A case series of symptomatic ocular tuberculosis and the response to anti-tubercular therapy

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Abstract

Objective To identify the clinical pattern of symptomatic ocular tuberculosis (OTB) and the outcome following anti-tubercular therapy (ATT) in an endemic setting.

Design A descriptive case series.

Setting Tuberculosis and ophthalmology clinics, Teaching Hospital, Kandy, Sri Lanka.

Method We followed up patients with OTB on standard six-month regimen of ATT, from January 2006 to December 2008. Serial opthalmological assessment were done at the beginning and end of therapy and in each clinic visit. Relevant investigations were performed. Objective improvement of visual acuity was considered the primary clinical outcome.

Results Tuberculous uveitis was the commonest manifestation observed in eighteen of twenty-three patients with symptomatic OTB. Retinal vasculitis (2), episcleritis (1), optic neuritis (1) and an inflammatory scleral nodule (1) were observed in the rest. Seventeen had Mantoux positivity over 15mm. Out of the seventeen patients (age range 25-74 years; 9 males) who completed ATT, fifteen had poor pre-treatment visual acuity, which improved in nine. Keratic precipitates, anterior segment cells, flaring, vitritis and macular oedema had resolved in majority. In patients who deteriorated despite therapy, retinal vasculitis with vitreous haemorrhage (1) and branch vein occlusion (1), persistent macular oedema (2), choroidal scar (1) and optic atrophy (1) were noted.

Conclusion OTB may present with varying manifestations, of which uveitis is the commonest. Majority with symptomatic OTB had a highly positive Mantoux test. Favourable clinical outcome with ATT was seen in patients who presented with uncomplicated disease. Standard regimen of ATT did not appear to be effective in patients with complications.

Introduction

The prevalence of symptomatic ocular tuberculosis (OTB) among tuberculosis patients is about 1.4%, though a higher percentage have asymptomatic choroiditis on routine examination [1,2,3,4]. Uveitis is the commonest manifestation in symptomatic OTB. Other presentations include keratoconjunctivitis, phlyctenular conjunctivitis, interstitial keratitis, episcleritis, nodular scleritis, multifocal choroiditis, exudative retinitis, retinal vasculitis and optic neuritis. Rarely orbital structures may be involved [5].

Drug therapy for OTB is similar to that for pulmonary tuberculosis. Anti-tubercular therapy (ATT) is used systemically in the treatment of OTB because it offers the best penetration of posterior ocular structures with least

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toxicity. Current guidelines recommend a six-month course of daily isoniazid (5mg/kg) and rifampicin (10mg/kg), in addition to pyrazinamide (15-30mg/kg) and ethambutol (15mg/kg) for the first two months. The therapy will also target other undiagnosed foci of disease which may co-exist [1, 6].

There are no clinical trials on treatment and prognosis of OTB. However, case studies suggest good resolution of ocular features and improvement of visual acuity with regimens described above. Majority of immunocompetent patients who completed the course of therapy had a successful outcome. Failure is commonly due to complications at presentation, poor treatment compliance, drug resistance and inadequate primary therapy [7].

In Sri Lanka, despite an effective national programme for tuberculosis control and mass scale immunoprophylaxis, tuberculosis still remains a growing public health issue with over 9000 new cases being detected annually [6]. Management of patients with OTB requires close liaison between the ophthalmologist and the respiratory physician, and is often a challenging effort, which may lead to the devastating consequence of blindness if not carried out optimally. The disease pattern of symptomatic OTB has not been described and the clinical outcome with ATT remains unevaluated in Sri Lanka. Our objective was to identify the clinical pattern of symptomatic OTB and the outcome following standard ATT.

Methods

We followed up all adult patients with symptomatic OTB presenting to tuberculosis and ophthalmology clinics, Teaching Hospital, Kandy, Sri Lanka from January 2006 to December 2008 (n=23), after taking informed consent.

All patients at presentation were seen by the Consultant Ophthalmologist. We recorded patient demography, co-morbidities, contact history, symptomatology and visual acuity using a standard Snellen's chart. Anterior and posterior segments were ophthalmologically assessed under higher magnification and findings including keratic precipitates, anterior segment cells, flaring, vitritis and macular oedema were documented. Structured data entry sheets filled by the investigators were used for data collection.

We performed relevant haematological investigations, including full blood count, fasting sugar level, erythrocyte sedimentation rate (ESR), serum calcium, liver and renal profiles, chest X-ray and tuberculin skin testing (Mantoux) in all patients. Sputum examination for acid-fast bacilli (AFB), fundal photography and histological evaluation were done where necessary. We excluded other possible aetiologies by performing urinary calcium excretion, anti-nuclear factor assay and treponemal, *Toxoplasma* and *Toxocara* serology when necessary.

The diagnosis of OTB was arrived at relying on a combination of features including the clinical picture, previous or present evidence of disease elsewhere and specific ocular findings by ophthalmological assessment, supported by positive tuberculin skin response, fundal imaging and histology, in the absence of an alternative diagnosis.

All patients were given a short, tapering course of oral prednisolone 0.5-1 mg/kg body weight and standard six-month regimen of ATT adjusted to body weight. They were reviewed monthly at the tuberculosis clinic and two-monthly at the eye clinic. We monitored them for disease progress, development of disease complications or medication related adverse effects. In each visit, routine clinical assessment, liver biochemistry and repeat haematological investigations were performed as necessary at the tuberculosis clinic and serial visual acuity and eye assessment performed at the eye clinic. At the end of six months the patients were reassessed by the Ophthalmologist and the post-treatment findings were recorded in detail.

We compared pre- and post-treatment ophthalmological findings in patients who have completed ATT by the end of study period (n=17), to assess the treatment outcome. Visual acuity was considered the primary clinical outcome. Resolution of specific ocular findings such as keratic precipitates, anterior segment cells, flaring, vitritis and macular oedema were also assessed.

Results

During the study period, we diagnosed 23 patients (15 males, 8 females) with symptomatic OTB, out of 2,130 total tuberculosis admissions. The mean age was 46 years. Eighteen (83%) had isolated eye disease. Two had coexisting pulmonary tuberculosis, and three had either past or contact history of tuberculosis. Only co-morbidity detected was diabetes mellitus in one patient. Tuberculous uveitis was the commonest manifestation, observed in eighteen (78%) patients. Fourteen of them had panuveitis, while three had anterior uveitis and one had posterior uveitis. Retinal vasculitis (2), episcleritis (1), optic neuritis (1) and an inflammatory scleral nodule (1) were observed in the rest. Two patients had superadded choroiditis. Bilateral involvement of eyes was seen in nine (39%) patients. Recurrent disease was noted in two. The main symptoms were deteriorated vision (87%), redness (57%), itching (17%), tearing (9%) and pain (9%) of the affected eye/s.

Sputum AFB were negative in all checked. Only four (17%) had erythrocyte sedimentation rate over 75mm/hour (mean±SE: 36.6±7.4). All had Mantoux skin reactions over 10mm (mean±SE; 16.3±3.7) while seventeen (74%) had high Mantoux positivity over 15mm. Three were immunoglobulin (Ig) G positive but IgM negative for *Toxoplasma* or *Toxocara* infection. Even though they did

not have evidence of past choroiditis, each had very poor visual acuity of the affected eye at presentation (6/36, 1/60 and hand movements only), with one having optic atrophy.

Seventeen patients who completed ATT were reassessed for improvement. They had a median post-treatment follow up of 14 (range 2-27) months. Fifteen (88%) of them had poor pre-treatment visual acuity (mode 6/12; range 6/9 to perception of light only) involving one or both eyes. Improvement of visual acuity was seen in nine (53%), and the acuity remained static in two mildly affected patients. Post-treatment ophthalmological findings, i.e. precipitates, cells, flaring, etc., were normal in all of them. Six (35%) showed deterioration of the visual acuity below 6/24 at the end of treatment. In these patients retinal vasculitis with vitreous haemorrhage (1) and branch vein occlusion (1), persistent macular oedema (2), choroidal scar (1) and optic atrophy (1) were noted at presentation.

In the treatment-completed group, tuberculous uveitis was the commonest manifestation seen in twelve patients. In pre-treatment assessment of uveitis patients, keratic precipitates were observed in nine, anterior segment cells in ten, flaring in five, vitritis in ten and macular oedema in six. Majority (75%) of uveitis patients had a good post-treatment outcome (Figure 1).

Discussion

Symptomatic OTB may present with varying manifestations. The majority in this series had isolated eye disease and only a few had present or past evidence of tuberculosis elsewhere. Highly positive Mantoux skin test was observed in a majority. Although the clinical outcome was satisfactory for patients with uncomplicated OTB, patients who presented with complications did not respond well to treatment.

The diagnosis of OTB in this study was based on multiple clinical and supportive evidence, in the absence of an alternative diagnosis. In order to make a definitive diagnosis of OTB, viable mycobacteria must be obtained from the eye through aqueous or vitreous sampling and should be processed for microscopy, culture or polymerase chain reaction (PCR) technique. However, obtaining adequate tissue samples is difficult and is often associated with significant ocular morbidity. Furthermore microscopy is less sensitive, while culturing is time consuming and PCR not freely available in the government hospitals. Therefore commencing treatment on a presumptive diagnosis using multiple clinical and supportive evidence in the absence of an established alternative diagnosis is acceptable in many instances, especially in a high prevalence setting [8].

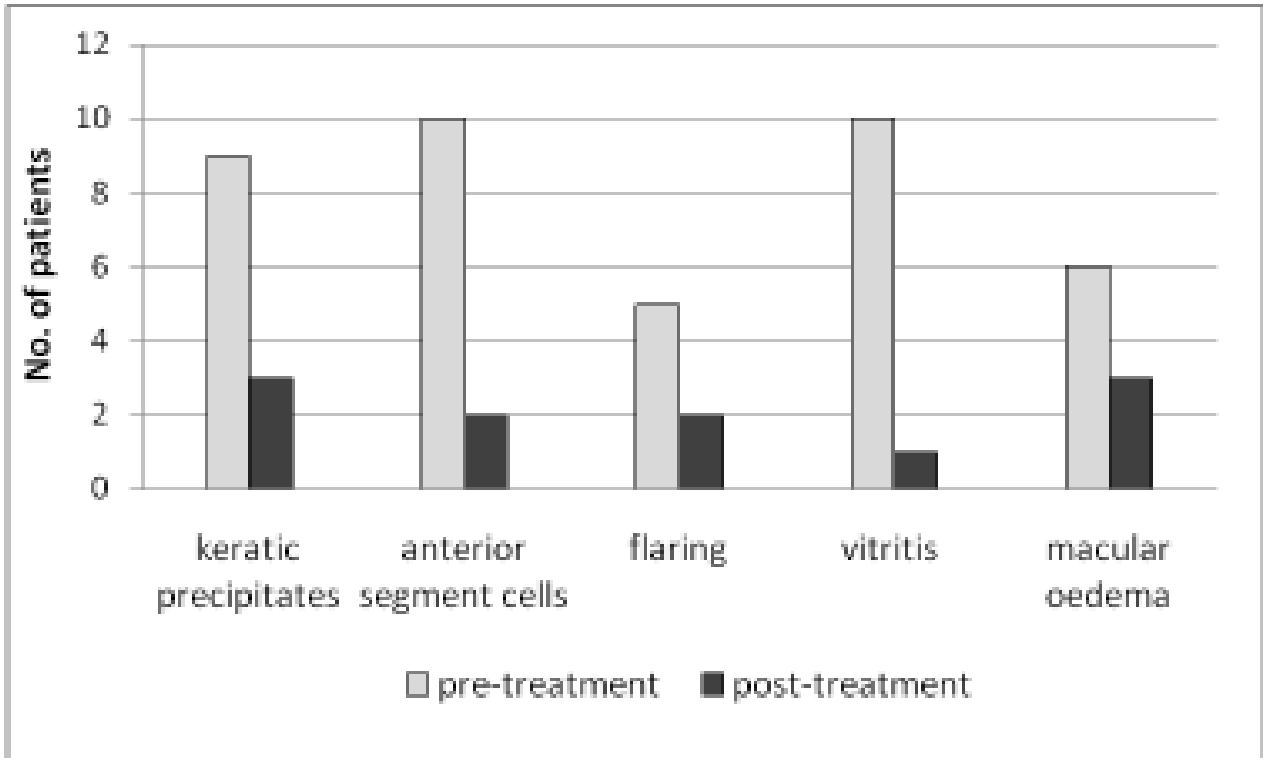

Figure 1. **Improvement of specific ocular findings in uveitis patients.**

Tuberculous uveitis was the main presentation in this cohort, as was the case in many other series with symptomatic OTB. Only two (8%) had superadded choroiditis, one with panuveitis and the other with retinal vasculitis.

According to this study, the majority of patients with uncomplicated ocular disease show a good response to ATT with improvement in visual acuity. Specific ocular findings (eg: keratic precipitates, anterior segment cells, etc.) also improved with treatment. These findings are similar to those of other series (7, 9). Primary clinical outcome in this study was the objectively assessed visual acuity using a standard Snellen's chart. Serial assessment of contrast sensitivity would be a better outcome measurement, but was not available to us. Serial fundal photography would be useful in selected patients with poor response, especially to assess the degree of macular oedema in the absence of gross macroscopic abnormalities [7].

This study has shown that the presence of early complications, like visible macular oedema or established damage to ocular structures, is a predictor of poor outcome. Furthermore the patients with *Toxoplasma/ Toxocara* IgG positivity also showed a poor outcome. This raises the possibility whether previous asymptomatic infection with these agents leads to a poor prognosis in OTB. It may be useful to assess the efficacy of using a different therapeutic regimen, such as a longer course of steroids, longer duration of ATT or different combination of drugs, in this subgroup of patients with a potentially poor prognosis.

In conclusion, symptomatic OTB usually presents with isolated eye involvement without systemic disease. Uveitis is the commonest disease manifestation. Highly positive tuberculin skin response (Mantoux test) is observed in the majority. A favourable clinical outcome with ATT is seen in patients presenting with uncomplicated symptomatic OTB. The standard regimen of ATT does not appear to be effective in patients presenting with complications.

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