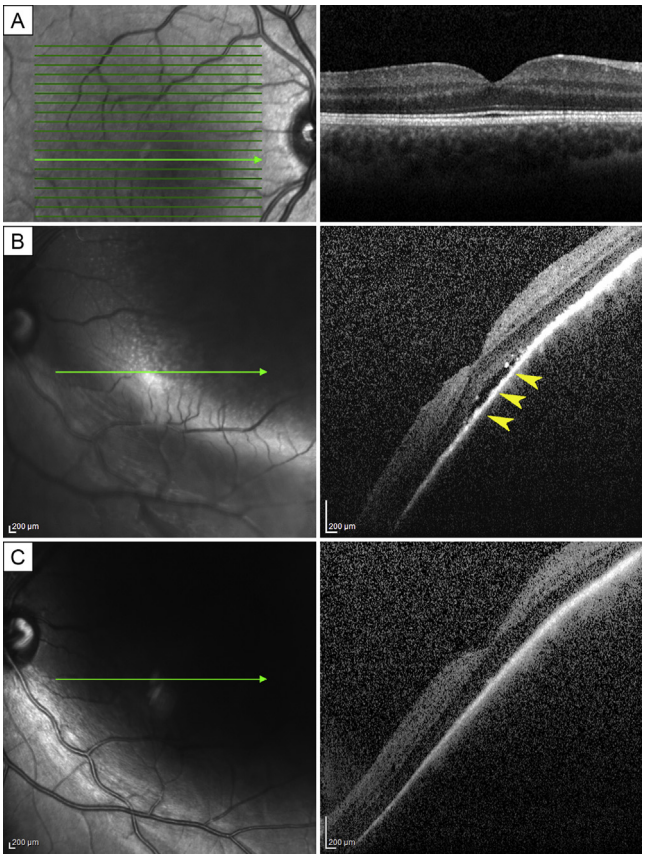

FIG 2. Response to therapy with propranolol. A, Optical coherence tomography (OCT) of the right eye showing normal retinal architecture. B, OCT of the left eye prior to therapy showing a pocket of subfoveal fluid (arrowheads). C, OCT 3 months after starting oral propranolol, with resolution of subretinal fluid.

incidentally on routine clinical examination, the majority of patients in a large series reported decreased vision.[3]

Established treatment modalities for symptomatic lesions include thermal laser photocoagulation and PDT, although antivascular endothelial growth factors have also been employed successfully.[2-5] However, in pediatric patients, these methods require use of general anesthetic.

Oral propranolol is a first-line therapy to treat infantile capillary hemangiomas. As a nonselective beta-2 blocker, it functions to reduce nitric oxide release and proangiogenic molecules, including hypoxia-inducible factor 1 and vascular endothelial growth factor, ultimately resulting in apoptosis of capillary endothelial cells.[1,6] This drug has been used to treat exudative retinal detachments related to circumscribed choroidal hemangiomas in adults with variable success. Sanz-Marco and colleagues[1] reported resolution of subretinal fluid and improvement of visual acuity to 20/20 from 20/100 using the same dose of propranolol. However, a study of 5 adults treated with propranolol for long-standing exudative detachments from choroidal hemangiomas found improvement in, but not resolution of, subretinal fluid volume on a maximum of 30 mg propranolol three times daily.[5] However, caveats of this study are the inclusion of chronic cases and the use of a low and potentially subtherapeutic dosage of propranolol.

Our patient presented at 10 years of age with a visually significant circumscribed choroidal hemangioma, with secondary exudative retinal detachment. A trial of oral propranolol was appropriate, because alternative treatments would have required use of general anesthetic. Using a weight-based dosage, our patient's subretinal fluid resolved, and his visual acuity improved to near baseline. Furthermore, his choroidal hemangioma remained stable for at least 3 years.

In the pediatric population, oral propranolol offers a relatively safe potential therapy for exudative retinal detachments related to circumscribed choroidal hemangiomas. As in our patient, this therapy may improve subretinal fluid accumulation and visual acuity in pediatric patients. A trial of oral propranolol may be considered prior to undertaking alternative therapies, such as laser therapy or intravitreal injections, which require general anesthesia.

References

1. Sanz-Marco E, Gallego R, Diaz-Llopis M. Oral propranolol for circumscribed choroidal hemangioma. Case Rep Ophthalmol 2011;2:84-90.
2. Karimi S, Nourinia R, Mashayekhi A. Circumscribed choroidal hemangioma. J Ophthalmic Vis Res 2015;10:320-28.
3. Shields CL, Honavar SG, Shields JA, Cater J, Demirci H. Circumscribed choroidal hemangioma: clinical manifestations and factors predictive of visual outcome in 200 consecutive cases. Ophthalmology 2001;108:2237-48.
4. Kwon HJ, Kim M, Lee CS, Lee SC. Treatment of serous macular detachment associated with circumscribed choroidal hemangioma. Am J Ophthalmol 2012;154:137-145.e1.
5. Tanabe H, Sahashi K, Kitano T, Tomita Y, Saito AM, Hirose H. Effects of oral propranolol on circumscribed choroidal hemangioma: a pilot study. JAMA Ophthalmol 2013;131:1617-22.
6. Storch CH, Hoeger PH. Propranolol for infantile haemangiomas: insights into the molecular mechanisms of action. Br J Dermatol 2010;163:269-74.

Juvenile idiopathic arthritis–related uveitis mimicking endophthalmitis

Vinod Kumar, MD,[a,b,c] Abhidnya Surve, MD,[a,b,c] Shorya Azad, MS,[a,b,c] Pradeep Venkatesh, MD,[a,b,c]

Author affiliations: [a]Vitreo-retina, Trauma and Uvea Services; [b]Dr. Rajendra Prasad Center for Ophthalmic Sciences; [c]All India Institute of Medical Sciences, Ansari Nagar, New Delhi, India [d]Pediatric Rheumatology

Submitted July 23, 2018.
Revision accepted March 21, 2019.
Published online April 5, 2019.

Correspondence: Abhidnya Surve, MD, Dr. RPC for Ophthalmic Sciences, AIIMS Ophthalmology, Ansari Nagar, New Delhi, India (email: abhidnyasurve@gmail.com).

J AAPOS 2019;23:238-241.

1091-8531/$36.00
https://doi.org/10.1016/j.jaapos.2019.03.001

Narendra Bagri, MD,[c,d] Priyanka Prasad, MBBS,[b,c] and Yogita Gupta, MD[a,b,c]

Juvenile idiopathic arthritis (JIA) is a group of disorders occurring in children with arthritis of more than 6 weeks' duration. JIA may have varied systemic and ocular presentations, which can pose a diagnostic challenge. Chronic uveitis with insidious onset is the most common type of ocular presentation. This report highlights a case of enthesitis-related arthritis, a type of JIA, in a 12-year-old boy who presented with severe intermediate uveitis that mimicked endophthalmitis.

Juvenile idiopathic arthritis (JIA) is a heterogeneous group of disorders with varied systemic and ocular presentations. Uveitis in JIA is common, with an overall prevalence of 4%-24.4%.[1-3] A population-based study demonstrated a high prevalence of anterior uveitis (83%), with panuveitis (7%), posterior uveitis (1%) and intermediate uveitis (9%) exhibiting low prevalence.[3] Chorioretinitis has also been reported.[4] We report a case of JIA presenting as sudden-onset severe joint involvement with severe intermediate uveitis.

Case Report

A 12-year-old boy presented at All India Institute of Medical Sciences, New Delhi, with pain, redness, and diminution of vision in his left eye of 10 days' duration. There was a history of pain in the right hip and fever for 20 days. The patient's gait was unstable, and he had tenderness in the hip joint. On ophthalmological examination, best-corrected visual acuity was 6/6 in the right eye and 6/18 in the left eye. There was mild discharge and ciliary congestion in the left eye, the anterior chamber of which showed few fine keratoprecipitates, 3+ cells, and flare; posterior segment examination revealed retrolental cells, media haze, and vitreous exudates prominently in the inferior area extending to the disk. The superior retina was normal. Right eye examination findings were within normal limits.

The initial blood examination revealed increased leukocyte count (14000/μL; normal range, 4000–11000/μL), an increased erythrocyte sedimentation rate (ESR; 76 mm/hr; normal range, 0–22 mm/hr), and C-reactive protein (CRP) (65 mg/L; normal, <10 mg/L). A provisional diagnosis of endogenous endophthalmitis with septic arthritis as primary foci was made. Because the patient was allergic to ceftriaxone, intravenous piperacillin-tazobactam 100 mg/kg/dose three times daily and vancomycin 40 mg/kg/day in two divided-doses was administered. Topical antibiotics (moxifloxacin 6 times daily), cycloplegic (homatropine 2%, 4 times daily), and steroid (prednisolone acetate 6 times daily) were also given. Vitreous tap was taken, and intravitreal vancomycin (1 mg/0.01 ml) and piperacillin-tazobactam (225 μ/0.01 ml) was administered. The vitreous fluid bacterial culture was sterile.

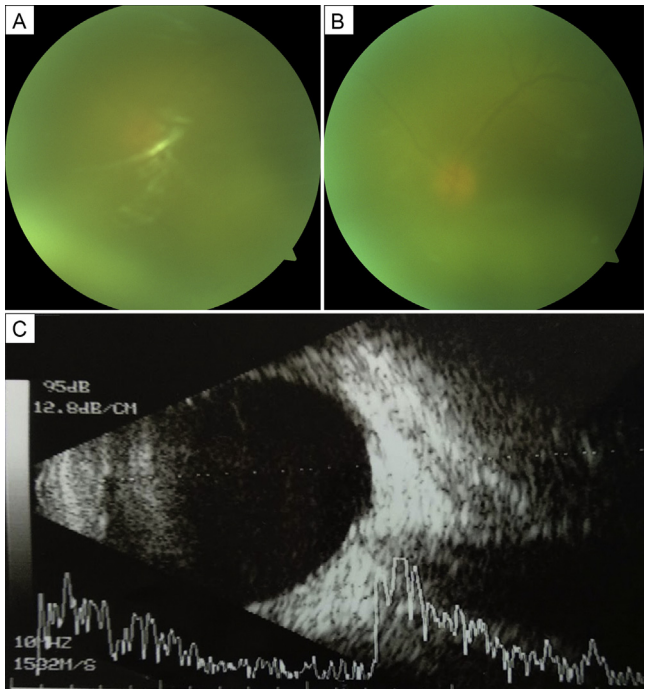

FIG 1. A, Fundus imaging of the left eye showing vitreous exudates, with disk hazily seen. B, On starting steroids, improvement was seen on fundus imaging within a week. C, B-scan ultrasonography prior to treatment with steroids showing mild-to-moderate amplitude spikes in vitreous cavity suggestive of vitreous exudates, seen after 3 days of systemic antibiotics.

Deterioration in best-corrected visual acuity (2/60) and increase in the vitreous exudates completely obliterating the media in the left eye was noted over the next 3 days (Figure 1A). The ultrasonography B-scan showed mild-moderate amplitude spikes in the vitreous cavity (Figure 1C). This was associated with increased pain in the hip joint and involvement of the right elbow joint. A history of right foot and ankle joint involvement for 2 months was elicited retrospectively. On musculoskeletal examination, the hip and elbow joints were tender and showed mild restriction of movement. X-ray revealed osteopenia and mild effusion at the mid-foot and elbow joint. However, no signs of periosteal reaction, erosion, or calcification were noted. The blood and urine bacterial culture was sterile. The Mantoux test was negative, and chest X-ray was normal, ruling out tuberculosis. Anti–cyclic citrullinated peptides titer, rheumatoid factor, and antinuclear antibodies (ANA) were negative, but human leukocyte antigen (HLA)-B27 was positive.

The clinical features, raised inflammatory markers, and HLA-B27 association suggested the diagnosis of enthesitis-related arthritis (ERA) with severe intermediate uveitis. The patient was started on oral prednisolone (1 mg/kg body weight), pantoprazole (20 mg), and weekly 15 mg methotrexate and folinic acid. At 1-week follow-up, inflammation and joint swelling had decreased, with

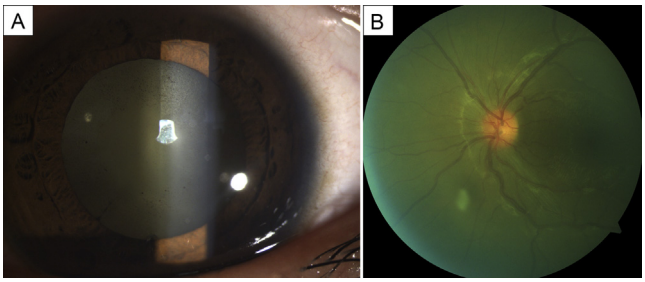

FIG 2. A, Anterior segment imaging showing quiet eye with resolution of anterior chamber inflammation, pigments on anterior capsule, and mild posterior subcapsular cataract. B, Fundus imaging showing resolution of the media haze at 1 month of treatment with steroids and methotrexate.

improved mobility of joints. Visual acuity improved to 6/9 at 1 month. The anterior segment inflammation had resolved with decrease in the media haze (Figures 1B and 2).

Discussion

In children, JIA is the most common systemic association with uveitis.[1] The diagnosis and classification of JIA are based on detailed history, complete physical examination, and required laboratory investigations. The International League of Associations for Rheumatology (ILAR) has classified JIA into seven clinical subtypes: rheumatoid factor (RF)–negative polyarthritis, RF-positive polyarthritis, oligoarthritis, systemic arthritis, psoriatic arthritis, ERA, and undifferentiated arthritis.[5]

The risk factors for JIA-related uveitis include younger age of onset, female sex, presence of circulating ANA, and HLA associations. The JIA-related uveitis is usually nongranulomatous, anterior in origin, and insidious in onset, with a chronic course.[6,7] Arthritis usually precedes the onset of uveitis, whereas JIA presenting as uveitis is rarely seen (3%-7%).[1] In our case, a 12-year-old boy had acute involvement of the joints and ocular involvement, with exudates in the vitreous. This unilateral acute presentation with raised leukocyte count and ESR suggested the diagnosis of endogenous endophthalmitis, but worsening was observed on antibiotic treatment.

ERA is a form of JIA having late childhood onset; it is the only category of JIA that affects males more often than females. It involves inflammation at the insertion site of tendon, ligament, or fascia, with adjacent arthritis. Most commonly involved areas are plantar fascia, tarsal area, Achilles tendon, and knees. Most common joints involved in arthritis include hips and other lower extremity joints. Many of these patients are HLA-B27 positive, but sacroiliac and spinal joint involvement is seen in 30%-40% of cases. Recurrent acute iridocyclitis, with a relatively good prognosis is seen in 7%-15% cases with JIA-ERA.[3,5,8] In our case, although the hip joint showed severe involvement, the ankle, mid-foot, and knee joint showed mild symptoms, which were unnoticed by the parents earlier. No sacroiliac or spinal involvement was seen, but HLA-B27 was positive. The presentation of a boy with acute involvement of joints along with severe uveitis, absence of ANA, and presence of HLA-B27 suggested the diagnosis of JIA-ERA.[5]

Appropriate classification of uveitis plays an important role in the evaluation, diagnosis, and management of patients with uveitis. Intermediate uveitis includes pars-planitis, hyalitis, posterior cyclitis, and vitritis, whereas posterior uveitis includes presence of retina or choroid involvement, including choroidits, retinochoroiditis, chorioretinitis, retinitis, and neuroretinitis.[9,10] Retinal changes in intermediate uveitis include tortuosity in arterioles and venules, sheathing of peripheral veins, neovascularizations, and retinal detachments.[11] The term *intermediate uveitis* is appropriate for that subset of uveitis where the vitreous is the major site of the inflammation, regardless of whether peripheral vascular sheathing and macular edema is present.[10] In our case, however, there were no signs of retinal or choroidal involvement. Only the presence of vitritis precluded its classification as posterior uveitis or panuveitis. Thus, the diagnosis of intermediate uveitis was made. That the anterior chamber had cells with few fine keratoprecipitates suggested anterior spillover of cells. The swelling of joints decreased, ocular inflammation resolved, and visual acuity showed drastic improvement with treatment. Worsening with antibiotics and dramatic response to steroids confirmed the inflammatory nature of the disease.

Uveitis has been associated with JIA mainly in the form of anterior uveitis. However, JIA may also be rarely associated with intermediate uveitis, posterior uveitis, and panuveitis.[2,3] Although ERA is known to present with acute anterior uveitis, the severe intermediate uveitis found in our case is rare. This case report highlights the need for careful history taking and meticulous clinical examination, because symptoms that may be initially ignored or unnoticed may be crucial to accurate diagnosis. A broad-spectrum and multidisciplinary approach, with involvement of a rheumatologist, helps in early recognition and management of the disease.

References

1. Heiligenhaus A, Heinz C, Edelsten C, Kotaniemi K, Minden K. Review for disease of the year: epidemiology of juvenile idiopathic arthritis and its associated uveitis: the probable risk factors. Ocul Immunol Inflamm 2013;21:180-91.
2. Heiligenhaus A, Niewerth M, Mingels A, et al. Epidemiology of uveitis in juvenile idiopathic arthritis from a national paediatric rheumatologic and ophthalmologic database [in German]. Klin Monbl Augenheilkd 2005;222:993-1001.
3. Heiligenhaus A, Niewerth M, Ganser G, Heinz C, Minden K. German Uveitis in Childhood Study Group. Prevalence and complications of uveitis in juvenile idiopathic arthritis in a population-based nation-wide study in Germany: suggested modification of the current screening guidelines. Rheumatology (Oxford) 2007;46:1015-19.

4. Thacker NM, Demer JL. Chorioretinitis as a complication of pauciarticular juvenile rheumatoid arthritis. J Pediatr Ophthalmol Strabismus 2005;42:183-4.
5. Petty RE, Southwood TR, Manners P, et al. International League of Associations for Rheumatology. International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. J Rheumatol 2004;31:390-92.
6. Kanski JJ. Juvenile arthritis and uveitis. Surv Ophthalmol 1990;34:253-67.
7. Vitale AT, Graham E, de Boer JH. Juvenile idiopathic arthritis-associated uveitis: clinical features and complications, risk factors for severe course, and visual outcome. Ocul Immunol Inflamm 2013;21:478-85.
8. Weiss PF. Evaluation and treatment of enthesitis-related arthritis. Curr Med Lit Rheumatol 2013;32:33-41.
9. Bloch-Michel E, Nussenblatt RB. International Uveitis Study Group recommendations for the evaluation of intraocular inflammatory disease. Am J Ophthalmol 1987;103:234-5.
10. Jabs DA, Nussenblatt RB, Rosenbaum JT. Standardization of Uveitis Nomenclature (SUN) Working Group. Standardization of uveitis nomenclature for reporting clinical data: results of the First International Workshop. Am J Ophthalmol 2005;140:509-16.
11. Nusenblatt RB, Palestine AG. Uveitis: fundamentals and clinical practice. Chicago: Yearbook Medical; 1989:279-88.

Heterochromia following intravitreal chemotherapy in two cases

David A. Camp, MD, Sara E. Lally, MD, and Carol L. Shields, MD

Intravitreal chemotherapy is recognized as an effective treatment for retinoblastoma with vitreous (and occasionally subretinal) seeding refractory to intravenous or intra-arterial chemotherapy. However, this treatment carries with it the risk of toxicity to both the posterior and anterior segments of the eye, including retinal pigment epithelial mottling, ischemic/hemorrhagic retinopathy, posterior synechia, cataract, scleral necrosis, and focal iris depigmentation. We report 2 cases of iris heterochromia secondary to profound iris stromal depigmentation following intravitreal melphalan and topotecan injections.

Author affiliations: Ocular Oncology Service, Wills Eye Hospital, Thomas Jefferson University, Philadelphia, Pennsylvania

Support provided in part by the Eye Tumor Research Foundation, Philadelphia, PA (CLS). The funders had no role in the design and conduct of the study, in the collection, analysis and interpretation of the data, and in the preparation, review or approval of the manuscript.

Submitted January 3, 2019.
Revision accepted March 26, 2019.
Published online April 27, 2019.

Correspondence: Carol L. Shields, MD, Ocular Oncology Service, 840 Walnut Street, Suite 1440, Philadelphia, PA 19107 (email: carolshields@gmail.com).

J AAPOS 2019;23:241-243.

1091-8531/$36.00
https://doi.org/10.1016/j.jaapos.2019.03.002

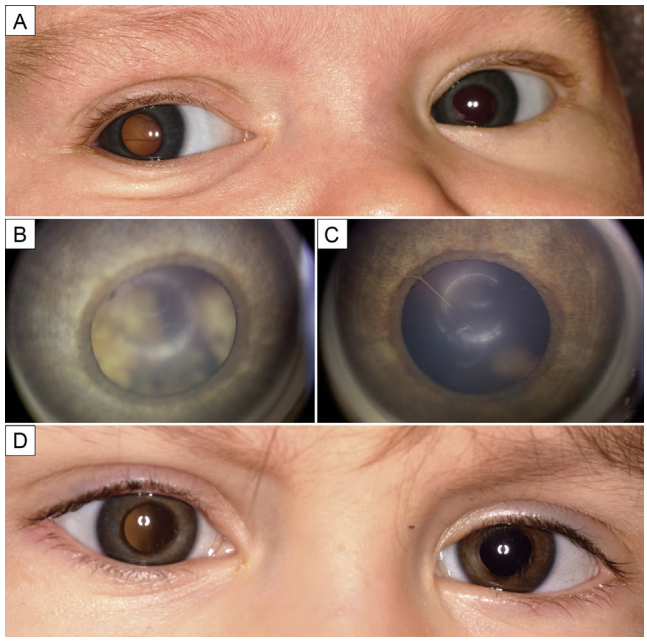

FIG 1. A 2-month-old white girl referred for evaluation of bilateral retinoblastoma. Prior to treatment (A), symmetric irides were noted; over time pigmentation increased. One month following intravitreal melphalan and topotecan in the right eye, diffuse iris stromal depigmentation led to heterochromia with lighter iris in the right eye (B), compared to the darker iris in the left eye (C). Following the third session of intravitreal injections (D), notable heterochromia was observed.

Case 1

A 2-month-old white girl with symmetric blue irides was referred to Wills Eye Hospital for evaluation of bilateral retinoblastoma (Figure 1A). On examination, the right eye showed a large, partially calcified retinoblastoma with total retinal detachment (group E); the left eye, 4 small retinoblastomas in the macula (group B). Despite intravenous chemotherapy (vincristine, etoposide, carboplatin) with consolidation and additional intra-arterial chemotherapy (melphalan, topotecan), the right eye demonstrated localized recurrent subretinal seeding. The seeding was managed with 6 sessions of trans pars plana precision intravitreal injections[1] of melphalan (20–30 mcg/0.1–0.15 cc) and topotecan (20–30 mcg/0.1–0.15 cc), using a 31-gauge needle directly on the recurrent seed with ultimate tumor control. At this time, the patient demonstrated symmetric hazel irides. One month after the first injection, slight heterochromia was observed (Figures 1B, 1C), leaving the affected right iris blue and unaffected left iris hazel. One month after the third injection, the heterochromia persisted (Figure 1D).

Case 2

A 10-month-old white boy with symmetric patchy light brown irides was referred for evaluation of bilateral