

Presumed ocular tuberculosis in an immunocompetent eight-year-old boy

Bukulmez A, Koken R, Melek H, Ozturk F, Konakci R, Dogru O

ABSTRACT

In recent years, tuberculosis has re-emerged as a serious public health problem, raising the possibility that tuberculous eye disease may also have become more prevalent. Ocular tuberculosis usually occurs in apparently healthy individuals. It is rarely observed in patients with active pulmonary disease. An eight-year-old boy was admitted to our department because of chronic granulomatous anterior uveitis on his left eye. His medical history was unremarkable. There were no systemic symptoms of tuberculosis. He had a positive purified protein derivative test reaction. In our case, the diagnosis of ocular tuberculosis was presumptive and depended upon indirect evidence. The patient was started on anti-tuberculosis therapy with three drugs, which were continued for 12 months, with complete healing of the ocular lesions, including a marked improvement in the gait of the patient. Tuberculosis remains one of the most important causes of morbidity and mortality in developing countries.

Keywords: chronic granulomatous anterior uveitis, ocular tuberculosis, tuberculosis, uveitis

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INTRODUCTION

Tuberculosis (TB) is the leading infectious cause of morbidity and mortality worldwide.⁽¹⁾ Despite important advances in its treatment over the last two decades, TB has remained a serious public health problem in recent years. The problem has been aggravated by the human immunodeficiency virus (HIV) pandemic and the recent increasing incidence of microbial resistance to antibiotics. The failure to control TB in both developed and developing countries represents one of our greatest public health failures. TB is defined by the US Centers for Disease Control and Prevention as a chronic bacterial infection caused by *Mycobacterium tuberculosis* (*M. tuberculosis*), characterised pathologically by the formation of granulomas. Ocular complications of TB, although less common than systemic involvement, are well recognised. The recurrence of TB as a major public health problem raises the possibility that ophthalmologists may encounter an increasing number of ocular complications.⁽²⁾



Fig. 1 Photograph of left eye before treatment. There are mutton-fat keratic endothelial precipitates.

CASE REPORT

An otherwise-healthy eight-year-old boy was referred to the Paediatric Department from the Ophthalmology Department for a confirmation of diagnosis. His main complaint was the redness in his left eye occurring intermittently during the last two years. He was diagnosed to have chronic granulomatous anterior uveitis on his left eye. His medical history was unremarkable and he had no systemic symptoms. He had been previously well and developing normally. He belonged to a family with poor socioeconomic status, but there was no history suggestive of TB in the family and the patient denied contact with anyone who had TB. His BCG vaccination history was positive. On his ocular examination, the right eye was totally normal. On slit lamp examination of the left eye, there was mutton-fat keratic endothelial precipitates (Fig. 1). The anterior chamber was quiet and no iris nodule was observed. There was a synechia posterior of iris with the lens and the pupil was vertically oval. The vitreous was also quiet and the retina was normal. His best corrected visual acuity was 20/20 on the right and 20/25 on the left eye. He had no palpable lymphadenopathy and organomegaly. His family subsequently discovered that a neighbour living in the flat below them was suffering from TB. Although he had no immediate risk factors for infection, living in the same building was sufficient for him to acquire the infection. His grandfather had a positive tuberculin skin test with an induration of 22 mm × 22 mm. His detailed systemic evaluation for infectious and inflammatory aetiologies was reported to be negative, so there was no systemic therapy. In our patient, detailed

Faculty of Medicine,
Department of
Pediatrics,
Afyon Kocatepe
University,
Afyon,
Turkey

Bukulmez A, MD
Associate Professor

Koken R, MD
Associate Professor

Melek H, MD
Associate Professor

Ozturk F, MD
Professor of
Ophthalmology

Konakci R, MD
Resident

Dogru O, MD
Associate Professor

Correspondence to:
Dr Aysegul Bukulmez
Tel: (90) 272 213 89 08
Fax: (90) 272 213 30 66
Email: aysegulbukulmez
@yahoo.com

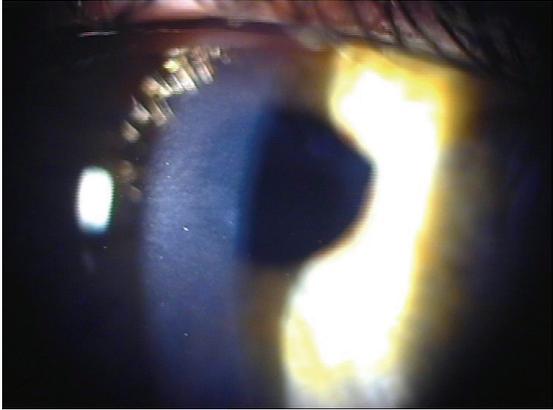


Fig. 2 Photograph of left eye after treatment. There is no sign of anterior uveitis. Mutton-fat keratic endothelial precipitates have disappeared.

systemic work-up was undertaken to investigate the underlying cause of the anterior granulomatous uveitis. No systemic source of infection was identified. Complete blood count, biochemical tests including serum calcium, and serological tests were normal. C-reactive protein was 2 mg/L. The sedimentation rate was 10 mm/hr and rheumatoid factor was negative. Sputum and gastric aspirate examination were negative for acid-fast bacilli. Polymerase chain reaction (PCR) of gastric aspirates was negative in our case. HIV infection was negative. There was no evidence of systemic TB in other parts of the body. Chest radiograph showed no significant pathological changes on the initial presentation. There was no suspicious change in the subsequent chest imaging. Tuberculin skin test was positive (18 mm × 20 mm).

In this case, the patient had symptoms attributable to a TB infection. In the differential diagnosis of chronic granulomatous anterior uveitis, sarcoidosis was considered, but we decided to evaluate our patient for sarcoidosis after administering anti-TB treatment. Since the diagnosis of TB was made based on the clinical diagnosis and supportive evidence from a positive Mantoux reaction, and the patient responded to the anti-TB treatment dramatically, we did not evaluate the patient for sarcoidosis. In our case, corticosteroid therapy was not given. Isoniazid, rifampin and pyrazinamide were administered for two months, followed by the continuation of isoniazid and rifampin for an additional ten months. The initial response occurred within two weeks. During treatment, he was closely monitored for drug toxicity. Anti-TB medication was continued for 12 months. After the completion of anti-TB therapy, there was no recurrence. There have been no complaints from our patient for the past one year. The patient was referred to the Ophthalmology Department for ocular consultation. The eyes were both quiet and there was no sign of previous anterior uveitis on the left eye (Fig. 2).

DISCUSSION

TB is an ancient infectious disease caused by *M. tuberculosis*. TB remains one of the most important causes of morbidity and mortality in developing countries. The recent re-emergence of TB as a public health problem has heightened interest in the disease.⁽³⁾ A high index of suspicion is very important in the detection of ocular TB to prevent ocular morbidity and visual loss. It is important to highlight the causes of ocular morbidity and blindness in ocular TB. Extrapulmonary TB, including ocular TB, occurs in less than 20% of cases. Ocular manifestations associated with TB are caused by an active infection or an immunological reaction in the absence of the infectious agent.⁽³⁾ The manifestations of anterior segment TB are chronic and insidious. The ocular findings may either follow the pulmonary TB or occur without evidence of pulmonary or other systemic signs or symptoms. Active TB may occur in extrapulmonary sites with or without evidence of chest disease. Sarvanathan et al reported that ocular TB may occur without pulmonary findings.⁽⁴⁾ Extrapulmonary disease is common in immunocompromised patients, infants and young children. Children acquire *M. tuberculosis* from adults in their environment.^(5,6) It occurs primarily as a pulmonary infection, but bacilli may be widely disseminated haematogeneously. Ocular involvement in TB occurs in only 1.4% of the population. All ocular tissues can be affected with diverse clinical manifestations.⁽⁷⁾

TB with ocular manifestations may involve various segments of the eye and cause severe visual loss if it is not treated properly. Ocular TB is an uncommon finding in children. Primary infection of the eye is very rare.^(1,5,6,8) The primary infection can be airborne or introduced into the eye by contaminated hands, fomites or exposure to dust or sputum particles containing the bacilli. Because our patient lived in a high-prevalence area of TB, the possibility of contact was very likely, although he denied such contact. Ocular manifestations of TB are likely to occur by either direct invasion or as a hypersensitivity reaction. Ocular tissue involvement is the result of systemic dissemination of the organism reaching the eye through blood circulation. The predominant route by which tubercle bacilli reach the eye is through the bloodstream, after infecting the lung. Pulmonary foci may not be evident clinically or radiographically.⁽⁹⁾

Intraocular TB is usually secondary to the haematological spread of a pulmonary or systemic TB infection, but in our case, the primary focus could not be demonstrated. This leaves chest radiographs and purified protein derivative (PPD) skin testing, which, although useful particularly in patients at a high risk of infection, have limited sensitivity and specificity. Most physicians have to depend on their own clinical skills supported by the time-honoured and judicious use of chest radiographs

and PPD testing. Its ocular manifestations are commonly associated with severe difficulties in diagnosis and therapy; moreover, it may cause blindness. Ocular TB is usually unilateral. TB of the eye may be acute but usually runs a chronic course with exacerbations and remissions. Children with ocular TB rarely show overt systemic manifestations and this may lead to difficulties in establishing the diagnosis. The clinical manifestations of ocular TB are protean and non-specific.

The most common clinical findings of intraocular TB are choroiditis, retinal vasculitis, optic disc nodules, solitary or multiple choroidal nodules, anterior and posterior uveitis.⁽⁴⁾ TB is an infrequent cause of uveitis, being responsible for approximately 1% of all uveitis cases. Where anterior uveitis develops, it is usually granulomatous, presenting with mutton-fat keratic precipitates and iris nodules. When TB manifests as uveitis, an accurate diagnosis becomes increasingly difficult. Moreover, because roughly 60% of patients with extrapulmonary TB have no evidence of pulmonary TB, negative chest radiograph and negative sputum culture results do not exclude the diagnosis.⁽¹⁰⁾ Our patient presented with anterior uveitis, which is quite unusual for his age group. The possibility that *M. tuberculosis* infection may have contributed to the development of intraocular inflammation in our patient with anterior uveitis cannot be ruled out.

Ocular TB usually occurs in apparently healthy individuals. It is rarely observed in patients with active pulmonary disease. Chest radiographical findings in patients with ocular TB are normal. The diagnosis of ocular TB is usually presumptive and depends on indirect evidence.⁽¹¹⁾ The diagnosis of TB begins with a complete physical examination, including a sputum smear and culture, PPD test and chest radiograph. The presence of a systemic TB infection strongly indicates but does not prove that TB is causative of ocular findings. Additionally, an initial work-up that yields negative results should not eliminate TB from the differential diagnosis. Abrams and Schlaegel reported that in 18 patients with presumed TB uveitis, the chest radiograph showed no active or inactive evidence of TB.⁽¹²⁾

The diagnosis of ocular TB is complicated by the difficulties associated with ocular sampling for microbiological evaluation. Culture and direct histopathological examination of infected tissue can provide definitive proof of ocular infection, but are often impractical given the risks of intraocular biopsy, particularly in the setting of active inflammation. Therefore, we did not take any samples for culture. PCR-based assays performed on ocular fluids provide strong

evidence of infection, but are not well standardised, and are available only at selected centres. Because of the difficulty in obtaining microbiological evidence, it has been suggested that a diagnosis of presumed intraocular TB be made on the basis of a good response to a clinical trial of isoniazid. The result of a gastric aspirate's PCR study was negative in our case. Here, the diagnosis was made through a positive tuberculin skin test and therapeutic isoniazid test. Supportive evidence included a strongly reactive tuberculin test and the positive tuberculin test results of the patient's grandfather. The diagnosis was reaffirmed by the dramatic response to anti-TB treatment. His ocular inflammation was resolved gradually and vision returned to normal in two weeks.

Despite the difficulties of diagnosis, the treatment of TB is relatively effective and cost-efficient. Ocular TB should be treated with multiple anti-TB chemotherapeutic drugs. The guidelines of the American Thoracic Society for treatment consist of a two-month initial phase of isoniazid, rifampin and pyrazinamide followed by isoniazid and rifampin, for a total of six months. In Taiwan, ocular TB therapy consists of an initial treatment phase with isoniazid, rifampin, ethambutol and pyrazinamide for two months followed by a continuation phase with the first three drugs for 10–16 months. During treatment, patients are monitored for drug toxicity.⁽⁹⁾ No adverse effects of the anti-TB medication have been found.

Recommended therapy for extrapulmonary Koch's disease consists of an initial treatment phase with four drugs (isoniazid, rifampicin, pyrazinamide and ethambutol/streptomycin) followed by a continuation phase with the first three drugs for 10–16 months.⁽⁹⁾ However, in our patient, isoniazid, rifampin and pyrazinamide were administered for two months, followed by the continuation of isoniazid and rifampin for an additional ten months. Our patient responded well to anti-TB therapy. The specific anti-TB treatment administered for 9–12 months is highly effective and helps in reducing recurrences in the eyes.⁽²⁾ The duration of treatment is longer than the World Health Organisation strategy because the incidence of TB in our country remains high (40 per 100,000 in 2003). A high degree of clinical suspicion is important in suspecting and managing this condition. Ocular examination should be routinely considered in patients with suspected and proven TB. Early diagnosis and prompt treatment of ocular TB may prevent serious complications and loss of vision. On the other hand, TB should be considered as a differential diagnosis in cases of uveitis and should be investigated accordingly.

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