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Ischemic Optic Neuropathy Associated with Low Dose Interferon Alfa: Report of Two Cases

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Keywords

Interferon Alfa; Ischemic Optic Neuropathy; Renal Cell Carcinoma

Case 1

A 70 year-old asymptomatic man presented for treatment of recurrent renal cell carcinoma, metastatic to the lungs. Low dose interferon alfa (IFN) was initiated at 0.5 million units subcutaneously (sc) twice daily on protocol. At the eight-week evaluation, he reported a 2 week history of precipitous decline of vision in the right eye. Visual acuity measured 20/80. Fundoscopic examination demonstrated diffuse disc edema with hemorrhage in the right eye (Fig 1). A right-sided relative afferent pupillary defect and altitudinal field defect were noted. The left optic nerve was normal. Neurological evaluation demonstrated no abnormalities. Complete blood count, C-reactive protein, erythrocyte sedimentation rate, rapid plasma reagin, fibrin split product, protein-S, lupus anticoagulant, factor-V Leiden, plasma homocystine level, antithrombin III, functional protein-C and $\beta 2$ glycoprotein were normal. MRI of the brain and orbit, carotid duplex and 2D echocardiogram demonstrated no abnormalities.

IFN was discontinued. Treatment with oral prednisone (80 mg daily), acetylsalicylic acid (325 mg daily), and brimonidine (1 drop three times daily) was initiated. Follow-up examination, six weeks later demonstrated a decline of vision in the right eye to 20/100 with resolution of disc edema (Fig 2). Automated Humphrey visual field testing demonstrated a residual altitudinal visual field defect. The patient was maintained on acetylsalicylic acid and brimonidine but visual acuity did not improve in the affected eye.

Case 2

A 72 year-old man presented with advanced renal cell carcinoma, metastatic to the sternum. After cytoreductive right nephrectomy, treatment with low dose IFN was initiated at 0.5 million units sc twice daily on protocol. After ten months of IFN therapy, subacute central visual loss in the left eye was described. Visual acuity measured 20/25 in the right eye and count fingers in the left eye. Fundoscopic examination demonstrated disc edema with associated hemorrhage in the left eye. A left sided centrocecal scotoma was detected on Humphrey visual field testing. Comprehensive neurological and serologic evaluation demonstrated no abnormalities. IFN was discontinued and a tapering course of steroids was started but the patient failed to recover his baseline visual acuity.

Discussion

Ocular side effects with IFN are uncommon. Most cases of decreased vision are transient, although permanent decline of vision has been reported. Ischemic changes have been demonstrated on fluorescein angiography. Permanent vision loss secondary to optic nerve edema, optic neuritis, and bilateral ischemic optic neuropathy has been reported in patients who received high dose IFN as adjuvant therapy for high-risk melanoma.¹ Our report demonstrates that optic neuritis may also occur in patients who receive low-dose IFN. Although the pathophysiology of IFN-associated anterior ischemic optic neuropathy remains unclear, an underlying immunological mechanism is suggested. It has been postulated that IFN is able to produce autoantibodies leading to the deposition of immune complexes in the small retinal or optic arteries.² IFN also has immunomodulatory properties capable of stimulating the production of other cytokines, such as various interleukins, and upregulating histocompatibility complex class II proteins.³ These interleukins can cause an inflammatory response affecting the blood vessels, leading to ischemia. It has also been proposed that IFN causes systemic hypotension, which may lead to optic vascular ischemia.⁴

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Figure 1.
CASE 1 Optic disc edema with associated hemorrhages

Figure 2.
CASE 1 Resolution of disc edema, 6 weeks later