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The Importance of an Ophthalmologic Examination in Patients With Juvenile Idiopathic Arthritis☆

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ABSTRACT

Uveitis occurs within the first year of arthritis onset in 73% of patients with juvenile idiopathic arthritis (JIA) considered at risk. The intraocular inflammation is characterized by an insidious onset and a silent and chronic clinical course capable of producing significant visual loss due to complications such as: cataract formation, secondary glaucoma, maculopathy and optic neuropathy. The absence of initial signs and symptoms, along with a deficient ophthalmic monitoring produces a delay in diagnosis with serious consequences. It has been estimated that 47% of JIA patients at risk for developing uveitis are legally blind (20/200 or worse) at least in one eye at the time of their first visit to the ophthalmologist. To reduce ocular complications and improve their visual outcome, it is necessary that rheumatologists refer all patients recently diagnosed (within the first month) with JIA for an ophthalmic evaluation, and maintain periodical follow-up visits based on classification and risk category of the disease.

Importancia de la evaluación oftalmológica en pacientes con artritis idiopática juvenil

Palabras clave:
Artritis idiopática juvenil
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RESUMEN

La uveítis ocurre dentro del primer año del inicio de la artritis en hasta el 73% de los pacientes con artritis idiopática juvenil (AIJ) considerados en riesgo. La inflamación intraocular se caracteriza por un inicio insidioso y un curso clínico silencioso y crónico, capaz de producir pérdida visual significativa debido a complicaciones como: formación de cataratas, glaucoma, maculopatía y neuropatía óptica. La ausencia de signos y síntomas oculares iniciales, aunado a una deficiente monitarización oftalmológica, producen un retraso diagnóstico de graves consecuencias. Se ha reportado ceguera legal (20/200 o peor) en al menos un ojo en hasta el 47% de aquellos pacientes en riesgo para desarrollar uveítis durante la primera visita oftalmológica. Para reducir las complicaciones oculares y mejorar el pronóstico visual, es necesario referir inmediatamente a pacientes recién diagnosticados con AIJ por el reumatólogo a evaluación oftalmológica y mantener visitas periódicas de seguimiento basadas en la clasificación y la categoría de riesgo de la enfermedad.

Introduction and Epidemiology

Juvenile idiopathic arthritis (JIA) is a chronic, debilitating inflammatory disease, which primarily affects the joints, and in varying degrees presents extra-articular involvement, affecting mainly children.[1]

Reports on the incidence and prevalence of JIA are difficult to compare between populations due to the heterogeneity of the disease, the different classification criteria employed, the nature of the ethnic groups studied and the diagnostic certainty in each case.[2] Consequently, the results shown in various studies vary significantly, with an incidence ranging from 0.8 to 22.6/100 000 persons <16 years per year and a prevalence ranging from 7 to 400/100 000 children and adolescents.[3]

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Table 1
Classification of JIA According to the International League of Associations for Rheumatology (ILAR).

JIA
Systemic onset JIA
Oligoarticular JIA
Persistent
Extended
Polyarticular JIA RF (−)
Polyarticular JIA RF (+)
Psoriatic arthritis
Enthesitis related arthritis
Undifferentiated
Does not fall into any category
Enters into more than one category

JIA, juvenile idiopathic arthritis; RF, rheumatoid factor.
Taken from Petty et al.[1]

In Mexico, there are no current figures for the prevalence of JIA; however, it is inferred that it could be at least 2 cases per 100 000 population and with an estimated annual incidence of 0.7–0.8 new cases per 100 000 population.[3]

JIA is a heterogeneous group of chronic arthropathies with an onset before age 16 and that must have a duration of at least 6 weeks. According to the classification of the International League of Associations for Rheumatology (ILAR), there are 7 subtypes of the disease (Table 1).[1] These subtypes differ in clinical manifestations, autoimmune features, genetic and prognostic determinants.[2] These clinical variants, along with some demographic characteristics, have been considered as risk factors for the development of uveitis,[4–6] the most frequent extraarticular manifestation of JIA 7. In patients with oligoarticular forms, and particularly in the presence of antinuclear antibodies (ANA), the occurrence of uveitis is approximately 20%, decreasing to 10.5% in patients with polyarticular disease with negative rheumatoid factor, being almost nonexistent in patients with systemic variants and with a positive rheumatoid factor.[8,9] In Mexico, prevalence of uveitis associated with JIA has been reported as 16.3%, being more frequent in girls (87.5%) at an early age (5.7 years) with oligoarticular forms (75.0%) and with the presence of ANA in 80% of cases.[10] These findings are consistent with the risk factors most associated with the occurrence of uveitis in JIA reported in the literature, namely: female gender, younger age of onset of arthritis, oligoarticular forms and the presence of ANA.[4,9] Finally, a meta-analysis of JIA studies published between 1980 and 2004 concluded that early age at onset, positive ANA and oligoarticular and polyarticular forms are the highest risk factors for developing uveitis, while ANA-negative patients with disease onset at 4 years of age are at a moderate risk category, regardless of the presentation of JIA.[11]

Although the highest prevalence of JIA has been reported in Scandinavian countries, followed by countries in northern Europe and North America it is unknown whether uveitis associated with JIA dominates in a particular ethnic group.[2] Moreover, to understand the role of genetic traits in the occurrence of uveitis associated with JIA, a large number of pairs of siblings with the disease has been analyzed[12] without sufficient evidence for a specific genetic component linked to the pathogenesis of uveitis associated with JIA.[13,14] However, the findings do not rule out a modest association with a specific genetic marker (relative risk genotype) because its frequency is relatively high.[15]

Regarding the association with alleles of major histocompatibility complex antigens (HLA), HLA profiles have been studied in patients with oligoarticular JIA associated to early uveitis. Some series found a significant increase in the frequency of HLA-DRB1*1104 (a fragment of HLA-DR5) in patients with chronic uveitis, compared with those without intraocular inflammation.[16,17] However, other studies have failed to demonstrate this fact.[18] Moreover, in all series examined, the frequency of HLA-DRB1*01[18] was reduced.

Intraocular Inflammation Associated With Juvenile Idiopathic Arthritis

Uveitis is one of the leading causes of preventable blindness in the world. In the pediatric population, the annual incidence of uveitis has been estimated between 4.3 and 6.9/100 000.[19–21] When analyzed in the context of the various causes of childhood uveitis, uveitis associated with JIA represents up to 47% of cases in the United States and Europe,[19,22] and from 1% to 11% of anterior uveitis in highly specialized centers worldwide.[23,24] It has been reported that up to 10% of cases, anterior uveitis is the first manifestation of JIA.[11] An important point to consider is that anterior uveitis is often detected during the first ophthalmology visit, early in the clinical course of JIA.[25] In a multicenter study conducted in 2007, in which 3271 patients with JIA from 35 centers were analyzed, it was found that 406 patients (12%) had uveitis, of which 115 (28%) patients with a documented clinical course of uveitis were analyzed. The vast majority (79%) had an oligoarticular form of arthritis, started early and were predominantly women with positive ANA. This study revealed that up to 73% of patients with JIA had uveitis before or within the first 12 months of the onset of arthritis, and 77% and 90% occurred within the first 2 and 4 years after its onset,[26] respectively. Moreover, at the time of presenting JIA, complications had been reported in 67% of uveitis affected eyes.[27]

The intraocular inflammatory process in patients with JIA is characterized by an insidious anterior uveitis, as well as a chronic silent clinical course which leads to a significant visual loss due to many serious complications, including formation of calcium band keratopathy, posterior and anterior iris synechia, cataract, secondary glaucoma, vitreitis, maculopathy and chronic optic neuropathy and ocular cyclitic hypotony by forming a membrane and complete loss of function with bulbar phthisis.[28–30]

Initially, the patient with intraocular inflammation associated with JIA shows no classic signs or symptoms associated with uveitis, specifically: red eye, eye pain, photophobia and blurred vision 9. This stage is critical in developing eye disease, because the lack of events can last from several months to years, and it is not until the first complications of uveitis appear that patients, their families or the attending physician detect its presence.[31,32]

It is during this stage of the disease that regular ophthalmologist visits are key for the early detection of intraocular inflammation, which can only be noted through careful observation under slit lamp examination which shows inflammatory cells floating in the aqueous humor of the anterior chamber[10,31] (Fig. 1A and B).

The first complications, such as calcium band keratopathy, the appearance of the posterior iris synechiae and the onset of cataract formation, can then produce photophobia and visual loss[27–29,33] (Fig. 2). In the only report of Mexican patients with uveitis associated with JIA, eye exams in the first visit found 55.2% of affected eyes with complications, the most common being formation of posterior synechiae of the iris (56.2%), followed by calcium band keratopathy (50.0%) and cataract formation (31.2%).[10] Then, if uveitis was still undetected, or if medical treatment was inadequate, more serious complications appeared, in addition to the progression of cataracts, such as vitreitis, cystoid macular edema, glaucoma secondary to pupillary blockage or angular closure through the formation of posterior and anterior iris synechia, respectively, and ischemic or inflammatory optic neuropathy, among others[5,33] (Fig. 3). In a study of 89 children with JIA-associated uveitis, maculopathy (edema and