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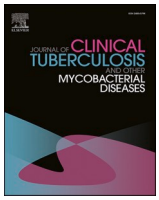

Characteristics and outcomes of the duration of treatment with adjunctive corticosteroids in intraocular tuberculosis

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ABSTRACT

Introduction: Intraocular tuberculosis (IOTB) is a common site of extrapulmonary tuberculosis and a main cause of infectious uveitis. It can result in severe visual morbidity if not recognized and treated properly. The clinical manifestations of IOTB are varied, and the duration of treatment is unclear. This study describes the clinical characteristics and outcomes of patients with IOTB and compares the duration of antituberculosis therapy (ATT) and steroid use.

Method: An 8-year retrospective study of IOTB patients in an endemic area of a tertiary hospital in Thailand. All patients had a complete treatment of ATT at least for 6 months.

Results: Forty-three patients with 57 eyes and a mean age of 43.72 years were included. Panuveitis (38.6 %), retinal phlebitis (31.6 %), and posterior uveitis (15.8 %) were common clinical characteristics. A significant difference between initial and final best corrected visual acuity (BCVA) after ATT in 6 months for therapy and at least 9 months for therapy was observed ($p = 0.004$, 0.003, respectively). Ninety point nine percent of patients who received ATT for 9 months achieved a successful treatment outcome, while 66.7 % of patients who received ATT for 6 months did ($p = 0.056$). Patients who received systemic and/or regional corticosteroids therapy during treatment had a higher rate of treatment failure ($p < 0.001$).

Conclusion: IOTB had a variety of clinical manifestations, including nongranulomatous inflammation. Patients who completed treatment with ATT for at least 6 months improved their final BCVA. There was no difference in treatment outcomes regarding the duration of treatment. Combined treatment with systemic and/or regional corticosteroids was significantly associated with failed treatment outcomes.

1. Introduction

Tuberculosis (TB) is one of the most burdensome infectious diseases, with high morbidity and mortality rates, caused by Mycobacterium tuberculosis. According to the global tuberculosis report 2022 from the WHO, as estimated 6.4 million people were affected by TB and estimated over 1.6 million people died from TB [1].

TB is a disease that predominantly affects the lungs and is treatable and preventable. Eighty-five percent of patients can be successfully treated with anti-tuberculosis therapy (ATT) [2]. Extrapulmonary TB accounts for 20 % of all tuberculosis cases, of those with extrapulmonary tuberculosis, around 3–5 % of cases involve the eyes [3]. Ocular TB can involve the orbit, eyelid, lacrimal gland, conjunctiva, sclera, uvea, or retina. Intraocular TB accounts for most of the ocular TB burden, with TB uveitis being a major cause of infectious uveitis in high TB burden areas, such as Southeast Asia [1,3–7]. Diagnosis of IOTB can be challenging given the heterogeneous clinical manifestations and difficulties obtaining microbiologic confirmation.

Despite the substantial morbidity of IOTB, the optimal ATT and corticosteroid regimen remains unclear [8]. This study aims to report the clinical characteristics of patients with IOTB and treatment outcomes of patients treated with ATT in different durations in a tertiary referral hospital in Bangkok, Thailand.

2. Materials and methods

This retrospective chart review was conducted at a uveitis clinic in Phramongkutklao Hospital, a tertiary hospital in Bangkok, Thailand.

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The protocol was approved by the Institutional Review Board of the Royal Thai Army Medical Department with the tenets of the Declaration of Helsinki. All patients diagnosed with IOTB and treated with ATT at least 6 months between January 2013 and December 2020, a total of 8 years, were analyzed. Patients who did not complete treatment or had incomplete records were excluded.

Patients were identified by searching for international classification of disease 10th edition (ICD-10) code A185, laboratory code for TB the interferon gamma release assay and ATT prescription records. The diagnosis of IOTB was based on the Classification of Intraocular Tuberculosis proposed by Gupta A, et al. in 2015 [9].

The demographic data consisted of age, gender, underlying diseases, disease laterality, history of pulmonary tuberculosis, and a history of contact with tuberculosis patients. The terminology and anatomical classification in this study were classified based on the Standardization of Uveitis Nomenclature (SUN) Working Group criteria [10]. All patients underwent a history-taking for specific ocular and systemic symptoms, together with full ocular examinations, including best-corrected visual acuity (BCVA), slit-lamp microscopy, intraocular pressure, and fundus examination. Fluorescein and/or indocyanine green angiography and optical coherence tomography were performed in certain cases, in particular posterior uveitis and panuveitis, with suspicion of retinal vasculitis and macular edema.

All patients with clinical suspicion in the uveitis clinic were screened for TB infection. HIV and syphilis infections were identified by serology tests (anti-HIV, VDRL, TPHA). Chest X-ray (CXR) and/or computer tomography (CT) imaging were performed, and immunological tests such as tuberculin skin test (TST) and interferon-gamma release assay (IGRA) in the form of QuantiFERON-TB Gold test and/or T-SPOT.TB tests were conducted. Polymerase chain reaction (PCR) or mycobacterial culture of tissue biopsy was performed only in cases of need for surgery together with purpose of improving vision in vitreous hemorrhage or could not see the fundus. Patients with a positive serology of syphilis were excluded.

The diagnosis of IOTB was classified into confirmed, probable, and possible IOTB according to the Classification of Intraocular Tuberculosis proposed by Gupta A, et al. in 2015 [9]. All patients had a clinical suspicion of IOTB and a positive TST or IGRA with varying degrees of responsiveness to ATT.

ATT was initiated, and adverse drug reactions were monitored by ophthalmologists together with respiratory or infectious disease physicians in our hospital. The duration of ATT depended on the physician's decision and clinical observation. We used two ATT regimens in our study. The first regimen is 2 months of a 4-agent regimen (isoniazid, rifampicin, pyrazinamide, and ethambutol (IRZE)), followed by at least 4 months of a dual-agent regimen (isoniazid, rifampicin). The second regimen is a fixed-dose-combination film-coated tablet composed of 75 mg of isoniazid, 150 mg of rifampicin, 400 mg of pyrazinamide, and 275 mg of ethambutol hydrochloride in the first 2 months, followed by a dual regimen.

Systemic corticosteroids might be prescribed after 2 weeks of initiating ATT, when inflammation had been persisting and affected visual acuity or caused inflammation in sight-threatening areas such as retinal vasculitis approaching the posterior pole. The dosage and duration of treatment depended on the clinical judgment of uveitis specialists. In case of anterior segment inflammation, topical corticosteroids were initiated and titrated according to the severity of inflammation. The frequency of the follow-up period was determined by the timing of ATT initiation, the severity of ocular inflammation, and dosage of systemic corticosteroids. We reviewed the frequency of follow-up at 2 weeks, 3 months, 6 months, 9 months, 12 months, and 24 months according to the duration of ATT. Adverse drug reactions were collected. The initial BCVA was defined as the BCVA from the first visit of the patient, and the final BCVA was the vision at the last visit or 24 months after treatment. All subjects were followed up for at least 6 months after the initiation of ATT.

Treatment response was defined according to the grading of the Standardization Uveitis Nomenclature (SUN) Working Group in anterior uveitis and intermediate uveitis [10]. Retinal vasculitis, and choroidal tuberculomas were identified as treatment response when ocular signs began to resolve. Fundus photographs were taken to compare clinical resolution/worsening. Inactive disease for $\geq$ 3 months after discontinuing all treatment signified remission. Recurrence was defined as a two-step increase in inflammation separated by periods of inactivity without treatment for $\geq$ 3 months. Definition of treatment failure was adopted from the Collaborative Ocular Tuberculosis Study (COTS) as any of the following [11].

1) persistence or recurrence of inflammation within 6 months of completing ATT,
2) inability to taper oral steroid to $<$ 10 mg/kg or topical steroid drops to $<$ 2 drops a day at 6th month
3) recalcitrant inflammation that requires steroid-sparing immunosuppressive therapy.

Data collection was done on Microsoft excel. A Shapiro-Wilk test was used to test whether continuous data were normally distributed. Frequencies of variables recorded on patients were tabulated for descriptive analysis. Mean and standard deviation (SD) were presented as normal distribution continuous variables, and median and interquartile range (IQR) for skewed continuous variables. The Mann-Whitney-Wilcoxon test was used to investigate the difference between initial and final BCVA within the group of 6 months and at least 9 months for the duration of therapy, as well as the difference in baseline clinical characteristics and degree of inflammation between the groups. Chi-square test was used for statistical analysis of treatment outcomes. A p-value of $<$ 0.05 was considered to be statistically significant. All analyses were performed using IBM SPSS Statistics for Windows, Version 29.0 (IBM Corp, Armonk, NY, USA).

3. Results

3.1. Demographic characteristics

Overall 49 patients with IOTB were identified, of those 43 patients and 57 eyes were included in the analysis. Of the included cases 1 patient (2.3 %) of cases had microbiologically confirmed IOTB with positive TB PCR from ocular fluid, 15 patients (34.9 %) had probable IOTB and 27 patients (62.8 %) had possible IOTB.

All patients were Thai, with 23 (53.5 %) men and 20 (46.5 %) women (Table 1). The mean age $\pm$ SD at presentation was 43.72 $\pm$ 14.05 years. Unilateral involvement was more common (67.4 %) than bilateral involvement (32.6 %). Almost all the patients (90.7 %) had no history of tuberculosis contact prior to infection. Most of the patients were healthy and had no underlying diseases. All four cases with pulmonary TB presented with posterior panuveitis or occlusive retinal phlebitis (Fig. 1A), and only one patient had tuberculoma (Fig. 1B).

Table 1
Demographic of intraocular tuberculosis patients.

	N = 43	%
Age (mean)	43.72 ± 14.05	
Min-max	12–70	
ender		
Male	23	53.5
Female	20	46.5
Laterality	29	67.4
Unilateral		
Bilateral	14	32.6
Pulmonary Tuberculosis	4	9.3
History of tuberculosis exposure	3	7
Human immunodeficiency virus infection	1	2.3

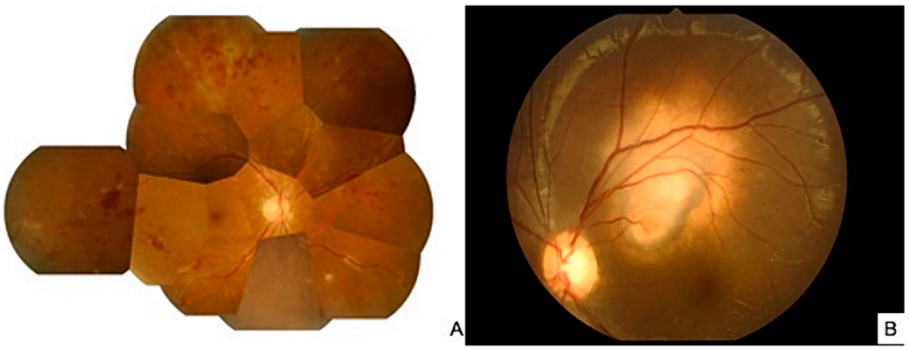

Fig. 1. A) The right fundus shows multiple occlusive retinal phlebitis at midperiphery. B) The left fundus shows tuberculoma size 2 disc diameter at superior of posterior pole.

3.2. Clinical presentations

Of the 57 eyes with IOTB; the most common presentations were panuveitis (38.6 %) and retinal vasculitis (31.6 %), followed by posterior uveitis (15.8 %). All of those with retinal vasculitis had phlebitis. Anterior segment findings showed mutton fat keratic precipitates in 8.8 %, iris nodules in 5.3 %, posterior synechia in 26.3 %, and anterior chamber cells in 56.1 %. For the posterior segment, the most common ocular presentation was vitritis (57.9 %), phlebitis (47.4 %), multifocal choroiditis (19.3 %), and macular edema (19.3 %). A fluorescein angiogram was performed in 32 eyes of 57 eyes (56.1 %). The most common clinical feature on FA was disc leakage (56.5 %), followed by ischemic areas (34.8 %), vasculitis (34.8 %), neovascularization (34.8 %), and capillary leakage (26.1 %) (Table 2).

3.3. Diagnostic modality

CXR was obtained in every patient and chest CT was obtained in 9 (20.9 %) patients. CXR was abnormal in 27.9 % and CT in 66.7 %. TB IGRA (QuantiFERON-TB Gold test and T-SPOT.TB) tests were obtained in 36 (83.7 %) patients, with 86.1 % being positive. TST was performed in 26 (60.5 %) patients, with 76.9 % being positive (Table 3). PCR for TB was obtained from intraocular fluid in 10 (23.3 %) patients, but only 1 (10 %) was positive.

Table 2
Clinical characteristics of intraocular tuberculosis per affected eye at presentation.

Clinical presentation by anatomical location	**N = 57**	**%**
Anterior uveitis	4	7
Intermediate uveitis	4	7
Posterior uveitis	9	15.8
Panuveitis	22	38.6
Retinal phlebitis	18	31.6
Ocular manifestation	**N = 57**	**%**
Anterior segment		
Anterior chamber reaction	32	56.1
Posterior synechiae	15	26.3
Ciliary injection	6	10.5
Iris nodule	3	5.3
Mutton-fat keratic precipitates	5	8.8
Hypopyon	1	1.8
Posterior segment		
Vitritis	33	57.9
Retinal phlebitis	27	47.4
Multifocal choroiditis	11	19.3
Macular edema	11	19.3
Vitreous hemorrhage	9	15.8
Tuberculoma	7	12.3
Focal Choroiditis	3	5.3
Serpiginous-like choroiditis	3	5.3
Retinitis	3	5.3
Exudative retinal detachment	2	3.5
Retinal abscess	1	1.8
Fluorescein angiography	**n = 32**	**%**
Disc leakage	13	56.5
Ischemic area	8	34.8
Capillary leakage	6	26.1
Vasculitis	8	34.8
Neovascularization	8	34.8

3.4. Management

All forty-three patients were treated with ATT for different durations, which were 6 months, 9 months, and the maximum at 12 months (48.8 %, 48.8 %, and 2.3 %, respectively). There were 20 (46.5 %) patients who received systemic steroid and/or regional steroid injections during treatment. There were no statistically significant differences in terms of the clinical characteristics and degree of inflammation between patients who received ATT for 6 months and at least 9 months and among patients who received steroid treatment or not (Table 4).

3.5. Adverse drug reactions of anti-tuberculosis therapy

There were 12 (27.9 %) patients who observed adverse drug reactions to ATT, but only minor side effects were found. Skin rash was the predominant adverse drug reaction with 11.6 %, followed by transaminitis with 7 %, gastrointestinal disturbance with 4.7 %, neutropenia with 2.3 %, and myalgia with 2.3 %.

3.6. Visual outcomes

Regarding the visual outcome, the median (IQR) initial BCVA expressed in LogMAR was 0.4 (0.2–1.0), 0.8 (0.4–2.0) in 6 months, and at least 9 months of therapy, with no significant difference between these two groups ($p = 0.19$). The final median (IQR) BCVA was 0.2 (0.2–0.4), 0.2 (0.2–0.9), with a significant difference between the initial and final BCVA within both groups, $p = 0.004$ and 0.003, respectively. Among patients with steroid administration, 65 % showed visual improvement, but there was no significant effect on gaining vision ($p = 0.19$).

Table 3
Investigations of intraocular tuberculosis patients.

	n	**%**
Abnormal CXR	12/43	27.9
Abnormal CT chest	6/9	66.7
Immunological Test	31/36	86.1
IGRAs		
PPD	20/26	76.9

CXR: Chest x-ray, CT chest: Computerized Tomography chest scan, IGRAs: Interferon-Gamma Release Assay, PPD:Purified Protein Derivative.

Table 4
Comparison of anatomical location and degree of inflammation of duration of anti-tuberculosis therapy and treatment of corticosteroids.

	Duration of ATT (N = 43)			Treatment (N = 43)		
	6 months (n = 21)	9 months (n = 22)	*p*-value	ATT alone (n = 23)	ATT with steroids (n = 20)	*p*-value
Anatomical location						
Anterior uveitis	1	1	0.9	1	1	0.9
Intermediate uveitis	1	2	0.6	2	1	0.6
Posterior uveitis	5	2	0.2	5	2	0.3
Panuveitis	9	9	0.9	8	10	0.3
Retinal vasculitis	5	8	0.4	7	6	1.0
Degree of inflammation						
Anterior chamber cell ≥ 2+	10	12	0.7	10	12	0.3
Presence of vitritis	13	13	0.9	12	14	0.2

The Mann-Whitney-Wilcoxon test.
ATT: anti-tuberculosis therapy.

3.7. Treatment outcomes

Treatment success was achieved in 90.9 % of those who received ATT for at least 9 months, compared to 66.7 % of those who received 6 months ($p = 0.056$). All patients who did not receive systemic and/or local steroid treatment in our study had 100 % treatment success; in contrast, only 55 % of patients using steroid had a successful treatment outcome ($p < 0.001$) (Table 5). There was no statistically significant difference in degree of inflammation between those who received ATT for 6 months compared to 9 months ($p = 0.9$) or in those who received steroids compared to those who did not ($p = 0.2$) (Table 4). There were 2 recurrent cases (4.7 %) in our study; 1 received 6 months and 1 received at least 9 months of ATT therapy, but both were using steroids.

4. Discussion

Our study of 43 patients with IOTB in a high TB burden area found no difference in treatment outcomes with longer duration of ATT or receipt of corticosteroids. The mean age of included patients in our study was 43.7 years, and the slight male predominance was similar to COTS at 41.3 years [12]. IOTB has various clinical presentations; most of our patients had unilateral involvement (55.55 %), as reported in other studies from South-East Asia [13,14] In contrast COTS and others reported predominantly bilateral disease [15,16]. In our study, mutton-fat precipitations were found in only 8.8 % and iris nodules in 5.3 % of patients. Therefore, IOTB should be included in the differential diagnosis for nongranulomatous uveitis cases. Panuveitis and retinal vasculitis are also common presentations of IOTB [9,17]. Posterior synechiae, which have been described as a sign of IOTB, were found in only 26.3 % in our study [18]. The association of retinal vasculitis with vitritis and choroiditis has been reported in many previous studies similar to the findings from our study [18–21]. Serpiginous like choroiditis was the most common form among choroidal involvement in COTS, however we observed multifocal choroiditis as the most common phenotype [12]. FA can detect IOTB complications; both ischemic areas and neovascularization were revealed by FA in 34.8 % in our study, which may benefit further management.

Table 5
Treatment outcome of intraocular tuberculosis patients.

	Success	Failure	*p*-value
ATT 6 month (n = 21)	14 (66.7 %)	7 (33.3 %)	
ATT ≥ 9 month (n = 22)	20 (90.9 %)	2 (9.1 %)	0.056
No systemic/regional steroid (n = 23)	23 (100 %)	0 (0 %)	
Combined systemic/regional steroid (n = 20)	11 (55 %)	9 (45 %)	<0.001*

Chi-square test.
ATT: anti-tuberculosis therapy.

The diagnosis of IOTB is typically challenging with cultures and PCR often negative due to the small volume and low bacillary concentration of intraocular fluid [22]. In our study, the positive IGRA (86.1 %) and tuberculin skin test (76.9 %) were very helpful for the diagnosis of presumed ocular TB; nevertheless, some authors believed that the tuberculin skin test was inaccurate, had a low positive predictive value and high false negative [22–24]. We found a positive CXR in 27.9 % of patients, similar rate to the previous reports [12,13,17]. We recommend chest imaging and IGRA or TST testing for those who have symptomatic vitritis or retinal phlebitis and an unexplained etiology. If any of this testing is abnormal, they should be considered for possible IOTB, particularly in TB- endemic areas.

We found an ATT adverse drug reaction rate of 28.9 %, considerably higher than the 8.3 %-10 % reported in previous studies [16,25,26]. Nevertheless, only minor adverse effects were observed and none lead to ATT discontinuation.

All patients in our study received ATT for a minimum of 6 months. Overall, patients had significantly improved their final BCVA compared to their initial BCVA, regardless of the duration of ATT. The finding that ATT was beneficial to patients with IOTB was consistent with several earlier research findings [15,27–29]. The optimal duration of ATT for IOTB is uncertain; however, the standard regimen entails IRZE for at least two months, followed by isoniazid and rifampicin for at least four months [8,16,30]. Some previous studies reported a favorable result for a longer 6-month ATT treatment [31,32] Our study showed no differences in the treatment outcomes between the different durations of treatment. Even with a group of minimum treatment at 9 months reached 90.9 % of successful treatment, it did not reach a statistical significance. This result might be due to the small number of patients in our study.

Treatment with corticosteroids is recommended for some other extrapulmonary TB conditions, such as TB meningitis and TB pericarditis. However, the benefit in IOTB is unclear [16,29]. In our study, combination treatment with oral prednisolone and/or regional steroid injections was found to be significantly associated with treatment failure, similar to some other studies [12,33]. The COTS Consenus Guidelines recommend initiation of oral corticosteroids at the same time or shortly after starting ATT, however this approach may need to be individualized [34]. The use of oral steroids in IOTB should be guided by the uveitis phenotype; those with more immune mediated disease such as serpiginous-like choroiditis, tubercular multifocal or unifocal choroiditis or occlusive retinal vasculitis may benefit from earlier initiation of corticosteroids together with or shortly after ATT initiation [34].

We recognize the limitations of our study, such as the retrospective nature, possibility of incomplete clinical documentation, incomplete investigations, and short follow-up duration. A longer follow-up period and larger number of cases may be better able to define the ideal duration of ATT. However, this 8-year retrospective study has found some important information regarding ATT duration and corticosteroid use in IOTB.

5. Conclusion

IOTB can have various manifestations; unilateral, panuveitis, and phlebitis were common presentations. IOTB should be considered as a possible cause of nongranulomatous uveitis, especially in areas with a high TB burden. ATT for at least 6 months was associated with a significant improvement in BCVA. There was no difference in treatment outcomes between the duration of ATT in our study. Combination

treatment with systemic and/or regional corticosteroids should be cautiously monitored as it may be associated with a higher chance of treatment failure, individualization based on the uveitis phenotype may lead to better outcomes.

6. Declarations

This work involving human data were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. It was approved by the Institutional Review Board, Royal Thai Army Medical Department (No. IRBRTA 520/2020). For data availability, please contact author for data requests.

7. Disclosure

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CRediT authorship contribution statement

Yaninsiri Ngathaweesuk: Writing – original draft, Project administration, Methodology, Data curation, Conceptualization. **Sitrapa Janthayanont:** Writing – original draft, Investigation, Data curation. **Narumon Keorochana:** Writing – review & editing, Visualization, Project administration, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] World Health Organization, 'Global Tuberculosis report 2022', 2022. [Online]. Available: http://apps.who.int/bookorders.

[2] World Health Organization, 'Global Tuberculosis report 2021', 2021. [Online]. Available: http://apps.who.int/bookorders.

[3] A. Abdisamadov and O. Tursunov, 'Ocular tuberculosis epidemiology, clinic features and diagnosis: A brief review', *Tuberculosis*, vol. 124. Churchill Livingstone, Sep. 01, 2020. doi: 10.1016/j.tube.2020.101963.

[4] S. Sukavatcharin, O. Kijdaoroong, K. Lekhanont, and S. Arj-Ong Vallipakorn, 'Pattern of Uveitis in a Tertiary Ophthalmology Center in Thailand', *Ocul Immunol Inflamm*, vol. 25, pp. S94–S99, Aug. 2017, doi: 10.1080/09273948.2016.1215475.

[5] I. Testi *et al.*, 'Ocular tuberculosis: Where are we today?', *Indian Journal of Ophthalmology*, vol. 68, no. 9. Wolters Kluwer Medknow Publications, pp. 1808–1817, Sep. 01, 2020. doi: 10.4103/ijo.IJO_1451_20.

[6] Keorochana N. Pattern and outcome of uveitis in a tertiary military hospital in thailand. Ocul Immunol Inflamm Apr. 2020;28(3):424–32. https://doi.org/10.1080/09273948.2019.1589527.

[7] Agrawal R, et al. Visual morbidity in ocular tuberculosis-collaborative ocular tuberculosis study (COTS)-1: Report #6. Ocul Immunol Inflamm 2020;28(sup1): 49–57. https://doi.org/10.1080/09273948.2020.1774905.

[8] M. Ang and S. P. Chee, 'Controversies in ocular tuberculosis', *British Journal of Ophthalmology*, vol. 101, no. 1. BMJ Publishing Group, pp. 6–9, Jan. 01, 2017. doi: 10.1136/bjophthalmol-2016-309531.

[9] A. Gupta, A. Sharma, R. Bansal, and K. Sharma, 'Classification of intraocular tuberculosis', *Ocular Immunology and Inflammation*, vol. 23, no. 1. Informa Healthcare, pp. 7–13, Feb. 01, 2015. doi: 10.3109/09273948.2014.967358.

[10] Jabs DA, et al. Standardization of uveitis nomenclature for reporting clinical data. Results of the first international workshop. Am J Ophthalmol Sep. 2005;140(3): 509–16. https://doi.org/10.1016/j.ajo.2005.03.057.

[11] Agrawal R, et al. Standardization of nomenclature for ocular tuberculosis-results of collaborative ocular tuberculosis study (COTS) workshop. Ocul Immunol Inflamm 2020;28(sup1):74–84. https://doi.org/10.1080/09273948.2019.1653933.

[12] I. Testi et al. 'Tubercular Uveitis: Nuggets from Collaborative Ocular Tuberculosis Study (COTS)-1', Ocular Immunology and Inflammation vol. 28, no. sup1 2020 Taylor and Francis Ltd. 10.1080/09273948.2019.1646774 8 16.

[13] Ang L, et al. Treatment outcome in patients with presumed tubercular uveitis at a tertiary referral eye care centre in Singapore. Int Ophthalmol Feb. 2018;38(1): 11–8. https://doi.org/10.1007/s10792-016-0401-6.

[14] Win MZA, Win T, Myint S, Shwe T, Sandar H. Epidemiology of uveitis in a tertiary eye center in myanmar. Ocul Immunol Inflamm Aug. 2017;25:S69–74. https://doi.org/10.3109/09273948.2015.1133839.

[15] Agrawal R, et al. Clinical features and outcomes of patients with tubercular uveitis treated with antitubercular therapy in the collaborative ocular tuberculosis study (COTS)-1. JAMA Ophthalmol Dec. 2017;135(12):1318–27. https://doi.org/10.1001/jamaophthalmol.2017.4485.

[16] Kee AR, et al. 'Anti-tubercular therapy for intraocular tuberculosis: A systematic review and meta-analysis', in *Survey of Ophthalmology*. Elsevier USA Sep. 2016: 628–53. https://doi.org/10.1016/j.survophthal.2016.03.001.

[17] C. J. Lin *et al.*, 'Clinical Manifestations and Outcomes of Tubercular Uveitis in Taiwan—A Ten-Year Multicenter Retrospective Study', *Medicina (Lithuania)*, vol. 58, no. 3, Mar. 2022, doi: 10.3390/medicina58030376.

[18] Gupta A, Bansal R, Gupta V, Sharma A, Bambery P. Ocular signs predictive of tubercular uveitis. Am J Ophthalmol Apr. 2010;149(4):562–70. https://doi.org/10.1016/j.ajo.2009.11.020.

[19] A. Gupta, V. Gupta, S. Arora, M. R. Dogra, and P. Bambery, 'PCR-POSITIVE TUBERCULAR RETINAL VASCULITIS Clinical Characteristics and Management'.

[20] Biswas J, Shome D. Choroidal tubercles in disseminated tuberculosis diagnosed by the polymerase chain reaction of aqueous humor. Ocul Immunol Inflamm 2003;10 (4):293–8.

[21] Y. Mao, X. Y. Peng, Q. S. You, H. Wang, M. Zhao, and J. B. Jonas, 'Tuberculous uveitis in China', *Acta Ophthalmol*, vol. 92, no. 5, 2014, doi: 10.1111/aos.12351.

[22] Alvarez GG, Roth VR, Hodge W. Ocular tuberculosis: diagnostic and treatment challenges. Int J Infect Dis Jul. 2009;13(4):432–5. https://doi.org/10.1016/j.ijid.2008.09.018.

[23] Huebner RE, Schein MF, Bass JB. 'The Tuberculin Skin Test' 1993.

[24] R. Long, 'The Canadian Lung Association/Canadian Thoracic Society and tuberculosis prevention and control', 2007.

[25] Redfield RR, et al. 'Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers Association and CDC. 2020 Morbidity and Mortality Weekly Report Recommendations and Reports Centers for Disease Control and Prevention MMWR Editorial and Production Staff (Serials) MMWR Editorial Board'. 2020.

[26] Gülbay BE, et al. Side effects due to primary antituberculosis drugs during the initial phase of therapy in 1149 hospitalized patients for tuberculosis. Respir Med Oct. 2006;100(10):1834–42. https://doi.org/10.1016/j.rmed.2006.01.014.

[27] R. Bansal, A. Gupta, V. Gupta, M. R. Dogra, P. Bambery, and S. K. Arora, 'Role of Anti-Tubercular Therapy in Uveitis With Latent/Manifest Tuberculosis', *Am J Ophthalmol*, vol. 146, no. 5, 2008, doi: 10.1016/j.ajo.2008.06.011.

[28] Morimura Y, et al. 'Tuberculin skin testing in uveitis patients and treatment of presumed intraocular tuberculosis in. Japan' 2002.

[29] F. I. Shakarchi, 'Ocular tuberculosis: Current perspectives', *Clinical Ophthalmology*, vol. 9. Dove Medical Press Ltd, pp. 2223–2227, Nov. 26, 2015. doi: 10.2147/OPTH.S65254.

[30] Lou SM, et al. Lack of consensus in the diagnosis and treatment for ocular tuberculosis among uveitis specialists. Ocul Immunol Inflamm Feb. 2015;23(1): 25–31. https://doi.org/10.3109/09273948.2014.926936.

[31] Agrawal R, et al. The role of anti-tubercular therapy in patients with presumed ocular tuberculosis. Ocul Immunol Inflamm Feb. 2015;23(1):40–6. https://doi.org/10.3109/09273948.2014.986584.

[32] Ang M, Hedayatfar A, Wong W, Chee SP. Duration of anti-tubercular therapy in uveitis associated with latent tuberculosis: A case-control study. Br J Ophthalmol Mar. 2012;96(3):332–6. https://doi.org/10.1136/bjophthalmol-2011-300209.

[33] Y. Fernández Zamora, L. Peixoto Finamor, L. M. P Silva, D. S. Rodrigues, R. P. Casaroli-Marano, and C. Muccioli, 'Clinical features and management of presumed ocular tuberculosis: A long-term follow-up cohort study in a tertiary referral center in Brazil', *Eur J Ophthalmol*, vol. 32, no. 4, pp. 2181–2188, Jul. 2022, doi: 10.1177/11206721211044624.

[34] Agrawal R, et al. Collaborative ocular tuberculosis study consensus guidelines on the management of tubercular uveitis-report 1: guidelines for initiating antitubercular therapy in tubercular choroiditis. Ophthalmology 2021;128(2): 266–76.