Jules Stein Eye Institute
U C L A

Clinical Update

May 2003
Volume 12, Number 2

Optic Neuritis: To Treat or Not to Treat?

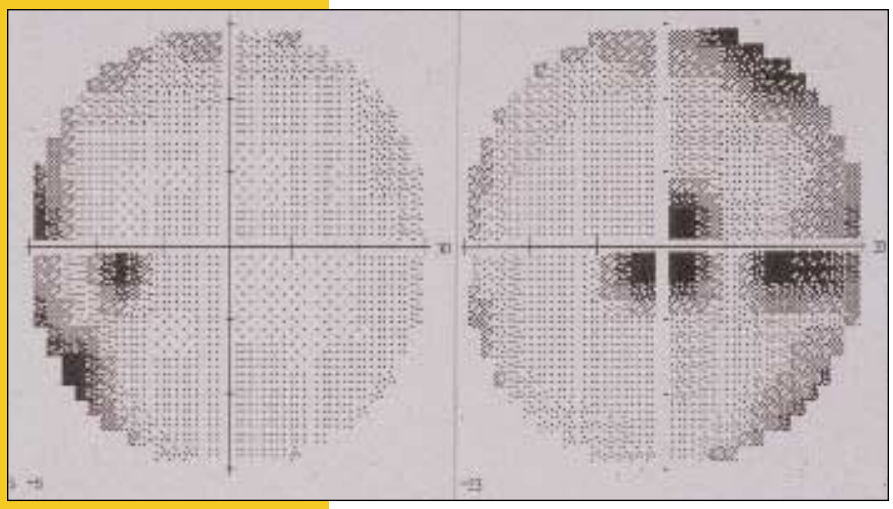

Figure 1: Visual fields from a patient with optic neuritis, right eye, showing central scotoma

"Garden-variety" optic neuritis is still somewhat of a management puzzle for ophthalmologists despite two excellent studies in recent years, says Anthony C. Arnold, MD, Professor of Ophthalmology, Chief of the Division of Neuro-Ophthalmology, and Director of the Optic Neuropathy Center at the Jules Stein Eye Institute. "Whether to treat typical monosymptomatic optic neuritis with steroids or not has always been controversial, and ophthalmologists may wonder if they can or should do anything about the patient's risk for developing Multiple Sclerosis (MS). The National Eye Institute-sponsored Optic Neuritis Treatment Trial (ONTT) and the industry-sponsored Controlled High-Risk Subjects Avonex Multiple Sclerosis Prevention Study (CHAMPS) clarified some issues, but raise additional questions."

Using Steroids to Speed Recovery

Uncomplicated optic neuritis (unilateral, without infection, and not associated with disease other than possible MS) is generally not treated for visual improvement because of its high spontaneous resolution rate. Dr. Arnold says, "The average person with a central scotoma in the affected eye (Fig. 1) can usually manage for a few weeks using the vision of the intact eye, and there are risks, albeit relatively small, to steroid treatment. The ONTT study showed that oral steroids (1mg/kg/day for 14 days) are virtually ineffective, while high-dose intravenous prednisolone (250 mg q.i.d. for three days), followed by oral prednisone, merely sped recovery short-term without changing the ultimate visual outcome."

Dr. Arnold has generally reserved IV steroids to speed healing for patients with severe, bilateral loss, or for those with less severe loss who require a high degree of depth perception for their work. While steroids were administered in the hospital in four IV doses daily during the ONTT, many medical clinics and emergency facilities are now equipped to provide outpatient, single, daily doses via heparin lock, obviating the cost and inconvenience of hospitalization.

Added Benefits and Interferon

In addition to faster visual recovery, the ONTT demonstrated that IV steroids reduced the risk of developing MS for up to two years. The CHAMPS study, says Dr. Arnold, went further to show that for patients at risk for MS, administration of steroids *plus* intramuscular interferon beta-1a (Avonex®—Biogen) reduced the rate of clinically definite MS

(*continued on page 2*)

Our web site address is
http://www.jsei.org

Physician's Direct Referral Line:

(310) 794-9770

OPTIC NEURITIS

(*continued from page 1*)

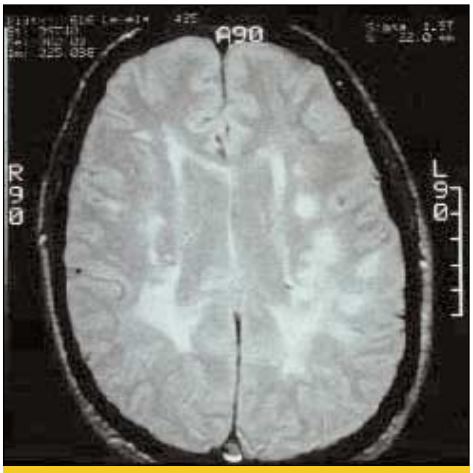

Figure 2: MRI scan of the brain in a patient with multiple sclerosis, showing multiple white matter lesions

within the next three years by about half. Dr. Arnold describes at risk patients as those with a first acute neurologic episode, including optic neuritis, spinal cord lesion, or brain stem lesion *and* an MRI showing significant white matter abnormalities. The decision to use interferon therapy is a complicated one. Dr. Arnold recommends that patients considering this treatment obtain neurological evaluation for other signs of MS, for general health assessment, for determining the appropriateness of steroids and/or interferon, and for monitoring treatment effectiveness and consequences.

Scan Regardless

The ONTT and the CHAMPS studies have clarified the use of MRI in optic neuritis. An MRI scan to look for white matter lesions is recommended for all patients presenting with any form of optic neuritis (Fig. 2). The volume of MRI white matter lesions predicts the risk of MS, and data on the value of steroids and interferons in reducing the risk of MS is valid only for patients with significant white matter abnormalities. "If the MRI is abnormal in a significant way, I'm much more aggressive in urging a neurological consult, which I can facilitate through our Optic Neuropathy Center," Dr. Arnold notes. "Conversely, if the scan is normal, I can advise the patient of the decreased risk of MS."

Cautionary Tales

Although some clinicians—ophthalmologists as well as neurologists—treat all cases of optic neuritis, regardless of scan results, Dr. Arnold believes that such a policy is not borne out by the trials.

"Neither study addressed people with normal MRI scans. What we don't know is whether these people with a lower risk for MS can benefit from interferon. Though its side effects are relatively mild, flu-like symptoms that usually wear off after initial use, interferon alters the immune system. Furthermore, the exact mechanism by which it reduces morbidity in MS patients is unclear, and we don't yet have data on its long-term effects. Currently, we must assume that patients will require lifelong immunomodulatory therapy to maintain a defense against MS. Committing someone indefinitely to interferon therapy is problematic, particularly when up to 50 percent of these at-risk patients will *not* develop MS within five years."

Dr. Arnold points out that key questions remain regarding the use of immunomodulatory agents:

1. Will ongoing follow-up from the ONTT and CHAMPS studies confirm a long-term, protective effect of steroids/interferon?
2. How long is therapy required?
3. Will a different interferon or another immune-suppressant (such as Betaseron® or Copaxon®) be as effective in lowering MS risk or severity with fewer side effects and easier administration?
4. Will reducing the number of attacks reduce the eventual permanent nerve damage and disability in those who go on to develop MS?

Different Measures

Dr. Arnold emphasizes that his protocol for most cases of idiopathic optic neuritis—MRI scanning followed by referral to a neurologist for management—differs from that of patients with ocular inflammation, associated retinal lesions, or signs of a systemic disease (such as lupus, sarcoid, or syphilis), which require different therapies. "Atypical optic neuritis cases, including patients who do not recover their vision within four to six weeks, those whose pain is persistent, and those who may respond initially to steroids but whose symptoms recur on attempted taper, fall into a different category and require workup for these specific diseases," he says.

For the typical case however, current knowledge suggests cautious optimism. Dr. Arnold says, "While a patient's five-year risk for developing MS after optic neuritis may be as high as 50 percent, we now have both a reliable way to estimate the risk (MRI) and a therapy which may substantially reduce it. Our hope for the future is that studies will produce agents even more effective, easier to administer, and with fewer side effects."

RECENT PUBLICATIONS:

CHAMPS Study Group. *Interferon beta-1a for optic neuritis patients at high risk for multiple sclerosis.* Am J Ophthalmol 2001;132:463-71.

Arnold AC. Optic neuritis. *Saudi J Ophthalmol* 2002;16:207-18.

Case Report: **Care of a Patient with Retinal Angioma and Secondary Exudative Maculopathy**

The following case report was submitted by Allan E. Kreiger, MD, Professor of Ophthalmology, in the Retina Division of the Jules Stein Eye Institute.

Figure 1: The right fundus with marked exudates in the macula (Coat's reaction) and a 1½ disc diameter red-orange mass located inferotemporal to the macula

In 1988, a 14-year-old girl presented to her ophthalmologist with a lump in the right lower lid. She was found to have a chalazion; and during the evaluation, poor vision in the right eye was detected. Her fundus showed exudative maculopathy and a probable retinal angioma in the posterior pole. She was referred to the Jules Stein Eye Institute for care.

An examination of the patient at the Jules Stein Eye Institute revealed her best-corrected vision to be 20/100 on the right and 20/15 on the left. Except for the fundus findings in the right eye, the remainder of her ophthalmic examination was within normal limits. Her family history was negative for eye disease, neurological disease, or abdominal cysts or tumors. There was no history of von Hippel-Lindau disease (VHL).

Her right fundus had marked exudates in the macula (Coat's reaction) and a 1½ disc diameter, red-orange mass located inferotemporal to the macula (Fig. 1). The inferior vascular arcade was markedly dilated, and the arteriole and venule entered the tumor at its nasal aspect. A diagnosis of retinal angioma with secondary exudative maculopathy was made. She was referred for medical evaluation to rule out systemic evidence of VHL. This evaluation, and several subsequently, have been normal.

Treatment

The tumor was treated on multiple occasions with argon laser photocoagulation, applying yellow wavelength directly to the tumor, using long exposure times (0.2 and 0.5 seconds) and large spot sizes (2 and 500 microns). The desired effect was to change the color of the lesion just slightly. Angiomas notoriously leak profusely after heavy treatment and can cause worsening of maculopathy, or even exudative retinal detachment. After several months of treatment, the tumor regressed into a fibrous mass, the macular exudates resorbed, and the feeder vessels returned to their normal diameters (Fig. 2).

When the patient was last seen in 2002 at the age of 28, the tumor was inactive and her vision was 20/200 as a result of pigmentary changes from the macular exudates. No other angiomas or manifestations of VHL had occurred.

Discussion

Retinal angiomas may occur sporadically, or as part of von Hippel-Lindau disease (VHL). Sporadic lesions should be differentiated from vasoproliferative tumors of the fundus, which resemble angiomas but tend to be seen in older patients, are more often in the far periphery, and do not usually have dilated feeder vessels. Otherwise, the characteristic appearance should differentiate the angioma from other ocular tumors. These can include astrocytic hamartoma, retinoblastoma, racemose hemangioma, retinal cavernous hemangioma, or melanoma. Since the presenting lesion of VHL is often a retinal angioma, its presence should prompt appropriate systemic evaluation.

Diagnostic workup for VHL should conform to the Cambridge screening protocol, which searches for the presence of non-ocular manifestations of the disorder, including CNS hemangioblastoma, renal cell carcinoma, cysts and tumors of the pancreas, pheochromocytoma, epididymal cystadenoma, and endolymphatic sac

(*continued on page 4*)

CASE REPORT

(*continued from page 3*)

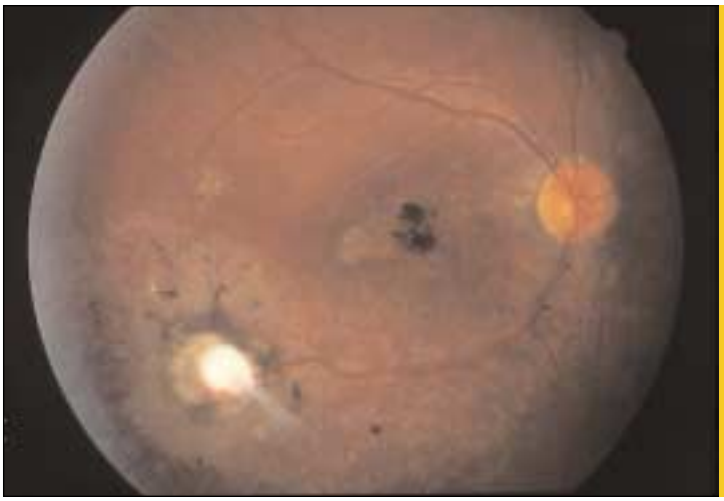

Figure 2: After treatment, the tumor regressed into a fibrous mass, the macular exudates resorbed, and the feeder vessels returned to their normal diameters.

tumors. Recently, diagnostic evaluation for VHL has been aided greatly by the ability to analyze the DNA of patients for the presence of the genetic defect, which is located on the short arm of chromosome 3. Testing is available through several laboratories in the United States. This knowledge is crucial to genetic counseling of patients and their families.

Treatment of retinal angiomas can be challenging. Small lesions can usually be managed through photocoagulation without complications. Larger tumors, because of their tendency toward exudation after treatment, must be managed patiently with multiple treatment sessions, rather than aggressive primary treatment. Cryotherapy may be used in more peripheral lesions. Tumors that are elevated from the retina into the vitreous may require an intraocular approach using vitrectomy techniques. Optic nerve head angiomas are particularly difficult to treat safely.

Early detection of retinal angiomas greatly facilitates their treatment. Furthermore, early diagnosis of VHL improves the prognosis of this multi-system disease.

PUBLICATIONS:

Shields CL, et al. *Vasoproliferative tumors of the ocular fundus. Classification and clinical manifestations in 103 patients.* Arch Ophthalmol 1995;113:615-623.

Maher ER, et al. *Clinical features and natural history of von Hippel-Lindau disease.* QJ Med 1990;77:1151-1163.

JSEI Continuing Education Programs 2002 – 2003

April 25-26, 2003
Annual Postgraduate Seminar and 34th Jules Stein Lecture

May 30-31, 2003
Fourteenth Annual Research and Alumni Day &
Seventh Annual Post ARVO Seminar

For more information, call Academic Programs at (310) 825-4617 or visit our website at http://www/jsei.org

Jules Stein Eye Institute UCLA
100 Stein Plaza
Box 957000
Los Angeles, CA 90095-7000
U.S.A.

First Class Mail
U.S. Postage
PAID
UCLA