Kyrieleis Plaques in Ocular Tuberculosis: A Case Report

Placas de Kyrieleis na Tuberculose Ocular: Relato de um Caso

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ABSTRACT

Kyrieleis plaques are a rare fundoscopic sign, in which multiple yellowish-white deposits are arranged in a beaded pattern along the branches of the central retinal artery. Their presence reflects severe intraocular inflammation, typically associated with infectious posterior uveitis. Here, we describe the case of a 58-year-old man who presented to our emergency department with a right red-eye, vision loss and floaters. The ophthalmological exam revealed unilateral panuveitis with the presence of Kyrieleis plaques. Laboratory evaluation was marked by a positive Mantoux skin test and a presumptive diagnosis of ocular tuberculosis was made. The patient was treated for active disease with a 4-drug anti-tuberculosis regimen, along with topical and oral corticosteroids, which allowed for the complete resolution of vitritis, gradual fading of the plaques and total vision recovery. Due to its rarity and strong association with infectious etiologies, the presence of Kyrieleis plaques in our patient´s eye fundus was crucial to narrow the range of possible differential diagnoses. Accurate diagnosis subsequently led to prompt and adequate treatment, with great visual outcomes.

KEYWORDS: Eye Infections; Tuberculosis, Ocular.

RESUMO

As placas de Kyrieleis são um achado fundoscópico raro, caracterizado pela presença de múltiplos depósitos amarelados, distribuídos num padrão segmentar ao longo dos ramos da artéria central da retina. A sua presença reflete um estado de inflamação ocular grave, tipicamente associada a uveítes posteriores infeciosas. Neste artigo, descreve-se o caso de um homem de 58 anos que recorreu ao serviço de urgência por olho vermelho, hipovisão e miodesópsias à direita. O exame oftalmológico revelou uma panuveíte unilateral associada a arteriolite de Kyrieleis. A avaliação laboratorial destacou-se por um teste de Mantoux positivo. Após exclusão de outras etiologias, estabeleceu-se o diagnóstico presuntivo de tuberculose ocular. Foi instituída terapêutica com 4 tuberculostáticos associados a corticoterapia oral e tópica, tendo-se assistido a uma resolução completa da vitrite, desaparecimento gradual das placas de Kyrieleis e recuperação

visual máxima. Pela sua raridade e forte associação a etiologia infeciosa, a presença das placas de Kyrieleis foi fundamental para afunilar a larga panóplia de diagnósticos diferenciais possíveis. O diagnóstico de tuberculose ocular permitiu instituir atempadamente o tratamento adequado, com excelentes resultados visuais.

PALAVRAS-CHAVE: Infecções Oculares; Tuberculose Ocular.

INTRODUCTION

Described for the first time in 1933, by the German ophthalmologist Werner Kyrieleis in a patient with presumed tuberculous uveitis,[1] Kyrieleis plaques, also referred to as "segmental retinal arteritis", are a rare fundus examination finding. In fact, almost 90 years after its first report, there are only about 20 cases published in the literature.[2]

Kyrieleis plaques reflect severe intraocular inflammation.[3] They have been classically reported in association with infectious posterior uveitis, *Toxoplasma gondii* being the most frequent etiology. Other agents include *Mycobacterium tuberculosis*, *Treponema pallidum*, *Cytomegalovirus*, *Varicella-Zoster Virus*, *Herpes Simplex Virus- 1 and 2*, and *Rickettsia conorii*.[2,4-10] A case of Kyrieleis arteritis associated with Behçet disease has also been published.[2]

Due to both the rarity of this condition and the absence of histopathological studies, the exact pathophysiology of these plaques remains to be found. Indeed, not much is known neither about the nature of these deposits nor about their precise location within the arteries, and various hypotheses have been proposed so far.[3,5,6]

In 1959, Griffin and Bodian suggested that the plaques were a consequence of the migration of exudates from a nearby chorioretinitis focus to the periarterial sheaths.[11] In the early '70s, Orzalesi and Ricciardi speculated that these deposits were composed of cellular and inflammatory material within the arterial walls.[12] Wise hypothesized that they constituted arteriosclerosis lesions.[13] A recent study, based on multimodal imaging findings, proposed that Kyrieleis plaques reflect the inflammatory involvement of the vascular endothelium, rather than periarteriolar or endoluminal damage.[3]

Kyrieleis arteritis, as the name suggests, solely affects the arterial vasculature, and on fundoscopic examination, they appear as multiple, segmental, and focal yellowish-white deposits, resembling atheromatous plaques, arranged in a beaded pattern, along the branches of the central retinal artery. An active chorioretinitis focus is usually present in the vicinity of the affected arteries.[2,3,6]

Fluorescein angiography (FA) is highly characteristic as there is neither leakage of fluorescein dye, nor occlusive phenomenon, differentiating this entity from other forms of retinal vasculitis.[2,3]

Kyrieleis plaques are benign and do not worsen the prognosis of the underlying uveitis.[6,14] With suitable treatment, there usually is complete vanishing of the plaques without sequelae.[2] However, they can sometimes persist long after the resolution of chorioretinitis and discontinuation of therapy.[7]

Here, going back to the beginning and resembling W. Kyrieleis' report, we describe the case of Kyrieleis plaques associated with presumed ocular tuberculosis infection.

CASE REPORT

A 58-year-old Caucasian male, with no relevant systemic or ophthalmological medical history, presented to our emergency department, complaining of a right red-eye, an uncomfortable impairment of visual acuity and floaters, for 5 days. There was no record of trauma or previous eye surgery. Detailed anamnesis disclosed the regular practice of high-risk sexual activities (unprotected intercourse with multiple sexual partners), as well as past consumption of smoked hashish.

On ophthalmic examination, the best-corrected visual acuity (BCVA) was 20/40 in his right eye and 20/20 in his left eye. The slit-lamp exam of the right eye revealed a violaceous ciliary flush, fine whitish precipitates in the inferior third of the corneal endothelium, and a 2+ cellular anterior chamber reaction. Left biomicroscopy was unremarkable.

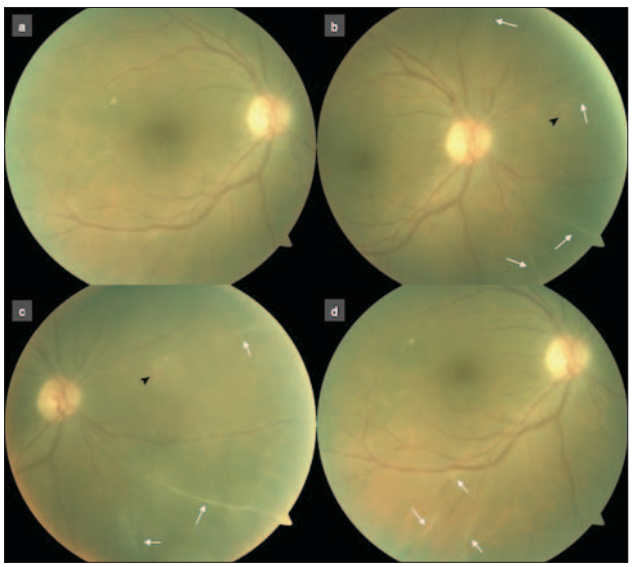

Fig. 1. (a-d). Right eye fundus retinographies showing 1+ diffuse vitritis and segmental retinal arteritis, characterized by the presence of multiple yellowish-white plaques placed in a beaded pattern along the branches of the central retinal artery (white arrows). Nasally to the optic disc, there is a small superficial retinal hemorrhage (black arrowhead).

Intraocular pressure was 14 mmHg in the right eye and 12 mmHg in the left eye. Fundoscopy on the right (shown in Fig. 1 a-d) was marked by mild vitreous haze, with 1+ diffuse vitritis, and the presence of segmental arteritis with Kyrieleis plaques affecting mid-peripherical retinal arteries. There were no signs of venous vasculitis neither of obvious retinitis, choroiditis, papilitis, or macular edema. Only a small, superficial temporal retinal hemorrhage, neighboring an area of segmental arteritis, was worthy of mention. Left eye fundoscopic findings were irrelevant.

FA displayed no typical signs of active vasculitis. Arterial branches containing the plaques had a normal vascular filling and there was no leakage of fluorescein dye nor late staining (shown in Fig.s 2a and 2b).

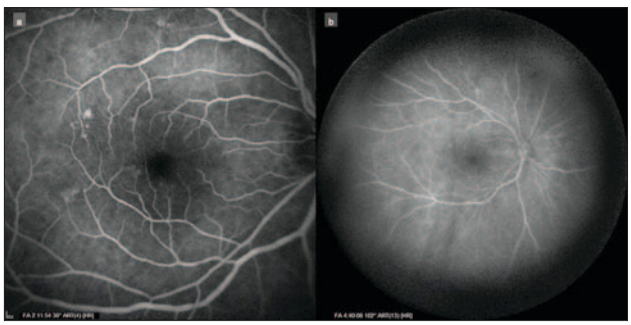

Fig. 2. Macular fluorescein angiography at 2:11 minutes (Fig. 2a) and wild-field fluorescein angiography at 4:40 minutes (Fig. 2b) revealing normal arterial filling and the absence of late staining or fluorescein dye leakage from the Kyrieleis plaques. Diffuse vitritis hampered better-quality images.

At this point, facing a unilateral panuveitis with Kyrieleis plaques, in a 58-year-old man with repeated high-risk sexual behaviors, the hypothesis of an infectious etiology seemed highly likely. The collaboration of an infectious disease specialist was requested and a further clinical investigation to reach for a definitive diagnosis continued.

His review of systems and physical exam were unremarkable. Laboratory evaluation was marked by a positive Mantoux skin test, with an induration area of 12 mm. The interferon gamma test (IGRA) was negative. All of the other blood tests for alternative infectious and non-infectious diseases, namely angiotensin-converting enzyme, serum calcium, lysozyme, auto-antibodies, serology for syphilis (both treponemal and non-treponemal tests performed twice, to exclude a false negative result), toxoplasmosis, cytomegalovirus, varicella-zoster virus, herpes simplex virus 1 and 2, HIV 1 and 2, HBV, HCV, *Bartonella* and *Borrelia*, were negative.

Chest radiography and chest computed tomography were innocent, as was the investigation for other foci of extrapulmonary tuberculosis (including cerebral magnetic resonance imaging and lumbar puncture).

A presumptive diagnosis of ocular tuberculosis was made, and the patient was started on a 4-drug anti-tuberculosis treatment (isoniazid, rifampicin, ethambutol, and pyrazinamide), along with topical and oral corticosteroids (1 mg/kg daily initially, and then slowly tapered over a period of 12 weeks).

Within a month of initiation of therapy, the patient showed a significant visual gain, with a right eye BCVA of 20/20. The anterior chamber inflammation and vitritis completely resolved, and Kyrieleis plaques became less numerous and prominent (shown in Fig. 3a). The last have been gradually fading and, in the third month of treatment, there is an evident fundoscopic improvement (shown in Fig. 3b).

This case report complies with the guidelines for human studies and was conducted ethically following the World Medical Association Declaration of Helsinki. The patient gave his consent to publish this report and accompanying images.

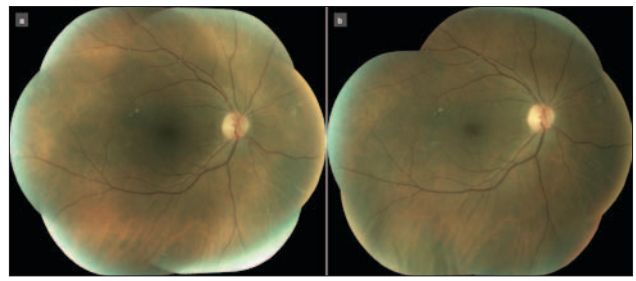

Fig. 3. Right fundus retinographies by the first (Fig. 3a) and third month (Fig. 3b) of treatment, showing complete vitritis resolution and progressive fading of Kyrieleis plaques, which are noticeable less numerous and prominent over time.

DISCUSSION/CONCLUSION

Tuberculosis (TB) is an airborne transmittable disease of great public health impact, caused by Mycobacterium tuberculosis. It is the major infectious cause of morbidity and mortality in adults, affecting more than 1.7 billion people worldwide.[15,16] The lungs are the Mycobacterium tuberculosis's favorite site of infection, but a variety of other organs can be affected.[16,17] Ocular TB is a form of extrapulmonary disease that can virtually affect every eye structure, posterior uveitis being the most frequent clinical presentation.[18]

Direct ocular inoculation from an exogenous font following an epithelial injury, or a hypersensitivity reaction to the mycobacterial antigens, are possible mechanisms of eye involvement. However, the most frequent mode of transmission to the eye is the hematogenous dissemination from a distant primary focus (pulmonary or extrapulmonary).[16] Nevertheless, the majority of patients with ocular TB do not present with systemic manifestations of the disease,[18] which was indeed our case. The definitive diagnosis of ocular TB is, therefore, extremely challenging, as it would require the isolation of the microorganism in eye tissue samples, such as the vitreous, aqueous humor, choroid or retina.[18] Herein, we considered that the intrinsic risks of such invasive procedures, along with their usual low sensitivity, would far outweigh its benefits in an otherwise healthy man, with unilateral impairment of visual acuity up to 20/40.

Thus, still bearing in mind the harmful consequences of a diagnostic delay, and according to the classification proposed by Gupta and colleagues,[19] we made a presump-

tive diagnosis of "possible intraocular TB" based on suggestive clinical signs along with a positive tuberculin skin test (given by induration of ≥10 mm in immunocompetent patients[18]) which, in our case, was of 12 mm in a patient who had not received BCG vaccination.

The detailed anamnesis and epidemiological background inquiry were also critical to develop a differential diagnosis *ad initium*. Although the patient denied recent contact with individuals with known tuberculosis, the fact that he confessed past drug consumption and current high-risk sexual behaviors, definitely alerted us to the possibility of this diagnosis, as well as other infectious etiologies that the laboratory tests later excluded.

Finally, TB is a great mimicker of other infectious and non-infectious intraocular inflammatory diseases.[18] Although some signs are more typical than others, a wide range of findings is possible. In combination with non-granulomatous anterior uveitis and vitritis, our patient presented with the very rare Kyrieleis plaques. Fundocopically, they appear as multiple, segmental, and focal yellowish-white deposits, exclusively affecting the retinal arteries, and characteristically, they are not associated with filling defects or leakage in fluorescein angiogram,[3] just like we observed them. The exact etiology of these plaques remains unknown but they are thought to be the result of an immunological response to an infectious agent.[3,5,6] Knowing this, our array of diagnostic possibilities was further reduced. Coincidently, our final diagnosis resembled that made by Werner Kyrieleis, in the early '30s.

With adequate management with both topical and systemic corticosteroids, in combination with a 4-drug scheme anti-tuberculosis treatment, anterior chamber inflammation and vitritis completely subsided within a month, and Kyrieleis plaques have been gradually disappearing in the third month of therapy. Actually, the favorable and fast response to TB treatment might be biased by simultaneous anti-inflammatory treatment. However, E.T. Cunningham Jr. *et al* showed that in patients with uveitis of undetermined etiology and a positive IGRA result, even without a history of previous TB or high-risk contacts, anti-tuberculosis drugs had a beneficial effect.[20] Besides, in a work of R Bansal *et al*, this treatment strategy significantly reduced the recurrence rate in patients with serpiginous-like choroiditis.[21] The value of this combined therapy remains undeniable and was, therefore, applied here with good outcomes so far.

In summary, we reported the exceptional case of Kyrieleis plaques occurring in association with presumed ocular tuberculosis. Herein, the presence of such a rare fundoscopic finding helped to narrow the wide range of possible differential diagnoses, especially when the isolation of *Mycobacterium tuberculosis* was not possible. This report also highlights the importance of a meticulous anamnesis, review of systems and epidemiological context investigation as the key to a successful diagnosis. Providentially, adequate and prompt treatment of active ocular tuberculosis allowed the complete resolution of vitritis and gradual disappearance of the plaques, with maximum visual outcome.

CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO:

All authors contributed to the study conception, commented on previous versions of the manuscript, read and approved the final manuscript design.

ML-D, ML-F, CO-F and LF: Material preparation, data collection and analysis.

ML-D: First draft of the manuscript.

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