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Juvenile Idiopathic Arthritis with Anterior Uveitis and Vasculitis

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Introduction

Juvenile idiopathic arthritis (JIA) is a chronic autoimmune condition that affects children younger than age 16. JIA is the most common comorbidity in the pediatric uveitis population, accounting for approximately 75% of all pediatric anterior uveitis.[1,2] JIA-associated uveitis places patients at an elevated risk of both anterior and posterior ocular complications, including band keratopathy, cataracts, glaucoma, posterior synechiae, cystoid macular edema (CME), epiretinal membrane, and hypotony.[1–3] JIA-associated uveitis more commonly presents with anterior segment involvement with chorioretinitis lesions described in only 1% of cases.[4] This can partially be explained by the difficulty in performing ophthalmoscopic examinations through cloudy ocular media and cataract formation secondary to inflammation.[4]

There is limited literature on posterior segment complications of JIA-related uveitis and very few reports regarding vasculitis involvement.[1,5,6] No animal model fully mirrors all features of JIA-associated uveitis; thus, pathophysiology is not yet well understood.[3]

Case Report

A 16-year-old female with history of JIA since age six presented with blurry vision and a diagnosis of chronic iridocyclitis and optic nerve drusen in both eyes. Prior to presentation, she had been initially treated with adalimumab (ADA) 40mg every other week. Then this was switched to infliximab (INF), and topical corticosteroid (difluprednate) was added due to frequent uveitis flare-ups. The INF dosage was then increased from 5mg/kg/month to 10mg/kg/month due to refractory uveitis; however, despite the higher dose, flare-ups persisted. She then commenced treatment with tofacitinib at a dose of 5mg twice daily, though flare-ups persisted. Tofacitinib was discontinued, and treatment with ADA at a dose of 40 mg every other week was reinitiated, in addition to topical and systemic corticosteroids. On presentation to our clinic, best corrected visual acuity (BCVA) was 20/70 in the right eye and 20/20 in the left eye. There were micro-granulomatous

keratic precipitates, band keratopathy temporal and medially in both eyes with posterior synechiae almost 360 degrees in the right eye. There was 0.5+ cell and 2+ flare in the anterior chamber in the right eye and 1+ cell and flare in the left eye. The anterior vitreous examination had +0.5 cell in both eyes. Dilated fundus exam, despite a poorer view in the right eye, revealed hyperemic and vascular sheathing in both eyes. Workup was normal/negative for various possible vasculitis etiologies, including beta-2 microglobulin in urine, syphilis, rheumatoid factor (RF), anti-neutrophil cytoplasmic antibodies (ANCA) profile, quantiFERON, angiotensin-converting enzyme (ACE), and lysozyme. The chest x-ray was normal.

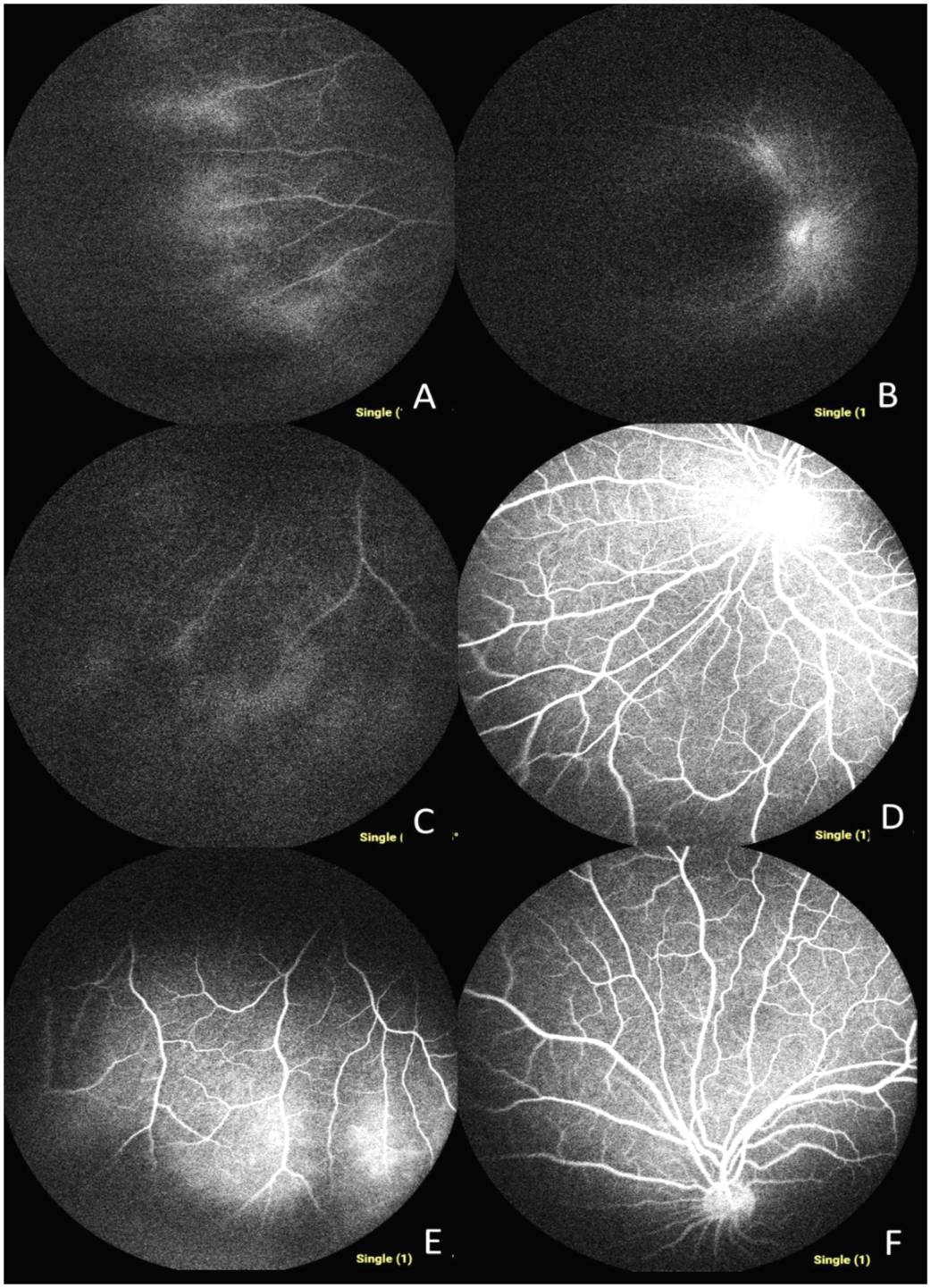

Figure 1. Fundus fluorescein angiography (FA) at presentation, revealing late leakage (6 min) of the optic disc in both eyes and late peripheral vascular leakage, more prominent in the right eye. FA images right eye: (A) temporal, (B) macula, and (C) inferior; left eye: (D) inferonasal, (E) inferior, and (F) superior.

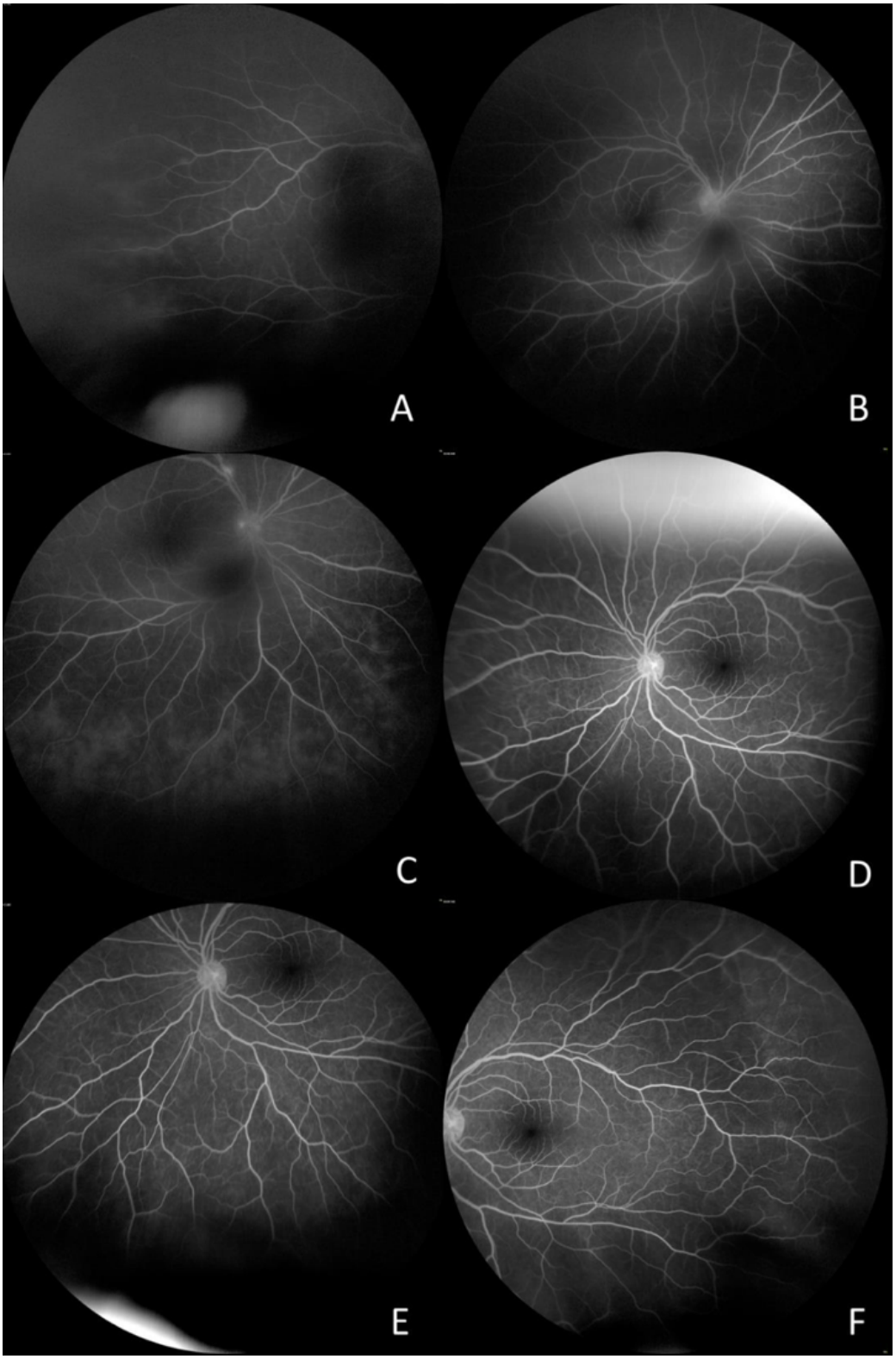

Figure 2. Ten-week follow-up fundus fluorescein angiography (FA) demonstrated improved late vascular leakage (6 min) in the right eye and no leakage in the left eye. FA images right eye: (A) temporal, (B) macula, (C) inferior; left eye: (D) macula, (E) inferior, (F) temporal.

Fundus fluorescein angiography (FA) was performed in both eyes. Late angiographic leakage was present on optic disc in both eyes, with late peripheral vascular leakage (right eye>left eye) (Figure 1). Optical coherence tomography (OCT) was also performed and revealed generalized macular thickening in both eyes with the presence of subretinal fluid (SRF) in the right eye. Central subfield thickness (CST) in the right eye was 378 microns, and the left eye was 332. The patient was started on ADA 40mg every other week and methotrexate (MTX) 20mg per week, oral corticosteroids 1mg/kg/day, and topical corticosteroids following presentation. At one-month follow-up, BCVA improved to 20/40 in the right eye and was stable at 20/20 in the left eye. At 10-week follow-up, exam findings demonstrated stable BCVA at 20/40 in the right eye and 20/20 in the left eye. The anterior chamber examination revealed no active inflammation in both eyes. No obvious vascular sheathing was seen on the exam in either eye. OCT showed resolved SRF in the right eye and improved retinal thickness in both eyes; CST was 308 in the right eye and 283 in the left eye. FA depicted improved leakage in the right eye, and the left eye showed no leakage (Figure 2). Treatment plan includes maintaining ADA 40mg every other week or increasing the dose to weekly, and continuing MTX 20mg per week, difluprednate eye drops every other day in both eyes, and atropine at night in the right eye.

Discussion

Herein we report a rare presentation of posterior segment involvement in a case of JIA-related uveitis. A thorough workup excluded other potential causes of vasculitis and promptly established an effective treatment plan.

Cystoid macular edema is identified as increased thickness of the macula and loss of its normal concave shape, a very frequent finding in eyes with JIA-associated uveitis. In a cross-sectional prospective study of 38 patients with JIA-associated uveitis, maculopathy was noted in 82% of eyes: perifoveolar thickening in 45 eyes (73%), CME in 29 eyes (47%), foveal detachment in 11 eyes (18%), and atrophic changes in six eyes (10%), which was higher than previous reports.[7,8] Our patient had subretinal fluid in the right eye and diffuse (sponge-like) macular thickening in both eyes at presentation, which improved with treatment.

The vasculitis component might have contributed to the refractory nature of uveitis in our patient. Tripathy et al. demonstrated that 70% of patients with JIA-associated uveitis in children less than 16 years old showed widefield FA evidence of posterior segment inflammation, which led to a change in management plans in 8 of 9 patients who had quiet anterior chambers, illustrating the importance of conducting a detailed posterior segment evaluation.[5] Another single case report highlighted a patient with reactivation of JIA-associated uveitis with posterior segment manifestations, specifically retinal vasculitis, following anti-SARS-CoV-2 vaccination.[6]

The reported incidence of posterior manifestations in JIA patients is low, and this may be due in part to the absence of routine FA screening for such, given that retinal vasculitis has not been commonly described in these eyes. While JIA-associated uveitis primarily manifests as chronic anterior uveitis, posterior segment manifestations may still develop. In some eyes with JIA uveitis, visualization and evaluation of the posterior segment may be limited by band keratopathy, small pupil due to posterior synechiae, and cataract formation.[6] In eyes with a view, evaluation of the posterior segment may detect the presence of involvement that may guide treatment decision-making.[4]

Incorporating the use of retinal imaging including FA for patients with JIA-associated uveitis may help identify subclinical vasculitis and other pathology, which would indicate an inadequate response to treatment or the need to change the treatment plan. This will ultimately lead to improved inflammatory control, thus improving visual outcomes.[6]

In the pediatric population, however, there is often associated challenges in obtaining FA, and thus OCT may be used to obtain retinal thickness maps which may serve as a proxy assessment of vasculitis in some eyes. Retinal vasculitis can lead to vascular leakage and exudation, as well as global "sponge-like" changes in the macula, resulting in overall increased retinal thickness with or without true CME. Quantifying retinal thickness allows the physician to gain information more easily.[9,10]

Conclusion

Retinal vasculitis is a rare finding in individuals with JIA-related uveitis; however, this may be under recognized in children without retinal imaging. The presence of retinal vasculitis may have contributed to the refractory inflammation observed in this 16-year-old female and thus identifying it may guide therapeutic decision-making to improve outcomes.

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Statement of Ethics

This case report adheres to patient confidentiality and ethical principles in accordance with the guidelines of the Declaration of Helsinki and relevant local regulations. Consent was obtained from the patient for the publication of this case report.

Conflict of Interest Statement

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Authorship

We attest that all authors contributed significantly to the creation of this manuscript, each having fulfilled the criteria as established by the ICMJE.