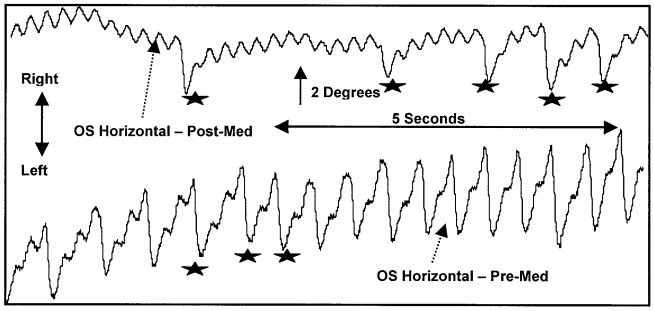

FIGURE 1. Horizontal position recordings of the left eye (OS) patient J.H. in primary position before and after Tenuate Dopsan (diethylproprionate; Watson Laboratories, Inc., Corona, California) administration. The top tracing in the figure shows the increase in the number of small foveation periods (pendular movements) in between the fast phases of nystagmus after Tenuate administration (represented by the arrows). This represents the fast phases ("jerk" portion of the nystagmus). The postmedication trace shows less "jerk" fast phases/unit of time, which result in longer periods of slow phases with increased foveation periods (pendular arrows) during the slow phases.

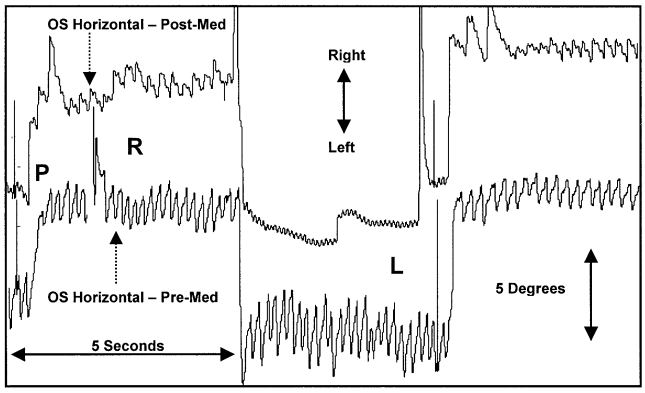

FIGURE 2. Horizontal position recordings of the left eye (OS) patient J.H. in primary position (P) and in right (R) and left (L) gaze before (bottom trace) and after (top trace) Tenuate Dopsan administration. An overall decrease occurs in the intensity of the nystagmus, and an increase occurs in foveation periods in primary position (P) and in right (R) and left (L) gaze seen in the top trace. This decreased amplitude of nystagmus across gaze represents an increased null zone breadth after Tenuate administration.

in common a desired effect of directly reducing the nystagmus intensity, and they indirectly show an increase in visual acuity. Tenuate Dospan is an adrenergic central nervous system stimulant.[4,5] It induces the release of norepinephrine and dopamine. As with other stimulant drugs, side effects of this drug may include abdominal discomfort, anxiety, blood pressure increase, blurred vision, bruising, changes in sex drive, chest pain, constipation, diarrhea, difficulty with voluntary movements, dryness of the mouth, hair loss, headache, irregular heartbeat, jitteriness, menstrual upset, muscle pain, nausea, nervousness, and vomiting. Similar to children with attention deficit disorder, patients with congenital nystagmus may respond to stimulant drugs "paradoxically." This intriguing observation may open new avenues of clinical investigation and treatment.

REFERENCES

1. Botulinum toxin therapy of eye muscle disorders. Safety and effectiveness. American Academy of Ophthalmology. Ophthalmol 1989;2:37–41.
2. Keltner JL. Neuro-ophthalmology for the pediatrician. Pediatr Ann 1983;8:586, 590–598, 600–602.
3. Larmande P, Pautrizel B. Treatment of congenital nystagmus with 5-hydroxytryptophan [letter]. Nouv Presse Med 1981;10: 3166.
4. Mousa GY. Effects of Tenuate (an anorexiant) on migraine. Am J Optom Physiol Opt 1983;6:538–539.
5. Albach E, Gianoli AC. Therapy of obesity. The initial and continued effectiveness of tenuate in intermittent therapy of moderately and severely obese patients. Double-blind study. Fortschr Med 1977;33:2040–2044.

Increased Endothelin-1 Plasma Levels in Giant Cell Arteritis: A Report on Four Patients

Mona Pache, MD, Hedwig J. Kaiser, MD, Timo Haufschild, MD, Patricia Lübeck, MD, and Josef Flammer, MD

PURPOSE: To test the hypothesis that endothelin-1 is increased in giant cell arteritis.

METHODS: Interventional case series. The medical history of four patients who presented to the University Eye Clinic Basel, Switzerland, with giant cell arteritis is reported. Endothelin-1 plasma levels were measured in all patients. The relevant medical literature was reviewed.

RESULTS: All patients presented with typical histopathological signs of giant cell arteritis in the temporal artery biopsy. The erythrocyte sedimentation rate was increased in two patients. All patients showed significantly increased endothelin-1 plasma levels, ranging between 3.13 to 4.82 pg/ml (reference value for females: 1.42 pg/ml ± 0.28 standard deviation, for males: 1.67 pg/ml ± 0.34 standard deviation).

CONCLUSION: The data obtained from the patients so far examined indicate that the level of circulating endothelin-1 is increased in giant cell arteritis. The clinical relevance of such an increase needs to be further evalu-

Accepted for publication Aug 1, 2001.

From the University Eye Clinic, Basel, Switzerland.

Inquiries to Josef Flammer, MD, University Eye Clinic Basel, Mittlere Str. 91, P.O. Box, CH-4012 Basel, Switzerland; fax: ++41/61/2658652; e-mail: Josef.Flammer@unibas.ch

TABLE 1. Clinical Data of Four Patients With Giant Cell Arteritis Show Significantly Increased Endothelin-1 Plasma Levels

	Case 1	Case 2	Case 3	Case 4
Gender	F	F	F	M
Age (years)	79	89	71	71
Temporal artery biopsy	+	+	+	+
Erythrocyte sedimentation rate [mm/h]	49	8	100	4
Endothelin-1 plasma level [pg/ml]	4.82	4.0	3.39	3.13

GIANT CELL ARTERITIS IS A SYSTEMIC VASCULITIS AFfecting large- and medium-sized arteries. The arteritic lesions lead to ischemic symptoms such as cephalgia, masseter pain, and mental depression. Often patients present with acute visual loss caused by anterior ischemic optic neuropathy or, less frequently, central artery occlusion. Another sign of ocular ischemia is amaurosis fugax.[1] A decrease of ocular perfusion, especially of the choroid, can be frequently observed.

Recently, it has been shown that infusion of endothelin-1 results in decreased ocular perfusion. If levels of circulating endothelin-1 are increased in patients with giant cell arteritis, we may hypothesize that endothelin-1 is at least partially involved in the observed ocular ischemia.

Therefore, we measured endothelin-1 plasma levels in four patients with biopsy-proven giant cell arteritis (Table 1). All patients showed significantly increased endothelin-1 plasma levels, ranging between 3.13 to 4.82 pg/ml (reference value for females: 1.42 pg/ml ± 0.28 standard deviation, for males: 1.67 pg/ml ± 0.34 standard deviation).[2] All four cases of giant cell arteritis revealed markedly increased levels of the potent vasoconstrictor endothelin-1. Endothelin-1 is not only synthesized by human endothelial cells, but also by a variety of other cell-types such as macrophages, mast cells, and synovialocytes. Increased production of endothelin-1 has been found in various vascular and autoimmune diseases,[3] which were excluded in our patients.

Endothelin-1 increases the sensitivity of blood vessels to other vasoconstrictive hormones such as norepinephrine, 5-hydroxytryptamine, and angiotensin II. Therefore, we presume that the symptoms of ocular ischemia associated with giant cell arteritis might be partially explained by an endothelin-1 modulated secondary vascular dysregulation. The prevalence of amaurosis fugax,[1] cotton–wool exudates, and nonthromboembolic retinal artery occlusion in giant cell arteritis supports this hypothesis. The alteration of choroidal perfusion found in giant cell arteritis[1] may be because endothelin-1 can permeate through the fenestrated choroidal endothelium. This anatomical situation

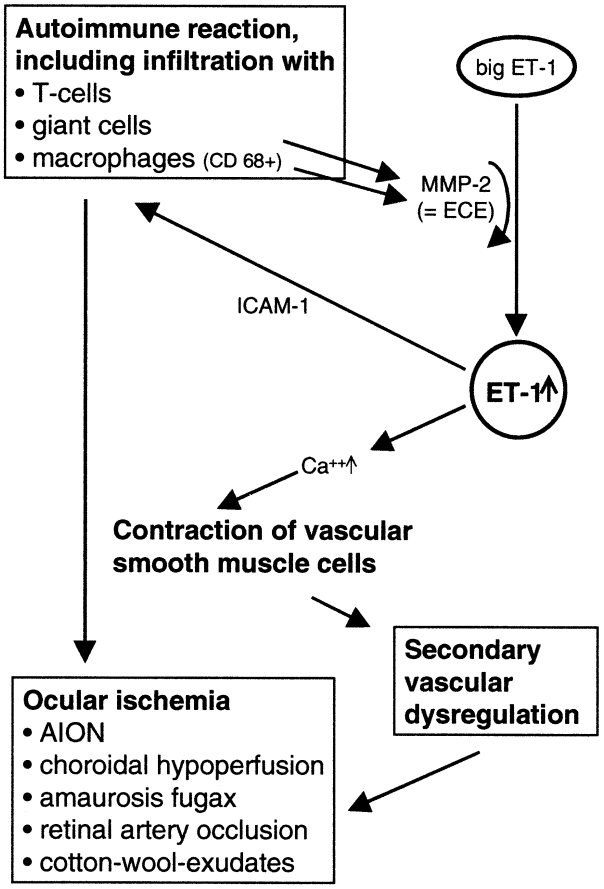

FIGURE 1. Hypothetical concept of ocular ischemia in giant cell arteritis.

predisposes the choroid and optic nerve head to vasospasm-induced damage. This may explain the glaucoma-like alterations of the optic nerve head seen in giant cell arteritis.[3] The reported positive effect of nitroglycerine on the visual defect also supports the hypothesis of a secondary vascular dysregulation in giant cell arteritis.

Giant cells and a subgroup of CD68+ macrophages located in focal arteritic lesions have been reported to synthesize matrix metalloprotease-2.[4] Matrix metalloprotease-2 is identical to the endothelin converting enzyme that cleaves the precursor protein big endothelin-1 to its active form endothelin-1.[5] We speculate, therefore, that matrix metalloprotease-2 expressed by giant cells and macrophages may be a cause for the increase of endothelin-1.

Besides influencing vessel function, endothelin-1 may also function as a pro-inflammatory mediator either by stimulating expression of intercellular adhesion molecule 1[6] or by direct enhancement of neutrophil adhesion by $endothelin_A$ receptors[7] (Figure 1).

We assume that endothelin-1, although involved in the inflammatory process, reduces ocular perfusion in giant cell arteritis. If further studies confirm that increased endothelin-1 plasma levels are indeed characteristic in patients

with giant cell arteritis, therapy with calcium channel blockers or possibly with endothelin-1 receptor blockers could be considered.

REFERENCES

1. Slavin ML, Barondes MJ. Visual loss caused by choroidal ischemia preceding anterior ischemic optic neuropathy in giant cell arteritis. Am J Ophthalmol 1994;117:81–86.
2. Haufschild T, Shaw SG, Flammer J. Endothelin-1 values in healthy subjects. In press.
3. Flammer J, Pache M, Resink T. Vasospasm, its role in the pathogenesis of diseases with particular reference to the eye. Prog Retin Eye Res 2001;20:319–349.
4. Rittner HL, Kaiser M, Sweda LI, Goronzy JJ, Weyand CM. Tissue-destructive macrophages in giant cell arteritis. Circ Res 1999;84:1050–1058.
5. Fernandez-Patron C, Radomski MW, Davidge ST. Vascular matrix metalloproteinase-2 cleaves big endothelin-1 yielding a novel vasoconstrictor. Circ Res 1999;85:906–911.
6. Xu SW, Denton CP, Dashwood MR, Abraham DJ, Black CM. Endothelin-1 regulation of intercellular adhesion molecule-1 expression in normal and sclerodermal fibroblasts. J Cardiovasc Pharmacol 1998;31:S545–S547.
7. Zouki C, Baron C, Fournier A, Filep JG. Endothelin-1 enhances neutrophil adhesion to human coronary artery endothelial cells: role of ET(A) receptors and platelet-activating factor. Br J Pharmacol 1999;127:969–979.

Atypical Anterior Optic Neuropathy Caused by Toxoplasmosis

Alice Song, MD, Ingrid U. Scott, MD, MPH, Janet L. Davis, MD, and Byron L. Lam, MD

PURPOSE: To report atypical anterior optic neuropathy due to toxoplasmosis.

METHODS: Interventional case report. A 33-year-old male presented with sudden painless loss of vision and floaters in the right eye. Examination demonstrated a best-corrected visual acuity of 20/200, optic nerve head edema, retinal hemorrhages, and vitreous opacities.

RESULTS: Nine days later, a granuloma at the optic nerve head was apparent, and the patient was treated with pyrimethamine, sulfadiazine, folinic acid, and prednisone. Six weeks after initiating therapy, best-corrected visual acuity had improved to 20/25.

CONCLUSION: Optic nerve involvement in toxoplasmosis is uncommon and, when it occurs, usually presents with a white inflammatory mass on the optic disk. The current case demonstrates the importance of including toxoplasmosis in the differential diagnosis of unilateral anterior optic neuropathy, even if a focal inflammatory mass is not apparent. (Am J Ophthalmol 2002;133:162–164.

Accepted for publication August 7, 2001.

Supported in part by Research to Prevent Blindness, Inc., New York.

From the Department of Ophthalmology, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida.

Inquiries to Ingrid U. Scott, MD, MPH, Bascom Palmer Eye Institute, PO Box 016880, Miami, FL 33101; fax: (305) 326-6417; e-mail: iscott@bpei.med.miami.edu

TOXOPLASMA GONDII IS A COMMON CAUSE OF FOCAL retinochoroiditis and posterior uveitis.[1] Typical presenting signs include chorioretinal scars with adjacent active retinochoroiditis and vitritis.[1,2] Periarteritis, arterial and vein occlusions, and choroidal neovascular membranes may also occur in patients with ocular toxoplasmosis.[1,3] Other less common manifestations of ocular toxoplasmosis include retinal neovascularization, vitreous hemorrhage, neuroretinitis, pars planitis, scleritis, and rhegmatogenous retinal detachment secondary to retinal necrosis.[4] Compared with immunocompetent individuals, immunocompromised individuals may have more severe and atypical presentations of ocular toxoplasmosis with papillitis, retinal necrosis, or bilateral or multifocal involvement, although with less inflammation histologically.[3]

Few reported cases of anterior optic neuropathy caused by toxoplasmosis exist.[1,2] In one case series of six patients with toxoplasmic anterior optic neuropathy, all patients demonstrated a localized white inflammatory mass on the optic disk with associated vitreous inflammation.[4] One patient with AIDS and cerebral toxoplasmosis presented with no light perception vision, optic nerve head swelling, and peripheral retinal hemorrhages.[5] The patients in these reports all had unilateral anterior optic neuropathy. We report an immunocompetent patient whose toxoplasmic anterior optic neuropathy presented as unilateral optic nerve head swelling, retinal hemorrhages, and vitreous opacities; an optic nerve head granuloma became apparent 9 days after presentation.

A 33-year-old Brazilian male presented with a 4-day history of sudden painless loss of vision and seeing "spider webs" in the right eye. The patient denied any history of trauma, ocular surgery, or photopsias. Medical, social, and ocular histories were unremarkable. Best-corrected visual acuity was 20/200 in the right eye and 20/25 in the left eye with no relative afferent pupillary defect. Intraocular pressures were 17 and 19 mm Hg, respectively. Slit-lamp examination was remarkable for moderately severe (3+) vitritis in the right eye. Funduscopic examination of the right eye demostrated a swollen optic nerve head with peripapillary retinal hemorrhages involving the posterior pole and extending to the midperiphery (Figure 1). Funduscopic examination of the left eye was unremarkable.

Fluorescein angiography demonstrated leakage from the optic disk, but no venous delay or leakage from the vessels. Laboratory studies, including a complete blood count, metabolic profile, fluorescent treponemal antibodies, erythrocyte sedimentation rate, and antinuclear antibodies, were within normal limits. Echography of the optic nerve and orbit was unremarkable.