CASO CLÍNICO/CASE REPORT

Bilateral Optic Neuropathy as First Manifestation of Tuberculosis

Neuropatia Óptica Bilateral como Manifestação Inaugural de Tuberculose

Luís Rufo Costa [1,*], Rui Pedro Silva [2], Sara Gomes [3], Isabel Amorim [3], Ana Filipa Santos [3], Gonçalo Cação [1], Cristina Almeida [2], Célia Machado [3]

1-Neurology department, Local Health Unit of Alto Minho, Viana do Castelo, Portugal
2-Ophthalmology department, Local Health Unit of Braga, Braga, Portugal
3-Neurology department, Local Health Unit of Braga, Braga, Portugal

DOI: https://doi.org/10.46531/sinapse/CC/195/2025

Informações/Informations:
Caso Clínico, publicado em Sinapse, Volume 25, Número 4, outubro-dezembro 2025. Versão eletrónica em www.sinapse.pt; Case Report, published in Sinapse, Volume 25, Number 4, October-December 2025. Electronic version in www.sinapse.pt

Keywords:
Antitubercular Agents; Immunocompromised Host; Mycobacterium tuberculosis; Optic Neuritis.

Palavras-chave:
Antituberculostáticos; Hospedeiro Imunocomprometido; Mycobacterium tuberculosis; Neurite Óptica.

***Autor Correspondente / Corresponding Author:**
Luís Rufo Costa
Hospital de Santa Luzia
Estrada de Santa Luzia,
4904-858 Viana do Castelo,
Portugal
luis.rufo95@gmail.com

Recebido / Received: *2025-10-19*
Aceite / Accepted: *2025-11-24*
Publicado / Published: *2025-12-31*

Abstract

Intraocular tuberculosis is a rare manifestation of *Mycobacterium tuberculosis* infection. We present a case of an immunocompetent male who presented with subacute binocular vision loss. On examination, he had a visual acuity of 6/10 bilaterally and optic disk edema. Initial workup was negative for structural, autoimmune, infectious or toxic etiologies. He was first treated with methylprednisolone, plasma exchange and intravenous immunoglobulin, without any clinical improvement. On the 20th day of admission, intraocular tuberculosis was presumed due to a positive interferon gamma release assay and chest tomography showing previous infection with *Mycobacterium tuberculosis*. He was started on an anti-tuberculosis drug regimen for 12 months, without any worsening of his visual acuity.

Resumo

A tuberculose intraocular é considerada uma manifestação rara da infeção por *Mycobacterium tuberculosis*. Apresentamos o caso de um homem imunocompetente que foi admitido com perda de visão binocular subaguda. Ao exame apresentava uma acuidade visual de 6/10 bilateralmente e edema bilateral da papila. A investigação inicial para uma potencial causa estrutural, autoimune, infecciosa e tóxica foi negativa. Foi tratado inicialmente com metilprednisolona seguida de plasmaferese e imunoglobulina intravenosa. No vigésimo dia de internamento, foi presumido um diagnóstico de tuberculose intraocular por apresentar um resultado positivo no IGRA e uma tomografia computorizada do tórax a revelar indícios de uma infeção pulmonar prévia por *Mycobacterium tuberculosis*. Iniciou tratamento com esquema de antituberculostáticos durante 12 meses, que resultou numa estabilidade da sua acuidade visual.

Introduction

Tuberculosis (TB) is an infectious disease associated with a myriad of clinical manifestations. Although it is most frequent in developing countries, its prevalence is also noted worldwide, commonly associated, among others with HIV infection, other immunodeficiencies and malnutrition.[1]

It affects most frequently the lungs and, in approximately 16%-20% of symptomatic infections, can also affect other organs (extrapulmonary tuberculosis).[2,3] In this group, intraocular tuberculosis is a rare manifestation, described in about 1.4% of extrapulmonary tuberculosis cases.[4] Intraocular involvement results frequently from hematogenous spread, affecting the ciliary body and the choroid.[5] Other mechanisms described include direct local extension or hypersensitivity reaction to the infection elsewhere.[5] The most common manifestation is a posterior uveitis, which includes retinitis, choroiditis, chorioretinitis and neuroretinitis.[6] On the other hand, involvement of the optic nerve is rarely described in the literature, typically secondary to choroidal, retinal or meningeal extension, is in most cases unilateral, associated with posterior uveitis and rarely as an isolated optic neuropathy.[5,7,8]

In this case, we aim to describe a patient presenting with bilateral optic neuropathy caused by a *Mycobacterium tuberculosis* infection.

Case Report

A 53-year-old white man arrived at the emergency department (ER) with subacute bilateral vision loss that began simultaneously 4 days prior and had progressively worsened, to the extent that he could no longer read, write, recognize objects or faces. He did not report any other symptoms, such as headache, eye pain, hearing loss, facial drooping, limb weakness, or sensory disturbances. There was no history of fever, weight loss, cough, or eye inflammation. There was no history of recent travel nor sick contacts.

He had no pre-existing conditions, was not on any medications and had no previous use of antibiotics. Additionally, he did not consume alcohol, tobacco, or any other toxic substances (such as nitrous oxide). His family history was unremarkable, particularly concerning neurological diseases or vision loss. He was not vaccinated with the Bacillus Calmette-Guerín (BCG) vaccine.

Ophthalmologic examination disclosed a visual acuity of 6/10 on both eyes, with normal conjunctiva, eyelids and cornea, no evidence of anterior chamber or vitreal inflammation, no relative afferent pupillary defect and normal direct and consensual pupillary reflexes. There was no impairment of extra-ocular muscles. Intraocular pressure was within normal limits. Direct ophthalmoscopy showed bilateral disc oedema without any evidence of hemorrhage or macular lesions. Further neurologic evaluation of the remaining cranial nerves as well as motor, sensory and coordination were unremarkable. There were no signs of meningeal irritation.

Initial blood workup in the ER showed blood counts and C-reactive protein and erythrocyte sedimentation rate within normal values. Kidney, liver function tests and electrolyte count were normal. A head computed tomography (CT) with CT angiography was performed, which showed no lesions and no evidence of cerebral venous sinus thrombosis. A lumbar puncture showed normal opening pressure (14.5 cmH_2O), 4 cells, 0.49 g/L protein and 65 mg/dL glucose (serum glucose of 100 mg/dL).

He was admitted to the neurology ward for additional investigation of bilateral optic neuropathy. Extensive testing which included kidney, liver and thyroid function, fasting glucose, electrolyte count, copper, vitamins B9 and B12 were within normal values. Autoimmune and inflammatory causes, which included assessment of serum angiotensin-converting enzyme, ANA, ANCA, anti-cardiolipin, lupus anticoagulant, anti-β2 glycoprotein and anti-neuronal antibodies (tested, among others, CV2/CRMP5, amphiphysin) and anti-ganglioside (including GQ1b antibodies) were all negative. Serum protein electrophoresis did not reveal any monoclonal peak and serology testing for HIV, HBV, HCV, rubella, EBV, CMV, HSV I and II, *Treponema pallidum*, *Toxoplasma* spp., *Rickettsia* spp., *Bartonella* spp. and *Borrelia burgdorferi* were all negative. We also tested serum and cerebrospinal fluid (CSF) for the presence of oligoclonal bands as well as anti-aquaporin-4 and anti-MOG (on cell-based assays), which were negative. CSF culture for bacteria and mycobacteria was negative. MRI of the brain, orbit and spine (with and without contrast) was performed before any treatment and repeated after treatment with methylprednisolone and plasma exchange, both completely unremarkable. Chest, abdomen and pelvis CT did not show any lesions suggestive of occult neoplasm. Although no family history was reported, Leber hereditary optic neuropathy genetic test was performed with no pathogenic variants found.

During the investigation, as no relevant infectious cause was apparent and the patient's visual acuity continued to worsen, he was started first on intravenous methylprednisolone (1 g) for 5 days, without any visual improvement. He was then started on 5 sessions of plasma exchange immediately followed by intravenous immunoglobulin (IVIg) for 5 days.

On the 20th day of admission, there was no improvement on the visual acuity despite treatment. On examination, he had worsened visual acuity, being able to detect hand movements on the right eye and 5/10 on the left eye. On direct ophthalmoscopy he maintained bilateral disc edema. Optic disc optical coherence tomography (OCT) showed retinal nerve fiber layer (RNFL) edema and fluorescein angiography showed hyperfluorescence of the optic disc and no relevant abnormalities on the retinal vessels (**Fig. 1**). Visual field testing with computerized perimetry showed a severe central scotoma, worse on the right eye.

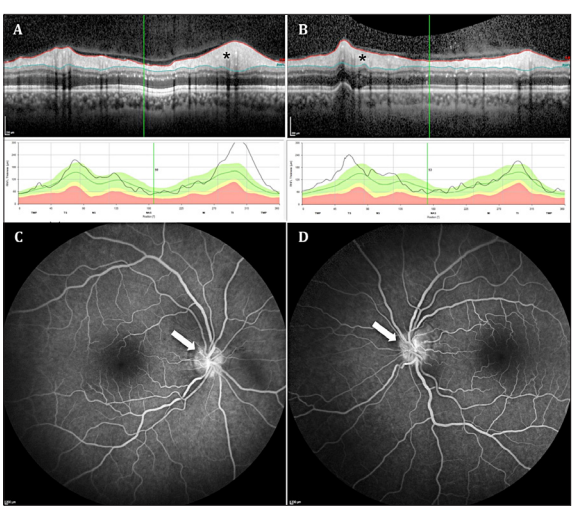

Figure 1. OCT showing increased thickness in the retinal nerve fiber layer (RNFL) in the right eye (OD, A, asterisk) and left eye (OS, B, asterisk). Fluorescein angiography showing optic disc hyperfluorescence in both eyes (C - OD, D – OS, arrows).

Although there were no relevant associated symptoms, intraocular tuberculosis was suspected following the exclusion of other possible causes and the absence of clinical response to treatment. Laboratory investigation revealed a positive interferon gamma release assay (IGRA) and chest, abdomen and pelvis CT showed calcification and loss of volume on the left middle and upper lung lobes, suggesting previous pulmonary involvement (**Fig. 2**).

On this basis, a diagnosis of intraocular tuberculosis

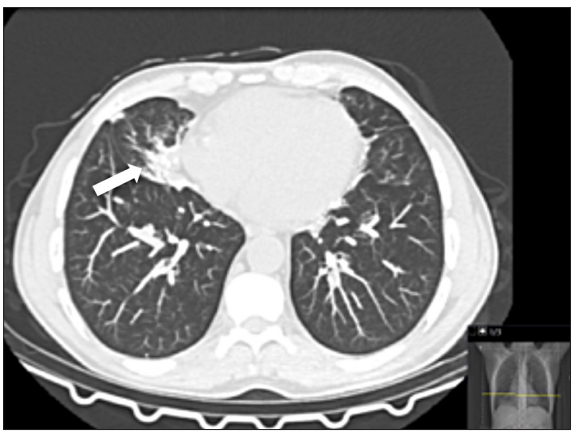

Figure 2. Chest CT showing calcification and loss of volume in the left middle lobe (arrow).

with bilateral optic neuropathy was assumed and the patient was started on antituberculous therapy (ATT), with isoniazid, rifampin, pyrazinamide and ethambutol, along with prednisolone. He was on treatment for one year, without any adverse effects. He maintained regular follow-up for more than one year and although the vision loss persisted, there was no further worsening of his visual acuity and no other symptoms. His last ophthalmologic assessment showed bilateral optic disc atrophy and, on OCT, a substantial reduction of RNFL thickness at the optic disc.

Discussion

Tuberculosis is an infectious disease typically observed in developing countries, affecting certain groups, in particular, people living with HIV or other conditions causing immunosuppression.[8,9] According to the World Health Organization, the incidence of tuberculosis worldwide was 134 per 100 000 people, with an increase from 10.7 million in 2022 to 10.8 million people diagnosed with TB in 2023.[1] In Portugal, in the same year, TB incidence was estimated at about 14.9 cases per 100 000 people.[10]

It is well known that the most common form of symptomatic infection is pulmonary TB, but other systems may be involved. Intraocular TB is a rare manifestation, with an incidence ranging from 1.4% to 18% in various case series.[4,8]

The pathophysiology of intraocular TB is postulated to be caused by direct extension of the infection (hematogenous or by contiguity) or a hypersensitivity reaction triggered by a systemic immune process.[8]

Intraocular TB has a very diverse clinical spectrum

and can affect any structure in the eye, ranging from a granulomatous uveitis (the most common manifestation) to other manifestations such as episcleritis, keratitis, choroiditis, granulomas of the optic disc, subretinal abscess, vasculitis and optic neuropathy.[8,11]

According to a review of 49 cases of tuberculous optic neuropathy, papillitis was the most frequent manifestation, in approximately half of the patients, often in association with other forms of ocular involvement (such as uveitis). The disease was more frequently unilateral but bilateral presentation, like our patient, was observed in 26.5% of the patients studied. Decreased vision was the most frequent symptom noted in the case series but other symptoms such as eye pain, ocular injection, ptosis or diplopia were also reported.[7]

Current or previous systemic symptoms such as fever, weight loss and cough can bring additional clues, confirming an active infection or indicating a previous untreated contact with *Mycobacterium tuberculosis*. In about 63.3%, along with the present report, these signs are either not present or not immediately recalled by the patient.[7]

In cases of isolated intraocular tuberculosis, definitive diagnosis is often difficult as it requires isolation of either the microorganism or its nucleic acid from ocular fluids. In these cases, a presumptive diagnosis can be established and allow for treatment if one of these features is present: (1) clinical ophthalmological signs consistent with intraocular tuberculosis; (2) confirmed exposure via a positive tuberculin skin test (TST) or IGRA; (3) evidence of a tubercular lesion on chest imaging.[5,6,12–14] Currently, Portugal has a high incidence of tuberculosis, so it must always be considered in the differential diagnosis. In this case, the clinical presentation was suggestive, we confirmed exposure with a previous pulmonary primary infection, a positive IGRA test and excluded other possible causes. Considering the differential diagnosis, more advanced testing such as F-fluorodeoxyglucose positron emission tomography, cerebrospinal fluid (CSF) examination for neoplastic cells was not performed as this hypothesis was considered less probable given the clinical presentation and results of initial CSF testing, negative serum antineuronal antibodies and a normal magnetic resonance imaging (MRI) of the brain and spine. In isolated intraocular tuberculosis, a negative PCR for *Mycobacterium tuberculosis* would not allow definite exclusion of this diagnosis, which was not performed in our patient.

Another factor to consider is the continuing clinical worsening despite empirical treatment with corticosteroid, plasma exchange or immunoglobulin in addition to a stabilization of visual acuity following ATT, which further supports the diagnosis.

First-line treatment of tuberculosis is a regimen of 4 antituberculous drugs for at least 6 months, with longer treatment durations reserved for more severe presentations such as tuberculous meningitis.[5,8] In the case of intraocular tuberculosis, there are no specific recommendations on the duration of treatment but generally, at least 9 months of ATT are suggested.[6,7,11] We aimed for a treatment duration of 12 months in this case, given the severity of the symptoms and lack of improvement.

In our case, because the initial suspicion was an inflammatory/autoimmune optic neuropathy, the patient was treated with methylprednisolone shortly followed by plasma exchange and IVIg before starting ATT regimen. It is not documented what the effect of plasma exchange and intravenous immunoglobulin might have on cases of intraocular tuberculosis but use of corticosteroid without ATT has been associated with disease progression and risk of recurrence.[5] On the other hand, the administration of corticosteroid as an adjuvant to ATT has been suggested as potentially helpful, particularly for management of ocular inflammation and also to minimize paradoxical worsening while on ATT.[6]

The prognosis of tuberculous papillitis is largely dependent on a number of factors such as: age > 50 years, female gender, longer duration of disease, severity of visual defect, delay in the diagnosis, presence of posterior or panuveitis, higher IGRA titers and also administration of corticosteroid therapy before ATT.[15] Visual outcomes were generally favourable, with most patients having improved visual acuity.[7] This underscores the importance of early suspicion, diagnosis and treatment to minimize complications and increase the chances of clinical improvement. In this case, the patients age, severity of visual defect, use of corticosteroid therapy and the delay on the diagnosis were definite factors that might have influenced poor visual outcome.

Long term follow-up is very important in these patients, given the need for continued monitoring of treatment effect, symptom improvement and complications. In patients with vision recovery, the process is frequently slow and very dependent on strict treatment adherence and management of complications.

Conclusion

In this report, we describe a case of bilateral optic neuropathy as an isolated manifestation of tuberculosis. Given its ubiquitous involvement of the eye structures, it can present with a wide range of signs and symptoms. Papillitis is a rare manifestation of intraocular tuberculosis, with a high propensity to cause severe vision loss if not adequately treated. In this regard, a low threshold for suspicion of this diagnosis and an appropriate treatment regimen with regular monitoring are absolutely crucial for better visual outcomes. ■

Previous Presentations

The clinical case reported in this article was previously presented as a poster at the "Congresso Nacional de Neurologia 2023" and at the 10th European Academy of Neurology Congress.

Contributorship Statement / Declaração de Contribuição

FA and IN: Design, data acquisition, content review, and approval of the final version to be published.

CC, ALR, and EV: Content review and approval of the final version to be published.

FA e IN: Desenho, aquisição de dados, revisão de conteúdo e aprovação da versão final a ser publicada.

CC, ALR e EV: Revisão de conteúdo, aprovação da versão final a ser publicada.

Responsabilidades Éticas

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

Fontes de Financiamento: Não existiram fontes externas de financiamento para a realização deste artigo.

Confidencialidade dos Dados: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.

Consentimento: Consentimento do doente para publicação obtido.

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

Ethical Disclosures

Conflicts of Interest: The authors have no conflicts of interest to declare.

Financing Support: This work has not received any contribution, grant or scholarship.

Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of patient data.

Patient Consent: Consent for publication was obtained.

Provenance and Peer Review: Not commissioned; externally peer-reviewed.

References / Referências

1. World Health Organization. Global tuberculosis report 2024. Geneva: WHO; 2024.
2. VidyaRaj CK, Vadakunnel MJ, Mani BR, Anbazhagi M, Pradhabane G, Venkateswari R, et al. Prevalence of extrapulmonary tuberculosis and factors influencing successful treatment outcomes among notified cases in South India. Sci Rep. 2025;15:8290. doi: 10.1038/s41598-025-92613-5.
3. Baykan AH, Sayiner HS, Aydin E, Koc M, Inan I, Erturk SM. Extrapulmonary tuberculosıs: an old but resurgent problem. Insights Imaging. 2022;13:39. doi: 10.1186/s13244-022-01172-0.
4. Donahue HC. Ophthalmologic experience in a tuberculosis sanatorium. Am J Ophthalmol. 1967; 64: 742–8.
5. Dalvin LA, Smith WM. Intraocular manifestations of mycobacterium tuberculosis: A review of the literature. J Clin Tuberc Other Mycobact Dis. 2017; 7: 13–21. doi: 10.1016/j.jctube.2017.01.003.
6. Alvarez GG, Roth VR, Hodge W. Ocular tuberculosis: diagnostic and treatment challenges. Int J Infect Dis. 2009; 13: 432–5. doi: 10.1016/j.ijid.2008.09.018.
7. Davis EJ, Rathinam SR, Okada AA, Tow SL, Petrushkin H, Graham EM, et al. Clinical spectrum of tuberculous optic neuropathy. J Ophthalmic Inflamm Infect. 2012; 2: 183–189. doi: 10.1007/s12348-012-0079-5.
8. Dhiman R, Lakra S, Panda PK, Hemachandran N, Sharma S, Saxena R. Neuro-ophthalmic manifestations of tuberculosis. Eye. 2022; 36: 15–28. doi: 10.1038/s41433-021-01619-6.
9. Sossen B, Kubjane M, Meintjes G. Tuberculosis and HIV coinfection: Progress and challenges towards reducing incidence and mortality. Int J Infect Dis. 2025; 155: 107876. doi: 10.1016/j.ijid.2025.107876.
10. Laboratório Nacional de Referência de Micobactérias. Vigilância Laboratorial da Tuberculose em Portugal. [consultado Maio 2025] Disponível: http://hdl.handle.net/10400.18/10456 (2025).
11. Reche-Sainz JA, Gracia García-Miguel MT, Pérez-Jacoiste MA. Papillitis and neuroretinitis of tuberculous etiology. Arch Soc Esp Oftalmol 2019; 94: 359–362.
12. Morimura Y, Okada AA, Kawahara S, Miyamoto Y, Kawai S, Hirakata A, et al. Tuberculin skin testing in uveitis patients and treatment of presumed intraocular tuberculosis in Japan. Ophthalmology. 2002; 109: 851–7. doi: 10.1016/s0161-6420(02)00973-9.
13. Aupy J, Vital A, Rougier MB, Gradel A, Meissner W, Marchal C, et al. Presumed tuberculous retrobulbar optic neuritis: a diagnosis challenge. J Neurol. 2015;262:481-4. doi: 10.1007/s00415-014-7611-5.
14. Sanghvi C, Bell C, Woodhead M, Hardy C, Jones N. Presumed tuberculous uveitis: Diagnosis, management, and outcome. Eye. 2011; 25: 475–80. doi: 10.1038/eye.2010.235.
15. Kee AR, Gonzalez-Lopez JJ, Al-Hity A, Gupta B, Lee CS, Gunasekeran DV, et al. Anti-tubercular therapy for intraocular tuberculosis: A systematic review and meta-analysis. Surv Ophthalmol. 2016; 61: 628–53. doi: 10.1016/j.survophthal.2016.03.001.