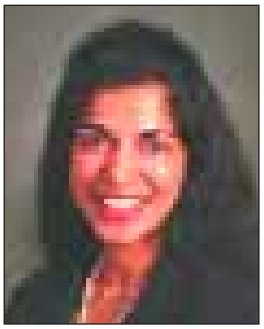
Successful Treatment of Retinal Neovascularization and Uveitis with Infliximab in a Patient with Crohn's Disase

Jared Z. Gold



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We report a case of a 32-year-old female with Crohn's disease who initially presented with an anterior uveitis. She later developed symptoms and signs of small bowel disease as well as a posterior uveitis and retinal neovascularization. She was treated with multiple topical and oral medications with minimal improvement. Finally, she was treated with infliximab 5 mg/kg IV which resulted in improvement of the gastrointestinal symptoms and complete resolution of her uveitis and retinal neovascularization.

INTRODUCTION

Inflammatory bowel disease (IBD) is associated with numerous extraintestinal manifestations. Ophthalmologic manifestations are reported to occur in approximately 4% to 6% of patients (1,2) and are more common in patients with Crohn's disease than ulcerative colitis (3). The two most common eye manifestations of IBD are episcleritis and uveitis (4), which are independent of intestinal disease activity. Other rare findings such as retinitis (5), optic neuritis (6) and retinal neovascularization (7) have been reported.

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Patients with refractory uveitis associated with IBD have been treated successfully with immunomodulators such as oral steroids, azathioprine, methotrexate and infliximab (8) (anti-tumor necrosis factor alpha). The standard therapy for retinal neovascularization is panretinal photocoagulation (6). There are no reports in the medical literature of use of infliximab for this rare extraintestinal manifestation of Crohn's disease.

We report a case of anterior and posterior uveitis with retinal neovascularization in a patient with newly diagnosed Crohn's disease that was successfully treated with infliximab.

CASE REPORT

The patient is a 32-year-old white female with a history of Hashimoto's thyroiditis who complained of

Figure 1. (left and right retina) Retinal examination from December 2003. The left retina shows a small physiologic cup, the optic disc appears very slightly hyperemic, normal appearing vessels, normal appearing macula, and patches of hyperpigmentation in parts of the periphery. The right retinal exam was relatively normal.

pain and redness of both her eyes. She was initially treated symptomatically for viral conjunctivitis but her symptoms continued. She was seen by an ophthalmologist who diagnosed bilateral iritis and uveitis and treated her with topical steroids and later, with oral methotrexate 32.5 mg once a week. Around the same time, she started experiencing abdominal pain, diarrhea and "gas." She was referred to a community gastroenterologist who performed a colonoscopy, which revealed mild inflammation of the terminal ileum and an upper gastrointestinal series with small bowel follow through which revealed mild terminal ileal disease. She was diagnosed with Crohn's disease and started on mesalamine 800 mg three times a day. This afforded her some relief for approximately one and a half years, until she developed worsening diarrhea, abdominal pain, loss of appetite, hip and back pain and a 30 pound weight loss over a six month period. She was therefore referred to our University based gastroenterology practice for further evaluation and treatment of her Crohn's disease.

At initial consultation, in addition to her gastrointestinal symptoms, the patient also complained of blurring of vision in her left eye. Examination of the left eye by her ophthalmologist revealed a visual acuity of 20/30, pupils equal, round, reactive and no afferent defect, normal slit lamp exam, a small or absent physiologic cup, slightly hyperemic optic disc, normal appearing vessels, normal appearing macula, patches of hyperpigmentation in some parts of the periphery and a normal scleral exam. Examination of the right eye was relatively normal (Figure 1). She was treated with methotrexate, topical steroids, lubricant eye drops and diclofenac eye drops. However, she continued to have blurring of vision and pain in her left eye. Two months later, dilated retinal examination of the left eye revealed a new finding of wiry looking telangiectactic vessels connecting the arteriole and venule. In addition, a mild cystoid irregularity in the macula was noted (Figure 2). Fluorescein injection showed prompt filling of the retinal vessels and choroids, early and prominent filling of the telangiectasia and a cystoid pattern of fluroscein accumulation in the macula. These finding were consistent with early neovascular proliferation and macular edema.

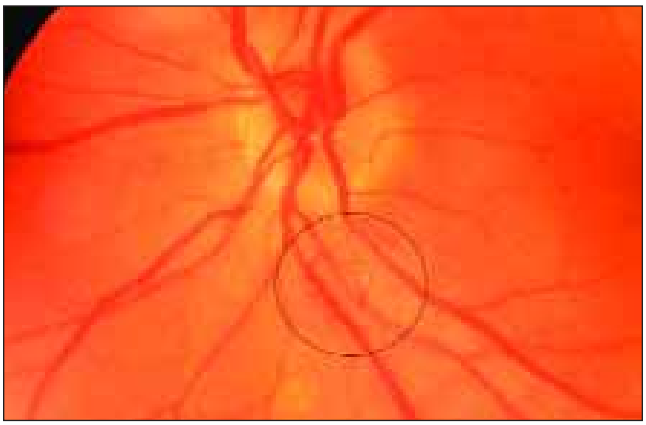

Figure 2. Left retinal examination from February 2004. Circle indicating area of neovascularization.

A CASE TO REMEMBER

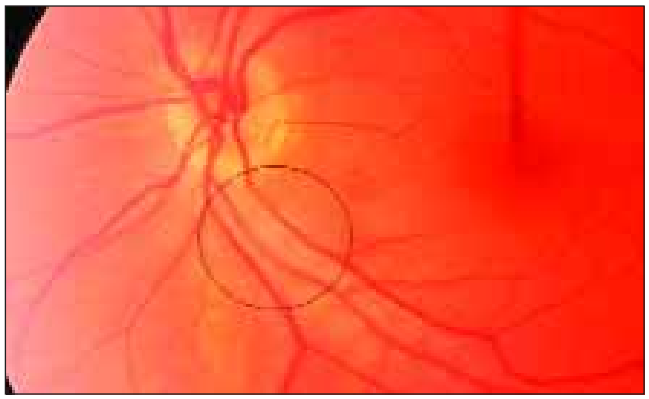

Figure 3. Left retinal examination from April 2004. Circle indicating area of resolved neovascularization.

The ophthalmologist suggested that the patient be started on oral cyclosporine for the uveitis. However, in view of the patient's continuing gastrointestinal complaints, we recommended treating her with infliximab instead of oral cyclosporine. The advantage of infliximab over oral cyclosporine is its greater efficacy in treating Crohn's disease and potential efficacy in treating uveitis. She was started on infliximab 5 mg/kg IV on weeks 0, 2, 6 and then every 8 weeks and continued on oral methotrexate 20 mg once a week, steroid eye drops, diclofenac eye drops and lubricant eye drops.

Approximately 4 weeks after starting infliximab, the patient reported improvement of the blurring and pain in her left eye. Dilated retinal examination of the left eye revealed resolution of the telangiectactic vessels seen previously, but the cystoid alteration of the macula remained (Figure 3). The topical steroid was increased to three times a day, and she continued the diclofenac drops, lubricant drops, oral methotrexate and infliximab. Several weeks after starting infliximab, she reported feeling very well. Fundal examination revealed no neovascularization, normal major vessels and macula and the cystoid alteration had resolved. She continues to have complete resolution of her eye symptoms while on the maintenance infliximab and her gastrointestinal symptoms are much improved.

DISCUSSION

This report describes a patient with multiple ocular manifestations of Crohn's disease, including retinal neovascularization, which resolved completely with infliximab treatment. Retinal neovascularization itself is a rare complication of Crohn's disease. We found one report in the literature of a 38-year-old woman with Crohn's disease and neovascularization secondary to retinal vasculitis and branch retinal arterial occlusion (7). She was treated with Argon green laser panretinal photocoagulation with complete regression of the neovascularization.

Our search in the English medical literature found no report of the use of infliximab in treating retinal neovascularization associated with Crohn's disease.

Infliximab and other tumor necrosis alpha inhibitors have become an important therapy for inducing and maintaining remission in moderate-to-severe Crohn's disease and inducing closure of fistulas in patients who have had an inadequate response to conventional therapy (9,10). There are several reports of improvement of extraintestinal manifestations of Crohn's disease with infliximab treatment (8,11,12). This case report describes another example of a rare, but important ocular manifestation of Crohn's disease that was treated successfully with infliximab. ■

References

1. Hopkins DJ, Horan E, Burton IL, et al. Ocular Disorders in a series of 332 patients with Crohn's disease. *Br J Ophthalmol,* 1974; 58:732-737.
2. Greenstein AJ, Janowitz HD, Sachar DB. The extraintestinal complications of Crohn's disease and ulcerative colitis: A study of 700 patients. *Medicine,* 1976;55:401-412.
3. Monsen U, Sorstad J, Hellers G, et al. Extracolonic diagnoses in ulcerative colitis: an epidemiological study. *Am J Gastroenterol,* 1990;85:711-716.
4. Petrelli EA, Mckinley M, Troncale FJ. Ocular manifestations of inflammatory bowel disease. *Ann Ophthalmol,* 1982;14:356.
5. Duker JS, Brown GC, Brooks L. Retinal Vasculitis in Crohn's Disease. *Am J Opthalmol,* 1987;103(5):664-668.
6. Ernst BB, Lowder CY, Meisler DM, et al. Posterior segment manifestations of inflammatory bowel disease. *Ophthalmology,* 1991;98(8):1272-1280.
7. Saatci OA, Kocak N, Durak I, et al. Unilateral retinal vasculitis, branch retinal artery occlusion and subsequent retinal neovascularization in Crohn's disease. *International Ophthalmology,* 2001;24(2):89-92.
8. Fries W, Giofre MR, Catonoso M, et al. Treatment of acute uveitis associated with Crohn's disease and sacroileitis with infliximab [letter]. *Am J Gastroenterol,* 2002;97(2): 499-500.
9. Targan SR, Hanauer SB, Van Deventer SJH, et al. A short-term study of chimeric monoclonal antibody cA2 to tumor necrosis factor alpha for Crohn's disease. *N Engl J Med,* 1997;337:1029-1035.
10. Present DH, Rutgeerts P, Targan S, et al. Infliximab for the treatment of fistulas in patients with Crohn's disease. *N Engl J Med,* 1999;340:1398-1405.
11. Kaufman I, Caspi D, Yeshurun D, et al. The effect of infliximab on extraintestinal manifestations of Crohn's disease. *Rheumatol Int,* 2004 Aug 12; [Epub ahead of print].
12. Sapienza MS, Cohen S, Dimarino AJ. Treatment of pyoderma gangrenosum with infliximab in Crohn's disease. *Dig Dis Sci,* 2004; 49(9):1454-1457.