Case Report

Anaphylaxis produced by Oxaliplatin

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Abstract. We are discussing two patients, with clinically compatible reactions, who display an immediate hypersensitive mechanism following the administration of oxaliplatin, confirmed by the performance of cutaneous tests.

Key words: anaphylaxis, allergy/ hypersensitivity, oxaliplatin

Introduction

Oxaliplatin, a compound derived from platinum salts, is used in the treatment of first line metastatic colorectal cancer.

Immediate hypersensitive reactions have been noted as often as up to 5 percent with other platinum analogues, such as carboplatin and cisplatin [1].

With oxaliplatin, the newest of them all, few cases of allergic reactions have been published and, in the majority of these cases, without performing allergenic studies [1-4].

We will now discuss two patients, with clinically compatible reactions, who display an immediate hypersensitive mechanism following the administration of oxaliplatin, confirmed by the performance of cutaneous tests.

Material and methods

Case 1

Male patient, 43 years old, diagnosed with adenocarcinoma of the colon with hepatic metastasis. He receives treatment with high doses of leucovorin and oxaliplatin administered over a period of two hours, followed by 5-flurouracil (5-FU) in continuous infusion during 48 hours in biweekly cycles. Antiemetic premedication, as usual, with 12 mg of dexamethasone was administered 10 minutes before the oxaliplatin.

A week after the third cycle, a generalized pruritus was experienced with the appearance of maculae which persisted in daily outbreaks without leaving a residual lesion.

On establishing the fourth cycle, intense and generalised pruritus along with erythema and swelling, respiratory problems and generalised discomfort occur immediately after administration of oxaliplatin.

This results in the suspension of the medication and the establishment of treatment with corticosteroids and antihistamines. Good tolerance to 5-FU and Polic acid is displayed afterwards.

Case 2

Female patient, 43 years old, diagnosed with metastatic carcinoma of the colon and having completed 11 treatment cycles with 12 mg of dexamethasone 10 minutes before oxaliplatin, 5-flurouracil and folic acid,

with good tolerance. A few months afterwards it is necessary to resume the treatment which, on the first day, immediately, causes shakes and shivers along with a measured temperature of 38 degrees, although without cutaneous outbreak, following the administration of oxaliplatin, due to which treatment with diazepam is established with good tolerance on that cycle. After 15 days, 20 minutes after the administration of oxaliplatin, itchiness is experienced along with erythema on the face and dyspnoea, due to which the medication is suspended, and treatment with corticosteroids and antihistamines is established. Afterwards, good tolerance is shown to a cycle of irinotecan and 5-FU.

Allergy Study

Skin-test

Having received previous consent in both cases, pricks and intradermal tests are performed with cisplatin, oxaliplatin, 5-flurouracil and folic acid. In the second case tests with carboplatin were included. In both cases positive results were obtained (papule of 14mm), following immediate reading, with oxaliplatin in intradermal tests with concentrations of 0.001mg/ml and 0.1 mg/ml respectively.

Tests with identical concentrations were performed, up to 0.1 mg/ml, on 6 controls, with negative result.

Discussion

Oxaliplatin is a complex of platinum II, under the form of oxalate, and with two amino groups belonging to a binding transporter of trans-1.2-diaminocyclohexane (DCH). It is related to other derivatives of platinum, such as cisplatin or carboplatin, although with the presence of the binding DCH it is a lot more voluminous than the simple aminic residues of its predecessors and with the particularity of being specific in the treatment of metastatic neoplastic diseases of the colon (Figure 1).

The most frequent adverse effect of oxaliplatin, with a frequency of 80-85 percent, is transient peripheral neuropathy, in the form of paraesthesia. The neurological toxicity is dose dependent and reversible in character [5]. Much less frequent, between 1.5 and 2 percent, are the idiosyncratic reactions which are potentially preventable with treatment prior to administration. Anaphylactic reactions are described in less than 1 percent of cases [6].

Based on the type and the immediateness of the clinical manifestations and the positivity of the cutaneous tests with oxaliplatin, following immediate reading, the reaction shown by our patients suggests a hypersensitive reaction mediated by IgE antibodies. In this type of IgE mediated reaction, prophylactic treatment with corticosteroids, as antiemetic medication,

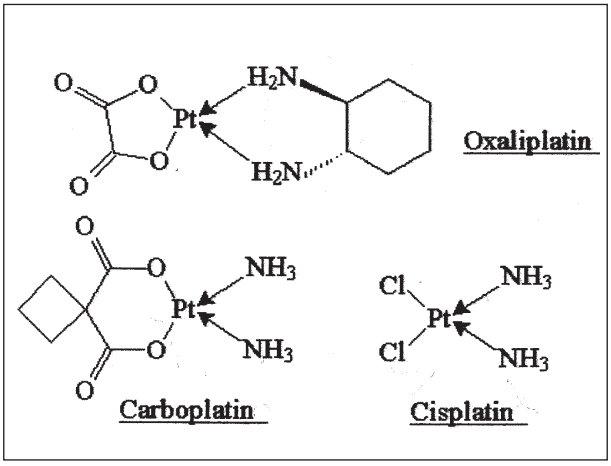

Figure 1. Molecular structure of platinum salts.

does not prevent recurrent allergic reactions [7]. In accordance with other authors [1, 8], the cutaneous tests help with the diagnosis of allergy in patients who have compatible clinical manifestations. In our patients a positive result was obtained with concentrations of 0.001 and 0.1 mg/ml, lower than those referred by other authors [1, 8], which vary between 0.003 and 3 mg/ml. In order to rule out irritation, six controls were performed with the same concentrations, which produced negative results. In the same way, other works [8] propose the use of cutaneous tests with oxaliplatin to predict the risk of allergic reaction.

In our two patients the negative results obtained from the cutaneous tests performed with the other platinum compounds, carboplatin and cisplatin, suggest the absence of a crossed reaction. The different molecular structure of oxaliplatin, including the presence of the binding DCH which is absent in its predecessors, could explain this fact, which has already been referred by other authors [8]. Nevertheless, according to the current oncology therapeutic criteria [5], the other platinum salts are not indicated for the treatment of metastatic colorectal cancer. The administration of cisplatin does not produce significant clinical benefit in terms of responses in colorectal cancer.

Conclusion

The tests performed on the two patients who have a suggested history of allergy to oxaliplatin are measurable and confirm the suspicion of an anaphylactic reaction which is possibly IgE mediated.

For the same reason, the negative results of these same tests support the lack of a crossed reaction with the other platinum salts and suggest that the sensitized portion is one of the lateral chains associated with the platinum atom.

Although the mechanism is still to be established, it is currently our most affordable and easily performed test.

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