ACUTE POSTERIOR MULTIFOCAL PLACOID PIGMENT EPITHELIOPATHY. STUDY OF 16 CASES

EPITELIOPATÍA PIGMENTARIA PLACOIDE POSTERIOR MULTIFOCAL AGUDA. ESTUDIO DE 16 CASOS

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ABSTRACT

Objective: Acute Posterior Multifocal Placoid Pigment Epitheliopathy (APMPPE) is a rare disease with a probable inflammatory component which mostly affects young patients. The aim of our study was to analyse the demographic and clinical features of this disease in a group of 16 patients.

Methods: Sixteen patients with APMPPE were included in this study. We analyzed their demographic data (age, sex) and the most relevant clinical findings: visual acuity and retinal disease outcome, association with other systemic diseases and response to treatment. We also collected data from fluorescence angiography, autofluorescence and optical coherence tomography (OCT) in some of the patients.

Results: Average age at diagnosis was 26.75 years with no sex predilection. Average final visual acuity (Snellen Scale) in our study was 0.73. Four patients presented with a systemic disease related to the APMPPE. Eleven patients were treated with oral steroids (one patient with steroids and cytotoxic agents) while the remaining 5 patients received no treatment.

Conclusions: In our patients, the average age at diagnosis was less than 30 years, with no sex predilection, as previously described by many authors.

RESUMEN

Objetivo: La Epiteliopatía Pigmentaria Placode Posterior Multifocal Aguda (EPPPMA) es una enfermedad infrecuente que afecta a individuos jóvenes y de probable etiología inflamatoria. El objetivo del estudio es analizar las principales características clínicoepidemiológicas de esta enfermedad en una serie de pacientes.

Métodos: Se presenta un estudio retrospectivo de 16 pacientes diagnosticados de EPPPMA. Se han estudiado sus características demográficas (edad, sexo) y clínicas: evolución de la agudeza visual y del cuadro retiniano, enfermedades sistémicas asociadas y respuesta al tratamiento. Se han recogido datos angiográficos, autofluorescencia y tomografía de coherencia óptica (OCT) en algunos pacientes.

Resultados: La edad media en nuestra serie es de 26,75 años sin preferencias por el sexo. La media de agudeza visual final en nuestra serie ha sido de 0,73. Cuatro pacientes presentaron enfermedad sistémica asociada a la EPPPMA. 11 pacientes recibieron tratamiento con corticosteroides (un paciente corticoesteroides e inmunosupresores) y cinco no recibieron tratamiento.

Conclusiones: En nuestra serie la edad media se encuentra por debajo de los 30 años y no hubo diferencias en cuanto al sexo, siendo estos resultados congruentes con lo descrito en la literatura.
The visual outcome is usually good regardless of the treatment given, although there are cases with a bad visual outcome, especially those with foveal involvement when initially seen (Arch Soc Esp Oftalmol 2007; 82: 291-298).

Key words: acute posterior multifocal placoid pigment epitheliopathy, retinal pigment epithelium, choroid, fluorescein angiography, indocyanine green angiography, optical coherence tomography, systemic vasculitis.

INTRODUCTION

Described for the first time by Gass in 1968 (1), Acute Posterior Multifocal Placoid Pigment Epitheliopathy (APMPPE) is a rare ailment with a potentially inflammatory etiology characterized by the emergence of several converging placoid injuries, white-yellowish in color, which involve the retinal pigment epithelium (RPE) and is preferably located at the posterior pole.

This disease tends to affect young individuals, usually under 30 years of age, and affects both genders equally. APMPPE’s initial symptoms include the rapid loss of visual acuity with central or para-central scotoma.

Other symptoms may also appear, such as myodesopsias and photopsias.

It is generally considered to be a disease with favorable prognosis, with resolution of injuries along the posterior pole in days or weeks and a good recovery of visual acuity, although there are cases with worse prognosis and a poor final visual outcome, especially in those cases where the fovea is prematurely compromised, onset in aged individuals or atypical manifestations (such as papillitis, retinal vasculitis, retinal vein occlusions, etc). (2,3).

APMPPE’s etiology is not well-known although there are many hints that suggest a potentially inflammatory nature. Temporary symptoms and the relatively frequent associations with previous prodomic viral conditions (above all those affecting the upper respiratory tract) have led several authors to consider APMPPE as an inflammatory disease at the RPE level or the superficial choroids. The characteristic premature hypofluorescence of injuries revealed in the fluorescein angiography and especially in the Indocyanine green angiography (4) suggest the presence of a choroidal ischemia, perhaps secondary to a choroidal vasculitis as the disease’s main mechanism. This hypothesis is supported by several associations described for APMPPE with different types of systemic vasculitis such as Wegener’s disease (5), sarcoidosis, cerebral vasculitis (6) and other conditions of stimulation of the immune system such as infections or reactions to vaccination.

Generally, this disease does not require treatment, although corticosteroids are usually prescribed in those cases presenting extensive injuries on the posterior pole, bilateral cases and cases involving the macula. Recurrence is rare but when it does occur it usually signals the worse prognosis.

SUBJECTS, MATERIAL AND METHODS

This retrospective study included 16 patients (26 affected eyes) diagnosed with APMPPE.

The purpose of this study is to explore these patients’ main epidemiological traits (age, gender), as well as their clinical traits: visual acuity and its evolution during follow-up, bilaterality rate, number of outbreaks during follow-up, potential associations with systemic diseases (as already explained in the previous section) and response to treatment. Angiographic findings and optical coherence tomography (OCT) were also assessed in those patients who were subjected to complementary explorations.
RESULTS

According to the results obtained during the follow-up of this series of 16 patients, it became clear that age at the time of diagnosis was below 30 years. The mean age in our series was 26.75 years, the youngest patient being 13 years old at the time of diagnosis and the eldest 44 years old.

No differences were found in terms of gender distribution: eight of the 16 patients were male (50 percent of patients) and the remaining eight were female (50 percent of patients). As for the distribution by age based on gender, again differences were not particularly significant although a certain tendency to a more premature debut of the illness was recorded among women, whose mean age was 24.65 years with respect to the mean age for diagnosis at 28.87 years for males.

As for the bilaterality of this illness, nine patients exhibited affection only in one eye, whereas the remaining seven showed alterations in both eyes. Out of these seven patients with bilateral affection, five presented bilateral affection at the time of diagnosis (figs. 1-4) and 2 began with a unilateral outbreak which soon bilateralized.

The average of outbreaks clinically well distinguished in time during progression was 1.44. Most patients (12 out of 16 patients) suffered one single outbreak, whereas two patients suffered two outbreaks and two patients suffered three and four outbreaks respectively during follow-up.

The time lapsed between outbreaks in those patients presenting more than one outbreak varied, ranging from 2 weeks to 5 years between outbreaks.

Figs. 1 to 4: Case 7: Images above: simultaneous bilateral involvement in both eyes during its active stage. Images below: self-fluorescent images revealing the RPE hypoautofluorescence in active inflammatory areas.
As for the patients' visual acuity (VA), VA results at the beginning of the outbreak and upon follow-up completion are summarized in Table I.

Total duration of the follow-up varied greatly, ranging from 1.5 months to 6 years. Final VA was defined as the VA exhibited by the patient whose retinal condition had completely stabilized, that is, pigmented injuries along the posterior pole with a scarred look and no sign of activity. A tendency to generally slight losses of visual acuity were observed, recovery was good and the mean VA on the Snellen scale at the time of the active outbreak was 0.45 and 0.73 at the end of follow-up, once the disease has become inactive.

Thus, at the time of diagnosis, around 47.61 percent of patients presented a VA lower than 0.5 whereas the remaining 52.38 percent had a VA equal to or greater than 0.5. At the end of follow-up, 78.26 percent of patients had recovered a vision of 0.5 or more whereas 21.73 percent retained a VA below 0.5.

Of the 16 patients, 12 did not show any systemic disease which could be linked to his/her ocular ailment, nor before nor after being diagnosed with APMPPE. Three patients exhibited a non-specific viral condition with fever and discomfort weeks prior to the APMPPE outbreak, progressing in one case with an increase in the sedimentation speed and erythema nodosum in the lower extremity. Another case was diagnosed with systemic vasculitis with positive c-ANCA based on the initial APMPPE diagnosis, but a biopsy of the nasal mucosa was negative for Wegener’s disease. This specific case presented the most difficulties in terms of therapeutic control, since the patient suffered four outbreaks very close to one another with a rapid progression of the disease which could only be controlled with immunosuppressants treatment (Prednisone, Methotrexate and bolus doses of Cyclophosphamide), although final VA was good, 1.2 and .9 in the RE and LI, respectively (figs. 5 to 10).

As for the treatment prescribed for these patients, five were not prescribed any treatment, nine patients were treated exclusively with oral corticosteroids (generally with 1mg/kg/day decreasing pattern), one patient was administered oral Prednisone plus one Subtenon Triamcinolone injection and another patient required multiple treatment with immunosuppressants (Prednisone, Methotre xate and bolus doses of Cyclophosphamide) in order to bring the disease under control.

Of the eyes treated, the final mean VA was 0.68, whereas those eyes untreated recorded 0.81.

A fluorescein angiography (FAG) was performed on 12 of the 16 patients during the disease’s active stage.

All patients showed to one extent or the other the typical pattern of FAG for APMPPE, with injury hypofluorescence in premature times due to the screen effect possibly caused by inflamed cells in the retinal pigment epithelium (RPE) and to the choroidal hypoperfusion. At later times in the FAG, a diffuse hyperfluorescence pattern appears along the injuries. During the disease’s inactive stage, angiographic findings are not as characteristic and reveal a diffuse hyperfluorescence without loss of contrast due to the window effect derived from the RPE atrophy in the injured areas.

One patient underwent an Indocyanine green angiography (figs. 11 to 15) where the characteristic choroidal hypoperfusion can be observed at the injury level.

Four out of 16 patients underwent an optical coherence tomography (OCT). The literature describes the presence of hyperreflectivity in the outer layers of the retina without an increase in retinal thickness at the level of the active plaques (7), although in our case no significant differences were

<table>
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<th>Case</th>
<th>VA at outbreak onset</th>
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The table shows visual acuity (VA) in the RE and LE for the 16 patients at the onset of the first outbreak and the final VA at the end of follow-up. The VA for the affected eyes appears in bold case, and in regular font those eyes which presented no outbreak during follow-up. Some unilateral cases at the onset of the disease bilateralized in time (cases 1 and 14), whereas there were only 5 bilateral cases from the start (cases 5, 7, 12, 13 and 15) and 9 unilateral cases (cases 2, 3, 4, 6, 8, 9, 10, 11 and 16).
Figs. 5 to 10: Case 14: Images above: appearance of the eye fundus in the RE and LE respectively during the first outbreak of the disease. Images in the middle: appearance of the eye fundus after 20 days. The appearance of injuries in the LE are clearly noticeable in their different stages, a typical trait in APMPPE; whereas the first injuries begin to pigment and exhibit a scarred look, appearing active injuries in the periphery of former injuries. Images below: appearance of the eye fundus once the condition has stabilized in both eyes. Injuries are already fully scarred and the patient’s VA is 1.2 and .9 in the RE and LE respectively.
no observed between the tomographic appearance of the healthy retina versus the affected retina.

**DISCUSSION**

The data obtained confirm the tendency described in the literature regarding the onset of APMPPE at early ages. According to our data, the mean age for onset was 26.75 years, a common factor in most checkups (8).

Similarly, no gender preference was observed for APMPPE. It is generally accepted that in most cases APMPPE is a bilateral ocular disease. Nevertheless, in the present series more than half of all cases (56.25 percent) were affected in a single eye. This might be due to the brief follow-up period for some patients, since affection of the contralateral eye may take place within months or even years after the first outbreak. Even so, frequently bilateralization, if not immediate, takes place after a little while, usually weeks, which might lead us to think that the rate of unilateral affection is not as unusual as previously described in the literature, at least in view of our findings.

The series also shows a tendency to a good VA recovery, in some cases the VA present before the outbreak being reestablished. This favorable visual prognosis is considered typical of the APMPPE, although one need to take into account that some of these patients do not recover a good VA. The main prognosis factor observed to predict a poor visual final result in our patients was affection of the fovea at the time of diagnosis.

As already pointed above, there are cases where systemic associations have been drawn with APMPPE. Of the 16 cases under study, only three patients clearly presented a viral condition prior to diagnosis and one patient was diagnosed with a systemic vasculitis of unknown origin.

Eleven patients were prescribed anti-inflammatory treatment (nine patients were administered oral corticosteroids, one patient Subtenon Triamcinolone + oral corticosteroids and another patient was administered corticoids and immunosuppressants) whereas five patients did not receive any
According to the observed results in the series, those patients who did not undergo treatment recorded the best VA (the mean VA was 0.81 versus a mean VA of 0.68 in those patients who did receive treatment). Although these findings may seem contradictory at first glance, it is possibly due to the fact that those cases were the ones with the worse initial prognosis (for instance, cases with foveal involvement) and were prescribed a steroid treatment, and thus the final visual outcome was more influenced by the initial fovea affection than by the treatment prescribed. Even so, several authors recommend administering corticosteroids due to the potential inflammatory nature of the disease, especially in those cases with poor initial visual acuity, manifestations with very extensive injuries and atypical manifestations of the disease (9).

REFERENCES