

Tuberculosis Uveitis Associated With Ocular Surface Squamous Neoplasia in an Otherwise Healthy Patient

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Abstract- We describe a 34-year-old woman with isolated tuberculosis (TB) uveitis who had unsuccessful resolution of her ocular surface squamous neoplasia after multiple shave excisions with a positive purified protein derivative (PPD) test and interferon-gamma (IFN- γ) release assays (IGRAs) proven tuberculosis. She was managed with wide local excision of the lesion. Histopathology confirmed conjunctival intraepithelial neoplasia (CIN) grade II. Topical interferon alpha-2b (4 times daily) and anti-tuberculous therapy was planned for her, and there was no sign of recurrence of the lesion at six months follow-up.

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Introduction

First proposed by Lee and Hirst in 1995, ocular surface squamous neoplasia (OSSN) represents a wide variety of conjunctival and corneal lesions ranging from mild epithelial dysplasia to invasive squamous carcinoma (1). Risk factors for OSSN include exposure to ultraviolet radiation, infection with human papillomavirus (HPV), immunosuppression, and infection with human immunodeficiency virus (HIV) (2).

Although a few studies have indicated an association of OSSN and pulmonary tuberculosis (TB), there are no reports in the literature regarding coexisting OSSN and isolated TB uveitis (3-5). We describe an unusual presentation of OSSN associated with TB uveitis in an otherwise healthy subject.

Case Report

A 34-year-old housewife was referred from the uveitis service of the ophthalmology department in October 2018 for cornea and anterior segment consultation with a newly diagnosed TB uveitis with no previous history of treatment. She first presented to her referring

ophthalmologist with a 4-month history of ocular mass on the surface of her right eye, which was accompanied by blurry vision and irritation. Over the past four months, she had undergone three times of shave excision of the lesion in an outpatient setting. However, she noticed the recurrence of the lesion rapidly after each procedure, for which she was referred to this center.

On examination, there was no lymphadenopathy, and other systemic examinations were all within normal limits. Laboratory tests were performed to diagnose autoimmune and infectious diseases and were all negative. A serology test for HIV showed a negative result. She had a positive Tuberculin Purified Protein Derivative (PPD) test (20 mm), and the sputum smear and culture result was negative. TB infection was documented with positive interferon-gamma (IFN- γ) release assays (IGRAs) results. Chest x-ray showed no infiltrates, consolidations, cavities, or lymphadenopathy in the lungs.

External ocular and anterior segment examination revealed a large leukoplakic mass at the nasal aspect of the right eye extending on to the peripheral cornea with no evidence of intraocular involvement (Figure 1).

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Figure 1. Ocular surface squamous neoplasia (right eye): preoperative appearance showing a leukoplakic mass at the nasal aspect of the right eye extending on to the peripheral cornea

In posterior segment examination, she had cystoid macular edema (CME), vitreous opacities, and disseminated choroiditis.

Provisional diagnosis of OSSN was made based on the clinical features. Impression cytology of the ocular surface was performed for the patient and keratin material was the only finding. Since the result was not diagnostic, ocular pathologist recommended excisional biopsy. Patient underwent a wide local excision, using standard "no touch technique". Double freeze- slow thaw cryotherapy of conjunctival margins and alcohol corneal epitheliectomy was performed. Amniotic membrane was secured in conjunctival defect by fibrin glue for reconstructing the ocular surface. Postoperatively, topical therapy with antibiotics, steroids, and lubricants for 2 weeks was commenced, and then subsequently tapered. Histopathology examination of the biopsy was compatible with conjunctival intraepithelial neoplasia (CIN) grade II (Figure 2).

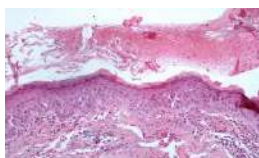


Figure 2. Photomicrograph showing conjunctival intraepithelial neoplasia II

With diagnosis of OSSN, topical interferon alpha-2b, 1 MIU [Million International Units]/mL, was prescribed 4 times daily for two months due to possible micro-invasion of the tumor. The two months regimen of Isoniazid, Rifampin, Ethambutol, and Pyrazinamide was prescribed followed by Isoniazid and Rifampin for four months. No recurrence noted in six months follow-up (Figure 3).



Figure 3. Six months after tumor excision

Discussion

In this study, we report a rare co-occurrence of massive leukoplakic CIN associated with isolated ocular tuberculosis in an immunocompetent young woman. In this patient, tuberculosis was confirmed via a positive PPD test and interferon-gamma release assay.

In the study by Meel *et al.*, the authors examined OSSN presentation in 7 patients. Two of them had a history of pulmonary tuberculosis, and one of them had HIV infection, too (5). They reported one patient with pulmonary tuberculosis having bilateral involvement with the intraocular and orbital extension of OSSN in the left eye.

The exact cause-effect relationship between tuberculosis and malignancy is not clear. However, based on plenty of experimental evidence, mycobacterium tuberculosis as a chronic inflammatory condition is capable of inducing DNA damage, (6) and reactive oxygen species (7). Moreover, it has been shown that mycobacterium tuberculosis can also increase the synthesis of BCL-2 (B-cell lymphoma 2) and anti-apoptotic activity (8).

In a retrospective study performed by Meel *et al.*, 57 eyes from 56 patients were diagnosed to have OSSN. Systemic predisposing factors were found in three patients included xeroderma pigmentosum (n=1), HIV (n=1), and renal transplantation (n=1). Other systemic associations were pulmonary tuberculosis (n=1), Berger's disease (n=1), and hepatitis B (n=1). The patient with pulmonary tuberculosis had bilateral involvement, with intraocular and orbital extension in the left eye (3).

In a case series done by Archarya *et al.*, they recorded 11 patients with OSSN over three years; one patient had OSSN associated with *Mycobacterium tuberculosis*. Patients with active TB and xeroderma pigmentosum had deeper invasion and hence had recurrences after surgery (4).

Primary excision still remains an important step in OSSN management. However, due to high recurrence rates (5%-66%) after surgery (9) and shifting toward conservative treatment, topical chemotherapeutic agents (interferon a-2b, 5-fluorouracil, and mitomycin C) are preferred choices for the management of OSSN (10). In the present case, there was no recurrence of the tumor at six months follow up. The recurrence rate of OSSN has been reported to be up to 36% during a follow-up time of one to 2.5 years (3). Tabin *et al.*, proposed that recurrence of OSSN lesions and the potential for malignant spread is sufficient reason to follow up all patients with a history of CIN for the rest of their lives (9).

In the present case, during six months follow-up after treatment, there was no recurrence of OSSN.

Association of isolated ocular TB and OSSN in the absence of any other definite predisposing factor in an immunocompetent patient made this case unique to report.

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