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Juvenile idiopathic arthritis-associated uveitis

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A B S T R A C T

Juvenile idiopathic arthritis (JIA) is the commonest rheumatic disease in children and JIA-associated uveitis its most frequent extra-articular manifestation. The uveitis is potentially sight-threatening and thus carries a considerable risk of morbidity with associated reduction in quality of life. The commonest form of uveitis seen in association with JIA is chronic anterior uveitis, which is almost always asymptomatic in the initial stages. Therefore, screening for JIA-associated uveitis in at-risk patients is essential. The aim of early detection and treatment is to minimise intraocular inflammation and to avoid complications that lead to visual loss, which can result from both disease activity and medications. The sight-threatening complications of JIA-associated uveitis include cataracts, glaucoma, band keratopathy, and macular oedema. There is increasing evidence for the early introduction of systemic immunosuppressive therapies to reduce topical and systemic use of glucocorticoids. A recently published randomised controlled trial of adalimumab in JIA-associated uveitis now provides convincing evidence for the use of this biologic in patients who fail to respond adequately to methotrexate. Tocilizumab and abatacept are being investigated as alternatives in children inadequately treated with anti–tumour necrosis factor drugs.

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Introduction

Uveitis is a condition characterised by inflammation of the uveal components of the eye, namely the iris, choroid and retina [1,2]. Classification has been defined in terms of the anatomy and time course of disease according to the Standardisation of Uveitis Nomenclature (SUN) International Working Group [3,4]. Anatomically, it can be described as anterior, intermediate, posterior or panuveitis (Fig. 1). Uveitis onset may be sudden or insidious and its duration limited ($\leq$3 months) or persistent (>3 months) [3]. The temporal pattern is described as acute (sudden onset and limited duration), recurrent (repeated episodes separated by periods of inactivity without treatment $\geq$ 3 months in duration) or chronic (persistent uveitis with relapse in <3 months after discontinuing treatment). Uveitis can also be classified by aetiology into infectious and non-infectious.

In children with rheumatologic disease, uveitis is seen associated with juvenile idiopathic arthritis (JIA), juvenile sarcoidosis/Blau syndrome and Behçet's disease [6]. The commonest form of uveitis is the chronic anterior type associated with JIA, and this will be the main focus of this review. This form of uveitis, which is usually asymptomatic, is most frequently associated with oligoarticular and rheumatoid factor (RF)–negative polyarticular categories of JIA. Acute anterior uveitis, which often presents with a painful, red eye, can also occur in JIA and is usually associated with enthesitis-related arthritis (ERA) and HLA–B27 positivity. If inadequately treated, JIA-associated uveitis (JIA-U) can lead to ocular complications including glaucoma, cataracts, band keratopathy and persistent cystoid macular oedema and can ultimately result in visual impairment and blindness [7]. Management of JIA-U involves the use of both topical and systemic agents, with clinical trials of biologic agents recently completed or underway [8,9].

Epidemiology

Children represent approximately 5–10% of all patients with uveitis [10]. The overall incidence of uveitis in the childhood population, reported in a study from Finland, was 4.3 per 100,000/year and prevalence of 27.9 per 100,000 [11]. Among all causes of paediatric uveitis, when stratified by aetiology, the prevalence of JIA-U ranged from 15% to 67% across centres in Europe, North America and Israel [10,12–15]. In a cohort of 642 children with uveitis in Tamil Nadu, India, infectious uveitis was most common representing 54.9%, followed by idiopathic and non-infectious uveitis at 32.5% and 12.6%, respectively [16]. It should be noted that uveitis can precede a diagnosis of arthritis in 3%–7% of children with JIA [17], and thus children presenting with uveitis need careful assessment for underlying systemic or infectious disease.

How common is uveitis associated with JIA?

In patients already known to have JIA, estimates of prevalence of uveitis range from 11.6% [18] to 30% [19], although overall it appears to be decreasing over the past decade. A longitudinal cohort study conducted in Nordic countries prospectively followed 435 children diagnosed with JIA in 1997–2000 for a median of 96 months [20]. Uveitis developed in 89 (20.5%) children. No patients with systemic or RF-positive JIA developed uveitis. The frequencies of chronic uveitis in other categories were as follows: 35.7% in juvenile psoriatic arthritis, 22.5% in RF-negative polyarticular, 20.5% in extended oligoarticular, 19.1% in persistent oligoarticular, 19.0% in undifferentiated and 8.3% in ERA. Regarding disease pattern, the majority (80 children) had chronic uveitis while the remaining nine patients had acute uveitis, all but one of whom had ERA. In another study where 13.1% of 1081 patients with JIA developed uveitis, chronic anterior uveitis was also predominant (68.3%) [21]. However, acute anterior disease (16.2%), recurrent anterior disease (12%), and panuveitis (3.5%) were also encountered.

What are the risk factors for the development of uveitis in JIA?

Several risk factors for JIA-U have been identified. These include age of onset, gender, JIA category, antinuclear antibody (ANA) and HLA–B27 positivity [7,17,19,22,23]. Young age, female gender,

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