

CLINICAL CASE

Anaphylaxis to calcitonin

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SUMMARY

Background: the calcitonin is an hormone produced by the thyroid gland C cells. The salmon calcitonin is used in some osteomuscular diseases. There are few references of allergic reaction to this hormone.

We introduce a case of a sixty years old woman with several previous episodes of rhinitis, conjunctivitis and perspiration immediately after the administration of salmon calcitonin with nasal spray or intramuscular administration (Calsynar®). There were some temporal periods of good tolerance between these episodes.

Methods: skin prick test (SPT), nasal and intramuscular challenge test with commercial salmon calcitonin (Miacalcic®) were performed.

Leukocyte histamine release test with salmon calcitonin and serum tryptase levels at baseline and after intramuscular challenge test were performed.

Results: the patient skin prick test with commercial calcitonin (Miacalcic®, 50 UI/ml) was positive and negative in controls. The nasal challenge test with a calcitonin nasal spray, up to 150 UI, was negative. The intramuscular challenge test with 25 UI of Miacalcic was positive with an immediate anaphylactic reaction. Whole blood histamine release studies were negative.

Serum tryptase levels after intramuscular challenge did not increase significantly with regard to the basal levels.

Conclusion: we have introduced a case of anaphylaxis by calcitonin that suggest an IgE mediated hypersensitivity reaction.

Key words: Anaphylaxis. Hypersensitivity. Skin prick test. Calcitonin.

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INTRODUCTION

The calcitonin is an hormone produced by thyroid gland C cells. It is a polypeptide containing 32 amino acids. Its most important action is the inhibition of bone resorption. Although the physiologic role of the hormone has still not been fully assessed, calcitonin acutely inhibits osteoclast function and diminishes their number when administered over a prolonged period (1). This action makes calcitonin to be used for a complementary treatment in some osteomuscular diseases as Paget diseases and osteoporosis. The most useful for treatment is salmon calcitonin due to it is twenty times more powerful than the human one.

Side effects included are: digestive disturbs as nauseas, vomiting, diarrhea and abdominal pain, face and hands erythema and local reaction on the point of administration (2). There are few reports of allergic reactions to this hormone recorded in the literature. We report an unusual case of allergy to exogenous administration of salmon calcitonin.

CASE REPORT

A sixty years old woman who suffered from high blood pressure, hipercolesterolemia, and osteoporosis, was referred to our service for rhinitis, conjunctivitis and perspiration immediately after the administration of salmon calcitonin with nasal spray or intramuscular administration.

The patient followed a daily treatment with 100 UI of salmon calcitonin with nasal spray (Calsynar® 100 UI/inhalation) six months a year, during four consecutive years with good tolerance. On the fifth year, once salmon calcitonin treatment with nasal spray started again, she developed hydrorrhea, watering, nasal and ocular pruritus, and perspiration immediately after the administration. The symptoms

were reproduced in each administration before the therapy was discontinued. On the sixth year after one year without treatment, the patient begun with intramuscular therapy of salmon calcitonin (Miacalcic®.100 UI per injection). The first 10 injections had a good tolerance but on the second month, after a twenty days break and after the first intramuscular injection (10 injections/month) there was an immediate reaction with rhinitis, conjunctivitis, perspiration and abdominal discomfort that was resolved with parental corticosteroids.

MATERIAL AND METHODS

Skin prick test with commercial salmon calcitonin (Miacalcic®.50 UI/ml), anisakis commercial extract and a battery of commercially available common inhalants (including grass pollen, an olive pollen, mixture of tree pollen, outdoor-indoor molds home ust mites and dogs and cats epithelia) with the allergy pricker lancet (Dome-Hollister-Stier) as described elsewhere (3) were performed. Histamine phosphate (10 mg/ml) served as positive control and negative control was NaCl (0.9%). The tests were read after 15 minutes. We considered a positive reaction if the wheal size was at least 3 mm diameter larger than negative controls. Ten atopic and ten non atopic controls were tested to SPT with commercial salmon calcitonin. Atopics were defined as having a SPT reaction of 3 mm or more to at least one common allergen.

SPT with cruce salmon was undertaken by prick-prick technique according to Dreborg and Foucard (4).

Total serum IgE analyzed with the CAP-FEIA System (Pharmacia, Uppsala, Sweden) was performed according to the manufacturers instructions.

Leukocyte histamine release test to salmon calcitonin was performed using an automated fluorometric method according to Siraganian (5) with the modifications previously described (6). A result higher than 10% release was considered positive.

Once the patient gave his written consent an intranasal challenge test with commercial salmon calcitonin (Miacalcic®.50 UI/inhalation) was performed reaching an accumulated doses of 150 UI.

After, an intramuscular challenge with 25 UI of commercial salmon calcitonin (Miacalcic 100 UI/ml) was performed.

Serum tryptase levels analyzed with Unicap tryptase FEIA system (Pharmacia & Upjohn Diagnostics AB, Uppsala, Sweden) was performed according to the manufacturers instructions. Blood was withdeawn in baseline conditions and 90 minutes following the reaction.

RESULTS

We observe a positive reaction to the SPT of salmon calcitonin with a 15 × 12 mm of wheal and 20 × 20 of erythema. The test was negative in all the atopic and non atopic controls.

There was a positive reaction to cat epithelia and negative for the rest of common pneumo allergens and anisakis commercial extract.

Skin prick by prick test with crude salmon was performed with negative results.

Total serum IgE was 203 KU/L.

Leukocyte histamine release test to salmon calcitonin was negative.

An intranasal challenge test with commercial salmon calcitonin was negative.

An intramuscular challenge test with commercial salmon calcitonin was performed showing an immediate response with symptoms of hidrorrea, watering, nasal obstruction, sneezes, abdominal discomfort, perspiration and hypotension (80/60). The reaction was resolved using subcutaneous epinephrine, antihistamines and corticosteroids in two hours. No late response was observed.

Serum tryptase levels after intramuscular challenge did not increased significantly with regards to the basal levels.

DISCUSSION

Calcitonin allergy is extremely rare and there are not well documented reports that demonstrate an allergic mechanism. In fact, there is only one clinical report without a complementary allergic study (7). Besides, some salmon calcitonin side effects could be similar to allergic reactions and made difficult the differential diagnosis. In our case the clinical history was confused. The patient had clinical reactions with salmon calcitonin, sometimes resolved spontaneously, followed by periods of good tolerance, with no time enough to loose specific antibodies. The patient suffered a serious osteoporosis and the treatment with salmon calcitonin was useful (8). In this case with a non-conclusive history the diagnosis with a challenge test was necessary.

We have introduced the first report where the positive skin prick test and immediate response in the challenge test strongly suggest that salmon calcitonin was the drug responsible of the clinical reaction produced by and IgE mediated hypersensitivity.

In vitro test to the medical allergy diagnosis as histamine release test could be useful but there is too many problems due to the low molecular weight of a lot of antigens, which cannot fit haptens.

The measurement of serum tryptase levels, as anaphylaxis mediator, is a test still being studied, its sensitivity and specificity was not sufficient for confirming the diagnosis of anaphylaxis (9) and nowadays there are not concluyent results in the literature (10).

RESUMEN

Antecedentes: la calcitonina es una hormona producida por las células C de la glándula tiroides. La calcitonina de salmón se administra en algunas enfermedades osteomusculares. Existen pocas referencias de reacciones alérgicas a esta hormona.

Presentamos el caso de una mujer de 60 años con antecedentes de varios episodios de rinitis, conjuntivitis y sudoración que aparecían inmediatamente después de la administración de calcitonina de salmón en aerosol nasal o por vía intramuscular (Calsynar®). Entre estos episodios se encontraron períodos de buena tolerancia.

Métodos: se realizaron pruebas cutáneas y de provocación nasal e intramuscular utilizando un preparado comercial de calcitonina de salmón (Miacalcic®).

Se realizó la prueba de liberación leucocitaria de histamina utilizando la calcitonina de salmón y los niveles séricos de triptasa en situación basal y después de una prueba de provocación intramuscular.

Resultados: las pruebas cutáneas con calcitonina comercial (Miacalcic®, 50 IU/ml) produjeron resultados positivos y negativos en controles. La prueba de provocación nasal con un aerosol nasal de calcitonina, hasta 150 IU, fue negativa. La prueba de provocación intramuscular con 25 IU de Miacalcic® fue positiva, produciendo inmediatamente una reacción anafiláctica. Los estudios de liberación de histamina en sangre entera obtuvieron resultados negativos.

Los niveles de triptasa sérica no aumentaron sig-

nificativamente después de la prueba de provocación intramuscular con respecto a los niveles basales.

Conclusión: en este caso de anafilaxia por calcitonina, el mecanismo probable parece ser una reacción de hipersensibilidad mediada por IgE.

Palabras clave: Anafilaxis. Hipersensibilidad. Pruebas cutáneas. Calcitonina.

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