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Successful Treatment of Chemotherapy-induced Symptoms with Granisetron as Alternative for Ondansetron Allergy

Ondansetron Alerjisinde Alternatif Granisetron ile Kemoterapiye Bağlı Semptomların Başarılı Şekilde Tedavisi

Öner Özdemir[1], Olena Erkun[2]

[1]Sakarya University Faculty of Medicine; Sakarya Training and Research Hospital, Department of Pediatrics, Division of Allergy and Immunology, Sakarya, Turkey
[2]Sakarya Training and Research Hospital, Clinic of Pediatrics, Sakarya, Turkey

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ABSTRACT

Ondansetron is a selective 5-hydroxy-tryptamine 3 receptor antagonist that is widely used as an antiemetic agent, especially for the preventive treatment of chemotherapy-induced nausea and vomiting. Side effects of ondansetron are headache, dizziness, constipation, diarrhoea and hypersensitivity reactions such as anaphylaxis, which are very rarely described in the literature. Herein, we present a patient with Hodgkin lymphoma who developed urticaria secondary to ondansetron intake, had been receiving chemotherapy and has safely used granisetron as alternative. Granisetron appears to be a safer potent alternative to ondansetron in patients with cancer receiving chemotherapy.

Keywords: Hypersensitivity, urticaria, drug hypersensitivity, ondansetron, granisetron

ÖZ

Ondansetron selektif 5-hidroksi-triptamin 3 reseptör antagonisti olan ve yaygın olarak, özellikle kemoterapiye bağlı bulantı ve kusmayı önlemede, kullanılan bir antiemetik ajandır. Ondansetronun yan etkileri baş ağrısı, baş dönmesi, kabızlık, diyare ve literatürde çok nadiren tanımlanan anafilaksi gibi hipersensitivite reaksiyonlarıdır. Bu raporda, kemoterapi alan ve ondansetrona bağlı ürtiker geliştiren ve güvenli şekilde alternatif granisetron kullanan Hodgkin lenfomalı bir olguyu sunmak istiyoruz. Granisetron kemoterapi alan onkoloji hastalarında güvenli ve güçlü bir ondansetron alternatifi olarak görünmektedir.

Anahtar kelimeler: Hipersensitivite, ürtiker, ilaç hipersensitivitesi, ondansetron, granisetron

INTRODUCTION

Ondansetron is a selective 5-hydroxy-tryptamine 3 (5-HT3) receptor antagonist that is widely used in haematology and oncology wards. Ondansetron has highly antiemetic (anti-emetogenic) effect (1). Thus, ondansetron is often used for the prevention and treatment of chemotherapy-induced nausea and vomiting (1). Ondansetron has several common side effects, which include headache, dizziness, diarrhoea, fever and constipation (1). There were reports of electrocardiographic changes in some patients (2). However, IgE- or non-IgE-mediated hypersensitivity reactions such as urticaria, anaphylaxis and anaphylactoid reactions are very rarely reported side effects of ondansetron (3-7).

Herein, we present the case of a patient with Hodgkin lymphoma who developed urticaria following ondansetron intake and was later successfully treated with granisetron for chemotherapy-induced nausea and vomiting.

CASE PRESENTATION

A 9-year-old boy was scheduled to undergo chemotherapy for nodular sclerosing Hodgkin lymphoma, which constitutes a combination of four drugs, namely, vinblastin, dacarbazine,

ORCID IDs of the authors: Ö.Ö. 0000-0002-5338-9561; O.E. 0000-0003-3067-3794.

Corresponding Author/Sorumlu Yazar: Öner Özdemir,
E-mail: ozdemir_oner@hotmail.com

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doxorubicin and bleomycin, as well as ondansetron for prevention of nausea and vomiting. Within the last 6 months, the patient has been receiving chemotherapy and using ondansetron as prophylaxis for severe nausea. He had no known history of hypersensitivity reactions to any food and/or drug allergens, including ondansetron. During the intravenous administration of the first dose of ondansetron (0.15 mg/kg; total, 4 mg) at the last chemotherapy course, after 2-3 min, the patient developed redness (flare) and wheals along with urticaria (Figure 1). There was no accompanying bronchospasm or hypotension. The patient was immediately treated with intravenous administration of 30 mg pheniramine (1 mg/kg). The reaction disappeared within a few minutes. The patient did not complain of any other symptoms and was discharged after a couple of hours of observation. He was asymptomatic within 24 h of follow-up.

According to the patient's mother, during the past one session of chemotherapy, the patient also demonstrated redness, swelling and mild rash over the body after injection of ondansetron. The patient has no individual or family history of atopy and asthma, but he has a history of common variable immunodeficiency disease. Thus, he has been receiving intravenous treatment with immunoglobulin.

After allergy consultation, the skin prick test to undiluted ondansetron (2 mg/mL concentration) with commercial product was performed, and the result was negative. Moreover, intradermal test showed a positive response to 0.02 mg/mL (100 times dilution of ondansetron) concentration, and a positive flare and wheal reaction were observed (hyperaemia, 35 mm; wheal, 20 mm) (Figure 2). Because of this positive response, intradermal test to 10 times dilution of ondansetron was not performed. Furthermore, the skin prick test and intradermal tests with an alternative drug granisetron (1 mg/mL, undiluted) were performed similarly for granisetron (1:100 and 1:10 dilution), and all test results were negative. The prick and intradermal test concentrations for both ondansetron and granisetron were defined based on previous clinical reports (5,8). All skin prick and intradermal tests were performed with original commercial preparations including excipients. Since our patient needed one of the 5-HT3 receptor antagonists, we provoked him the same day with granisetron as an alternative. He was given intravenously cumulative doses of granisetron at 20-min intervals under strict scrutiny, beginning with 1 mg up to the therapy dose of 100 mg, as described earlier (9). As a result, granisetron was successfully administered to the patient for prevention of chemotherapy-induced nausea and vomiting.

Verbal and written informed consents were obtained from the patient's parents for publication of this case report and any accompanying images.

DISCUSSION

The 5-HT3 receptor antagonists (ondansetron, tropisetron, granisetron, dolasetron and palonosetron) are well-tolerated, potent antiemetic drugs that are used for the prevention of chemotherapy-induced nausea and vomiting. They are highly safe and have rare side effects, such as dizziness, headache, dystonia, constipation, chest pain and prolongation of the QT period on electrocardiogram (1,2). In our case, the side effect was a localised

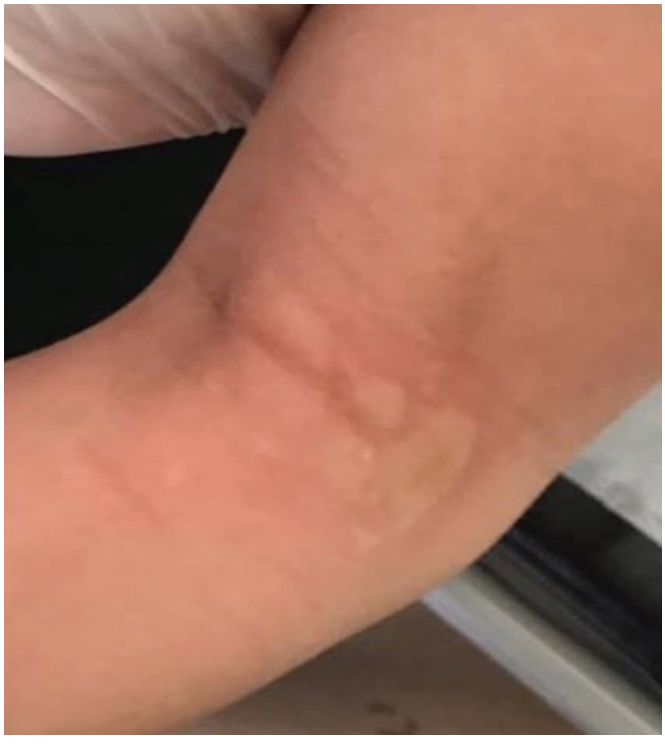

Figure 1. Redness and wheals after administration of ondansetron

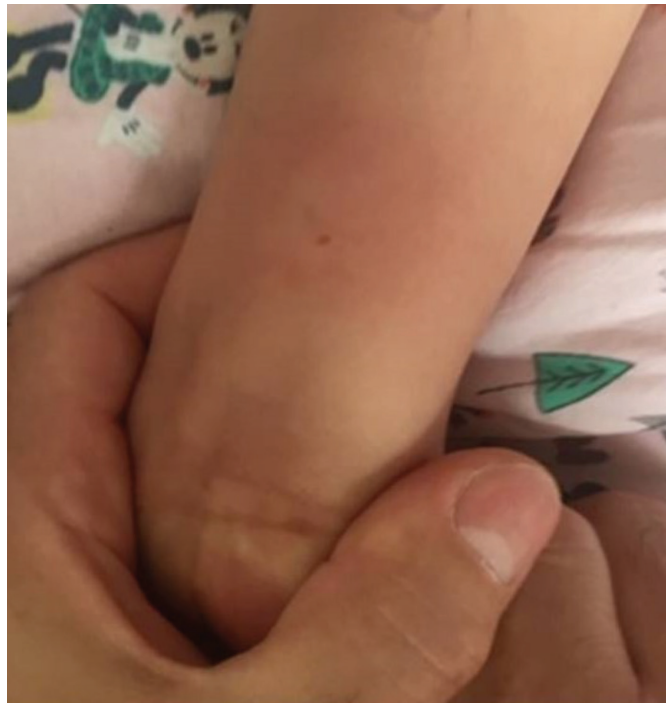

Figure 2. Positive result to intradermal test with 0.02 mg/mL (100 times dilution) of ondansetron (hyperaemia, 35 mm; wheal, 20 mm)

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urticarial wheal near the injection site. It was successfully treated with administration of antihistaminic drug without any need of further medications such as epinephrine and/or prednisolone.

In the literature, hypersensitivity reaction induced by ondansetron has been reported in patients with cancer, who are undergoing chemotherapy with a prior history of ondansetron exposure (3-10). However, some authors hypothesise that hypersensitivity may be a class effect, while some others suggest that it is drug-specific effect as long as ondansetron and tropisetron contain indole ring, whereas granisetron does not (5). Thereby, some authors advise avoidance of all 5-HT3 antagonists after developing hypersensitivity to ondansetron. Others have demonstrated the successful utilisation of granisetron (9,10).

Before giving a substitute drug to a patient with drug allergy, it is compulsory to first learn possible cross-reactivity by performing skin tests and provocation tests (6). Granisetron might be an alternative antiemetic agent for patients with cancer who are undergoing chemotherapy (9,10).

In conclusion, we describe a rare case of IgE-mediated type I hypersensitivity to ondansetron that presents as isolated urticaria (9). In consistent with the literature, granisetron can be considered a safer potent alternative to ondansetron in patients with cancer who are receiving chemotherapy.

Informed Consent: Verbal and written informed consents were obtained from the patient's parents for publication of this case report and any accompanying images.

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