Section: Ophthalmology

Original Research Article

CLINICAL FEATURES OF OCULAR TUBERCULOSIS IN MANTOUX-NEGATIVE BUT QUANTIFERON-TB GOLD POSITIVE PATIENTS

Chethan N Murthy[1], Ranjitha K. C.[1], Shalini G[2]

[1]*Assistant Professor, Department of Ophthalmology, Madhusudan Sai Institute of Medical Sciences and Research Centre, Chikkaballapur, Karnataka, India*
[2]*Senior Resident, Department of Ophthalmology, Madhusudan Sai Institute of Medical Sciences and Research Centre, Chikkaballapur, Karnataka, India*

Received *: 08/10/2025*
Received in revised form *: 23/11/2025*
Accepted *: 09/12/2025*

Corresponding Author:
Dr. Chethan N Murthy,
Assistant Professor, Department of Ophthalmology, Madhusudan Sai Institute of Medical Sciences and Research Centre, Chikkaballapur, Karnataka, India.
Email: chethanthegreat@gmail.com

DOI: 10.70034/ijmedph.2025.4.446

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2025; 15 (4); 2470-2472

ABSTRACT

Background: Ocular tuberculosis (TB) presents with diverse clinical manifestations, making diagnosis challenging. Conventional tests such as the Mantoux skin test have limited diagnostic accuracy. Interferon-gamma release assays (IGRAs), particularly the QuantiFERON-TB Gold (QFT-G) test, have emerged as valuable adjuncts in identifying latent and extrapulmonary TB. The objective is to describe the clinical features of ocular TB in patients who tested negative on the Mantoux test but positive on QuantiFERON-TB Gold.

Materials and Methods: A retrospective review of 110 patients with ocular inflammation was conducted. All were Mantoux-negative but QuantiFERON-positive. Clinical features were documented and analyzed descriptively with additional subgroup comparison.

Results: Retinal vasculitis (25.6%), multifocal choroiditis (22.5%), and posterior uveitis (21.2%) were the most common findings. A significant portion (83%) had QuantiFERON levels >2 U/mL. The QFT-positive subgroup showed a predominance of posterior segment disease.

Conclusion: Mantoux-negative but QuantiFERON-positive patients often show posterior ocular inflammation. This highlights the diagnostic utility of QFT in TB-endemic areas and suggests the need to reevaluate reliance on Mantoux testing alone.

Keywords: Ocular tuberculosis, QuantiFERON-TB Gold, Mantoux test, retinal vasculitis, uveitis, choroiditis.

INTRODUCTION

Ocular tuberculosis (OTB) represents one of the most elusive manifestations of Mycobacterium tuberculosis infection, owing to its variable clinical presentations and lack of pathognomonic features. The global burden of TB remains substantial, particularly in endemic countries where latent infection is prevalent. The Mantoux tuberculin skin test (TST), though widely used, suffers from poor specificity due to prior Bacille Calmette–Guérin (BCG) vaccination and cross-reactivity with nontuberculous mycobacteria. In contrast, interferon-gamma release assays (IGRAs), such as the QuantiFERON-TB Gold (QFT-G) test, measure immune reactivity to M. tuberculosis-specific antigens and are unaffected by BCG vaccination.[1,2]

Recent studies suggest that QFT may play a crucial role in identifying ocular TB, especially in cases where conventional diagnostic tools fail. However, the subset of patients who are Mantoux-negative but QFT-positive remains under-characterized.[3,4]

This study aims to describe the spectrum of ocular inflammation in such patients, providing insights into the diagnostic value of IGRAs in this unique cohort.

MATERIALS AND METHODS

Study design: Retrospective, observational study conducted on 110 consecutive patients presenting with ocular inflammation at a tertiary eye care center between January 2020 and December 2024.

Inclusion Criteria

Evidence of ocular inflammation (anterior uveitis, posterior uveitis, choroiditis, or retinal vasculitis). - Negative Mantoux test (< 10 mm induration). - Positive QuantiFERON-TB Gold test.

Exclusion Criteria

Patients with systemic immunosuppression or HIV infection. - Prior anti-tubercular therapy. - Other identifiable infectious or autoimmune uveitic etiologies.

Data Collection: Demographics, ocular findings, and laboratory test results were recorded. QuantiFERON levels were categorized as < 2 U/mL or > 2 U/ml. Ocular findings were grouped by anatomical classification of uveitis (anterior, intermediate, posterior, and panuveitis).

Statistical Analysis: Descriptive statistics were used to summarize data. Subgroup comparisons were performed between QuantiFERON >2 U/mL and ≤2 U/mL groups. Results were expressed as percentages.

RESULTS

Table 1: Demographic characteristics

Demographic characteristics	Number	%
Male	66	60
Female	44	40
Mean age (years)	39.8 ± 12.1	

Demographics: Of the 110 patients, 66 were male (60%) and 44 were female (40%) The mean age was 39.8 ± 12.1 years.

Table 2: Ocular manifestations

Ocular manifestations	Number	%
Retinal vasculitis	28	25.5
Multifocal choroiditis	25	22.7
Posterior uveitis	23	20.9
Vitritis	16	14.5
Anterior uveitis	11	10
Panuveitis	7	6.4

Retinal vasculitis was seen in (25.6%), multifocal choroiditis was seen in (22.5%), posterior uveitis was seen in (21.2%), vitritis was seen in (15%), anterior uveitis was seen in (10%), and panuveitis was seen in (5.7%).

Table 3: Quantiferon results

Quantiferon results	Number	%
Quantiferon level > 2 U/ml	91	82.7
Quantiferon level < 2 U/ml	19	17.3

Mean QuantiFERON level was 5.7 U/mL. 83% of patients had values >2 U/mL, indicating strong immune sensitization.

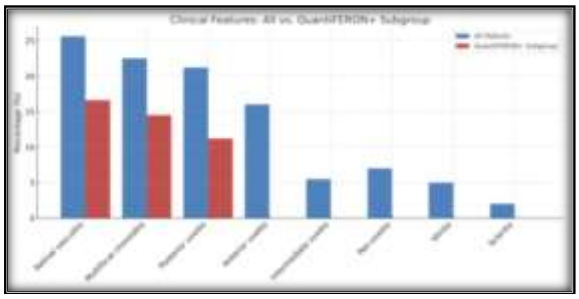

Figure 1: Subgroup analysis

Subgroup analysis: Patients with QuantiFERON >2 U/mL had a higher frequency of posterior segment disease.

DISCUSSION

The diagnosis of ocular tuberculosis (OTB) remains challenging, primarily because Mycobacterium tuberculosis rarely involves ocular tissue directly and microbiological confirmation is seldom obtained.[1,2] This study focused on patients who were Mantoux negative yet QuantiFERON-TB Gold positive and highlights the clinical relevance of such cases. Significance of Mantoux-Negative, QuantiFERON-Positive Status: The Mantoux skin test is limited by cross-reactivity with BCG and environmental mycobacteria, as well as false negatives due to anergy or immunosuppression.[3,4]

IGRAs, like QFT-G, provide higher specificity and detect immune reactivity even when TST fails.[5,6]

In our cohort, all patients were Mantoux-negative but QFT-positive, with 83% showing levels >2 U/mL, indicating latent or active TB sensitization. Predominance of Posterior Segment Involvement: Posterior segment inflammation— retinal vasculitis (25.6%), multifocal choroiditis (22.5%), and posterior uveitis (21.2%)— was predominant. This aligns with COTS-1 findings and other studies from India.[2,4-6] High QFT levels may correlate with posterior localization of ocular inflammation.[6]

Pathophysiological Considerations: Ocular TB manifestations are often immune mediated rather than due to direct infection. Delayed hypersensitivity

to mycobacterial antigens can trigger choroidal or retinal granulomatous inflammation.[7]

Mantoux negative patients may still exhibit circulating sensitized T-cells detectable by QFT.[5] Clinical and Diagnostic Implications: QFT testing is critical in TB-endemic areas, particularly when Mantoux is negative. High QFT titers may indicate disease activity and support the initiation of anti-tubercular therapy when ocular findings are compatible.[2,4,5,8]

Comparison with Previous Studies: Our results align with Ang et al,[5] and Bansal et al,[4] who found QFT positivity in patients with presumed OTB even when Mantoux was negative. Western cohorts show lower positivity due to lower endemic exposure, but posterior uveitis remains the predominant finding in QFT-positive patients.[6] Therapeutic Implications: While treatment outcomes were not studied here, evidence supports ATT initiation in QFT-positive patients with compatible ocular features, often with adjunctive corticosteroids.[2,7-9]

Limitations and future directions: Retrospective design and lack of microbiologic confirmation are limitations. Future prospective studies and molecular diagnostics such as PCR on intraocular fluids could further validate QFT as a diagnostic tool for ocular TB. Summary: Mantoux-negative but QuantiFERON-positive patients often show posterior ocular inflammation. QFT testing is valuable in TB-endemic regions and should complement, not replace, clinical assessment.

CONCLUSION

Mantoux-negative but QuantiFERON-TB Gold positive patients frequently demonstrate posterior ocular inflammation. IGRA testing provides an essential diagnostic adjunct in TB endemic settings, and its inclusion in ocular TB evaluation is recommended.

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