Mode of Presentations and Management of Presumed Tuberculous Uveitis at a Referral Center

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ABSTRACT:

BACKGROUND:

The diagnosis of tuberculous uveitis is often presumptive, because of the difficulty in obtaining microbiological evidence. The diagnosis has to rely on characteristic ocular findings, and possibly a therapeutic treatment trial.

OBJECTIVE:

To illustrate the mode of presentations and management of presumed tuberculous uveitis at a referral eye center in Iraq.

METHOD AND SUBJECTS:

This prospective case series study included patients with presumed ocular tuberculosis presented consecutively at uveitis clinic/ Ibn Al-Haetham teaching eye hospital, from January 2007-January 2013. Ocular tuberculosis was presumed when findings were consistent with possible intraocular tuberculosis, intractable to steroid therapy, and no clinical or laboratory evidence for other causes of uveitis. Strongly positive tuberculin skin test result (more than14 mm area of induration/necrosis) supported the diagnosis, but was not a prerequisite for initiating therapy. All patients were treated with anti tuberculosis therapy. Clinical findings and response on treatment were documented in a special follow up cards.

RESULTS:

64 patients with presumed TB uveitis were included in this study. Mean age of the patients was 35.7 years with no significant sex predominance. Majority of patients were from urban places (79.7%).

Bilateral involvement was recorded in 62 patients. Vitritis was a universal finding, while multifocal choroiditis was the most common fundus lesions (104 eyes; 82.5%).

All patients responded well to anti tuberculosis therapy. Systemic corticosteroids were added after few days in 14 patients to decrease inflammatory reaction, retinal vasculitis, macular edema and macular scaring.

CONCLUSION:

According to this study; vitritis with multifocal choroiditis is the most common mode of presentation in patients with presumed TB uveitis. All cases responded well to anti-tuberculosis therapy, systemic corticosteroids can be added to decrease inflammatory reaction, retinal vasculitis, macular edema and macular scaring.

KEY WORDS: uveitis, ocular tuberculosis, tuberculin skin test.

INTRODUCTION:

Tuberculosis (TB) is the leading infectious cause of morbidity and mortality worldwide. The World Health Organization (WHO) currently estimates that nearly two billion people, or one third of the world's population, are infected by tuberculosis, and that roughly 10% of these infected people will develop clinical disease at some point during their lifetime. [1,2] TB is endemic in Iraq.

Uveitis may be seen concurrently with TB, but a direct association may be difficult to prove.[3] The diagnosis of ocular TB is often problematic and in nearly all reported cases, the diagnosis was only presumptive, because of the difficulty in obtaining microbiological evidence and chest X-rays are normal in cases of latent TB.[4,5,6] The absence of clinically evident pulmonary TB does not rule out the possibility of ocular TB, as approximately 60% of patients with extra pulmonary TB have no

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evidence of pulmonary TB.[7] Intraocular TB is a great mimicker of various uveitis entities and it can be considered in differential diagnosis of any type of intraocular inflammation. It is still unknown if ocular manifestations result from a direct mycobacterium infection or hypersensitivity reaction and this is reflected on the management of TB uveitis. The aim of this study is to illustrate the mode of presentations and management of presumed TB uveitis at a referral eye center in Iraq.

METHOD AND SUBJECTS:

This prospective case series study was conducted at the uveitis clinic at Ibn Al-Haetham teaching eye hospital (IAHTEH) in Baghdad, Iraq. The study followed the principles of the Declaration of Helsinki. Institutional review board and ethics committee approval was granted by the Scientific Committee of IAHTEH.

Uveitis clinic at IAHTEH receives referral cases of uveitis from outpatients' clinics in the hospital, and some patients are directly referred to this clinic from various eye centers in the country.

Successive new patients referred to uveitis clinic at IAHTEH, from January 2007-January 2013 were enrolled in this study, if they had clinical signs of presumed ocular tuberculosis. All patients underwent a complete ocular examination, which included visual acuity assessment, examination the anterior segment with a Slit Lamp, fundus examination with indirect ophthalmoscopy and indirect Slit Lamp biomicroscopy. Intraocular pressure was measured using Goldman applanation tonometer.

If clinical pictures did not indicate a specific etiology, patients were sent for a routine set of tests including: Complete blood count (CBC) with differential, erythrocytes sedimentation rate (ESR), urinalysis, chest X-ray, tuberculin skin test (T.T.) and serological tests for syphilis (fluorescent treponemal antibody absorption test). Ancillary tests including fluorescein angiography, ultrasonography, MRI, CT scan, and antiphospholipid antibodies were carried out when needed.

Ocular tuberculosis was presumed when findings were consistent with possible intraocular tuberculosis, intractable to steroid therapy, and no clinical or laboratory evidence for other causes of uveitis.[3] Strongly positive tuberculin skin test result (more than14 mm area of induration/necrosis) supported the diagnosis, but was not a prerequisite for initiating therapy. Numerous variables were assessed including age, sex, demographical features, onset, course and presence of related systemic diseases.

Patients with presumed ocular tuberculosis were sent to the Tuberculosis Institute in Baghdad, for starting treatment with anti tuberculous therapy (ATT) (2 months of rifampicin, isoniazid, pyrazinamide, and ethambutol followed by 4 months of rifampicin and isoniazid). Clinical findings and response on treatment were documented in a special follow up cards.

RESULTS:

Out of 506 patients with active uveitis attended uveitis clinic during the period of this study, 64 patients (12.7%) with presumed TB uveitis were consecutively included in this study. Patients age ranged between 12-60 years with mean age of 35.7 years), and there was no significant sex predominance. Majority of patients were from Urban places (79.7%) and more than half of them (53.2%) had intermediate or high education levels. The demographic characteristics of these patients are shown in table one.

At presentation two patients had military TB, and one patient had history of pulmonary TB with incomplete treatment. All other patients had normal chest radiographs with no evidence of active systemic disease, but 24 patients (37.5 %) reported that they had previous contact with patients with pulmonary TB, sometimes this contact was several years before eye complaining started. .

Bilateral simultaneous involvement was recorded in 49 patients (76.6%), in 13 patients (20.3%) bilateral involvement was un-simultaneous; one eye was involved months or years after the primary one. In 2 cases (3.1%) unilateral uveitis was recorded. Total number of eyes with presumed ocular TB was 126 cases.

At presentation 116 eyes (92.1%) had panuveitis, 6 eyes (4.7%) had posterior uveitis, and 4 eyes (3.2%) had intermediate uveitis. Clinical findings at presentation are illustrated in table 2. Vitritis was a universal finding, while multifocal choroiditis was the most common fundus lesions (104 eyes; 82.5%).

Strongly positive T.T. (more than 14 mm) was recorded in 58 patients, while 3 patients with T.T 10-14 mm, and 3 patients had negative T.T. Two patients with negative T.T. were using oral corticosteroid therapy, while the third patient was debilitating 12 years old girl. T.T. was strongly positive in only 4 out of 95 patients with other causes of uveitis sent for T.T. three of them proved latter to have Behçet's disease.

All patients treated initially with ATT. In 50 patients (100 eyes) with multifocal choroids treatment continued with ATT only, while systemic corticosteroids (oral prednisone) were added after few days in 14 patients (26eyes) to decrease inflammatory reaction, retinal vasculitis, macular edema and macular scaring. All patients had favorable response on treatment. In 62 patients uveitis resolved completely within 3-6 month, only 2 patients required ATT for one year and in all patients uveitis did not recur for more than 6 months after completion of treatment. After controlling of the inflammation, phacoemulsification with intra-ocular lenses implantation was performed on 12 eyes with dense cataract, and there was no post-operative activation of inflammation.

Table 1: Demographical characteristics of 64 patients with presumed TB uveitis.

Character	Number (%)	Character	Number (%)
Age		Occupation	
<20	1 (1.5%)	Governmental employee	17 (26.6%)
21-40	52 (81.3%)	Free jobs	17 (26.6%)
41-60	11 (17.2%)	Housewife	14 (21.9%)
>60	0 (0%)	Farmer	9 (14.1%)
Total	64	Militant	3 (4.7%)
Gender		Physician	2 (3.1%)
Male	29 (45.3%)	Other medical staff	1 (1.5%)
Female	35 (54.7%)	Student	1 (1.5%)
Total	64	Total	64
Residence		Educational level	
Urban	53 (82.8%)	Illiterate	12 (18.7%)
Rural	11 (17.2%)	Read and write	18 (28.1%)
Total	64	Intermediate education (primary or secondary schools)	29 (45.4%)
		Higher education	5 (7.8%)
		Total	64
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Table 2: Clinical finding at presentation.

Clinical findings	Number of eyes with presumed TB uveitis	Percentage out of 126 eyes with presumed TB uveitis
Muttan fat KPs*	72	57.1
Posterior synaechae	87	69.1
Iris nodules	8	6.3
Dense cataract	12	9.5
Vitritis	126	100
Multifocal choroiditis	104	82.5
Retinal vasculitis	20	15.9
Proliferative retinopathy	4	3.2
Serpigenous choroidits	4	3.2
Choroidal granuloma	2	1.6

*Keratic precipitate

DISCUSSION:

Tuberculosis (TB) is one of the most widely distributed infectious diseases in the world, and it is endemic in Iraq. TB uveitis is one of the important causes of uveitis in the neighboring countries.[8,9,10] The diagnosis of ocular TB is frequently presumptive.[11] Definite diagnosis relies on demonstration of tubercle bacilli in tissue but this is fraught with the difficulty of obtaining ocular tissue

for biopsy in seeing eyes due to the invasive nature of the procedure.[12] In most cases the clinician has to rely on a combination of evidence of systemic disease, characteristic ocular findings, and possibly a therapeutic treatment trial to make the diagnosis.

It is unknown if ocular manifestations result from a delayed hypersensitivity reaction or due to infectious agent. Uncommonly, live mycobacteria or their DNA may be accessible from intraocular samples.[13] More commonly, intraocular inflammation is either presumed to be a hypersensitivity response rather than direct infection, or possibly mycobacteria are sequestered within the retinal pigment epithelium as has been anecdotally reported.[14]This is reflected in the absence of information on ocular TB management in any of the TB guidelines of the UK, USA or Canada.[15]

False positive T.T. can occur as the test uses a mixture of antigens from mycobacterium and some patients have already received bacille Calmette-Guerin (BCG), but strongly positive T.T. is unlikely to be due to prior BCG vaccination.[16] The predictive value varies depending on the population TB incidence and local BCG vaccination policy; in the United States, the routine use of TB skin testing in patients with uveitis is considered unhelpful[17] whereas in India it is considered mandatory.[14]

In this study multifocal choroiditis was the most important clinical sign for TB uveitis as it was presence in 82.5% of cases. All cases with multifocal choroiditis and positive TT responded well to anti TB therapy.

In the current study, 61 out of 64 patients (95 .3%) with presumed ocular tuberculosis had positive T.T, while it was negative in 3 immuno-compromised patients. T.T. may be weakly positive or negative in patients using systemic corticosteroids, and it may be false positive in patients with Behçet's disease as it may act as a pathargy test.http://bjo.bmj.com/content/85/2/127.full?sid=ae850efe-a217-42ff-93e9-60b383dd9806 - ref-16

Recent advances in diagnostic tools for ocular TB as detection of antibodies against purified cord factor and use of polymerase chain reaction can provide strong evidence of the infection.[18,19]

Previous studies reported favorable response tohttp://bjo.bmj.com/content/85/2/127.full?sid=ae850efe-a217-42ff-93e9-60b383dd9806 - ref-16 anti tuberculous therapy when administrated concomitantly with systemic steroids in patients with presumed TB uveitis. In this study, out of 64 patients with presumed TB uveitis, 50 patients presented with multifocal choroiditis were treated with ATT drugs only. All patients treated with ATT drugs only had favorable response without concomitant use of systemic corticosteroids, and no recurrence was recorded; this strongly favors the diagnosis of ocular tuberculosis, and this may indicate that ocular manifestations in these patients were due to direct mycobacterium invasions. Systemic steroids were added to anti-TB therapy in 14 patients to decrease inflammatory reaction, retinal vasculitis, macular edema and macular scaring. The use of oral steroid in the majority of patients is clearly a confounding issue.[14]Oral prednisone can be used in treatment of ocular TB, in order to control coexisting inflammatory reaction, and reduce macular edema.[3] It might be desirable diagnostically to delay steroid treatment in order to assess the response to ATT, this must be balanced with the risk of loss of sight.[11] The use of steroids at the same time as ATT is recommended in other situations where inflammation and fibrosis caused by TB may lead to long-term complications, for example, tuberculous meningitis or pericarditis.[20]

CONCLUSION:

According to this study; vitritis with multifocal choroiditis is the most common mode of presentation in patients with presumed TB uveitis. All cases responded well to anti-TB therapy, systemic corticosteroids can be added to decrease inflammatory reaction, retinal vasculitis, macular edema and macular scaring.

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