Retrospective Study Evaluating Treatment Decisions and Outcomes of Childhood Uveitis Not Associated with Juvenile Idiopathic Arthritis

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Objective To evaluate treatment, ocular complications and outcomes of children with pediatric uveitis not associated with juvenile idiopathic arthritis.

Study design This was a retrospective chart review of pediatric uveitis in children under 16 years of age, recruited from the pediatric rheumatology department at Bicêtre Hospital from 2005 to 2015. Patients with juvenile idiopathic arthritis-associated and infectious uveitis were excluded. We used the Standardization of Uveitis Nomenclature Working Group to classify uveitis, disease activity, and treatment end points.

Results We enrolled 56 patients and 102 affected eyes. The mean age at diagnosis was 10 ± 3.5 years (range 3-15), and the mean follow-up 4.2 ± 3.3 years (1-15). The main diagnoses were idiopathic (55%), Behçet disease (15%), and sarcoidosis (5%). The main localization was panuveitis in 44 of 102 eyes (43%). Corticosteroid sparing treatment was needed in 62 of 102 eyes (60%). Second-line therapies included methotrexate and azathioprine, and the third-line therapy was a biologic agent, mainly infliximab, in 33 of 102 eyes (32%). Infliximab achieved uveitis inactivity in 14 of 18 eyes (80%), in all etiologies. Severe complications were present in 68 of 102 eyes (67%). The most common were synechiae 33% of eyes, cataract (20%), and macular edema (25%). Of these, 37% were present at diagnosis. Remission was achieved in 22 of 102 eyes (21%).

Conclusions Conventional therapies were insufficient to treat many of the cases of posterior or panuveitis. This study underlines the need for earlier and more aggressive treatment and antitumor necrosis factor-α therapy was rapidly efficient in most cases of refractory uveitis. *(J Pediatr 2017;186:131-7).*

Pediatric uveitis is a rare but severe disorder that accounts for 2.1%-13.8% of all cases of uveitis.[1] Ocular complications are frequent, such as retinopathy, cataract, and glaucoma and causes 20% of cases of blindness.[2,3] Pediatric uveitis must be distinguished from adult uveitis with regard to its etiology and management.[4] The overall incidence and prevalence of pediatric uveitis are estimated to be 6 and 30 per 100 000 children, respectively.[1,5,6] The clinical presentation can vary and eye redness (25%), a painful eye (7%), and vision loss (23%) are the most commonly reported. However, the disease is usually insidious and remains asymptomatic.[7] The main causes are idiopathic (30%-50%), juvenile idiopathic arthritis (JIA) (20%-40%), and pars planitis (15%-17%).[7-9] Chronic silent anterior uveitis, associated with antinuclear antibody positive oligoarticular JIA, has been extensively described and requires accurate monitoring and early treatment.[10] Although it is rare, non-JIA-associated pediatric uveitis represents a challenge, but lack of knowledge and the absence of appropriate validated diagnosis tools often lead to diagnosis delays and poor visual outcomes.[2-4] Corticosteroids (CS) and immunomodulatory drugs are the most common treatment for pediatric uveitis.[11,12] Topical or systemic CS had been traditionally indicated for acute pediatric uveitis and is first-line therapy, regardless of the etiology.[11,12] Methotrexate (MTX) and azathioprine (AZA) are second-line therapies for up to 78% of CS-refractory uveitis.[7,11-15] Mycophenolate mofetil can also be administered as a CS-sparing agent or as an alternative treatment to MTX.[16-18] Many cases are chronic. It is rare for treatment to lead to remission or prevent complications and the sequelae may be devastating.[2,3,7,19] In contrast to the severity of pediatric uveitis, labeled treatment options are limited and are not evidence based. The extremely poor visual outcome and side effects of CS are changing the traditional approach toward the early introduction of biological agents.

Most pediatric uveitis studies have reported the experience of biology in JIA but have usually been limited to trials of small groups of patients.[20-22] This study

AZA	Azathioprine
CS	Corticosteroids
DMARDs	Disease-modifying antirheumatic drugs
JIA	Juvenile idiopathic arthritis
MTX	Methotrexate
SUN	Standardization of Uveitis Nomenclature
TNF	Tumor necrosis factor

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The authors declare no conflicts of interest.

http://dx.doi.org10.1016/j.jpeds.2017.03.052

evaluated the treatment and visual outcomes of non-JIA uveitis in a large cohort of patients followed in a reference center for pediatric rheumatology and uveitis.

Methods

We performed a retrospective chart review of patients under the age of 16 years, with a diagnosis of non-JIA uveitis. Patients were seen between 2000 and 2015 at our tertiary center for pediatric rheumatology in Bicêtre Hospital and were followed in one of the following 3 departments of ophthalmology: Pitié Salpêtrière Hospital, Bicêtre Hospital, and Rothschild Ophthalmologic Foundation. The diagnosis of uveitis was performed according to the international Standardization of Uveitis Nomenclature (SUN) Working Group.[23] Patients with JIA-associated uveitis and patients with incomplete data were excluded from the analyses (**Figure 1**). Patient charts were reviewed by a pediatric rheumatologist and an ophthalmologist to minimize the risk of information bias. Ethics committee approval was not required for this noninterventional study, according to French regulations.

The demographic data that were collected included the sex of the patient, age at disease onset, ethnic origin, and personal and family medical history. The clinical characteristics collected were the ophthalmologic symptoms, including vision loss, red-eye, painful eye and myodesopsia, and extra-ophthalmologic symptoms, meaning nonophtalmologic symptoms including oral and/or genital ulcers, cutaneous signs, headache, arthralgia/arthritis, and fever.

Clinical descriptions of uveitis were recorded according to the SUN Working Group[23] and included the anatomic localization (anterior, intermediate, posterior, or panuveitis) and the laterality of intraocular inflammation, defined by anterior chamber cells, vitreous haze, choroiditis, and retinitis. The best corrected visual acuity and the presence of granuloma (ie, mutton-fat keratic precipitates, Koeppe, or busacca nodules) were also noted.

We collected treatment options including topical, oral or intravenous CS, immunomodulatory agents, and biological agents. Complications such as band keratopathy, epiretinal membrane, posterior synechiae, cataract, vitreous hemorrhage, cystoid macular edema, macular ischemia, ocular hypertension (defined as intraocular pressure >21 mm Hg), glaucoma (defined as ocular hypertension and optic nerve damage),[7] hypotony (defined as intraocular pressure ≤5 mm Hg), retinal detachment and vision loss (best corrected visual acuity <20/40), were analyzed. Ophthalmologic characteristics were collected at the time of diagnosis and at any change of treatment. Etiologies were recorded if available. Note, pars planitis and

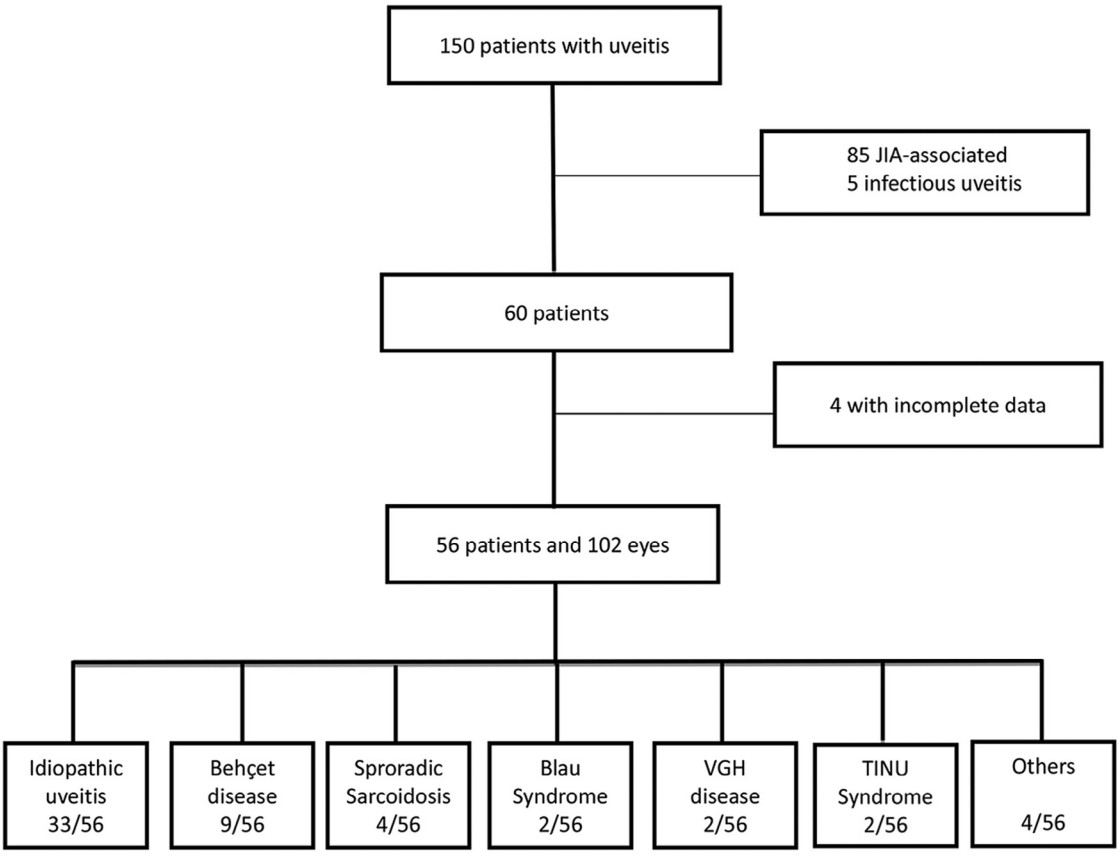

Figure 1. Patient flowchart. *Others*, uveitis, with neurologic disease; *TINU*, tubulointerstitial nephritis; *VGH*, Vogt-Koyanagi-Harada.