

Unilateral acute posterior multifocal placoid pigment epitheliopathy in a patient with a strongly positive purified protein derivative test

Epiteliopatia pigmentar placóide multifocal posterior aguda unilateral na presença de reação forte positiva para o teste tuberculínico

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ABSTRACT | A 27-year-old man presented with a complaint of decreased visual acuity in the right eye. Best-corrected visual acuity was 20/60 in the right eye and 20/20 in the left eye. Right eye funduscopy revealed mild vitritis, multifocal yellowish lesions, and macular serous retinal detachment. Left eye evaluation was normal. Acute posterior multifocal placoid pigment epitheliopathy was diagnosed in the right eye. Complementary exams revealed a strong reaction to the *Mycobacterium tuberculosis* purified protein derivative test, thus treatment for tuberculosis was initiated. Baseline fluorescein angiography of the right eye revealed early hypofluorescence and late staining of the lesions. Optical coherence tomography of the right eye demonstrated the accumulation of subretinal and intraretinal fluid associated with cystoid macular edema. During follow-up, the retinal fluid and cysts disappeared, which was followed by disorganization of foveal interdigitation and ellipsoid zones. This is the second described case of unilateral acute posterior multifocal placoid pigment epitheliopathy in a patient with a strong positive result to the *M. tuberculosis* purified protein derivative test.

Keywords: Tuberculin test; *Mycobacterium tuberculosis*; Uveitis, posterior; Tuberculin; Tomography, optical coherence; Fluorescein Angiography; Retinal diseases; Humans; Case report

RESUMO | Um homem de 27 anos apresentou uma queixa de diminuição da acuidade visual no olho direito. A acuidade visual melhor corrigida foi 20/60 no olho direito e 20/20 no olho esquerdo. A fundoscopia do olho direito revelou vitreíte leve, lesões amareladas multifocais e descolamento seroso da retina em região macular. A avaliação do olho esquerdo foi normal. Epiteliopatia pigmentar placóide multifocal posterior aguda foi diagnosticada no olho direito. Os exames complementares revelaram forte reação ao teste do derivado proteico purificado *Mycobacterium tuberculosis*, iniciando terapia antibiótica contra tuberculose. A angiografia fluoresceínica basal do olho direito revelou hipofluorescência precoce e tardia das lesões. A tomografia de coerência óptica do olho direito demonstrou fluido sub- e intrarretiniano associado a edema macular cistóide. Durante o seguimento, os fluídos e cistos retinianos desapareceram, seguido da desorganização das zonas de interdigitação e elipsóide em região foveal. Este é o segundo caso descrito de epiteliopatia pigmentar placóide multifocal posterior aguda unilateral em um paciente com um forte resultado positivo para o teste tuberculínico.

Descritores: Teste tuberculínico; *Mycobacterium tuberculosis*; Uveíte Posterior; Tuberculina; Tomografia de Coerência Óptica; Angiofluoresceínografia; Doenças retinianas; Humanos; Relato de caso

INTRODUCTION

Acute posterior multifocal placoid pigment epitheliopathy (APMPPE) is an idiopathic disease likely associated with an altered immune response to an infectious agent⁽¹⁾. It that was first described by Gass in 1968 as a sudden bilateral decrease of visual acuity in young patients following flu-like symptoms⁽²⁾. In most cases, despite the persistence of visual field defects and the risk of disease

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recurrence, the prognosis of APMPE is favorable with a good visual outcome and total resolution of retinal and choroidal lesions⁽²⁾.

On fluorescein angiography (FA), acute lesions have a pattern of early hypofluorescence and late staining, which becomes hyperfluorescent in the subacute and healed stages due to retinal pigment epithelium (RPE) atrophy. Following resolution, lesions may persist as hypoautofluorescent or may become hyperautofluorescent (occurrence of lipofuscin deposition and/or RPE dysfunction)⁽³⁾. Spectral-domain optical coherence tomography (SD-OCT) shows, at disease onset, elevations to the ellipsoid zone (EZ) corresponding to the placoid lesions that overlay the accumulation of subretinal fluid and material. Disorganization of the RPE and outer retinal layers may also be observed over the course of the disease⁽⁴⁾.

Although its etiology is unknown, a great range of conditions is reported to be associated with APMPE, such as vaccination and sarcoidosis^(5,6). Here, we report multimodal image findings of unilateral APMPE in a patient with a strong reaction to the *Mycobacterium tuberculosis* purified protein derivative (PPD) test.

CASE REPORT

A 27-year-old black Brazilian man complained of a 5-day duration of decreased visual acuity in his right eye, but no ocular pain or flu-like symptoms. Ocular and medical history, including recent vaccination and contact with animals, were unremarkable. He denied contact with someone with active tuberculosis but had close contact with a 2-year-old child under pediatric investigation for a 2-month duration of a persistent cough. On ocular examination, best-corrected visual acuity (BCVA) was 20/60 in the right eye and 20/20 in the left eye. Pupillary reactions, slit-lamp biomicroscopy, and intraocular pressure were normal. Right eye fundus examination revealed 1+ vitreous cells and creamy multifocal lesions between the temporal vascular arcades that were associated with macular serous retinal detachment. FA of the right eye demonstrated early hypofluorescence and late staining lesions. Right eye SD-OCT (Cirrus HD-OCT; Carl Zeiss Meditec, Dublin, CA, USA) revealed the accumulation of subretinal and intraretinal fluids associated with cystoid macular edema. Dome-shaped elevation of the EZ was also observed within the macular area (Figure 1). Multimodal imaging of the left eye was normal.

Laboratory tests revealed elevation of C-reactive protein and normocytic-normochromic anemia with a nor-

mal leukocyte count. Serologies for syphilis, cytomegalovirus, herpes simplex virus, human immunodeficiency virus, *Bartonella*, *Histoplasma capsulatum*, *Toxoplasma gondii*, *Toxocara canis*, and *Borrelia burgdorferi* were negative. The result of the *M. tuberculosis* PPD skin test was strongly positive (20 mm of induration). Computed tomography of the chest was normal and no scarring of prior Bacillus Calmette-Guérin vaccination was observed. Tuberculosis therapy was initiated (RIPE scheme-2 months of rifampin, isoniazid, pyrazinamide, and ethambutol, followed by 4 months of rifampin and isoniazid) in combination with a 2-month tapering dose of oral prednisone (60 mg).

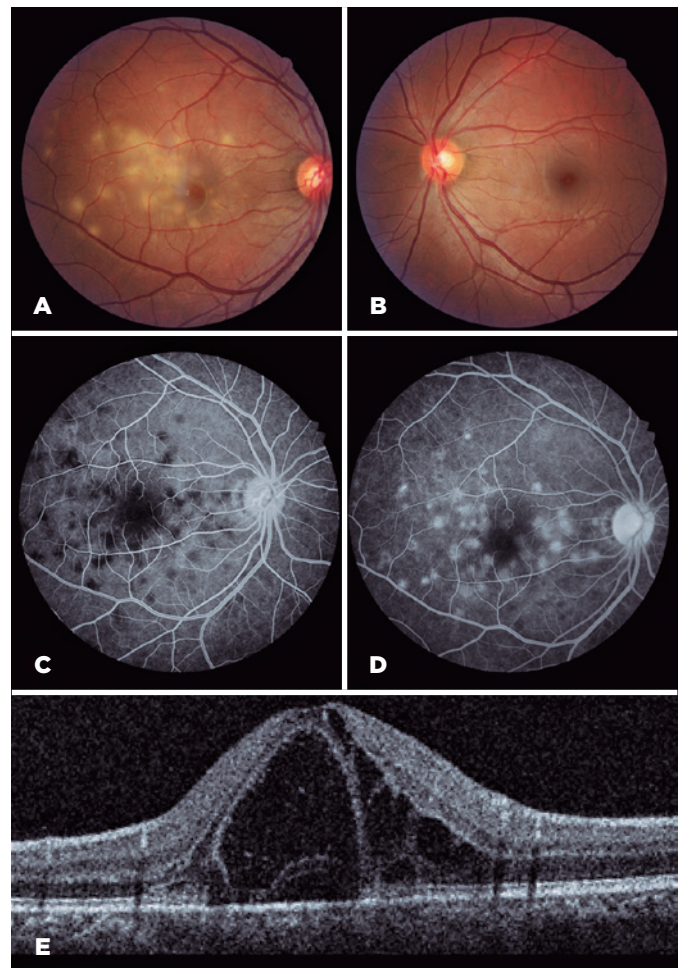


Figure 1. (A) Baseline color fundus photograph of the right eye showing multifocal and creamy lesions associated with serous retinal detachment within the macular area. (B) Color fundus photograph of the left eye was normal. (C and D) Fluorescein angiogram of the right eye revealed early hypofluorescence and late hyperfluorescence of the corresponding lesions, as demonstrated in the color photograph. (E) Optical coherence tomography of the right eye showing dome-shaped elevation of the EZ, subretinal, and intraretinal fluid associated with cystoid macular edema.

Four months after treatment, right eye BCVA improved to 20/40, and there was a significant decrease in the extent of the lesions, which became grayish-green and less delimited. FA showed early hyperfluorescent spots and maintenance of late hyperfluorescence. On SD-OCT, the intraretinal and subretinal fluid resolved, and the foveal interdigitation zone (IZ) and EZ were disrupted (Figure 2). At a 6-month follow-up, BCVA was 20/20 and the fundal lesions were reduced in number and size. SD-OCT revealed a normal appearance of the EZ and IZ (Figure 3).

DISCUSSION

APMPPE is an idiopathic disease that typically manifests in young adults as bilateral acute vision loss,

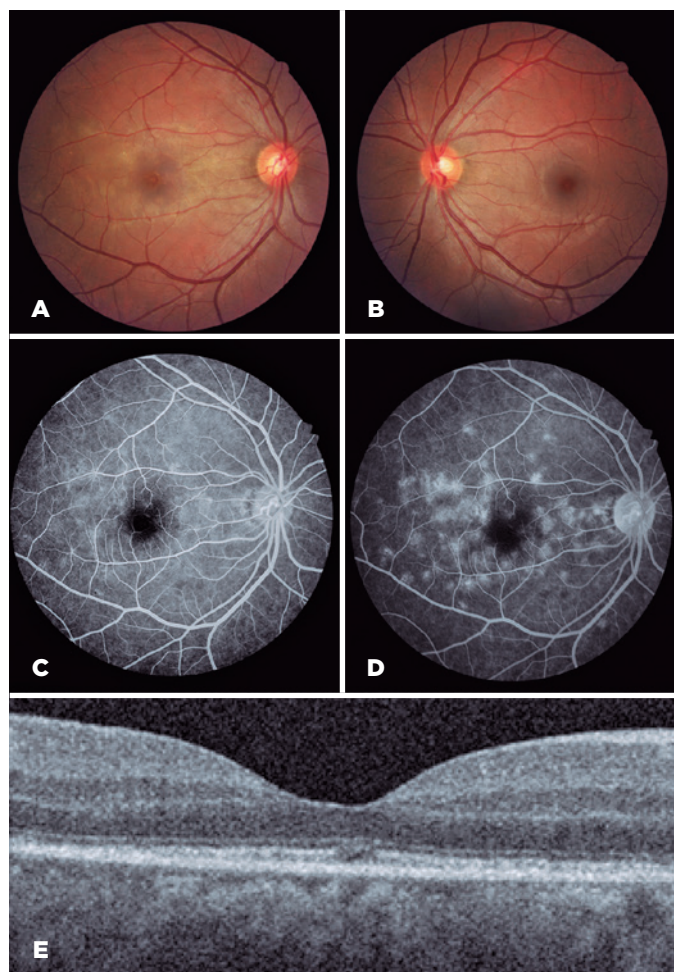


Figure 2. (A and B) At a 4-month follow-up examination, color fundus photography of the right eye demonstrated a decrease in the extent of the yellowish-white lesions. (C and D) Fluorescein angiogram of the right eye showing early hyperfluorescent spots and maintenance of late hyperfluorescence. (E) Optical coherence tomography of the right eye showing complete resolution of the intraretinal and subretinal fluid, but with interdigitation and EZ disruption in the fovea.

scotomas, photopsia, and metamorphopsia, preceded by a viral prodrome⁽²⁾. In the present case, the clinical features of disease presentation corresponded to the characteristics of APMPPE. A diagnosis of APMPPE was confirmed after exclusion of other infectious/inflammatory retinal and choroidal diseases. Since a laboratory investigation revealed a strong reaction (20 mm) to the PPD test, presumed intraocular tuberculosis was considered a possible differential diagnosis in this case. The use of the interferon-gamma release assay (IGRA) in endemic countries has demonstrated similar sensitivity and specificity to that of the PPD test. The combination of both may increase the specificity for the detection of ocular tuberculosis and is considered the most cost-effective strategy⁽⁷⁾. Unfortunately, the IGRA test was not available in the present case. However, the patient's clinical features, the strong reaction to the PPD test, and the treatment response reinforced tuberculosis as a possible differential diagnosis.

Intraocular tuberculosis has a wide spectrum of presentations, and despite new diagnostic approaches, laboratory confirmation remains challenging⁽⁸⁾. Serpiginous-like choroiditis due to tuberculosis may mimic APMPPE with multifocal choroidal lesions at the posterior pole⁽⁹⁾. This form of tuberculosis is very different from

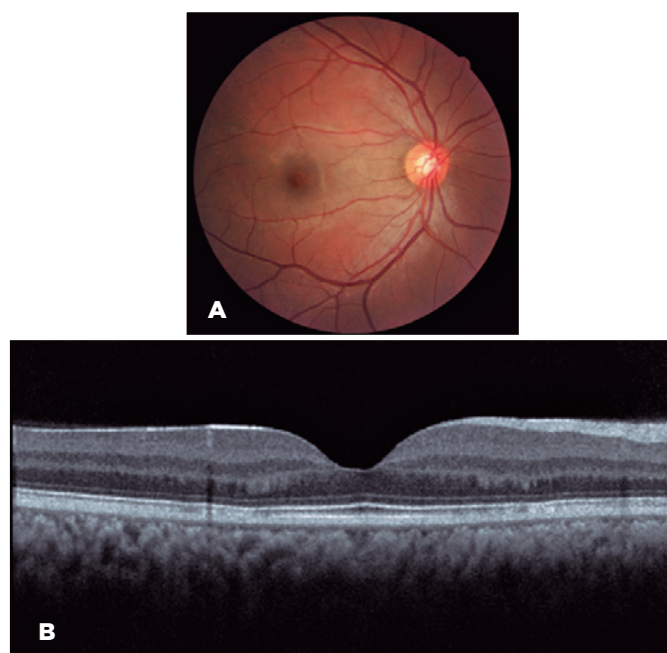


Figure 3. (A) At a 6-month follow-up, color fundus photography of the right eye showing a significant reduction in number and size of placoid lesions, which were almost absent. (B) Optical coherence tomography of the right eye showing complete resolution of the intraretinal and subretinal fluid, but with interdigitation and the normal appearance of the EZ had returned to normal.

APMPPE since it is often associated with severe vitritis, the lesions present at different stages of inflammatory activity, and healing with marked sequelae. Conversely, our case demonstrated mild vitritis and retinochoroidal lesions of the same inflammatory stage that healed without leaving marked sequelae. In some cases, fundoscopic features of APMPPE may also resemble the acute phases of punctate inner choroidopathy (PIC). However, on FA, the PIC lesions show early hyperfluorescence with staining in late phases. Furthermore, upon healing, the lesions leave atrophic and deep scars with depigmented halos that are often associated with subretinal neovascular membranes⁽¹⁰⁾.

Recent studies have shown various stages of retinal morphologic changes in APMPPE, specifically in the RPE and outer retina⁽⁴⁾. At presentation, SD-OCT demonstrates dome-shaped elevations of the EZ band associated with hyperreflective material and subretinal fluid accumulation. Over time, the dome-shaped lesion flattens and the EZ, RPE, and outer nuclear layer show hyperreflectivity followed by thinning. The resolution phase starts at 3 months with the reformation of the outer retina and minor RPE irregularities. At baseline, our case showed dome-shaped elevations of the EZ band associated with a considerable accumulation of intraretinal and subretinal fluids within the macular area, compatible with the acute phase of APMPPE. At a 4-month follow-up, retinal fluids were reabsorbed, and the foveal EZ and IZ appeared disorganized. At a 6-month follow-up, SD-OCT demonstrated complete reformation of the EZ and IZ.

Although the etiology of APMPPE is obscure, it seems to be associated with a delayed type hypersensitivity reaction to an infectious agent⁽¹¹⁾. The significance of a positive PPD test is unknown, but it is reasonable to believe that APMPPE may be triggered by an immunological hypersensitivity reaction to *M. tuberculosis*. Interestingly, two of the first three APMPPE cases reported by Gass had positive PPD test results, but no evidence of pulmonary disease⁽²⁾. Additional studies are necessary to better understand the relationship between APMPPE and positive PPD test results. It is difficult to determine

whether antibiotic therapy and the use of oral corticosteroids affected the course of the disease in our case.

We are aware of only one case of unilateral APMPPE in a patient with a positive PPD test result⁽¹²⁾. Moreover, this is the first report of SD-OCT and FA findings in unilateral placoid lesions and seems to not differ from those bilateral cases. The present case highlights the importance of careful investigation of *M. tuberculosis* infection in APMPPE, even with atypical features.

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