Original Article

Spectrum of Ocular Tuberculosis in Tertiary Care Hospitals of Khyber Pakhtunkhwa Peshawar

PJO – Official Journal of Ophthalmological Society of Pakistan

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ABSTRACT

Purpose: To describe the spectrum of ocular tuberculosis (TB) and highlight the difficulty in diagnosis and treatment of such cases encountered in a tertiary care hospital of Peshawar, Pakistan.

Study Design: Descriptive Case series.

Place and Duration of Study: Khyber teaching hospital MTI Peshawar from Jan 2021 till July 2022.

Methods: Eleven cases with Ocular tuberculosis are described. At presentation, complete history was taken and detailed examination was done including fundus examination and OCT macula. For diagnosis, a combination of Tuberculin skin test (TST) and QuantiFERON-Gold was performed. On the basis of results of both tests Anti-TB treatment (ATT) was started and continued for an average of 9 months.

Results: This study highlights the diverse ocular manifestations of TB in patients, even without a known history of systemic disease. Among 11 patients, 3 presented with panuveitis, 6 with posterior uveitis, and 2 with serpiginous-like choroidopathy with uveitis. Notably, only 2 had a known history of systemic TB. The patients were treated primarily with Anti-Tuberculosis Therapy (ATT) along with steroids or other adjunct therapies. Most cases showed improved vision and stable disease post-treatment, with visual acuity ranging from 6/24 to 6/6. However, two patients were lost to follow-up, leaving their outcomes unknown.

Conclusion: In this case series, we explore different cases of Ocular Tuberculosis (OTB) seen at a busy hospital in Peshawar, Pakistan. There are variety of symptoms with which the patients present. The combined use of TST and QuantiFERON-Gold proved an effective and affordable approach for diagnosis and timely initiation of ATT in ocular TB.

Key words: Ocular Tuberculosis, Uveitis, Serpiginous like Choroiditis, Panuveitis, Tuberculin Skin Test, QuantiFERON-Gold.

How to Cite this Article: Bibi H, Zafar F, Iqbal M, Tanveer S, Luqman F. Spectrum of Ocular Tuberculosis in Tertiary Care Hospitals of Khyber Pakhtunkhwa Peshawar. 2024;40(4):376-384. **Doi: 10.36351/pjo.v40i4.1805**

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Received: January 28, 2024
Accepted: September 24, 2024

INTRODUCTION

Across the globe, the spectrum of tuberculosis (TB) casts a long shadow, claiming countless lives each year. In Pakistan, this infectious entity holds a particularly strong grip, ranking it fifth among high-burden countries (EMRO, WHO).[1] This phenomenon, known as ocular tuberculosis (OTB), presents a complex diagnostic puzzle, with its prevalence fluctuating from a whisper of 1% in pulmonary cases to roaring 20% in those battling extrapulmonary forms.[2,3] Gupta et al and Cunningham JR et al, boldly tackle this diagnostic challenge in their respective studies.[4,5] Their framework recognizes the powerful telltale signs like retinal perivasculitis and multifocal serpiginous choroiditis, which boast predictive values rising as high as 90%. OTB tuberculosis is more complex than just these two aspects. It involves

various elements like granulomas, scleritis, and interstitial keratitis and tubercles in the choroid. There are also adhesions forming between the iris and lens (posterior synechiae), damage to the nerves in the eye (optic neuropathy), and signs of inflammation on the optic disc, resembling a granuloma. All of these details hint at the quiet invasion of tuberculosis in the eye.[4]

In this case series, we embark on a journey through the diverse landscapes of OTB encountered at a bustling tertiary care hospital in Peshawar, Pakistan. In this series we will observe a diverse range of clinical manifestations and delve into the diagnostic tools used to diagnose this disease.

Case 1

A 50-year-old female, known case of secondary open angle glaucoma with right fully cupped optic disc presented with sudden decrease in vision of left eye for 1 week with associated photophobia. On examination (O/E) visual acuity (VA) was perception of light (PL+) right eye (OD) and 6/24 left eye (OS) with no further improvement on refraction. Relative afferent pupillary defect (RAPD) was noted in OD. Anterior chamber (AC) was deep and quiet in both eyes (OU). Intraocular pressure (IOP) was 38 OD and 18 OS. +2 cells in vitreous of left eye was noted while posterior segment of right eye was clear beside fully cupped disc while left optic disc was swollen.

VF 30-2 were done and showed generalized decreased sensitivity in right eye and inferior altitudinal defect OS. QuantiFERON-TB Gold (QFT) was positive. Mantoux test along with baseline investigations were unremarkable. Patient was started on oral Anti-Tuberculous Therapy (ATT) after pulmonologist's consultation. Systemic intravenous methylprednisolone 1gm was given for 3 days followed by tapering dose of oral steroids for 11 days. Patient was followed up after 2 months. VA was markedly improved to 6/12 OS. A/C was deep and quiet in both eyes. Vitreous was clear in both eyes and optic nerve revealed improved swelling in OS.ATT was continued for 6 months with tapering oral steroids. Marked improvement in VA and optic nerve functions was observed. The final VA was PL+ OD and 6/9 OS with no RAPD left eye.

Case 2

A 34-years-old young male with no known co-morbidities presented with sudden painless decrease in vision OD for 3 days. On examination, VA was 6/9 OD and 6/12 OS. Both pupils were reactive to light. IOP was 12 OU. Both the anterior chambers were deep and quiet. Posterior segment was unremarkable OD while +2 cells were noted in OS vitreous with inferotemporal (IT) BRVO and macular star. CT Macula showed macular edema. QFT was positive, rest of the investigations were within normal range. Intravitreal Bevacizumab was given OS and the patient was started on ATT after the pulmonologist's review. The patient was reviewed after 2 months when VA was 6/6p OD and 6/6 OS.IOP was 14OU.The posterior segment of the left eye showed resolving retinal blot hemorrhages along the inferotemporal vascular arcade. Rest of the anterior and posterior segment examination was unremarkable. After completing ATT for 6 months, OS remained stable with no remarkable findings and VA of 6/6.

Case 3

A 24-years-old young male presented with sudden painless decrease in vision OD with floaters for 3 days. BCVA was 6/12 OD and 6/6 OS. Both pupils were reactive to light. IOP was 15 OU. Anterior and posterior segment were unremarkable OS but +2 cells in both the anterior chamber and vitreous with yellowish placoid lesion between optic disc and fovea was noted OD.

QFT was positive. Mantoux was 6mm after 72 hours whereas rest of the investigations were unremarkable. CT macula showed subretinal fluid and disruption of outer retinal layers OD while OS was unremarkable **(Figure 1).**

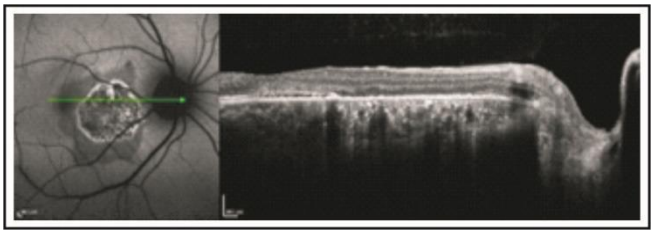

Figure-1: OD BAF image on left side shows a hypo-autofluorescent placoid lesion with central hyper-autofluorescence and well-defined area of hyper-autofluorescence around the placoid lesion. OCT macula on right shows disruption of outer retinal layers and slither of subretinal fluid.

Patient was started on ATT and right sub-tenon triamcinolone acetonide (ST-TCA) was given. After 02 weeks patient presented again with decrease vision

OD. VA was 6/12 OD and 6/9 OS. IOP was 12 OD and 14 OS. Anterior segments were unremarkable in both eyes. Vitreous was clear in both eyes. Posterior pole left eye showed the same placoid lesion between Optic disc and fovea with increase in subretinal fluid on OCT from the previous visit. Oral steroids were started at the dose of 0.75mg/kg body weight along with ATT. Patient was followed 4 weekly for 2 months and vision improved to 6/9 OD and 6/6 OS. Hyper-autofluorescence was seen around the margins of the placoid lesion in the first 5 months followed by the complete hypo-autofluorescence of the entire lesion. The patient was kept on ATT for 9 months in consultation with the physician. The final visual was 6/6p OD and 6/6 OS after the completion of ATT with no active lesion in both the eyes.

Case 4

A 34-years-old female presented with decrease in vision OS with associated photophobia for 1 week. BCVA was 6/6 OD and 6/18p OS. Anterior and posterior segment was quiet OD while there were broad anterior synechiae OS. Vitreous had snowballs inferiorly with swollen optic disc and macular edema OS. Mantoux test was positive (16mm induration), rest of the investigations were unremarkable. QFT was advised but the patient did not comply because of financial constraints. Patient was started on ATT and systemic steroids; however, the patient was lost to follow-up.

Case 5

A 52-years-old female presented with photophobia, red eye and decrease in vision OD for the past 1 month with decreased vision OS for 2 years. BCVA was 6/60 OD and PL+ OS. RAPD was positive OS. IOP was 17mm Hg OU. Cornea was clear OD and KPs were noted OS. Anterior segment was deep and quiet OU. PSC+3 was noted OD with pre-lenticular membrane while there was mature cataract OS. Posterior segment showed snowballs with normal optic disc and normal macular reflex OD. No fundus view was available OS.B-scan revealed vitreous opacities with flat retina OS. Mantoux was negative. QFT was positive and rest of the investigations were unremarkable. Patient was started on ATT and was given sub-tenon triamcinolone. At follow up, vision improved to 6/24 OD and no improvement OS. Both anterior and posterior segments were quiet OU. Right cataract extraction with intraocular lens implantation was done under steroid cover once the eye was quiet for 3 months. Final VA was 6/12 OD. However, OCT revealed disruption of IS/OS junction and loss of photoreceptors. Patient completed the ATT for 9 months with no recurrence.

Case 6

A 25-years-old male presented with the complaint of blurred vision and floaters OD for 3 months. He had been diagnosed with posterior uveitis and started on topical and oral steroids. The patient showed improvement within 45 days but presented again with decreased vision, photophobia and redness OD. Patient was kept on oral dexamethasone 1mg/kg body weight with recurrence.VA was 6/60 OD and 6/6 OS with no further improvement on refraction. IOP was 10 OU. Patient had KPs, +3 cells in A/C, +3 cells in vitreous and snow banking along with serous retinal detachment (SRD) on fundus examination OD. OS was unremarkable. ESR was raised 52mm/1st hour (cut off limit of 15mm/1st hour). Mantoux Test was negative. QFT was positive. Patient was started on ATT and sub-tenon triamcinolone was given. Patient was followed 2 weekly (Figure 2**)**.VA was improved to 6/18 OD after 2 weeks. Cornea showed KPs, no cells in A/C, +1 cells in vitreous with the improvement in serous retinal detachment. No remarkable findings were there in left eye. Patient was lost to follow-up after initial 2 visits.

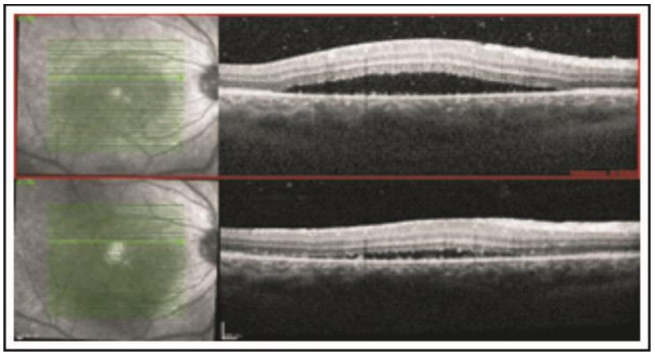

Figure 2: Right Eye. OCT macula. The above image (red outlined) is pretreatment OCT macular showing serous fluid. The image underneath is post-treatment OCT macula showing marked decrease in Serous fluid.

Case 7

A 35-years-old male presented with decrease in vision left eye for 10 days. O/E VA was 6/9p OD and 6/36p OS with improvement to 6/6 OD and 6/24p OS on refraction. Both the anterior and posterior segments were unremarkable except NS++OD. OS anterior

segment was unremarkable, +2 cells OS vitreous cells and swollen optic disc along with swelling of nerve fiber layer superior and temporal to the disc with macular exudates. OCT RNFL showed swollen optic disc in OS.OCT (M) showed a slither of subretinal fluid and intraretinal exudates in OS.

VF 30-2 was done and were normal in OD but inferior altitudinal defects OS.

QFT turned out positive, rest of the laboratory investigations were unremarkable. Diagnosis of left Tuberculous Optic Neuritis/Neuroretinitis was made and patient was started on oral ATT and was given left sub-tenon triamcinolone.

Patient was called for 2 monthly follow up with no relapse and VA of 6/9 and 6/12p OS with unremarkable findings right eye except NS++ lens opacities. Left A/C was quiet, +1 cells in vitreous with the decrease in left optic disc swelling. Patient continued to take ATT for 6 months in consultation with the physician. Final VA after completion of treatment was 6/9 OU with no recurrence.

Case 8

A 55-year-old male presented with decrease in vision OD for the past 2 years which worsened over the last 20 days with floaters. BCVA was 6/60 OD and 6/6p OS. Anterior segments were unremarkable OU. However, +2 cells were noted in vitreous OD. There was choroiditis with evolving and burnt-out lesions on the posterior pole. Patient was managed with systemic dexamethasone but had multiple recurrences. QFT was positive. OCT OD revealed photoreceptor layer loss with disrupted outer retinal layers and intraretinal cystoid spaces. Serpiginous like choroidopathy with hypo-autofluorescent snakelike lesions on BAF were seen in OD. Guarded prognosis was explained to the patient and ATT was advised but the patient was lost to follow-up.

Case 9

A 22-year-old female with a history of TB contact and treated Hepatitis B presented with reduced vision, pain, redness, watering, and floaters OS for 2 months. Her BCVA was 6/6 OD and 6/60 OS. Both pupils were reactive, and intraocular pressure was 14 mmHg OD and 16 mmHg OS. Examination revealed sectoral conjunctival hyperemia, anterior vitreous cells, and vitreous haze in OS, with an unremarkable OD. Ultra-wide field imaging confirmed vitritis in OS. Her ESR was 22 mm in the first hour, hepatitis B surface antigen was positive, and QFT test was positive. A diagnosis of TB scleritis and vitritis in OS was made. Treatment included Flurbiprofen, Dexamethasone eye drops, sub-tenon triamcinolone (ST TCA), anti-tuberculosis therapy (ATT), and Entacavir for Hepatitis B. After 4 weeks, visual acuity improved to 6/9 OS with improved scleritis and reduced vitreous inflammation. At 6 weeks, her vision remained stable. However, at 10 weeks, she reported difficulty focusing, with VA of 6/6 OD and 6/18 OS. Mild vitreous haze and macular exudates were observed, and OCT revealed new macular edema. Treatment was continued, including sub-tenon triamcinolone.

After 6 months of ATT, her final VA was 6/9 OS, with no further disease activity.

Case 10

A 50-years-old male, known hypertensive and diabetic for the past 2 years presented with decreased vision OU for 6 years with associated on and off red eye and photophobia. VA was 6/9 OD and 6/60 OS improving to 6/6 OD with refraction and no further improvement OS. There were +3 cells in vitreous and chorioretinitis scars and unremarkable optic disc OD. OS posterior segment showed chorio-retinal burnt-out peri-papillary and posterior pole scars with no activity in vitreous.

OD sub-tenon triamcinolone was given. OCT (M) both eyes showed subretinal fibrosis along with photoreceptor loss and intraretinal cystoids spaces OD (Figure 3). QFT was positive and other baseline investigations were unremarkable. ATT was started. At 4 months, patient had photophobia and headache. BCVA was 6/9 OD and CF at 3 meters OS. There were +1 cells in anterior chamber, +3 cells in the vitreous and chorio-retinal scars on fundus OD. Both the anterior and posterior segments were unremarkable OS. Patient was given OD sub-tenon triamcinolone and started on topical prednisolone in tapering dose

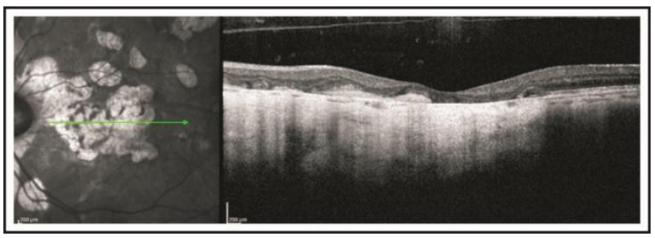

Figure 3: OD IR image on left shows areas of chorio-retinal atrophy over green arrow. Image on right is OCT macula showing subretinal fibrosis with photoreceptor loss.

Table 1: *Summary of the Ocular Tuberculosis: Presenting Symptoms and Ocular Findings.*

Case	Age/Sex	Presenting symptoms	VA-OD, OS	Ocular Findings	Investigations
1.	50F	Sudden vision loss LE, photophobia	PL+,6/24	Swollen LO, vitreous cells	QFT (+) Mantoux (-)
2.	34M	Sudden painless vision loss LE	6/9,6/12	IT BRVO, Macular star, vitreous cells	QFT (+) OCT: Macular edema LE
3.	24M	Sudden vision loss RE, floaters	6/18,6/6	Placoid lesion near OD Optic disc	QFT (+) Mantoux (+) OCT: subretinal fluid OD
4.	34F	Vision loss LE, photophobia	6/9,6/18p	Broad anterior synechiae, vitreous snowballs, swollen OD and macula edema	Mantoux (+)
5.	52F	Vision loss RE, Photophobia, red eye	6/60, PL+	PSC+3 OD, pre-lenticular membrane, OD vitreous snowballs, mature cataract OS	QFT (+) Mantoux (-)
6.	25M	Blurred vision, Floaters RE	6/60,6/6	KPs, vitreous cells, snow-banking, serous retinal detachment	QFT (+) Mantoux (-)
7.	35M	Vision loss LE	6/9p,6/36p	Swollen left OD, vitreous cells, macular exudates	QFT (+) OCT RNFL and macula abnormalities
8.	55M	Vision loss RE, floaters	6/60,6/6p	Choroiditis with evolving and burnt-out lesions OD	QFT (+) OCT Macula: PR layer loss
9.	22F	Reduced vision LE, pain, redness, watering, floaters	6/6,6/60	Scleritis, vitreous haze and snowballs OS	QFT (+) ESR raised HBsAg (+)
10.	50M	Decreased vision BE, red eye, photophobia	6/9,6/60	Chorio-retinal scars BE, vitreous cells OD	QFT (+)
11.	26M	Blurred vision, Photophobia BE	6/9, 6/18	Mild flare AC and pigment on OS lens	QFT (+)

Legends: VA: Visual acuity, LE: Left eye, RE: Right eye, OD: Right eye, OS: Left eye, QFT: QuantiFERON-TB Gold, ATT: Anti-tuberculous therapy, IT BRVO: Inferior temporal branch retinal vein occlusion, PSC: Posterior subcapsular cataract, OCT: Optical coherence tomography.

Table 2: *Ocular Tuberculosis Cases: Treatment and Response Summary*.

Cases	Treatment Provided	Response
1.	Oral ATT, IV methylprednisolone	Improved (VA 6/12 OD), quiet AC, clear vitreous and reduced Optic Disc swelling
2.	Intravitreal Bevacizumab, ATT	Marked improvement (stable VA 6/6pOD and 6/6 OS after ATT
3.	Oral ATT, Oral Steroids and sub tenon triamcinolone	Improved VA 6/9 OD. Stable disease after ATT
4.	Oral ATT, systemic steroids (lost to follow-up)	Outcome unknown
5.	Oral ATT, sub tenon triamcinolone and cataract extraction	Improved VA 6/24 OD. Stable disease after ATT
6.	Oral ATT, sub tenon triamcinolone	Improved VA 6/18 OD Lost to follow-up
7.	Oral ATT, sub tenon triamcinolone	Final VA 6/9 OU with no recurrence
8.	ATT (lost to follow-up)	Outcome unknown
9.	Tab. Flurbiprofen, E/D dexamethasone, S/T triamcinolone and ATT	Improved VA 6/9 OS. Stable disease after ATT
10.	Oral ATT, S/T triamcinolone	Stable burnt-out lesion with persistent Macular edema
11.	Topical prednisolone, timolol–dorzolamide, ATT	Improved VA 6/6 OU with no recurrence

Legends: VA: Visual acuity (presented as OD/OS), A/C: Anterior chamber, ST TCA: Sub-Tenon Triamcinolone Acetonide.

and cyclopentolate TDS along with ATT. OCT (M) was advised and no new cystoid spaces were noted on follow up. The patient had subretinal fibrosis and photoreceptor loss in both eyes.

Case 11

A 26-years-old young male presented with blurred vision and photophobia both eyes for the past 6 months. BCVA was 6/6 OU. Anterior and posterior segments were unremarkable OD. There was mild flare in the anterior chamber and pigments on the lens OS. However, posterior segment was unremarkable. IOP was 25 OD and 40 OS. Patient was started on tapering dose of topical prednisolone and timolol plus

dorzolamide combination BD in OS and topical dexamethasone was stopped. QFT was positive. ATT was started. After 1 month, VA was 6/9 OU and IOP was 12 OU. On completing ATT after 6 months the final VA was 6/6 both eyes and no relapse was noted.

DISCUSSION

We present 11 cases of Ocular Tuberculosis, 8 among them presented with posterior uveitis and its sequelae; commonest being maculopathy (macular edema). None of the case's had pulmonary involvement and likewise the inflammatory markers were in normal range. The presenting features of these patients were panuveitis (3 patients), posterior uveitis (7 patients) and serpiginous like choroidopathy associated with uveitis (2 patients). Of these 11 cases, one had a known history of systemic tuberculosis, while the ocular findings in the other cases were the presenting manifestation of systemic tuberculosis. Multi-drug ATT regimen was employed in all cases for a mean of 9 months (median 6 months, range 6–12 months).

Diagnosis of ocular TB is a challenge. According to Gupta V, et al, Acid-Fast Bacilli (AFB) detected by Ziehl-Neelsen or Auramine–rhodamine stains have a low yield from the aqueous or vitreous.[3] An even lower yield is obtained by cultures, that are laborious and may take 6–8 weeks.[6] In addition, the histopathological evidence of necrotizing granulomatous inflammation from an ocular biopsy is rarer to obtain, which needs to be reasonably patent to support OTB diagnosis according to Wroblewski et al and Biswas J, et al.[7,8] The low sample volume and the pauci-bacillary nature of the disease challenges the techniques used to isolate Mycobacterium tuberculosis (MTB) from ocular samples.[9]

Hence, the results with low positive yield may be explained by the second hypothesis of OTB being an immune-mediated mechanism of inflammation as analyzed by Ang M, et al, where the author concluded that uveitis associated with TB and responding to ATT do not have an active ocular tuberculous infection, but rather an autoimmune-related ocular inflammation that may be triggered by TB.[10]

Nucleic acid amplification test is another modality aimed to detect MTB DNA from ocular sample but it lacks comparisons with gold standard and is unable to distinguish latent from active infection. It has variable specificities and sensitivities and is affected by sample volume, method of DNA extraction and variable other factors as highlighted by Parashar D et al and Arora SK et al.[11,12]

Sarvananthan N, et al, in their study deduced that in 70% of the OTB patients, the images obtained by the chest X-ray (CXR) is normal.[13] Radiological signs such as hilar lymphadenopathy and parenchymal scarring may not be specific of pulmonary TB.[14]

Immunological tests such as the tuberculin skin test (TST) lack specificity and do not distinguish latent from active TB disease.[15] Newer blood tests are objective, reproducible and require only one visit, such as the interferon-γ release assays (IGRA) that include the QuantiFERON-Gold In-Tube (Cellestis, Carnegie, Australia) or T-SPOT.TB (Oxford Immunotec, Abingdon, UK) have gained popularity in recent years.[16,17] Ang M, et al, has shown that IGRA have better sensitivities and specificities compared with the TST. But with regard to the screening and diagnosis of TB there is currently no consensus on its use (single versus combination with TST or CXR).[17] Due to difficulty in its diagnosis, the investigative approach to OTB is heterogeneous worldwide.[18] For example, TST may be preferred over IGRA in low/middle-income countries, and CT chest may be more commonly ordered in high-income countries to detect subtle pulmonary involvement.[19] The most cost effective diagnosis of TB is the combination of an IGRA with TST and that is what we have found in our own study as well.[20]

Currently no reconciliation has been done on the clinical approach to the diagnosis of OTB but most clinicians agree that careful ocular evaluation provides an important role. In some endemic regions, the identification of clinical signs such as broad-based synechiae, retinal vasculitis, multifocal choroiditis and serpiginous choroiditis may be suitable. A patients may present with a whole spectrum of clinical signs due to the protean nature of OTB infection that is, from granuloma, nodular scleritis and interstitial keratitis in the anterior segment to caseating granulomas in the ciliary body or choroidal tubercles in the posterior segment.[4] A suggested clinical approach involves first identifying these suggestive clinical signs, followed by a step-ladder approach to confirm the diagnosis: 1) after the exclusion of other causes of uveitis, 2) the results of TST, IGRA, CXR or CT chest and (3) biopsy with molecular testing would be considered, before confirming a 'definite' case of OTB.[21]

According to National Guidelines for control of tuberculosis in Pakistan, revised 2019, chapter 8, all newly diagnosed patients should undergo rifampicin sensitivity testing, before initiating ATT, by Xpert testing. The Guidelines recommend four essential 1st line ATT drugs namely Isoniazid, Ethambutol, Pyrazinamide and Rifampicin. These 04 drugs are considered as Standard First Line Treatment regimen. However, this is not effective in case of rifampicin resistance (RR) or multidrug resistance cases (MDR), the management of which is beyond scope of this article. The guidelines highlight use of combination antimicrobial therapy in fixed dose combination according to patient's body weight, to have a fixed dosing time and to employ directly observed treatment (DOT) technique in which the patient is under a caretaker supervision throughout the duration of treatment to ensure proper management and to avoid risk of drug resistance. Recommended duration of treatment is 06 months in these guidelines, which has minimal chance of relapse and the entire treatment duration is split into two phases: 1) Initial phase for first 02 months in which all 04 agents are given and 2) Continuation phase of 04 months in which only Isoniazid and Rifampicin are administrated. However, it is critical to note that exact treatment regimen, drug agents and dosing and total treatment duration need to be tailored according to patient's sensitivity and response in collaboration with infectious diseases specialist. It is also recommended in the guidelines that systemic steroids be used in cases of extrapulmonary TB in tapering dose for 6-8 weeks.[21]

Lack of treatment response may be because of drug resistance, which is reported in up to 40% of patients with definite OTB, especially in patients originating from endemic countries. Pakistan ranks 4th among 30 high Drug Resistant (DR) TB burden countries in the world and thus drug resistance and lack of treatment response is frequently encountered. DOT is one such management technique to mitigate the risk of drug resistance as discussed in detail in the guidelines, chapter 9.[21]

Another important aspect of ATT is paradoxical worsening which is defined as "a paradoxical reaction" while on ATT and consisting of clinical or radiological worsening of pre-existing TB lesions or the development of new lesions in patients who showed an initial response or improvement with treatment.[22] These paradoxical reactions are common after initiating ATT and are most common in extra pulmonary TB. Variety of underlying mechanisms for this worsening have been proposed which include delayed hypersensitivity, decreased suppressor mechanism and increased response to mycobacterial antigens mediated by host's immune reaction. It is therefore important that clinician be aware of this aspect of disease and its management. Of challenge here is the recognition of deterioration due to paradoxical reaction, from worsening that results from treatment failure, drug resistance, poor compliance or secondary diagnosis.

A case report by Yilmaz et al described a case of paradoxical worsening of choroidal lesions with overlying serous retinal detachment in young Turkish patient treated with ATT who after 1 month of ATT initiation showed enlargement of choroidal lesion with worsening of VA and described a localized Jarisch–Herxheimer like reaction for this worsening.[23] Although first described for syphilis, this reaction has also been noted in various other bacterial infections. Similar reports of paradoxical worsening have also been described by Cheung and Chee in 2009 where they stated worsening of chorioretinitis following initiation with ATT. In order to combat this dilemma, it has been suggested by Ganesh S.K et al and National guidelines for TB control, (revised, 2019), that systemic steroids in tapering dose be used in OTB cases.[21,22]

In conclusion, ocular tuberculosis can have variable clinical manifestations and occasionally appears as an intraocular tumor or other inflammatory conditions. A high degree of clinical suspicion is important, especially in developing countries. In our clinic, a combined Mantoux and QuantiFERON-Gold test offers the most cost-effective approach for OTB diagnosis, as suggested in our research.

Treatment typically involves anti-tuberculous therapy (ATT) for 9 months, leading to symptom resolution. We monitor patients for complications, with macular edema being the most common side effect. This paradoxical worsening of vision may be a Jarisch-Herxheimer-like reaction, manageable with steroids.[22,23]

CONCLUSION

Ocular tuberculosis (OTB) poses a diagnostic challenge due to its varied and often non-suggestive symptoms. Several factors contribute to this:

- Isolated ocular manifestation: Patients may lack

systemic TB symptoms.

- Lack of standardized diagnosis: No consensus exists on the clinical approach.
- Biopsy limitations: Small sample size and pauci-bacillary nature hinder cultures.
- Mimicry of malignancy: OTB can resemble intraocular tumors.

Funding: This study was not funded by any organization.

Patient's Consent: Researchers followed the guidelines set forth in the Declaration of Helsinki.

Conflict of Interest: Authors declared no conflict of interest.

Ethical Approval: The study was approved by the Institutional review board/Ethical review board **(02/DME/KMC)**.

ACKNOWLEDGMENTS

The authors would like to acknowledge the specialist opinion and supervision of Dr. Mustafa Iqbal.

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