Lepromatous Uveitis Diagnosed by Iris Biopsy

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Leprosy, a chronic granulomatous infectious disease caused by Mycobacterium leprae, mainly involves skin, peripheral nerves, mucous membranes, and ocular structures. As early as 1873, Bull and Hansen drew attention to leprous eye complications, which may be present in up to 100% of patients with longstanding disease. Ocular damage occurs through four mechanisms: direct bacterial infection leading to keratitis, scleritis, and uveitis; facial and trigeminal nerve involvement; hypersensitivity reactions such as erythema nodosum leprosum (type I) or reversal reactions (type II) complicated by corneal hypoesthesia, superficial punctate keratitis, episcleritis/scleritis, nerve paralysis, and/or iridocyclitis; and secondary infections. Early subtle signs of ocular involvement are autonomic dysfunctions, including diminished pupillary reactions and reduced accommodation. Although leprosy is regarded primarily as a tropical disease, 2469 cases were reported in the United States from 1981 to 1990. Imported rather than indigenous cases are responsible for the growing incidence of leprosy in the United States, reflecting the increase in numbers of refugees and immigrants and increased world travel by American citizens.

We reported the long-term follow-up of a man presenting with bilateral uveitis, glaucoma, and keratitis refractive to conventional therapy. Skin, iris and aqueous humor biopsies disclosed abundant Wade-Fite-positive organisms consistent with M. leprae.

CASE REPORT: Three months after emigration from St. Lucia to the United States, a 38 year-old black male presented complaining of progressive decrease in visual acuity in his left eye (OS) over the preceding 8 months. His past ocular history included blunt trauma to his right eye (OD) in 1980 with resultant substantial visual loss.

The patient's visual acuities were finger counting at 2 fee (OD) and 20/100 (OS). Intraocular pressures were elevated in both eyes. Examination of the right eye revealed bullous corneal edema and corneal neovascularization, a fibrovascular membrane on and behind the endothelium, 3+ anterior chamber inflammation, Rubeosis iridis and a secluded miotic pupil. The left eye showed corneal pannus formation superiorly with inferior anterior stromal infiltrates, 3+ anterior chamber inflammation, posterior synechiae and cystoid macular edema.

The patient was treated with topical prednisolone acetate 1%, flurbiprofen sodium 0.03%, timolol 0.5%, diflunisal and transseptal triamcinolone 40 mg to the left eye. extensive laboratory investigations were normal except for elevated circulating immune complexes and a nodular apical density on the chest X-ray, suggestive of granulomatous disease; a skin test for tuberculosis with purified protein derivative (PPD) was reported to be negative with the use of positive controls. Serological tests for syphilis were negative. the patient was referred to a pulmonologist for further evaluation of the pulmonary lesion.

Over the next 2 weeks frank iris granulomas developed in the left eye. The vision in the right eye fell to light perception due to an intraocular pressure of 52 mm Hg secondary to complete angle closure. Bronchoscopy and possible lung biopsy were considered by the pulmonologist to evaluate the pulmonary lesion.

At this point the patient revealed a history of lepromatous leprosy which had been treated 15 years previously for 2 • years with Dapsone and clofazimine. After a 5-year period of post treatment evaluation he had been told he was cured. He reported a reluctance to reveal his disease for fear that it might jeopardize his efforts to obtain citizenship to the United States.

Biopsies of mildly hypopigmented skin of the upper extremities, as well as aqueous humor and iris of the right eye, disclosed abundant Wade-Fite-positive organisms consistent with M. leprae. Mycobacterial culture did not yield any growth, but with the help of molecular biological techniques (PCR amplification and slot-blot hybridization) M. leprae could be identified in the iris specimen. Multidrug therapy with

Dapsone (100 mg/day), clofazimine (50 mg/day), and rifampin (600 mg monthly) was instituted. Topical anti-inflammatory and anti-glaucomatous treatment was continued. The uveitis improved over the following 6 months. The rubeosis iridis regressed on the right, though the vision remained at light perception from corneal opacification, cataract, and presumed glaucomatous optic nerve damage. On the left, the corneal pannus and infiltrates remained stable with fluctuating intraocular pressures requiring the addition of methazolamide therapy. No visual field abnormalities were detectable. the visual acuity of the left eye stabilized at 20/30.

DISCUSSION: Even today, the social stigma of leprosy and the lack of suspicion of this rare disease on the part of physicians in developed societies may delay appropriate diagnosis and care. Although leprotic affection of the iris is less common than corneal manifestation of the disease, iridocyclitis is the most frequent cause of blindness in leprosy patients. Lepromatous iridocyclitis may be caused by persistent M. leprae in ocular structures, may be neuroparalytic, or can be autoimmune. This is evidenced by the reduction of T-suppressor cells during acute lepromatous uveitis and vasculitis/perivasculitis in iris biopsies of leprosy patients with low-grade iridocyclitis, suggesting an immune-complex-mediated reaction. The chronic iridocyclitis in our patient with borderline lepromatous leprosy could have been caused by a combination of persistent organisms as demonstrated by iris biopsy, resulting in cell-mediated reactions such as iris granuloma formation by macrophages, epithelioid cells, and T-lymphocytes, and (b) autoimmune phenomena as evidenced by increased circulating immune complexes. The worsening of symptoms after the application of periocular steroids, however, suggests that infection was the main pathogenic factor in our patient's ocular disease. Transseptal corticosteroids should be used with the utmost caution in uveitis cases in which infection has not completely been ruled out.

Miliary lepromas of the iris or "iris pearls", which developed in our patient during follow-up, are pathognomonic features of leprous eye involvement. M. leprae may localize to the iris very early during dissemination of the organisms throughout the body and may multiply in stromal mononuclear cells which take on the appearance of foam cells. Such cells containing "globi" composed of closely packed acid-fast bacilli coalesce and become clinically visible as iris lepromas. "Iris pearls", however, are rarely discovered without evidence of previous or acute iris inflammation as in our patient.

Glaucoma is supposedly an uncommon complication of leprosy, and decreased intraocular pressures were found in the majority of patients with leprous iridocyclitis in one study. Walton and coworkers, however, reported glaucoma in 10% of their leprosy patients which in most cases was secondary to uveitis.

The eyes of patients with lepromatous leprosy may harbor living organisms or antigen long after the skin is bacteriologically negative. In one study 24% of patients had ongoing eye problems after completion of multidrug therapy, indicating that regular ocular examinations are necessary even after the systemic disease is controlled. The appearance of new ocular lesions in a leprosy patient may be the first sign of incomplete treatment or relapse of the leprous disease, as demonstrated in our patient. Our patient was treated with Dapsone and clofazime, two drugs weakly bactericidal against M. leprae. the duration of his two-drug therapy was probably adequate to achieve an intermittent bacteriological "cure" as evidence by negative skin smears immediately after treatment, but inadequate to eliminate M. leprae from the eye. The WHO study group recommends treatment of "borderline" lepromatous leprosy with a multidrug regimen consisting of Dapsone (100 mg/day), rifampicin (600 mg once monthly) and clofazimine (300 mg once monthly, 50 mg/day) for at least 2 years and, whenever possible, up to skin smear negativity. They emphasize that one of the drugs combined with Dapsone should always be rifampicin because it has the greatest potency. In addition to not having received rifampicin as part of his therapy, our patient may have been infected by a Dapsone-resistant strain of M. leprae, and his two-drug regimen may have been inadequate to eradicate the organisms. Moreover, longer treatment courses than suggested by the WHO for the therapy of the systemic disease may be necessary to cure ocular leprosy.

Acid-fast organisms have been reported in the aqueous humor and in a scleral nodule of a patient with lepromatous iridocyclitis. The diagnosis in our patient was ultimately established by demonstrating M.

leprae in aqueous humor and involved iris tissue. Leprosy must be considered in the differential diagnosis of keratitis and uveitis.