



## OLGU SUNUMU/CASE REPORT

# Carboplatin hypersensitivity in children with glial tumors: a report of two cases

Glial tümörlü çocuklarda karboplatin hipersensitivitesi: iki olgu sunumu

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### Abstract

Carboplatin, commonly used chemotherapeutic agent in treatment of pediatric cancers, can cause life-threatening hypersensitivity reactions. Carboplatin hypersensitivity is protocol-specific and associated with repeated doses and prolonged use of the drug. Vincristin and carboplatin combination is used efficiently in treatment of pediatric low-grade gliomas. However, hypersensitivity reactions are frequently observed during usage of this protocol. Desensitization strategies with variable success rates were reported. Failure of these strategies may lead to cessation of carboplatin. Here, we report two cases with carboplatin hypersensitivity treated with epinephrine administration, in whom carboplatin was discontinued after hypersensitivity reaction.

**Key words:** carboplatin, hypersensitivity, glial tumors

### Öz

Pediyatrik kanserlerin tedavisinde sıklıkla kullanılan kemoterapi ajanlarından biri olan karboplatin, yaşamı tehdit edici hipersensitivite reaksiyonlarına neden olabilir. Karboplatin hipersensitivitesi protokole özgü olup, ilacın uzun süreli ve tekrarlı dozlarda kullanımı ile ilişkilidir. Karboplatin ve vinkristin kombinasyonu pediyatrik düşük gradeli gliomların tedavisinde etkin bir şekilde kullanılmaktadır. Ancak, bu protokolün kullanımı sırasında hipersensitivite reaksiyonları sıklıkla gözlenmektedir. Değişen oranlarda başarı elde edilen desensitizasyon stratejileri bildirilmiştir. Bu stratejilerin başarısız olması durumunda karboplatin tedavisinin kesilmesi söz konusu olabilir. Burada, epinefrin uygulaması ile tedavi edilen ve hipersensitivite reaksiyonu gelişmesi sonrasında karboplatin tedavilerine devam edilemeyen iki karboplatin hipersensitivitesi olgusu sunulmuştur.

**Anahtar kelimeler:** karboplatin, hipersensitivite, glial tümörler

## INTRODUCTION

Carboplatin is one of the second generation platinum compounds that produces inter- and intra-strand DNA links, inhibits DNA synthesis and causes cytotoxicity<sup>1</sup>. Carboplatin is widely used in treatment of childhood cancer and takes place as various dosages in treatment schedules of central nervous system tumors, retinoblastoma, neuroblastoma, germ cell tumors, sarcomas in children<sup>2</sup>.

Carboplatin hypersensitivity (CH) is a well-known entity observed especially in long term usage of the drug. CH has been reported up to %30 in pediatric case series<sup>3</sup>. CH may result in cessation of the drug.

Therefore, it is important to develop strategies for desensitization in these patients in whom carboplatin is essential in treatment<sup>4</sup>. Herein we report two children receiving weekly carboplatin for treatment of glial tumors who developed CH after repeated doses.

## CASE 1

A-sixteen-month-old female presented with multiple cafe-au-lait spots. Physical examination findings were unremarkable except for cafe-au-lait spots. Neurofibromatosis type 1 (NF1) diagnosis was also present in her father, grandmother and aunt. Cerebral magnetic resonance imaging (MRI)

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revealed multiple hamartomatous lesions and bilateral thickening of canalicular and intracranial segments of optic nerves. Visual evoked potential test showed N70 and P100 components were severely affected with normal amplitudes. Carboplatin (175 mg/m<sup>2</sup> day 1) with vincristine (1.5 mg/m<sup>2</sup> day 1) were started. During the 18th week of chemotherapy (at the end of maintenance course 1), cough was observed immediately after the starting infusion of carboplatin. Shortly after cough, maculopapular rash on the face and upper trunk and slight swelling of the lips and eyebrows were noticed. Infusion was stopped and epinephrine (0,3 mg, intramuscular) was administered. Symptoms resolved in fifteen minutes. Carboplatin was ceased after development of anaphylaxis. Orbital MRI revealed stable thickening in optic nerves and VEP showed mild improvement in N70 and P100 components. Follow-up was made by MRI in 6-months-intervals. No progression was reported neither on MRI nor with VEP during 24 months without treatment.

## CASE 2

Nine-year-old female had admitted to another hospital with history of convulsions two years earlier than admission to our department. She had been operated for temporal mass detected on cranial MRI for the first time. After the operation, a residual mass was observed in the primary tumor location and second operation was performed. Low grade glioneuronal tumor was reported in histopathological examination. Fifteen months after second surgery, progression was noticed in the temporal mass. She was operated for the third time. Radiotherapy was given to tumor location. After radiotherapy, chemotherapy with carboplatin (175 mg/m<sup>2</sup> day 1) and vincristin (1.5 mg/m<sup>2</sup> day 1) were started. At the 10th month of treatment, cough, hyperemia on the face and neck and swelling on the lips and eyelid were noticed during carboplatin infusion. Epinephrine (0,3 mg, intramuscular) was administered. MRI examination revealed stable mass located in temporal region and treatment was ceased due to family's refusal.

## DISCUSSION

Hypersensitivity reactions with carboplatin is a well-known condition observed in patients with low grade glioma treated with carboplatin-based

chemotherapy. However, majority of reports on this subject in English medical literature includes adults and there are a few pediatric case series<sup>5-9</sup>. The exact underlying mechanism in the carboplatin hypersensitivity and delayed type reactions are not known. However, IgE-mediated immediate type hypersensitivity is thought to be involved<sup>9,10</sup>. Repeated doses of the drug increases the risk of hypersensitivity with highest risk reported at 8th course of carboplatin<sup>11,12</sup>.

Hypersensitivity symptoms include cutaneous erythema, urticaria, maculopapular rash, palmar erythema, facial flushing and swelling, itching, cough, wheezing, dyspnea, chills, rigor, throat and chest tightness, blood pressure changes<sup>13</sup>. Weekly or monthly administration of the drug were found to be equally affecting hypersensitivity incidence. However, weekly administration resulted earlier hypersensitivity development<sup>5,12</sup>. Carboplatin hypersensitivity was reported more frequently in females than males<sup>5,14</sup>. In our patients, CH was noticed during 12th and 24th carboplatin infusions and both of our patients were females similar to findings reported in literature.

It is difficult to make an accurate decision about continuation of treatment with carboplatin in these patients who have developed mild or severe allergic reactions. It has been reported that the frequency of a more severe allergic reaction after re-exposure was 32%<sup>5</sup>. Carboplatin is one of the most effective chemotherapeutic agent in treatment of low grade gliomas in children. Therefore in case of hypersensitivity reaction, a desensitization protocol is required as the replacement of the drug with another agent with same efficacy is not possible. Various desensitization protocols have been reported<sup>10,15,16</sup>. Confino-Cohen et al.<sup>10</sup> used different diluted concentrations of carboplatin and started with the lowest dilution with premedication including antiemetic and dexamethasone. Success rate was reported to be 95% with desensitization. However, a current study reported low efficacy with desensitization protocol<sup>17</sup>. Shah et al.<sup>18</sup>, proposed a clinical algorithm using carboplatin challenge with H1 and H2 antagonists, corticosteroids and prolonged infusion instead of abandoning carboplatin.

Hypersensitivity reactions are more common than it is reported. Repeated doses of carboplatin and combination with vincristin increases the risk. The possibility of hypersensitivity reactions should be

kept in mind especially in children with low grade glioma treated with this combination. Desensitization strategies can be used in case of CH in appropriate clinical conditions.

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