Very Early Development of Carboplatin-Associated Hypersensitivity Reaction in a Patient with Relapsed Ovarian Cancer: Case Report

Nükseden Over Kanserli Bir Hastada Karboplatin İlişkili Cilt Hipersensitivite Reaksiyonunun Çok Erken Gelişmesi

Ali Osman KAYA,[a]
Aysun KAYA[b]

[a]Clinic of Medical Oncology, Bahçelievler Medicana Hospital,
[b]Department of Medical Microbiology, Istanbul University İstanbul Faculty of Medicine, İstanbul

Geliş Tarihi/*Received:* 07.06.2012
Kabul Tarihi/*Accepted:* 04.01.2013

Yazışma Adresi/*Correspondence:*
Ali Osman KAYA
Bahçelievler Medicana Hospital, Clinic of Medical Oncology, İstanbul, TÜRKİYE/TURKEY
aosmankaya@gmail.com

ABSTRACT Carboplatin-related hypersensitivity reactions usually occur following multiple infusions. These infusions rarely cause acute or severe cutaneous reactions. Premedication therapy with dexamethasone and diphenhydramine are utilized to avoid possible side effects of this drug. The patient in our case study initially received six cycles of chemotherapy consisting of carboplatin plus paclitaxel as first line therapy between the dates of February 2010 and June 2010. However in August 2011, the disease had reoccurred. The same treatment regimen was started due to the prior platinium sensitivity. Within the second minute of the third cycle of the chemotherapy carboplatin infusion, an erythematous cutaneous eruption appeared widely on the trunk and arms. The carboplatin infusion was immediately discontinued. Dexamethasone, diphenhydramine and ranitidine therapy was rapidly administered. In the two hour follow-up examination, all the erythematous lesions disappeared. In this article, we will present the very early onset of carboplatin hipersensitivity reaction in a female patient with relapsed ovarian cancer.

Key Words: Carboplatin; hypersensitivity; ovarian epithelial cancer

ÖZET Karboplatin ilişkili hipersensitivite reaksiyonları, genellikle çok sayıda infüzyonlar sonrasında gözlenir. Bu infüzyonlar akut veya ciddi cilt reaksiyonlarına nadiren yol açar. Bu ilacın yan etkilerinden kaçınmak için tedavi öncesi, deksametazon ve difenhidraminli premedikasyon tedavisi kullanılır. Olgu çalışmamızdaki hasta, birinci basamak tedavi olarak Şubat 2010 ile Haziran 2010 tarihleri arasında karboplatin ve paklitakselden oluşan kemoterapiyi 6 siklüs olarak almıştı. Hastalık, Ağustos 2011 tarihinde nüks etti. Platin duyarlı olması nedeniyle aynı tedavi rejimi başlandı. Üçüncü siklüs karboplatin infüzyonunun ikinci dakikasında, gövde ve kollarda yaygın eritematöz cilt döküntüleri ortaya çıktı. Karboplatin infüzyonu hemen sonlandırıldı. Deksametazon, difenhidramin ve ranitidin tedavisi hızlıca verildi. İki saat takip sonrası, tüm eritematöz lezyonlar kayboldu. Bu makalede, biz nüks eden over kanserli bir kadın hastada çok erken başlangıçlı karboplatin hipersensitivite reaksiyonunu sunduk.

Anahtar Kelimeler: Karboplatin; aşırı duyarlılık; ovaryum epitel kanseri

Turkiye Klinikleri J Gynecol Obst 2013;23(2):103-5

Carboplatin is widely used for the treatment of several solid tumors such as lung and ovarian cancer. Although carboplatin is usually well tolerated and has moderate toxicity, the greater and prolonged use of carboplatin is associated with an increased incidence and severity of carboplatin-related hypersensitivity reactions.[1] However, although the rapid administration of dexamethasone and diphenhydramine for premedication therapy, the risk of carboplatin-related hypersensitivity reactions is in-

creased following several cycles of chemotherapy (in most cases >6).[1,2] We reported the very early onset of carboplatin-related cutaneous hypersensitivity reaction in a 57-year-old female patient with relapsed ovarian cancer that received treatment with carboplatin plus paclitaxel in the second-line setting.

CASE REPORT

The patient has received six cycles of chemotherapy consisting of carboplatin plus paclitaxel as the first line therapy between the dates of February 2010 and June 2010. Premedication therapy consisted of dexamethasone 20 mg and diphenhydramine 50 mg prior to all cycles of chemotherapy. During the first line treatment period, hypersensitivity reaction was not observed and other toxicities were well tolerated. Because of clinical and marker complete response to first line chemotherapy, the patient underwent a total abdominal hysterectomy (TAH) and bilateral salpingo-oopherectomy (BSO) in July 2010. During her follow-up care in August 2011, peritoneal implants and liver metastases were detected. In addition, CA-125 levels were elevated (CA-125: 68 IU/mL). The same treatment regimen was planned due to the platinium-sensitive nature of the tumors. Premedication therapy of dexamethasone 20 mg and diphenhydramine 50 mg was utilized once again. Because partial response (PR) was achieved after two cycles of chemotherapy, it was decided to continue the same treatment regimen. For the third cycle of second line chemotherapy, the same premedication therapy was used again. Severe pruritus began on the palmar and back surfaces in the first minute of carboplatin infusion. Shortness of breath, anxiety and fear were also observed in the patient. An erythematous cutaneous eruption appeared widely on the trunk and arms in the second minute of carboplatin infusion (Figure 1, 2). The carboplatin infusion was immediately discontinued. A 16 mg dose of dexamethasone, 50 mg of diphenhydramine and 150 mg of ranitidine was administered. The patient was monitored and by the two hour follow-up, all of the erythematous lesions disappeared. After this experience the patient refused

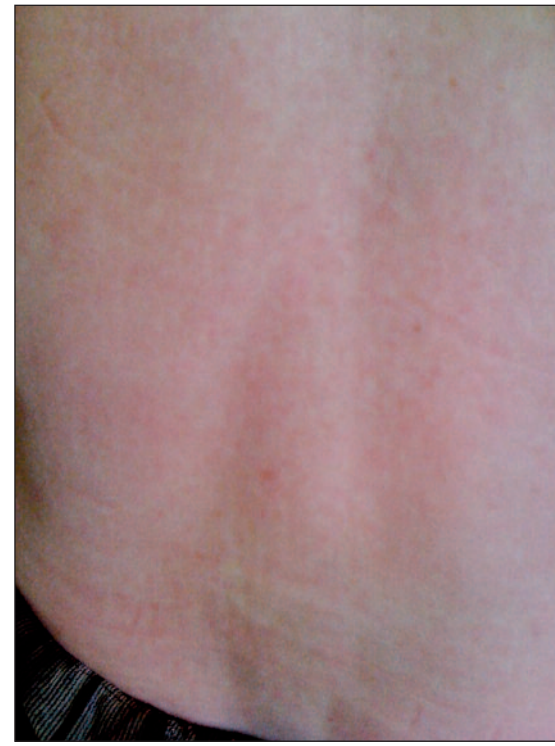

FIGURE 1: The erythematous cutaneous eruptions appeared widely on the trunk.
(See for colored form http://jinekoloji.turkiyeklinikleri.com/)

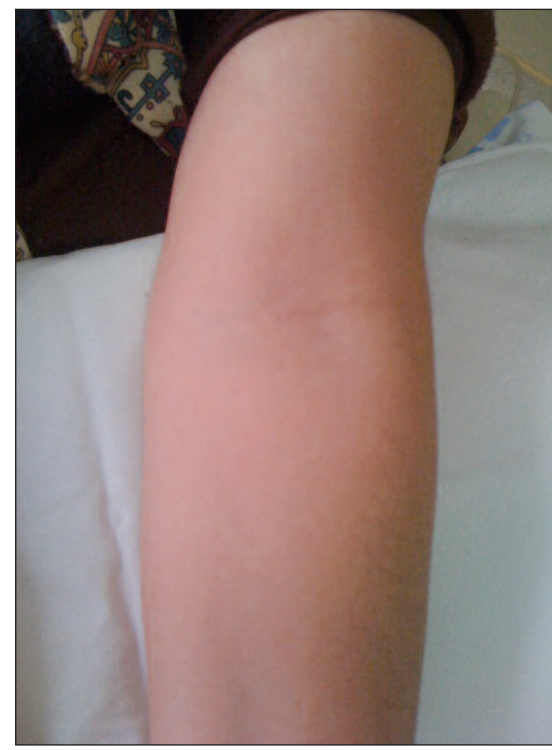

FIGURE 2: The erythematous cutaneous eruptions appeared widely on the arms.
(See for colored form http://jinekoloji.turkiyeklinikleri.com/)

another intravenous chemotherapy cycle, thus oral etoposide therapy was started. Clinical and biomarker complete response was achieved after the completion of six cycles of chemotherapy. The patient is still alive and currently under follow up care plan.

DISCUSSION

The exact mechanism of carboplatin hypersensitivity reactions remains unclear. It is hypothetically possible that several immune pathways such as type I response mediated by immunoglobulin E or mast cell degranulation leading to histamine and cytokines release could be the cause.[3,4] Platinum agent-induced advers events may appear with several clinical findings from mild rash and diffuse erythroderma to serious anaphylactic reactions.[1,5] Although the administration of premedication treatment consisting of dexamethasone and diphenhydramine, the carboplatin-associated hypersensitivity reactions usually occur following several cycles of chemotherapy.[1,2] In addition, the incidence and severity of carboplatin-associated hypersensitivity reactions have been noted to follow six cycles of chemotherapy.[1,2,6] In a current study, the mild, severe and lethal hipersensitivity reactions caused by carboplatin and oxaliplatin were reported more than cisplatin. Furthermore, in the same study, it was found that dexamethasone and diphenhydramine were an effective therapy for the treatment of platinum-related hypersensitivity reactions.[6]

In our case, at the beginning of third cycle of second line chemotherapy during the first few minutes of of intravenous carboplatin infusion,the reaction occured. This reaction included severe pruritus of the palms and a diffuse erythematous eruption on the back. The carboplatin infusion was immediately discontinued; then the dexamethasone 16 mg, diphenhydramine 50 mg and ranitidine 150 mg therapy was administered to treat the hypersensitivity reaction. By the two hour follow-up examination, all of the erythematous lesions disappeared. In fact, the hypersensitivity reaction was related to the cumulative number of infusions rather than the cumulative dose of carboplatin.[2] Therefore, it is recommended that skin testing should be considered prior to the infusion of the eighth cycle, preferably before the sixth cycle. This testing could accurately predict patients who will develop carboplatin hypersensitivity reactions.

In conclusion, because the hypersensitivity reactions to carboplatin are very significant, the prospective studies that use prolonged carboplatin-containing protocols should include screening and management recommendations for carboplatin-related allergic reactions.

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