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Original Research Article

Ocular Manifestations in Patients with Extrapulmonary Tuberculosis

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ABSTRACT :

Introduction : The study was done to find out the ocular manifestation in patients with extrapulmonary tuberculosis visiting a tertiary eye centre. **Methods:** A hospital based descriptive observational study was done among newly diagnosed extrapulmonary tuberculosis cases after approval from the institutional review board. After a detailed ocular evaluation, findings including patient demographics, presenting complaints, best corrected visual acuity, colour vision, contrast sensitivity, Goldman visual field and Optical Coherence tomography Retinal nerve fibre layer analysis of the optic nerve head were recorded in a semi-structured proforma. Data were expressed in frequency and percentage. **Results:** Out of 50 eyes of 25 patients included in the study, the mean age was 26.92±14.2 years (11-73 years). Sixty four percent were female. Two cases had ocular findings at the time of diagnosis. One case of tuberculous lymphadenitis had phlyctenular conjunctivitis and one case of tubercular meningitis had diplopia with right lateral rectus muscle paresis secondary to raised intracranial pressure. All the patients had best corrected visual acuity better than 6/12 at presentation. Color vision was normal in 72% cases in both eyes. Goldman visual field done at presentation were normal in both eyes in 88% cases while retinal nerve fibre layer thickness and contrast sensitivity were normal in all cases. **Conclusion:** The prevalence of ocular findings in patients with extrapulmonary tuberculosis was 8% in this study. Ocular examination is important in cases with extrapulmonary tuberculosis since a significant number of cases have ocular findings.

Keywords: Cranial nerve palsy, Extrapulmonary tuberculosis, Ocular findings, Phlyctenular conjunctivitis

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INTRODUCTION :

Tuberculosis (TB) is an airborne infectious disease caused by *Mycobacterium tuberculosis* (MTB) that most commonly affects the lungs. However, extrapulmonary manifestations of TB can affect the eye and surrounding orbital tissues. Extra-pulmonary TB involves locations such as the lymph nodes, pleura, central nervous system and the eyes and accounts for around 15% of TB.[1] TB occurrence is a result of a complex interaction between the host immune response

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and the bacillus leading to either clearance of the bacillus, latent infection, subclinical disease or active disease.

In a previous study from Nepal, the authors had reported ocular manifestations in 2.6% of the patients with TB under anti-tubercular therapy (ATT); 1.2% in cases of pulmonary TB and 5.3% in extra pulmonary TB cases.[2] Tuberculosis can affect nearly any tissue in the eye, and a high index of suspicion is required for accurate diagnosis.[3] Ocular TB shares many of the characteristics of TB elsewhere in the body, and when MTB causes direct infection of the eye, the predominant structures involved are the uvea and retina.[3] Uveitis, papilloedema (in cases of tubercular meningitis due to raised intracranial pressure), oculomotor nerve paresis (commonly the sixth cranial nerve with associated raised intracranial pressure in cases with TB meningitis), scleritis and episcleritis were the common ocular findings in cases with extrapulmonary tuberculosis in one study done in Nepal.[2] This observational study was done to find out the ocular manifestation in patients with extrapulmonary tuberculosis taking ATT visiting a tertiary eye centre.

METHODS:

A hospital-based descriptive observational study was done among newly diagnosed extrapulmonary TB cases taking ATT from their local directly observed treatment short-course (DOTS) centre for less than one month visiting B.P. Koirala Lions Center for Ophthalmic Studies (BPKLCOS), Tribhuvan University Teaching Hospital (TUTH), Kathmandu Nepal for a duration of 22 months from September 2019 to June 2021 after approval from institutional review board of Institute of Medicine (IRC no -67/(6-11)E2/076/077). Patients who had pre-existing ophthalmologic problems (diabetic retinopathy, visually significant cataract, glaucoma or optic nerve head abnormalities), ocular TB cases and drug resistant TB cases were excluded.

Detail ocular evaluation of the cases was then conducted by an ophthalmologist. Best Corrected Visual acuity (BCVA) was assessed by Snellen Vision Chart with multiple optotypes. Any evidence of ocular misalignment and abnormality of extra-ocular movement was evaluated with extra ocular motility and cover tests. Periorbital area and anterior segment was first examined with diffuse torchlight. Haag Streit 900 slit lamp was used in appropriate magnification and illumination for further evaluation of anterior and posterior segments. Posterior vitreous and fundus were evaluated under dilatation using 90 diopters and 20 diopters Volk aspheric lenses. Any evidence of posterior uveitis, retinal vasculitis and optic nerve abnormalities like papilloedema or optic neuropathy were also evaluated.

Color vision was tested monocularly with the Farnsworth Dichotomous D-15 test at arm's length. Contrast sensitivity was recorded using Pelli-Robson contrast sensitivity chart at 1m distance. Visual field test was done using Goldman visual fields (Takagi company) at 30 cm. Optical coherence tomography (OCT) of optic nerve head and retinal nerve fiber layer was performed. Peripapillary retinal nerve fiber layer (RNFL) thickness of each eye was measured for the four quadrants using spectral-domain optical coherence tomography (SD-OCT; Spectralis® OCT, Heidelberg Engineering, Heidelberg, Germany). OCT test results with a good signal strength and good centration were included for analysis. Confidentiality of the participants was ensured by de-identifying the data in records and securing them in password protected software.

Data were analyzed using Statistical Package for Social Sciences (SPSS^{TM}) version 14 software. Data were presented in frequency and percentage. Continuous variables were

expressed in means with standard deviation (SD).

RESULTS:

A total of 50 eyes of 25 patients meeting the inclusion criteria were included in our study. The mean age ± SD of the patients was 26.9 ± 14.2 years (11-73 years). Out of them, 64% were female.

The mean weight ± SD of the patients in the study was 52.4 ± 9.9 kilograms. Out of different types of extra pulmonary TB, tubercular lymphadenitis was present in 44% of the patients (Table 1).

Table 1: Distribution of different categories of extrapulmonary tuberculosis (N=25)

Types of Tuberculosis	Frequency (%)
Endometrial tuberculosis	1 (4)
Renal tuberculosis	1 (4)
Pott's spine	1 (4)
Tuberculous meningitis	2 (8)
Tuberculous Pericarditis	2 (8)
Tuberculous osteomyelitis	3 (12)
Abdominal tuberculosis	4 (16)
Tubercular lymphadenitis	11 (44)

Out of the 25 cases of extrapulmonary TB, only two cases had ocular findings at the time of diagnosis. One case of TB lymphadenitis had phlyctenular conjunctivitis and one case of TB meningitis had diplopia with right lateral rectus muscle paresis secondary to raised intracranial pressure. All the patients had best corrected visual acuity better than 6/12 at presentation except for one case that had history of eye injury in childhood in the left eye and had no perception of light in the eye (Table 2). Table 3 shows the color vision and goldman visual fields of the patients and Table 4 shows the distribution of OCT RNFL thickness of the patients taking ATT. The mean contrast sensitivity in the right eye was 1.9 ± 0.1 log units (1.50-2.25 log units) and 1.9 ± 0.1 log units (1.5-2.2 log units) in the left eye.

DISCUSSION:

Tuberculosis is still one of the major causes of morbidity in Nepal with serious public health implications. Clinical manifestations of TB may vary and depend on the status of host immunity, environmental factors and microbial factors.[4] Various studies have reported that extrapulmonary TB is on the rise and factors like being female gender, younger age, Human Immuno-deficiency Virus (HIV) co-infection and better diagnostic facilities may be associated with increased incidence and reporting of extrapulmonary TB.[5,6,7] The estimated incidence reported in National TB prevalence survey report 2020 was 245.1 (147.4 - 367.3) per 100,000 population with extrapulmonary TB accounting for 32% of new cases.[8]

Although pulmonary TB is more common than extra-pulmonary TB, studies have shown that ocular manifestations are more common in cases of extra pulmonary TB.[2] Ocular TB is also a type of extrapulmonary TB which can lead to visual loss from the irreversible destruction of intraocular tissues.[3] We did not include cases of primary ocular tuberculosis in this study as our aim was to find the ocular manifestations in other types of extrapulmonary tuberculosis which has been found to affect relatively younger and the economically productive age groups.

In our study, the mean age of the patients with extrapulmonary TB was 26.9 ± 14.2 years (11-73 years). The females accounted for 64% of the cases which is similar to other literature where females and younger age groups were commonly affected by extrapulmonary TB.[5,9] The common types of extrapulmonary TB cases were tubercular lymphadenitis followed by bone TB (Pott's spine and tuberculous osteomyelitis), abdominal TB and tuberculous meningitis.

Table 2: Best Corrected Visual acuity of patients with newly diagnosed extrapulmonary TB (N=25)

BCVA	**Right Eye: Frequency (%)**	**Left eye: Frequency (%)**
NPL*	0 (0)	1 (4)
6/12	0 (0)	2 (8)
6/9	2 (8)	0 (0)
6/6	23 (92)	22 (88)

**BCVA= Best Corrected Visual Acuity; NPL= No Perception of Light*

Table 3: Visual functions of patients with newly diagnosed extrapulmonary TB (N=25)

Variable		Right Eye Frequency (%)	Left Eye Frequency (%)
Colour Vision Test	Normal	18 (72)	18 (72)
	Non specific	7 (28)	6 (24)
	Could not be assessed	0 (0)	1 (4)
Goldmann Visual Field Test	Normal	22 (88)	22 (88)
	Superior Constriction	3 (12)	2 (8)
	Could not be assessed	0 (0)	1 (4)

Table 4: Distribution of OCT RNFL thickness of patients with newly diagnosed extrapulmonary TB

OCT findings (µm) Mean± SD	Right Eye	Left Eye
Superior	135.1 ± 17.9	141.6 ± 18.4
Inferior	138.0 ± 16.9	142.0 ± 19.5
Nasal	83.8 ± 17.7	83.5 ± 16.4
Temporal	72.8 ± 11.6	72.1 ± 14.9
Mean	109.8 ± 13.0	107.4 ± 12.1

All the patients had best corrected visual acuity (BCVA) better than 6/12 at presentation except for one case who had history of eye injury in childhood in the left eye and had no perception of light in the eye. Two cases had BCVA 6/12 in left eye due to cataract. Color vision was normal in 72 % cases in both eyes and the rest had non-specific color vision deficit which was not attributable to TB. Goldman visual field done at presentation were normal in both eyes in 88% cases and showed mild superior

constriction in three and two cases in right eye and left eye respectively. These findings were considered normal as the patients had no visual complaints and rest of ocular examination and visual function were normal. Optical Coherence Tomography (OCT) Retinal nerve fibre layer thickness (RNFL) done at baseline showed normal findings in both eyes.

Two patients had ocular findings. One case was a 16 year old female with TB meningitis with right lateral rectus paresis due to involvement of sixth cranial nerve. Tuberculosis is one of the common etiologies of meningitis in Nepal, more so in children.[10] In tubercular meningitis, there is hematogenous seeding of bacilli to the meninges or brain parenchyma resulting in formation of subpial or subependymal foci of metastatic caseous lesions which have propensity to enlarge and rupture into the subarachnoid spaces, leading to meningitis.[11] Basal meningitis leads to cranial nerve pathologies resulting in paresis or palsy.[11,12] Other studies have also reported that cranial nerve palsies were present in a third to quarter cases of patients with tubercular meningitis at initial presentation with cranial nerve VI to be most commonly affected cranial nerve in tubercular meningitis.[2,10,11,12]

The other case with ocular finding was a 20 year old male with recently diagnosed TB lymphadenitis who had phlyctenular conjunctivitis. Phlyctenulosis is a type IV hypersensitivity response to tuberculous antigen and is an uncommon presentation of TB in the eye.[13] Phlyctenules have been most commonly associated with *Mycobacterium tuberculosis* antigen and a study in India where there is a high prevalence of TB, 76.7% of cases of phlyctenular eye disease was associated with TB.[14]

Small sample size and the cross-sectional nature of the study were some of the limitations of the study. Future studies including a larger sample of TB patients would help identify the true ocular burden of this condition.

CONCLUSION:

The prevalence of ocular findings in patients with extra pulmonary tuberculosis was 8% in this study. Ocular examination is important in cases with extrapulmonary tuberculosis since a significant number of cases have ocular findings. Presence of ocular findings may give us clue to diagnosis in cases with diagnostic challenge which is common is these cases by ocular findings such as phlyctenules in conjunctiva.

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Conflict of Interest: The authors report there are no competing interests to declare.

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