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Case report

Negative Mantoux test in a patient with definite pulmonary and ocular tuberculosis

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ABSTRACT

The case is reported of a patient with pulmonary and ocular tuberculosis presenting with blurred vision in both eyes. A 27-year-old well-nourished male nursing-home resident with a previous history of traumatic intracerebral hemorrhage was brought to the ophthalmological clinic due to progressively blurred vision. His best-corrected visual acuity was 20/400 in the right eye with only light perception in the left eye. Fundus examinations revealed retinal segmental periphlebitis and hemorrhagic retinitis in the right eye and dense vitreous hemorrhage in the left eye. The Mantoux test was negative; however, the results of an interferon gamma release assay were positive. Ocular tuberculosis was suspected. Although he had never had any respiratory symptoms, his chest radiograph and computed tomography scan showed a multiple centrilobular glandular and ground-glass appearance with air-space consolidations and atelectasis in both lower lobes. Pulmonary tuberculosis was confirmed by a positive acid-fast stain of a bronchial alveolar lavage sample. A GEN-PROBE amplified *Mycobacterium tuberculosis* direct test of the vitreous fluids was also positive. Ocular tuberculosis was confirmed. After treatment for tuberculosis and vitrectomies, his final best-corrected visual acuity improved to 20/30 in the right eye and 20/200 in the left eye. Ocular tuberculosis is rarely reported as the primary presentation of systemic tuberculosis in young patients. A negative Mantoux test may lead to misdiagnosis and delayed treatment. Doctors should become more familiar with the manifestations of systemic tuberculosis and use advanced diagnostic tools in cases of clinical suspicion.

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1. Introduction

Tuberculosis (TB) usually infects the lungs and is a slowly progressive, chronic, necrotizing or nonnecrotizing, and granulomatous or nongranulomatous infection caused by *Mycobacterium tuberculosis* (MTB). Alveolar macrophages acquire phagocytic and bactericidal functions and may limit the pulmonary infection. However, some organisms may escape through the lymphatic or blood systems or hematogenously, resulting in seeding of the organisms in other organs, including the cardiovascular system, the gastrointestinal system, the musculoskeletal system, the genitourinary tract, the central nervous system, the skin, and the eyes.[1,2] In regions with a naturally high immunity to MTB, reactivation of the latent infection may occur. In developing countries where a high ratio of TB infection and low natural resistance exist, the risk of inhaling bacilli on several occasions is high and may cause reinfection. Ocular TB can be acquired by direct infection or by an indirect immune-mediated hypersensitivity response to mycobacterial antigens; it is a great mimicker of various uveitis entities.[3,4] The Mantoux test (a tuberculin purified protein derivative test) is a screening tool for TB and is one of the major tuberculin skin tests used around the world.

We report the case of a patient with definite pulmonary plus ocular tuberculosis who had a negative Mantoux test result. We also review the currently available laboratory methods for the confirmation of tuberculosis.

2. Case report

The patient presented here was a 27-year-old well-nourished male nursing-home resident with a previous history of traumatic

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intracerebral hemorrhage. He was mentally and physically disabled. He was brought to the ophthalmological clinic of the local hospital as a result of progressively blurred vision in both eyes for 2 weeks. Based on our impression of branch retinal vein occlusion in the right eye and vitreous hemorrhage in the left eye, an intravitreal bevacizumab injection and laser photocoagualtion were performed in the right eye; however, a vitreous hemorrhage was seen to have developed at the 6-month follow up. He was therefore referred to a tertiary care center for further evaluation and management.

On examination, his best-corrected visual acuity was 20/400 in the right eye with only light perception in the left eye. The intraocular pressure was within the normal range. Slit-lamp examination showed broad-based posterior synechiae in the left eye, which obscured the details of the fundus. Reviewing the presenting fundus photographs revealed retinal segmental phlebitis with perivenous clustering and hemorrhagic retinitis (Fig. 1). Fluorescein angiography revealed occlusive retinal phlebitis with late leakage (Fig. 2). A B-scan examination showed vitreous hemorrhage in his left eye.

The results of his blood investigations, including a complete blood count, random blood sugar, and routine serum biochemistry, were within normal limits. The results for the lupus anticoagulant, anticardiolipin antibody, rapid plasma regain, and HIV Ag/Ab combo tests were negative. A culture of the anterior chamber fluid showed no growth. The Mantoux test was negative, but an interferon gamma release assay (IGRA) was positive. Ocular TB was therefore suspected.

Although the patient had no respiratory problems, his chest radiograph revealed a multiple centrilobular glandular and ground-glass appearance in both lungs (Fig. 3). A chest computed tomography scan showed air-space consolidations and atelectasis in both lower lobes (Fig. 4). Definite pulmonary TB was confirmed due to the positive acid-fast stain from bronchial alveolar lavage by bronchoscope. Drugs for treating TB, including ethambutol, pyrazinamide, rifamycin, and isoniazid, were prescribed.

The vitreous hemorrhage and tractional retinal detachment worsened in both eyes. Small gauge vitrectomies, membrane peeling, and endolaser photocoagulation were performed. Definite ocular TB was confirmed by the positive results of the GEN-PROBE amplified MTB complex (MTBC) direct test of the vitreous humor approximately 1 year after the onset of symptoms. After treatment for TB and surgery, his final best-corrected visual acuity improved to 20/30 in the right eye and 20/200 in the left eye.

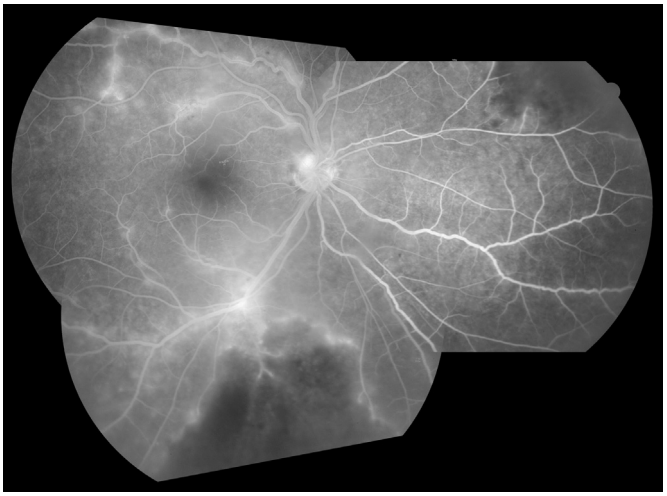

Fig. 2. Fluorescein angiography results showing occlusive retinal phlebitis with late leakage.

3. Discussion

TB is a slowly progressive chronic infection caused by MTB. It mainly affects the lungs, but can also affect other organs and systems, including ocular tissue.[1,2] Ocular TB can be acquired by direct infection or via an indirect immune-mediated hypersensitivity response to MTB antigens. It is a great mimicker of various kinds of uveitis.[3,4] MTB can thrive in the retinal pigment epithelium (RPE), which is similar to the alveolar macrophage environment in which the bacteria normally develop and grow.[5] RPE may serve as a sanctuary for MTB. Reactivation of dormant organisms in the RPE or reinfection from a pulmonary origin with the dissemination of microorganisms may cause ocular TB.[6]

The clinical manifestations of ocular TB include necrotizing and nonnecrotizing diffuse or nodular scleritis, episcleritis, peripheral ulcerative keratitis, interstitial keratitis, phlyctenulosis,

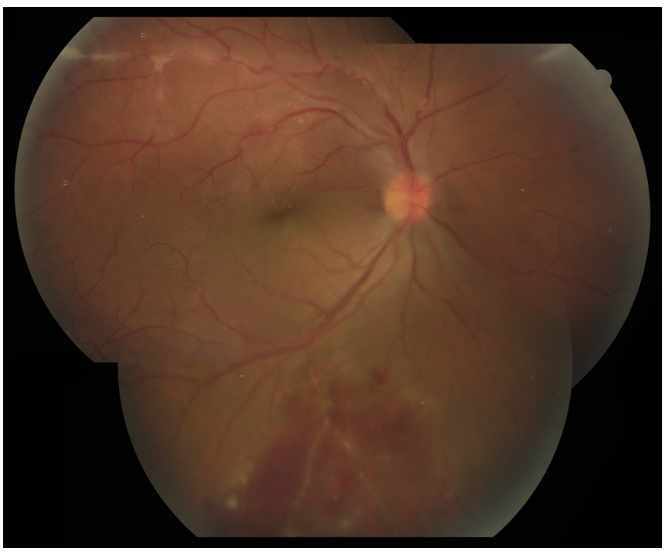

Fig. 1. Fundus photographs showing retinal segmental phlebitis with perivenous clustering and hemorrhagic retinitis.

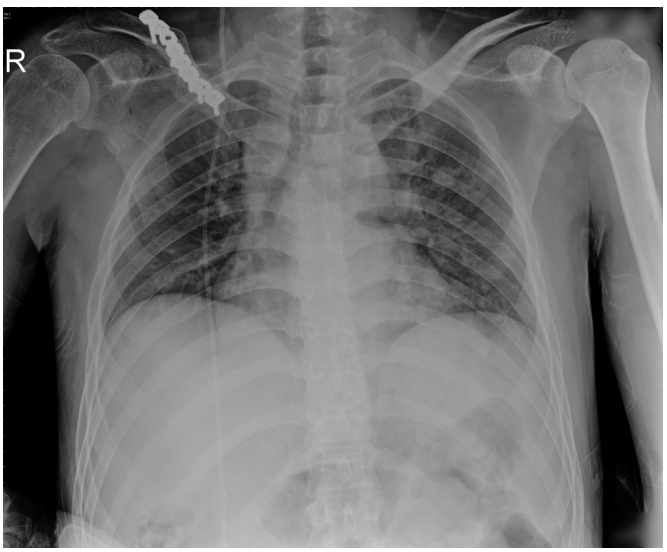

Fig. 3. Chest radiograph of our patient showing a multiple centrilobular glandular and ground-glass appearance in both lungs.

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