DIAGNOSING AND MANAGING PEDIATRIC RETINAL VASCULITIS

High-quality fundus imaging and aggressive treatment of inflammation is critical for children with retinal vasculitis.

BY DILRAJ S. GREWAL, MD

Pediatric uveitis is relatively uncommon, with a prevalence of 30 in 100,000 children and accounting for only 5% to 10% of all uveitis cases.[1,2] However, the vision-threatening complications are disproportionately higher, and up to 25% of children can progress to a VA of 20/200 or worse due to cataracts, ocular hypertension, glaucoma, macular edema, and amblyopia. Thus, ocular inflammation must be treated aggressively to prevent the occurrence of these ocular sequelae.

Unfortunately, pediatric uveitis can be challenging to manage because of the often delayed diagnosis, chronic course, examination difficulties, and side effects of medical treatment. It is also usually idiopathic, accounting for 30% to 50% of cases.[3] The pearls included in this article can help you to catch this condition early and treat it appropriately.

THE CRITICAL IMAGING TOOL

The advent of widefield imaging systems has improved our ability to obtain high-quality fundus imaging in children, even in-office and without the use of anesthesia. While multimodal imaging—including fundus photography, OCT, and OCT angiography (OCTA)—is important, fluorescein angiography (FA) remains the critical tool for diagnosing and monitoring retinal vasculitis.[4-7]

The benefits of obtaining FA in children outweigh the logistical concerns, as FA provides substantial additional information beyond what the clinical examination can find. Nearly 80% of children with posterior uveitis deemed quiescent based on their clinical examination demonstrate persistent subclinical inflammation on FA that requires further treatment with immunomodulatory therapy (IMT) to obtain full disease control and true quiescence.[8]

Physicians may use oral fluorescein when venous access for FA is not feasible in a child. However, oral FA images are not directly comparable with intravenous FA images and may not be suitable for detecting subtle inflammation, particularly for peripheral findings in the later (10- to 20-minute) phases.

AGGRESSIVE AND ADEQUATE TREATMENT OF OCULAR INFLAMMATION IS CRITICAL TO OPTIMIZE LONG-TERM VISUAL OUTCOMES IN CHILDREN WITH RETINAL VASCULITIS.

Failing to identify and adequately control occult retinal vasculitis may contribute to the higher incidence of long-term complications in children with intermediate, posterior, or panuveitis and to the subsequent poorer prognosis compared with patients whose disease is isolated to the anterior segment.

WHAT TO LOOK FOR

According to the Standardization of Uveitis Nomenclature Working Group, the presence of perivascular sheathing and vascular leakage or occlusion on a fundus FA may be used for the classification of retinal vasculitis.[9] Retinal vasculitis can be accompanied by retinal vascular sheathing, leakage, occlusion, or neovascularization. Features of active inflammation seen on FA include perivascular staining (venous or arterial), peripheral capillary leakage, late optic disc staining, peripheral retinal nonperfusion, and angiographic cystoid macular edema (Figure 1). In eyes apparently quiescent based on a dilated examination, 79% had FA activity.[8] Almost 80% of pediatric patients with idiopathic uveitis show some manifestations of retinal vasculitis, which is associated with a lower probability of inflammation control at 1 year, resulting in a worse visual prognosis.[10]

When performing FA, it is important to capture the

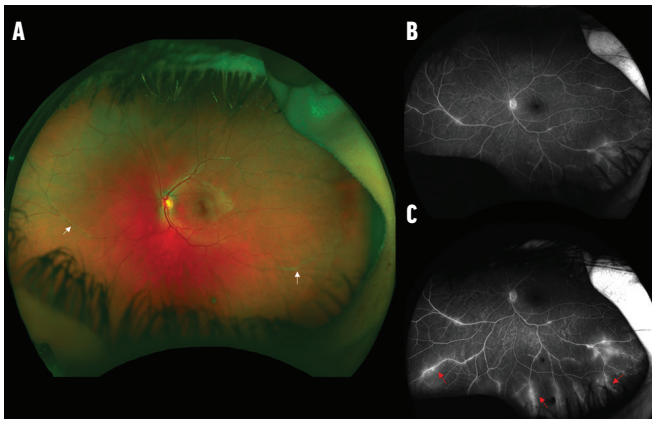

Figure 1. This fundus photograph shows perivascular sheathing (A, white arrows). Widefield intravenous FA with an on-axis view shows a perivascular leak in the posterior pole and the nasal and temporal periphery (B). Inferior-steered widefield FA shows additional areas of perivascular leakage not seen on the on-axis image (C).

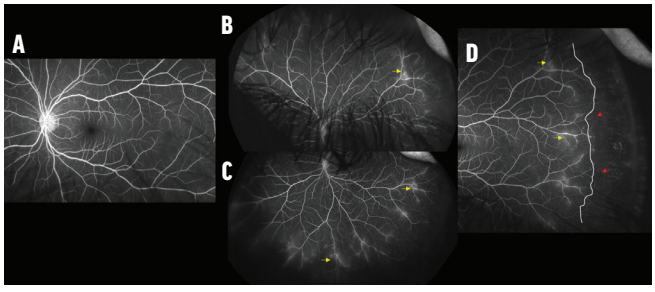

Figure 2. FA shows an unremarkable posterior pole with no optic disc leakage or angiographic macular edema (A). The peripheral-steered images show a perivascular leak superiorly (B, yellow arrows), inferiorly (C), and temporally (D). The white line temporally demarcates an area of retinal nonperfusion.

retinal periphery using steered images to accurately detect and monitor peripheral leakage (Figures 2 and 3) until complete quiescence is demonstrated on both FA and clinical examination.

Another useful marker to detect inflammatory activity is noncystic thickening (thickening of retina in absence of intraretinal fluid or intraretinal cysts) seen on thickness maps and the central subfield thickness value on OCT (Figure 4). When assessing noncystic thickening, clinicians must ensure that the segmentation lines on the OCT image are correct; otherwise, it may lead to erroneous measurements and thickness maps.

In children with intermediate uveitis and retinal vasculitis, it is also important to evaluate for retinoschisis, particularly in the inferior periphery in areas of snowbanks, as poor inflammatory control may lead to the progression of retinoschisis and retinal detachment. A vitreous hemorrhage may also develop due to traction and neovascularization because of peripheral nonperfusion. OCT and OCTA are helpful to evaluate for inflammatory choroidal (or macular) neovascular membranes that, if active, may require treatment.

Failure to fully control retinal vasculitis leads to recalcitrant cases that cannot taper IMT, which causes long-term complications and a poor prognosis. It is critical to objectively assess

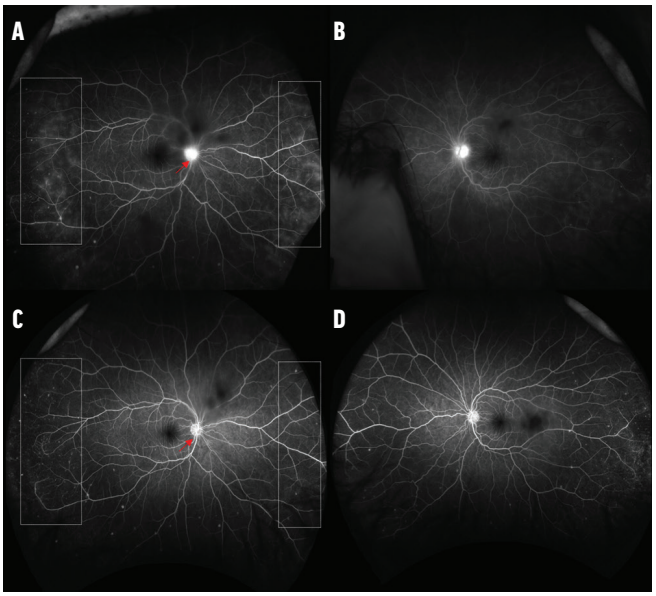

Figure 3. The widefield FA of an 8-year-old boy with active intermediate uveitis shows leakage at the optic disc (red arrow) and perivascular leakage in the periphery (white rectangles) in both the right (A) and left (B) eyes. After initiation and titration of IMT, there is improvement with resolution of the optic disc leakage (red arrow) and peripheral perivascular leakage (white rectangles) in both the right (C) and left (D) eyes.

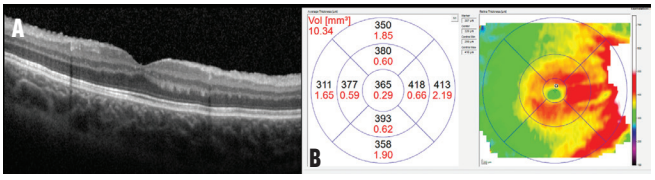

Figure 4. Although OCT shows no cystoid macular edema (A), the thickness map shows increased thickness in the corresponding scale on the right (B), consistent with noncystic thickening, which is a marker of active inflammation.

inflammation to titrate IMT and avoid premature cessation of therapy. In children, clinicians can't rely on symptoms or the anterior segment examination alone.

THE TREATMENT

Treatment of pediatric uveitis and retinal vasculitis is individualized based on the patient and the severity of intraocular inflammation using a stepladder approach. It is important to consider the side effect profile of each treatment option. For example, systemic steroids are a good first-line treatment as a bridge to IMT. However, long-term use of steroids is not recommended due to the systemic side effects such as growth retardation, Cushingoid effects, behavioral changes, and related psychosocial problems.

Our systemic immunosuppressive therapy armamentarium includes antimetabolites (azathioprine, methotrexate, and mycophenolate mofetil [CellCept, Genentech/Roche]); calcineurin inhibitors (cyclosporine and tacrolimus), and biologics (adalimumab [Humira, AbbVie],

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infliximab [Remicade, Janssen], rituximab [Rituxan, Roche], and tocilizumab [Actemra, Genentech/Roche]). Alkylating agents such as cyclophosphamide and chlorambucil are rarely used in the pediatric population.

Local therapies such as intravitreal or periocular steroids are not usually a good option in the pediatric population. This is due to the risk of IOP elevation and cataract formation and the need to administer these injections under general anesthesia. However, in certain situations—and when used judiciously—local therapy can be an effective tool and a useful adjunct to IMT.[11,12] Dexamethasone can cause less IOP elevation compared with triamcinolone and fluocinolone. The effect of the dexamethasone implant has been shown to last for more than 6 months.

There is a higher risk of steroid-induced glaucoma in children, so it is important to involve our glaucoma colleagues early in the management plan in the event incisional glaucoma surgery is required. In addition, due to the need for chronic treatment and the risk of amblyopia, children should be followed regularly for the development of lens opacities.

The goal of IMT in pediatric uveitis is steroid-free remission without any active or recurrent inflammation (on both clinical examination and FA) on a stable IMT dose for 2 to 3 consecutive years. Once this is achieved, specialists can attempt to slowly taper the IMT off with the final goal of durable drug-free remission.[13] It is important to accurately detect the level of inflammatory activity in such children using FA during the taper.

Aggressive and adequate treatment of ocular inflammation is critical to optimize long-term visual outcomes in children with retinal vasculitis. ■

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DILRAJ S. GREWAL, MD
■ Retina Surgeon and Uveitis Specialist, Duke University Eye Center, Durham, North Carolina
■ dilraj.grewal@duke.edu
■ Financial disclosure: Consultant (Allergan/AbbVie, EyePoint)