Original article

Association of epiretinal membranes with macular edema in pars planitis

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A R T I C L E   I N F O

Article history:
Received 22 January 2013
Accepted 17 September 2013
Available online 12 April 2014

Keywords:
Pars planitis
Epiretinal membrane
Cystoid macular edema
Optical coherence tomography
Fluorescein angiography

A B S T R A C T

Introduction: Pars planitis (PP) is a form of intermediate uveitis that manifests with several posterior segment complications, including cystoid macular edema (CME) and epiretinal membrane formation (ERM). On the presence of CME the patient is usually treated with anti-inflammatory and/or immunosuppressive drugs. However the presence of CME may coexist with ERM formation, and therefore the treatment could be different.

Purpose: To determine the association between ERM and CME in PP.

Materials and methods: Case control series. The charts of patients diagnosed with PP were retrospectively reviewed. All patients had fluorescein angiogram (FA) and spectral domain optical coherence tomography (SD-OCT). The presence of ERM was determined by SD-OCT, while CME was determined by FA. Contingency tables were used to determine the risk of developing CME with ERM.

Results: 31 eyes presented ERM. 16 eyes presented CME. Relative risk to have CME and ERM was 0.971, with a P value of 0.77 ($\chi^2$).

Conclusions: There is no association between ERM formation and the development of CME. There is no evidence to suggest a surgical approach as first line of treatment with the presence of ERM in PP.

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Asociación de membranas epirretinianas con edema macular en pars planitis

R E S U M E N

Introducción: La pars planitis (PP) es una uveíta intermedia idiopática que presenta múltiples complicaciones en el segmento posterior, las cuales incluyen el edema macular quístico o cistóide (EM) y la formación de membranas epirretinianas (MER). Comúnmente se decide realizar tratamiento antiinflamatorio o inmunosupresor ante la presencia de EM. Sin embargo, este puede coexistir con la presencia de MER y, por lo tanto, existe la posibilidad de que el enfoque del tratamiento deba ser diferente.

Palabras clave:
Pars planitis
Membrana epirretiniana
Edema macular
Tomografía de coherencia óptica
Angiografía con fluoresceína


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Objetivos: Determinar la asociación que existe entre la presencia de MER con EM en PP.
Materiales y métodos: Serie de casos y controles donde se analizaron de manera retrospectiva los expedientes de pacientes con PP, todos ellos seguidos con angiografía con fluoresceína (AF) y tomografía de coherencia óptica de dominio espectral (SD-OCT). Se determinó la presencia de MER por SD-OCT, mientras que el EM fue determinado por AF. Se realizaron tablas de contingencia para determinar cómo influyen las MER como factores de riesgo para desarrollar EM.
Resultados: 31 ojos presentaron MER. 16 ojos presentaron EM. La razón de riesgo para presentar EM por MER fue de 0,971 con un valor de p determinado por $\chi^2$ de 0,77.
Conclusiones: No existe una asociación significativa entre la formación de MER y el desarrollo de EM. No existe evidencia que sugiera considerar un abordaje quirúrgico como primera línea de tratamiento ante la presencia de MER en PP.
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Introduction

Pars planitis (PP) is a type of uveitis which occurs frequently in pediatric and young adult patients. Its diagnosis is mainly based on the anatomic inflammation site, predominantly the vitreous and peripheral retina. The working group for the Standardization of Uveitis Nomenclature [SUN] defines PP as an intermediate, idiopathic, unilateral or bilateral uveitis without associated systemic disease, with the presence of snowbanks in at least one eye.

Some of the frequently observed complications in the posterior segment are inflammatory cells in the vitreous (89.1–93%); snowbanks (97.8–99.7%); retina vasculitis, mainly peripheral (15.7–88%); macular edema (ME) (26–83%); cataract (46%) and retina detachments (RD) (1.6–8.3%).

The formation of epiretinal membranes (ERM) has also been observed as a frequent complication in this disease. ERM are defined as fibrotic cellular proliferations in the internal layers of the retina and are considered to be an anomalous tissue repair or cicatrización. ERM cell components include fibroblasts and glyal retina cells. Extracellular components include different collagen varieties such as types I and III, mainly observed in contractile membranes. In addition, other adhesion-promoting proteins include laminine, vitronectin and fibronectin.

Donaldson et al. found that ERM formation in PP is the most frequent complication, with a prevalence of 44.4% in 15 years. However, patients referred diminished visual acuity for several reasons such as cataracts, ME or vitritis. For this reason it is believed that ERM could be underdiagnosed.

The association that could exist between the presence of ME together with ERM in PP is not known. In many cases the presence of ME is observed as a frequent complication without establishing that it could be influenced by the presence of a mechanical effect or traction by ERM. It is possible that ERM could promote greater development of ME. If this were the case, the treatment of refractory chronic ME cases with ERM could be surgical in order to remove the mechanical stress.

The objectives of the study are to determine the association of ERM and the presence of ME in patients diagnosed with PP.

Subjects, materials and methods

A case and control series. A retrospective analysis was made of patients diagnosed with PP in the Ocular Inflammatory Disease Clinic [Clínica de Enfermedades Inflamatorias Oculares (CEIO)] of the Association for Preventing Blindness [Asociación Para Evitar la Ceguera (APEC)], Dr. Luis Sánchez Bulnes Hospital (Mexico). All the patients had a clinical diagnosis in accordance with the SUN criteria: a full ophthalmological examination, fluorescein angiography (FA) and macular spectral domain optic coherence tomography (SD-OCT). The study included patients with clinically inactive inflammation (6 months or more) and transparent optic media enabling posterior segment assessment.

The structural analysis of the macula by means of SD-OCT was performed with Cirrus HD OCT (Carl Zeiss Meditec Inc, Dublin, CA, USA). Macular thickness was analyzed with 512 x 128 line scans. All the patients were analyzed on pharmacological pupil dilatation. Tomography measurement results were obtained and macular alterations recorded.

The obtained SD-OCT measurements were:

1) Minimum foveal thickness, defined as the smallest foveola point, manually measured from the internal limiting membrane up to the retina pigment epithelium.
2) Central foveal thickness of the 9 section map of the Early Treatment Diabetic Retinopathy Study.
3) Macular volume.

The last 2 points were calculated automatically by the system segmentation software.

The tomographs of each patient were analyzed to assess the presence of macular abnormalities. ERM were defined as the presence of hyper-reflecting material or line over the internal surface of the retina, parallel to the plane thereof.

ME was defined on the basis of the FAA analysis in the presence of hyperfluorescence secondary to intraretinal fugue.

Results

Overall, the study comprised 90 eyes of 53 patients with previous PP diagnosis who visited the CEIO between March and
April 2009. All the patients were clinically free of inflammation for over 6 months (interval: 7–24 months). Twenty-three patients (43.3%) were female and 30 male (56.6%). The mean age was 14.54 years (interval: 6–39 years).

The average minimum foveal thickness was 167.69 μm (89–453 μm). The average central foveal thickness was 273.73 μm (43–941 μm), while the average macular volume was 10.91 mm³ (range: 7.3–19.4 mm³).

Of all the macular alterations analyzed by SD-OCT, ERM was the most frequent as it was identified in 31 eyes (34.4%). The remaining alterations were vitreomacular traction syndrome (VMTS) in 10 eyes (11.1%); ME (tomographic, observed as hypo-reflecting spaces matching intraretinal liquid) in five eyes (5.5%); RD in one eye (1.1%); epiretinal fibrosis (RF) in 3 eyes (3.3%).

The presence of ME was established by FA. ME was identified in 16 eyes with angiographic edema. The joint presence of angiographic and tomographic ME was identified in only 3 cases (Table 1).

Of all the eyes with angiographic ME (16 patients), 6 cases included the presence of ERM (Table 1). The eyes which did not exhibit ME Word 74, of which 25 exhibited ERM.

The odds ratio was of 0.8503. The risk ratio was of 0.971. The P value established by the \( \chi^2 \) test gave a value of 0.77, while Fisher’s exact test gave 0.49. Both values were considered statistically not significant.

<table>
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<th>Table 1 – Contingency tables.</th>
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<tr>
<td>ERM</td>
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<tr>
<td>ME</td>
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<tr>
<td>No ERM</td>
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<td>Total</td>
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Fisher’s exact test \( p = 0.49 \).

ME: edema macular, ERM: epiretinal membrane.
Discussion

Visual loss in patients with PP can be due to several reasons. ERM are a frequent complication and sometimes can diminish VA. However, a number of complications can also affect vision. A study carried out in the Mayo clinic indicated that the alterations associated to the visual reduction below 20/40 were cataracts, optic neuritis, ERM and EM.

The most frequent macular alteration in our study was ERM, observed in 31 eyes (34.4%). This result was similar to that reported by Donaldson et al. (36.9%) and Malinowsky et al. (34.4%). In contrast, findings for ME were quite the opposite: overall, 16 eyes exhibited ME in comparison with 26.06 and 50.9% reported by Donaldson and Malinowsky, respectively. The differences in these findings could be due to the presence of active inflammation. Our study included only patients who had been clinically inactive for 6 months or more and had optically transparent media. This could be one reason to explain the lower incidence of angiographic ME as well as higher detection of structural abnormalities on the macula.

The ERM diagnosis was obtained by SD-OCT. Even though medium transparency is important for obtaining a reliable clinical examination and adequate signals for tomography, the presence of ERM is easy to detect due to its hyperreflectiveness. The use of SD-OCT has increased sensitivity for detecting ERM. Clinical diagnosis of this complication was obtained only in 6 eyes, as compared with 31 eyes obtained with SD-OCT. Such a marked difference between biomicroscopy and indirect ophthalmoscopy as compared to tomography can be explained by the fact that patients with PP usually associate other more severe complications with greater visual repercussions. As this was a retrospective study, its intrinsic limitations involve not having clinical assessments by a single observer. It is likely that ERM are underdiagnosed or not taken into account as an important cause of visual loss in these patients. As in our environment this disease mainly affects pediatric patients, posterior segment examination could be laborious, leaving subtle details such as slight ERM unnoticed. It should be taken into account that many of these patients exhibited variable degrees of cataract of vitreous condensation which do not prevent an adequate view of the retina but increase the difficulty for an assessment thereof.

Risk factors for poor vision in patients with uveitis and ERM are the presence of ERM over the fovea, focal adhesions to the internal retina layers and alterations in the ellipsoid portion of photoreceptors, also known as the joining line of the external and external photoreceptor segments. Focal ERM adhesions have also been associated to higher ME frequency. However, there is no correlation between retina thickness and the visual acuity.

Additional complications observed in this study include the presence of VMTS, RD and RF. Both VMTS and RF can be considered as the different expressions of a same pathophysiopathological process observed in ERM. Malinowsky et al. separated slight and moderate ERM from severe ones, which were observed in 7 cases (6.5%). Said authors did not find a relationship between the degree of ERM and patient age, disease duration, choroidal neovascularization, cataracts or ME degree. This study found 3.3% of patients with RF, the equivalent of a severe ERM presentation.

The most significant limitation of this study is its retrospective nature. There is an important bias in considering that the clinical assessments were made by different observers within the CEIO. However, the FAA readings as well as the tomographic studies were carried out by a single observer (GSV). Other important bias factors were the exclusive inclusion of cases with an active inflammation and transparency of media, which means that the behavior of patients with active inflammation should also be measured. A prospective study comparing the response of ME resolution with surgical early removal of ERM, compared with medical treatment alone would be necessary. However, the results of this study did not justify a study of this nature. This is in contrast with the study by Dev et al. which retrospectively analyze the results of 7 patients with PP treated with vitrectomy for removal of ERM, who exhibited visual improvements.

To conclude, ERM is a frequent complication which should always be considered when examining patients with PP. Despite being a mechanical factor that could produce traction and inflammation on the internal layers of the retina, an association between the presence of ERM and ME could not be found. Accordingly, the results do not suggest that the medical management of patients with edema and posterior segment inflammatory diseases should be different. There is no evidence to consider a surgical approach as the first line of treatment in the presence of both complications.

Conflict of interests

No conflict of interests has been declared by the authors.

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