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Bacillary layer detachment in serpiginous-like choroiditis of presumed intraocular tuberculosis: Report of two cases

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ABSTRACT

Purpose: To describe the presence of bacillary layer detachment (BALAD) in serpiginous-like choroiditis (SLC) in presumed intraocular tuberculosis.
Observations: Clinical and multimodal imaging including fundus photography, fundus autofluorescence, and spectral domain and enhanced-deep imaging optical coherence tomography (OCT) of two cases of SLC in presumed intraocular tuberculosis. Two patients (26 and 38-year-old woman) presented with unilateral, decreased vision of acute onset. They were diagnosed with SLC in presumed intraocular tuberculosis, and OCT revealed splitting of the ellipsoid zone, resembling BALAD. All two patients showed complete resolution after treatment with antitubercular therapy (ATT).
Conclusions and Importance: BALAD appears in the acute stage of SLC in presumed intraocular tuberculosis and resolves rapidly at the beginning of ATT.

1. Introduction

Tuberculosis is an infectious disease of worldwide capital importance. It is the leading cause of death from a single infectious agent worldwide. The World Health Organization estimates that approximately a quarter of the world's population is infected with *Mycobacterium tuberculosis*.[1]

Intraocular tuberculosis produces a wide spectrum of clinical signs, including anterior granulomatous uveitis, chronic anterior uveitis, intermediate uveitis, retinal vasculitis, serpiginous-like choroiditis (SLC), choroidal granuloma, and panuveitis.[2]

The diagnosis of intraocular tuberculosis is often presumptive. Confirmatory test results, such as the demonstration of acid-fast bacilli, culture of *M. tuberculosis*, or histopathologic evidence, are seldom available from ocular specimens. Presumed tubercular uveitis is diagnosed in patients with supportive clinical findings and a positive clinical response to antitubercular therapy (ATT) with no recurrence of inflammation thereafter.[2]

SLC is a multiple choroidal lesion with outer retinal and inner choroidal involvement progressing in the serpentine aspect, unlike classical serpiginous choroiditis (SC), lesions do not start from the optic disc, and they are generally multifocal in nature, associated with vitritis, and affect younger adults.[3]

The bacillary layer is synonymous with the retinal photoreceptor layer and represents the inner and outer segments of the photoreceptor unit. Bacillary layer detachment (BALAD) has been described in sparse reports and represents a possible separation between the myoid and ellipsoid components of the inner segment, following injury or insult to the outer retina.[1,2]

The presence of BALAD has been identified on optical coherence tomography (OCT) in inflammatory or infiltrative lesions of the choroid, which decreases the perfusion of the outer retina.[4,5] BALAD has been reported in retinochoroiditis due to toxoplasmosis, infiltratory choroidal granuloma in Vogt-Koyanagi-Harada disease, pachychoroid-associated serous chorioretinopathy, trauma, acute posterior multifocal placoid pigment epitheliopathy, and tubercular choroidal granuloma.[5]

We report the presence of BALAD in two cases of SLC in presumed intraocular tuberculosis with a retinal detachment that apparently separated the photoreceptor inner segment myoids from the inner segment ellipsoids, possibly exacerbated by the acute stage of inflammation.

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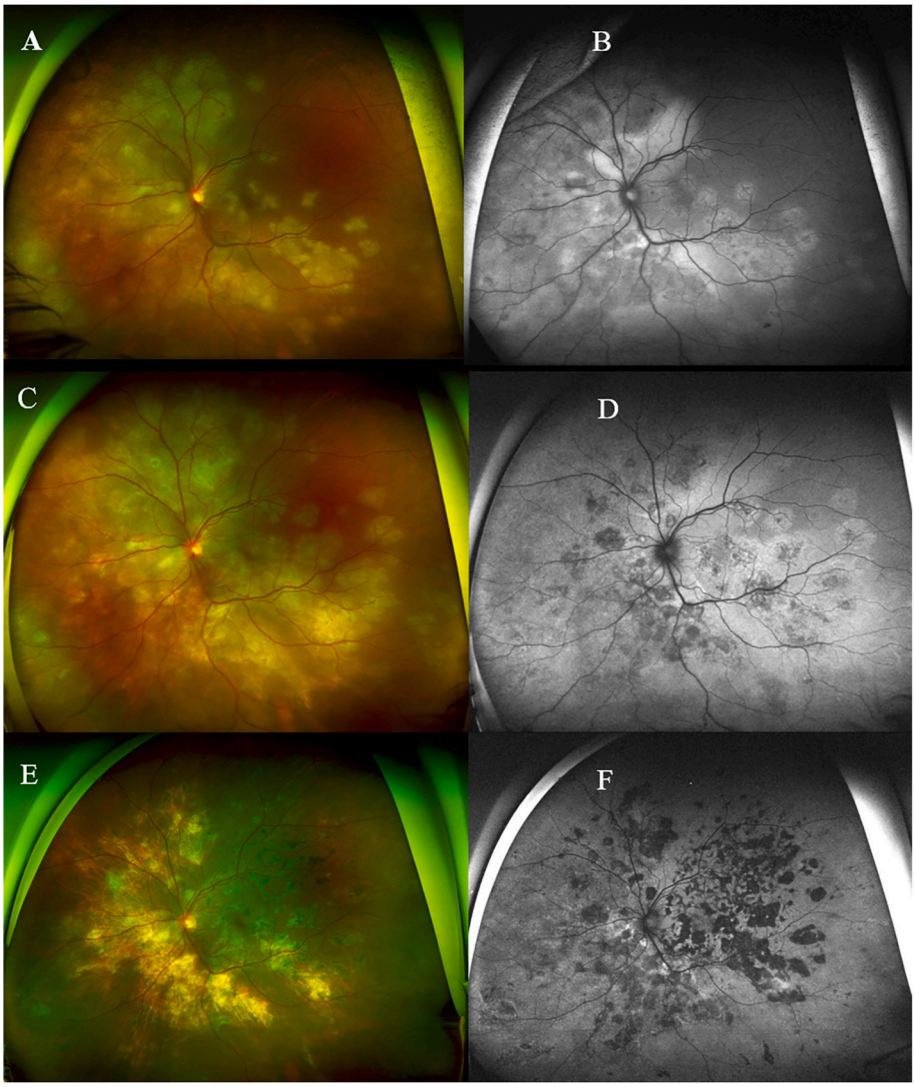

Fig. 1. (A) Ultra-wide-field fundus retinography of the left eye of the patient in case 1, at presentation showing multiple deep ill-defined yellowish lesions, from the optic disc toward the posterior pole and nasal retina
(B) Ultra-wide-field autofluorescence showing multiple hyperfluorescent diffuse lesions, corresponding active lesions. (C, D) Retinography after 1 month without treatment showing more active lesions. (E) The pigmented lesions after 2 months of treatment. (F) The lesions show total hypoautofluorescence after healing.

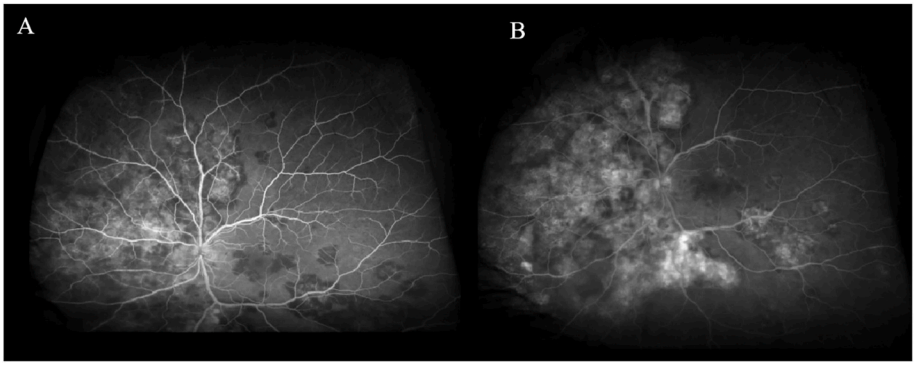

Fig. 2. Ultra-wide-field fluorescein angiography at presentation. In the early phase (A) the multifocal lesions show early hypofluorescence with late hyperfluorescence (B) indicating active choroidal inflammation.

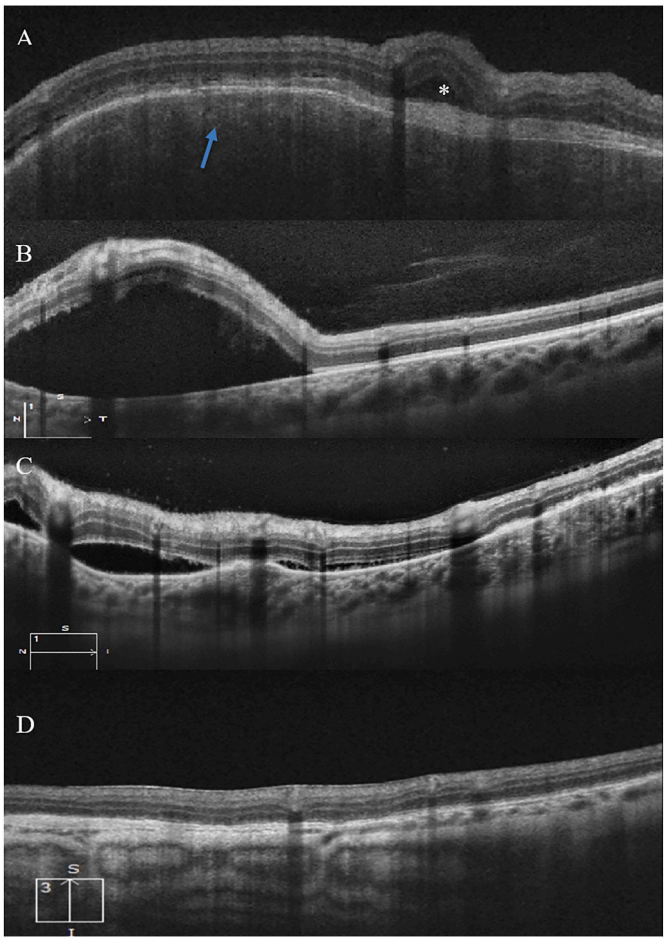

Fig. 3. Optical coherence tomography at presentation. (A) In the scan at the nasal retina, there is presence of BALAD (white asterisk). The outer retina split occurs at the level of the hyporreflective myoid zone (MZ) leaving the remaining photoreceptor layers adherent to subretinal hyperreflective material anterior to the retinal pigment epithelium (RPE)-basal lamina-Bruch membrane complex at the base of the BALAD. A choroidal lesion is causing an elevation of the retina (blue arrow). (B) A dome-shaped cystic retinal hyporreflective space superiorly to the macula. (C) Subretinal fluid accumulation is observed inferiorly to the macula. (D) Optical coherence tomography at 2 months of follow-up, shows a resolution of the BALAD and a hyperreflective material is noted over the RPE. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

2. Case 1

A 26-year-old healthy White woman, from Rio de Janeiro, Brazil, presented with decreased vision in her left eye (OS) associated with photopsias and headache for the past 10 days. At presentation, the best corrected visual acuity (BCVA) was 20/20 in the right eye and counting fingers in the left eye. Slit-lamp examination showed no anterior segment inflammation in the right eye and 2+cels in the anterior chamber of the left eye. The intraocular pressure was 14 mmHg bilaterally. Fundoscopy of the left eye and multimodal imaging are described in Figs. 1A, 2A and 2B, and 3A, 3B and 3C. We conducted VDRL, FTA-ABS, sorology for toxoplasmosis, sorology for human immunodeficiency virus, and chest computer tomography, and found that these test results were normal, but the tuberculin skin test (TST) was performed with a size 17mm. The diagnosis of SLC due to presumed intraocular tuberculosis was made based on a positive TST, aspect of the lesions, and good response to ATT and systemic steroids. Following treatment, the lesions healed completely at 2 months of follow-up (Fig. 1E–F).

Spectral domain OCT performed 2 months later demonstrated resolution of the serous retinal detachment and clinical improvement of the lesions as visual acuity in the left eye to 20/40 (Fig. 3D).

3. Case 2

A 38-year-old woman presented with a history of progressive visual loss in her left eye for 1 month. The medical history was relevant for pulmonary tuberculosis treated 10 years before. At presentation, her BCVA was 20/20 in the right eye and counting fingers in the left eye. There were 2+ cells in the anterior vitreous of the left eye. There were no signs of inflammation in the anterior chamber. The intraocular pressure was 16 mmHg in both eyes. Fundoscopy of the left eye and multimodal imaging are described in Figs. 1A, 2A and 2B, and 3A and 3B. The QuantiFERON-TB Gold test results were positive. The tuberculin sensitivity test (TST) was positive with a 15mm induration. Tests for toxoplasmosis, syphilis, and human immunodeficiency virus were negative. Treatment with rifampicin, isoniazid, pyrazinamide, ethambutol and prednisone (60mg/day) was initiated. After 7 days, the visual acuity was 20/200 (Figs. 4B and 5C). At the 14-day follow-up visit, the visual acuity improved to 20/80 (Fig. 4C) and no signs of intraocular inflammation were observed on biomicroscopy. After 45 days of treatment, the visual acuity was 20/60 (Figs. 4D, 5D and 6C).

4. Discussion

Bacillary detachment, considered as intra-retinal splitting, has been demonstrated to occur at the level of the EZ, which was named the bacillary layer by neuroanatomist Polyak in 1941.[4,15] Moreover, Mehta et al. also demonstrated artefactual retinal detachment in histological specimens. They reported splitting of the bacillary layer at the level of the myoid, the OCT findings of which were similar and corroborated to the BALAD seen in our cases.[6,9,11,15]

Freund et al. postulated that the main pathophysiological mechanism in BALAD is comparable to exudative retinal detachment and involves breakdown of the retinal pigment epithelium (RPE) component of the outer blood-retina barrier, leaving the external limiting membrane (ELM) component intact.[15]

In the patients reported herein, multimodal imaging revealed a large, dome-shaped retinal detachment with a continuous hyperreflective line at the level of the EZ in two patients with SLC in presumed intraocular tuberculosis.[8]

In the face of an inflammatory choroidopathy in a young female patient without comorbidities, tuberculosis is a possible diagnosis, considering that intraocular tuberculosis with involvement of the posterior segment can show a spectrum of manifestations, including a serpiginous-like one.[7]

Ocular inflammation due to tuberculosis occurs either because of direct invasion by the tubercle bacilli or because of an immunogenetic reaction due to the extraocular infective foci. Ocular tuberculosis manifests as heterogeneous clinical findings that can involve various ocular structures. The diagnosis of ocular tuberculosis is often delayed because

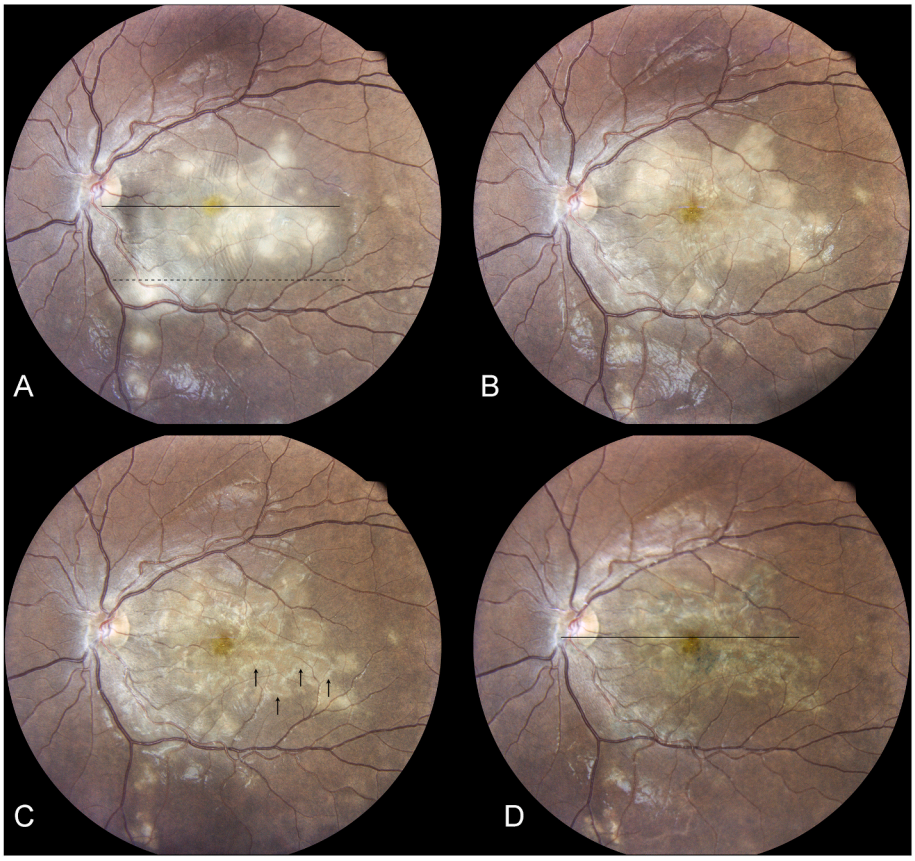

Fig. 4. Confocal digital fundus retinography of the left eye of patient 2. (A) At presentation, the fundus photograph showing deep ill-defined multifocal and confluent yellowish lesions involving the macula. A choroidal lesion is causing an elevation of the retina (white arrow) (B) and (C) at 7 and 14-day follow-up, respectively. The border of the lesions becomes progressively more distinct, and an amoeboid-like pattern can be noted (arrows). (D) At 45-day follow-up the healing of these lesions is evident. Irregular retina pigment epithelium (RPE) perturbations, diffuse RPE mottling with extensive atrophy of RPE and choriocapillaris are observed.

of its protean ocular manifestations that can mimic other uveitis entities. Intraocular tuberculosis produces a wide spectrum of clinical signs, including anterior granulomatous uveitis, chronic anterior uveitis, intermediate uveitis, choroiditis, SLC, retinal vasculitis, choroidal granuloma and panuveitis.[7,12]

Fluorescein angiography is capable of identifying active lesions that present early hypofluorescence with late hyperfluorescence.

The patient (case 1) had a diffuse choroiditis with yellowish-white, subretinal lesions scattered on the posterior pole and nasal peripapillary region showing the centrifugal spread characteristic of SC. The posterior location of retinal lesions and the presence of vitritis account for poor vision at presentation. Patient 2 presented with multiple peripheral hyperautofluorescent lesions observed on ultra-wide-field autofluorescence retinography, with a pattern mimicking multiple evanescent white dot syndrome (MEWDS) (Fig. 6C and 6D). These lesions completely resolved, with no visible sequelae. This MEWDS-like retinal response may represent an epiphenomenon, and it has been described in various inflammatory, infectious and neoplastic conditions.[13,14]

Elevations of the RPE have been described before in cases of tuberculous SLC.[16]

The choroiditis in the SLC phenotype is explained by the presence of the *Mycobacterium tuberculosis* in the choroid after a hematogenous spread of the disease. The bacilli in the choroid lead to an immune-mediated hypersensivity reaction which may either be focal or diffuse. The focal reaction is related to the RPE elevation observed with OCT, as seen in patient 2. In some patients, especially those not treated with antibiotic therapy, the focal lesions may become confluent and be responsible for a diffuse choroiditis which can present an advancing edge that resembles serpiginous choroiditis.[17] The presence of BALAD is a novel finding in patients with tuberculous SLC.

In SLC due to presumed ocular tuberculosis, intraocular inflammation was controlled with the use of ATT as soon as the diagnosis was suspected in case 2 (Fig. 4A and 4B). In case 1 the patient had a worsening of the lesions, due to the delay in starting ATT treatment (Fig. 1C, and1D). Unlike what one sees in the lesions of idiopathic SC, the tuberculous lesions tend to not recur after the ATT treatment.[9,10]

Aggressive chorioretinal inflammation, choroidal thickening and accumulation of fluid may lead to splitting detachment occurring at the level of the MZ, resulting in BALAD.[5]

Litts et al. histologically observed mitochondrial migration following ischemic stress of the outer retina, which was evident on in vivo imaging.[11]

In our cases, it is possible that a combination of inflammation and choroidal ischemia could be participatory to the photoreceptor stress and splitting. The photoreceptors receive their nutrients from the choriocapillaris and in the acute stages, the compromised perfusion could lead to splitting of the bacillary layer. The BLD then resolves once the inflammation subsides and the blood flow improves.

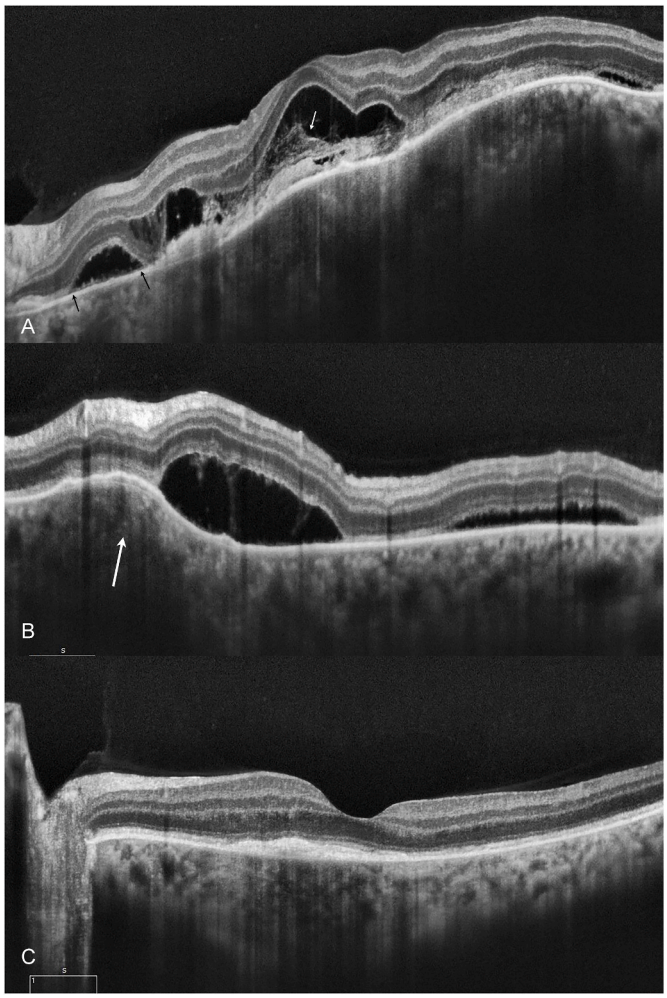

Fig. 5. (A and B). Optical coherence tomography at presentation (scan sites are the solid and dashed lines in Fig. 1A, respectively). (A) A dome-shaped cystic retinal hyporreflective space. A thin line of reflectivity at the base of the cystic space appears continuous with the flanking ellipsoid zone (black arrow). In the subfoveal area, the retinal cavity contains an amorphous hyperreflective material along the outer retinal surface (white arrow). (B) Subretinal fluid accumulation is observed inferiorly to the fovea. A choroidal lesion is causes retina elevation (white arrow). (C) Optical coherence tomography at the 45-day follow-up. A subretinal hyperreflective material is noted under the fovea.

5. Conclusions

In conclusion, we describe two patients with presumed intraocular tuberculosis with SLC and a photoreceptor splitting detachment that we consider BALAD in the acute stage of the disease, with rapid resolution over days.

After 2 months of ATT, the patients showed improvement in their visual acuity with absorption of serous retinal detachment but with persistent damage, with disorganization and thickening of the external retinal layers. Closer follow-up with multimodal imaging, including enhanced-depth imaging spectral domain optical coherence tomography, fundus autofluorescence, and fluorescein angiography may be warranted for patients presenting with this atypical form of the disease.

Patient consent

Written consent to publish potentially identifying information, such as details or the case and photographs, was obtained from patient's legal guardian.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship. We confirm that the manuscript has been read and approved by all named authors.

We confirm that the order of authors listed in the manuscript has been approved by all named authors.

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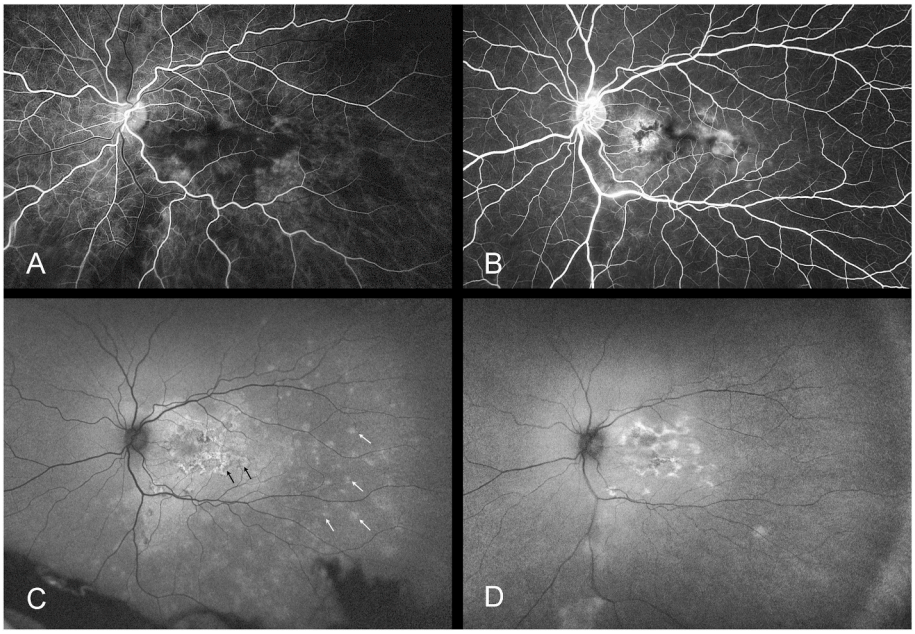

Fig. 6. (A and B). Fluorescein angiography at presentation. In the early phase (A) the macular lesions show early hypofluorescence. In the late phase (B), the lesions become progressively hyperfluorescent. (C) Ultra-wide-field autofluorescence at the 7-day follow-up. The central inactive lesions present a hyperfluorescent amoeboid-like pattern. They are surrounded by a hypofluorescent area, corresponding to active lesions (black arrows). There are peripheral patches of hyperfluorescence in a pattern mimicking multiple evanescent white dot syndrome (white arrows). (D) Ultra-wide-field autofluorescence at the 45-day follow-up. The areas of macular hyperfluorescence corresponding to healed lesions are observed. No peripheral lesions are noted.

Declaration of competing interest

The following authors have no financial disclosures: da Costa D.S.; Silva A. G., Melichar A., Neves D. B., Correa P. A., Moraes R. T.

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