

Monolateral Ocular Tuberculosis in an Immunocompetent Patient: A Case Report

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Abstract

Introduction - A rare case of monolateral tubercular choroiditis in a 25 year old Bengali man without pulmonary involvement was reported.

Case presentation - Ocular pain, lacrimation, and conjunctival hyperaemia, without any other systemic sign or symptoms, were the first illness manifestations. Multiple yellowish lesions, at the posterior pole and in the mid-periphery of the retina were the most relevant manifestations at fundus examination. The diagnosis of ocular TB was presumptive based on the ocular findings, the patient history, and the positive Mantoux skin test and interferon-gamma release assay. Polymerase chain reaction for *M. tuberculosis* on vitreous humour, collected by sterile vitrectomy, was negative. After six months of anti-tubercular therapy visual acuity remained limited to light perception, but no more signs of inflammation in the patient's left eye anterior to the vitreous chambers were present. The loss of vision was likely due to irreversible macular involvement.

Conclusion - In this age of global migration, TB is also becoming more common in countries with previously low prevalence of the disease. Ophthalmologists and specialists in infectious diseases should increase their awareness and understanding of the ocular manifestations of TB, because the disease is curable.

Introduction

Tuberculosis (TB) is a disease, most often involving the lungs, caused by infection with *Mycobacterium tuberculosis*. Extrapulmonary involvement, including lesions of the gastrointestinal tract, genito-urinary tract, cardiovascular system, skin, central nervous system, and eyes may occur in association with clinically apparent pulmonary tuberculosis or in isolation, with no clinical or laboratory evidence of pulmonary infection. Ocular involvement is an uncommon extrapulmonary manifestation of tuberculosis (1-2%) [1]. Choroiditis is common in patients with miliary tuberculosis, especially in immunocompromised patients, and can be uni or bilateral. We present a case of monolateral tubercular choroiditis in an immunocompetent man without systemic disease or pulmonary involvement. The relevant aspects of ocular tuberculosis in terms of diagnostic tools, treatment and evolution of the disease are discussed through a review of the literature.

Case report

A 25-year-old Bengali man lived in Italy for two years before presenting with clinical symptoms. He presented with a four-week history of ocular pain, lacrimation, and conjunctival hyperaemia in his left eye. He was diagnosed with conjunctivitis in the emergency room and was treated with lomefloxacin, 0.3% eye drops three times daily, for five days. He also used diclofenac, one eye drop three times daily, for five more days without any benefit. Two weeks later, the patient continued to have the same symptoms and began to lose visual acuity. He was admitted to our hospital on the 10th of April, 2007. He never reported fever, cough or chills. Ocular examination showed a visual acuity of 0.0 LogMar in his right eye (10/10), and 1.0 LogMar in his left eye (0.5/10). There were signs of anterior uveitis, with cells seen in the anterior chamber, and there was involvement of the ocular posterior segment, which showed evidence of vitre-



Fig 1. Fundus examination and FAG of left eye at admission

ous Tyndall. Examination of the fundus showed multiple yellowish lesions of various sizes under the retina, at the posterior pole, and in the mid-periphery that ranged from 0.3-3.0 mm in diameter. There were two kinds of lesions: some were nodular, while others had a grey central nucleus, fibrotic features, and edematous white perilesional rings (Fig.1) Fundal fluorescein angiography (FAG) of the left eye showed, in the early phase, foci of hypofluorescence due to lack of perfusion of the posterior pole. Subsequent onset of progressive hyperfluorescence with sharp borders was observed in the posterior pole and papillary area (Fig.1 and 2). There was no involvement of the right eye. Optical coherence tomography (OCT) did not demonstrate oedema at the posterior pole. A cerebral Magnetic Resonance Imaging (MRI), performed to search for tubercular lesions in the central nervous system and exclude signs of vasculitis, showed multiple punctiform areas of signal alteration with hypersignalling in T2-weighted images in the subcortical white matter, the frontal regions of both brain hemispheres, and in the right external capsule. These findings are consistent with foci of gliosis due to ischemic microangiopathic events. The orbital region showed a normal and symmetric ocular globe, normal extrinsic ocular musculature, and no signal alteration in the optic nerve or optic chiasma. There was a normal distribution of intra- and extra-conic fat, with no highlighted areas in the post-contrast phase of the test. A Mantoux skin test read at 48 hours displayed a 20 mm diameter of induration, and the patient had a normal appearing chest X-ray. An Interferon- γ release assay (QuantIFERON-TB GOLD[®]) was performed, which provided a value of 2.05 IU/ml (normal value <0.35 IU/ml). Other laboratory tests showed: a white blood cell count of 7.800/mm³ with 4.240/mm³ neutrophils and 2.840/mm³ lymphocytes, a red blood cell count of 5.670x10³/mm³, a

haemoglobin of 17.2 g/dl, a platelet count of 214.000/ μ l, an ESR 5 of mm/h, a CRP of 0.8 mg/dl, an AST of 19 IU/L, an ALT of 22 IU/L, a normal urine test, and a negative HIV test. The detection of antibody to Varicella-Zoster and Herpes Simplex viruses, Cytomegalovirus and Toxoplasma have revealed past infections, the detection of antibodies to nuclear, smooth muscle, anti-neutrophil cytoplasm and mitochondrial membrane resulted negative. The VDRL was negative. Ziehl-Neelsen acid-fast stain and polymerase chain reaction (PCR) for *M. tuberculosis* results were negative for 1 ml of vitreous humour, collected by sterile vitrectomy. Based on the patient's demographic data (young age, recent migrant, coming from highly endemic country), strongly positive tuberculin skin-test, and ocular symptoms unresponsive to non-specific therapy, he was started on anti-tubercular therapy. The initial regimen consisted of isoniazid (350 mg/die), rifampicin (450 mg/die), ethambutol (1.2 gr/die), pyrazinamide (1500 mg/die), and pyridoxine (300 mg every second day). Pyrazinamide and ethambutol were discontinued after two months, while isoniazid and rifampicin were continued for four more months. He also took prednisone, 25 mg daily, for one week with a progressive dose reduction to treat his ocular pain. Response to treatment was evident within six weeks and there were no side effects. One month later, the patient reported a subjective improvement in his visual acuity. This improvement was not confirmed by the visit that showed only light perception in the left eye and 0.0 LogMar (10/10) in the right eye. The anterior segment of the left eye showed a reduction in the number of cells and no vitreous inflammation was evident in the posterior chamber.

The second FAG showed a hypofluorescent posterior pole and mid-periphery of the left eye with subsequent diffuse hyperfluorescence emanating from small focal lesions also involving the papilla. Three months later his visual acuity remained light perception in the left eye. Fluorescein angiography of the left eye revealed general atrophy of the pigmented retinal epithelium and light residual papillary hyperfluorescence. Uveitis was also noted to be resolving. The patient completed anti-tubercular therapy in six months, and there was no recurrence of infection noted after eighteen months of follow-up. His visual acuity remained light perception. There were no signs of inflammation in the anterior chamber or the vitreous chamber. The sight loss was irreversible due to macular involvement. However, the patient could see lights and discern different colours in his peripheral vision. (Fig.5)

Discussion

M. tuberculosis infects one third of the world's population and causes 8 million new cases of

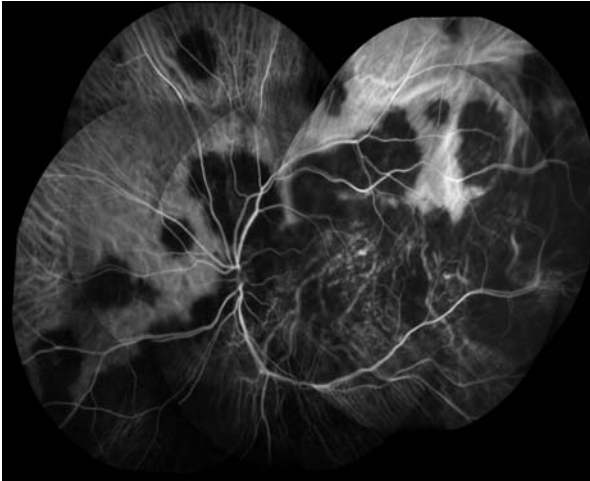


Fig 2. FAG of left eye at admission

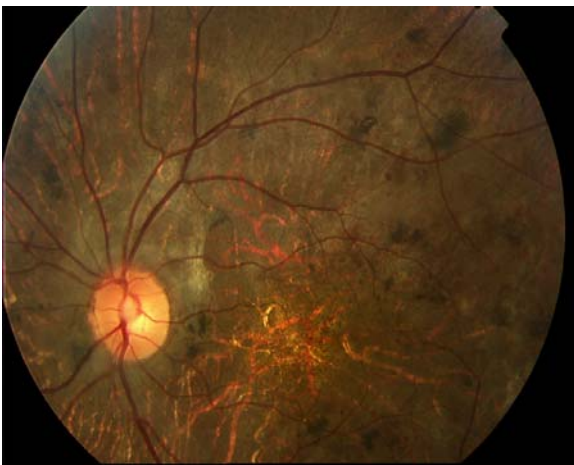


Fig 3 . Fundus examination 10 months after of the start of therapy.

tuberculosis and approximately 2 million deaths per year [2]. Although ocular involvement is an uncommon extrapulmonary manifestation of infection, it is important to recognise it because a 1-2% incidence has been reported [3]. The most common manifestation of ocular involvement is uveitis, which usually presents as chronic anterior uveitis, panuveitis, or choroiditis [4,5]. The presence of choroidal lesions is strongly correlated with systemic disease and is an indicator of haematogenous spread of *M. tuberculosis*. Choroidal involvement is common as the choroid has the highest blood flow per volume in the body. The ocular inflammatory response may be unilateral or bilateral. Association with systemic TB occurs in 9 to 19% of patients, ocular involvement can occur in asymptomatic patients (no ocular symptoms) in up to 2-3% of the cases, particularly in immunosuppressed individuals [5]. Diagnosis of ocular TB is difficult due to its widely variable clinical presentation and the lack of uniformity in diagnostic criteria [6]. In most cases, diagnosis requires both corroborative evidence, such as a

positive PPD and chest x-ray, and the exclusion of other causes. Furthermore, ocular TB often occurs asymptotically, is usually bilateral, and usually appears in patients with miliary tuberculosis. The diagnosis of tuberculosis rests mainly on the demonstration of acid-fast bacilli in Ziehl-Neelsen-stained smears, or culture of mycobacterium bacilli from the clinical specimen. The sensitivities of the AFB smear and culture are very low, especially in specimens like ocular fluid where the amount of sample drawn varies between only 50 and 100 μ l and the cellularity is low [7]. Direct microscopy of the smears is often not helpful in the diagnosis of intraocular tuberculosis because of the low yield of organisms from intraocular fluids [8]. Despite the use of highly sensitive molecular tools, such as PCR, for the detection of *M. tuberculosis*, ocular tuberculosis remains a subject of controversy. PCR is an auxiliary diagnostic tool that should be evaluated along with ophthalmological findings in the patient. The highest reported PCR-positivity for *M. tuberculosis* (66.6%) is in cases of granulomatous panuveitis, followed by multifocal choroiditis, granulomatous iridocyclitis, and lastly vasculitis (33.3%). Samples might be negative simply because of the very low number of organisms in the ocular fluid [9]. The presence of characteristic ocular findings, even in the absence of mycobacteriologic evidence, could be sufficient, with a positive Mantoux skin test, to justify initiating anti-TB therapy, unless another aetiology is found. Furthermore, the absence of clinically evident pulmonary TB does not rule out the possibility of ocular TB, as approximately 60% of patients with extrapulmonary TB have no evidence of pulmonary TB [10,11]. In our patient, the diagnosis of ocular TB was presumptive based on ocular findings, patient history, and a positive Mantoux skin test and interferon- γ release assay. Our patient presented no sign of involvement of the eyelids, lacrimal gland or conjunctiva which has necessitated the implementation of further investigation. Numerous other viral infections (herpes viruses) and protozoal (toxoplasmosis) as well as immune disease (sarcoidosis) may lead to granulomatous uveitis. We excluded these conditions in our patient by performing a work-up including antinuclear antibodies detection, syphilis serology, herpes simplex, varicella zoster, cytomegalovirus and Epstein-Barr virus serologies. Drug regimens for ocular tuberculosis are similar to those for pulmonary or extrapulmonary tuberculosis, and a combination of drugs should be given for several months [5, 12]. The CDC recommends the use of all four drugs (isoniazid, rifampicin, pyrazinamide, and ethambutol) for an initial 2-month period followed by a choice of different options over next 4 to 7 months for treatment of tuberculosis [13]. Although in Bangladesh a prevalence of multi-drug-resistant TB is reported in 3.6% of new cases

and in 19% of previously treated cases [14], there is no indication to start treatment for drug-resistant tuberculosis in the absence of a drug-resistant isolate or without a demonstrated evidence of poor clinical response to conventional treatment. Our patient therefore received a four-drug therapy for first 2 months, continuing with 2 drugs for another 4 months. Low-dose systemic corticosteroids were added to limit damage to ocular tissues caused by delayed-type hypersensitivity. This treatment is supported by various clinical and experimental studies that have addressed the utility of adjunctive corticosteroid therapy in the management of ocular tuberculosis [15, 16]. The patient responded well to the anti-tubercular treatment, and after six weeks he had reduction of retinal oedema and a stable visual acuity. At the end of his therapy, ocular examination established resolution of the inflammatory process with residual scars on the retina.

Conclusions

There is little data on the prognosis of ocular TB, again because of the low prevalence of cases. Intraocular tuberculosis can cause complications seen in other types of uveitis: cataracts, glaucoma, and in posterior disease, retinal detachment. It is reasonable to assume that TB in the eye requires prolonged treatment to eradicate the organism, just as it does in other organs. Therefore, a high index of suspicion is needed for timely diagnosis and treatment. Ocular TB should be part of the differential diagnosis for any chronic or recurrent uveitis, especially in an at-risk patient. In this age of the HIV pandemic and global migration, TB is also becoming more common in countries with previously low prevalences of the disease. Ophthalmologists and specialists in infectious diseases should increase their awareness and understanding of the ocular manifestations of TB, because the disease is curable.

Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare that they have no competing interests.

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