

## NEURO-OPHTHALMOLOGY

# The Balancing Act of Managing Giant Cell Arteritis

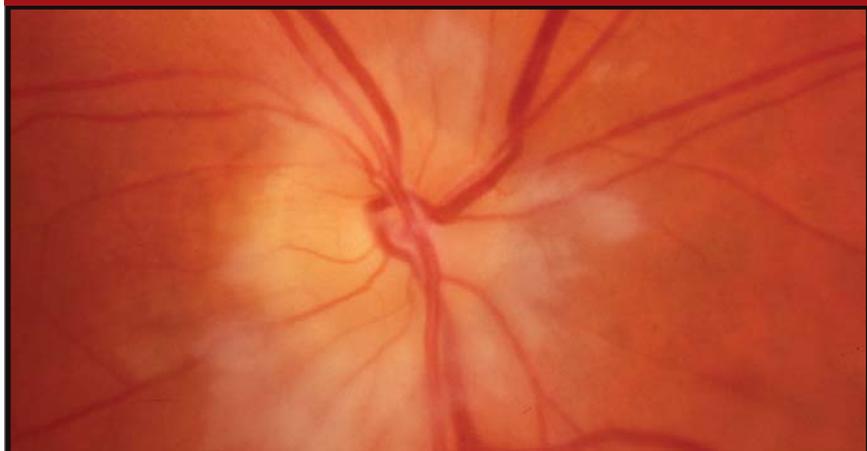
BY BARBARA BOUGHTON, CONTRIBUTING WRITER

**G**iant cell arteritis (GCA), a well-known vasculitis, can be a true medical emergency in ophthalmology. Also called temporal arteritis, GCA causes devastating vision loss in one of five patients. If left untreated, up to 50 percent of patients will experience vision loss in the opposite eye within days or weeks of onset. While the use of corticosteroid treatment is well-established in GCA, controversy remains over whether intravenous or oral administration of treatment is more effective. There is also controversy over what role steroid-sparing anticoagulants may play.

### Who and What to Suspect

GCA is sometimes seen in people in their 50s, but it is most common in those over 65. It should be suspected in any patient with sudden vision loss as well as various symptoms that often accompany the disease—jaw claudication, headache, scalp tenderness, recent weight loss, fevers, chills and sweats, said Steven A. Newman, MD, professor of ophthalmology at the University of Virginia in Charlottesville. In 25 percent of cases, however, there are no systemic symptoms. Ophthalmologic symptoms, in addition to vision loss, can include problems with motility leading to diplopia. And examination will sometimes reveal a pale, swollen optic nerve, said Jonathan D. Trobe, MD, professor of ophthalmology and neurology at the University of Michigan in Ann Arbor.

### White and Fluffy



Cotton-wool spots and whitish appearance of the nerve presenting acutely are highly suggestive of GCA-related anterior ischemic optic neuropathy, Dr. Blouise said.

Serologic tests that include erythrocyte sedimentation rate, C-reactive protein and platelet count can help make the diagnosis of GCA. While the sed rate is sensitive for GCA, it is not specific. If C-reactive protein suggests inflammation and the platelet count is elevated, the physician should suspect GCA, Dr. Newman said.

**Treat presumptively.** The only definitive confirmation of GCA is temporal artery biopsy. However, because of the possible devastating consequence of GCA, steroids should be started before biopsy in patients who show clinical signs and whose blood work is consistent with the disease, Dr. Newman said. Biopsies can be positive even 14 to 28 days after starting steroids. Importantly, in 15 percent of patients with GCA, the sed rate and even

C-reactive protein may be normal, Dr. Newman said, so given substantial clinical suspicion, those patients should be treated and biopsied anyway.

**Treat aggressively.** One argument for aggressive treatment is to prevent involvement of the opposite eye. And some studies have reported up to 15 percent of patients may experience improved vision in the affected eye with aggressive treatment, said Dr. Newman.

### The Steroid Question

A looming question in treating GCA, especially in those who are elderly, is how best to use steroid treatment aggressively but with enough care to minimize side effects, such as osteoporosis, hyperglycemia, diabetes, hypertension and even mania. “In elderly

patients with giant cell arteritis, more than 50 percent are ultimately going to have complications due to steroid therapy," Dr. Newman said. "The art in taking care of these patients is how to taper the steroids fast enough to minimize the complications because the complications can be severe, even possibly fatal."

**How to deliver the drug.** The route of administration of steroids has also become a matter of some controversy, said Dr. Newman. Although many physicians prefer to treat patients who have GCA with an initial intravenous treatment of steroids, there are no prospective trials that show this is superior to oral steroids. The key question is whether IV steroids actually provide better outcomes. One controlled, randomized trial showed that induction treatment with high-dose, pulsed IV methylprednisolone allowed a shorter course of high-dose therapy. Oral steroids could then be tapered more quickly to minimize side effects.<sup>1</sup>

**The typical approach.** According to Valerie Biousse, MD, professor of neurology and ophthalmology at Emory University in Atlanta, most patients are started on a p.o. dose of 1 mg/kg per day and reach about 20 mg per day at six months and then 10 mg per day at one year. "During this time it's important that the ophthalmologist follow the patient closely and coordinate treatment with his or her primary care physician so that complications of steroids can be minimized," Dr. Biousse said. That includes providing adjunctive treatment such as vitamins or bisphosphonates to reduce the risks associated with osteoporosis, or even providing an oral hypoglycemic agent or insulin if blood sugar is persistently elevated.

**Careful tapering, douse the smoldering.** Dr. Biousse added that close monitoring during steroid tapering is a necessity because GCA is considered a smoldering disease. More than half of patients with the disease have at least one recurrence during tapering.<sup>2</sup> Serologic tests that show subclinical disease activity, even without symptoms, can predict such a recurrence. Even after

steroids are discontinued, it's wise to follow patients for at least one year, Dr. Biousse said.

Dr. Newman said that because of the danger of recurrence, patient education is vital. "You have to emphasize to your patients that if they experience any recurrent symptoms, they need to let their physician know about it right away," he said.

### The Anticoagulant Question

Another area of controversy in GCA is the use of anticoagulants, Dr. Biousse said. There are few data on anticoagulants, but there are some hints in the scientific literature that antiplatelet therapy may reduce the inflammation seen in GCA. In two clinical studies, patients with GCA who were treated with both steroids and aspirin also had a reduced risk of presenting with ischemic complications such as stroke.<sup>3</sup> Other studies have shown that antiplatelet or anticoagulant therapies produced a lower incidence of ischemic events, including vision loss or stroke.<sup>3</sup>

"We know that aspirin is protective in terms of risk of systemic vascular complications in GCA, so it makes sense to provide patients with giant cell arteritis with antiplatelet agents, particularly those who have vascular risk factors," Dr. Biousse said. She recommends the use of aspirin as an adjunct to corticosteroids in the treatment of GCA, unless it is contraindicated.

**Bigger guns.** Dr. Biousse said that there is no reason to think that other antiplatelet agents besides aspirin would not be helpful in patients with GCA. Dr. Trobe said that on occasion he has used heparin for acute treatment and warfarin for three months in GCA, but only when the patient has lost vision in one eye and is showing signs of losing vision in the opposite eye. "That's part of the art of managing GCA, rather than the science," he said.

### Looking for Alternatives

Because standard therapy currently involves a very big commitment to steroids, clinicians have searched for other agents that may be effective, Dr.

Biousse said. It is a search that has not gone very far.

**Methotrexate—probably not.** The drug that perhaps has gotten the most attention is methotrexate, but so far studies for treating GCA have not been promising, said Dr. Biousse.

**TNF inhibitors—maybe.** Because examinations of the vessel walls of GCA-positive pathology specimens have isolated the cytokine tumor necrosis factor-alpha within T cells, giant cells and macrophages, drugs directed against TNF-alpha, such as infliximab, have been proposed as a possible solution. There have been some positive case reports of remission with this drug, but a recent controlled, randomized, multicenter trial showed no benefit.<sup>3</sup>

**Methylprednisolone—yes.** "The best steroid-sparing drug is really IV methylprednisolone, which allows you to taper oral prednisone faster," Dr. Biousse said.

### Don't Tarry With Treatment

Paradoxically, some of the systemic symptoms can be relatively well tolerated by patients, leading to dangerous neglect of the situation. "Sometimes there's an unwillingness or inability to express the nonophthalmic symptoms, or a desire of patients not to bother their physicians, so that these symptoms are not reported. Then the patients suddenly become blind," Dr. Trobe said.

Consequently, it's vital that acute vision loss in patients over age 65 be assessed urgently, Dr. Trobe said. "These patients have to be seen immediately, even if it's Friday night or Saturday because you could be in the position to save vision in the opposite eye by getting high-dose steroids to the patient immediately. With giant cell arteritis, you can intervene and truly make a difference."

1 Mazlumzadeh, M. et al. *Arthritis Rheum* 2006;54(1):3310-3318.

2 Fraser, J. A. et al. *Rev Neurol Dis* 2008;5(3):140-152.

3 Kawasaki, A. and V. Purvin. *Acta Ophthalmol* 2009;87:13-32.