

Grand Rounds

A 45-year-old man with spontaneous hyphema of the right eye

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History

A 45-year-old white man with a history of iritis of the right eye presented to the Massachusetts Eye and Ear Emergency Department for a new, spontaneous hyphema of the right eye. The patient reported that he had previously experienced approximately 4 episodes of iritis of the right eye each year for the last 4 years; each time these episodes resolved with topical steroid therapy. He did not recall any blood work having been performed or any cause of his recurrent iritis having been identified.

The current episode started 1 week prior to presentation with pain, redness, and right eye photosensitivity. He was examined by his ophthalmologist 3 days later and was started on topical prednisolone acetate 1% every 2 hours. His symptoms did not improve with this treatment, and 1 day prior to presentation he was noted by his ophthalmologist to have a new hyphema of the right eye and was referred to our institution.

The patient did endorse a history of intermittent joint pains, worse in the morning but improving with movement. He had a history of back surgery 20 years prior for a herniated disc. He otherwise denied a history of autoimmune disease, fever or chills, joint pains, rashes, muscle aches, or oral ulcers. He denied a history of trauma, use of blood thinners, history of bleeding disorders, or sickle cell disease. His past medical history was unremarkable, and he did not have a history of diabetes. He did not take any medications. His family history was significant for his mother having rheumatoid arthritis.

Examination

On examination, visual acuity was 20/50 in the right eye and 20/20 in the left eye. His pupils were equal, round, and reactive; there was no relative afferent pupillary

defect. Intraocular pressure was 18 mm Hg in the right eye and 16 mm Hg in the left eye. Anterior segment examination of the right eye revealed 2+ diffuse conjunctival and scleral injection, with tenderness, fine keratic precipitates, diffuse anterior stromal haze of the cornea, and Descemet folds centrally. Prominent iris blood vessels were noted superiorly with 360 degrees of posterior synechiae, but there were no iris transillumination defects. The anterior chamber was notable for 4+ cell and flare and a 1 mm inferior clot, with 2 mm layering hyphema from 2 to 9 o'clock (Figure 1A). Gonioscopy showed fine blood vessels traversing the superior angle, which did not cross over the scleral spur onto the trabecular meshwork. There were no peripheral anterior synechiae. Posterior segment examination of the right eye was somewhat limited because of the anterior segment pathology and poor pupillary dilation. Only a small, intraretinal hemorrhage inferior to the optic nerve was noted. There was no evidence of vitritis or pars planitis. Anterior segment examination (Figure 1B) and gonioscopy of the left eye were normal. Posterior segment examination of the left eye was unremarkable.

Ancillary Testing

Laboratory results revealed positive HLA-B27 and HLA-B7 and slightly elevated complement C3c. Polymerase chain reaction (PCR) tests for cytomegalovirus, Epstein-Barr virus, Herpes simplex virus (HSV-1), and varicella zoster virus from an anterior chamber tap were negative. All other tests were negative, including Lyme serologies, rheumatoid factor, HSV-1 IgM, anti-neutrophil cytoplasmic antibody, anti-nuclear antibody, complement C4, toxoplasma IgG, anti-cyclic citrullinated peptide IgG, angiotensin converting enzyme, lysozyme, rapid plasma reagin (RPR), and fluorescent treponemal antibody absorbent (FTA-ABS). Basic bloodwork did not reveal an anticoagulated state. Fluorescein and

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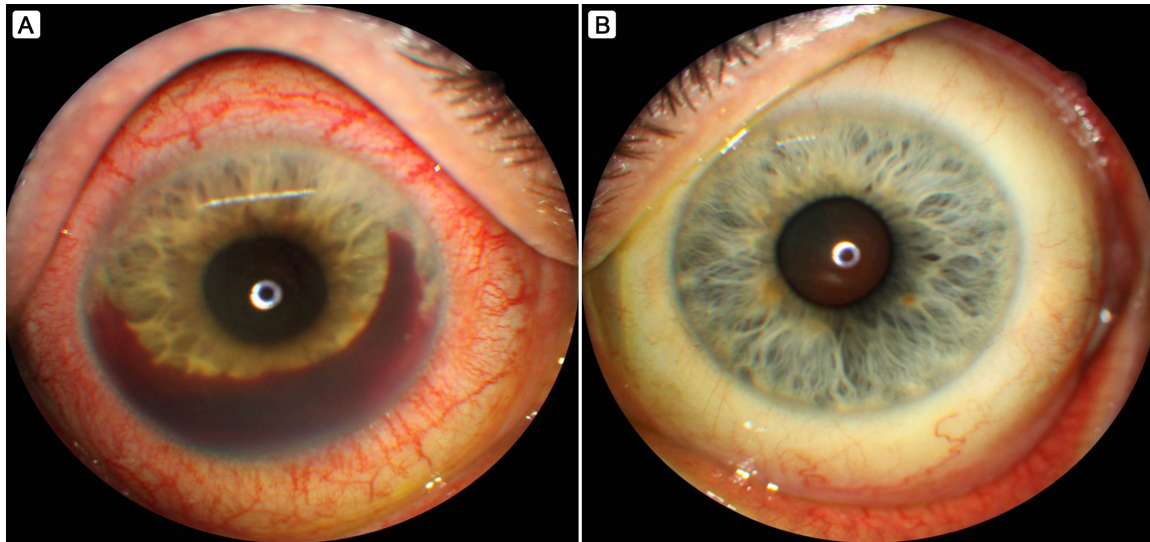


Figure 1. Anterior segment photographs of the right eye (A) and the left eye (B).

indocyanine green angiography did not reveal any signs of retinal ischemia, vasculitis, or choroidal pathology.

Treatment

The patient was initially switched from prednisolone acetate to difluprednate 0.05% drops every 2 hours and started on cyclopentolate 1% drops 3 times per day in the right eye. Additionally, he was started on oral valacyclovir 1000 mg 3 times a day. He did not symptomatically improve with this therapy; therefore, he was started on 3 days of 1 g intravenous methylprednisolone infusion followed by an oral prednisone taper, with noticeable improvement. On tapering of oral prednisone, inflammation recurred, and he was started on systemic corticosteroid-sparing therapy with methotrexate. Subsequently he was also started on adalimumab for better control of his inflammation.

Differential Diagnosis

The differential diagnosis for spontaneous hyphema in the setting of a unilateral anterior uveitis includes infectious and inflammatory causes. Viral infections, such as herpes simplex and herpes zoster, must also be considered, because these can present with a keratouveitis and, rarely, hyphema. Inflammatory causes include Fuchs heterochromic iridocyclitis, HLA-B27-associated uveitis, lens-induced uveitis, juvenile xanthogranulomatosis, and juvenile idiopathic arthritis in young patients. In patients who are pseudophakic, uveitis-glaucoma-hyphema syndrome is also part of the differential diagnosis.

Diagnosis and Discussion

The occurrence of a spontaneous hyphema with an anterior uveitis is uncommon. One must first rule out other more common causes of hyphema, such as trauma. In addition, the iris should be carefully inspected for any signs of neovascularization from proliferative diabetic retinopathy, retinal vein occlusion, anterior segment ischemia, or other causes, such as a mass or tumor in the anterior segment. Once these causes for hyphema have been eliminated, one can be more confident that the hyphema is more likely associated with a uveitis. Our patient did not report a history of trauma, and there was no evidence of a mass in the anterior segment. The prominent dilated iris vessels observed were within the stroma and radial in orientation, differentiating them from neovascularization of the iris, which appears as small, fine, disorganized vessels on the anterior surface of the iris. With immunomodulatory treatment, the vessels were no longer prominently noted.

Fuchs heterochromic iridocyclitis was initially considered, given the presence of fine keratic precipitates and what appeared to be fine blood vessels traversing the angle. There was also an asymmetry in the color of the iris, although the iris was darker in the affected eye. A hyphema can occur due to bleeding of fine vessels traversing the iris and angle during anterior chamber paracentesis, or even spontaneously, also known as Amsler's sign. However, the anterior uveitis in Fuchs is typically mild and rarely presents with visual acuity worse than 20/40.¹

In our patient, the anterior chamber inflammation was quite significant and could not be adequately controlled with topical difluprednate. Due to the possibility of a viral infection, the patient was empirically started on oral antiviral therapy. It was important to obtain a sample of the aqueous humor to rule out a viral infection with PCR tests for herpes simplex and varicella zoster virus, because these have been implicated in keratouveitis and spontaneous hyphema.^{2,3} In children, juvenile xanthogranulomatosis and juvenile idiopathic arthritis can also present with uveitis and spontaneous hyphema, but our patient is out of this age group.^{4,5} Lens-induced uveitis and hyphema with resolution upon cataract extraction has been reported, but there was not a significant cataract in our patient.⁶

Labwork revealed our patient to be HLA-B27 positive. The uveitis associated with HLA-B27 is typically unilateral and can be severe. Spontaneous hyphema has been reported, especially in patients with ankylosing spondylitis.^{3,7} It is thought that hyphema occurs in the setting of severe anterior uveitis secondary to breakdown of the blood–aqueous barrier and increase in capillary permeability.⁸ Our patient did not carry a diagnosis of ankylosing spondylitis, although he did have a history of intermittent mild joint pains, improving with movement. It is not known whether recent spinal imaging has been performed to evaluate for this, but it should be considered.

Our patient's uveitis was severe and could not be controlled with topical steroids. He required systemic corticosteroids in the acute phase and additional long-term steroid sparing therapy with methotrexate and adalimumab. Recent studies have shown anti-TNF- α agents such

as infliximab, adalimumab, and etanercept to be effective in the treatment of uveitis associated with HLA-B27.^{9,10} However, these agents increase the risk of severe infection and should be used with caution. Coordination with a rheumatologist can be helpful in the management of these patients.

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