Uveitis in juvenile idiopathic arthritis

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Abstract

Objective: to evaluate the frequency of chronic anterior uveitis in patients with juvenile idiopathic arthritis and its association with the presence of antinuclear antibodies.

Patients and methods: we retrospectively studied 72 patients with juvenile idiopathic arthritis. All of them were submitted to slit-lamp examination of the anterior chamber at diagnosis. Both antinuclear antibodies and rheumatoid factor were determined. Patients with positive results for antinuclear antibodies were evaluated every three months and those with negative results were assessed every six months.

Results: forty patients were male (55.5%) and 36 were Caucasoid (50%). The mean age at the onset of juvenile idiopathic arthritis was 6.4 years (range = 1 to 14 years) and the mean age at the beginning of the study was 10.4 years (1 to 19 years). According to the type of disease at onset, 32 were pauciarticular (44.4%) (17 boys and 15 girls), 30 were polyarticular (41.6%) (17 boys and 13 girls) and 10 were systemic (14%) (6 boys and 4 girls). We observed chronic anterior uveitis in five patients (6.5%) (mean age = 11.4 years). Among them, four (80%) had pauciarticular juvenile idiopathic arthritis at disease onset (three girls with type I juvenile idiopathic arthritis and positive antinuclear antibodies and one boy with type I juvenile idiopathic arthritis and negative antinuclear antibodies) and one girl with polyarticular juvenile idiopathic arthritis (negative antinuclear antibodies and rheumatoid factor). In this group, the mean age at the onset of juvenile idiopathic arthritis was 5.1 years and the mean age of uveitis onset was 9 years. Antinuclear antibodies were positive in 3/5 patients (60%) with uveitis. Antinuclear antibodies were positive in 12% of the patients without uveitis (n = 67). Among the patients with uveitis, three had only one flare and the other two had four flares with cataract. The frequency of antinuclear antibodies was statistically higher in the patients with uveitis (P < 0.05).

Conclusion: although the incidence of uveitis in our study was lower than that reported in the literature, the frequency of uveitis was higher in females, in those with pauciarticular juvenile idiopathic arthritis and in patients with positive antinuclear antibodies.


Introduction

Juvenile idiopathic arthritis (JIA) is the most common chronic arthropathy during childhood; it is characterized by inflammation of joints and involvement of other organs.

Chronic nongranulomatous uveitis is among the most frequent manifestations of JIA (iridocyclitis), which often leads to visual impairment of patients.¹ Chronic iridocyclitis consists of an inflammation of the iris and the ciliary body
that can last for over three months. The incidence of JIA varies. In Brazil, JIA is responsible for 1.5% to 5.2% of cases of uveitis in children.\textsuperscript{2,3} Uveitis occurs more frequently in girls with pauciarticular JIA, aged less than six years, and with presence of antinuclear antibodies (ANA).\textsuperscript{4} Allemann et al. carried out a nine-year study of 77 JIA patients, out of which only eight (10.4%) showed eye involvement with five (62.5%) of the pauciarticular type and three (37.5%) of the polyarticular type.\textsuperscript{5} In another study, uveitis was diagnosed in 20% of children with pauciarticular JIA and 5% with polyarticular JIA.\textsuperscript{6} Uveitis is rare in children with systemic onset JIA.

Chronic anterior uveitis develops bilaterally in 65% of cases.\textsuperscript{7} The earlier manifestations occur due to the accumulation of inflammatory cells in the anterior chamber and synchiae formation and are usually asymptomatic. Less than 2% of patients complain of lacrimation, pain, photophobia, headaches, conjunctival hyperemia, or visual acuity loss. There may also be cases of recurrent acute iridocyclitis and there is no direct relation between the action of arthritis and uveitis.\textsuperscript{8}

Uveitis may precede the appearance of arthritis or, more frequently, appear during the first five to ten years of the disease.\textsuperscript{4,7}

It is estimated that 25% of patients with JIA associated with chronic anterior uveitis develop severe and irreversible complications, such as cataract, band keratopathy, posterior synechiae, glaucoma, edema, cystoid macular degeneration, and even blindness.\textsuperscript{9}

There are few studies on the histology of uveitis in JIA. Some alterations, such as the vascularization of the iris with lymphocytic infiltrates and plasma cells, have been described.\textsuperscript{8} Immunoglobulin levels (especially IgG) are increased in aqueous and vitreous humor. According to Bloom et al., these antibodies are significantly more prevalent in the population of pauciarticular and polyarticular JIA patients than in that of systemic JIA patients and normal controls.\textsuperscript{8} The activation of complement components (C3 and C1q) in vitreous humor suggests the presence of immunocomplexes.\textsuperscript{4}

Positive ANA is associated with chronic uveitis. The ANAs are significantly more prevalent in children with pauciarticular JIA and uveitis (65-88%) than in those with JIA without uveitis.\textsuperscript{3}

The objective of our study was to assess the prevalence of chronic anterior uveitis in JIA patients and its association with the presence of ANA.

Patients and methods

Patients

We carried out a retrospective investigation of 72 children diagnosed with JIA and classified according to the American College of Rheumatology 1986 criteria. Patients were followed-up at the Pediatric Rheumatology department of the School of Medicine, Universidade Federal do Estado de São Paulo (UNIFESP-EPM) and evaluated at the Ophthalmology department at the same institution.

Methods

The study consisted of clinical and ophthalmologic evaluation of patients with confirmed diagnosis of JIA and determination of ANA (direct immunofluorescence) and rheumatoid factor (RF) (latex agglutination test) during the initial stage of the disease.

Ophthalmologic evaluation consisted of biomicroscopy of anterior chamber. Patients positive for ANA were submitted to biomicroscopy every three months and those with negative ANA, every six months.

Biomicroscopy is carried out using a device that emits a potent ray of light through a slit, hence the name slit lamp; this device allows microscopic examination of live tissues. Slit lamp biomicroscopy is the choice method for examination of the cornea, anterior eye segment, and even the vitreous and the tunica intima and media; it favors direct observation of the normal histologic structure and critical analysis of the existing pathologic alterations.\textsuperscript{10}

Statistical analysis

We applied Fisher’s exact test for the comparison of positive ANA in patients with JIA and uveitis to those with JIA and without uveitis.

Results

Out of the 72 pediatric patients with confirmed diagnosis of JIA, there were 40 (55.5%) boys and 36 (50%) Caucasians. The average age of onset of JIA was 6.4 years (one to 14 years); the average age of patients in the study was 10.4 years (one to 19 years). Results related to the type of onset of JIA indicated 32 (44.4%) pauciarticular (17 boys, 15 girls); 30 (41.6%), polyarticular (17 boys, 13 girls); and 10 (14%), systemic (six boys, four girls) patients.

Table 1 shows the clinical characteristics of patients with JIA.

The presence of chronic anterior uveitis was detected in five (6.5%) children (age average 11.4 years). Out of the five children, four (80%) had pauciarticular onset (three girls with type 1, positive ANA; one boy type 1, negative ANA), and one had polyarticular onset (negative ANA and RF). In this group of children, the average age at onset of JIA was 5.1 years (three to 12 years), and the average age at onset of uveitis was nine years (four to 16 years). One female patient presented uveitis 13 years after diagnosis of JIA in remission; the remaining patients, one year after diagnosis of disease activity.
Table 1 - Clinical characteristics of patients with JIA

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Pauciarticular n=32</th>
<th>Polyarticular n=30</th>
<th>Systemic n=10</th>
<th>Total n=72</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/Female</td>
<td>17/15</td>
<td>17/13</td>
<td>6/4</td>
<td>40/32</td>
</tr>
<tr>
<td>With uveitis</td>
<td>4</td>
<td>1</td>
<td>–</td>
<td>5</td>
</tr>
<tr>
<td>Positive ANA</td>
<td>9</td>
<td>2</td>
<td>–</td>
<td>11</td>
</tr>
<tr>
<td>Positive RF</td>
<td>2</td>
<td>1</td>
<td>–</td>
<td>3</td>
</tr>
<tr>
<td>Positive HLAB27</td>
<td>3</td>
<td>1</td>
<td>–</td>
<td>4</td>
</tr>
</tbody>
</table>

ANA - antinuclear antibodies; RF - rheumatoid factor

ANA was positive in three of the five patients (60%) with uveitis. Two presented homogeneous and speckled pattern, whereas one presented speckled pattern. Out of the patients with JIA and without uveitis (67 children), eight (12%) were ANA positive (six pauciarticular and two polyarticular), and three (4.5%) were RF positive (two pauciarticular and one polyarticular) (Tables 2 and 3).

In relation to the clinical evolution of patients with uveitis, three children had only one episode of uveitis (one pauciarticular girl, one polyarticular girl, and one pauciarticular boy). Two pauciarticular children showed two episodes of recurrence of uveitis, without associated joint activity; these two patients developed cataract as a late ophthalmologic complication.

ANAs were more prevalent in the population of patients with JIA and uveitis (60%) in comparison to that of patients with JIA and without uveitis (12%); this difference was statistically significant (P<0.05).

Discussion

The incidence of uveitis (6.5%) in children who were assisted at our services was smaller than that reported in the literature. Cabral et al. reported uveitis in 20% of children with pauciarticular onset JIA, and in 5% of those with polyarticular onset JIA. This finding may be explained by the characteristics of our population or by failure in the referral of patients (patients followed-up only by ophthalmologists).

Table 2 - Patients with JIA according to the presence or absence of uveitis

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Pauciarticular</th>
<th>Polyarticular</th>
<th>Systemic</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>With uveitis</td>
<td>4</td>
<td>1</td>
<td>–</td>
<td>5</td>
</tr>
<tr>
<td>Without uveitis</td>
<td>28</td>
<td>29</td>
<td>10</td>
<td>67</td>
</tr>
<tr>
<td>Total</td>
<td>32</td>
<td>30</td>
<td>10</td>
<td>72</td>
</tr>
</tbody>
</table>
In our study, uveitis was diagnosed in four children with pauciarticular onset JIA and one child with polyarticular onset JIA; uveitis was not diagnosed in children with systemic onset JIA. This finding is in agreement with the literature, which describes a higher prevalence of uveitis in pauciarticular onset JIA.5,6

The determinant risk factors for uveitis in JIA pediatric patients are related to the female sex, age less than six years at onset of inferior arthritis, pauciarticular onset, duration of the disease less than four years, positive ANA, and presence of HLA DR5.1,6,7,11,12 The risk factors referred in the literature were also observed in our study: 80% of children with uveitis were of the female sex; all had onset of arthritis before age six years and pauciarticular onset; and all had a minimum duration of one year for the disease.

Allemann et al. observed that positivity for ANA was four-fold higher in patients with ophthalmologic involvement than in controls with JIA (5.8%). Others have also shown the importance of frequent ophthalmologic examinations in patients with positive ANA, especially in cases of pauciarticular onset. In this sub-group of patients, the presence of ANA was high (approximately 80% of patients) and associated with the high incidence of chronic iridocyclitis.2

In our population, ANA was detected in three girls with pauciarticular onset JIA type 1 and chronic anterior uveitis; ANA was statistically more prevalent in JIA patients with uveitis than in those without uveitis (60% and 12.5%, respectively). Antinuclear antibodies are considered a marker of ophthalmologic involvement.4

All children with eye involvement presented negative rheumatoid factor (RF); this finding is in agreement with the study by Galea et al.9 Positive RF is apparently associated with less risk for uveitis, which is similar to the case of rheumatoid arthritis in adult patients.13

In relation to the complications of chronic uveitis, two girls with pauciarticular JIA type 1 (both ANA positive) had two episodes each of recurrence of uveitis with cataract. In 1989, Kanski described 277 patients with juvenile chronic arthritis and iridocyclitis, out of which 42% developed cataract and 17%, glaucoma.13

The importance of periodical biomicroscopy examination of JIA patients is related to the fact that ophthalmologic involvement is usually asymptomatic and that uveitis is usually detected during routine ophthalmologic examinations.14 These examinations should be carried out every three months for patients with positive ANA and every six months for those with negative ANA; the examination routine should be maintained for seven to 10 years, even in cases of remission of joint inflammation.4 Early diagnosis and treatment reduce the appearance of sequelae.12,15

We concluded that despite the small number of cases of chronic anterior uveitis (6.5%), there was a higher prevalence in the female sex and in pauciarticular onset JIA (with ANA detected in most cases).

References

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