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Case report

Unilateral papilledema after bone marrow transplantation

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Summary:

We describe a patient who developed unilateral papilledema after allogeneic BMT. This is a rare manifestation of pseudotumor cerebri, which results from elevated intracranial pressure caused by cyclosporin A. The papilledema usually involves the fundi bilaterally, but unilateral involvement has been described. Congenital anomalies, compression and adhesion of the optic nerve sheath are its causes. In this patient, the right optic fundus was spared although leukemic infiltration was present on this side and high-dose irradiation (72 Gy) was given. Although papilledema is a sensitive marker of elevated intracranial pressure, this sign may be masked by constriction of the optic sheath in patients who suffer from leukemic infiltration of the central nervous system and receive high doses of cranial irradiation.

Keywords: unilateral papilledema; pseudotumor cerebri; cyclosporine

Ocular complications after BMT have been well described. Acute and chronic graft-versus-host disease (GVHD), conditioning therapy, prophylaxis and treatment of GVHD (corticosteroids and cyclosporin A) and a variety of infections may cause the ophthalmologic problems.

The adverse ophthalmologic effects of cyclosporin A (CsA) are frequently reported. These include cortical blindness,[1] microvascular retinopathy,[2] ocular flutter[3] and pseudotumor cerebri.[4] Because they potentially progress to cause life-threatening central nervous system (CNS) complications CsA must be discontinued in some cases.

Papilledema is a sign of elevated intracranial pressure. Infection and infiltration by malignant cells in the CNS are the chief causes of this complication. Sometimes, patients who have no definite signs of intracranial problems develop papilledema, which usually involves the fundi bilaterally. These are diagnosed as pseudotumor cerebri. However, unilateral involvement has also been reported,[5,6] but the exact pathomechanism is unknown. Here, we report a patient who developed unilateral papilledema after allogeneic BMT. This is the first report of this rare ocular complication after BMT.

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Case report

In July 1996, a 26-year-old male with t(8;21) positive acute myeloid leukemia in second relapse was transferred to our hospital for allogeneic BMT. He had received 40 Gy of whole brain irradiation for the leukemic infiltration in the CNS and an additional 20 Gy for residual leukemia in the right mastoid sinus. We succeeded in controlling the CNS lesions with the radiotherapy and intrathecal MTX. No abnormalities were noted on the pre-transplant ophthalmologic examination.

He underwent an allogeneic BMT in August 1996. Conditioning was with G-CSF, cytarabine, MCNU and fractionated TBI. GVHD prophylaxis was the combination of short-term MTX and cyclosporine.

The patient was seen at day 65 after BMT for routine ophthalmologic examination. At that time, he had no visual symptoms and was receiving 125 mg of cyclosporine daily. Ophthalmologic examination revealed a visual acuity of 20/20 bilaterally and normal pupillary responses. The anterior segment was also normal in both eyes. Papilledema was observed of the left but not in the right fundus (Figure 1). A subsequent fluorescein angiogram revealed early hyperfluorescence of the left optic disk which persisted throughout the angiogram (Figure 2). Results of Goldmann perimetry showed enlargement of the Mariotte's blind spot. Neurological examination and computed tomography of the head were unremarkable. Although the opening pressure of the lumbar puncture was elevated to 310 mm of water, cytological examination was normal, and protein and glucose levels of the cerebrospinal fluid and cell counts were also normal. Chimeric mRNA of AML-MTG8 was not detected in the cerebrospinal fluid by the RT-PCR assay. Cerebrospinal culture was negative. Pseudotumor cerebri was therefore diagnosed and the cyclosporine was discontinued. Thereafter, the elevated intracranial pressure gradually decreased and the unilateral papilledema finally normalized in April 1997.

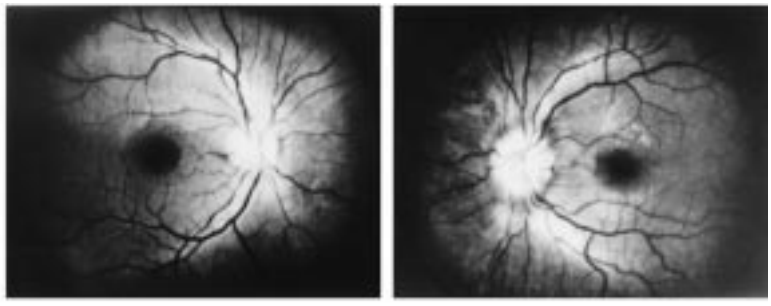

Figure 1 (Left panel) Funduscopic examination of the right eye, showing a normal optic disc. (Right panel) Funduscopic examination of the left eye showing a marked disc edema with dilated capillaries.

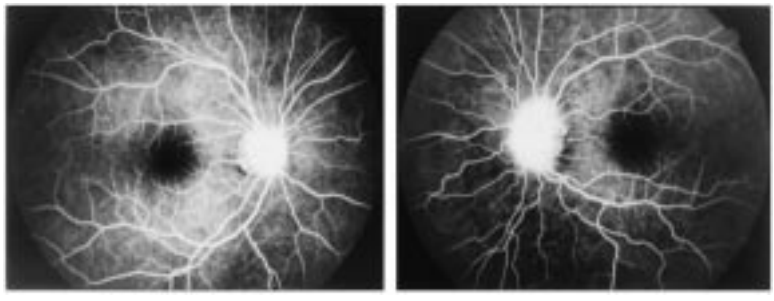

Figure 2 (Right panel) Fluorescein angiogram of the left eye demonstrating marked leakage of fluorescein from the swollen optic nerve. (Left panel) Fluorescein angiogram of the right eye demonstrating a normal fundus.

Discussion

Papilledema is a rare complication after BMT, which usually involves the optic fundi bilaterally, impairs visual acuity and is frequently associated with the use of CsA.[4,7] In a retrospective study Coskuncan *et al*[8] reported that 11 of 397 patients (2.8%) had bilateral optic disc edema after BMT, with eight cases attributed to the toxic effects of CsA and three to other causes.

Because pre-transplant ophthalmologic examination revealed normal fundi, this ocular complication was considered due to the transplantation procedure. The optic disc edema resolved with decreasing the dose of CsA, which suggested an association between this immunosuppressive agent and the edema. With the history of cranial irradiation radiation-induced optic neuropathy was considered, which usually manifests acutely as disc swelling with surrounding exudate, hemorrhages, and subretinal fluid.[9] However, the papilledema developed in the left eye and the local irradiation had mainly been given to the opposite side, the right mastoid sinus. Thus, we did not consider radiation toxicity as the primary cause of the papilledema.

This patient satisfied the diagnostic criteria of pseudotumor cerebri:[10] (1) papilledema, (2) increased intracranial pressure ($>200\ mmH_2O$) without a mass or ventricular enlargement, (3) normal cerebrospinal fluid cytology and chemistry, (4) normal mental status. The most common symptom in patients with pseudotumor cerebri is headaches, occurring in more than 90% of cases. Visual symptoms occur in 35–70% of patients.[11] Although the fundi are usually involved bilaterally there have been case reports of unilateral papilledema in pseudotumor cerebri[12] and even less frequently the absence of papilledema has been reported.[13] Lepore[5] compared six patients with pseudotumor cerebri and unilateral papilledema with 20 such patients with bilateral papilledema. Except for age, there were no significant differences between the two groups. Although the exact mechanism of unilateral papilledema is unknown, obstruction of CSF circulation, which usually occurs via the subarachnoid spaces of the optic nerve to the lamina cribrosa,[14] may result in elevated intracranial pressure. They hypothesized that in patients with unilateral papilledema, one optic nerve may be protected from pressure effects by a congenital abnormality of the optic nerve sheath, compression from tumor or adhesions following inflammation. In our case, local irradiation or leukemic infiltration of the right frontal lobe including the mastoid sinus might have induced fibrous changes in the right optic nerve sheath or lamina cribrosa, which might have protected the right optic disk from the effects of elevated intracranial pressure caused by CsA.

Papilledema has been considered a sensitive marker of elevated intracranial pressure. In the light of this case, however, this finding may not be as reliable as accepted, especially in patients with a history of leukemic infiltration and irradiation to the central nervous system. This case demonstrates that CsA may cause pseudotumor cerebri and that it may present as unilateral papilledema in an asymptomatic patient after BMT. Lessell and Rosman[15] described visual loss as being the most important long-term consequence of pseudotumor cerebri and that awareness of pseudotumor cerebri should prompt investigation and treatment of raised intracranial pressure. Although the mechanism of unilateral papilledema remains to be elucidated,

unilateral papilledema should be added to the list of ocular complications after BMT and further information about it should be sought.

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