Optic nerve degeneration caused by supraophthalmic carotid artery infusion with cisplatin and ACNU

Case report

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A 28-year-old woman with a left frontoparietal anaplastic astrocytoma was treated postoperatively with a combination of cisplatin and 1-(4-amino-2-methylpyrimidine-5-yl) methyl-3-(2-chloroethyl)-3-nitrosourea hydrochloride (ACNU). The drugs were infused via the left supraophthalmic internal carotid artery in an attempt to avoid ocular toxicity. The patient subsequently developed blindness in the left eye and a right temporal hemianopsia from marked degeneration of the left optic nerve and tract. It is apparent that the placement of a catheter into the supraophthalmic carotid artery does not exclude visual complications.

KEY WORDS ▪ anaplastic astrocytoma ▪ intra-arterial infusion ▪ cisplatin ▪ ACNU ▪ optic nerve degeneration ▪ toxicity

THE efficacy of infusion of chemotherapeutic agents into the carotid artery for the treatment of malignant brain tumors has been reported. However, drugs infused into the cervical internal carotid artery (ICA) also perfuse the ophthalmic artery, causing ocular toxicity in some cases; reported instances include loss of vision, retinal vasculitis, formation of cataracts, and neovasculization of the anterior chamber. To avoid these complications, infusion of drugs into the ICA above the origin of the ophthalmic artery has been advocated. We report a patient treated with supraophthalmic intracarotid infusion of chemotherapeutic agents. Subsequently, degeneration of the optic nerve and tract developed to cause blindness of the left eye and a right temporal hemianopsia. We report this case and review the literature.

Case Report

This 28-year-old woman visited Kobe West Municipal Hospital with a chief complaint of speech disturbance following a seizure on August 10, 1987.

First Admission and Operation. Neurological examination revealed a slight motor aphasia which resolved 1 hour later. Magnetic resonance imaging and computerized tomography (CT) demonstrated a left frontal lobe tumor. One week later, a left frontoparietal craniotomy was performed and the tumor was subtotally removed. Histological examination revealed that the tumor was an anaplastic astrocytoma.

Postoperative Course. The patient received 4500 rads of whole-brain irradiation supplemented by intra-arterial infusion of cis-diammine dichloroplatinum (cisplatin) and 1-(4-amino-2-methylpyrimidine-5-yl) methyl-3-(2-chloroethyl)-3-nitrosourea (ACNU). Prior to drug infusion, 1 liter of fluid and 10 gm of mannitol were given intravenously over 2 hours and 10 minutes, respectively. The left ICA was cannulated by direct puncture of the common carotid artery using a fluoroscopy-guided leak-balloon catheter. The leak-balloon was negotiated up to the ICA above the origin of the ophthalmic artery (Fig. 1) in order to avoid the drugs being delivered into the ophthalmic artery. Thereafter, 150 mg ACNU and 100 mg cisplatin were infused continuously into the supraophthalmic portion of the ICA at the rate of 10 and 2 mg/min, respectively. The location of the leak-balloon was intermittently ascertained with fluoroscopy during the infusion.
A leak-balloon is placed between the ophthalmic artery and the posterior communicating artery (right). After the procedure, the patient was well except for moderate bone marrow suppression. About 40 days later, she started to complain of blurred vision which progressed within a week to blindness of the left eye and a right temporal hemianopsia. Extraocular movements were normal and ophthalmological evaluation revealed no retinal abnormalities. Left carotid angiography and CT were normal. Magnetic resonance studies demonstrated bilateral swelling of the optic nerves on T1-weighted images, and the T2-weighted images demonstrated high signal intensity in the chiasm and left optic tract (Fig. 2). These findings confirmed the presence of a mass in the chiasmal region.

**Second Operation.** A left frontotemporal craniotomy was performed on November 30, 1987. The chiasmal arachnoid membrane, left ICA, middle cerebral artery, and anterior cerebral artery were normal. The optic chiasm and bilateral optic nerves were slightly whitish and swollen but no neoplasm was found. Biopsy of the left side of the optic nerve and chiasm was performed. Postoperatively, the patient developed no additional neurological deficits.

**Pathological Examination.** The biopsy specimen was stained with hematoxylin and eosin (H & E), phosphotungstic acid hematoxylin, Bodian, and Luxol fast blue. Staining with H & E was poor. Microscopic examination revealed that the normal anatomical structures of the optic nerve were obscure and several focal areas of macrophage accumulation were found. The axons were partially destroyed and the myelin was completely disintegrated leaving only a small number of myelin droplets (Fig. 3). Degenerated areas adjacent to the perineurium were associated with gliosis. From these findings, marked degeneration of the optic nerve was diagnosed.

**Discussion**

Intra-arterial infusion of chemotherapeutic agents reduces systemic toxicity of the drugs but ocular toxicity may occur. In our case, cisplatin (60 mg/sq m) and ACNU (3 mg/kg) were infused via a leak-balloon catheter inserted through the common carotid artery into the supraophthalmic ICA under fluoroscopic control. Before infusion of these drugs, contrast medium was infused at a rate of 3 ml/min. It was ascertained under fluoroscopy that the contrast medium was mixed diffusely with circulating blood (Fig. 1). The drugs were delivered in the direction of bloodstream into the anterior cerebral and posterior communicating arteries, the branches of which fed the optic nerves and chiasm. Histological findings of the specimen obtained at biopsy from the optic nerve revealed that destructive changes were more extensive in the myelin than in the axons. These findings were consistent with demyelination. Ax-
Optic nerve degeneration due to supraophthalmic chemotherapy

FIG. 2. Magnetic resonance images demonstrating swelling of bilateral optic nerves on the T1-weighted image (left) and high signal intensity in the optic chiasm and the left optic tract on the T2-weighted image (right).

FIG. 3. Photomicrographs of the optic nerve obtained at biopsy. Left: Partially destroyed axons are seen in the optic nerve. Bodian stain, × 150. Right: Completely disintegrated myelins with several myelin droplets are visible (arrows). Luxol fast blue stain, × 150.

Axons and myelin are damaged to the same degree in ischemic neuropathy from arterial thrombosis or vasculitis, while axons are more severely affected than myelin in optic nerve changes following retinopathy. Therefore, the discrepancy of changes between the myelin and axons in our case confirmed that the degeneration was induced by the infused drugs.

There are no reports of permanent ocular toxicity associated with infusion of ACNU into the cervical ICA in the treatment of malignant brain tumors, whereas cisplatin and/or 1,3-bis(2-chloroethyl)-1-nitrosourea (BCNU) are often complicated by deterioration of vision, with an incidence of 10% to 50%. To avoid ocular toxicity, Kapp and associates have used the supraophthalmic intracarotid infusion of chemotherapeutic agents with excellent results. However, they also reported that 10 of 31 patients treated with supraophthalmic infusion of BCNU and/or cisplatin developed Marcus-Gunn pupils. They suggested that Marcus-Gunn pupils were secondary to optic tract damage from toxicity of BCNU and cisplatin delivered into the anterior choroidal artery. Our patient developed blindness of the left eye and a right temporal hemianopsia. Magnetic resonance imaging disclosed abnormal intensity in the optic nerves, chiasm, and left optic tract, and histological findings revealed marked degeneration of
the optic nerve. These results strongly suggest that the placement of a catheter distal to the ophthalmic artery with intra-arterial infusion of chemotherapeutic agents may affect the vision of that eye.

References


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