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SHORT COMMUNICATION

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Severe ocular and orbital toxicity after intracarotid injection of carboplatin for recurrent glioblastomas

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Abstract *Background*: Glioblastoma is a malignant tumor that occurs in the cerebrum during adulthood. With current treatment regimens including combined surgery, radiation and chemotherapy, the average life expectancy of the patients is limited to approximately 1 year. Therefore, patients with glioblastoma sometimes have intracarotid injection of carcinostatics added to the treatment regimen. Generally, carboplatin is said to have milder side effects than cisplatin, whose ocular and orbital toxicity are well known. However, we experienced a case of severe ocular and orbital toxicity after intracarotid injection of carboplatin, which is infrequently reported. *Case*: A 58-year-old man received an intracarotid injection of carboplatin for recurrent glioblastomas in his left temporal lobe. He complained of pain and visual disturbance in the ipsilateral eye 30 h after the injection. Various ocular symptoms and findings caused by carboplatin toxicity were seen. *Results*: He was treated with intravenous administration of corticosteroids and glycerin for 6 days after the injection. Although the intraocular pressure elevation caused by secondary acute angle-closure glaucoma decreased and ocular pain diminished, inexorable papilledema and exudative retinal detachment continued for 3 weeks. Finally, 6 weeks later, diffuse chorioretinal atrophy with optic atrophy occurred and the vision in his left eye was lost. *Conclusion*: When performing intracarotid injection of carboplatin, we must be aware of its potentially blinding ocular toxicity. It is recommended that further studies and investigations are undertaken in the effort to minimize such severe side effects.

Introduction

Today, carcinostatics are necessary for the treatment of malignant tumors. Intravenous administration is usual, but patients sometimes receive a local intra-arterial injection of carcinostatics to obtain stronger efficacy against localized lesions.

Intracarotid injection is a mode of intra-arterial administration for brain tumors. Dozens of reports have noted that intracarotid injection of cisplatin can cause severe ocular and orbital toxicity [3, 4, 6, 7]. Although carboplatin is a platinum complex like cisplatin, it is reported that in patients with malignant gliomas carboplatin injected by the intra-arterial route seems less toxic than cisplatin [2]. However, we experienced a rarely reported case of severe reaction to intracarotid carboplatin.

Case report

A 58-year-old man with recurrent glioblastoma in his left temporal lobe received an intracarotid injection of carboplatin on 9 August 2001. He had been diagnosed with glioblastoma in his left temporal lobe on 23 April 2001 and then underwent surgery on 30 April 2001.

The patient was injected with carboplatin via the left carotid artery after placement of a catheter using a percutaneous transfemoral arterial approach. The tip of the catheter was placed distal to

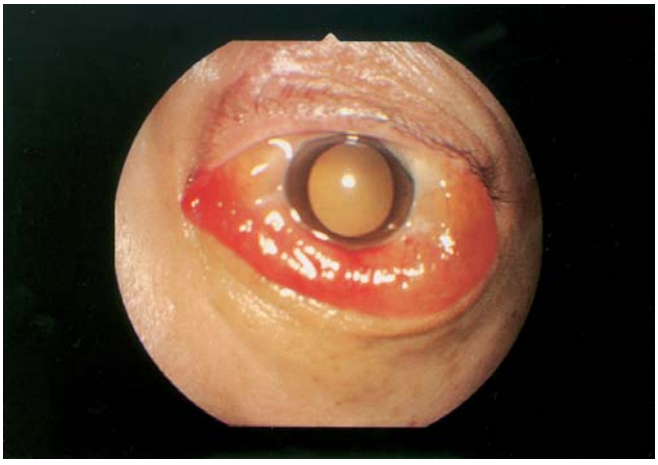

Fig. 1 Marked chemosis and acute angle-closure glaucoma with mydriasis were seen in the left eye. The intraocular pressure was kept relatively low by intravenous administration of betamethasone phosphate and glycerin, and the cornea maintained its clarity. There was also ocular motility disturbance in all directions

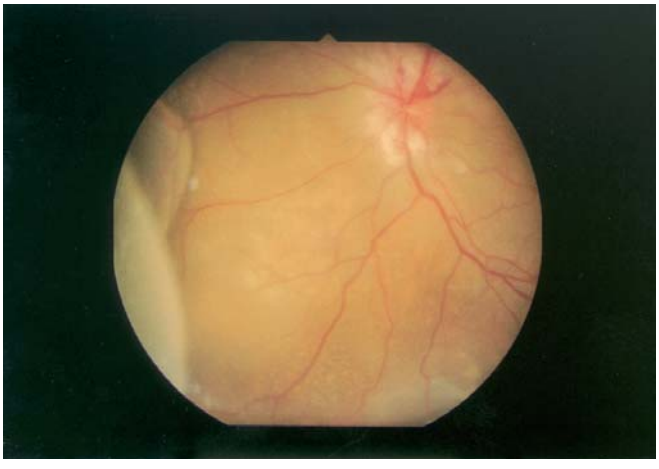

Fig. 2 There was bullous exudative retinal detachment at the nasal and inferior region. There were neither tears nor holes in the retina. The optic disc was edematous and its margin was not clear

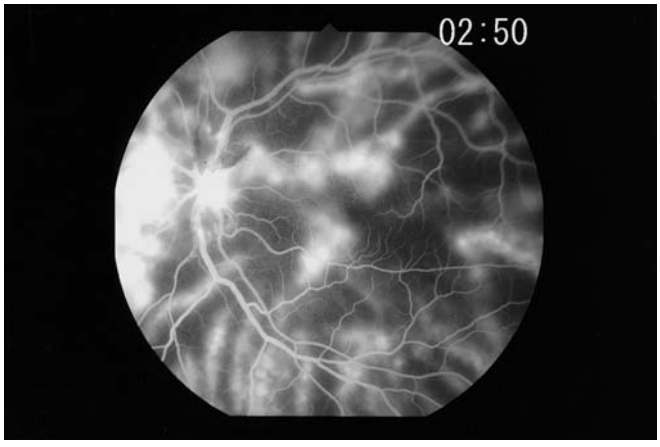

Fig. 3 Fluorescein angiography showed prolonged choroidal hyperfluorescence with dye leakage. This image is similar to that of typical vasculitis

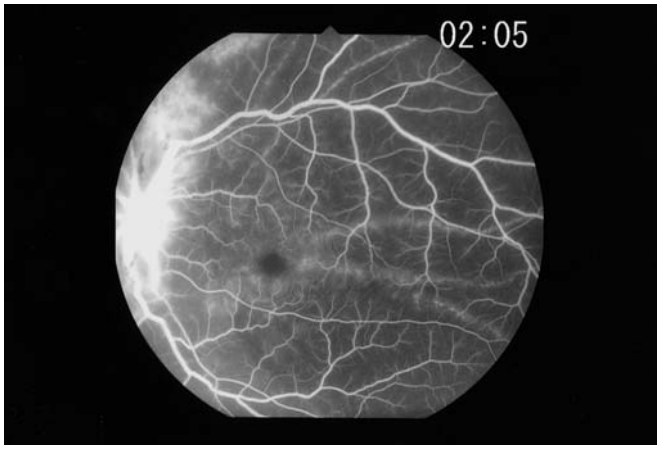

Fig. 4 The marked dye leakage seen in Fig. 3 decreased. The vasculitis subsided markedly

the ipsilateral ophthalmic artery. A test injection of the contrast medium did not demonstrate the ophthalmic artery. Then, 550 mg of carboplatin dissolved in 137 ml of 5% glucose solution and filtered prior to use was prepared, and 76 ml of the carboplatin solution, in which there was 306 mg of carboplatin, was injected with the contrast medium intermittently over a 60-min period. The remaining solution was injected into other regions.

The patient complained of pain and severe visual disturbance in the left eye 30 h after the injection and was referred to us by his neurosurgeon on 13 August 2001. Various ocular and orbital symptoms and findings such as ocular pain, marked visual disturbance, ocular motility disturbance in all directions, marked chemosis (Fig. 1), acute angle-closure glaucoma, papilledema and exudative retinal detachment (Fig. 2) were seen. His visual acuity was 1.5 OD and hand motion OS. Intraocular pressure was 12 mmHg OD and 33 mmHg OS. His right eye was unremarkable. He had already been treated with intravenous administration of 8 mg of betamethasone phosphate and 200 ml of glycerin after the intracarotid carboplatin before his first visit. This treatment was continued for 6 days.

Ocular pain diminished and the intraocular pressure decreased to 24 mmHg OS on the day after his first visit. Fluorescein angiography in his left eye showed prolonged choroidal hyperfluorescence, with dye leakage into the subretinal space, as well as areas of choroidal non-perfusion, retinal capillary non-perfusion, and leakage from the optic disc with dilated retinal veins, together suggestive of severe choroidal inflammation (Fig. 3). External ophthalmoplegia, chemosis, papilledema and exudative retinal detachment continued for 3 weeks.

Gradually the vasculitis subsided (Fig. 4), and the papilledema and exudative retinal detachment had disappeared 3 weeks later. Finally, 6 weeks later, his left fundus showed diffuse chorioretinal atrophy with optic atrophy (Fig. 5), and the vision in his left eye was lost.

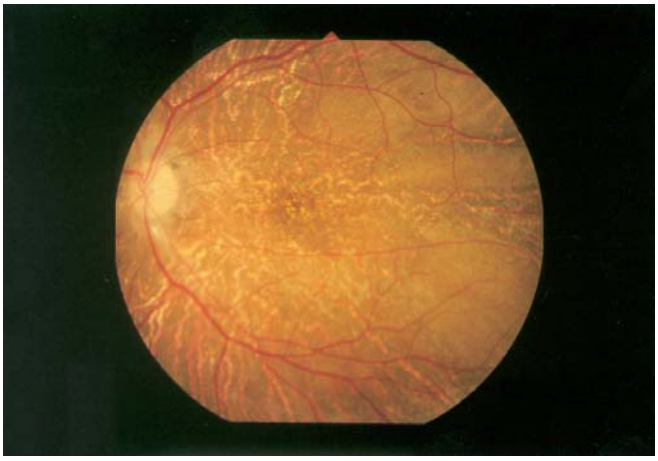

Fig. 5 Inflammation subsided and exudative retinal detachment disappeared, but diffuse chorioretinal atrophy with optic atrophy remained

Discussion

It is suspected that the severe ocular and orbital toxicity in this case was caused by an influx of carboplatin to the ophthalmic artery. Although the injection was performed carefully by a skilled neurosurgeon, there could have been an influx of carboplatin backwards to the ophthalmic artery because its viscosity is lower than that of the contrast medium. Placement of a catheter above the ophthalmic artery does not guarantee that the ipsilateral eye and orbit can be protected from potentially blinding side effects [6].

Carboplatin is an alkylating agent that inhibits DNA replication and fragments DNA, leading to cell death. Intravenous administration of carboplatin has been associated with maculopathy, optic neuritis, and cortical blindness [8]. But its cytotoxic mechanisms do not explain the acute ocular and orbital inflammation seen in this case.

Subconjunctival administration of carboplatin for the treatment of intraocular retinoblastoma has been reported. The authors stated that a transient periorbital edema is common, but did not refer to the posterior segment disorder [1].

Various symptoms and findings in this case may be the results of vasculitis caused by carboplatin toxicity. We suggest the following explanations: the vasculitis of orbital soft tissue caused the chemosis; extraocular muscular inflammation and the increase in volume disturbed ocular motility [5]; inflammatory ciliochoroidal effusion displaced the lens-iris diaphragm forward and caused acute angle-closure glaucoma; and the choroidal effusion also caused the exudative retinal detachment at the posterior fundus.

There are dozens of reports of severe ocular and orbital toxicity after intracarotid cisplatin [3, 4, 6, 7]. However, there are not many cases of severe ocular and orbital toxicity after intracarotid carboplatin. Recently only a case involving intracarotid etoposide phosphate and carboplatin has been reported [5]. In contrast, in our case severe toxicity was caused by carboplatin alone and the ipsilateral eye showed exudative retinal detachment, which was not seen in that case.

Our observations confirm the ocular and orbital toxicity of intracarotid carboplatin injection. When performing intracarotid injection of carcinostatics, which now is becoming a common method of chemotherapy for brain tumors, we must be aware of carboplatin's ocular and orbital toxicity. It is important for ophthalmologists and neurosurgeons to remember its potentially blinding side effects and to minimize them. We expect that further studies and investigations will lead to intracarotid chemotherapy becoming a safer and more effective method of treatment for brain tumors in the near future.

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