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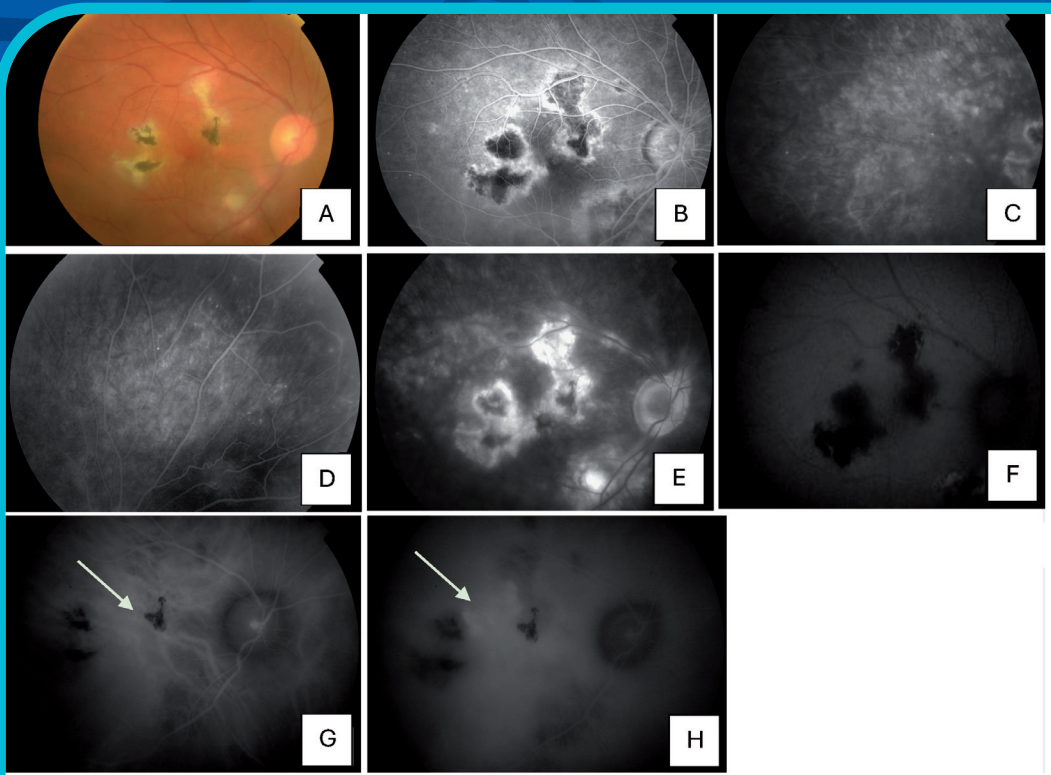

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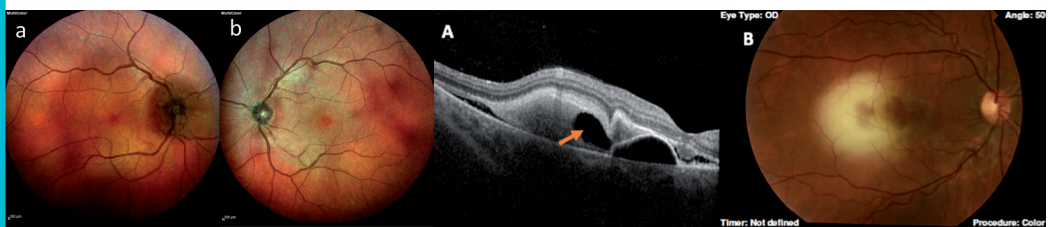

CASOS CLÍNICOS

CASE REPORTS

Seeing Beyond the Surface: The Role of Multimodal Imaging in Diagnosing and Managing Myopic Retinochoroidopathies

Ver Além da Superfície: O Papel da Imagiologia Multimodal no Diagnóstico e Gestão das Retinocoroidopatias Míopes

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ABSTRACT

Globally, the prevalence of myopia is on the rise, and this condition can lead to serious, vision-threatening complications. In young women, differentiating between neovascular and inflammatory conditions remains a diagnostic challenge.

We present a case of a 28-year-old high myopic patient with recurrent retinochoroidal events over a decade, including macular neovascularization (MNV), acute macular outer retinopathy (AMOR), and multiple evanescent white dot syndrome (MEWDS). MNV was effectively treated with intravitreal anti-VEGF injections, while other episodes resolved spontaneously.

Multimodal imaging—including spectral domain optical coherence tomography (SD-OCT), autofluorescence (FAF), fluorescein angiography (FA), indocyanine green angiography (ICGA), multicolour retinography, and visual field (VF) testing—was crucial to distinguish and manage these entities, underscoring the importance of a comprehensive diagnostic approach for optimal patient care.

KEYWORDS: Multimodal Imaging; Myopia/diagnosis; Myopia, Degenerative/diagnosis.

RESUMO

Globalmente, a prevalência da miopia está a aumentar, e esta condição pode levar a complicações graves que ameaçam a visão. Em mulheres jovens, a distinção entre condições neovasculares e inflamatórias continua a ser um desafio diagnóstico.

Reportamos o caso de uma paciente de 28 anos, com alta miopia, que apresentou episódios recorrentes com atingimento da retina e da coroide ao longo de uma década, incluindo neovascularização macular (MNV), retinopatia macular externa aguda (AMOR) e síndrome dos múltiplos pontos brancos evanescentes (MEWDS). A MNV foi tratada com sucesso com injeções intravítreas de anti-VEGF, enquanto os restantes episódios foram autolimitados.

A imagiologia multimodal — incluindo tomografia de coerência óptica de domínio espectral (SD-OCT), autofluorescência (FAF), angiografia fluoresceínica (FA), angiografia com verde de indocianina (ICGA), retinografia multicor e perimetria — foi essencial para distinguir e monitorizar estas entidades, reforçando a importância de uma abordagem diagnóstica abrangente para um cuidado otimizado do doente.

PALAVRAS-CHAVE: Miopia; Imagiologia Multimodal; Miopia/diagnóstico; Miopia Degenerativa/diagnóstico.

INTRODUCTION

Myopia is an escalating global health issue, projected to affect nearly half of the global population (4.76 billion people) in 2050.[1] This rising trend significantly strains healthcare systems, especially as younger, working-age individuals face higher risks of serious vision loss from its related complications.[2,3]

The definition of high myopia is primarily based on biometric criteria, notably a spherical equivalent refractive error of ≤−6.00 diopters (D) or an axial length greater than 26.5 mm.[4,5] Although earlier classifications of pathologic myopia focused on these biometric values, they were frequently inconsistent and of limited clinical relevance. The current conceptual framework places greater emphasis on the identification of characteristic structural abnormalities in the retina. Presently, pathologic myopia is characterized by myopic maculopathy of a severity equivalent to or greater than diffuse chorioretinal atrophy.[6] Myopic maculopathy itself represents a spectrum of progressive degenerative changes, including, but not limited to, diffuse and patchy chorioretinal atrophy, lacquer cracks, myopic macular neovascularization (myopic MNV), and choroidal macular atrophy secondary to MNV.

Epidemiological data suggest that young myopic women may be more predisposed to certain inflammatory and neovascular complications, although the reasons and the underlying pathophysiological link remain incompletely understood.[7-10] Moreover, due to the clinical overlap between these myriads of pathologies, it is often challenging to establish a definitive diagnosis based solely on an initial assessment. This diagnostic ambiguity can complicate both the management and prognosis of affected patients, particularly in cases with atypical presentations or evolving clinical features over time.

In this context, the advent and refinement of multimodal imaging techniques—including spectral domain optical coherence tomography (SD-OCT), OCT angiography (OCT-A), fundus autofluorescence (FAF), fluorescein angiography (FA), indocyanine green angiography (ICGA) and multicolour retinography - have revolutionized routine clinical practice.[11] The integration of these tools enabled detailed structural and functional assessment of the retina and choroid, facilitating early diagnosis, guiding management decisions, improving disease monitoring, and helping avoid unnecessary or invasive interventions.

This case report, with a follow-up period spanning nearly 10 years, highlights the essential role of multimodal assessment in clarifying complex ophthalmic presentations and guiding appropriate management in a high myopic patient.

CASE REPORT

We report the case of a 28-year-old female rheumatologist with high myopia (-7.0D). Her medical, social, and epidemiological histories were unremarkable; she denied any recent systemic illness, regular medication use, exposure to pets, recent travel, or known contact with tuberculosis. She was first seen in our ophthalmology department in June 2014 with a one-week history of decreased vision in her right eye (OD) with central scotoma. Best corrected visual acuity (BCVA) was 66 letters (ETDRS) in the OD and 83 letters (ETDRS) in the left eye (OS). SD-OCT and FA imaging revealed a classic type 2 MNV, associated with subretinal and intraretinal fluid and hemorrhage. (Fig. 1A-C).

The patient was treated with three monthly intravitreal injections of bevacizumab (dose 1.25 mg/0.05 mL), resulting in resolution of symptoms. Visual acuity improved to 85 letters in the OD. Post-treatment SD-OCT and Infrared imaging revealed an inactive and cicatricial MNV, with no signs of exudation, accompanied by a small halo of retinal pigment epithelium (RPE) atrophy (Fig. 1D). FA with no leakage was also consistent with the resolution of the condition and treatment efficacy (Fig. 1E).

Following a clinically stable period of almost 4 years, the patient presented with new visual complaints characterized by a new scotoma in the OS (contralateral to the previously affected side). The patient denied any recent systemic illness or prodromal symptoms. Visual acuity was 85 letters (ETDRS) OD and 84 letters (ETDRS) OS.

A new multimodal imaging workup was conducted and the integration of findings across modalities supported a presumptive diagnosis of acute macular outer retinopathy (AMOR) (Fig. 2).

This episode was self-limited, with spontaneous and favourable resolution within three weeks.

In March 2022, the patient returned to the emergency department with new reported complaints of paracentral scotomas in the OS. Notably, she reported a confirmed COVID-19 infection approximately three weeks prior to symptom onset. A comprehensive multimodal imaging

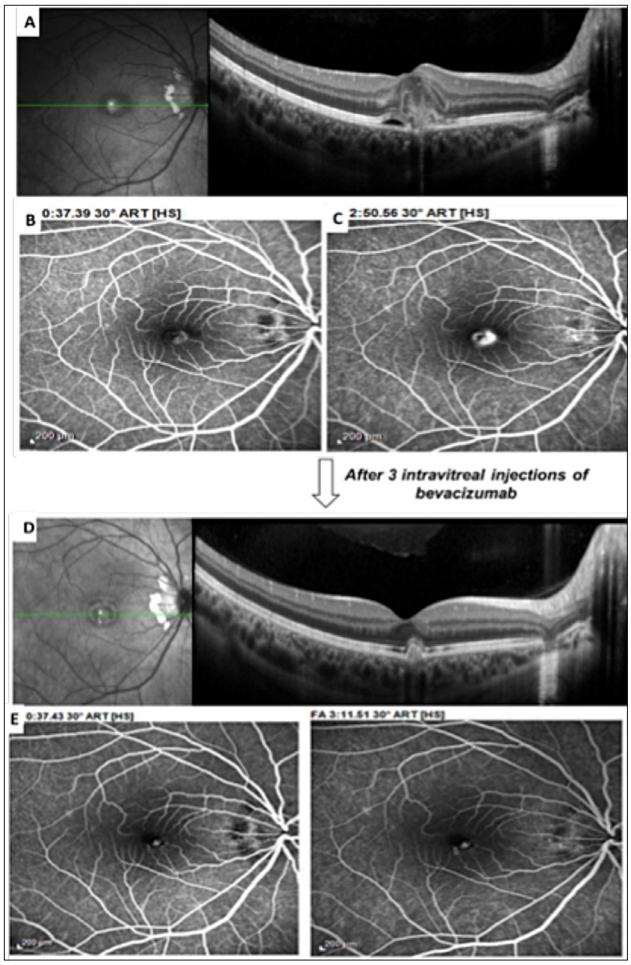

Figure 1. **A)** SD-OCT scan through the fovea shows a hyperreflective lesion in the outer nuclear layer and subretinal space, with some intraretinal fluid and subretinal fluid. These findings are consistent with an active type 2 MNV. In the Infrared reflectance image, it is possible to observe patchy hyperreflective areas nasal to the fovea, towards the optic disc, likely representing myopic peripapillary chorioretinal atrophy. **B and C)** FA with a well-defined hyperfluorescence subfoveal lesion (A) followed by late leakage (B), confirming the classical angiographic pattern of an active type 2 MNV. **D)** Restoration of the outer retinal layers is noted, with a well-defined lesion, recovered by RPE and absence of intraretinal or subretinal fluid, consistent with inactive type 2 MNV. **E)** FA shows a discrete well-demarcated area of hyperfluorescence in the subfoveal region, but without evidence of active leakage.

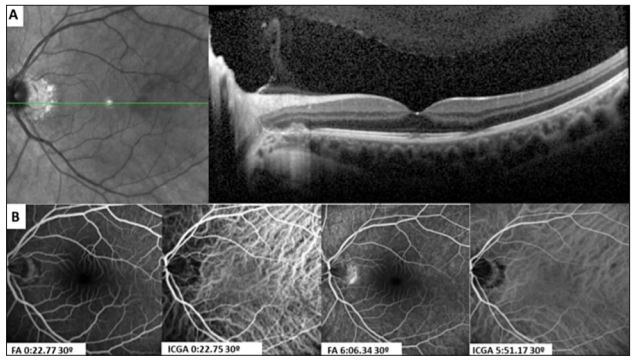

Figure 2. SD-OCT scan and Infrared (A) revealed hyperreflective, petaloid-shaped lesions located temporal to the fovea. Corresponding SD-OCT scan demonstrated disruption of the ellipsoid zone and thinning of the RPE in the affected area. Additionally, subtle hyperreflectivity was observed in the outer nuclear layer of the parafoveal region. A well-defined hyperreflectivity in the outer nuclear layer was also noted in the peripapillary area. The identified lesions showed no corresponding abnormalities on FA or ICGA studies (B).

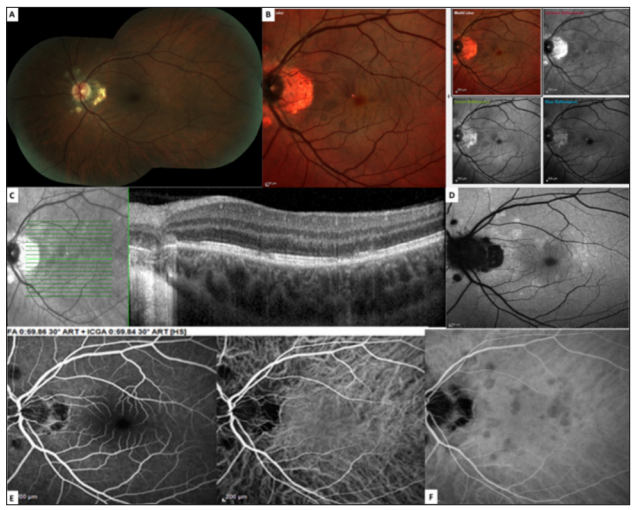

Figure 3. Multimodal imaging study including seven-field colour fundus photography (A), multicolour imaging (B), SD-OCT and InfraRed (C), FAF (D) and FA+ICGA (E-F). **A)** Seven-field colour fundus photograph shows multiple yellowish-white lesions of varying sizes distributed in the posterior pole and in the nasal retina, as well as the previous peripapillary pigmentary alteration. **B)** Multicolour imaging revealed multiple hyporeflective, multifocal lesions, located nasal to the fovea. On reflectance decomposition, these lesions were most pronounced in the infrared and green channels, suggesting outer retinal involvement. **C)** SD-OCT scan through the affected areas of the lesions demonstrated hyper-reflective lesions extending from the RPE, into and/or through the ellipsoid zone and into the outer nuclear layer of the retina, like a "smoke/volcano" sign. **D)** FAF image demonstrates multiple hyperautofluorescent spots corresponding to the lesions seen in multicolour and fundus photography. Additionally, there are patchy areas of hypoautofluorescence in the supra-, infrapapillary and temporal regions, indicating regions of RPE atrophy. **E)** In the early phases of FA and ICGA, there is an unremarkable angiographic background with no signs of active leakage or staining. **F)** The late phase of ICGA reveals multiple, well-circumscribed hypofluorescent lesions dispersed across the macular region, which correspond to the structural changes seen in the other modalities. These findings are consistent with a diagnosis of MEWDS.

study was conducted (Fig. 3), and the integration of the findings led to the diagnosis of multiple evanescent white dot syndrome (MEWDS). As with the previous episode, this condition resolved spontaneously within three weeks.

Since the last episode and up to the most recent follow-up in March 2025 — more than 10 years after the initial manifestation — the patient remained clinically stable, with no further inflammatory or neovascular events. BCVA was 85 letters (ETDRS) bilaterally (OU), and the ophthalmologic examination was otherwise unremarkable.

A comprehensive systemic evaluation was performed, including a basic metabolic panel, an extensive autoimmune workup, as well as an infectious disease screening targeting a wide range of viral, bacterial, and mycobacterial (specifically tuberculosis) agents. Although extensive, all investigations were negative, ruling out any identifiable systemic infectious or autoimmune aetiology.

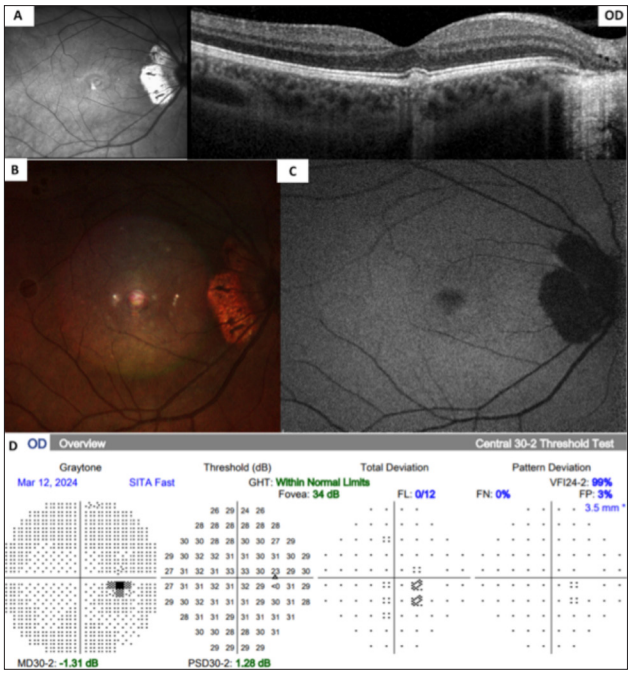

Figure 4. Multimodal imaging study including SD-OCT and InfraRed (A), multicolour imaging (B), FAF (C) and VF test (D) of the OD. **A)** SD-OCT and InfraRed reveal a small macular scar with mild distortion of the outer retinal layers, but overall retinal architecture appears stable without active fluid or other signs of neovascular activity. **B)** Multicolour imaging reveals a central hyperreflective lesion corresponding to the fibrotic scar. **C)** FAF image demonstrates a well-defined area of hypoautofluorescence corresponding to the macular scar, with no signs of new hyperautofluorescent activity, consistent with a chronic, inactive lesion. **D)** The 30-2 SITA Fast VF demonstrates a reliable test, within normal limits. The glaucoma hemifield test (GHT) is normal, and the grayscale map shows no significant defects. Overall, this test is interpreted as normal.

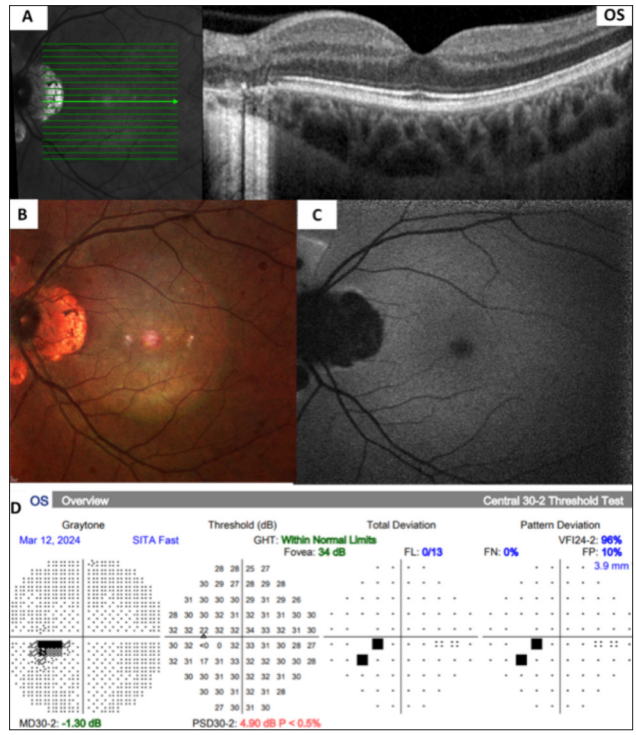

Figure 5. Multimodal imaging study including SD-OCT and InfraRed (A), multicolour imaging (B), FAF (C) and VF test (D) of the OS. **A)** SD-OCT and InfraRed shows preservation of the foveal contour, with an overall intact outer and inner retinal layers. **B)** Multicolour imaging reveals mildly hyperreflective perifoveal lesions that are most likely artefactual, as they lack corresponding findings on other imaging modalities; however they might suggest outer retinal involvement, though less extensive than previously documented. **C)** FAF image demonstrates small hypoautofluorescent areas in the peripapillary region suggesting residual retinal pigment epithelium (RPE) alterations. No hyperautofluorescent lesions are noted, supporting a stable, inactive status. **D)** The 30-2 SITA Fast visual field demonstrates a reliable test (fixation losses 0/13, false positives 3%, false negatives 0%) with a MD of -1.30 dB. A mild focal defect is indicated by a PSD of 4.90 dB ($p < 0.5\%$) and a few points depressed on the pattern deviation map in the blind spot region. The GHT is within normal limits, and visual field index (VFI) remains high at 96%, suggesting preserved global function. Findings are consistent with a stable, clinically insignificant paracentral scotoma, likely from prior retinal changes (peripapillary atrophy).

Residual findings included a cicatricial macular lesion in the OD and peripapillary pigmentary changes OU, with no signs of active disease. Most recent multimodal imaging (Figs. 4 and 5) confirmed the stability of previously documented structural alterations. A 30-2 VF test was also performed.

DISCUSSION

This case highlights the complexity of pathologic myopia, where neovascular and inflammatory entities may co-occur or mimic one another. The sequential presentation of myopic MNV, AMOR and MEWDS in a single patient suggests a unifying pathophysiological environment driven by structural fragility, vascular compromise, and immune predisposition.

In high myopia, axial elongation and choroidal thinning impose mechanical stress that disrupts the RPE–Bruch's membrane–choriocapillaris (RPE–BrM–CC) complex. This disruption facilitates subretinal antigen exposure and fosters a pro-angiogenic and pro-inflammatory microenvironment.[12-14] Within this context, mMNV likely arose from ischemia-induced VEGF upregulation, genetic susceptibility (e.g., VEGF, CFI variants), and local and mechanical damage.

The subsequent episode of AMOR, associated with outer retinal ischemia involving both the deep capillary plexus and choriocapillaris,[15] likely reflects progression of the same vascular fragility. The later development of MEWDS aligns with the concept of "secondary MEWDS"— a term used to describe an immune response triggered by prior disruption of the RPE–BrM–CC interface.[16] Unlike primary MEWDS described by Jampol *et al*,[17] secondary MEWDS emerges in the context of preceding retinal pathology, as likely occurred in this case. Rather than being isolated pathological events, the three episodes appear to be interlinked, forming a continuum of immune and ischemic sequelae within a structurally vulnerable retina.

Interestingly, the patient's profession as a rheumatologist introduces another immunological dimension to consider. Chronic occupational exposure to immunocompromised individuals and latent infections — such as tuberculosis — may contribute to a heightened antigenic burden, potentially amplifying local immune responses. Although extensive sys-

temic investigation — including autoimmune and infectious testing — was negative, this background offers a plausible context for increased ocular immune reactivity.

Equally important, this case highlights the pivotal role of multimodal imaging in the diagnosis and treatment of complex myopic retinal disease. Imaging enabled precise differentiation between active neovascular pathology, requiring anti-VEGF treatment, and self-limited inflammatory events, for which observation was appropriate, thereby avoiding unnecessary intervention.

In conclusion, this case supports an evolving paradigm that favours individualized, imaging-guided, and adaptive management strategies for complex myopic retinal disorders. It also emphasizes the importance of maintaining a high index of suspicion in individuals with risk exposures, even in the absence of confirmed systemic disease.

CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO:

DRA: Conception and design of the work, draft of the paper, critical review, and approval of the final version

JO: Critical review, and approval of the final version

JNB: Patient care, critical review, and approval of the final version.

LF: Patient care, critical review, and approval of the final version.

AC: Conception of the work, patient care, critical review, and approval of the final version.

DRA: Conceção e desenho do trabalho, rascunho do artigo, revisão crítica e aprovação da versão final.

JO: Revisão crítica e aprovação da versão final.

JNB: Cuidados ao paciente, revisão crítica e aprovação da versão final.

LF: Cuidados ao paciente, revisão crítica e aprovação da versão final.

AC: Conceção do trabalho, atendimento ao paciente, revisão crítica e aprovação da versão final.

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ETHICAL DISCLOSURES

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Misfortune Never Comes Alone

O Infortúnio Nunca Vem Sozinho

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ABSTRACT

Tuberculous uveitis remains a diagnostic challenge, as Mycobacterium tuberculosis is rarely isolated from ocular samples due to the inherently low bacterial load and the difficulty of obtaining adequate intraocular specimens for microbiological confirmation.

We report the case of a 48-year-old male with unilateral recurrent posterior uveitis initially diagnosed and treated as ocular toxoplasmosis, who later presented with bilateral intraocular inflammation. Despite the absence of an unequivocal workup for systemic tuberculosis, a presumptive diagnosis of ocular tuberculosis was made based on multimodal imaging findings and disease presentation and progression. This case was particularly interesting because it involved a combination of two distinct phenotypes. The patient was started on anti-tubercular therapy (ATT) combined with systemic corticosteroids and intravitreal therapies tailored to each eye. Significant visual and anatomic improvement was observed, with final best-corrected visual acuity reaching 20/25 in the right eye and 20/20 in the left eye.

KEYWORDS: Choroiditis; Multimodal Imaging; Retinal Vasculitis; Tomography, Optical Coherence; Tuberculosis, Ocular / diagnosis.

PALAVRAS-CHAVE: Corioidite; Imagem Multimodal; Tomografia de Coerência Óptica; Tuberculose Ocular/diagnóstico; Vasculite Retiniana.

INTRODUCTION

Despite substantial advances in diagnostic imaging, laboratory methodologies, therapeutic interventions and molecular engineering, tuberculous uveitis remains challenging to diagnose and treat.[1] This complexity is largely due to the protean clinical manifestations of the disease and its potential to affect virtually any anatomic segment of the eye and periocular structures, including the sclera, orbit, and adnexal tissues. Isolation and culture of *Mycobacterium tuberculosis* (TB), the etiological agent, are often hampered by the low organism load typical of this condition and the difficulty of obtaining adequate ocular biological samples for analysis.[1,2] Moreover, in regions with a high prevalence of latent tuberculosis infection, as is the Oporto area, clinical differentiation between true TB-induced uveitis and uveitic manifestations coinciding with unrelated latent TB poses a considerable diagnostic dilemma. We present a case of ocular TB with weak evidence of systemic infection and distinct ocular manifestations in each eye that was successfully treated with systemic antibacillary and intravitreal therapy.

CASE REPORT

A 48-year-old male was referred to our uveitis clinic in March 2015 for evaluation of decreased visual acuity (VA) in the right eye (RE) with three months' duration. The patient was employed as a car mechanic in Oporto. His past medical history included hypertension, dyslipidemia, and a recent diagnosis of essential thrombocytosis. He had no history of pet ownership, international travel outside Europe, high-risk behaviors, or known exposure to tuberculosis (TB). He received the Bacillus Calmette–Guérin (BCG) vaccination in early childhood.

In December 2012, the patient had previously presented with similar visual complaints in the RE. Best-corrected visual acuity (BCVA) at that time was 20/400. Fundoscopic examination revealed macular chorioretinal infiltrates with associated vitritis, leading to a clinical diagnosis of presumed ocular toxoplasmosis. He was treated with oral trimethoprim-sulfamethoxazole (800/160 mg) and prednisolone (1 mg/kg/day). Fundus fluorescein angiography (FFA) showed early diffuse hypofluorescence of the macular lesions with late hyperfluorescence of the borders (Fig. 1). The patient showed improvement in BCVA to 20/25 in February 2013 and was subsequently lost to follow-up.

In December 2014, he presented again to the emergency department with recurrent visual loss in the RE. BCVA was 20/63, and the fundus exam revealed recurrence of posterior uveitis with macular involvement, 1+ vitreous haze, and multifocal chorioretinal lesions at the posterior pole with variable degree of pigmentation and two creamy lesions adjacent to the temporal inferior arcade, (Fig. 2). Treatment with oral trimethoprim-sulfamethoxazole and prednisolone was re-initiated. The left eye (LE) remained unaffected, with BCVA of 20/20 and a normal examination. Fundus autofluorescence (FAF) revealed hypoautofluorescent lesions corresponding to areas of chorioretinal scarring and atrophy, while active lesions showed hyperautofluorescent borders that resolved with treatment. Indocyanine green angiography (ICGA) demonstrated persistent hypofluorescent choroidal lesions, with some lesions exhibiting late hyperfluorescent borders (Fig. 3). Optical

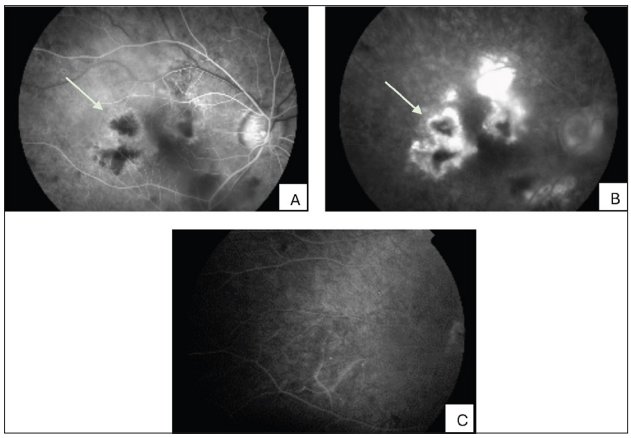

Figure 1. FFA before discharge: A – 20 sec; B – 5 minute 11; C – 1 minute. Note the early hypofluorescence of the lesions with late hyperfluorescence of the borders (arrow) – block early and stain late pattern.

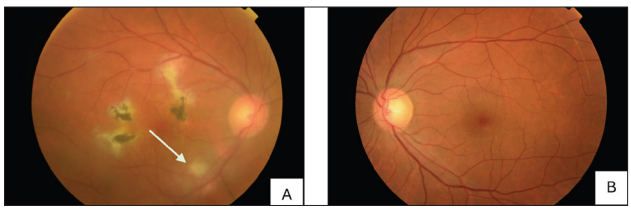

Figure 2. Fundus photo: RE (A) showing multifocal chorioretinitis involving the macular area with lesions with varying degrees of pigmentation; note to the lesion adjacent to the temporal inferior arcade (arrow), with a creamy appearance and indistinct borders suggesting a more active state Left eye (B) without pathological changes.

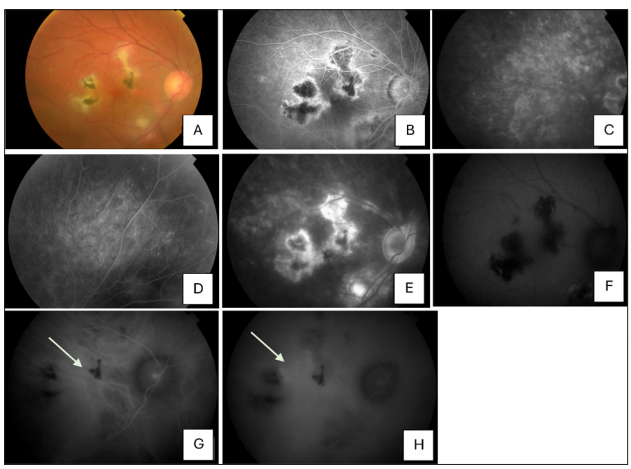

Figure 3. Multimodal imaging of the RE in early 2015: Fundus photo (A); FFA – early block and stain late pattern with evidence if macular periphlebitis and some extent of peripheral capillary dropout (B – 29 seconds, C –2 minute 15; D – 3 minute; E – FA 5 minute), FAF (F) and ICGA (G – 1 minute; H – 15 minute). The arrows in G and H outline the hypofluorescent choroidal lesions with late hyperfluorescence.

coherence tomography (OCT) of active lesions revealed the absence of the choriocapillaris and variable thickening of the outer retina and retinal pigment epithelium (RPE). In inactive lesions, partial reconstitution of the choriocapillaris was observed.

At presentation to our clinic, BCVA was 20/50 in the RE and 20/20 in the LE. Slit-lamp examination revealed no signs of anterior uveitis in either eye, with intraocular pressure (IOP) of 18 mmHg bilaterally. Fundus examination of the RE demonstrated multifocal macular chorioretinal lesions, 1+ vitreous haze, and focal retinal vasculitis. Given the atypical clinical course and multimodal imaging findings, the diagnosis of ocular toxoplasmosis was reconsidered, and serpiginous-like choroiditis was suspected. Further systemic investigation, including laboratory workup and chest imaging, was initiated.

Serologic testing was negative for syphilis, HIV-1/2, HLA-B27, HLA-B51, and angiotensin-converting enzyme (ACE). Inflammatory markers including complete blood count, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) were within normal limits. Positive IgG titers were noted for HSV-1, CMV, and Toxoplasma gondii. Interferon-gamma release assay (IGRA) testing yielded two indeterminate and two negative results. A chest computed tomography (CT) scan revealed mild fibrotic changes in the inferior lung lobes and a spiculated 11-mm nodule in the right lung apex.

In April 2015, during a follow-up visit while still on systemic corticosteroids, the patient reported decreased visual acuity in the LE. BCVA remained 20/50 in the RE and was reduced to 20/25 in the LE. There were no signs of anterior segment inflammation or elevated IOP. Fundus examination of the LE demonstrated occlusive temporal retinal vasculitis with segmental periphlebitis, confirmed by fluorescein angiography (Fig. 4). The patient was referred to the Pneumologic Diagnostic Center for TB screening evaluation. Repeat IGRA testing was again negative and chest radiography was unremarkable, but a Mantoux test result of 12 mm was detected. Despite weak evidence of *Mycobacterium tuberculosis* infection, a presumptive diagnosis of ocular tuberculosis was made based on clinical and multimodal imaging findings suggestive of serpiginous-like choroiditis in the RE and tubercular retinal vasculitis in the LE. In June 2015, the patient was initiated on a 6-month course of standard anti-tubercular therapy (ATT) in combination with systemic corticosteroids. Additionally, he received an intravitreal dexamethasone implant in the RE to treat macular edema and decrease posterior segment inflammation (Fig. 5) and, off-label, as-needed, intravitreal anti-VEGF combined once with triamcinolone (2 mg) in the LE.

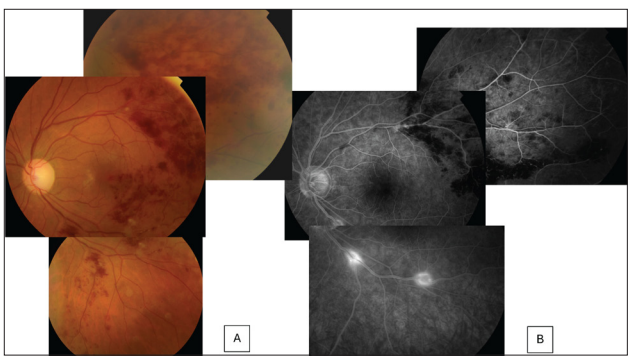

Figure 4. Fundus photography of the LE (A) and FFA (B) showing temporal retinal vasculitis with segmental periphlebitis and peripheral capillary occlusion.

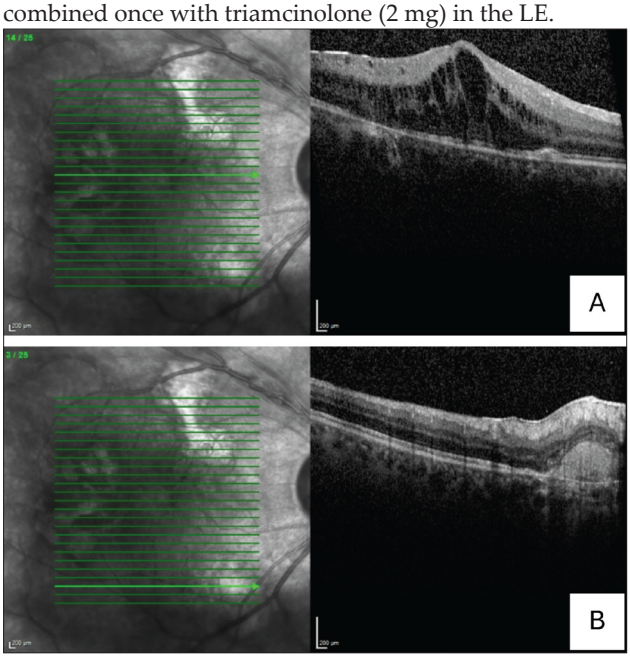

Figure 5. OCT of the RE showing macular edema (A) and extrafoveal choriocapillaris and outer retina involvement (B).

At follow-up in January 2016, the patient showed significant anatomical and functional improvement, with BCVA of 20/25 in the RE and 20/20 in the LE (Fig. 6). Over the subsequent years, he developed recurrent macular edema in the LE (Fig. 7). Treatment was switched from bevacizumab to ranibizumab, and ultimately to aflibercept in September 2021, with good anatomical and functional response.

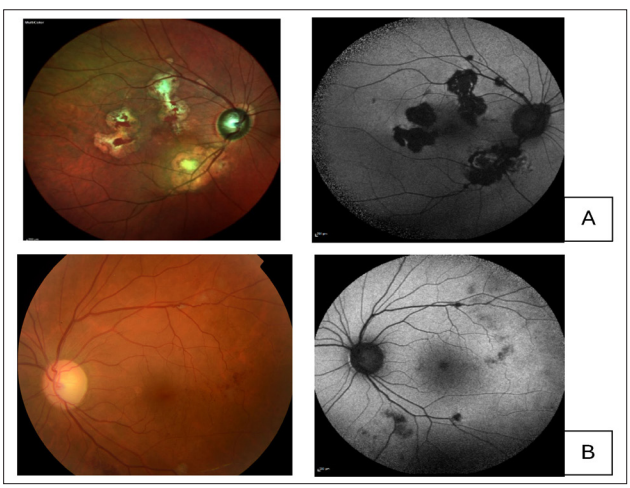

Figure 6. Fundus photography and blue-peak FAF of the RE (A) and LE (B).

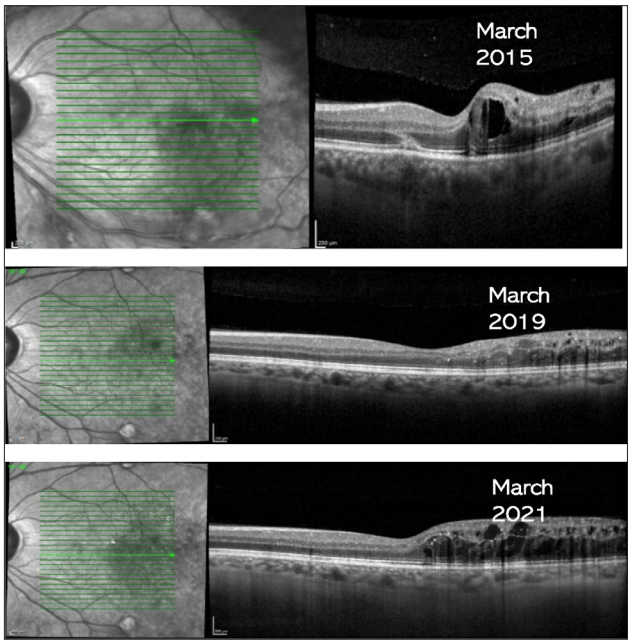

Figure 7. Macular OCT of the LE throughought the years, revealing chronic recurrent macular edema.

DISCUSSION

Tuberculous uveitis presents a significant diagnostic challenge, often requiring a presumptive diagnosis based on clinical features, supporting investigations, and therapeutic response rather than direct microbiologic confirmation. Our patient developed bilateral posterior uveitis, initially managed as ocular toxoplasmosis, but with subsequent clinical evolution suggestive of serpiginous-like choroiditis (SLC) in the RE and occlusive retinal vasculitis complicated with chronic macular edema in the LE — phenotypes increasingly recognized as manifestations of presumed ocular tuberculosis (TB).[2,3]

Ocular tuberculosis can manifest in a variety of phenotypic forms, particularly involving the choroid. The Collaborative Ocular Tuberculosis Study (COTS) group has outlined a standardized nomenclature for these presentations, including standardized terminology for defining the spectrum of lesions and choroidal involvement in tubercular choroiditis: tubercular serpiginous-like choroiditis (TB SLC), tubercular multifocal choroiditis (TMC), tubercular focal choroiditis (TFC), and tuberculoma.[1] TB SLC is a particularly important phenotype in ocular TB, as it can be easily misdiagnosed as autoimmune serpiginous choroiditis or infectious causes such as toxoplasmosis. Clinical features favouring a tubercular etiology include unilateral presentation (at least initially), vitreous inflammation, lack of systemic autoimmune markers, and a positive response to anti-tubercular therapy (ATT).[1,2,4] In our patient, these features were present, prompting re-evaluation of the initial diagnosis and leading to a revised working diagnosis of presumed ocular TB.

The presence of retinal vasculitis, particularly segmental periphlebitis, in the contralateral eye further supports the diagnosis of ocular TB. Retinal vasculitis is a well-recognized but underreported manifestation of ocular TB. Tubercular retinal vasculitis typically presents as exudative, segmental, hemorrhagic retinal vasculitis, frequently associated with peri ou subvascular choroiditis, vitritis, and when more posteriorly located, with disc and macular edema.[5] The simultaneous presentation of two distinct phenotypes — TB SLC in one eye and retinal vasculitis in the other — further supports the diagnosis. This multifocal, bilateral and phenotypically diverse involvement is highly suggestive of *Mycobacterium tuberculosis* infection.[1,2]

Multimodal imaging played a critical role in the diagnostic process, as techniques such as FAF, FFA, IGCA, and OCT help provide complementary insights into lesion pattern, activity, extent, and evolution, allowing a better recognition of the phenotypic patterns suggestive of ocular TB and helping to differentiate tubercular choroiditis from mimickers. In active SLC the OCT may reveal outer retina hyperreflectivity with loss of inner segment and outer segment junction, with intact inner retina, while in inactive disease, decreased retinal thickness due to atrophy of the outer nuclear layer with disruption of photoreceptor layer, RPE loss, cystic changes, and subretinal fibrosis may appear. The OCT changes can be correlated with FAF imaging.[6]

Our patient's clinical and anatomical improvement following systemic ATT and corticosteroid therapy further supports this diagnosis. The subsequent recurrence of macular edema in the left eye required long-term intravitreal anti-VEGF and switch among different drugs highlighting the chronic and relapsing course that tuberculous uveitis can follow despite appropriate anti-tubercular therapy. The initially adopted PRN treatment regimen in the LE was replaced for a proactive, *treat and extend* approach due to the chronicity of macular edema.

Diagnostic confirmation of ocular TB is notoriously difficult and requires a multidisciplinary approach that includes not only the ophthalmologist but also infectious diseases, pneumology and other medical specialities. In the absence of positive microbiological testing or unequivocal systemic involvement, diagnosis relies on a constellation of findings. The British Thoracic Society (BTS) and COTS have proposed diagnostic criteria that include typical ocular manifestations, evidence of TB infection (e.g., IGRA, chest imaging), exclusion of other causes, and therapeutic response to ATT.[1,3] In the presented case, although repeated IGRA results were negative/undetermined and pulmonary imaging was nonspecific, the clinical presentation and excellent response to ATT were consistent with presumed ocular TB. It is important to note, however, that systemic corticosteroid use can affect the reliability of TB screening tests so it is generally recommended that screening should be performed while the patient is on a prednisone dose inferior to 20 mg/day, whenever clinically feasible.[7]

This case reinforces the importance of considering ocular TB in patients with unexplained, recurrent posterior uveitis, particularly in the presence of choroiditis with a serpiginous pattern and/or associated retinal vasculitis,

even when conventional TB tests are negative. Empirical ATT, in carefully selected cases, may serve both diagnostic and therapeutic purposes. Multimodal assessment can help recognise characteristic patterns of ocular tuberculosis and plays a fundamental role in differential diagnosis.

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ETHICAL DISCLOSURES

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Atypical Ocular Syphilis with Bilateral Posterior Staphylomas and Chorioretinal Atrophy: A Case Report in a Non-Myopic Patient

Sífilis Ocular Atípica com Estafilomas Posteriores Bilaterais e Atrofia Coriorretiniana: Relato de um Caso em Paciente Não Míope

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ABSTRACT

Ocular syphilis is characterized by a highly heterogeneous clinical presentation, potentially affecting virtually any ocular structure and mimicking various ocular pathologies. We report the case of a 56-year-old immunocompetent, non-myopic woman with progressive, asymmetric visual loss. Ophthalmological examination revealed well-defined "punched-out" chorioretinal atrophic lesions involving the macula. Multimodal imaging showed complete loss of the retinal pigment epithelium, choroidal thinning, and bilateral posterior staphylomas corresponding to atrophic areas. Serological tests confirmed active syphilis infection, with no evidence of neurological involvement. Intravenous penicillin treatment led to serological improvement and stabilization of ocular lesions, although irreversible macular damage persisted. This case highlights the diverse ocular manifestations of syphilis, its ability to mimic hereditary dystrophies and inflammatory chorioretinitides, and the need to include it in the differential diagnosis of unexplained chorioretinal atrophy, even in immunocompetent patients. Posterior staphylomas in non-myopic eyes are rare, and this case allows us to hypothesize an inflammatory scleral remodeling process associated with syphilis infection.

KEYWORDS: Choroid Diseases; Eye Infections, Bacterial; Multimodal Imaging; Syphilis; Tuberculosis, Ocular.

RESUMO

A sífilis ocular caracteriza-se pela sua apresentação clínica altamente heterogénea, podendo afetar virtualmente qualquer estrutura ocular e mimetizar várias patologias oculares. Apresenta-se o caso de uma mulher imunocompetente, não míope, de 56 anos, com perda visual progressiva e assimétrica. O exame oftalmológico evidenciou lesões atróficas coriorretinianas bem delimitadas, do tipo *punched-out*, com atingimento macular. A imagem multimodal revelou perda completa do epitélio pigmentar da retina, afinamento coroideu e estafilomas posteriores bilaterais correspondentes às áreas atróficas. Os testes serológicos confirmaram infeção ativa por sífilis, sem envolvimento neurológico. O tratamento com penicilina intravenosa resultou na melhoria serológica

e estabilização das lesões oculares, persistindo o dano macular irreversível. Este caso destaca as variadas manifestações oculares da sífilis, a sua capacidade de mimetizar distrofias hereditárias e coriorretinites inflamatórias, e a necessidade de considerar a sífilis no diagnóstico diferencial de atrofia coriorretiniana inexplicada, mesmo em doentes imunocompetentes. Estafilomas posteriores em olhos não míopes são raros e, com este caso, coloca-se a hipótese de um possível processo inflamatório de remodelação escleral associado à infeção por sífilis.

PALAVRAS-CHAVE: Doenças da Coroide; Imagem Multimodal; Infecções Oculares Bacterianas; Sífilis; Tuberculose Ocular.

INTRODUCTION

Syphilis, a chronic and multi-system disease caused by the spirochete *Treponema pallidum*, has undergone a global resurgence in recent decades, including in Portugal, primarily due to evolving sexual habits and rising rates of HIV co-infection.[1,2] Ocular involvement, however rare, can occur at any phase of the disease and exhibits a broad spectrum of clinical manifestations, earning syphilis the moniker "the great imitator".[3]

The disease can affect almost any ocular structure. The predominant ocular manifestations include uveitis (posterior or panuveitis), optic neuritis, and vitritis, with acute syphilitic posterior placoid chorioretinitis (ASPPC), although uncommon, being a hallmark manifestation associated with poor visual prognosis.[4] Chronic, untreated cases may occasionally progress to chorioretinal atrophy, as reported in some studies.[4,5]

Posterior segment involvement is particularly challenging, since it may mimic several infectious, inflammatory, or degenerative retinal disorders, including viral retinitis, autoimmune retinopathies, and hereditary chorioretinal dystrophies.[6,7] Multimodal imaging, which includes color fundus photography, fundus autofluorescence, optical coherence tomography (OCT), and fluorescein angiography, is crucial for precisely delineating the extent and nature of retinal and retinal pigment epithelium (RPE) involvement, guiding both diagnosis and therapeutic decisions.[8]

Recent studies from Portuguese tertiary centers have highlighted an increasing incidence of ocular syphilis, often bilaterally, with a spectrum of posterior involvement exhibiting considerable variability.[2,4] Globally, similar patterns have emerged, particularly in high-risk groups.[3] Loss of visual acuity is frequently the initial complaint, and a delayed diagnosis strongly correlates with irreversible structural damage, including macular atrophy or optic nerve fibrosis.[4,9] Early recognition and prompt initiation of intravenous penicillin are critical, as ocular syphilis is considered a form of neurosyphilis and may progress to permanent vision loss within weeks if untreated.[3] Serological testing (non-treponemal rapid plasma reagin [RPR] and reactive treponemal assay [CLIA]/ Fluorescent Treponemal Antibody Absorption [FTA-ABS]) is mandatory for all patients exhibiting unexplained ocular inflammation or chorioretinal atrophy, regardless of systemic symptoms.[3,4] Analysis of cerebrospinal fluid is not universally required. According to Faria Pereira *et al*[4] lumbar puncture should be reserved for cases with neurological symptoms, atypical clinical evolution (e.g., treatment failure), or high-risk comorbidities (e.g., HIV coinfection), a practice supported by recent international guidelines.[10,11]

Here, we report a case of bilateral, asymmetric chorioretinal atrophy with macular involvement in a middle-aged immunocompetent woman, where a comprehensive multimodal imaging approach and systemic serological testing were crucial for diagnosing ocular syphilis. This case highlights the diagnostic challenges of rare, atypical chorioretinal presentations and underscores the necessity of considering infectious etiologies, especially syphilis, in the differential diagnosis of chorioretinal atrophy, even in immunocompetent patients.

CASE REPORT

A 56-year-old female presented to the emergency department with complaints of decreased visual acuity in the left eye for several months. Her medical history was notable for osteoarthritis and generalized anxiety disorder, with no prior ophthalmological complaints. According to the patient, previous eye examinations were unremarkable. There was no family history of significant ocular disease. Best-corrected visual acuity (BCVA) was 80 ETDRS letters (with -0.50 × 90°) in the right eye (OD) and 50 ETDRS letters (with -0.75 -0.50 × 145°) in the left eye (OS). Intraocular pressure was 14 mmHg OD and 16 mmHg OS. Pupils were equal and reactive to both light and accommodation, with no relative afferent pupillary defect. Anterior segment examination revealed incipient cataracts in both eyes, with no evidence of active inflammation or signs of previous anterior segment inflammation.

Fundus examination (Fig. 1) revealed bilateral peripapillary myelinated retinal nerve fibers, more prominent in the OS. Both eyes showed sharply demarcated, "punched-out" chorioretinal atrophic lesions adjacent to the vascular arcades. In the OD (Fig. 1a), these atrophic areas were mainly superotemporal, with exposed large choroidal vessels and subtle macular pigmentary changes. The OS (Fig. 1b) exhibited more extensive atrophy involving the superotemporal, inferotemporal, and central macular regions, with atrophic zones exhibiting a diffuse yellow-whitish

scleral reflex and granular pigmentary changes at the borders. Atrophy extended into the macula, resulting in loss of normal foveal architecture and scattered pigment clumping; additional smaller atrophic foci were also present throughout the posterior pole. In both eyes, the optic discs had well-defined margins, and the retinal vasculature appeared normal.

Fundus autofluorescence (FAF) imaging (Fig. 1c, d) demonstrated pronounced areas of hypoautofluorescence corresponding to regions of chorioretinal atrophy in both eyes, indicating complete loss of RPE. The borders of the main lesions were sharply demarcated, and a background of granular hypoautofluorescence with smaller, patchy areas of relative hyperautofluorescence was observed, suggestive of ongoing RPE dysfunction or transitional zones. In the OD macular region, stippled hypoautofluorescence correlated with the clinically observed pigmentary alterations, indicating early RPE impairment. Conversely, in the OS, the macular region was extensively affected, with hypoautofluorescence spreading across the fovea.

B-scan ultrasonography (Fig. 2) revealed bilateral posterior staphylomas, defined by localized outpouching of the posterior ocular wall corresponding precisely to the areas of chorioretinal atrophy observed fundoscopically. The staphylomatous configuration was asymmetric between eyes, with the OS exhibiting a more pronounced posterior ectasia with greater axial depth and steeper transitional borders.

Spectral-domain optical coherence tomography (OCT) of the OD (Fig. 3a) reveals preserved central foveal architecture with focal disruption of the ellipsoid zone (EZ) in parafoveal/temporal regions. Extensive RPE atrophy and choroidal thinning are evident, corresponding with fundoscopic and autofluorescence-defined chorioretinal lesions. The OS (Fig. 3b) exhibits advanced degeneration, with near-complete EZ/external limiting membrane (ELM) loss and multifocal RPE atrophy extending into the macula. Furthermore, outer retinal tubulations confirm chronic degeneration. A posterior staphylomatous contour is observed, corresponding with the B-scan-identified posterior staphyloma.

Fluorescein angiography (FA) (Fig. 4) demonstrated bilateral, sharply demarcated hypofluorescent lesions indicative of chorioretinal atrophy, persisting unchanged throughout all angiographic phases. Retinal vasculature in both eyes crossed atrophic regions without exhibiting leakage, exudation, or neovascularization. The OD exhibited progressive hyperfluorescence at the lesion borders, indicative of late scleral staining resulting from the degeneration of the overlaying RPE and choriocapillaris. Minimal heterogeneity in macular fluorescence was also noted, indicating potential early RPE disruption. The structural integrity of the macula was maintained. In the OS, atrophy extended into the macular region, corresponding with outer retinal/RPE disruption observed on OCT. As in OD, mild marginal hyperfluorescence due to late scleral staining was observed. This angiographic pattern of continuous hypofluorescence, intact vasculature, and lack of exudative characteristics confirms chronic, non-exudative chorioretinal degeneration. The asymmetric macular involvement

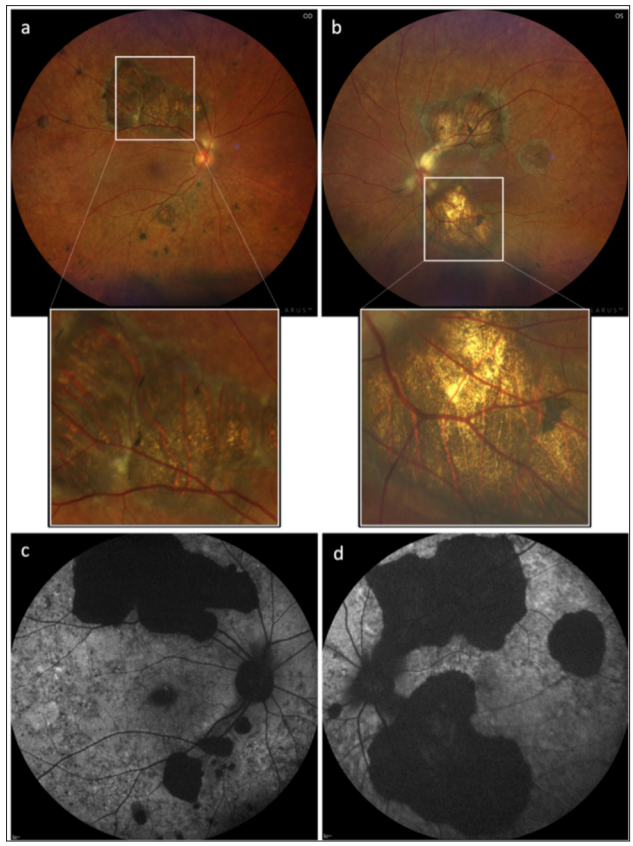

Figure 1. Fundus photography and fundus autofluorescence reveal pronounced areas of chorioretinal atrophy in both eyes. **a)** Fundus photograph OD: Extensive areas of chorioretinal atrophy are present, predominantly in the superotemporal and inferior quadrants, characterized by well-demarcated, "punched-out" lesions with exposed choroidal vessels and peripheral pigment clumping. The macular region shows focal RPE mottling and small hyperpigmented foci, while the foveal contour is preserved. **b)** Fundus photograph OS: More confluent and extensive chorioretinal atrophy is observed, involving the superotemporal, inferotemporal, and central macular regions. These atrophic zones display loss of the normal foveal reflex, central pigment clumping, and granular RPE changes. Bilateral peripapillary myelinated retinal nerve fibers are visible in both eyes, more prominent in OS. **c)** Fundus autofluorescence OD: Sharply demarcated areas of hypoautofluorescence are seen in the superotemporal and nasal quadrants, corresponding to complete RPE loss. Stippled hypoautofluorescence in the nasal macula indicates early RPE dysfunction. Transitional hyperautofluorescence at the margins of the atrophic lesions suggests ongoing RPE remodeling. **d)** Fundus autofluorescence OS: Panmacular hypoautofluorescence with foveal involvement is evident, along with extensive hypoautofluorescence in the superotemporal and inferotemporal quadrants. Hyperautofluorescent border zones are observed at the margins of the atrophy, indicating transitional RPE changes.

(relative OD preservation versus OS extension) aligns with clinical and multimodal imaging findings.

A systemic workup revealed normal complete blood count, renal function, serum electrolytes, erythrocyte sedimentation rate, and C-reactive protein levels. The interferon-gamma release assay (IGRA) and HIV serology were negative. Syphilis serology was positive, with a RPR titer of 1:16 and a CLIA value of 23.52.

The patient was assessed by the infectious diseases team, which indicated no systemic or neurological involvement, allowing for the deferral of a lumbar puncture. She was hos-

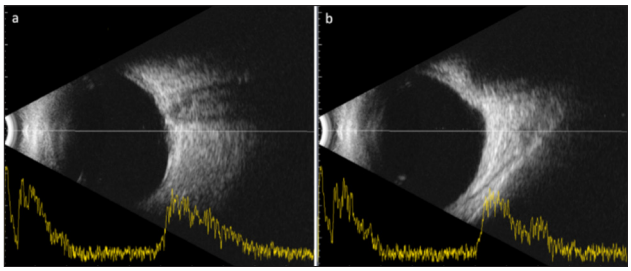

Figure 2. The B-scan images reveal bilateral posterior staphylomas, defined as localized posterior scleral ectasia with outward convex curvature. The OD **(a)** demonstrates a moderately deep staphyloma, exhibiting a gradual transition from the normal scleral contour. In contrast, the OS **(b)** displays a more pronounced staphyloma with greater axial depth, steeper walls, and abrupt demarcation between normal and ectatic sclera. Both eyes show an attached retina, clear vitreous, and normal optic nerve morphology.

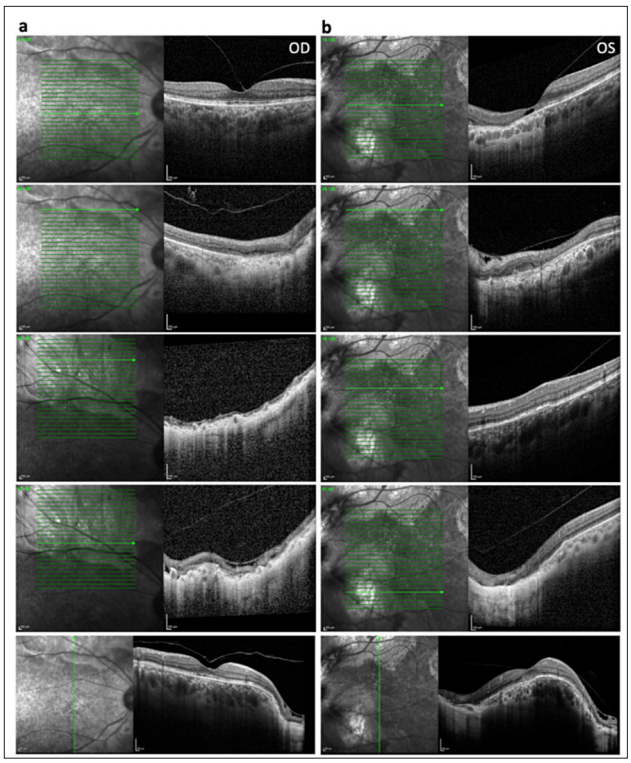

Figure 3. High-resolution spectral-domain OCT scans. **a)** OD: Preserved central foveal architecture. Focal EZ and interdigitation zone (IZ) disruption aligns with superotemporal chorioretinal atrophy observed fundoscopically. RPE thinning and choroidal hypertransmission are most pronounced in the superotemporal quadrant, extending into the temporal periphery. Peripheral scans reveal full-thickness chorioretinal atrophy (abrupt transition zones) and choroidal thinning, correlating with hypoautofluorescent FAF zones. **b)** OS: Advanced structural disruption with EZ/ELM loss extending from the peripapillary region into the superotemporal macula, matching FAF-defined atrophy. Diffuse RPE atrophy spans superotemporal, inferotemporal, and nasal macular quadrants, with outer retinal tubulations at atrophic margins. Posterior staphylomatous configuration aligns with B-scan findings. No exudative changes or vitreomacular interface abnormalities were observed (OD/OS).

pitalized and treated empirically for presumed neurosyphilis with intravenous benzylpenicillin (4 million IU every 4 hours for 10 days), followed by adjunctive intramuscular benzathine penicillin (2.4 million IU). Her hospitalization

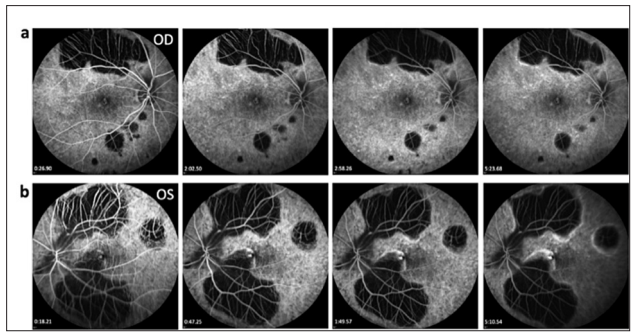

Figure 4. Serial fluorescein angiography frames. **a)** OD: Multiple sharply demarcated hypofluorescent lesions correspond to chorioretinal atrophy with complete RPE/choriocapillaris loss. Mild hyperfluorescence at the lesion borders, which gradually increases in intensity throughout the angiographic phases while maintaining well-defined margins, is consistent with late staining of the sclera rather than leakage/exudation. This pattern reflects scleral staining due to overlying RPE and choriocapillaris loss. The macular region shows subtle background fluorescence heterogeneity without structural disruption. **b)** OS: Extensive hypofluorescent plaques with marginal hyperfluorescence, which is consistent with late scleral staining. Atrophy involves the macula, where heterogeneous fluorescence reflects RPE/choriocapillaris loss. In both eyes, retinal vessels are preserved and cross atrophic areas without leakage or neovascularization.

proceeded without complications. At the first post-discharge follow-up, the RPR titer had diminished to 1:4, indicating a therapeutic response. Ophthalmological examination revealed improved visual acuity in the OD (85 ETDRS letters with -0.50 × 90°) and stable vision in the OS (50 ETDRS letters with -0.75 -0.50 × 145°). The fundus examination and OCT revealed no new lesions, indicating structural stability of the pre-existing areas of chorioretinal atrophy.

DISCUSSION

This case of bilateral, asymmetric chorioretinal atrophy with posterior staphylomas in a non-myopic, immunocompetent patient demonstrates the challenging diagnosis of ocular syphilis and reinforces its status as a "great imitator".[1,3] The diagnosis was confirmed with multimodal imaging and serological analysis, which indicated a reactive treponemal assay and decreasing RPR titers following penicillin treatment, emphasizing the importance of integrating clinical, imaging, and laboratory data in atypical presentations.

The extensive areas of chorioretinal atrophy observed on OCT in this case align with prior descriptions of chronic syphilitic chorioretinitis, characterized by RPE atrophy and choroidal thinning in untreated or late-stage ocular syphilis.[4,8,12] Fundus autofluorescence delineated areas of complete RPE loss, while fluorescein angiography confirmed the non-exudative nature of the atrophy. These findings are consistent with end-stage syphilitic chorioretinal degeneration but introduce a novel observation: the coexistence of multiple posterior staphylomas in a non-myopic patient. B-scan ultrasonography revealed asymmetric posterior ectasia, with OS exhibiting a more pronounced staphyloma corresponding topographically with the extent of chorioreti-

nal damage. While staphylomas are traditionally associated with high myopia,[13] we hypothesize that their occurrence in this non-myopic patient could potentially indicate inflammatory scleral remodeling, as in myopic patients and other chronic inflammatory chorioretinopathies.[14] Nonetheless, such cases remain exceptional, and this association in syphilis should be interpreted cautiously, as extensive clinical studies on ocular syphilis—particularly those highlighting delayed inflammation as a contributor to structural sequelae like chorioretinal atrophy,[4] do not identify staphylomas as a recognized complication. The staphylomas in this case likely resulted from persistent inflammation and biomechanical stress, as evidenced by the topographic correlation between atrophy and ectasia, which is more pronounced in the OS.

The differential diagnosis for chorioretinal atrophy included hereditary dystrophies such as retinitis pigmentosa, choroideremia, and gyrate atrophy. Gyrate atrophy was excluded due to the lack of mid-peripheral circular lesions, hyperpigmented borders, and childhood-onset nyctalopia, features inconsistent with this patient's presentation.[15] Recent Portuguese studies emphasize that ocular syphilis is frequently misdiagnosed as hereditary dystrophies due to overlapping imaging findings, reinforcing the need for serological testing in atypical cases.[4,7] Although syphilis can mimic retinitis pigmentosa,[16] this etiology was ruled out due to preserved retinal vasculature and the absence of bone-spicule pigmentation. Infectious etiologies like tuberculosis and toxoplasmosis were dismissed due to lack of vitritis or hyperpigmented scars.[17] This case exhibited multifocal chorioretinal atrophy, initially suggesting the potential diagnosis of serpiginous choroiditis or infectious multifocal serpiginoid choroiditis. Nazari and Rao[6] emphasize the importance of differentiating between idiopathic and infectious forms, as the latter, frequently linked to tuberculosis, requires specific antimicrobial treatment. In our patient, the absence of active lesion borders on FA and negative IGRA, combined with positive syphilis serology, supported the diagnosis of syphilitic chorioretinitis. This case reinforces the necessity of integrating multimodal imaging and comprehensive laboratory evaluation in atypical chorioretinal presentations.

The patient's clinical course highlights several critical lessons. Firstly, syphilis must be considered in instances of unexplained chorioretinal atrophy, even in immunocompetent individuals devoid of systemic symptoms. Secondly, a delayed diagnosis is significantly associated with irreversible structural damage, exemplified by OS's macular atrophy and loss of foveal architecture. Third, multimodal imaging is indispensable for distinguishing syphilitic lesions from mimics: fundus autofluorescence delineated areas of RPE loss, OCT revealed RPE atrophy and choroidal thinning, and FA confirmed the non-exudative nature of the atrophy.

The decision to defer lumbar puncture, based on absent neurological symptoms, adheres to current guidelines.[3,4] The favorable serological response to penicillin (RPR reduction from 1:16 to 1:4) confirms the efficacy of prompt treatment following diagnosis. However, the irreversible visual loss in the OS emphasizes the consequences of diagnostic delay.[3] At follow-up, structural stability of the chorioretinal atrophy was observed, with no new lesions, reinforcing the arrested progression of syphilitic damage after appropriate treatment of the infection.

In conclusion, this case aligns with emerging data from Portuguese tertiary centers, indicating a significant increase in ocular syphilis incidence, often presenting posterior segment involvement, and mimicking degenerative or inflammatory conditions. Clinicians must maintain high suspicion for syphilis in atypical chorioretinal atrophy, particularly in regions with rising incidence. Multimodal imaging and serology are fundamental to diagnosis, while prompt penicillin treatment is crucial to prevent irreversible vision loss. Further studies are needed to elucidate the mechanisms linking *Treponema pallidum* infection, scleral remodeling, and atrophy. The speculative association between syphilis and posterior staphylomas, which is not documented in large studies, underscores the necessity for more extensive research into the inflammatory factors driving scleral ectasia in non-myopic patients.

CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO:

AM-S: Contributed to the study conception, conducted the clinical analysis of the case, and wrote the manuscript.

AMS and MVP: Participated in the critical revision and scientific discussion.

JFC: Was responsible for patient follow-up, supervised the entire project, and reviewed the manuscript. All authors read and approved the final manuscript.

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Coriorretinite Placóide Posterior Sifilítica Aguda: Relato de Caso

Acute Syphilitic Posterior Placoid Chorioretinitis: Case Report

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RESUMO

A coriorretinite placóide posterior sifilítica aguda é uma forma de sífilis ocular que apresenta características clínicas e imagiológicas bem definidas. Apresentamos um caso clínico onde a clássica lesão placóide não era evidente à fundoscopia e não apresentava hiperfluorescência progressiva na angiografia fluoresceínica. No entanto, após realização de uma abordagem imagiológica multimodal, nomeadamente da imagem *Multicolor*, da autofluorescência e da tomografia de coerência ótica de domínio espectral, os achados característicos permitiram orientar o diagnóstico e iniciar o tratamento atempadamente.

PALAVRAS-CHAVE: Coriorretinite; Sífilis.

ABSTRACT

Acute syphilitic posterior placoid chorioretinitis is a form of ocular syphilis with well-defined clinical and imaging features. We present a case in which the classic placoid lesion was not evident on fundoscopy and did not present progressive hyperfluorescence on fluorescein angiography. However, after a multimodal imaging approach, including *Multicolor* imaging, fundus autofluorescence, and spectral-domain optical coherence tomography, the characteristic findings guided the diagnosis and allowed initiation of the appropriate therapy.

KEYWORDS: Chorioretinitis; Syphilis.

INTRODUÇÃO

O número de casos de sífilis ocular tem vindo a aumentar na sequência do aumento da incidência da infeção pelo *Treponema pallidum* na Europa e, especificamente, em Portugal.[1,2] Os sintomas oftalmológicos são a primeira manifestação em 81%-97% dos casos de sífilis ocular, que pode afetar qualquer uma das estruturas intraoculares, pelo que se preconiza testar, para esta infeção, todos os casos de inflamação intraocular.[3,4] Apesar das várias formas de apresentação que pode ter, em 1990, Gass *et al*[5] descreveram 6 casos de sífilis ocular que se apresentaram com uma ou mais lesões subretinianas placóides solitárias amareladas que demonstravam uma hiperfluorescência progressiva na angiografia fluoresceínica (AF). Nomearam estes achados de coriorretinite placóide posterior sifilítica aguda (CPPSA), definindo um padrão clínico e angiográfico típico, e quase patognomónico, desta infeção. Desde então, um total de 387 casos foram descritos na literatura com a caracterização dos achados noutros exames de imagem, nomeadamente na tomografia de coerência ótica de domínio espectral (SD-OCT) e na autofluorescência (FAF).[6-8]

Neste caso clínico, apresentamos um caso de CPPSA onde a clássica lesão placóide era pouco evidente à fundoscopia e não apresentava a típica hiperfluorescência progressiva na AF, mas os achados da imagem *Multicolor*, da FAF e da SD-OCT foram suficientes, e fundamentais, para orientar para o diagnóstico mais provável.

CASO CLÍNICO

Homem de 55 anos, recorre ao Serviço de Urgência por diminuição progressiva da acuidade visual do olho esquerdo, com um mês de evolução. Em termos de antecedentes patológicos apresentava infeção pelo vírus da imunodeficiência humana, encontrando-se medicado e acompanhado na consulta externa de Infeciologia. No estudo analítico mais recente apresentava contagens dos linfócitos T CD4+ de 787/mm^3 e carga vírica indetetável. Apresentava ainda antecedentes de asma e alergia ao conservante metilisotiazolinona. Desconhecia antecedentes oftalmológicos de relevo.

Ao exame objetivo, apresentava uma melhor acuidade visual corrigida de 10/10 do olho direito e de contagem de dedos a 1 m do olho esquerdo. Não apresentava defeito pupilar aferente relativo. À biomicroscopia não foram observados achados de relevo no segmento anterior do olho direito. No olho esquerdo, foram observados precipitados queráticos finos e células 0,5+. A pressão intraocular era normal em ambos os olhos. À fundoscopia, apresentava edema do disco óptico bilateral, mais exuberante à direita e alterações pigmentares da mácula à esquerda.

Relativamente aos exames auxiliares de diagnóstico, a imagem *Multicolor*, à direita, demonstrou edema exuberante do disco óptico e áreas amareladas, de limites mal definidos e profundas na emergência das arcadas vasculares temporais, assim como manchas e pontos amarelados distribuídos pela retina em torno da arcada vascular temporal superior (Fig. 1a). A imagem *Multicolor*, à esquerda, demonstrou uma área amarelada profunda peripapilar e macular, com manchas e pontos amarelados também distribuídos para além da arcada vascular temporal superior (Fig. 1b). A SD-OCT do disco óptico revelou espessamento

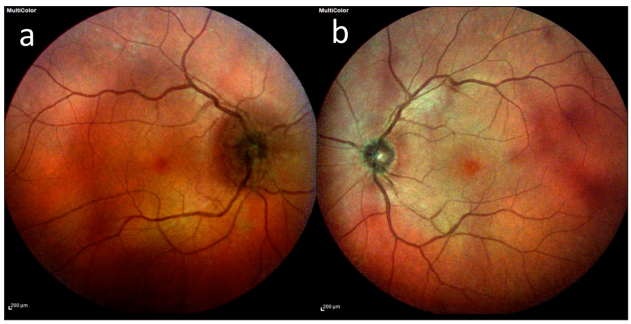

Figura 1. Imagem *Multicolor*: a) olho direito, edema exuberante do disco óptico direito e áreas amareladas profundas na emergência das arcadas vasculares temporais e manchas e pontos amarelados distribuídos para além da arcada vascular temporal; b) olho esquerdo, área em placa amarelada profunda peripapilar e macular, com manchas e pontos amarelados distribuídos para além da arcada temporal superior.na emergência das arcadas vasculares temporais e manchas e pontos amarelados distribuídos para além da arcada vascular temporal; b) olho esquerdo, área em placa amarelada profunda peripapilar e macular, com manchas e pontos amarelados distribuídos para além da arcada temporal superior.

exuberante da camada de fibras nervosas à direita e, menor, à esquerda (Fig. 2a e 2b). A SD-OCT macular, à direita, evidenciou alguns pontos hiperrefletivos no vítreo e fluído intrarretiniano peripapilar (Fig. 2c), à esquerda, revelou disrupção da zona elipsóide com disrupção intermitente da membrana limitante externa (MLE) e granularidade do epitélio pigmentar da retina (EPR) envolvendo toda a área peri-foveal (Fig. 2d). A AF demonstrou hiperfluorescência progressiva do disco óptico em ambos os olhos, mais acentuada à direita, sem outras alterações aparentes (Fig. 3). A FAF revelou, à direita, vários pontos e manchas hiperautofluorescentes para além das arcadas vasculares e duas áreas mais confluentes, uma peripapilar e uma temporal à má-

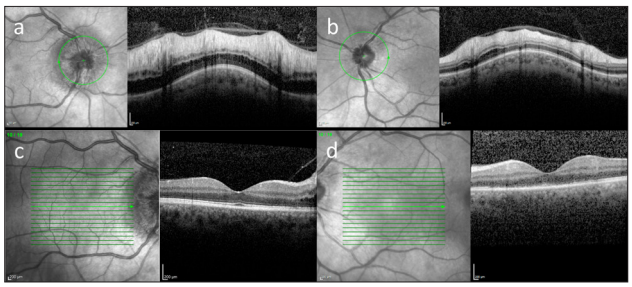

Figura 2. Tomografia de coerência ótica de domínio espectral: a) Nervo óptico direito: camada de fibras nervosas com aumento da espessura. b) Nervo óptico esquerdo: camada de fibras nervosas com ligeiro aumento da espessura; c) Mácula direita: alguns pontos hiperrefletivos no vítreo, fluído intrarretiniano peripapilar; d) Mácula esquerda: disrupção da zona elipsóide com disrupção intermitente da membrana limitante externa e granularidade do epitélio pigmentar da retina.

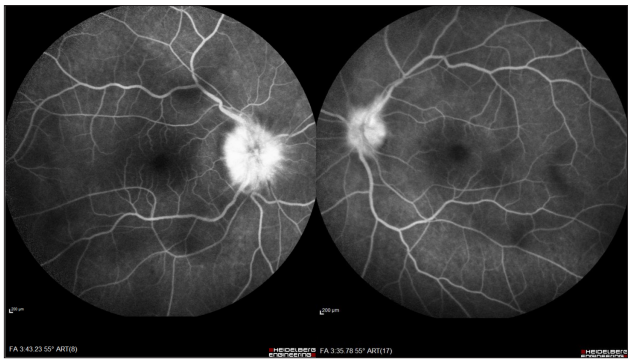

Figura 3. Angiografia fluoresceínica demonstrou hiperfluorescência do disco em ambos os olhos, mais acentuada à direita.

cula (Fig. 4a), à esquerda, uma placa hiperautofluorescente peripapilar com atingimento foveal, com manchas e pontos hiperautofluorescentes menores em torno das arcadas vasculares (Fig. 4b).

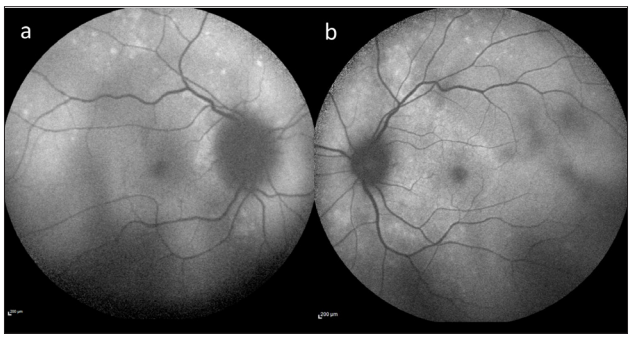

Figura 4. Autofluorescência: a) Olho direito: vários pontos e manchas hiperautofluorescentes para além das arcadas vasculares e duas áreas mais confluentes, uma peripapilar e uma temporal à mácula b) Olho esquerdo: placa hiperautofluorescente peripapilar e macular e manchas e pontos hiperautofluorescentes distribuídas para além de ambas as arcadas vasculares temporais.

Os achados imagiológicos foram essenciais para a identificação das lesões placóides bilaterais e suspeita do diagnóstico de CPPSA. Foi encaminhado para o Serviço de Urgência de Medicina Interna para avaliação global e colheita de estudo analítico. Nesta avaliação, foi encontrado um *rash* urticariforme exuberante do tronco e membros superiores. O estudo analítico revelou um *rapid plasma reagent* (RPR) positivo (1/128) e anticorpos IgM e IgG positivos para sífilis. A tomografia computadorizada do crânio e a punção lombar não revelaram alterações.

Foi confirmado o diagnóstico de sífilis secundária, com atingimento ocular, e iniciado o tratamento endovenoso com penicilina benzatínica 24 milhões de unidades por dia, durante 14 dias, em regime de internamento. Fez ainda um curso de prednisolona oral em desmame.

A evolução do quadro clínico foi favorável após iniciar a antibioterapia, com progressiva melhoria da acuidade visual e resolução das alterações ao exame oftalmológico. Dois meses depois de completar o tratamento antibiótico apresentava uma melhor acuidade visual corrigida de 10/10 em ambos os olhos, com um exame oftalmológico normal (Fig. 5).

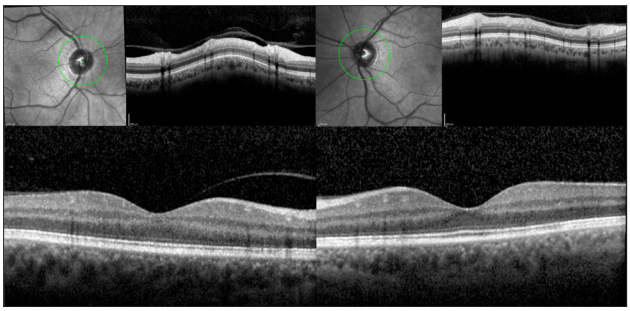

Figura 5. Tomografia de coerência ótica de domínio espectral do disco óptico e macular 2 meses após o término do tratamento antimicrobiano, evidenciando resolução anatómica completa.

DISCUSSÃO

A CPPSA é um quadro típico da sífilis ocular cujos achados clínicos e imagiológicos estão bem caracterizados na literatura: à fundoscopia são visíveis lesões placóides extensas, amareladas, ovais ou circulares, ao nível da retina externa e EPR; a AF mostra hipofluorescência nos tempos precoces seguida de hiperfluorescência tardia com impregnação das lesões; a angiografia com verde de indocianina revela uma lesão hipofluorescente durante todo o exame; a FAF mostra uma lesão hiperautofluorescente; a SD-OCT revela disrupção da zona elipsóide, com ou sem disrupção da MLE, espessamento e elevações nodulares hiperrefletivas do EPR e lesões hiperrefletivas em pinpoint ao nível da coróide.[7,8]

No nosso caso clínico, as lesões placóides não eram facilmente identificadas à fundoscopia. Esta dificuldade já foi reportada por Wells *et al*,[9] onde mostraram que à fundoscopia as lesões podem ser subtis e que as imagens de pseudo-cor e a autofluorescência poderão mais facilmente detetá-las, como no nosso caso. Outro achado curioso, foi a falta de impregnação das lesões placóides na AF. Apesar de haver outros casos descritos com impregnação ligeira na AF, achamos que o facto da captação das imagens ter terminado antes dos 4 minutos pode ser a razão pela qual não observamos uma impregnação mais intensa.[10]

Em conclusão, este caso ilustra a importância da avaliação multimodal nas doenças do segmento posterior, que permitiu um diagnóstico e tratamento célere com recuperação total da visão e das estruturas oculares envolvidas.

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VL: Responsável pela recolha de dados, redação do texto, obtenção e edição de imagens clínicas, revisão crítica do conteúdo intelectual importante.

MR: Responsável pela supervisão deste projeto, revisão crítica do conteúdo intelectual importante e contribuiu com a sua experiência para a conclusão do manuscrito.

JP: Responsável pela supervisão deste projeto, revisão crítica do conteúdo intelectual importante e contribuiu com a sua experiência para a conclusão do manuscrito.

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Acute Macular Neuroretinopathy Related to COVID-19 Infection: Case Report

Neuroretinopatia Macular Aguda Associada à Infeção por COVID-19: Relato de Caso

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ABSTRACT

Acute macular neuroretinopathy (AMN) is a relatively rare condition characterized by the sudden onset of acute scotomas, which commonly affects young women. More recently, AMN has been reported in association with COVID-19. The diagnosis is based on typical imaging features. We present a case of presumed COVID-19 associated bilateral AMN.

A 20-year-old female presented with a right eye scotoma, after COVID-19 infection. Multimodal imaging showed dark grey, petaloid, perifoveal lesions in near infra-red, which corresponded anatomically to the red brown lesions in the fundus, the scotomas drawn on the Amsler grid and the lowest sensitivity points in the perimetry. Hyperreflectivity of the outer plexiform/nuclear layers and ellipsoid zone rarefaction were observed on optical coherence tomography. Visual acuity remained maximal during follow-up and the scotoma and typical features subsided 9 months after the diagnosis.

KEYWORDS: COVID-19; Macula Lutea; Retina; Retinal Diseases.

RESUMO

A neurorretinopatia macular aguda (AMN) é uma condição relativamente rara caracterizada pelo aparecimento súbito de escotomas agudos, que geralmente afeta mulheres jovens. Mais recentemente, a AMN foi reportada em associação com a COVID-19. O diagnóstico é baseado em características típicas de imagem. Apresentamos um caso de AMN bilateral presumivelmente associada à COVID-19.

Uma mulher de 20 anos apresentou um escotoma no olho direito após o diagnóstico de COVID-19. A imagiologia multimodal mostrou lesões perifoveais cinza-escuras e petaloides no infravermelho próximo, que correspondiam anatomicamente às lesões vermelho-acastanhadas na fundoscopia, aos escotomas desenhados na grelha de Amsler e aos pontos de menor sensibilidade na perimetria. Hiperrefletividade das camadas plexiformes/nucleares externas e rarefação da zona elipsoide foram observadas na tomografia de coerência óptica. A acuidade visual permaneceu máxima durante o acompanhamento e o escotoma e as características típicas atenuaram 9 meses após o diagnóstico.

PALAVRAS-CHAVE: COVID-19; Doenças da Retina; Macula Lutea; Retina.

INTRODUCTION

Acute macular neuroretinopathy (AMN), first reported in 1975 by Bos and Deutman, is a relatively rare condition characterized by the sudden onset of acute scotomas, which commonly affect young women.[1] Although the pathogenesis of AMN is complex, recent research suggests a microvascular etiology, with ischemia of the deep capillary plexus.[2]

Proposed etiologic factors include a preceding respiratory or influenza-like illness, although oral contraceptives, epinephrine or ephedrine, trauma, dehydration, hypovolemia, systemic shock, and systemic lupus erythematosus have also been reported to be associated with AMN.[2,3] More recently, AMN has been reported in association with COVID-19, both with the infection and after vaccination. [4,5]

We present a case of presumed COVID-19 associated bilateral AMN.

CASE REPORT

A 20-year-old Caucasian female presented with right eye (RE) scotoma for 1 week, starting 48 hours after COVID-19 infection diagnosis. Her initial complaints of odynophagia and bilateral frontal headache had subsided with symptomatic medication during initial evaluation. Her neurological exam was otherwise unremarkable. She had no relevant past medical or ocular history, including family history, and no regular drug intake.

The best corrected visual acuity was 20/20 in both eyes. However, using the Amsler grid she reported bilateral central scotoma, larger in the RE. Standard automated perimetry (SAP) documented decreased sensitivity of the central points in the RE (Fig. 1). Intraocular pressure was 15 mmHg in the RE and 16mmHg in the left eye (LE). Pupils were equal and reactive to light, with no afferent relative pupillary defect. Her chromatic vision assessed through Ishihara plates was normal, scoring 17/17 plates bilaterally.

Anterior segment examination revealed a transparent cornea, an anterior chamber without cells or flare and a clear lens. Fundus observation through clear media (no vitreous cells or haze) uncovered multiple petaloid red brown perifoveal lesions in the RE and an isolated small oval red lesion in the papillomacular bundle of the LE.

Near-infrared reflectance (NIR) showed well-demarcated, dark grey lesions around the fovea (hyporeflectant), in the described fundoscopic distribution. Macular spectral-domain optical coherence tomography (SD-OCT) revealed a disturbance of the outer retinal architecture within the lesions, namely a hyperreflective outer plexiform layer, thinned outer nuclear layer and disrupted ellipsoid and interdigitation zones. OCT-angiography demonstrated flow voids in deep capillary plexus. Fundus autofluorescence (FAF) exhibited a subtle increase in autofluorescence over the lesions (Fig. 2). Fluorescein and indocyanine green angiography were unremarkable (Fig. 3). Head computed tomography and cerebral venogram were normal.

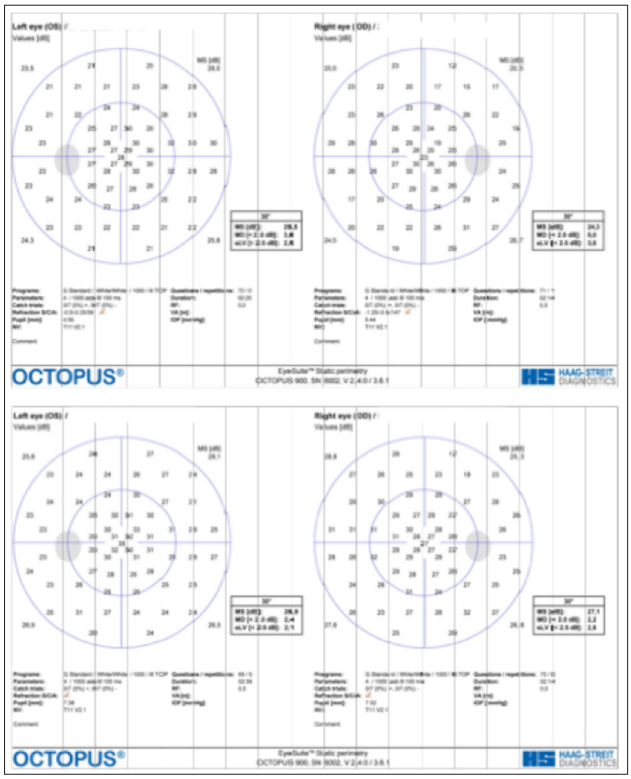

Figure 1. Visual fields in standard automated perimetry at presentation (top) and 6 months of follow-up (bottom).

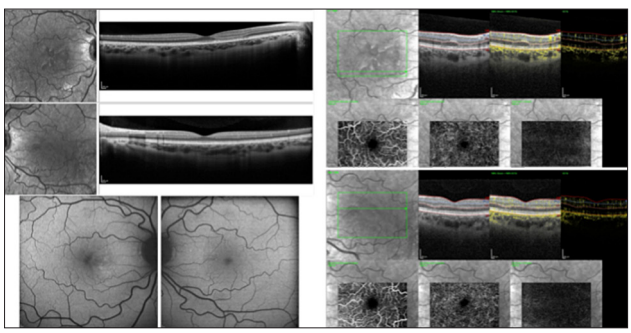

Figure 2. Multimodal imaging at diagnosis, SD-OCT (top, left), OCT-angiography (right) and FAF (bottom, left).

A presumed diagnosis of bilateral AMN superimposed on COVID-19 infection was established and the patient remained on observation. The COVID-19 infection itself was mild in severity, with the initial symptoms resolving after symptomatic medication.

Throughout the subsequent follow-up, at 6 weeks and 9 months, the patient reported subjective improvement of the scotoma. Visual acuity remained excellent since presentation. There was objective improvement of the central sensitivities in SAP, no alterations were seen at fundoscopy (Fig. 4) and the retinal exam findings were less prominent (NIR, SD-OCT, FAF), leaving a subtle outer nuclear layer atrophy noted in SD-OCT (Fig. 5).

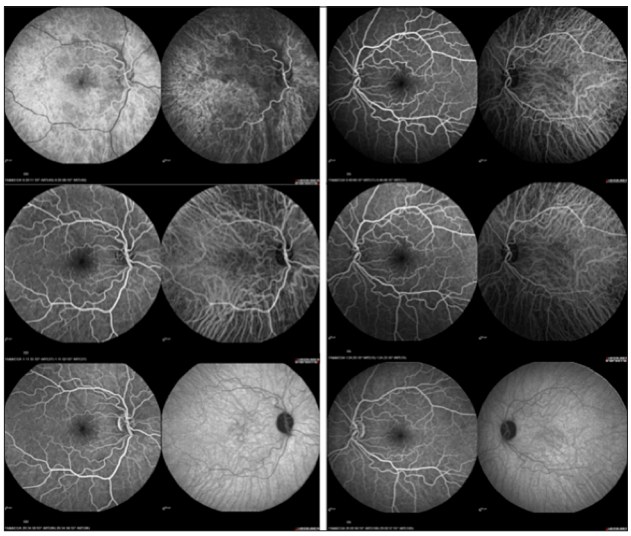

Figure 3. Fluorescein and indocyanine green angiography at diagnosis.

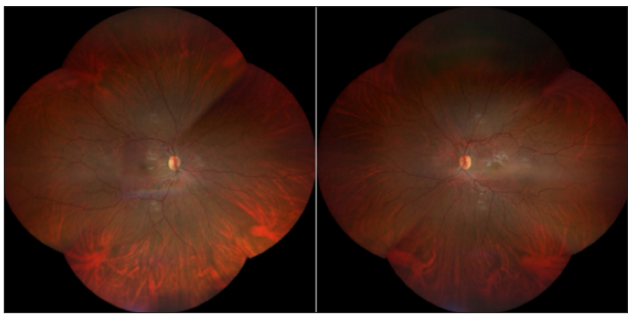

Figure 4. Retinography at 9 months follow-up visit.

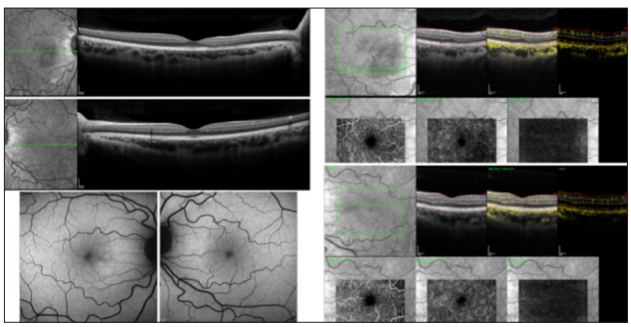

Figure 5. Multimodal imaging at 9 months follow-up visit, SD-OCT (top, left), OCT-angiography (right) and FAF (bottom, left).

DISCUSSION

The exact mechanism underlying AMN has not been elucidated, but the occlusive microvascular theory is the most widely accepted hypothesis. It remains unknown which circulation is primarily affected, but there is a focal compromise in perfusion of the deep retinal capillary plexus or choriocapillaris at the sites of the lesions, both circulations supplying the photoreceptors.[5] Infectious diseases like COVID-19 stimulate the production of type I interferon, a cytokine responsible for the activation of acute phase proteins that lead to vascular endothelium damage, producing a hypercoagulable state predisposing to AMN.[5]

The increased number of AMN cases reported during or after COVID-19 infection raised the suspicion of a causal association, particularly when considering that viral illnesses often preceded the retinal findings.[4] In our case report, we showed a close temporal relationship between COVID-19 diagnosis and AMN onset, but a causal relationship cannot be inferred. This limitation was also pointed out in the largest published cohort of COVID-19 possibly associated AMN, due to the rarity of the diagnosis and presence of concurrent risk factors.[6]

Focusing on COVID-19 related AMN, our patient developed a scotoma 48 hours after COVID diagnosis, according to what has been reported in the literature (time of ocular symptom onset was 2.62 days and 87.9% of COVID-19 related AMN exhibited scotomas in the study).[3]

Irrespective of controversies regarding etiology, multimodal imaging safeguards the diagnosis of AMN. We presented a well-documented case illustrative of this diagnosis. Dark grey, petaloid, perifoveal lesions with the tip pointed towards the fovea were observed in NIR, which corresponded anatomically to the red brown lesions in the fundus, the scotomas drawn on the Amsler grid and the lowest sensitivity points in SAP. Hyperreflectivity of the outer plexiform/nuclear layers and ellipsoid zone rarefaction were observed on OCT. Fluorescein and indocyanine green angiography were noted to be normal, like in most cases of AMN.

Differential diagnosis for AMN includes paracentral acute middle maculopathy (PAMM), acute macular outer retinopathy (AMOR) and acute retinal pigment epitheliitis (ARPE). Unlike AMN, an outer retina pathology, PAMM has a distinct inner retina involvement, first with hyperreflectivity of the inner nuclear and inner plexiform layers, which later may transform into atrophy.[7] AMOR, also known as AMN type 2, differs from AMN because ellipsoid zone loss occurs without outer plexiform layer hyperreflectivity. However, this term is also used as a substitute for AMN by some authors to emphasize the outer retina involvement.[8] Lastly, ARPE is typically unilateral presenting with a focal retinal pigment epithelium hyperreflectivity with upward extension named the "moustache sign". Again, this disease has recently been revisited due to diagnostic criteria that fit well within other preexisting retinal diseases.[9]

In conclusion, our case report illustrates a presumed COVID-19 associated bilateral AMN, with typical findings in multimodal imaging, namely SAP, NIR, FAF and SD-OCT.

RESPONSABILIDADES ÉTICAS

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

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Confidencialidade dos Dados: Os autores declaram ter

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Consentimento: Consentimento do doente para publicação obtido.

Proveniência e Revisão por Pares: Não comissionado; revisão externa por pares.

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Patient Consent: Consent for publication was obtained.

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Síndrome de Múltiplas Manchas Brancas Evanescentes Bilateral e Recorrente

Recurrent and Bilateral Multiple Evanescent White Dot Syndrome

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RESUMO

A síndrome de múltiplas manchas brancas evanescentes (SMMBE) é uma uveíte posterior, idiopática e autolimitada, geralmente unilateral.

O caso clínico relata uma doente de 21 anos que desenvolveu uma diminuição súbita da acuidade visual (AV), inicialmente do olho esquerdo (OE). Os achados na fundoscopia, correlacionados com as alterações na tomografia de coerência ótica (OCT), autofluorescência do fundo ocular (FAF) e angiografia com verde de indocianina (ICG) eram compatíveis com o diagnóstico de SMMBE. Aproximadamente um mês após o início dos sintomas, a doente recuperou a AV e verificou-se a regressão das lesões.

Após 5 meses do início dos sintomas no OE, a doente apresentou-se com diminuição AV, desta vez no olho direito (OD). Os achados nos exames de imagem eram compatíveis com SMMBE bilateral e recorrente, descrito em apenas 10% dos casos.

Este caso ilustra a importância da imagem multimodal para diagnóstico e seguimento de coriocapilaropatias inflamatórias.

PALAVRAS-CHAVE: Síndrome de Manchas Brancas/diagnóstico; Síndrome de Manchas Brancas/tratamneto.

KEYWORDS: White Dot Syndromes/diagnosis; White Dot Syndromes/therapy.

INTRODUÇÃO

A síndrome de múltiplas manchas brancas evanescentes (SMMBE) constitui uma uveíte posterior, idiopática e autolimitada. Salvo raras exceções descritas, habitualmente tem envolvimento unilateral. Afeta maioritariamente jovens adultos, com predomínio no sexo feminino e míopes. Em até 50% dos casos é antecedido por pródromo viral. Pode manifestar-se por diminuição súbita da acuidade visual (AV), escotomas, fotopsias e metamorfopsias. Na fundoscopia é característica a ocorrência de múltiplas lesões retinianas amarelo-esbranquiçadas, mal definidas e dispersas. O diagnóstico é confirmado por imagem multimodal, nomeadamente: tomografia de coerência ótica (OCT), autofluorescência do fundo (FAF) e angiografia com verde de indocianina (ICGA). A recuperação completa da AV ocorre habitualmente dentro de três a nove semanas, com resolução espontânea das lesões. As recorrências são raras (10%).

CASO CLÍNICO

Doente do sexo feminino, 21 anos, saudável, com antecedentes oftalmológicos de miopia e astigmatismo, com acuidade visual corrigida: olho direito (OD) 10/10 (-2,75-1,25x100º), olho esquerdo (OE) 10/10 (-3,50-0,75x55º).

A doente recorreu ao serviço de urgência (SU) por diminuição aguda da AV OE com duas semanas de evolução e escotoma OE. Não havia história de trauma ou síndrome gripal recente.

Da avaliação oftalmológica realizada, destacava-se: melhor acuidade visual corrigida (MAVC) OD: 10/10, MAVC OE: 4/10, biomicroscopia sem alterações. Fundoscopia (FO) OE sem vitrite, papila com bordos nítidos, mácula com alteração central de pigmentação. Foram realizados retinografia (Fig. 1), OCT mácula (Fig. 2), angiografia fluoresceína (AF) (Fig. 3), ICG (Fig. 4) e FAF (Fig. 5)– foi colocada hipótese de SMMBE no OE.

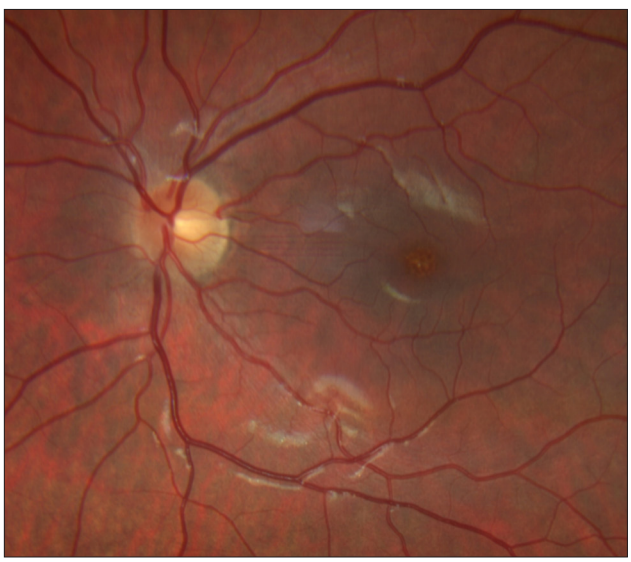

Figura 1. Retinografia OE: documenta granularidade foveal.

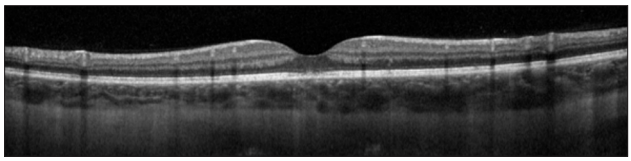

Figura 2. Tomografia de coerência ótica (OCT) OE: demonstra alterações nos segmentos externos dos fotorrecetores - disrupção da zona elipsoide e atenuação da linha do epitélio pigmentar da retina (EPR) subfoveal.

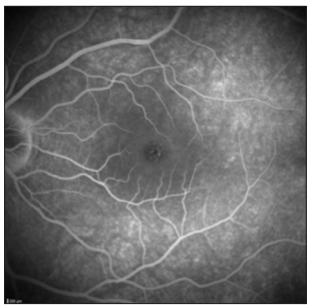

Figura 3. Angiografia com fluoresceína OE: demonstra lesões irregulares hiperfluorescentes na fase intermédia-tardia.

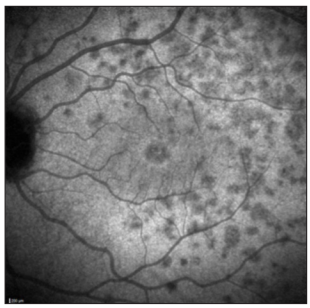

Figura 4. Angiografia com verde indocianina OE: demonstra áreas dispersas de hipofluorescência mais evidente na fase angiográfica tardia.

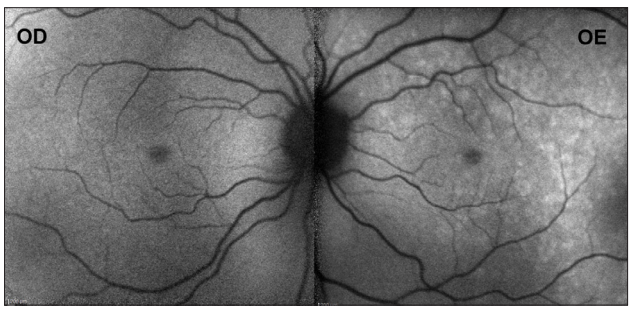

Figura 5. Autofluorescência do fundo ocular ODE: OE com evidência de lesões hiperautofluorescentes dispersas pela mácula.

Na consulta de reavaliação, realizada após um mês da avaliação inicial, verificou-se resolução da sintomatologia, MAVC OD 10/10, MAVC OE 10/10 e a fundoscopia do OE revelou papila e mácula sem alterações. Repetiu OCT mácula (Fig. 6) e autofluorescência do fundo ocular (FAF) (Fig. 7).

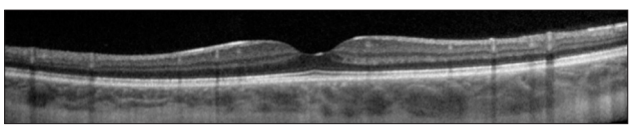

Figura 6. OCT OE: resolução das alterações nos segmentos externos dos FR (linha elipsoide e EPR).

Foi reavaliada dois meses após o evento inicial. Mantinha-se assintomática, sem alterações no exame objetivo e com normalização dos achados na FAF.

Após cinco meses do início dos sintomas no OE, a doente recorreu novamente ao SU por diminuição da acuidade visual e escotoma, desta vez no olho direito (OD), com uma semana de evolução. A avaliação oftalmológica revelou: MAVC OD 6/10, MAVC OE 10/10. A biomicroscopia do segmento anterior e a fundoscopia do ODE não apresentaram alterações significati-

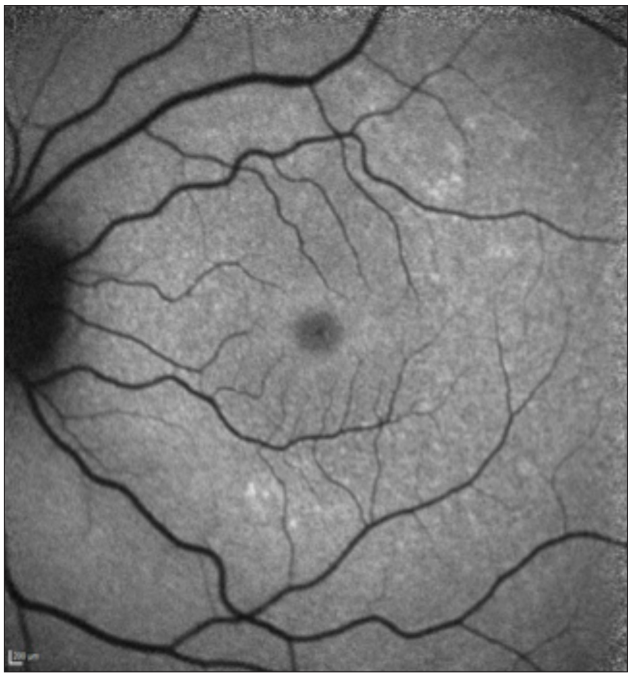

Figura 7. Autofluorescência azul OE: lesões hiperautofluorescentes residuais.

vas, assim como a avaliação laboratorial revelou-se inocente.

Realizou OCT mácula (Fig. 8), retinografia (Fig. 9) e FAF OD (Fig. 10) que demonstraram lesões hiperautofluorescentes dispersas na mácula. Foi colocada a hipótese de SMMBE recorrente sequencial. A doente manteve seguimento em consulta, com resolução espontânea e completa do quadro clínico após um mês do início da sintomatologia, sem evidência de lesões residuais no OCT e na FAF. Sem novos episódios de diminuição súbita da acuidade visual durante um ano de seguimento.

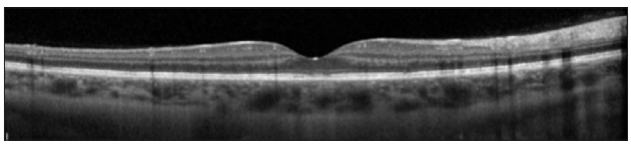

Figura 8. OCT OD: demonstra disrupção dos segmentos externos (zona elipsoide e EPR).

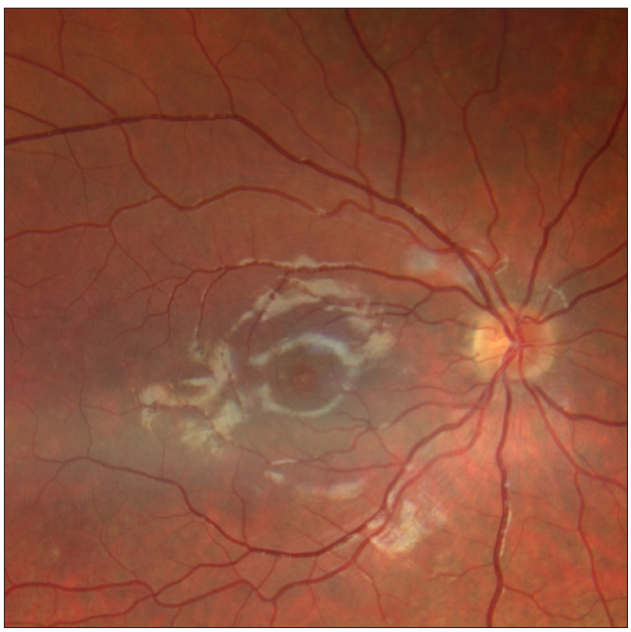

Figura 9. Retinografia OD: não documentava granularidade da fóvea ou manchas brancas na mácula.

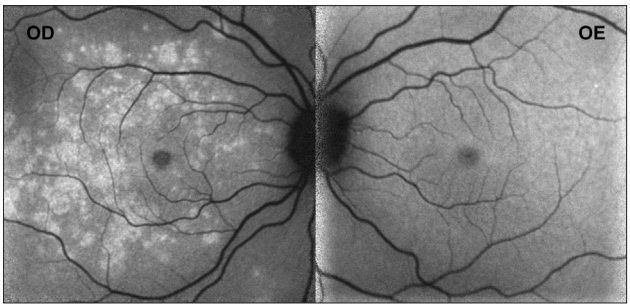

Figura 10. Autofluorescência do fundo ocular ODE: OD com evidência de lesões hiperautofluorescentes dispersas pela mácula.

DISCUSSÃO

A SMMBE foi inicialmente descrita em 1984 por Lee Jampol e Paul Sieving, que publicaram as características clínicas e eletrofisiológicas desta síndrome.[1] Historicamente, em 1995, a SMMBE viria a ser integrada no grupo das *White dot syndromes* (WDS). Esta seria uma forma de agrupar um grupo alargado de doenças que tinham em comum a aparência da fundoscopia: manchas brancas, que variavam em dimensão e configuração.[2] Mais recentemente, com o advento da imagem multimodal, foi possível demonstrar que os mecanismos fisiopatológicos das diferentes doenças englobadas nas WDS são muito heterogéneos. Atualmente advoga-se que a terminologia WDS é incorreta, devendo ser classificadas de acordo com o respetivo mecanismo fisiopatológico em: coriocapilaropatias (p.e. SMMBE, epiteliopatia pigmentar placóide multifocal posterior aguda, coroidite multifocal idiopática, coroidopatia serpiginosa) e coroidopatias estromais (p.e. síndrome de Vogt-Koyanagi-Harada, retinocoroidite *birdshot* HLA-A29).[3]

O SMMBE pode manifestar-se por escotomas temporal ou paracentral, fotopsias, metamorfopsias e perda aguda indolor da AV unilaterais. É caracterizado por múltiplas lesões retinianas amarelo-esbranquiçadas, isoladas ou confluentes, entre 100 µm – 200 µm, mais concentradas na região peripapilar e paramacular, mas pode ter atingimento da média periferia. Também pode estar associada a *flare* da câmara anterior, vitrite ligeira e edema do disco ótico. Numa fase pós-aguda, pode ser evidente apenas o aspeto granular da fóvea, descrito em 70%-94% dos casos.[4]

Em cerca de 50% dos doentes, o envolvimento ocular é antecedido por síndrome gripal, pelo que se suspeita que a SMMBE possa ser desencadeado por agentes virais ainda não identificados. Quanto à sua fisiopatologia, advoga-se que resulte de fenómenos vaso-oclusivos ao nível da coróide interna, com consequente isquémia da retina externa e dano dos segmentos externos dos fotorrecetores. Esta teo-

ria é corroborada pelos achados na ICGA, em que são evidentes múltiplas áreas hipofluorescentes no polo posterior, peri-disco e média periferia e, mais evidentes em fases angiográficas tardias. Estas lesões têm uma correspondência com as áreas de hiperautofluorescência na FAF e disrupção dos segmentos externos dos fotorrecetores (zona elipsoide e interdigitação) no OCT.[5]

Já a AF pode demonstrar uma hiperfluorescência punctiforme, resultado da vasodilatação reativa e consequente difusão secundária à isquémia induzida pela hipoperfusão coriocapilar. Como está dependente da gravidade do processo vaso-oclusivo, os sinais na AF podem estar ausentes, pelo que a sua utilidade no diagnóstico de SMMBE é limitado.[6]

Da mesma forma, a angiografia-tomografia de coerência ótica (OCT-A) não tem alterações aparentes na SMMBE, uma vez que a circulação coroideia afetada são os capilares terminais, onde o fluxo não é significativo, pelo que não é possível de ser documentado por esta técnica. Assim, o OCT-A não tem relevância no diagnóstico de SMMBE, ao contrário das restantes coriocapilarites.[6]

Deste modo, a ICGA e FAF são as principais modalidades de imagem no diagnóstico, avaliação da extensão da lesão e impacto na acuidade visual na SMMBE. Mesmo na ausência de alterações na fundoscopia, a evidência de lesões características na FAF e ICGA podem sugerir o diagnóstico.

Na maioria dos casos, a SMMBE tem resolução espontânea, sem necessidade de terapêutica. A FAF e o OCT, enquanto métodos não invasivos, rápidos e com elevada sensibilidade, têm um papel relevante no seguimento, de forma a detetar os raros casos em que existe progressão. Nestes, deve ser ponderada a terapêutica com corticoterapia sistémica e/ou injeções intravítreas com anti-VEGF (no caso de neovascularização coroideia inflamatória- NVC-associada).[7]

Das coriocapilarites, a coroidite multifocal idiopática (CMI) é o principal diagnóstico diferencial, uma vez que pode ter os mesmos achados na ICGA e FAF. Já no OCT, as lesões ativas demonstram elevação do EPR devido à deposição de material no espaço sub-EPR. A CMI inicialmente pode ter uma apresentação semelhante ao SMMBE, no entanto é caracterizada por maior extensão das lesões, não resolução, recorrências, bilateralidade e cicatrizes coriorretinianas (evidenciadas por lesões hipoautofluorescentes na FAF), a longo prazo. Devido às recorrências e múltiplas cicatrizes, existe maior risco de desenvolvimento de NVC (em até 30%).[5,7] De destacar ainda a doença de Krill (epitilite pigmentar da retina aguda) como um importante diagnóstico diferencial, uma vez que também se pode apresentar com ponteado de pigmento foveal na fundoscopia e alterações no OCT comuns com o SMMBE. A realização da ICGA e FAF é imperativo, uma vez que as lesões, se presentes, estão limitadas à zona da fóvea. No entanto, persistem dúvidas quanto à sua verdadeira entidade nosológica.[8]

O caso descrito parece tratar-se de um caso raro de SMMBE com envolvimento sequencial de ambos os olhos, que pode ocorrer em até 10%.[9] É ilustrativo da importância da imagem multimodal no diagnóstico diferencial e seguimento das coriocapilaropatias inflamatórias primárias, ao permitir uma caracterização precisa da coróide e respetiva compreensão do processo patológico, através do maioritariamente de ICGA, FAF e OCT.

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Punctate Inner Choroiditis with Choroidal Neovascularization Following COVID-19 Vaccination

Coroidite Punctata Interna com Neovascularização Coroideia Após Vacinação Contra a COVID-19

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ABSTRACT

We report a case of a 23-year-old myopic female with inaugural punctate inner choroiditis complicated by bilateral choroidal neovascularization (CNV). She presented 5 weeks after COVID-19 vaccination with ongoing symptoms for 3 weeks. The patient was treated with bilateral aflibercept 2 mg intravitreal injections and oral corticosteroids and underwent immunosuppression with mycophenolate mofetil (MMF). Twelve months after the last anti-VEGF injections and while on MMF, the CNV remained quiescent in both eyes, with no signs of new inflammatory lesions on multimodal imaging. We speculate that COVID-19 vaccine triggered PIC in this patient with a likely genetic susceptible background.

KEYWORDS: Choroidal Neovascularization; COVID-19 Vaccines; White Dot Syndromes.

RESUMO

Apresentamos o caso clínico de uma mulher míope de 23 anos diagnosticada com coroidite punctata interna (PIC) inaugural complicada por neovascularização coroideia (NVC) bilateral. A apresentação ocorreu 5 semanas após a vacinação contra a COVID-19, estando sintomática há 3 semanas. A doente foi tratada com injecções intravítreas bilaterais de aflibercept 2 mg e corticóide oral, tendo iniciado posteriormente imunossupressão com micofenolato mofetil (MMF). Doze meses após as últimas injecções intravítreas e sob MMF, a NVC permanecia quiescente em ambos os olhos, sem sinais de novas lesões inflamatórias na imagiologia multimodal. Consideramos que a vacina contra a COVID-19 terá despoletado um quadro de PIC nesta doente com provável susceptibilidade genética prévia.

PALAVRAS-CHAVE: Neovascularização Coroidal; Vacinas Contra a COVID-19; Síndrome de Manchas Brancas.

INTRODUCTION

Punctate inner choroiditis (PIC) consists of a relatively uncommon type of multifocal choroiditis that affects the posterior pole, characterized by multiple punctate choroidal lesions smaller than 250 μm in diameter. It is noninfectious, nonsystemic and immunomediated. Intraocular inflammation signs are very mild or absent.[1] PIC is included in the umbrella term of white dot syndromes.[2]

We report a well-documented case of inaugural PIC complicated by CNV with sequential bilateral involvement, in close temporal relation with COVID-19 vaccination.

CASE REPORT

A 23-year-old female attended the Emergency Department, reporting blurred vision in the left eye (LE) for 3 weeks. She was originally from Brazil and had been living in Portugal for a year, working as an assistant in a nursing home. She had undergone simultaneous flu and COVID-19 vaccination 5 weeks before. She denied night sweats, weight loss, joint pain, shortness of breath, mouth or genital ulcers, skin changes, genitourinary symptoms or gastrointestinal symptoms. The patient was a myope of -6.00 diopters in both eyes (BE). The past medical history was negative and she did not take any medication.

On clinical examination, her visual acuity was 20/20 in the right eye (RE) and 20/125 in the LE. Pupils were isocoric and isoreactive, with no rapid afferent pupillary defect. Biomicroscopy was unremarkable in both eyes. On Goldmann applanation tonometry, intraocular pressure (IOP) was 15 mmHg in the RE and 14 mmHg in the LE.

Fundus examination did not show any apparent changes in the RE. The LE fundoscopy showed small, ill-defined creamy multifocal choroidal lesions with less than 250 um in diameter, located at the posterior pole (Fig. 1-C). It was also possible to observe a grey lesion inferotemporal to the fovea suggestive of CNV. The RE spectral domain ocular coherence tomography (SD-OCT) showed a focal attenuation of the ellipsoid, interdigitation zone and retinal pigment epithelium (RPE) layer with hyper-transmission, superior to the fovea (Fig. 1–B). The LE SD-OCT through the fovea revealed subretinal hyperreflective material (SRHM) and a hyperreflective inflammatory PED (Fig. 1-D). The OCT-Angiography (OCT-A) at the same location depicted an extensive subretinal neovascular network consistent with CNV (Fig. 1 – F). Also in the LE, SD-OCT B-scan through the choroidal lesions showed fluffy SRHM with EZ disruption and RPE splitting, typical of active inflammatory lesions (Fig 1 – E).

The clinical and imaging findings were therefore consistent with LE multifocal choroiditis with secondary CNV, with a possible RE early choroiditis lesion. The patient underwent a 2 mg aflibercept intravitreal injection in the LE and was reassessed in the Uveitis Clinic.

Four weeks after presentation and ten days after the LE injection (Fig. 2), she reported a subjective improvement in the

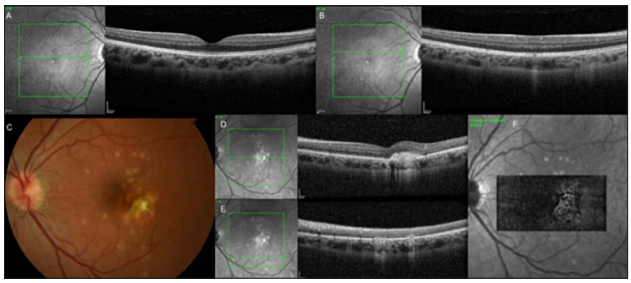

Figure 1. Patient's multimodal imaging on presentation. CFP of the RE did not show any changes (not show). The LE CFP showed small ill-defined creamy multifocal choroidal lesions with less than 250um in diameter, located at the posterior pole as well as a grey lesion inferotemporal to the fovea suggestive of CNV (C). Macular SD-OCT B-scan of the RE was unremarkable at the fovea (A) but showed a focal attenuation of the ellipsoid, interdigitation zone and RPE with hyper-transmission, superior to the fovea (B). The LE SD-OCT B-scan through the fovea revealed SRHM and a hyperreflective inflammatory PED (D). The OCT-Angiography at the same location depicted an extensive neovascular network located at the avascular plexus, consistent with CNV (F). OCT B-scan through the choroidal lesions observed on fundoscopy showed fluffy SRHM with EZ disruption and RPE splitting, consistent with active inflammatory lesions (E).

LE vision, with a new onset deterioration in the RE vision. At this stage, the BCVA was 20/32 in the RE and 20/200 in the LE. The RE SD-OCT showed new SRHM superior to the fovea, associated with intraretinal fluid (IRF) as well as subfoveal

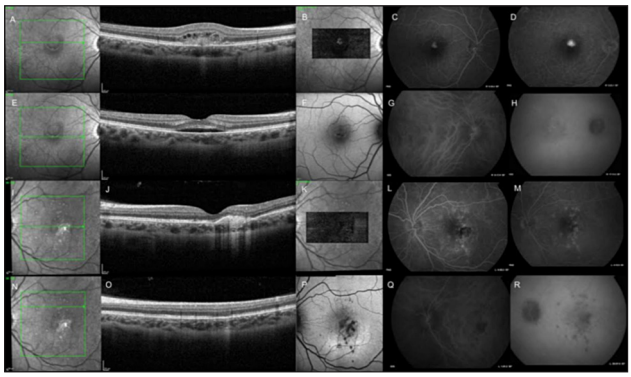

Figure 2. Multimodal imaging 4 weeks after presentation. The RE SD-OCT showed SRHM superior to the fovea, associated with IRF as well as subfoveal SRF fluid (A, E). CNV was confirmed on OCT-A (B). The LE SD-OCT showed reabsorption of the SRHM and PED with more defined borders (I) and the choroidal inflammatory lesions started to fade (N). The LE OCT-A showed a decrease in the CNV (K). RE Fundus autofluorescence showed central macular non circumscribed areas of hyper-autofluorescence (hyper-FAF) corresponding to the SRF and hypo-autofluorescence (hypo-FAF) corresponding to the CNV (F). FAF in the posterior pole was otherwise normal. The LE FAF showed central hypo-FAF which corresponded to the CNV as well as focal hypo-FAF spots corresponding to the inactivation of choroiditis lesions (P). Some of these lesions had a hyper-FAF cuff which may persist in inactive lesions. There were also several hyper-FAF lesions in the inferior macular area, suggestive of new inflammatory lesions. RE Fluorescein angiography (FFA) revealed early macular hyperfluorescence with late leakage, consistent with type 2 CNV (C,D). LE FFA showed macular early and late hypofluorescence, suggestive of blockage due to fibrovascular PED/CNV as well as multiple hypofluorescent dots which persisted hypofluorescent in the late frames (L,M). Signs of vasculitis were absent in both eyes. Indocyanine green angiography (ICGA) of the RE showed multiple early hypofluorescent dots, not visible fundoscopically as well as late irregular hyperfluorescence juxtafoveally, which corresponded to the CNV location (G,H). LE ICGA showed early central irregular hypofluorescence and multiple hypoautofluorescence dots. Hypofluorescence areas persisted in the late frames (Q,R).

subretinal fluid (SRF) (Fig. 2-A, E). The OCT-A confirmed the presence of a CNV (Fig. 2-B). On the other hand, the LE SD-OCT showed improvement in the CNV activity signs (Fig. 2-I), while the choroidal inflammatory lesions started to fade (Fig. 2-N). The OCT-A confirmed a decrease in the CNV (Fig 2-K). RE Fundus autofluorescence showed central macular non circumscribed areas of hyper-autofluorescence (hyper-FAF) and hypo-autofluorescence (hypo-FAF) corresponding to the CNV (Fig. 2-F). FAF in the posterior pole was otherwise normal. The LE FAF showed central hypo-FAF as well as focal hypo-FAF spots corresponding to the inactivation of choroiditis lesions (Fig. 2-P). There were also several hyper-FAF lesions in the inferior macular area, suggestive of new inflammatory lesions. RE Fluorescein angiography (FFA) was consistent with type 2 CNV (Fig 2-C,D). LE FFA showed macular early and late hypofluorescence due to fibrovascular PED/CNV as well as multiple hypofluorescent dots which persisted hypofluorescent in the late frames (Fig 2-L,M). Indocyanine green angiography (ICGA) of the RE showed multiple early hypofluorescent dots consistent with choroiditis lesions, not visible fundoscopically as well as late irregular hyperfluorescence juxtafoveally, which corresponded to the CNV location (Fig. 2-G,H). LE ICGA showed early central irregular hypofluorescence and multiple hypoautofluorescence dots. Hypofluorescence areas persisted in the late frames (Fig. 2-Q,R).

Blood test results were all within normal limits, namely erythrocyte sedimentation rate, C-reactive protein, serum angiotensin converting enzyme, human immunodeficiency test, venereal disease research laboratory test, Treponema pallidum hemagglutination assay, toxoplasma IgG/IgM and interferon gamma release assay (IGRA, QuantiFERON TB-gold).

The multifocal choroiditis clinical diagnosis was narrowed to bilateral PIC with CNV. The patient was started on 60 mg oral prednisolone with a tapering regimen and sent to bilateral monthly intravitreal aflibercept injections.

She was reassessed after a total of three monthly 2 mg aflibercept intravitreal injections in each eye and while on 10 mg of oral prednisolone daily (Fig. 3). The BCVA had improved to 20/25 in the RE and 20/100 in the LE. The RE SD-OCT showed complete resolution of the CNV activity (Fig. 3-B) with an intact foveal ellipsoid (Fig. 3-A). The LE SD-OCT revealed fibrosis, associated with ellipsoid damage (Fig. 3-D), while the SD-OCT through the previously choroiditis lesions showed resolution of the fluffy SRHM, with RPE and ellipsoid disruption, consistent with inactive lesions (Fig. 3-E). The LE CNV on OCT-A had markedly decreased in size (Fig. 3-F).

As there was an improvement of the choroiditis lesions on steroids, the patient was assessed in Rheumatology for immunosuppression and was started on oral Mycophenolate mofetil. Oral steroids were tapered over 4 months. It was advised to treat the RE with an aflibercept treat and extend regimen. However, the patient did not attend any further scheduled injections and missed several appointments. She was reassessed 6 months after the last injection in both eyes. As there were no signs of active CNV in either eye, it was decided to observe and not proceed with further anti-VEGF treatment.

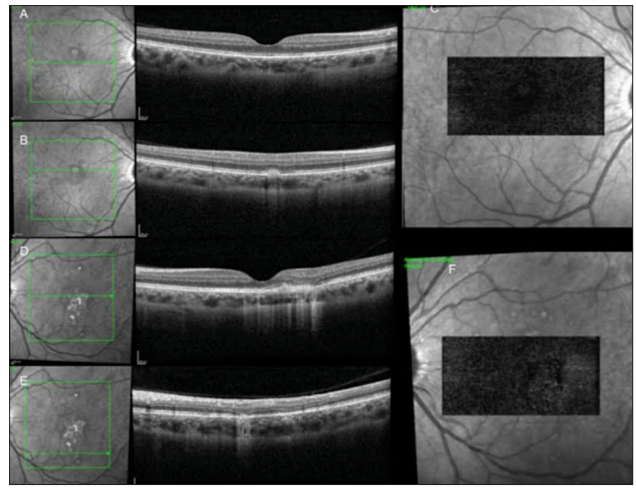

Figure 3. Multimodal imaging after three monthly 2mg aflibercept intravitreal injections in each eye and while on 10mg of oral prednisolone daily. The RE SD-OCT B-scan showed complete resolution of the intra and subretinal fluid (B) with an intact foveal ellipsoid (A). The subretinal hyperreflective area which corresponded to the CNV was smaller and with defined borders. OCT-A showed a resolution of the CNV lesion (C). In the LE, SD-OCT B-scan revealed subretinal hyperreflectivity consistent with fibrosis, associated with ellipsoid damage (D). SD-OCT imaging through the previously choroiditis lesions showed resolution of the fluffy SRHM, with RPE and ellipsoid disruption, consistent with inactive lesions (E). The LE CNV on OCT-A had markedly decreased in size (F).

The latest assessment was performed twelve months after the last anti-VEGF treatments. The patient was on MMF 1 g twice a day for 7 months and off oral steroids for 5 months. BCVA was 20/40 in the RE and 20/125 in the LE. The RE ellipsoid was completely intact and the CNV remained small and quiescent (Fig. 4-A,B). In the LE, the CNV was larger than previously on OCT-A, however, with no signs of exudation (Fig.4-C,D). There were no new choroiditis lesions. The patient remains of MMF and under close monitoring.

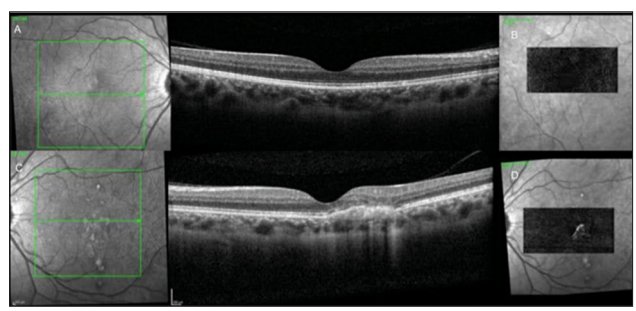

Figure 4. Multimodal imaging performed twelve months after the last anti-VEGF treatments and while on MMF. On SD-OCT, the RE ellipsoid was completely intact (A) and the CNV remained small and quiescent (B). In the LE, the CNV was larger than previously on OCT-A (D), however with no signs of exudation (C).

DISCUSSION

PIC is an uncommon type of multifocal choroiditis that is more frequent in young myopic females.[3]

Multimodal imaging is extremely useful in the diagnosis, monitoring and assessment of complications of multifocal choroiditis, including PIC. In this context, guidelines for the use of multimodal imaging in PIC have been recently published in April 2025, in a consensus publication by the Multimodal Imaging in Uveitis (MUV) task force.[4] Typical findings on OCT, OCT-A, FAF and ICG-A correspond to biomarkers of active and inactive lesions. OCT through the PIC lesions is regarded as the preferred imaging modality to detect active inflammation in new and recurrent disease.4 Active lesions on OCT are characterized by fluffy SRHM overlying the RPE or as an inflammatory PED. EZ disruption may extend beyond the lesion edges while focal thickening of the choroid may be visible under the lesions. When inactive, the SRHM resolves, with residual focal disruption of EZ and RPE.[4]

PIC prognosis is variable, depending on the frequency of recurrences, location of inflammatory lesions and secondary complications.[5] CNV in particular may complicate PIC and compromise visual acuity irreversibly.[1,6] PIC management is therefore challenging and should be tailored to each patient. In the current case, the patient presented with a LE CNV. Treatment of the LE with aflibercept IVT injections allowed inactivation of the macular CNV, with improvement of BCVA. Unfortunately, it was not possible, however to prevent fibrosis formation.

PIC is commonly unilateral at presentation.[5] However, approximately one-third of individuals who develop either CNV or subretinal fibrosis in one eye also experienced the same complication the other eye.[7] At this patient's presentation, the RE showed a possible early choroiditis lesion. Just four weeks after presentation, it was possible to observe the development of a marked CNV, in the absence of other choroiditis lesions. Early treatment with intravitreal aflibercept injections in the RE enabled a total reconstitution of the ellipsoid zone and foveal and perifoveal macular architecture, as well as improvement in the BCVA.

In PIC, while CNV complications are primarily treated with anti-VEGF injections,6 acute inflammatory PIC lesions are managed by corticosteroid treatment.[5,8] Corticosteroid treatment also has an antiangiogenic effect.[9] Our patient presented with extremely aggressive PIC, with bilateral sequential involvement in 4 weeks and foveal damage. After successful control of the choroiditis lesions with oral corticosteroids, it was decided to treat the patient with immunosuppression, namely MMF, to prevent relapses, which could potentially further damage the fovea. Controlling the inflammation also prevents secondary CNV.[5] In our patient, early immunosuppression has prevented further choroidal inflammation and CNV exudation, avoiding the need for anti-VEGF injections for a year.

PIC aetiology remains unclear. It is regarded as an autoimmune disease that emerges in the context of genetic susceptible background triggered by an environmental stimulus, such as infection, immunization or stress.[3] In this case, there was a close temporal relation between COVID-19 vaccination and PIC manifestations. Previous publications have reported on the association between this particular vaccine and the broad group of white dot syndromes.[10] PIC has also been reported to occur after COVID-19 infection.[11] Our patient was a young myopic female and PIC is known to be more common in this group. In this particular case, we speculate that the COVID-19 vaccine triggered PIC in a patient with a susceptible background. The simultaneous administration of the flu jab was likely a cumulative trigger effect. Exploring these associations may allow a more comprehensive understanding of PIC pathophysiology.

CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO:

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SH, MJG, ML: Data Collection, Analysis and Critical Revision.

FR: Manuscript Writing.

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Atypical Presentation of Central Serous Chorioretinopathy: Insights from Multimodal Imaging: A Case Report

Apresentação Atípica de Coriorretinopatia Serosa Central: Imagem Multimodal: Caso Clínico

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ABSTRACT

Central serous chorioretinopathy (CSC) is a self-limiting retinal condition that can be precipitated by elevated endogenous corticosteroids, such as those occurring during pregnancy. Subretinal fibrin is a relatively rare finding in CSC and may mimic inflammatory or neovascular pathologies, complicating diagnosis. Early recognition is essential to avoid unnecessary treatments and ensure appropriate management.

We report the case of a 34-year-old woman who presented at 18 weeks of gestation with metamorphopsia in the right eye. Visual acuity was 10/10, and OCT revealed a serous pigment epithelial detachment (PED). Over subsequent weeks, BCVA fluctuated, and at 29 weeks of gestation, new subretinal fibrin was observed on OCT, along with the "lucency sign," suggestive of active exudation. Fluorescein angiography confirmed findings consistent with exudative CSC, showing pooling and mild late-phase leakage. Alternative diagnoses, including infectious and inflammatory causes, were excluded. After multidisciplinary discussion, including consultation with obstetrics, a conservative "watch-and-wait" approach was adopted. The patient underwent cesarean delivery at 39 weeks, and three weeks postpartum, her vision improved to 10/10 with complete resolution of subretinal fluid and PED.

This case illustrates an atypical, early-pregnancy presentation of CSC complicated by subretinal fibrin deposition. Multimodal imaging was crucial for diagnosis and exclusion of mimicking entities. Although treatment with photodynamic therapy was considered, a conservative approach was favored due to the known favorable prognosis of pregnancy-associated CSC. This case highlights the value of clinical vigilance and multidisciplinary collaboration in managing complex retinal pathology during pregnancy.

KEYWORDS: Central Serous Chorioretinopathy; Multimodal Imaging; Pregnancy Complications.

RESUMO

A coriorretinopatia serosa central (CSC) é uma patologia retiniana autolimitada que pode ser causada por níveis elevados de corticosteroides endógenos, como ocorre durante a gravidez. A presença de fibrina sub-retiniana é uma manifestação rara na CSC e pode simular patologias

inflamatórias ou neovasculares, dificultando o diagnóstico. O reconhecimento precoce é essencial para evitar tratamentos desnecessários e garantir uma abordagem adequada.

Apresentamos o caso de uma mulher de 34 anos que recorreu ao serviço de oftalmologia às 18 semanas de gestação com metamorfopsias no olho direito. A acuidade visual era de 10/10, e a tomografia de coerência óptica (OCT) revelou um descolamento seroso do epitélio pigmentar (DEP). Nas semanas seguintes, a acuidade visual corrigida variou, e, às 29 semana de gestação, foi observada fibrina sub-retiniana na OCT, juntamente com o sinal de lucency, indicativo de exsudação ativa. A angiografia fluoresceínica confirmou achados compatíveis com CSC exsudativa, evidenciando pooling e leakage de contraste na fase tardia. Diagnósticos diferenciais inflamatórios e infecciosos foram excluídos. Após discussão multidisciplinar, incluindo a equipa de obstetrícia, optou-se por uma abordagem conservadora. O parto por cesariana ocorreu às 39 semanas, e, três semanas após o parto, a visão era de 10/10 com resolução completa do fluido sub-retiniano e do DEP.

Este caso ilustra uma apresentação atípica de CSC em fase precoce da gravidez, com deposição de fibrina sub-retiniana. A imagiologia multimodal foi fundamental para o diagnóstico e exclusão de entidades miméticas e de neovascularização coroideia. Embora tenha sido equacionado tratamento com terapia fotodinâmica, optou-se por uma abordagem conservadora, dada a evolução geralmente favorável da CSC associada à gravidez. Este caso destaca a importância da imagem multimodal e da colaboração multidisciplinar na gestão de patologia retiniana complexa durante a gravidez.

PALAVRAS-CHAVE: Complicações na Gravidez; Coriorretinopatia Serosa Central; Imagem Multimodal.

INTRODUCTION

Central serous chorioretinopathy (CSC) with subretinal fibrin is a relatively uncommon presentation. It was first described by Yannuzzi *et al* in 1993 in a series of 11 patients who exhibited subretinal plaques, presumed to represent fibrin exudation. Notably, all cases demonstrated complete resolution of these plaques over time.[1] In another cohort of 16 CSC patients, half were initially misdiagnosed with alternative conditions such as posterior uveitis or exudative retinal detachment, underscoring the diagnostic challenge posed by fibrinous variants of CSC. Key distinguishing features include a dark lesion on color fundus photography and the presence of a hyporeflective subretinal "vacuole" on optical coherence tomography (OCT), both of which can aid in avoiding misdiagnosis.[2]

Pregnancy-associated CSC is typically self-limiting, with resolution expected postpartum.[3] However, early-onset or atypical variants with extensive exudation and fibrin deposition may require more nuanced diagnostic and therapeutic considerations.

In this report, we present the case of a pregnant woman who developed CSC with subretinal fibrin at 18 weeks of gestation. We describe the clinical course, multimodal imaging findings, and the multidisciplinary management strategy that led to a favorable visual and anatomical outcome.

CASE REPORT

A 34-year-old woman presented to the ophthalmology department with a 2-day history of metamorphopsia in the right eye (OD). She was 18 weeks pregnant following a spontaneous conception. Her past medical history was unremarkable, with no known systemic or ocular diseases. She denied any previous episodes of visual disturbances, ocular trauma, intraocular procedures, or corticosteroid use. Her only medications were folic acid and iodine supplementation.

Best-corrected visual acuity (BCVA) was 10/10 in both the OD and left eye (OS). Anterior segment biomicroscopy was unremarkable in both eyes. Fundoscopic examination of the right eye revealed a subtle parafoveal elevation suggestive of subretinal fluid accumulation, while the left eye appeared normal.

OCT of the right eye revealed a serous pigment epithelial detachment (PED) (Figs. 1A and 1B). Over the course of serial follow-up visits, both BCVA and PED dimensions demonstrated fluctuating patterns (Table 1). At 29 weeks of

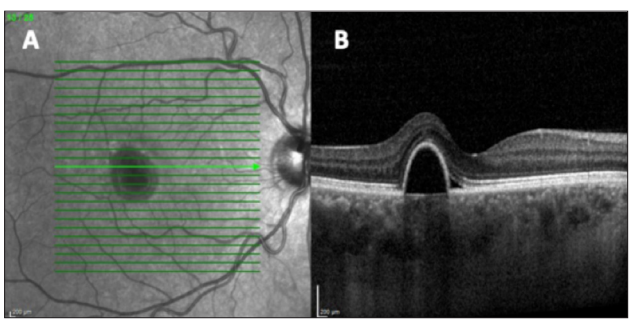


Figure 1. Multimodal imaging of the macula. A. Red-free photograph showing a darkened macular area corresponding to the pigment epithelial detachment seen in panel B; B. Optical coherence tomography (OCT) demonstrating a serous pigment-epithelial detachment.

gestation, OCT imaging showed new subretinal fibrin deposition with the characteristic "lucency sign," indicative of active exudation (Figs. 2A and 2B).

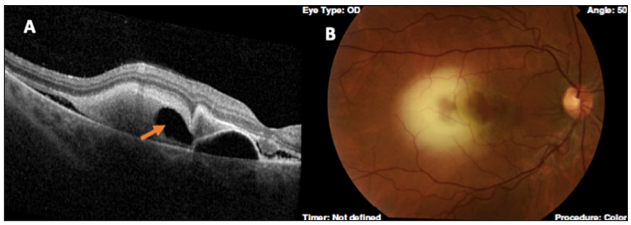


Figure 2. A- OCT image at 29 weeks of gestation revealing subretinal fibrin deposition and the "lucency sign" (orange arrow), indicative of active exudation. B- Color Fundus at 29 weeks revealing subretinal foveal fibrin.

Although CSC remained the leading diagnostic consideration, alternative etiologies such as choroidal neovascularization, Vogt-Koyanagi-Harada disease, unilateral acute idiopathic maculopathy, and acute syphilitic posterior placoid chorioretinitis were also evaluated. Following a detailed discussion of the risks and benefits of fluorescein angiography (FA) during pregnancy and with informed written consent obtained, FA was performed. The angiogram demonstrated a broad hypofluorescent area caused by masking from the fibrin-PED complex, with pooling and mild late-phase leakage—findings consistent with an exudative variant of CSC (Fig. 3).

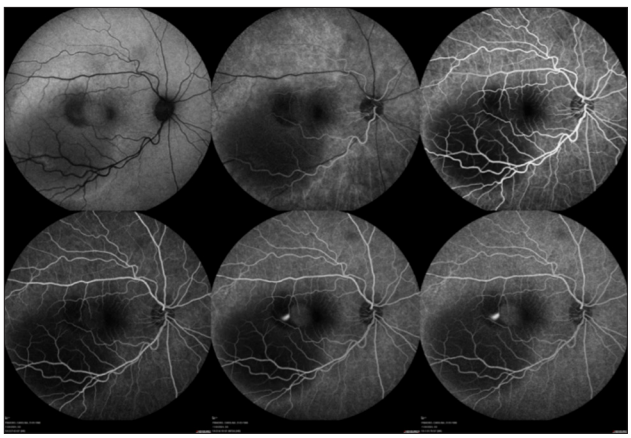
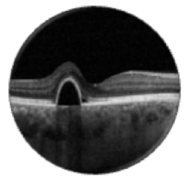
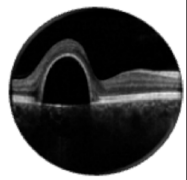
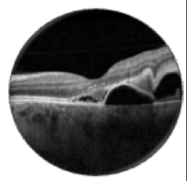
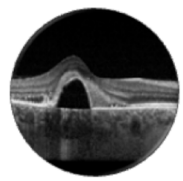
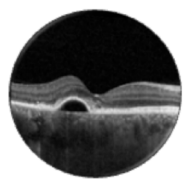
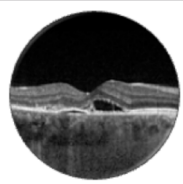
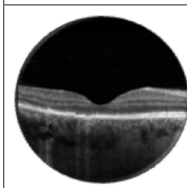


Figure 3. Fluorescein angiography demonstrating a large area of hypofluorescence, consistent with a masking effect caused by subretinal material. Late-phase images reveal pooling of dye and mild leakage, findings characteristic of exudative central serous chorioretinopathy.

Non-dye photodynamic therapy was discussed in a retinal specialist meeting but ultimately not pursued. Instead, a conservative approach with close clinical monitoring was adopted. The case was further reviewed in collaboration with the patient's obstetrician to exclude preeclampsia and autoimmune pathology, and to ensure coordinated multidisciplinary planning for labor and delivery. A cesarean was initially scheduled for 37 weeks of gestation; however, the patient elected to delay the procedure for personal reasons. Delivery was successfully performed via cesarean at 39 weeks. At a follow-up visit three weeks postpartum, the patient reported a BCVA of 10/10 in OD without metamorphopsia. OCT demonstrated complete resolution of subretinal fluid, with persistent irregularities of the outer retinal layers (Table 1).

Table 1. OCT and BCVA evolution during pregnancy and after delivery.

	14th February | 18W BCVA OD 10/10 with metamorphopsias OCT: PED
	1st April | 25W BCVA 8/10 OCT: PED at maximum size
	1st May | 29W BCVA 9/10 OCT: PED + subretinal fibrin + lucency sign (arrow)
	17th June | 36W BCVA 8/10 OCT: PED + subretinal fibrin + PED rip (arrow)
	27th June | 37W BCVA 9/10 OCT: PED + subretinal fibrin + hyperreflective foci
	1st July | 38W BCVA 9/10 OCT: PED + subretinal fibrin + hyperreflective foci
	OCT: PED resolution + external retinal layer' irregularities

OCT- optic coherence tomography; BCVA- best corrected visual acuity; PED – pigment epithelium detachment; W- weeks.

DISCUSSION

This case highlights an atypical presentation of CSC during pregnancy, complicated by subretinal fibrin deposition.

Pregnancy has been shown to increase the risk of CSC up to 9 times and it is mostly observed in the third trimester of pregnancy.[4] The main cause of this condition is attributed to the high concentration of cortisol during pregnancy.[3] It was reported that 90% of pregnant patients with CSC had fibrinous subretinal exudate in comparison with the 20% non-pregnant patients with CSC.[5] In our case, a pregnant woman developed exudative CSC at 18 weeks of gestation, with the additional finding of subretinal fibrin, a feature known to complicate diagnosis and mimic other inflammatory or neovascular pathologies.

Subretinal fibrin in CSC was first described by Yannuzzi et al., and although uncommon, it can mimic other inflammatory or neovascular conditions, leading to potential misdiagnosis.[1] The characteristic OCT finding of a hyporeflective cleft within hyperreflective subretinal material—often referred to as the "lucency sign"—is a valuable clue toward fibrinous CSC.[6] In our patient, this imaging sign guided diagnostic certainty and helped avoid unnecessary treatment.

Given the atypical features, differential diagnoses such as Vogt-Koyanagi-Harada disease, unilateral acute idiopathic maculopathy, and infectious posterior uveitis (e.g., syphilitic placoid chorioretinitis) were considered. Multimodal imaging —particularly FA—was pivotal in confirming the diagnosis and excluding neovascularization. Although FA is generally avoided in pregnancy due to theoretical risks, studies suggest that fetal exposure is minimal and not associated with adverse outcomes when clinically justified.[7-9] The United States Food and Drug Administration (US FDA) and Therapeutics and Goods Administration (TGA) in Australia have placed fluorescein under category 3 and 2 B, respectively.[8]

CSC during pregnancy is typically self-limiting, with spontaneous resolution of subretinal fluid and visual recovery occurring postpartum in most cases.[3] In our patient, the clinical course followed this pattern, with complete anatomical and functional recovery after delivery. However, due to the substantial exudative activity and the early stage of pregnancy at presentation, our retina specialist team considered the possibility of treatment with photodynamic therapy (PDT) without verteporfin. Recent global shortages of verteporfin, as well as concerns regarding its safety profile—particularly in pregnant patients, given its FDA B3 classification—have led to interest in alternative approaches such as no-dye PDT.[10] A comparative study has shown that short-term anatomical and functional outcomes of no-dye PDT are comparable to those achieved with half-dose verteporfin full-fluence PDT (HDFF-PDT) in the treatment of CSC.[10] Although this technique was hypothesized as a potential therapeutic option in our case, a multidisciplinary discussion with the patient and obstetrics team was held. Considering the lack of robust data in pregnancy, the known favorable prognosis of pregnancy-associated CSC, and the absence of significant visual compromise, a conservative approach was deemed appropriate. Therefore, we opted for close observation, which ultimately led to complete resolution without the need for intervention.

This case underscores the importance of recognizing atypical presentations CSC in pregnancy, particularly those complicated by subretinal fibrin, which may mimic other inflammatory or neovascular diseases. Multimodal imaging, especially OCT and fluorescein angiography, proved essential for accurate diagnosis and management planning. Despite early onset and significant exudation, a conservative, multidisciplinary approach resulted in full visual and anatomical recovery. This case highlights that, in selected patients, careful monitoring can be a safe and effective strategy, avoiding unnecessary interventions during pregnancy.

CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO:

RA, CX and AB: Contributed to the conception and supervision of this rase report.

PBS, RF and RA: Were responsible for data collection and clinical follow-up.

RA, ML and PBS: Conducted the literature review and drafted the initial manuscript.

All authors contributed to manuscript revision, read, and approved the final version.

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