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**Case Report**

# Reactivation of Multifocal Choroiditis Associated with Treatment in Latent Tuberculosis

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**Keywords**
Chorioretinitis · Choroid · Tuberculosis · Retina · Infectious disease

**Abstract**
Tuberculosis (TB) causes significant morbidity and mortality worldwide. Ocular manifestations of TB can lead to severe and sight-threatening complications. Initiating treatment in ocular TB with anti-tubercular therapy (ATT) may be necessary to prevent long-term visual complications. We present a case of the reactivation of bilateral multifocal choroiditis (MFC) in a patient with latent TB after commencing ATT. An asymptomatic 36-year-old Indian male was referred to an ophthalmologist with extensive inactive bilateral MFC close to his fovea despite no previous medical or ocular history. Latent TB was subsequently diagnosed via TB specific antigens and antibodies. After a period of stable observation without evidence of active eye or systemic disease, the patient was commenced on quadruple ATT with the aim of reducing the risk of visual loss with the MFC. However, after commencing treatment, MFC reactivation was observed. This settled with the addition of high-dose oral prednisone. The steroid was slowly weaned and ceased with the cessation of ATT. There have been no further episodes of active choroiditis since treatment was ceased. TB is a significant cause of mortality worldwide, and ocular manifestations can cause severe and sight-threatening complications in active and latent TB. The treatment of TB, however, may lead to further complications. We present the case of a visually asymptomatic patient with latent TB, with before and after fundal images, demonstrating the reactivation of the MFC after commencing ATT.



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## Introduction

Tuberculosis (TB) infects over a third of the world's population and is the leading cause of death by an infectious disease [1]. It is caused by *Mycobacterium tuberculosis,* an intracellular bacillus that leads to a caseating granulomatous infection [1–3]. The prevalence of TB was estimated in the National TB Prevalence Survey in India to be 316 per 100,000 in 2019–2021 [4]. Considering the high prevalence of TB, ocular manifestations are uncommon and are seen in both active and latent TB. Ocular presentations of TB can affect all parts of the eye and surrounding adnexa [2, 5, 6] including the eyelids which can present with reddish-brown nodules or a fluctuant mass without inflammation [5]. Similarly, common corneal presentations include phlyctenular keratoconjunctivitis or interstitial keratitis [2, 5]. Tubercular uveitis is often a chronic granulomatous condition causing mutton-fat keratic precipitates, posterior synechiae, iris nodules and secondary glaucoma. Choroidal tubercles and tubercular choroiditis have been reported to occur without systemic involvement. Additionally, retinal disease can be result of choroidal extension or haematogenous spread, presenting with tubercles or diffuse retinal vasculitis [2, 5, 6].

Chorioretinitis such as multifocal choroiditis (MFC), however, can have numerous infective and non-infective aetiologies [6]. Patients may present with metamorphopsia, photopsias, and floaters with variable visual acuity (VA) [7]. Examination of the posterior pole and periphery demonstrates chorioretinal lesions with minimal anterior uveitis or vitritis [8]. Without intervention, the natural course will cause progressive vision loss [8, 9]. Treatment of MFC is dependent on the underlying cause as antimicrobials, antivirals, and antifungals are often used if an infective cause is suspected. Similarly, the use of systemic immunosuppression can be utilized to minimize the damage caused by the accompanying inflammation [7–9].

Tuberculosis is one of the numerous causes of MFC, though targeted anti-tubercular treatment (ATT) used to prevent severe and sight-threatening complications [2] has been described to cause a paradoxical exacerbation of disease [3, 10]. We present a case of the reactivation of bilateral MFC in latent TB after commencing ATT.

## Case Report

A 36-year-old Indian man living in Sydney, Australia was referred by an optometrist with scars in both fundi after he had presented for reading glasses. The gentleman was born in India and had been living in Australia for the previous 2 years. He had no significant past medical or ocular history and had not had an eye examination previously. On examination, his Snellen VA was 6/6 with normal anterior segment examination. Dilated fundoscopy, however, demonstrated inactive bilateral MFC with lesions close to his foveae (Fig. 1). Fundus photography, fundus fluorescein angiography, optical coherence tomography, and computed tomography (CT) imaging were performed to determine the aetiology of the MFC. Syphilis, toxoplasmosis, anti-nuclear antibody, extractable nuclear antigen panel, antineutrophil cytoplasmic antibodies were negative. However, an interferon gamma releasing assay (QuantiFERON®-TB Gold, Qiagen, Germantown, MD, USA) was positive and CT of the chest demonstrated prominent mediastinal lymph nodes. The patient was subsequently referred to a tubercular clinic where a diagnosis of latent TB was confirmed. The patient was closely monitored and the MFC remained inactive over the following 4 months. However, the decision was made to start quadruple ATT with rifampicin, isoniazid, pyridoxine, and moxifloxacin to reduce the risk of vision loss from future reactivation of the MFC. Although he remained asymptomatic, new active MFC lesions developed 3 months after the initiation of ATT (Fig. 2).

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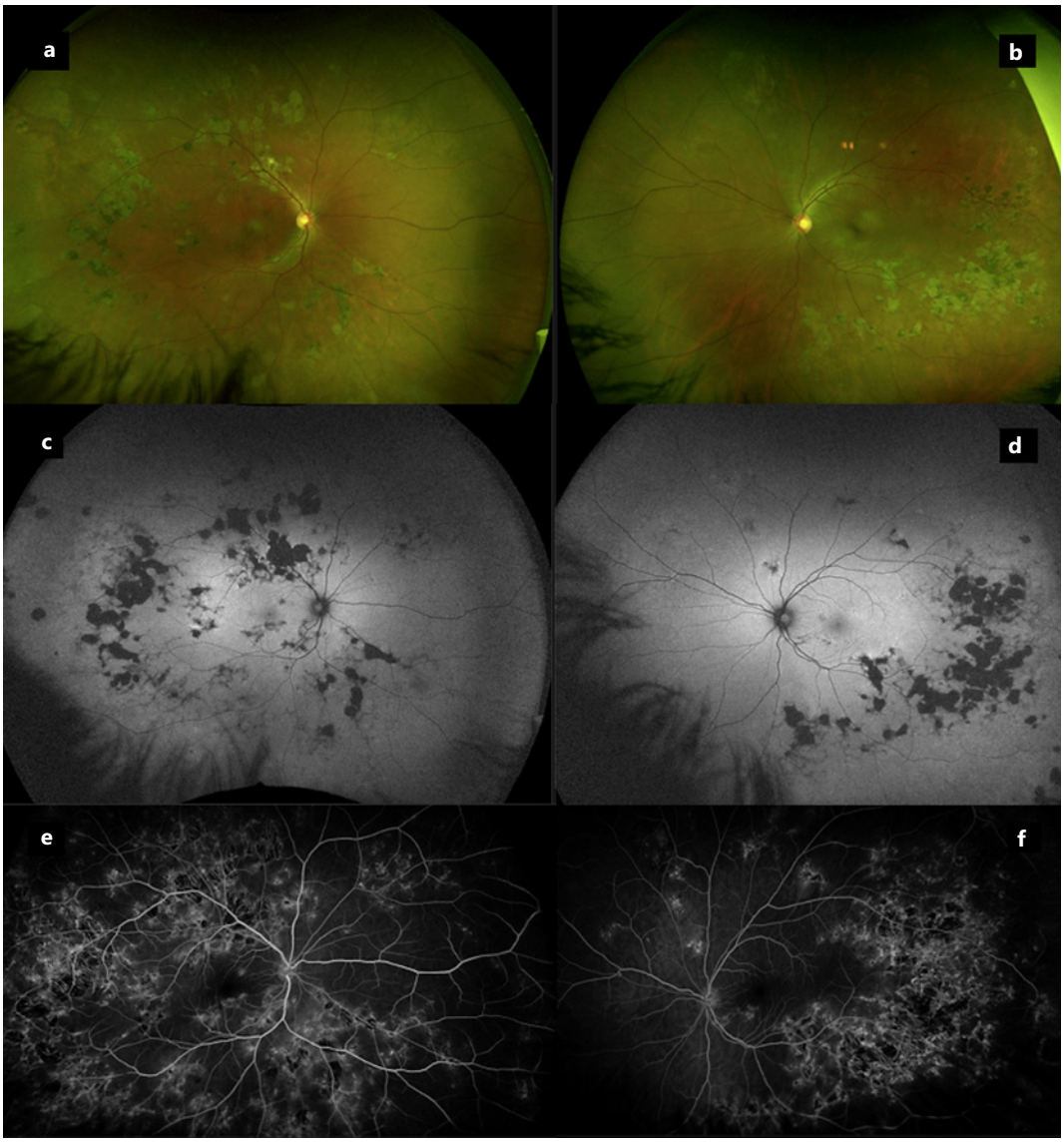


**Fig. 1.** Wide field colour fundus photos (**a**, **b**), fundus autofluorescence (**c**, **d**), and FFA (**e**, **f**) of the first presentation of right eye (**a**, **c**, **e**) and left eye (**b**, **d**, **f**). Lesions consistent with inactive multifocal choroiditis evidenced by areas of abnormal pigmentation on colour photos (**a**, **b**) which are hypo-autofluoresent (**c**, **d**) and stain rather than leak on FFA (**e**, **f**). Note that lesions in the right eye are close to but not involving the foveal centre.

Daily oral prednisone (80 mg per day) was commenced. The areas of active MFC responded to this treatment. Prednisone was tapered by 5 mg per week and ceased coinciding with cessation of ATT. The MFC has remained inactive during 2 years of follow-up (Fig. 3).

## Discussion

Multifocal Choroiditis is one of the many presentations of ocular TB [5, 6]; however, the differential diagnosis of chorioretinitis is broad with numerous infective and non-infective aetiologies [6]. Infective causes such as bacteria, viruses, fungi, and protozoa may present

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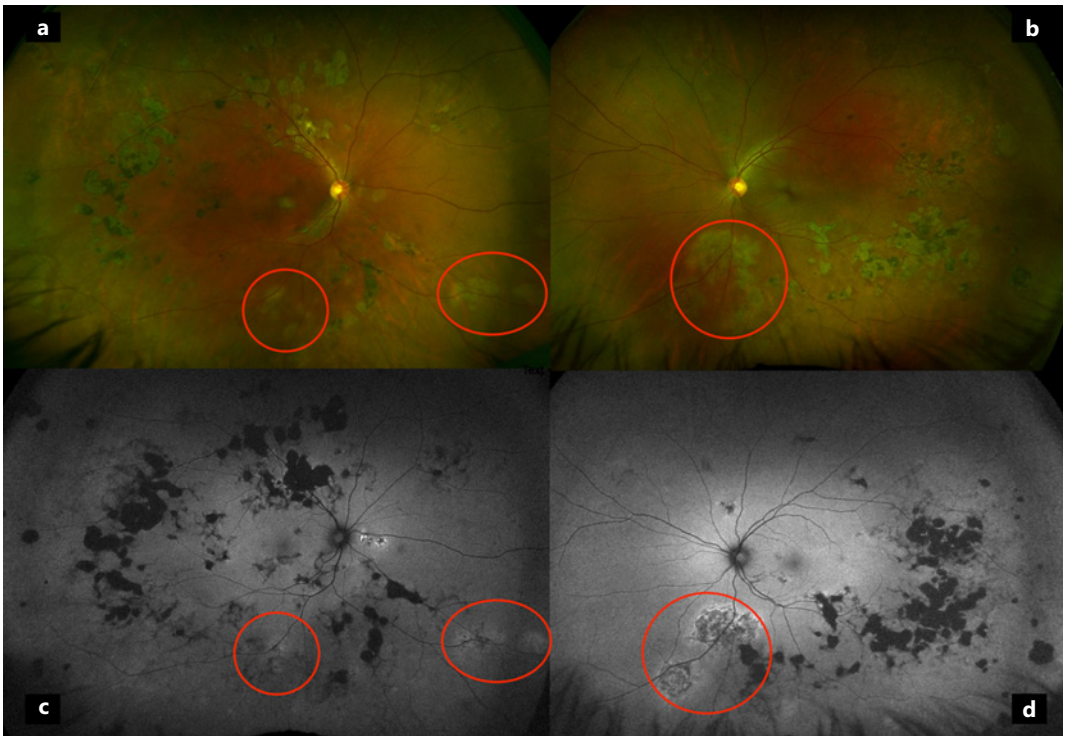


**Fig. 2. a**, **b** Wide field images taken 3 months after commencing anti-tubercular treatment showing new active multifocal choroiditis lesions (red circle). **c**, **d** Active multifocal choroiditis lesions are hyperautofluoresent.

with similar features making clinical differentiation difficult [2, 5]. Furthermore, autoimmune conditions including sarcoidosis, Adamantiades-Behcet's disease may present with similar clinical features [7, 9]. Additionally, posterior uveitis without systemic illness such as birdshot chorioretinopathy, acute posterior multifocal placoid pigment epitheliopathy, and multiple evanescent white dot syndrome are further examples of differential diagnoses that can further cloud the clinical picture [9]. Therefore, investigations including serological, immunological, and imaging tests are performed to determine the specific cause of the chorioretinopathy while excluding other possible diagnoses [4, 7, 8, 10].

Ocular TB may precede any other evidence of systemic tubercular manifestations. Performing thorough investigation and incorporating subspecialist respiratory and/or infectious disease reviews allows for the prompt diagnosis and treatment, which in turn minimises the potential of poor outcomes [6]. Furthermore, the decision to treat ocular TB with ATT is determined by the risk of disease progression [9–11]. The Collaborative Ocular Tuberculosis Study guideline provides recommendations on commencing treatment in ocular TB based on the results of immunologic (Mantoux, QuantiFERON®-TB Gold) and radiologic investigations (X-ray, CT) as well as considering community prevalence of TB [11]. There is moderate consensus in commencing ATT in patients with MFC from an endemic or non-endemic area with 1 positive immunologic test and positive radiologic results [11, 12]. Given there was only moderate consensus for commencing ATT in our case, our patient was closely monitored with ongoing multidisciplinary reviews before being commenced on ATT. During this monitoring period, the MFC remained inactive.

Anti-tubercular treatment, although necessary for the treatment of TB, has been described to cause a worsening of disease [3, 6]. Cheung and Chee [3] presented the case of a

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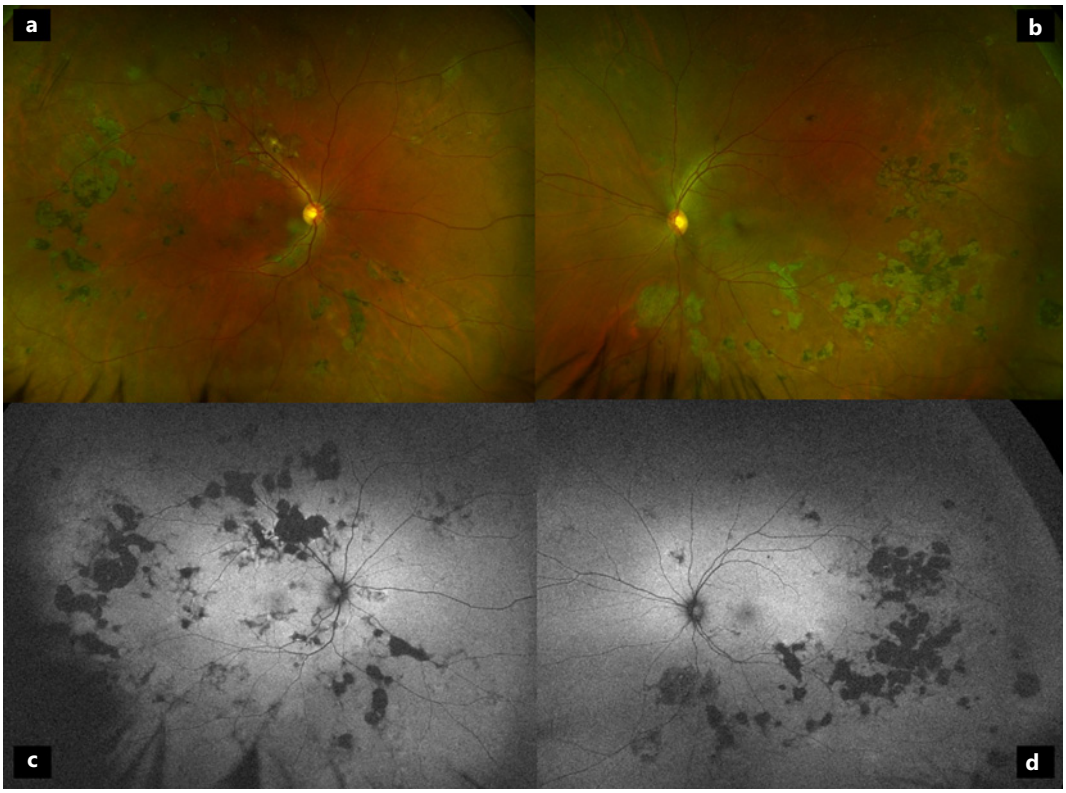


**Fig. 3.** Wide field colour (**a**, **b**) and autofluorescent images (**c**, **d**) of right (**a**, **c**) and left (**b**, **d**) fundi demonstrate that all multifocal choroiditis lesions are now inactive after cessation of anti-tubercular treatment and prednisone.

77-year-old female with biopsy-proven tubercular cervical lymphangitis that experienced reduced vision after commencing ATT. Examination demonstrated anterior chamber and vitreous cells with numerous areas of retinitis and pigmented chorioretinal scars. Testing of vitreous identified *Mycobaterium tuberculous* DNA and investigations for other infective and non-infective causes were negative. Treatment with oral prednisone with a tapering course leads to the resolution of the vitritis and chorioretinitis. Similarly, Yilamz et al. [13] reported the case of a 20-year-old male presenting with decreased VA and distorted vision. He was noted to have multiple hypofluorescent choroidal lesions. Systemic investigation demonstrated miliary lesions in both lungs and positive TB serologies. After commencing ATT, however, his VA decreased and he was noted to have progression of a choroidal tuberculoma after commencing ATT. Interestingly, his treatment was not altered as his systemic TB was resolving. The ocular TB did improve, though his VA remained poor [13]. Furthermore, Aggarwal et al. [14] conducted a prospective observational study using ultra-wide field imaging to assess TB uveitis. Through their study, they found that 36% demonstrated paradoxical worsening of chorioretinitis after commencing ATT. Additionally, all of the patients demonstrated resolution of the chorioretinitis after treatment with immunosuppressive therapy [12].

These progressions of disease after commencing ATT have been proposed to be similar to Jarisch-Herxheimer reactions (JHR), which are a paradoxical worsening of disease after commencing antibiotic therapy. JHR are postulated to be triggered by a delayed hypersensitivity to the release of antigens and endotoxin [3, 10, 15]. They have been described to occur

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in intracellular bacterial infections, often early in the antibiotic treatment and are associated with a worsening of systemic symptoms such as fever, rash, and diaphoresis [6, 13, 14, 16]. In our case, we demonstrate the reactivation of inactive bilateral MFC after commencing ATT (Fig. 1, 2). Our patient, however, did not report systemic symptoms that would normally be described in JHR. Because of lack of symptoms, the precise time that reactivation of MFC occurred is also unknown but was diagnosed on ocular surveillance.

In ocular manifestations of TB, ongoing surveillance must be prioritized to prevent poor visual outcomes [5, 10, 13–16]. Patients should have routine follow up with physicians and ophthalmologists to observe for systemic and ocular disease progression, in addition to monitor systemic and ocular toxicity of therapy [5, 11, 12]. Multidisciplinary care and communication between specialists are imperative for best outcomes [11, 12]. In our case, it is worth noting that the patient remained asymptomatic despite the worsening MFC, emphasizing the need for continued vigilance.

## Conclusion

TB is a significant cause of mortality worldwide and can cause severe ocular morbidity in latent and active TB. In rare cases, the initiation of therapy can cause a worsening of ocular disease that if not detected can lead to significant morbidity. Our case emphasises the importance of thorough examination even in asymptomatic patients and the awareness of the ocular sequelae of TB and its treatment.

## Statement of Ethics

Ethics approval was not required in accordance with local or national guidelines. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

## Conflict of Interest Statement

We declare no competing or conflicts of interests.

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## Author Contributions

Christopher Bartimote, Samantha Fraser-Bell, and Hamish Dunn were involved in conceiving the study. Christopher Bartimote researched the literature. Christopher Bartimote wrote the first draft of the manuscript. Christopher Bartimote, Samantha Fraser-Bell, and Hamish Dunn reviewed and edited the manuscript and approved the final version of the manuscript.

## Data Availability Statement

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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