

## Primary Conjunctiva Tuberculosis & Review of Literature

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**Abstract.** The causes of chronic conjunctivitis are exhaustive, infection being the commonest. Primary tuberculosis (TB) involving the conjunctiva is rare. History of chronicity, worsening symptoms with steroids and clinical signs of subconjunctiva nodules could point towards the diagnosis of primary conjunctiva tuberculosis especially in endemic countries. Clinicopathological diagnosis is imperative to confirm this diagnosis. We report a case of a young lady who presented with a non-resolving chronic conjunctivitis that was proven to be TB and responded well to anti-tuberculosis treatment.

### INTRODUCTION

It has been estimated that about a third of the world's population is infected by *Mycobacterium tuberculosis*, which predominantly involves the lungs (World Health Organization, 2016). The infection is worldwide, but the largest number of new cases occur in developing countries (World Health Organization, 2016).

Ocular TB is uncommon and its incidence varies widely among different populations and geographical locations (Donahue, 1967; Bouza *et al.*, 1997; Beare *et al.*, 2002). *Mycobacterium tuberculosis* can infect any part of the eye and may occur as a primary infection or secondary spread (Bodaghi, L. Hoang, 2000; Faiz, 2015). The definition of primary ocular TB can be varied, with some authors describing it as the eye being the initial site of entry for the organism while others describe it as ocular disease in the absence of systemic manifestation (Bodaghi, L. Hoang, 2000; Faiz, 2015). Secondary ocular tuberculosis is defined as ocular involvement due to direct spread from adjacent areas or distant spread through various channels for example haematogenous spread.

Here we describe a rare case of primary conjunctiva tuberculosis which was successfully treated. We believe this is the first reported from this region.

### CASE SUMMARY

A 23-year-old healthy lady presented in the eye clinic with left eye redness, swelling and foreign body sensation for the past 2 months. It was associated with mild pain and discomfort. There were no complaints of reduced vision or history of ocular trauma.

On presentation, her vision was 6/9 both eyes. Relative afferent pupillary defect was absent and her visual fields were normal in both eyes. Her left eye was diffusely injected with a nodular swelling of the inferior bulbar conjunctiva measuring 2x1.5cm (Figure 1). The cornea was clear with no epithelial defects or keratic precipitates and there was no anterior chamber reaction. Her right eye was unaffected. Intraocular pressure was 16 mm Hg in both eyes. Fundus examination revealed normal optic discs and retina bilaterally, with no evidence of vitritis, retinitis or choroiditis. On further physical examination, there was no lymphadenopathy



Figure 1. Left eye conjunctiva appearance; injected, swollen with multiple nodules.

or organomegaly. No other abnormalities were found on a full systemic review.

She was initially treated with antibiotics and steroid eyedrops but her condition continued to worsen.

The total white count (TWC) was normal, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) as well as a negative viral screening. Her Mantoux test was non-reactive and chest radiography were normal as well.

We proceeded with an excisional biopsy of the conjunctiva, which revealed intraepithelial and stromal neutrophilic infiltration with multiple epithelioid granulomas within the stroma. There was also presence of lymphoplasmacytic cell infiltration within the stroma as well as Langhans type multinucleated giant cell with pathognomonic areas of suppurative and necrotizing centre (Figure 2, 3, 4, 5) within the granuloma, highly suggestive of *Mycobacterium tuberculosis* (Figure 4, 5). However, the Ziehl Neelsen stain was negative.

Treatment was initiated with Akurit -4 which consists Ethambutol 275 mg, Isoniazid 75mg, Rifampicin 150mg and Pyrazinamide 400mg. Remarkable clinical improvement was shown after 2 months of anti-tuberculosis

treatment (Figure 6). The patient successfully completed 6 months of treatment with no adverse effects and had complete resolution of her symptoms.

## DISCUSSION

Primary ocular infection by *Mycobacterium tuberculosis* is uncommon and usually affects the younger age group (Eyre, 1912; Chandler, Locatcher-Khorazo, 1964; Woods, 1972; Fernandes *et al.*, 2003). Any part of the eye can be involved but commonly manifests as uveitis, which is usually in the form of chronic anterior uveitis, panuveitis or choroiditis (Donahue, 1967; Ang *et al.*, 2012; Faiz, 2015). It can present at any age, is chronic in duration, and there is no gender bias (Helm, Holland, 1993). Primary conjunctiva tuberculosis is rare (Sorsby, 1963; Archer, Bird, 1967; Rao, Bhat, 1967). It can be ulcerative, nodular polypoidal, hypertrophic capillary or pedunculated type (Eyre, 1912). The most common site for conjunctiva tuberculosis is usually at the palpebral conjunctiva of the upper eye lid (Eyre, 1912). Most cases are accompanied by enlargement of the preauricular lymph nodes (Eyre, 1912).

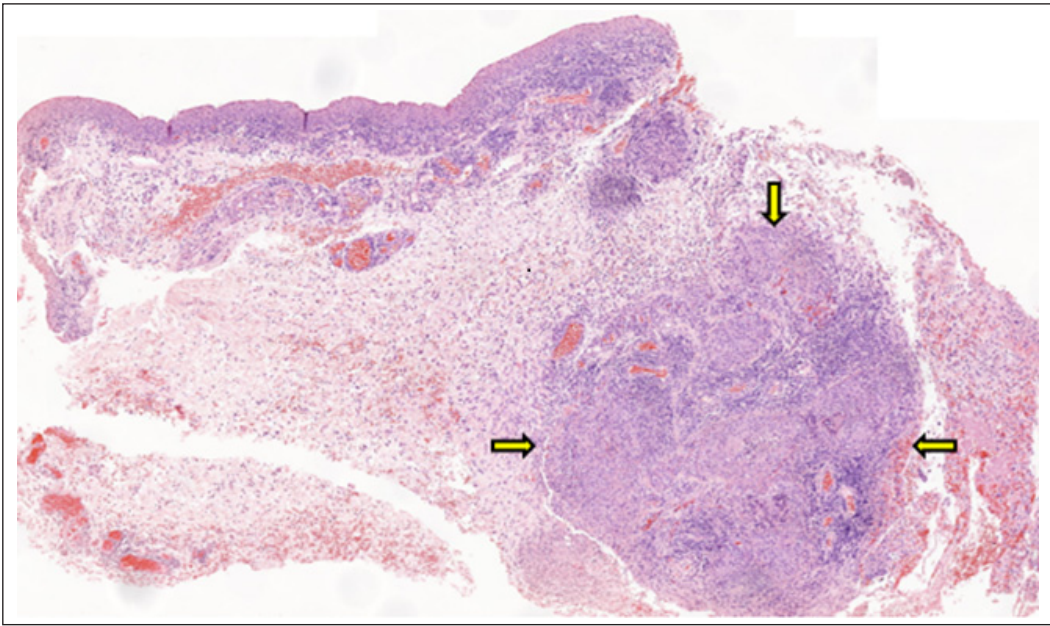


Figure 2. Hematoxylin and Eosin (H&E) 40x: Low power view showing granuloma formation surrounded by an infiltrate of both acute and chronic inflammatory cells. Arrow points to a multinucleated giant cell.

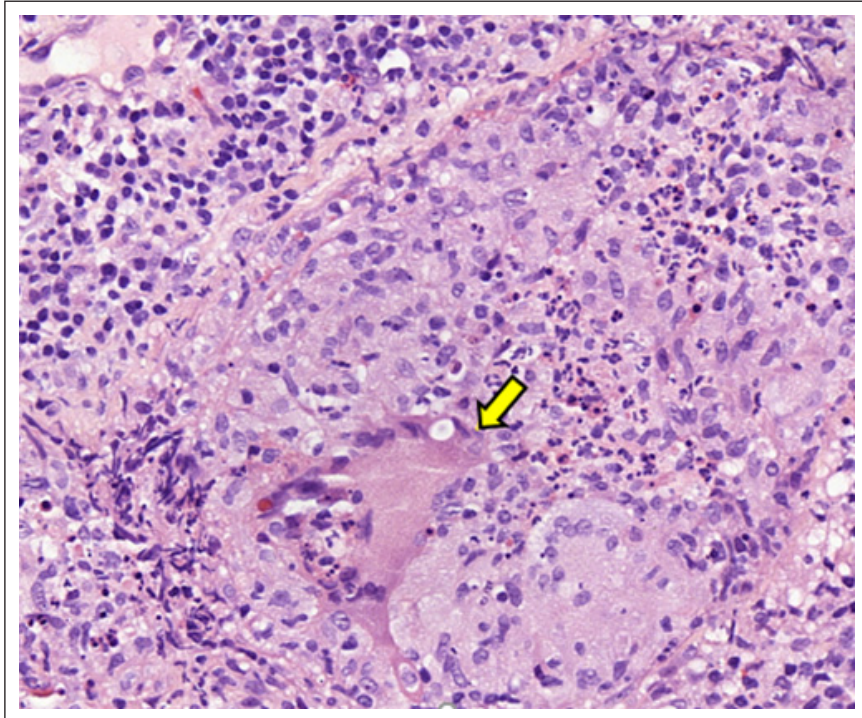


Figure 3. Hematoxylin & Eosin 40x: A granuloma formation made up of epithelioid histiocytes surrounded by patchy infiltrates of both acute and chronic inflammatory cells. Arrow points to a multinucleated giant cell.



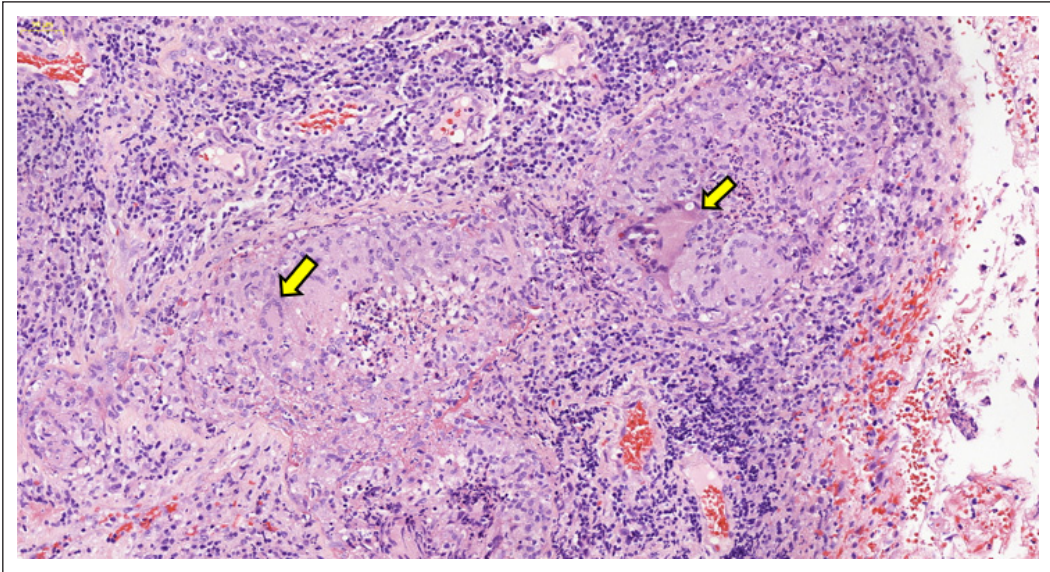


Figure 4. H&E x 200: Arrows pointing to the multinucleated giant cells which appear Langhan's type.

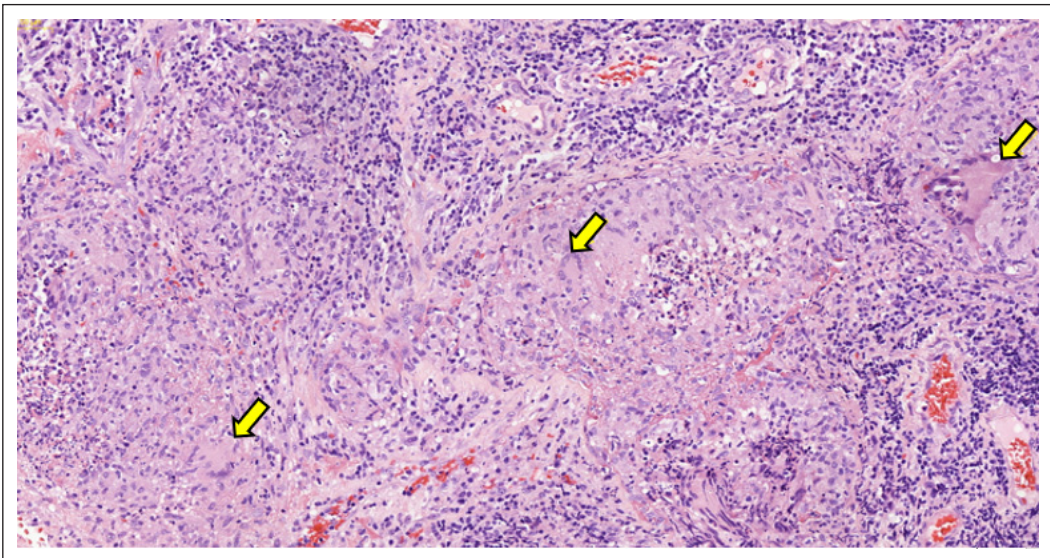


Figure 5. H&E x 400: High power view showing a the well formed granuloma made up of epithelioid histiocytes, Langhan's type multinucleated giant cell (arrow) and central suppurative material and neutrophilic debris.

Ocular diagnosis of TB can be challenging as most cases occur without ongoing active pulmonary tuberculosis (Jun-ichi *et al.*, 2001; Mao *et al.*, 2014). Diagnosis of TB is still dependent on Mantoux test in many countries (Ang *et al.*, 2012). However, Mantoux test has a low

specificity because of false positivity in non-tuberculous mycobacterium infections and BCG vaccinated individuals (Morimura, 2002). The current diagnostic tests available for detecting active TB infection is interferon-gamma release assay (IFN- $\gamma$ ) such as T-SPOT.TB (Oxford Immunotec, Oxford,



Figure 6. Less chemotic and injected conjunctiva seen after treatment.

UK) and QuantiFERON-TB Gold In-tube or QFT (Cellestis Incorporated, Carnegie, Australia). They are more specific and sensitive compare to Mantoux test in detecting active pulmonary TB patient (Ang *et al.*, 2012). T-SPOT.TB is more specific for tuberculosis associated uveitis, it serves as a better diagnostic tool if used in conjunction with the Mantoux test. Additional investigative test such as acid-fast bacilli smear or polymerase chain reaction detection of *Mycobacterium tuberculosis* DNA for ocular samples have low sensitivities (Ang *et al.*, 2012). The use of this interferon-gamma release assay (IFN- $\gamma$ ) tests in conjunctival TB has not been documented in view of its rarity.

In our case, the diagnosis was suspected by the chronic duration and worsening with steroid treatment. In the conjunctiva biopsy, there was multiple epitheloid granulomas in the stroma layer with lymphoplasmacytic cell infiltration. Multinucleated giant cell of Langhan's type with areas of caseous necrosis are seen too within the granulomas. This patient most probably had a direct inoculation of organisms into the conjunctiva as there was no evidence suggestive of endogenous or contiguous spread.

Identification of the bacilli in the tissue is important for diagnosis (David *et al.*, 2001). However, failure to demonstrate the mycobacterium in biopsy is not against a TB

aetiology and this can be due to reduction in size or number of the bacilli which result in technical difficulties of acid fast tissue staining as seen in this particular case (Singh, 1989; Ang *et al.*, 2012).

Besides the histopathological diagnosis, full recovery of the patient after commencing the treatment of anti-tuberculosis therapy confirms the diagnosis of conjunctival tuberculosis in our patient.

## CONCLUSION

We highlight a rare case of primary conjunctival tuberculosis that was successfully treated. Clinicians should have high index of suspicion of conjunctiva TB in cases of chronic conjunctivitis not responding to standard treatment especially if it worsens with steroid therapy as in our case. This is especially so in countries where the disease is endemic. Failure to treat this condition can have disastrous effect not only on the eye, but also systemically. It is fortunate our patient responded well to treatment.

## Funding sources

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## REFERENCES

- Ang, M., Wong, W., Ngan, C.C.L. & Chee, S.P. (2012). Interferon-gamma release assay as a diagnostic test for tuberculosis-associated uveitis. *Eye* **26**(5): 658-665.
- Archer, Bird. (1967). Primary Tuberculosis of Conjunctiva. *British Journal of Ophthalmology* **51**: 679-684.
- Beare, Kublin, Lewis, Schijffelen, Peters, Joaki, Kumwenda, E.E.Z. (2002). Ocular disease in patients with tuberculosis and HIV presenting with fever in Africa. *British Journal of Ophthalmology* **86**(10): 1076-1079.
- Bodaghi, L. Hoang. (2000). Ocular tuberculosis. *Current Opinion in Ophthalmology* **11**: 443-8.
- Bouza, Merino, Munoz, Sanchez-Carrillo, Yanez, C.C. (1997). Ocular tuberculosis: a prospective study in a general hospital. *Medicine (Baltimore)* **76**: 53-61.
- Chandler, Locatcher-Khorazo. (1964). Primary tuberculosis of the conjunctiva. *Archives of Ophthalmology* **71**: 202-205.
- David, Shashidhar. (2001). Primary tuberculosis of the conjunctiva. *Eye* **15**: 674-676; doi:10.1038/eye.2001.215.
- Diel, R., Wrighton-Smith, P. & Zellweger, J.P. (2007). *European Respiratory Journal* **30**(2): 321-32.
- Donahue. (1967). Ophthalmologic experience in a tuberculosis sanatorium. *American Journal of Ophthalmology* **64**: 742-748.
- Eyre. (1912). Tuberculosis of the conjunctiva: its aetiology, pathology and diagnosis. *Lancet* **1**: 1319-28.
- Faiz. (2015). Ocular tuberculosis: current perspectives. *Clinical Ophthalmology* **9**: 2223-2227.
- Fernandes, Vemuganti, Pasricha, Bansal & Sangwan. (2003). Unilateral tuberculous conjunctivitis with tarsal necrosis. *Archives of Ophthalmology* **121**: 1475-1478.
- Helm, Holland. (1993). Ocular tuberculosis. *Survey of Ophthalmology* **38**(3): 229-56.
- Jun-ichi, S., Suguru, M., Masahiko, U. & Ikuya, Y. (2001). New diagnostic approach for ocular tuberculosis by ELISA using the cord factor as antigen. *British Journal of Ophthalmology* **85**: 130-133.
- Mao, Y., Peng, X.Y., You, Q.S., Wang, H., Zhao, M. & Jonas, J.B. (2014). Tuberculous uveitis in China. *Acta Ophthalmologica* **92**(5): e393-7.
- Morimura, Y., Okada, A.A., Kawahara, S., Miyamoto, Y., Kawai, S., Hirakata, A. & Hida, T. (2002). Tuberculin skin testing in uveitis patients and treatment of presumed intraocular tuberculosis in Japan. *Ophthalmology* **109**(5): 851-7.
- Rao, Bhat. (1967). Active systemic lesions in cases of suspected ocular tuberculosis. *Journal of All India Ophthalmological Society* **15**: 175-180.
- Singh, Chaudhary & Arora. (1989). Tuberculoma of the conjunctiva. *Journal of the Indian Medical Association* **87**: 265-6.
- Sorsby. (1963). Ocular tuberculosis. *Modern Ophthalmology* **117**: 456-457.
- World Health Organization. (2016). Global health observatory data repository: global tuberculosis report 2016. Geneva ([http://www.who.int/tb/publications/global\\_report/en/](http://www.who.int/tb/publications/global_report/en/)).
- Woods. (1972). Ocular tuberculosis. In: Sorsby A, ed. *Modern Ophthalmology*. Philadelphia, Pa: JB Lippincott; **1972**: 105-140.