigation. On the contrary, skin tests demonstrated IgE mediated allergy to Interferon beta 1a.
After clinical evaluation and Neurological assessment the patient underwent copaxone therapy, as alternative maintenance drug, with good tolerance. Currently, the clinical condition of the patient is satisfactory and the disease is under control.

Methods and Results

We did skin prick tests (Alk®) and prick by prick tests for food eaten at the restaurant. The results were negative.
After the patient underwent the Challenge test with single foods ingested at the restaurant: the results were negative.
Finally the patient underwent Skin tests (prick test, intradermal test) with beta 1a Interferon (R.® 22 micrograms/milliliter): the results were positive at 1:100 (intradermal) corresponding to 0.22 micrograms/milliliter.
The Neurology department of our hospital follows one hundred patients with multiple sclerosis. In the group treated with beta 1a interferon , which has tolerated the drug for years, we found 10 volunteers for skin tests.
We performed Skin tests in the control group. The results were negative up to 1:1 concentration in 9 cases; up to 1:10 in 2 cases (in the control after 48 h). Finally, in order to extend the number of control subjects and to enhance the sensibility of the test, we performed skin control tests in 2 healthy volunteers without multiple sclerosis or other diseases and not in therapy with beta 1a interferon . Skin tests were negative up to 1:1 concentration.

Discussion

In the literature, there are several reports of hypersensitivity reactions to interferon beta 1a. The use of this drug for the treatment of Multiple sclerosis is currently increasing. In the case described herein we have demonstrated an IgE mediated reaction. This mechanism wasn't demonstrated in the previous case report described by Corona (4); equally it was only hypothesized in the case report of Kalpaklioglu (6) that underwent desensitization procedure.
Also, we have established, for the first time in the literature, the non-irritating concentration to perform skin tests.
We conclude that the NIC (non- irritating concentration) for beta 1a Interferon (R.®) is 1:100 intradermal, corresponding to 0.22 micrograms/milliliter.

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