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Macular Thickness in Patients with Idiopathic Juvenile Rheumatoid Arthritis without Uveitis: Is There any Alteration?

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Abstract

Introduction: The Juvenile Idiopathic Arthritis (JIA) is the most common rheumatic disease in children. One of the most common causes of Secondary Uveitis is JIA, in fact uveitis is the most common extraarticular manifestation in all groups of JIA [1-3]. The visual loss secondary to a complicated uveitis is a major concern and has resulted in recommendations to regulate ophthalmologic examination. Among the possible complications is clinical and subclinical macular edema [2,4,5]. It has been reported increase in Macular Thickness (MT) in eyes with Anterior Uveitis in JIA patients [5-7]. This observation was also found in the contralateral eyes even though they did not had a current episode of uveitis, suggesting that the increase in MT could be explained by the immune response to systemic inflammatory process [5].

Purpose: This study aims to document the MT in patients with JIA wich present a systemic inflammatory response, but unlike what has been done in previous studies, this research was performed in eyes that did not have uveitis at the time of ophthalmologic examination and therefore seeking changes in MT arising from systemic situation.

Results: In a 11-month period 14 patients with JIA, 7 female and 7 male were reviewed. With an average of 10.5 years (range 3-16 years) with a mean age at diagnosis of 7.8 years (range 2-4 years). The range of time between diagnosis of JIA and the first ophthalmologic examination was 0.5-9.0 years. The most common type of JIA was persistent oligoarticular in 14.3% of cases. Active disease in 4 patients (28.6%) and 10 patients (71.4%) was found. Optical coherence tomography (OCT) was performed in patients with JIA and 14 controls matched for age and sex The Mann-Whithney was performed without finding difference in central macular thickness JIA patients and control patients, with p=0.548 for the right eye (RE) and p=0.378 for the left eye (LE). There was no relationship between macular thickness and the presence of positive rheumatoid factor, erythrocyte sedimentation rate or C-reactive protein.

Conclusion: There was no statistically significant difference in macular thickness in JIA patients without prior or current episode of uveitis and control patients. Likewise, there was no relationship between the activity or inactivity of the disease and macular thickness in such patients. Further research would find association between macular thickness and probability of developing uveitis or impared vision.

Keywords: International league of associations for rheumatology (ILAR); Mean foveal thickness (MFT); C-Reactive protein (CRP)

Introduction

The International League of Associations for Rheumatology (ILAR) defines Juvenile Idiopathic Arthritis as a group of chronic childhood arthropathies with no apparent cause, lasting for a minimum of 6 weeks and with disease onset prior to age 16 Although an incidence of just 3 to 23 per 100,000 children and a prevalence of 16 to 140 per 100,000 children, Juvenile Idiopathic Arthritis is the most common rheumatic disease in children. Uveitis is the most common extra-articular involvement found in patients with Juvenile Idiopathic Arthritis [1,2] and Juvenile Idiopathic Arthritis is the most common systemic cause of pediatric uveitis [3,4].

The cumulative incidence of Juvenile Idiopathic Arthritis associated uveitis is 8.3% [3] and it is reported that 13 - 36% of the patients with Juvenile Idiopathic Arthritis will develop uveitis [1].Thirty seven percent (37%) of these patients will present secondary ocular complications, with significant visual impairment in 3% to 66% [2].

Among the complications of uveitis is macular edema, which is initially reported in 5% [2]. In the other hand, with the use of the Optical Coherence Tomography (OCT), it has been found that while macular edema is clinically detected in 13%, by OCT examination actually 25% of eyes with anterior uveitis of any origin present macular edema and that macular alterations can be found in 84% of the eyes of children with Juvenile Idiopathic Arthritis and uveitis. Also, has been studied the macular thickness of the fellow eye in patients with unilateral anterior uveitis of any cause, finding that also in the quiet fellow-eyes there is subclinical macular alteration, probably as a reflect of systemic immune-mediated response to the inflammatory disorder in anterior uveitis and that this seems to be larger in HLA-B27 positive patients [5].

The purpose of our study was to transversely analyze by means of OCT scanning the macular thickness in children with Juvenile Idiopathic Arthritis without current or previous episode of uveitis in order to describe the measurements of macular thickness resulting from the systemic condition.

Methods and Materials

This was a case-control study where 30 eyes of patients with Juvenile Idiopathic Arthritis and 60 eyes of control subjects matched by sex and age (2:1) underwent Macular Optical Coherence Tomography. Twenty patients with Juvenile Idiopathic Arthritis where transversally referred from Rheumatology service and evaluated between November 2012 and December 2013 at the Hospital Civil Fray Antonio Alcalde, Guadalajara, Jalisco. Subjects with current or previous ophthalmic history of Anterior Uveitis, intraocular surgery or any ocular complication of previous uveitis were excluded. Five patients were excluded: Three patients for having complication of uveitis, two of them with previous intraocular surgery, and 2 for having incomplete file.

The study of 30 eyes of 15 patients with Juvenile Idiopathic Arthritis and 60 eyes of 30 control subjects matched by age and sex, underwent a complete ophthalmological examination during their first visit, including visual acuity assessed using HTOV charts, slit-lamp examination, aplanation tonometry, and fundoscopy with dilated pupils. The informed consent of the parents was obtained in each case before undergoing ophthalmic examination and OCT.

OCT scanning was performed with Cirrus OCT, Carl Zeiss Meditec and comprised in all patients a 6mm mapping of the macula. The retinal map analysis protocol was used, with numeric averages of the measurements for each of the 9 map sectors as defined by the Early Treatment Diabetic Retinopathy Study. The regional variables that were analyzed were Mean Foveal Thickness (MFT=F1); Mean Central Thickness, composed by the inner ring of 3mm diameter (MCT= (F2+F3+F4+F5)/4); and Mean Peripheral Thickness, the outer ring of 6mm diameter (MPT=F6+F7+F8+F9/4).

Data was analyzed with T-Student test, two tail/two-sided and p-value < 0.05 was set to be statistically significant. SPSS v.17.0 was used for statistical analysis. Institutional review board approval was obtained for the design of this study, conducted in accordance with Declaration of Helsinki recommendations.

Results

The sample group was composed by thirty eyes of 15 patients with Idiopathic Juvenile Arthritis, eight (53.3%) female and seven (46.7%) male, and the control group formed by 60 eyes of 30 subjects matched by sex and age. The mean age at the time of ophthalmological examination was 10.6±3.5 years, ranging from 3 to 16 years. The mean age of the onset of symptoms of Idiopathic Juvenile Arthritis was 6.2±3.4 years (range 2-13), while the mean age of diagnosis of Idiopathic Juvenile Arthritis was 8.2±3.6 years (range 2-14).The average time from diagnosis of Idiopathic Juvenile Arthritis to the first ophthalmological examination was 3.1±2.6 years (range 0-9).

The oligoarticular persistent type was the most frequent with a 40%, the seronegative polyarticular with a 33% while the oligoarticular extended and polyarticular seropositive arthritis with a 13% each one. Non systemic, psoriatic or enthesitis related was found. The 93.3% of the patients were under systemic rheumatologic treatment, the majority received both sulfasalazine and methotrexate in a 57%, sulfazalazine 36% and 7% with oral steroids. Active disease was found in 26.6%. The mean erythrocyte sedimentation rate (ESR) was 13.92mm/hr (0-10mm/hr). The mean C-Reactive protein (CRP) was 1.37mg/L, (0-0.80) no association was found between the ESR and CPR with macular thickness.

Mean Visual Acuity in LogMAR was +0.10 for right eye and +0.20 for left eye with HTOV chart. Mean intraocular pressure was 11mmHg (range 10-21mmHg) in right eye and 15.2mmHg in left eye. (Range 12-22mmHg). No posterior pole alteration was found in fundoscopy. Macular OCT was done in 30 eyes of the 15 case patients and in 60 eyes of the 30 patient's age and sex matched controls. Mean foveal thickness was 239±17microns while mean thickness in control group was 238±25 microns with a p=0.80. Mean central thickness was 311±14 microns and 313±19 in the control group P=0.54. The mean peripheral thickness was 276±14 microns and 277±19 microns in control group. p=0.65. No statistical significance was found between the two groups.

Discussion

The incidence of macular edema in patients with Idiopathic Juvenile Arthritis as a complication of a uveitic process is approximately 3%, as reported in a retrospective study by Sylvia R. Kodsi et al. In 2002, 158 patients were included, of which 25% developed uveitis, 5% according to a 2007 publication in a cohort of 1081 patients with Idiopathic Juvenile Arthritis, 13% had uveitis, and 5% had macular edema [6-10].

In 2007, however, a cross-sectional study was conducted, which showed that the incidence of maculopathy in patients with JIA and uveitis was greater in 82% of patients with peripheral thickening (73%), Macular edema (47%), foveal detachment (18%) or atrophic changes (10%), these data being quite different

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from what was found only by clinical evaluation [3]. Similarly, in a retrospective series carried out in 2010, which included 67 patients with Idiopathic Juvenile Arthritis, 13.8% presented macular edema secondary to a uveitic process. However, macular edema incidence was documented at 25%. In 2012, a retrospective study was carried out in which OCT was performed in 14 eyes with unilateral anterior uveitis of non-infectious origin, finding a statistically significant increase in macular thickness compared to healthy contralateral eye thickness [10].

On the other hand, also in 2012 Alexandra Wexler carried out a prospective study in which macular OCT was performed on eyes with anterior uveitis and healthy contralateral eye in patients with HLA-B27 positive and HLA-B27 negative compared to control patients matched by age and sex. It was found that there is an increase in macular thickness of both the uveitic process eye and the healthy contralateral eye, in comparison to the control eyes of patients without uveitis, suggesting that the anterior uveitis episode is accompanied by an autoimmune systemic response, it was also discovered that the increase in macular thickness was greater in HLA-B27 positive patients [8]. Likewise, evidence from animal models supports that the non-infectious uvetic inflammatory process is related to alteration in systemic immunity, which leads to damage of ocular autoimmunity [11].

To date, there is no previous study that documents the macular thickness of patients with Idiopathic Juvenile Arthritis and without uvetic process, seeking to describe the incidence of maculopathy and / or posterior pole pathology resulting from a systemic inflammatory and systemic immune process.

According to our results, there is no alteration in the macular thickness of patients with Idiopathic Juvenile Arthritis and no ocular inflammatory process. However, it is important to note that 73.4% of our patients had inactive and controlled Idiopathic Juvenile Arthritis and that 93% were on rheumatologic medication. Finally, it is important to note that in 86% of the patients the ophthalmologic assessment performed in the present study was the initial assessment, with a delay between the diagnosis of Idiopathic Juvenile Arthritis and referral to the ophthalmologist of 3 years on average, with guidelines indicating ophthalmologic assessment at the time of diagnosis of Idiopathic Juvenile Arthritis [4,12-15].

Conclusion

No differences were found in the macular thickness of the eyes of patients with Idiopathic Juvenile arthritis and without uveitic process and eyes of control subjects. Future research will be required with a larger sample of patients with active disease or who are not taking rheumatologic medication at the time of macular OCT. It is important to promote and promote the ophthalmologic assessment of the patient with Idiopathic Juvenile Arthritis.

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