

The Patient Who Preferred to Act *Locally* Rather Than Think *Globally*

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Paula Douglas* is a 40-year-old African-American female. She initially presented to a rural clinic with a two-year history of blurred vision and floaters in both eyes. At that time she had a vision of 20/40 in the right eye and 20/50 in the left, as well as bilateral vitreous cells, bilateral peripheral periphlebitis and scattered intraretinal hemorrhages. She was started on topical steroids and referred in for an evaluation.

We Get a Look

The patient's past medical and ocular histories were unremarkable with the exception of hypertension. She was given a uveitis questionnaire.¹ Her answers were unrevealing, although she did have a daughter who had been diagnosed with systemic sarcoidosis.

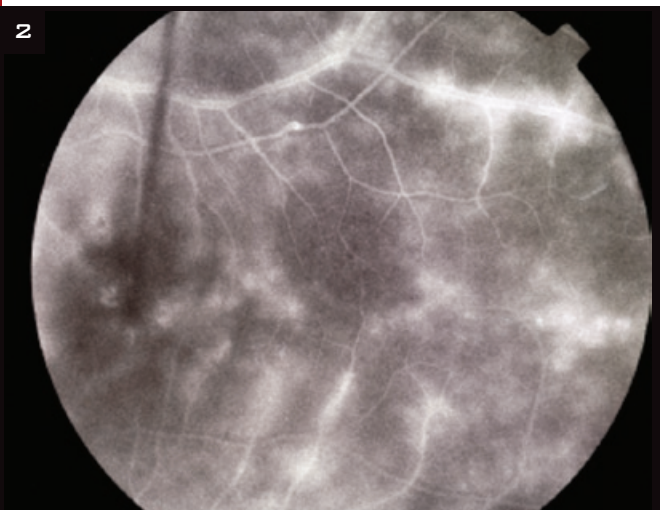
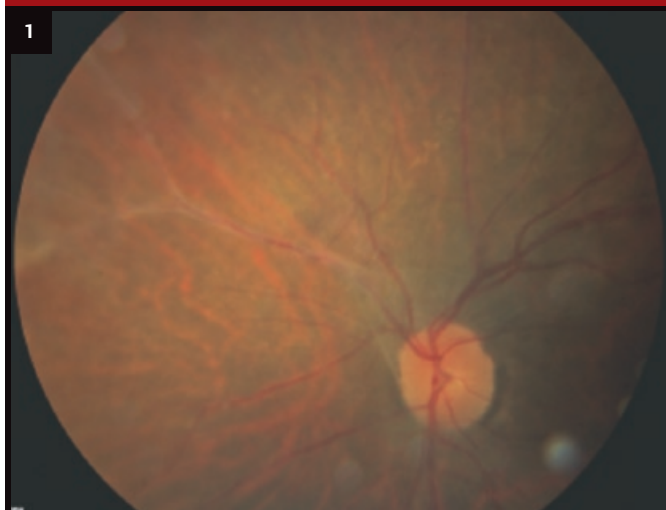
When we examined her, she had the findings that had been noted at the referring practice plus a trace of anterior chamber cells with no synechia, iris nodules or keratic precipitates. She also had pronounced macular edema and scattered vitreous snowballs in both eyes, but no pars plana snowbanking.

Her laboratory evaluation in-

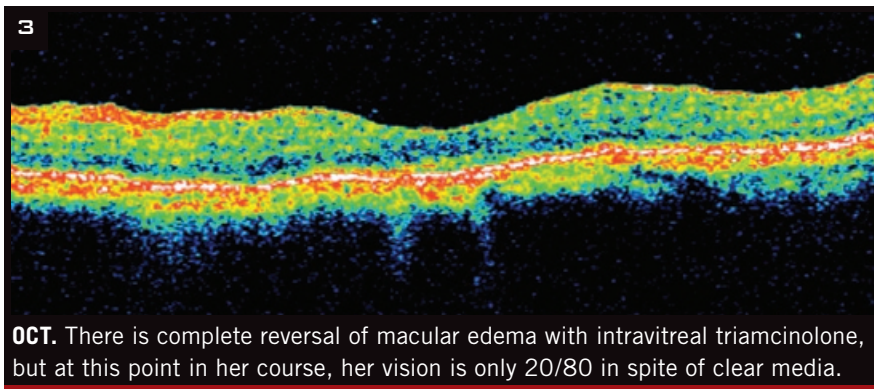
cluded CBC, liver function tests, chest x-ray, angiotensin converting enzyme, serum lysozyme, Lyme titer, VDRL, FTA-ABS, PPD and antibodies to HIV.

The test results were unremarkable with the exception of a positive PPD. Because of this positive result and the fact that her presentation was suggestive of sarcoidosis, we arranged for Ms. Douglas to be seen by a pulmonary specialist. He did not find any evidence of active tuberculosis or sarcoidosis. Given her age, and the fact that her uveitis might represent a hypersensitivity response to latent tuberculosis, she was treated with isoniazid. She tolerated the medication, but it did not have any significant effect on the activity of her ocular disease.

What's Your Diagnosis?



WE GET A LOOK. We noted periphlebitis (1) and diffuse perivenular staining, which can be seen in this late-phase fluorescein angiogram (2). Cystoid macular edema can also be seen as well as focal dilation of one of the arteries.



OCT. There is complete reversal of macular edema with intravitreal triamcinolone, but at this point in her course, her vision is only 20/80 in spite of clear media.

Treatment

At first, her inflammation responded surprisingly well to topical steroids alone. She did have problems with ocular hypertension on the steroids, but the pressure was controlled with topical medications. But her disease eventually became more aggressive with a return of the inflammation, vascular sheathing and macular edema.

We had a number of discussions with the patient about systemic treatment vs. local ocular therapy. The patient was very reluctant to be treated systemically, so over the next year she received a series of periocular steroid injections. These controlled her disease for a while, and she did not have significant pressure elevations.

However, her disease became more aggressive and the combination of topical and periocular steroids became less and less effective. There were also problems with adherence to the medication regimen and making scheduled appointments. The importance of close follow-up was discussed with her, and it turned out that she had lost her job and insurance and was unable to afford her care. In order to maintain appropriate follow-up, she was reassured that she would be seen gratis and she was provided with sample medications as much as possible.

As her uveitis worsened, she presented with flare-ups that reduced her vision to count fingers in the right eye and 20/400 in the left eye. Repeat systemic testing remained unremarkable. We recommended treatment with immunosuppressive agents, but she was very worried about side effects, and she opted for intravitreal triamcinolone

injections, preferring to accept the risk of glaucoma and cataract over the risk of systemic therapy. Once again, this approach was initially successful and she did not have pressure elevations that required surgery. But the treatment effect wore off after two months and her vision dropped back to the 20/200 to 20/400 range in both eyes.

We again encouraged Ms. Douglas to undergo systemic treatment, but she again declined. So we performed a vitrectomy with peripheral laser treatment in the left eye in hopes of controlling the disease activity. The vitrectomy specimen was sent for cytology, and it was negative for malignancy. She also required cataract surgery, but even with surgery and continued intravitreal triamcinolone her vision ranged between 20/200 and 20/70 in the left eye. At one point her vision did not improve at all after an intravitreal steroid injection in spite of resolution of her macular edema and vitritis (Fig. 3). Vision was better in the right eye than in the left, but was still hovering between 20/60 and 20/80 in spite of treatment with both topical and periocular steroids.

The patient was again encouraged to consider the use of systemic immunosuppressives. She finally agreed and was seen by a rheumatologist who treated her with methotrexate, using a relatively moderate dose of 17.5 mg per week. Within two months she stopped having flare-ups and, remarkably, once her disease was controlled on a consistent basis her vision improved to 20/20- in the right eye and 20/25+ in the left. She has remained stable for the past two years on this regimen.

Discussion

This case demonstrates a number of points in managing uveitis patients.

First, not every patient ends up with a definitive diagnosis. In this case, the clinical presentation and course was suggestive of ocular sarcoidosis, but the patient never had any systemic manifestations of that condition.

The positive PPD is also interesting. While Eye M.D.s tend to be conscientious about getting blood tests on uveitis patients, they sometimes overlook the PPD, which is a crucial test when tuberculosis may be a possibility. Patients can have intraocular tuberculosis without active systemic disease, and the ocular disease can manifest in protean ways. Patients may also have intraocular inflammation as a hypersensitivity response to latent tuberculosis elsewhere in the body. Appropriate antituberculosis therapy can cure the disease in both types of patients.² Knowledge of the PPD status is also important when planning systemic therapy because of the risk of converting latent disease to active disease, especially with newer treatments such as the tumor necrosis factor-alpha inhibitors.

This case also reinforces the need to discuss compliance issues with patients. This can be a problem under the best of circumstances, but especially when there are financial obstacles. These difficulties can go unvoiced by the patient because of embarrassment, and physicians may need to specifically ask about the situation. It is incumbent on physicians to find ways for patients to be followed regardless of their ability to pay in order to avoid vision loss (see Practice Perfect, p. 49).

Local ocular therapy with the Retisert fluocinolone implant may be more effective for some patients than systemic immunosuppression.³ In the case presented here, the implant was not used because during most of the patient's course she had no insurance (nor could she have afforded the inevitable glaucoma surgery). Also, the fact that intravitreal triamcinolone did not completely treat the disease made it seem that the Retisert implant would

have been less effective in this case.

Most important, this case is a cautionary tale about the effectiveness of local ocular therapy vs. systemic immunosuppression.⁴ For years this patient declined systemic treatment. As ophthalmologists, it is easy to resort to local treatments because such treatments are most familiar to us, but treating only the eye does not always control the recruitment of immunoreactive cells from the rest of the body. In this case, moderate doses of methotrexate had a dramatic effect.

Strong consideration should be given to referring problematic patients to a regional uveitis specialist for guidance about the role of systemic treatment when needed. Even if the community ophthalmologist is not familiar with immunosuppressive therapy, it is usually fairly simple to find specialists such as rheumatologists or nephrologists who are willing to help monitor the patient's systemic status. These doctors often worry that they will be asked to manage the patient exclusively, but they will be much more willing to help if they understand that the ophthalmologist monitors the eyes closely to assist with titrating treatment.

In this case the patient is far happier now that her disease is controlled, her vision is better, and she is no longer running back and forth to the ophthalmology office for treatment of flare-ups and monitoring of IOP.

* Patient name is fictitious.

1 The questionnaire was similar to the one that appears in the *Basic and Clinical Science Course, Section 9* (San Francisco: AAO, 2009), pp 142–146.

2 Varma, D. et al. *Eye* 2006;20:1068–1073.

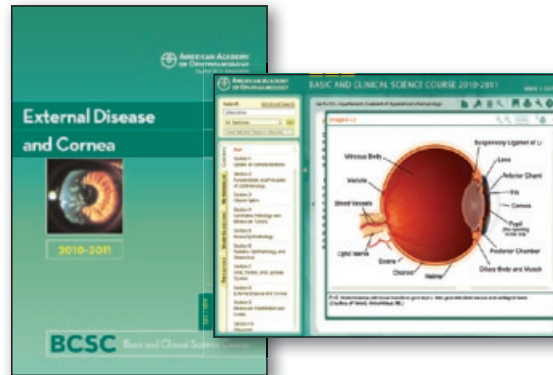
3 Pavasio, C. et al. *Ophthalmology* 2010;117:567–575.e1.

4 Okada, A. A. *Ocul Immunol Inflamm* 2005;13:335–351.

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