Ocular Tuberculosis Initially Presenting as Central Retinal Vein Occlusion

Muiz Mahyudin May May Choo Norlina Mohd Ramli Sharifah S. Omar

University Malaya Medical Centre, Kuala Lumpur, Malaysia

Key Words
Ocular tuberculosis · Central retinal vein occlusion · PCR analysis · Vitreous tap

Abstract
A 23-year-old man presented with central retinal vein occlusion. The retinal haemorrhages worsened and signs of retinal vasculitis appeared later as vision dropped from 6/60 to Counting Fingers. No signs of systemic disease were observed. Routine Mantoux test and chest radiograph were negative for tuberculosis. Fundus fluorescein angiogram confirmed presence of retinal vasculitis. Both systemic and topical corticosteroid therapy were ineffective. Polymerase chain reaction analysis of vitreous fluid showed presence of *Mycobacterium tuberculosis*. A full 6-month course of antituberculosis therapy was given and inflammation subsided. Vision improved to 3/60. This is a rare case of ocular tuberculosis without evidence of systemic infection, presenting first as a central retinal vein occlusion.

Introduction
Central retinal vein occlusion (CRVO) in a young patient warrants extensive investigation to look for an underlying cause. Retinal vasculitis is one possible underlying pathology. How extensive should the diagnostic work-up be in the absence of systemic features? A study by George et al. [1] showed 24 out of 25 patients with retinal vasculitis had no systemic features and only one patient was proven to have systemic lupus erythematosus. Hayreh et al. [2] advocated that unless there was clear indication, routine haematologic evaluation was sufficient for patients with retinal vein occlusion. This case illustrates the diagnostic dilemma of how extensive these investigations should be. Ocular tuberculosis presenting first as CRVO is also rare. This is the first case of ocular tuberculosis in which no clinical systemic signs of tuberculosis were detected.
Case Report

A 23-year-old man presented to the Ophthalmology Clinic with a 4-month history of blurring of vision in his right eye. The onset had been sudden and painless. There were no symptoms of cough, night sweats, joint pains or recent exposure to people with chronic cough. He had seen an ophthalmologist who had made a diagnosis of CRVO secondary to glaucoma.

Vision was 6/60 OD, 6/6 OS. Right relative afferent pupillary defect was present. Intraocular pressures were 14 mm Hg OU. No iritis or vitritis were seen. There were retinal haemorrhages, cotton wool spots, venous engorgement and a swollen optic disc. The left fundus was normal. Both optic discs showed a cup–disc ratio of 0.7.

Blood investigations including full blood count, venereal disease research laboratory (VDRL), collagen vascular screen and coagulation profile (homocysteine, antithrombin III activity, protein C and protein S activity and IgG anticardiolipin) were normal. The erythrocyte sedimentation rate (ESR) was 3 mm/1st hour. A chest radiograph performed did not reveal the presence of active tuberculous infection in the lungs. Mantoux test which measured 5–6 mm was not indicative of active tuberculosis infection.

Two weeks later, right vision became Counting Fingers. Cell activity of 2+ was noted in the anterior chamber and vitritis of 2+ was present. Fresh retinal haemorrhages were also seen. There was retinal vessel sheathing and some preretinal whitish opacities were noted in the inferior retina (fig. 1a). The left fundus was normal (fig. 1b). A fundus flourescein angiogram (FFA) performed revealed leakage of flourescein from retinal vessels and staining of vessel walls confirming retinal perivasculitis (fig. 2). A virology test for both Herpes and Varicella IgG and IgM were negative. Cytomegalovirus, toxoplasmosis, VDRL/TPHA and HIV tests were also negative. The patient was commenced on oral corticosteroids of 1 mg/kg and topical dexamethasone eye drops to the right eye q.i.d.

Three weeks from initial presentation, it was decided to proceed with a diagnostic vitreous tap as there was no change. The fundal haemorrhages persisted and vascular sheathing was more prominent (fig. 1c). Polymerase chain reaction (PCR) analysis of vitreous fluid was positive for Mycobacterium tuberculosis. The patient was commenced on antituberculosis treatment and oral corticosteroids were stopped. Intensive phase antituberculosis treatment which consisted of ethambutol (1 g), isoniazid (300 mg), rifampicin (600 mg) and pyrazinamide (1.5 g) was continued for 2 months followed by maintenance therapy of isoniazid and ethambutol for 4 months.

The signs of inflammation subsided. At 8 months, the patient’s right vision was 3/60. Fundus showed sclerotic vessels with resolving retinal haemorrhages (fig. 1d). The left eye was normal throughout.

Discussion

Ocular tuberculosis usually manifests as a granulomatous uveitis. Even if there is retinal vasculitis, there are signs of uveitis [3]. A first presentation of CRVO attributed to tuberculosis is rare. There have only been 2 reported cases of CRVO associated with tuberculosis [4, 5]. These cases were associated with underlying pulmonary tuberculosis.

Our case is one of PCR-positive ocular tuberculosis presenting first as a CRVO in a patient with no signs of a systemic infection. Further observation showed a progression of retinal findings leading to a diagnosis of retinal vasculitis.

Young patients presenting with CRVO require extensive investigations to rule out conditions like homocystinuria, collagen vascular disorders and blood coagulopathies. In a study by Gupta et al. [6] on CRVO patients aged below 40 years, 5 out of 8 patients who had ischaemic CRVO had an underlying systemic problem.

The FFA was initially deferred to await further resolution of retinal haemorrhages. However, as the signs showed further progression, it was performed and signs of retinal perivasculitis were confirmed with the finding of staining of vessel walls and leakage from retinal vessels. Oral corticosteroid therapy was commenced as routine screening tests for
tuberculosis and systemic signs of infection were negative. This proved to be ineffective and led to worsening of ocular findings.

There is a worldwide resurgence of tuberculosis infection [7]. According to Kremer and Besra [8], approximately one third of the world’s population is infected with *M. tuberculosis* and despite the availability of effective chemotherapy, 3.5 million tuberculosis deaths occur each year.

In view of this trend, it is perhaps not adequate to stop further tests to confirm presence of a tuberculosis infection when routine tests were normal. As shown in our case, the decision to perform a further diagnostic test for an underlying cause of the retinal vasculitis turned out to be fruitful and important to ensure that a recurrence of symptoms would not occur, as well as to prevent a similar occurrence in the fellow eye.

PCR analysis is a valuable tool in the investigation of those cases that do not show systemic signs of tuberculosis. PCR analysis was first reported as a useful technique to detect *M. tuberculosis* in clinical specimens in 1989 by Brisson-Noel et al. from the Pasteur Institute [9]. The sensitivity and specificity for chest specimens of PCR is reported to be 87.2 and 97.7%, respectively, by Forbes and Hicks [10]. The use of PCR analysis to detect *Mycobacterium* in aqueous samples in a large series in 1999 by Arora et al. [11] showed a 37.7% (20/53) detection rate in patients with uveitis presumed to be ocular tuberculosis, compared to a weak positive in 5.7% (1/17) in healthy controls.

As vitreous tap is an invasive procedure, it should be reserved for cases where it is justified as shown in this case, where the involved eye showed worsening of signs with the use of corticosteroids. As the prognosis for visual recovery was poor in the affected eye, it was important to exhaust all possible investigations to look for an underlying cause in order to prevent a similar occurrence in the fellow eye. The prior use of corticosteroids could also have increased the yield of organism to detect presence of *M. tuberculosis*.

This case illustrates the possible need for young patients with CRVO caused by retinal vasculitis to undergo an invasive procedure to reach a definitive diagnosis, especially in areas in which tuberculosis cases show resurgence.
Fig. 1. Fundus photographs of patient’s right and left eye. a Right eye 2 weeks after initial presentation of CRVO, showing worsening of retinal haemorrhages. b Left eye was normal, showing an enlarged cup-disc ratio of 0.7. c Three weeks after initial presentation, the haemorrhages had not resolved. A vitreous tap was performed and vitreous fluid sent for PCR analysis to identify *M. tuberculosis*. d Eight months after presentation, haemorrhages have resolved, there is preretinal fibrosis and vascular sclerosis.
Fig. 2. Composite showing FFA done 2 weeks after presentation when retinal haemorrhages worsened. 
\(\textbf{a}\) Right eye at 15 seconds; laminar flow. \(\textbf{b}\) Right eye at 30 seconds; late venous phase, extensive 
ischaemia and perivasculitis seen as stained vessels. \(\textbf{c}\) Right eye at 5 minutes; late phase. \(\textbf{d}\) Left eye; no 
abnormal findings.
References


