

Corneal Manifestations of Tuberculosis: About 2 Cases

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Abstract Corneal tuberculosis is a rare ophthalmic manifestation of tuberculosis. The purpose of this study is to present clinical and histopathological findings in two cases of corneal tuberculosis. We reported corneal manifestation of tuberculosis in two patients including granulomatous lesion at upper third of the cornea in the first case, and sectorial interstitial keratitis in the second one. The diagnosis was based on various anamnestic, clinical, histological and evolutive arguments. An anti-tuberculosis treatment was prescribed.

Keywords: *ocular tuberculosis, corneal manifestations, interstitial keratitis, granuloma*

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1. Introduction

Tuberculosis (TB), a multisystem infectious disease caused by *Mycobacterium tuberculosis* (MTB). It is a disease that primarily affects the lungs, but may also affect extra-pulmonary organs, including the eye. [1] The true incidence of ocular TB is unknown due to the difficulty obtaining specimens, and inexact diagnostic criteria. [2] Corneal tuberculosis is a rare ophthalmic manifestation of TB. [3] Because the treatment of TB is relatively effective and cost efficient, [4] Early diagnosis and rapid treatment are the keys to saving the sight of patients with ocular manifestations of TB.

2. Case Report

The two cases were diagnosed and treated in university hospital Mohammed VI, Marrakech, Morocco.

2.1. Patient 1:

A 50-years-old man was admitted with loss of vision, redness and pain in his left eye since 5 month. He was treated for pulmonary TB in 1970. At presentation, the best-corrected visual acuity was 20/20 in his right eye and 14/20 in the left eye. The right eye was unremarkable except for cortical lens opacification. Slit-lamp biomicroscopic examination of the left eye revealed a congested conjunctiva, an unfiltered cornea and a granulomatous lesion at the limbus and the upper third of the cornea (Figure 1). A shallow anterior chamber with 1 + flare and cells. The intraocular pressure was 12 mmHg in the right eye and 16 mmHg in the left eye. Fundus examination was normal.



Figure 1. OS: granulomatous lesion at the limbus and the upper third of the cornea

The dermatological examination found an erythematous noures at both legs, with local heat in favor of erythema nodosum. A skin biopsy was done revealing a septal panniculitis.

A detailed systemic investigation was undertaken to identify the underlying causes. The results of a complete blood count, biochemical tests, antistreptolysin O titer (ASO), erythrocyte sedimentation rate (ESR) and angiotensin converting enzyme (ACE) were normal. A chest roentgenogram showed bilateral fibro-productive changes with infiltration. Sputum culture was negative.

TB skin test was positive and a phlyctenular reaction has been associated. Quantiferon test was positive as well.

Corneal scraping was performed; histopathological results showed granulomatous inflammation with epithelioid cells and langhans giant cells (Figure 2). The patient started antituberculosis treatment with isoniazid (H), rifampin (R), pyrazinamide (Z) and ethambutol (E) according to the following protocol 2RHZE / 4RH. The left eye improved to 20/20 of vision with sectoral and peripheral interstitial keratitis (Figure 3).

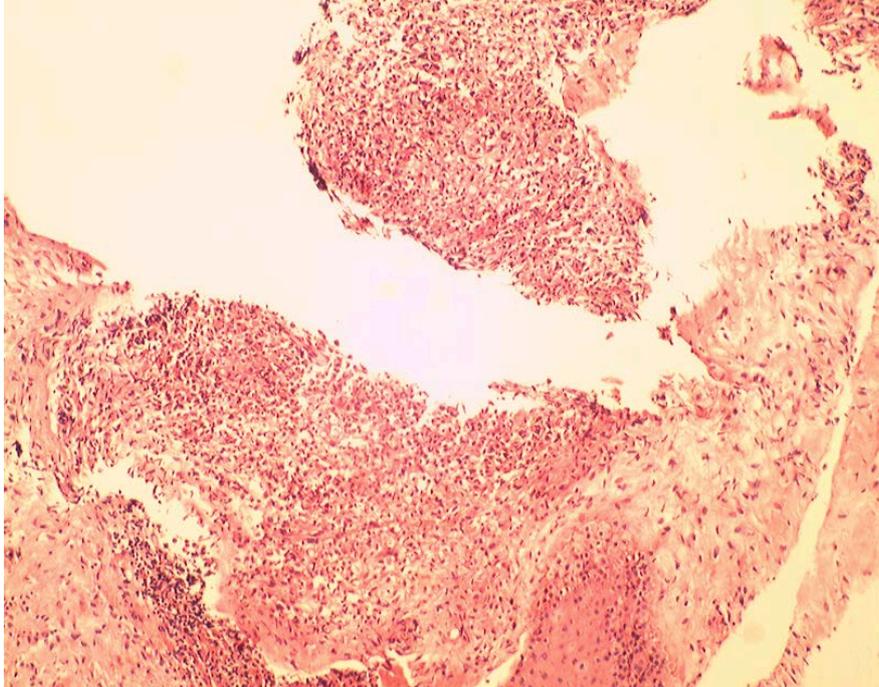


Figure 2. histopathological examination revealed granulomatous inflammation with epithelioid cells and langhans giant cells

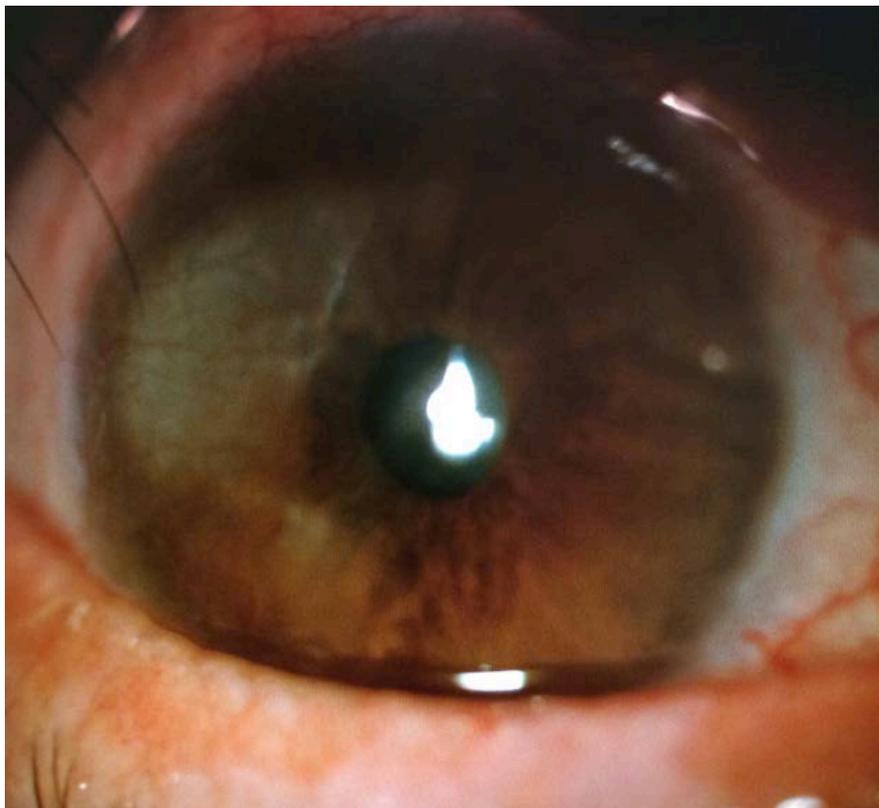


Figure 3. OS: peripheral interstitial keratitis

2.2. Patient 2:

A 14-years-old girl was referred to our hospital for nasal granuloma with blurred vision and pain in both eyes since 6 months. Apart of a skin rash around her eyes 6 years ago, medical history was non-significant.

Ophthalmic evaluation revealed best-corrected visual acuity of 18/20 in the right eye and 16/20 in the left eye.

Slit-lamp examination showed ciliary injection of conjunctiva, sectoral and peripheral interstitial keratitis with vascularization (Figure 4), and a shallow anterior chamber with 2 + flare and cells. The intraocular pressure was 12 mmHg in the right eye and 11 mmHg in the left eye. Fundus examination was normal.

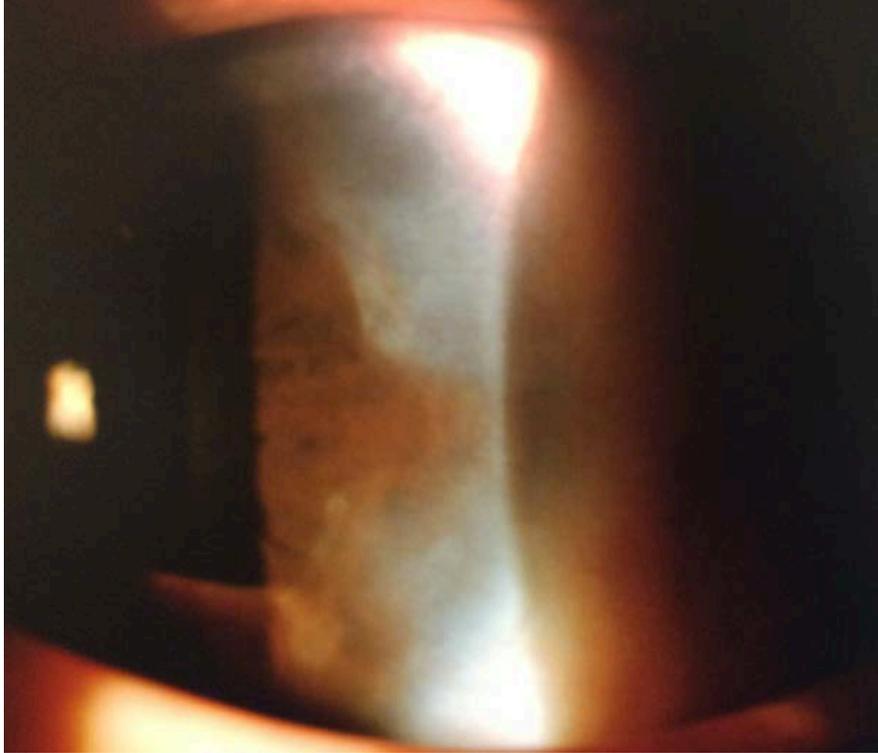


Figure 4. OS: Sectoral and peripheral interstitial keratitis

Dermatological examination objectified erythematous papules on the nose, lupoid to vitropression with telangiectasias surface, infiltrating nasal mucosa (Figure 5). A biopsy with 3 fragments was performed, mycological and bacteriological tests were negative.



Figure 5. Erythematous papules on the nose, lupoid to vitropression with telangiectasic surface, covered with pustules

The anatomopathological tests showed granulomatous inflammation composed of epithelioid cells and langhans giant cells without caseous necrosis (Figure 6). A complete systemic workup was performed. An elevated erythrocyte sedimentation rate and C-reactive protein were found. A chest roentgenogram showed no significant pathological changes on the initial presentation. TB skin test was positive (20 mm) and a phlyctenular reaction has been observed. The AFB sputum was negative. TB treatment was started according to the 2RHZE / 4RH protocol.

Vision returned to normal 3 months after the beginning of the treatment. Skin lesions regressed 4 months after the antituberculosis treatment.

3. Discussion

Tuberculosis with ocular manifestations is likely to occur by either direct invasion or as a hypersensitivity reaction [5], this shows a spectrum of ocular diseases caused by *M. tuberculosis*. In primary ocular TB, there are no other systemic lesions, however, secondary ocular TB is defined as an infection resulting from contiguous spread from an adjacent structure or hematogenous spread. Tuberculosis may involve any part of the eye and may appear in different clinical forms [6]. TB may affect the cornea, leading to interstitial keratitis that may be seen as an isolated finding or in association with scleritis and uveitis.

This association is probably related to the presence of tubercular antigen in aqueous humor [7]. TB affecting cornea may also present as disciform keratitis. [8] Corneal tuberculosis is part of rare ophthalmic signs of TB. The

pathogenesis is thought to be related to hypersensitivity to tuberculo-proteins, rather than a direct effect of the active disease. [9]

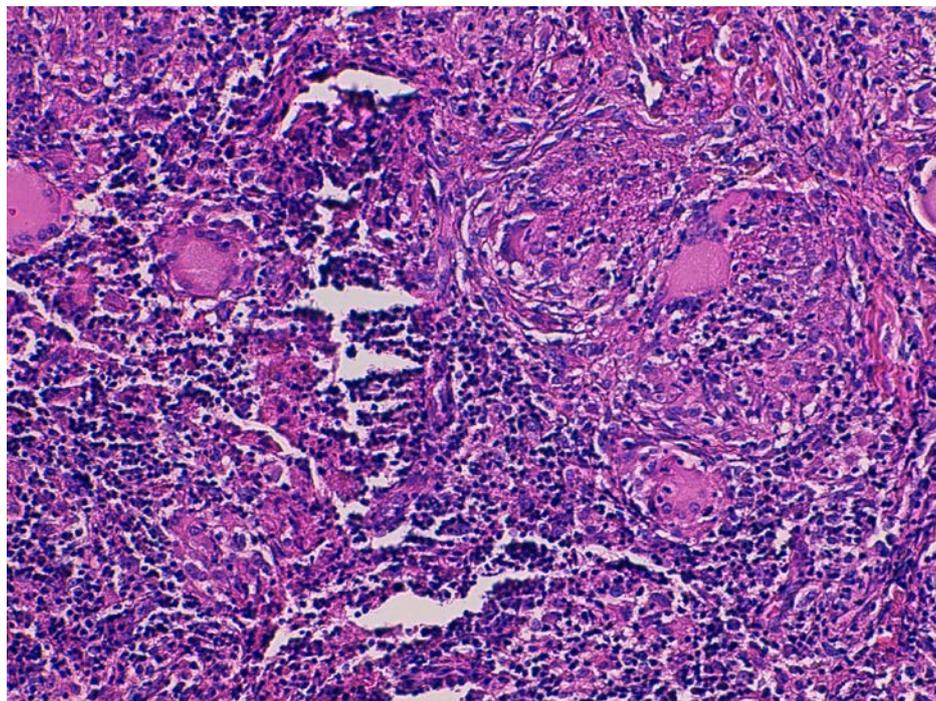


Figure 6. Histopathological examination showed granulomatous inflammation composed of epithelioid cells and langhans giant cells without necrosis caseating

In this report, we presented two cases of corneal TB. The diagnosis was made using results of histopathological tests, Tuberculin skin test and Quantiferon test.

The diagnosis of ocular TB is often problematic due to a wide spectrum of presentations and it is impractical to take uveal biopsy for culture and direct histopathological examination to provide definitive proof of ocular infection. [10] In nearly all reported cases, the diagnosis of ocular TB was only presumptive.

Guidelines for interpreting of TST vary in different countries where different strengths are used. The predictive value varies depending on the incidence of TB in the population and local BCG vaccination policy. In the USA, the routine use of TB skin testing in patients with uveitis is considered unhelpful, [11] whereas in India it is considered mandatory. [12] Polymerase chain reaction techniques were used for the detection of MTB in aqueous and vitreous samples from patients with presumed tuberculous uveitis. Detection of antibodies against purified cord factor, the most antigenic and abundant cell wall component of MTB, can provide strong evidence of the infection. [13] However, the sensitivity was reported to be low, as many ocular manifestations may represent a delayed hypersensitivity reaction rather than a direct mycobacterial infection, making the analysis of a fluid sample from the eye less sensitivity. [14]

Despite the difficulties of diagnosis, the treatment of TB is relatively effective and cost efficient. Five major drugs are considered the first-line agents to treat TB: isoniazid, rifampin, pyrazinamide, ethambutol, and streptomycin. Corticosteroids are sometimes used prudently in combination with antimicrobial therapy. [15]

The treatment of ocular TB is largely presumptive and there are no rationalized standard guidelines governing management principles for presumed ocular tuberculosis. In the absence of randomized clinical trials, a wide range of treatment practice patterns have been reported in the literature and, as a matter of fact, there are no national TB guidelines about ocular TB diagnosis and treatment in many nonendemic regions, including Canada, the United Kingdom, and the United States [15]. There is some published literature on use of mono versus multiple drug therapy and also debate about treatment duration with ATT (6–18 months). But the outcomes are inconsistent due to lack of standard guidelines for diagnosis of ocular TB, concomitant immunosuppressive therapy, and variation in severity of ocular inflammation prior to initiating treatment [10,16].

Conflicts of Interest

None.

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