ABSTRACT

Purpose: The purpose of this paper is to describe the frequency and characteristics of uveitis associated with juvenile idiopathic arthritis at a tertiary referral centre in Spain.

Methods: Review of clinical records. 205 children diagnosed with chronic juvenile arthritis over the last 15 years, of whom 26 presented anterior uveitis. Patients were classified according to their pattern of evolution, the time the uveitis was diagnosed with respect to the onset of arthritis, and the severity of uveitis at diagnosis.

Results: The prevalence of uveitis was 12.7%. Of the patients affected with uveitis 71% were girls. The average age at which the arthritis was diagnosed was significantly earlier in the group of patients who developed uveitis (4.06 years). No differences were observed in the incidence of uveitis in girls and boys, nor in pauci/polyarticular affectionation. ANA positivity was found in 84.6% of the uveitis-affected patients, this being significantly different to the ANA- group. The average age at which uveitis was diagnosed is 5.87 years. 48.1% of uveitis patients develop uveitis within 12 months of the onset of arthritis. This group presented more complications during the evolution of the condition.

RESUMEN

Objetivo: Describir la frecuencia y características de la uveítis asociada a la artritis idiopática juvenil en un centro de referencia terciario en España.

Métodos: Se estudiaron 205 niños diagnosticados de artritis idiopática juvenil en los últimos 15 años, de los cuales 26 desarrollaron uveítis anterior. Se clasificó a los pacientes según su patrón de evolución, el momento de diagnóstico de uveítis y la gravedad de la misma al diagnóstico.

Resultados: La prevalencia de uveítis entre los niños con artritis idiopática juvenil fue de 12.7%, de las cuales el 71% eran niñas. La edad media del diagnóstico de artritis fue significativamente menor en el grupo de pacientes que desarrollaron uveítis (4 años).

No se observaron diferencias en la incidencia de uveítis en niños/as ni en la afectación pauci/poliarticular. Se encontraron ANA+ en el 84.6% de los pacientes con uveítis, presentando diferencias significativas con el grupo ANA-.

La edad media de diagnóstico de uveítis fue de 5,87 años. El 48,1% de los pacientes desarrollaron la uveítis en los primeros doce meses del diagnóstico de artritis. Este subgrupo de pacientes presentó más complicaciones en su evolución. El 84,7% del total...
total of 84.7% of the uveitis-affected patients presented with a final visual acuity of >0.5 during the observation period.

Conclusions: In our study, the development of uveitis was significantly associated with an earlier age of diagnosis of the arthritis and with the presence of ANA positivity. No differences were observed between boys and girls, or between pauci and polyarticular groups. A greater prevalence of complications was observed in cases presenting with a shorter time interval between the diagnosis of arthritis and uveitis and in those that presented with complications on diagnosis (Arch Soc Esp Oftalmol 2009; 84: 133-138).

Key Words: uveitis, juvenile idiopathic arthritis, cataract, glaucoma.

INTRODUCTION

Uveitis associated with juvenile idiopathic arthritis is the most common cause of uveitis in pediatric populations. Tugal-Tutkun (1) published a series of 130 children suffering from uveitis, of which 41% corresponded to this group, which was also the one developing most complications.

The association existing between both entities was reviewed by Rosenberg (2) (1987) and Kanski (3) (1990), and more recently by Kotaniemi (4) (2003). Most studies report a higher incidence of uveitis in pauciarticular JA, females and ANA-positive subjects. However, in Kotaniemi’s series, one of the broadest series to date, uveitis appeared with the same frequency in both genders and pauci- as well as poly-articular JIA. In a case-control study, Chia (5) found a higher incidence of severe uveitis at diagnosis among boys. As already suggested by Rosenberg, Wolf (6) found a correlation in 1987 between the existing degree of inflammation during first check-ups and severe loss of final visual acuity, while observing worse evolution in those cases in which uveitis preceded arthritis. In a recent study authored by Edelsten (7), the most significant prognosis factor was severe uveitis at diagnosis. Thus, there is no uniformity in terms of epidemiology and prognosis criteria in uveitis associated with juvenile idiopathic arthritis. Therefore, additional studies are needed to determine the prognosis and the occurrence of uveitis among patients diagnosed with juvenile idiopathic arthritis.

SUBJECTS, MATERIAL AND METHODOLOGY

The present study includes 205 children examined by the ophthalmology and pediatric rheumatology units at H.U. La Paz over the past 15 years.

The following data were compiled from clinical histories: gender; group of articular involvement; presence of ANA; presence of rheumatoid factor; presence of HLA B27; date of birth and arthritis diagnosis; date of first and last check-ups at the rheumatology and ophthalmology units; date of uveitis diagnosis and surgical procedures performed; presence of complications during first ophthalmologic examination; number of outbreaks; presence of symptoms; uni/bilaterality; overall duration of involvement in months; type and overall duration of topical treatment in months; type, dosage and overall duration of systemic treatment in months; treatment side effects; complications during evolution; need for surgery; type of surgery performed; annual visual acuity of all children; monthly visual acuity in those children who underwent surgery during one year after surgery; intraocular pressure; and papillary excavation in ocular hypertensive patients.

The diagnosis of juvenile idiopathic arthritis was established using the criteria defined by the International League Against Rheumatism (ILAR) (8,9), i.e., as arthritis of unknown cause appearing in patients under 16 years of age with at least six weeks’ duration.
Children diagnosed with juvenile idiopathic arthritis were referred to the pediatric ophthalmology unit for slit lamp examination and early detection of asymptomatic uveitis.

The uveitis diagnosis was established by means of biomicroscopic examination in the presence of flare or cells (Tyndall +) in the anterior chamber or recent keratic precipitates.

Isolated inflammatory episodes taking place with at least one month intervals and registering no activity were considered as uveitis outbreaks.

Children diagnosed with uveitis during the first year or prior to the arthritis diagnosis were included in the group of «early» uveitis.

Children presenting uveitis-related complications during the first ophthalmic examination were included in the group of «severe» uveitis at diagnosis. Uveitis complications include the presence of synechiae, cataracts, glaucoma, band keratopathy and cystoid macular edema.

Statistical Analysis

Data were analyzed using SPSS 9.0. (SPSS Inc., Chicago, Illinois, USA) statistical software. Qualitative data are expressed as absolute frequencies and percentages. Quantitative data are expressed as means, median and typical deviation according to their distribution.

Comparison of qualitative data was performed using Fisher’s exact test; quantitative data between two groups were compared with the Mann–Whitney U test (non-parametric test). The correlation between quantitative data and final visual acuity was analyzed using Spearman’s rank correlation coefficient.

All statistical tests were bilateral and significant values were set at p<0.05.

RESULTS

Mean follow-up time at the ophthalmology unit for patients suffering from uveitis was 64.2 months (range 6-174 months).

Mean age at diagnosis for juvenile idiopathic arthritis among the 205 children followed up at the Rheumatology Unit was 5.5 years. 71.7% of the total sample were girls while 28.3% were boys. Table I summarizes group distribution based on ocular involvement.

Prevalence of uveitis among children suffering from idiopathic arthritis was 12.7%. Mean age at the onset of arthritis was 5.73 years in the group not suffering from uveitis versus 4.06 years in the group suffering from uveitis, this difference being statistically significant (p< 0.05).

Of all children suffering from uveitis, 70.4% belong to the pauciarticular subgroup versus 25.9% and 3.70% of polyarticular and psoriasis arthritis. Although the majority of patients suffering from uveitis clearly belong to the pauciarticular group, the fact that this is the largest group ought to be taken into account. When observing the percentages of uveitis for each subgroup, 15.7% of children in the pauciarticular group presented uveitis versus 17.90% in the polyarticular group, the difference not being statistically significant. No uveitis cases were observed in the systemic group.

Concerning gender, of all patients checked at the Ophthalmology Unit 85.20% were girls versus 14.80% boys, mainly due to the greater prevalence of juvenile idiopathic arthritis among girls. Thus, 7.10% of boys presented uveitis versus 15.90% of girls. This difference is not statistically significant.

As for the presence of ANA+, a significant relation was found (p< 0.001), 84.6% of boys suffering from uveitis being ANA +. 23.7% of ANA+ children developed uveitis versus 3.70% of ANA-. No significant relation was found between the presence of ANA and gender. Of all ANA+, 82.7% were girls. The percentage of ANA+ boys is 30% versus 51.7% ANA+ girls. Mean age at the time of uveitis diagnosis is 5.87 years. The average delay for the first ophthalmology check-up after the arthritis diagnosis is 6.6 months.

The average time lapsed between the arthritis and the uveitis diagnosis was 21.83 months.

48.1% of patients had been diagnosed with uveitis previously or within one year from the arthritis diagnosis. The most frequently observed phenome-

| Table I. Articular involvement based on subgroups |
|-----------------------------------|--------|--------|
| Frequency | Percentage |
| Pauciarticular | 122 | 60 |
| Systemic | 37 | 18 |
| Polyarticular | 41 | 20 |
| Others | 4 | 2 |
| Total | 205 | 100 |
non was that of diagnosis during the first ophthalmic check-up after the arthritis diagnosis.

«Early» development (during the first year or prior to the arthritis diagnosis) was observed in 75% of boys and 43.5% of girls. However, the presence/absence of ANA does not seem to exert any influence on the duration of this interval.

52% of uveitis cases did not present complications at diagnosis versus 48% which presented synechiae, band keratopathy, cataracts or ocular hypertension during the first check-up. 76.9% of children diagnosed during the first year or prior to the arthritis diagnosis suffered complications versus 50% who presented with uveitis at a later stage. Of all patients with complications, 58.8% had been diagnosed during the first year or prior to the arthritis diagnosis.

Although differences were not statistically significant, in the group of children who had developed early uveitis the total recurrences, time of involvement and duration of treatment with topical corticosteroids were greater than the other group’s.

Complications were observed in 17 children and 27 eyes. No significant differences were found in terms of final visual acuity related to the presence of ANA, gender or early diagnosis.

Average visual acuity in patients without complications was 0.85 for girls and 0.718 for boys. In total, eight eyes presented final visual acuity under 0.5 versus 46 eyes whose final visual acuity was greater than 0.5. Eight children and eleven eyes required surgery. Cataract surgery in eight eyes; glaucoma surgery in two eyes; vitreo-retinal surgery in one eye.

Children who underwent surgery belonged to the group classified as severe at diagnosis (with complications during first check-up) and were diagnosed with uveitis less than one year after the arthritis diagnosis.

Eight eyes underwent secondary cataract surgery by means of lensectomy-vitrectomy with posterior capsulorrhexis. No IOL was implanted at first.

Mean evolution time between the onset of uveitis and the need for cataract surgery was 54.8 months. The average age of patients undergoing surgery was 8.9 years. Visual acuity in the optotype after surgery improved on average by 4.25 lines at six months after cataract surgery.

Two cases out of twelve eyes required glaucoma surgery, while the remaining cases were adequately controlled with topical treatments.

**DISCUSSION**

The frequency of uveitis in children suffering from juvenile idiopathic arthritis reported in the literature ranges from 2 to 25%, while the present study found this rate to be 13% (3,9). Traditionally, a higher incidence of uveitis among girls suffering from arthritis has been described (3,6) thus considering the female gender as a risk factor (regardless of the higher incidence of arthritis among girls) for the development of uveitis. Belonging to the pauciarticular involvement group was also considered to increase the risk of developing uveitis.

Nevertheless, Kotaniemi (4) found no differences in the incidence of uveitis among girls and boys or the pauci and polyarticular groups, not so in the case of ANA-positive subjects.

Our sample presented no significant differences in terms of incidence of uveitis among boys and girls or between the different groups with articular involvement (except in the systemic form), thus supporting the latter hypothesis. Results point at a younger age for arthritis diagnosis among children who will develop uveitis; therefore, age is a factor to be taken into account when screening these children (3,6,10). The average age at the time of the arthritis diagnosis for children who would eventually develop uveitis is 4.06 years versus 5.73 for those who did not present ocular involvement (p<0.05). In the present study, the presence of ANA is associated with the development of uveitis (p<0.001), 84.6% of ANA+ children presenting ocular involvement. ANA values range in the literature between 71 and 93% for the group suffering from uveitis and is considered to be one of the most important parameters in screening programs. Worse evolution has been suggested for ANA- children suffering from uveitis, although this could not be confirmed in the present study (11). ANA counts are not correlated with the severity of articular and ocular diseases.

On the other hand, many publications have sought to identify potential factors associated with the development of severe uveitis, i.e. predictors for worse evolution (5,6,12,13), including the time interval between the arthritis and uveitis diagnosis, severity at diagnosis, gender and increase of a-2 globulins.

Edelsten (7) and Chia (5) report that male gender is a risk factor for the development of severe uveitis and that boys’ evolution is worse than girls’ (4,6).
In the present sample, 75% of the children followed-up presented complications during their evolution. All children developed uveitis less than one year after the arthritis diagnosis and presented complications during the first check-up. One of them required surgery. It should thus be considered a prognostic factor for complications.

48.1% of patients were diagnosed with uveitis less than 12 months after and even prior to the arthritis diagnosis (two cases). Those patients who developed uveitis in a shorter time interval developed more complications, presented more recurrences and required more surgical procedures than those who developed uveitis at a later stage. This finding is in agreement with most of the studies available on the subject, and apparently there is no doubt about the fact that children who develop uveitis early on after the arthritis diagnosis will have a worse evolution. The study authored by Vela (14) also described this phenomenon, whereby patients suffering from early onset uveitis presented twice the number of episodes.

Similarly, 48% of the children examined presented complications at diagnosis, which in turn is related to a worse evolution of uveitis, greater need for treatment and surgical procedures. This result matches other series and reflects the need to improve screening programs. According to Edelsten’s study, the severity of uveitis at diagnosis was the most significant predictor of worse evolution (7). Therefore, based on the findings above, ANA+ boys/girls under four years of age at the time of the arthritis diagnosis, whether pauci or polyarticular, could be considered as high-risk patients for uveitis. Slit-lamp examinations are recommended every three months. Two years later, examinations could be performed every six months instead. Children over four years of age or ANA- may be considered medium-risk patients and should be examined every six months, while those presenting systemic involvement would benefit from annual check-ups. Thorough follow-up is recommended for those cases already diagnosed with uveitis presenting bad prognosis factors: short interval from the time of arthritis diagnosis, complications at diagnosis, males…

Broader studies would allow for establishing protocols and specifying the profile of patients who might benefit from continued ophthalmic care.

With respect to complications, 48% of children suffered from cataracts during their evolution. This is the most commonly described complication, being related to the chronic inflammatory process and corticoids treatment. Other authors report scarcely homogeneous values ranging from 20% to 84% (7,13,15), but the largest series yield similar values to those observed in the present survey (13,16). The percentage of secondary glaucoma reported in the literature varies from 15 to 45% and in most cases it has been described as the most devastating complication (3,14,15). In the present sample, 33% of children suffered episodes of ocular hypertension, which were easily brought under control with topical antihypertensive medication.

The present series revealed that eight out of 52 eyes presented final visual acuity below 0.5 and six under 0.4.

In the present series, visual outcome after cataract surgery was good. The available literature reports very different outcomes, which could be explained by the small size of series (16-18). Early and intensive treatment following the zero-tolerance model for intraocular inflammation proposed by Foster (19) is needed to reduce complications.

In five eyes out of eight (62.5%) undergoing cataract surgery, visual acuity was greater than 0.5. Visual prognosis for children suffering from juvenile idiopathic arthritis and uveitis has not improved as expected in the past years. Complications remain high in spite of the new systemic treatments.

Since prevention of one of the main causes of childhood blindness is possible, it is necessary to put great effort into early detection of the disease, establishment of treatment protocols and improvement of surgical techniques to prevent complications.

REFERENCES

Sendagorta E, et al.


