



## Asymptomatic occlusive retinal vasculitis in newly diagnosed active tuberculosis

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### ABSTRACT

**Introduction:** Worldwide, tuberculosis is the leading cause of death from an infectious disease. Ocular involvement can cause significant and permanent vision loss. Ocular manifestations of tuberculosis often present with visual symptoms. Asymptomatic ocular tuberculosis is uncommon and yet can have serious consequences if missed.

**Case report:** An immunocompetent 26-year-old Filipino man living in regional Australia who was diagnosed with active pulmonary tuberculosis and started on antitubercular therapy. He was referred to an ophthalmologist for baseline ethambutol screening to exclude pre-existing optic neuropathy. Despite having no visual symptoms, when examined, the patient had vision threatening occlusive retinal vasculitis. He was initially commenced on localised therapy via bevacizumab intravitreal injections and retinal photocoagulation. Following completion of antitubercular therapy, high dose prednisone was commenced and slowly tapered.

**Conclusions:** We present the case of an asymptomatic sight threatening occlusive vasculitis that was discovered on pre-treatment ophthalmology review. This case emphasises the need for referral for full ophthalmic screening in newly diagnosed tuberculosis to exclude vision-threatening complications.

### 1. Introduction

Tuberculosis infects over a third of the world's population and is the leading cause of death by an infectious disease [1–3]. It is caused by *Mycobacterium tuberculosis*, an intracellular bacillus [1,2] that leads to a granulomatous pulmonary infection. Due to the haematogenous spread of the bacteria, however, tuberculosis can infect any structure in the body [4]. Ocular tuberculosis can cause significant morbidity from the active infection and subsequent inflammatory response. It often presents with visual symptoms, such as blurry vision, diplopia flashes and/or floaters [2,3,5]. Asymptomatic ocular manifestations of tuberculosis have been described [4], although it usually occurs in immunocompromised patients or where the lesions develop in the periphery of the retina [5,6]. Treatment of ocular tuberculosis involves anti-tubercular treatment (ATT) combined with local and/or systemic immunosuppression [2,7]. We present the case of an asymptomatic sight threatening occlusive retinal vasculitis presenting soon after an active tuberculosis diagnosis.

### 2. Case report

An immunocompetent 26-year-old Phillipino man living in regional Australia was diagnosed with active pulmonary tuberculosis and was commenced on ATT consisting of 2 months of ethambutol and pyrazinamide with 6 months of isoniazid and rifampicin (2HRZE/4HR). After 2 weeks of ATT, he presented to the local ophthalmologist for baseline ethambutol screening. At the time of review, he did not report any visual symptoms. Physical examination demonstrated visual acuity of 20/20 in each eye. Corneae and anterior chamber examination was normal. However, fundal examination revealed temporal blot haemorrhages and multiple inferior and superonasal nodules at the veins that were suspicious for occlusive retinal vasculitis (Fig. 1). Fundus fluorescein angiography (FFA) confirmed periphlebitis with staining of the vessel walls, and a secondary branch retinal vein occlusion (BRVO) with diffuse areas of capillary non-perfusion indicating retinal ischaemia (Fig. 2).

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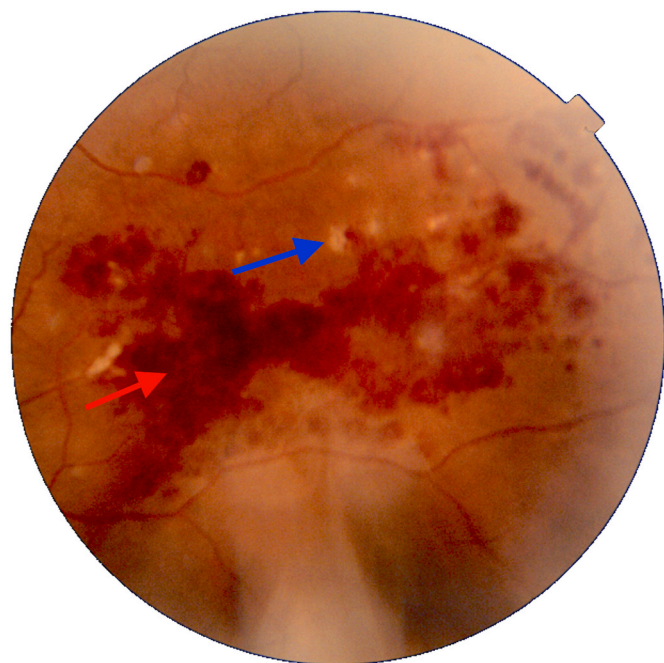
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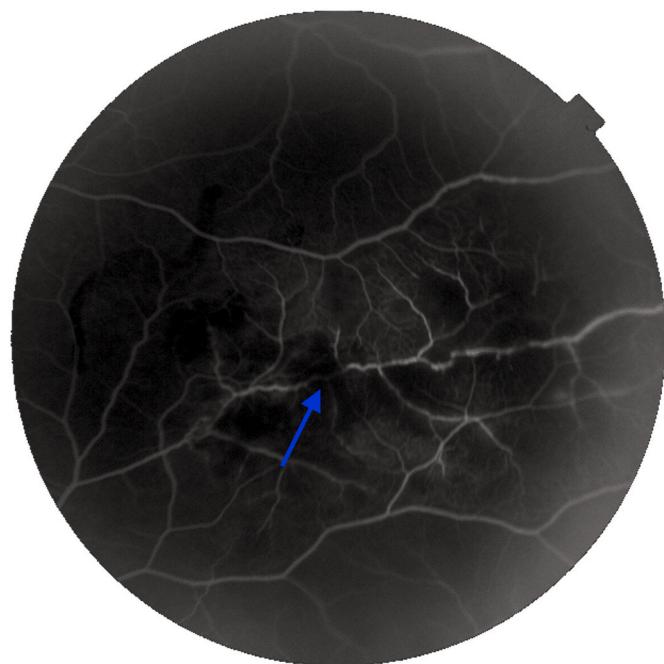
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**Fig. 1.** Colour fundus photograph demonstrating Occlusive Vasculitis with retinal nodules (blue arrow) and temporal blot haemorrhages (red arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)



**Fig. 2.** Fundus fluorescein angiography demonstrating Branch Retinal Vein Occlusion with surrounding capillary non-perfusion (blue arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

steroid is often used. In discussion with the treating respiratory physician, the use of systemic steroids was avoided to prevent immunosuppression in active tuberculosis. Instead, the off-label use of bevacizumab 4mg as an intravitreal injection (IVI) was utilised to provide localised treatment for the vasculitis. With the IVI, the periphlebitis and temporal haemorrhages were settling, however, extensive whitening of the retina

developed from the BRVO. Sectoral scatter laser therapy was applied to the areas of retinal ischaemia to prevent extension and the risk of retinal detachment. Throughout this period, visual acuity remained normal and the patient asymptomatic.

Six weeks after the initiation of ATT, systemic steroids (1mg/kg) were initiated with gastric protection (pantoprazole 40mg). In the preceding reviews of the eye, peripheral whitening and vascular sheathing reduced but remained present until the cessation of the 6 months of ATT. There was a recurrence of retinal whitening and perivascular nodules when the prednisone dose was reduced after 3 weeks, but abated following medical retina subspecialty advice of a small increase in steroids and a prolonged wean. The slow wean of steroids was conducted over 4 months after the cessation of ATT. Over 28 months of follow-up there were no further recurrences of ocular inflammation or signs of vasculitis after completing the 9 months total of systemic steroids.

### 3. Discussion

*Mycobacterium tuberculosis* can infect all parts of the eye leading to a myriad of presentations known as ocular tuberculosis. Ocular tuberculosis, however, can range from cutaneous nodules and abscesses on the eyelids, mucopurulent and chronic conjunctivitis, choroiditis, uveitis and endophthalmitis [8]. The seemingly localised infections may initially present in a single area of the eye but can spread haematogenously or by local extension to other ocular structures [8]. Additionally, the spread of *M. tuberculosis* can trigger an immunoreaction to tuberculosis antigens with an unclear pathophysiology as it can be seen in both active and latent tuberculosis. It has been found to cause anterior uveitis, anterior scleritis, serpiginoid choroiditis, occlusive vasculitis and severe vitritis [9,10]. Therefore, therapies must target *M. tuberculosis* infection as well as suppress the immune response [3,9].

Unfortunately, the complications of these pathologies can be devastating, increasing the likelihood of poor visual outcomes [8,9,11]. For example, occlusive retinal vasculitis predominantly affects retinal venules [9] and can be complicated by retinal vein occlusion, such as BRVO as seen in this case. In turn, the associated ischaemia can lead to retinal neovascularisation and its complications [11]. Although the effect on vision may initially be minimal, it can progress to permanent vision loss [6]. Yaacob et al. reported the only other case of an asymptomatic occlusive retinal vasculitis caused by tuberculosis [12]. The vasculitis occurred in the periphery of the retina which can often present with no symptoms [6]. In our case, however, the vasculitis was sight threatening on presentation leading to our concern, as it was an asymptomatic vasculitis with the potential for severe morbidity.

The collaborative ocular tuberculosis study developed a guideline for treatment of ocular tuberculosis based on tuberculosis community prevalence and the results of radiologic and immunologic tests [13]. Using these guidelines, instituting ATT in the treatment of ocular tuberculosis is a calculated decision based on the risk of disease progression and the likelihood of a poor prognosis [7,9,13]. Additionally, systemic steroid regimes or the localised use of vascular endothelial growth factor inhibitors, such as the off-label use of intravitreal bevacizumab as in our case, can be used to minimise the severe visual complications from vasculitis caused by tuberculosis [3,14,15].

It is important to note, however, that numerous other entities may present with similar retinal and/or choroidal pathology [16,17]. Agarwal et al. characterised the aetiology and epidemiology of occlusive retinal vasculitis from two tertiary institutions [16]. Forty-three percent were caused by tuberculosis, however, there were a multitude of other aetiologies including Systemic Lupus Erythematosus, Bechet's disease, Sarcoidosis, Eales disease, Herpes simplex and zoster viruses [16]. Differentiating the aetiology of the ocular disease is extremely important as without appropriate treatment the prognosis is very poor [16,17].

The prognosis of retinal vasculitis in tuberculosis patients usually depends on the risk of that pathology developing complications [14–17]. Pathologies that are prone to develop ischaemia, such as

occlusive retinal vasculitis as seen in our case, have a very guarded prognosis as the neovascularisation and retinal ischaemia can lead to irreparable damage to the retina [14,16]. Aggressive and novel treatments are indicated in these circumstances due to the high risk of poor visual outcomes [14]. Early assessment and diagnosis is paramount to maximise recovery and minimise complications.

In the management of tuberculosis, however, visually asymptomatic patients are usually only referred to an ophthalmologist for Ethambutol screening to document a baseline assessment of the optic nerve before or soon after the initiation of ATT, as the doses of ethambutol utilised can lead to optic nerve toxicity [7,17,18]. The examination will concentrate on the appearance of the optic nerve and functional tests of the eye such as visual field and colour vision [17,18]. From this case, we demonstrate the value of a full ocular examination and fundus imaging regardless of whether visual symptoms are present. Further health economic research is indicated to determine the public health value of such practice.

#### 4. Conclusions

We present the case of an asymptomatic sight threatening occlusive vasculitis caused by active tuberculosis. Although asymptomatic ocular manifestations of tuberculosis are uncommon, the consequences of missed diagnoses can be devastating. By incorporating referrals for full retinal examination and investigation into practice, it would allow for early detection and treatment of ocular tuberculosis complications.

#### Declaration of competing interest

We declare no competing or conflicts of interests.

All authors were involved in conception, writing and critical review of the report.

Informed consent was obtained from the patient for the publication of the clinical pictures and case report.

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