Anti-Cancer Drugs 1995, **6**, pp. 775–776

Case report

Carboplatin-related idiosyncrasy

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Side effects of cisplatin and carboplatin include nausea, vomiting, peripheral neuropathy, nephrotoxicity, hearing loss, bone marrow depression, and rarely Lhermitte's sign and allergic reactions. A unique case of idiosyncrasy related to carboplatin administration was observed in a young woman treated for ovarian cancer. Symptoms and signs included skin rash, shortness of breath, and redness of face and upper trunk, without drop in blood pressure or change in heart rate, and were resolved within a short time following administration of hydrocortisone and promethazine.

Key words: Carboplatin, idiosyncrasy, toxicity.

Introduction

Platin-containing drugs have been widely introduced into common regimes used for treating ovarian cancer, germ cell tumors and other malignancies. This resulted in improved control of the disease and improval of patients survival. A wide spectrum of toxic manifestations has been attributed to the use of cisplatin, carboplatin and newer analogs. The side effects include nausea, vomiting, peripheral neuropathy, nephrotoxicity, hearing loss, bone marrow depression and more rarely Lhermitte's sign.[1] Allergic reactions and idiosyncrasy were only seldom reported, mainly in association with exposure to platin-compounds in industrial workers and in patients receiving cisplatin.[2–4] Idiosyncrasy to carboplatin, an extremely rare manifestation, is herewith reported in a patient with ovarian cancer.

Case presentation

A 47 year old woman patient, mother to one boy, suffered from right upper quadrant (RUQ) abdominal pain, unrelated to food intake, but aggravating during the night time. No associated nausea, vomiting, change in bowel habits or weight loss were reported by the patient. Upper gastrointestinal series, ultrasound of the abdomen and pelvis, and physical, including gynecological, examinations were unrevealing. Six weeks following the onset of the RUQ pain, she underwent an emergency laparotomy due to severe and diffuse abdominal pain and clinical signs of pertonitis. Bloody ascites containing adenocarcinoma cells was found. The abdominal cavity, omentum, liver and pelvic organs were infiltrated by tumor, which was diagnosed as moderately differentiated serous papillary cystadenocarcinoma compatible with ovarian origin. In May 1992 she started on combination chemotherapy, based on three-weekly courses of cisplatin 75 mg/m^2 and cyclophosphamide 750 mg/m^2. Granisetron (Kytril) 3 mg and dexamethasone 20 mg i.v. were prescribed to control emesis. Partial response was achieved after six courses as documented by ancillary studies, leaving a residual mass of 1.1 × 1.4 cm in the left parametrium. CA 125 level returned to its normal range following the fourth course. Second look laparotomy was carried out in November 1992. Total abdominal hysterectomy, bilateral salpingo-oophorectomy and omentectomy were performed, leaving behind no macroscopic disease. Pathological examination showed bilateral ovarian moderately differentiated adenocarcinoma, which also involved the omentum. Chemotherapy consisting of three-monthly carboplatin 300 mg/m^2 and cyclophosphamide 750 mg/m^2, and Kytril and dexamethasone to control emesis as before, was prescribed for two consecutive years. Following the sixth course, peripheral neurotoxicity was diagnosed. During the seventh course, while on carboplatin infusion, the patient developed an acute reaction manifested by skin rash and shortness of breath. Interruption of the infusion and administration of hydrocortisone 250 mg and promethazine 25

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mg i.v. resulted in complete recovery. A late idiosyncratic reaction was suspected, but could not be proven. After a thorough anamnesis that revealed no change in drug and food habits, we decided that this episode could have happened by chance, and the eighth course was given as planned. The eighth course started with infusion of Kytril followed by cyclophosphamide, but while on carboplatin (600 mg dissolved in 500 ml glucose 5%), after a dose of 250 mg, she developed redness of face and upper trunk, shortness of breath without drop in blood pressure or change in heart rate. The symptoms and signs resolved within a short time following administration of hydrocortisone and promethazine. Since there was no evidence for disease at this time, chemotherapy was stopped and the patient remained on follow-up.

Discussion

Our patient represents a rare case of idiosyncrasy related to administration of carboplatin. We have no doubt that our patient developed late idiosyncrasy to carboplatin. We have no definite explanation for the late occurrence. It is possible that antibodies to platin-compounds developed after repeated courses of cisplatin (six courses of 75 mg/m^2 each) and carboplatin (six courses of 300 mg/m^2 each), and were responsible for this phenomenon.

Only two cases have been reported previously in the literature. Saunders *et al.* observed generalized pruritus in a 36 year old woman having a second relapse following a total number of nine courses of cisplatin and five courses of carboplatin. The relapsing disease was treated by carboplatin and during the third course pruritus developed. Since the pruritus was mild and was not accompanied by more severe phenomena, treatment was continued with prophylactic administration of steroids and antiemetics.[3] A second case, reported by Windom *et al.*, was a 69 year old non-atopic woman with ovarian cancer, who relapsed following treatment with eight courses of cisplatin. The relapsing disease was treated by carboplatin, but during the first course pruritus in the hands developed. Prophylactic treatment by steroids and anti-histamines did not prevent the symptoms and signs during the next dose. These included perioral tingling, palmar pruritus, dyspnea, cyanosis, urinary incontinence, hypotension and hypoxemia. In this case treatment was completed by using escalating doses of carboplatin.[5]

The mechanism responsible for the reaction to *cisplatin* is undetermined. It was claimed to be type 1 hypersensitivity reaction combined with direct release of histamine from mast cells and basophils, unrelated and unmediated by IgE production.[2] The mechanism responsible for the reaction to *carboplatin* was assumed to be type 1 hypersensitivity reaction or idiosyncrasy. Hypersensitivity was suggested by the findings in the second case.[5] Skin tests were positive for platinum compounds and serum level of IgE was high.[5] However, Kawano *et al.*[6] found that carboplatin did not have antigenic or haptenic properties in animal model, in a dose that did not suppress the immune reactions, and excluded the possibility of allergy to carboplatin.

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(Received 29 June 1995; received in revised form 25 July 1995; accepted 27 July 1995)