

## Panuveitis: A case of suspected ocular tuberculosis

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### ABSTRACT

A 32-year-old incarcerated man was evaluated for decreased vision in both eyes at a tertiary care facility. He presented with uveitis and the initial work up indicated that tuberculosis was the most likely etiology. This report will discuss the frequency, presentation, diagnostic procedures and yield, and treatment of ocular tuberculosis.

**Keywords:** *Mycobacterium tuberculosis*, panuveitis, uveitis, ocular tuberculosis, Ozurdex, Quantiferon Gold

### INTRODUCTION

Despite advances in diagnostic techniques and treatment regimens, tuberculosis (TB) continues to present numerous challenges. It is estimated that *Mycobacterium tuberculosis* (MTB) infects 1.7 billion people worldwide but only 5-15% develop tuberculosis disease during their lifetimes. In the United States, the annual incidence of TB is between 2.7-3.6 cases/100,000.<sup>1</sup> Pulmonary involvement accounts for most cases of tuberculous disease. However, as the diagnostic tests have improved, TB has become increasingly implicated in extrapulmonary manifestations, including skin, cardiovascular system, gastrointestinal tract, and eye involvement.

There is considerable inconsistency in the literature about the incidence of ocular involvement in patients with either pulmonary or disseminated tuberculosis with reported incidences ranging from 1.4% to 18%.<sup>2,3</sup> A 1987 California review of 600 cases of uveitis reported that MTB caused less than 0.5% of the cases.<sup>4</sup> Historically, TB was thought to involve the eye by hematogenous spread from loci of infection elsewhere, but more recently it has been suggested that

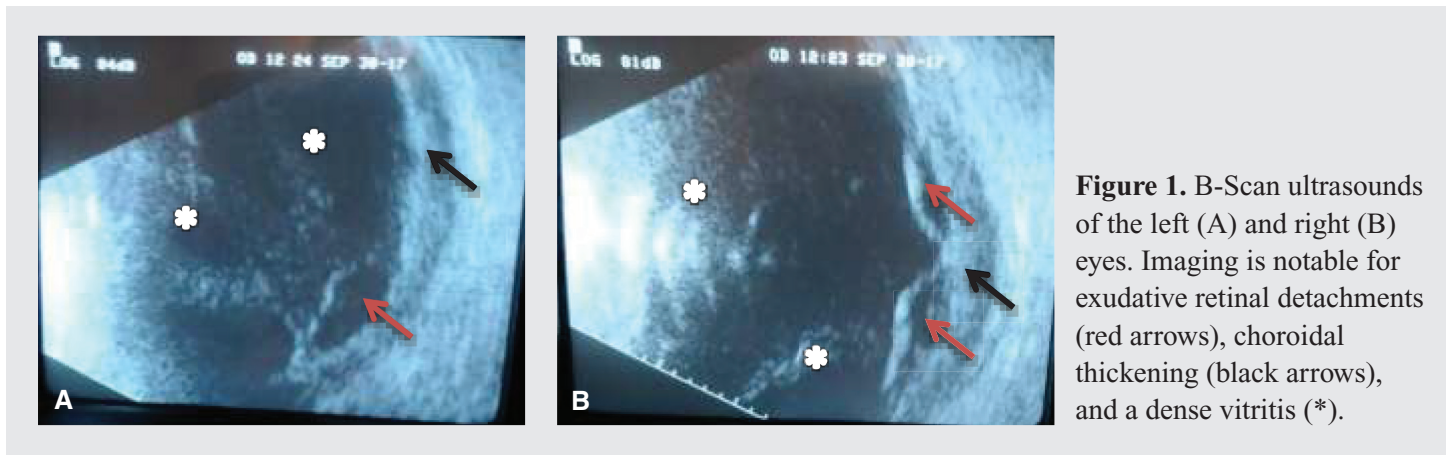
ocular complications can result from an immunologic response to MTB elsewhere in the body.<sup>5,6</sup> The following case report explores the diagnostic and therapeutic challenges posed during a patient encounter.

### CASE

A 32-year-old incarcerated Hispanic man presented to the emergency room with a six-week history of blurry vision and ocular pain, which had rapidly worsened over the preceding 10 days. He noted that his initial symptoms began in the left eye (OS) and later involved the right eye (OD). Review of systems revealed photophobia, floaters in both eyes (OU), fatigue, anorexia, weight loss, chills, and night sweats. He had no prior ocular, medical, surgical, or relevant family history.

Physical examination revealed hand motion vision and unreactive pupils OU. Examination of the anterior segment revealed mild conjunctival injection, trace endothelial pigment deposition, significant anterior chamber cells, and flare without hypopyon. The iris demonstrated 360 degrees of posterior synechia with fibrous lens deposits. There was no view of the posterior segment OD; OS presented a challenging view with 2+ cell and an inferior retinal detachment (RD) about 4-5 clock hours in size. B-scan demonstrated diffuse exudative RDs, choroidal thickening, and vitritis OU (Figure 1).

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**Figure 1.** B-Scan ultrasounds of the left (A) and right (B) eyes. Imaging is notable for exudative retinal detachments (red arrows), choroidal thickening (black arrows), and a dense vitritis (\*).

The patient was hospitalized to initiate management of panuveitis with systemic corticosteroids (IV methylprednisolone), topical atropine drops (gtts), and topical prednisolone acetate gtts. He underwent an extensive evaluation, including CBC, ESR/CRP, *Treponema pallidum* hemagglutination test, rheumatoid factor, antinuclear antibody, cyclic citrulline peptide, HIV, HLA-B27, toxoplasmosis antibody, Quantiferon Gold, angiotensin converting enzyme level, Lyme antibody, and chest x-ray. While in the hospital, the patient's lab tests were all negative, except for the reference lab tests for toxoplasmosis, Quantiferon Gold, HLA-B27, and Lyme disease that had not yet returned. After receiving three days of systemic corticosteroids, he was discharged on oral corticosteroids, topical atropine, and prednisolone acetate gtts. At the time of discharge, his visual acuity remained hand motion OU, the vitritis had decreased, and he had modest improvement in many of his presenting symptoms.

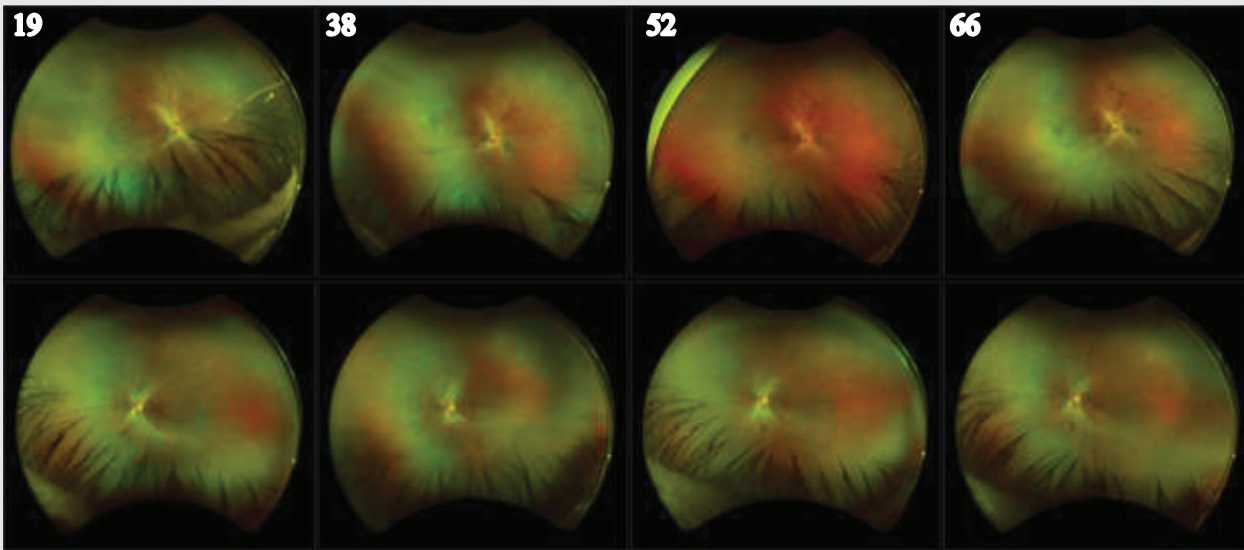
By day 7 following discharge, the Quantiferon Gold returned positive, which prompted a discussion about treatment for either active or latent tuberculous infection. Due to the acuity of his presentation and the possible risk of reactivation, if latent infection were present, he was started on rifampin, isoniazid, pyrazinamide, and ethambutol (4-drug therapy) for MTB and had x-rays of the lumbar spine, which were negative. By day 12, on corticosteroid therapy and anti-tuberculous treatment, his best corrected visual acuity had improved to 20/80 in both eyes. The patient was then followed monthly in the clinic and

monitored with serial ultra-wide field fundus imaging (Figures 2, 3). He received 4-drug therapy for 55 days and then rifampin and isoniazid during the continuation phase of treatment; the corticosteroid regimen was also gradually tapered over the following 102 days to prednisone 20 mg PO daily.

At day 106, the patient had a flare of his original symptoms and decreased visual acuity. His topical and systemic corticosteroid regimen was increased. Re-evaluation on day 129 revealed worsening of symptoms requiring hospitalization and the resumption of IV corticosteroids. While in the hospital, he underwent additional work up, including syphilis, HIV, toxoplasmosis, and coccidioides tests that were negative. On IV corticosteroids, his symptoms improved, and on day 133, he was discharged on prednisone 60 mg PO daily, topical prednisolone acetate, and a cycloplegic drug. Due to a recurrence of symptoms on corticosteroid taper, intravitreal Ozurdex (dexamethasone) implants were placed on day 151. The implants were tolerated well and allowed a gradual taper of the corticosteroids to prednisone 20 mg PO daily with no recurrence of uveitis, full resolution of chronic retinal detachments at day 206, and visual acuity of 20/150 OD and 20/200 OS.

## DISCUSSION

The diagnosis of ocular tuberculosis remains challenging. A clinical diagnosis is typically not possible



**Figure 2.** Ultra-wide field fundoscopic imaging with the right eye superiorly, left eye inferiorly at days 19, 38, 52, and 66, respectively. Day 19, demonstrates exudative RD inferiorly, that gradually improves over the series.

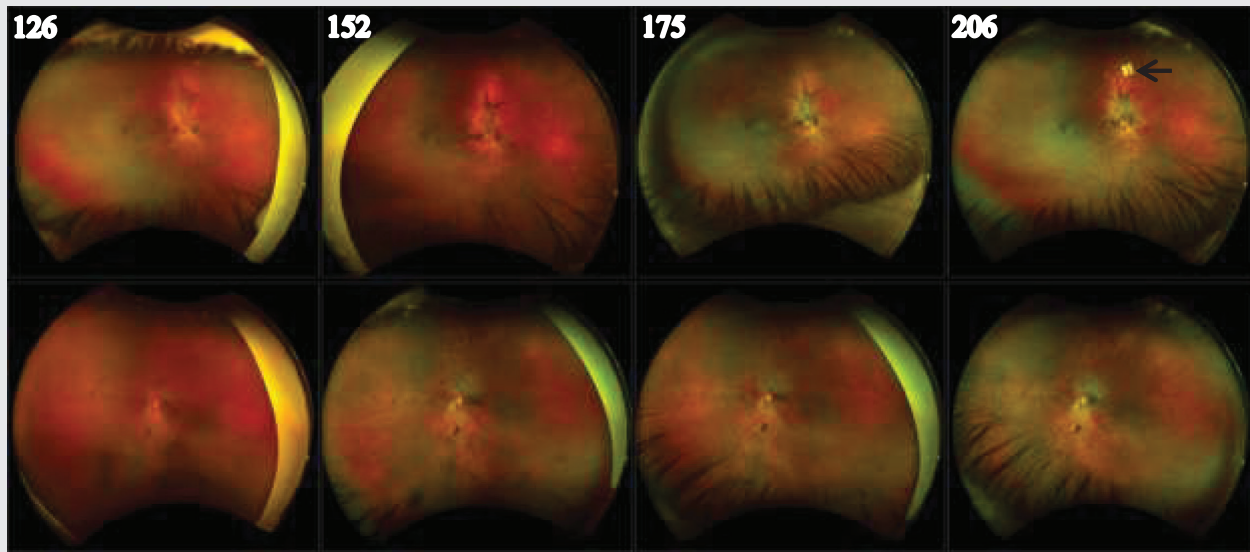
as the disease presentation is often indistinguishable from other etiologies of uveitis. One retrospective study identified broad-based posterior synechiae, retinal vasculitis without choroiditis, retinal vasculitis with choroiditis, and serpiginous-like choroiditis as four clinical features of ocular tuberculosis with specificities of 93%, 97%, 99%, and 98%. However, all four had poor sensitivities.<sup>7</sup> The lack of sensitive and specific clinical findings prompts a broad workup to rule out other etiologies, as in this case. Assuming a negative workup of other etiologies, a positive result from chest x-ray, tuberculin skin test, or the interferon-gamma release assay often directs additional diagnostic studies and therapy.

The gold standard for the diagnosis of ocular TB is a positive culture from ocular tissue. However, a definitive diagnosis by this approach is rarely obtained due to the small sample size of either aqueous or vitreous fluid that can be safely obtained (100-200  $\mu$ L) and potential risks of obtaining uveal tissue. The diagnostic yield is further decreased by the paucity of bacilli in ocular tissues or by the possibility that the inflammation is induced by tubercular antigens rather than the actual organism. Even if a sample is culture

positive, this result is mitigated by the fact that it often takes 6-8 weeks to isolate these slow growing bacteria. These difficulties have led to the use of polymerase chain reaction (PCR) tests as a more efficient method for diagnostic confirmation.

In recent years, PCR has become increasingly utilized in both research and clinical evaluations for TB diagnosis. The advantages of PCR include improved sensitivity and specificity over culture, small sample requirement, and diagnostic expedience (2-3 days). Due to the challenges of culture or demonstration of MTB on smear, early PCR studies compared PCR results to pre-test probability.<sup>8</sup> Sensitivities and specificities for tuberculosis reported in the literature ranged from 71.4 to 73.3%, and 76.77 to 100%, respectively.<sup>9-11</sup> However, the gold standard used in these studies was a positive PCR, clinical gestalt, and response to antituberculous therapy rather than a positive culture or the demonstration of MTB on smears. Due to sampling complexity and the poor yield from cultures or the demonstration of MTB on smears, a definitive study comparing PCR to culture is not likely.

The reported regimens for the treatment of ocular tuberculosis vary in the literature. A 2015



**Figure 3.** Ultra-wide field fundoscopic imaging, the right eye superiorly, left eye inferiorly at days 126, 152, 175, and 206, respectively. A comparison of day 66 to 126, reveals blurring of the disc/vessels at day 126 which corresponds to the flare experienced by the patient. Black arrow at 206 indicates Ozurdex implant that migrated into field of view.

meta-analysis of 28 studies concluded that the most frequent regimen was 4-drug therapy with isoniazid, rifampicin or rifampin, ethambutol, and pyrazinamide for a minimum of 2 months (up to 3-4 months) followed by 2-drug therapy with isoniazid and rifampicin for a minimum of 4 months in 18 of the studies. An alternative therapy included the 4-drug regimen combined with fluoroquinolones, particularly with the goal of preventing or treating drug-resistant MTB.<sup>12</sup> These meta-analysis results support CDC recommendations on treatment duration and regimen, though the regimen recommended by the CDC did not specifically target ocular tuberculosis.<sup>13</sup> In a survey of international uveitis experts, a plurality of respondents in developing and developed countries suggested a 9 month regimen; the second most common duration was 6 months.<sup>14</sup> A 9 month course was also supported by a case-control study of latent tuberculosis that demonstrated a decreased rate of uveitis recurrence following 9 months of treatment.<sup>15</sup> The use of corticosteroids in tuberculous infections is also controversial. However, the predominant consensus is

that if corticosteroids are used, they should be begun concurrently or after initiation of antituberculous therapy.<sup>12,14,16-18</sup> In cases of latent tuberculous infection, TB antigen induced uveitis, or uveitis refractory to corticosteroid tapers similar to our case, localized long-acting corticosteroids have been shown to be effective.<sup>19,20</sup>

In conclusion, there remains significant controversy about many aspects of ocular tuberculosis. A recent article by Ang does an excellent job of summarizing three significant controversies that exist in ocular tuberculosis. First, terminology used in ocular tuberculosis requires standardization and consensus among clinicians to understand the disease burden. Second, the diagnosis of ocular TB needs to distinguish between a TB infection of the eye and inflammation associated with a remote or systemic TB infection. Finally, guidelines need to be established for the treatment regimen and duration of therapy for ocular tuberculosis.<sup>21</sup> Despite advances in diagnostic and therapeutic techniques, ocular inflammation associated with tuberculosis remains a challenging disorder.

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