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CASE REPORT

Optic nerve involvement in a borderline lepromatous leprosy patient on multidrug therapy

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Summary Amidst the plethora of ocular complications of leprosy, involvement of the posterior segment or optic nerve is extremely rare. The mechanism of optic neuritis in leprosy is poorly understood. A 47 year-old man presented with a single lesion suggestive of mid-borderline (BB) leprosy over left periorbital region; the histology showed borderline lepromatous (BL) leprosy with a BI of 3+. After initial improvement with WHO MDT-MB and prednisolone (40 mg/d) he developed sudden and painless diminished vision in the left eye, about 3 weeks later. His visual acuity was 6/9 in the left and 6/6 in the right eye, and there was left optic disc edema, hyperemia and blurred disc margins. Treatment with prednisolone (60 mg/d) along with WHO MDT-MB continued. A month later he returned with painless diminished vision in the other eye as well. Visual acuity was 6/6 in the right and 6/12 in the left eye, and there was right optic disc edema and left optic disc atrophy. CT of the head and MRI of the brain were normal. Inflammatory edema of the orbital connective tissue or other surrounding structures, or direct infiltration of vasa nervosa with resultant vascular occlusion leading to optic nerve ischemia, seems the most plausible explanation of optic nerve involvement in this case.

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Introduction

Nerve involvement in leprosy occurs prior to any clinical manifestation and nerves which are superficial, traversing through relatively cooler areas are liable to trauma; the supra orbital, great auricular, ulnar, median, radial cutaneous, lateral popliteal, posterior tibial nerves are mostly affected. *Mycobacterium leprae* gains entry into the nerve and multiplies inside the Schwann cells. The initial segmental demyelinating neuropathy leads to axonal degeneration manifesting clinically as mononeuritis, mononeuritis multiplex or symmetrical polyneuropathy. Cranial nerve involvement occurs along with any of these three types of peripheral neuropathy or rarely as an isolated feature.[1] Involvement of the facial or trigeminal nerves has been commonly reported in borderline tuberculoid (BT) leprosy while olfactory nerve involvement is observed frequently in borderline lepromatous or lepromatous (BL, LL) leprosy.[2] In rare instances auditory, oculomotor, glossopharyngeal, vagus, spinal accessory and hypoglossal nerves may be affected.[1] Optic nerve involvement in leprosy is considered extremely rare.[3]

Case Report

A 47 year-old man was hospitalised with an erythematous, infiltrated, annular plaque over the left periorbital region, of 1 month duration (Figure 1). He had no other skin lesions, peripheral nerve thickening or sensory loss over the lesion or hands/feet. A slit-skin smear examination from the lesion showed BI 3+. He had diabetes for the last 7 years. Systemic examination including ophthalmic examination, chest x-rays and laboratory work up were essentially normal except for elevated erythrocyte sedimentation rate (ESR 35 mm in the first hour, normal 5–10 mm in the first hour by Westergren method) and fasting blood sugar levels (FBS) varying between 78 and 363 mg/100 ml (HbA_1C 15%) during 10 days of hospitalisation. A biopsy from the skin lesion showed histologic features of borderline lepromatous (BL) leprosy in Type-1 lepra reaction. With the diagnosis of BT leprosy downgrading to mid borderline (BB) leprosy, multidrug therapy (WHO MDT-MB, rifampicin 600 mg, clofazimine 300 mg and dapsone 100 mg once a month given supervised, and clofazimine 50 mg/d and dapsone 100 mg/d given unsupervised) and prednisolone (40 mg/d) were started along with insulin (12 units before breakfast and 10 units before dinner) for diabetes mellitus. After adequate control of his skin symptoms and blood sugar levels he was discharged. He was hospitalised 3 weeks later with sudden and painless vision loss in

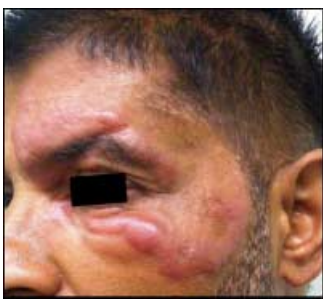

Figure 1. An erythematous, infiltrated, annular plaque over the left periorbital region. Irregular margins suggest downgrading to BL Leprosy.

the left eye. His visual acuity was 6/9 in left and 6/6 in right eye and the anterior chamber showed no abnormality. The right eye and color vision were normal. There was relative afferent pupillary defect (RAPD). Direct ophthalmoscopy revealed left optic disc edema, hyperemia and blurred inferio-nasal disc margins and no diabetic retinopathy (Figure 2A). There was decreased generalised sensitivity, and constriction of left visual field (Figure 3). Repeat laboratory investigations showed elevated ESR (39 mm in the first hour) and FBS levels varied between 65 and 340 mg/100 ml. With a diagnosis of anterior ischemic optic neuropathy the dose of prednisolone was increased to 60 mg/d and treatment with WHO MDT-MB continued. Metformin (1000 mg/d, PO) was added along with increased doses of insulin (24 units before breakfast and 18 unit before dinner). A month later he presented again with painless diminished vision in the right eye and no significant improvement in left eye vision. Repeat ophthalmic examination showed visual acuity of 6/6 in right and 6/12 in the left eye, optic disc edema of right eye and partial optic atrophy of left eye (Figure 2A) and no features of diabetic retinopathy. Computed tomography and MRI of the head showed no abnormality of brain parenchyma, ventricles, vasculature, optic chiasma or other cranial nerves. During the next 3 months of treatment with WHO-MDT- MB, oral prednisolone (60 mg/d, tapered to 10 mg/d), insulin and oral hypoglycemic agents his vision improved or remained stable (6/9 in the left eye, 6/6 in the right eye) while disc pallor persisted, more in the left than in the right eye (Figure 2B).

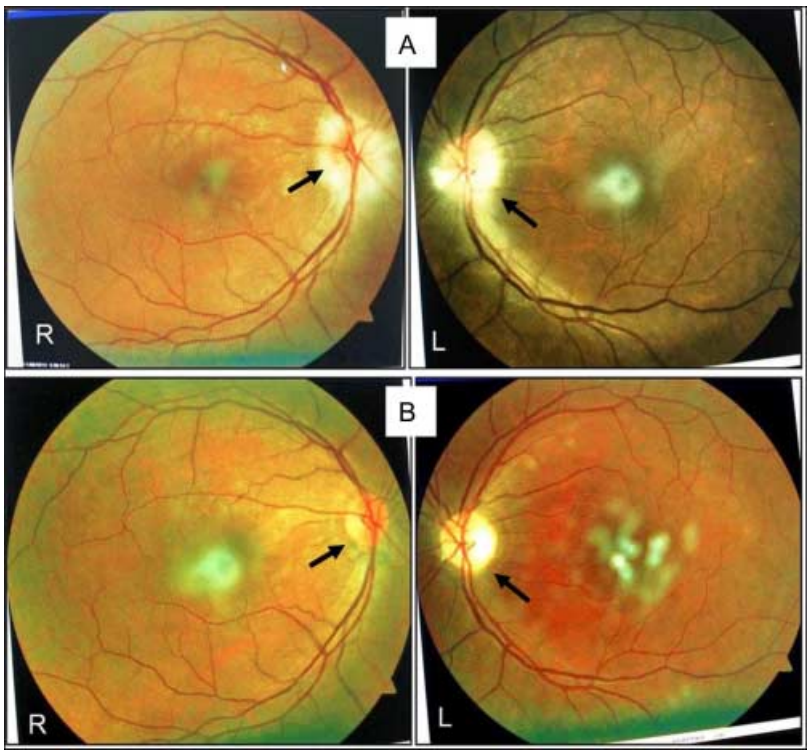

Figure 2A. Both right (R) and left (L) optic discs show acute edema, hyperemia, blurred disc margins and normal foveal region at the time of onset of optic neuritis (arrows). **2B:** Both right (R) and left (L) optic disc pallor (more in left than right) due to optic atrophy at 10 and 12 weeks respectively after the onset of optic neuritis. Disc margins have become well demarcated (arrows).

Discussion

The ophthalmic complications in leprosy may be due to direct infiltration by *M. leprae* or leprosy reactions.[4] Direct invasion of the cornea by *M. leprae* or involvement of trigeminal

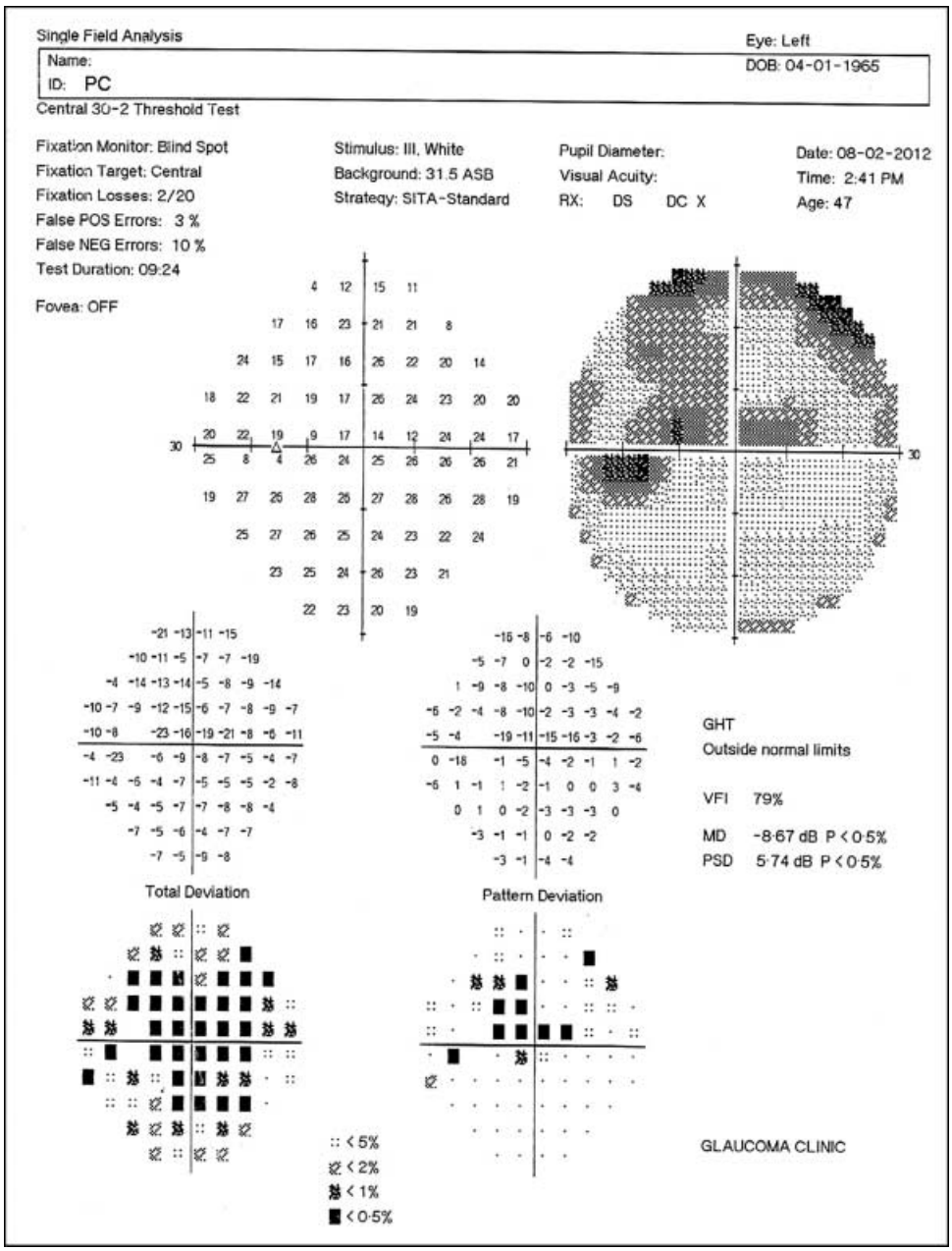

Figure 3. Perimetry field of the left eye of the patient at onset of the optic neuritis shows decreased generalised sensitivity, constriction of left visual field and no centrocaecal scotoma.

and facial nerves results in stromal/punctate keratitis, opacities, or corneal ulcer. Uveitis with its complications may be due to direct invasion by *M. leprae* or from Type-2 lepra reaction. Invasion by *M. leprae* also causes dacryoadenitis and supra-cilliary or cilliary madarosis while facial nerve involvement will manifest in lagophthalmos and eyelid deformity (ectropion, entropion, or trichiasis). Involvement of the posterior segment or the optic nerve is extremely rare in leprosy. However, some reports suggest that there may be subclinical optic nerve involvement particularly during reactions.[5,6] Early diagnosis and management of optic neuritis from any cause is of paramount importance in preventing blindness. Clinically, nearly 65% of patients with optic neuritis may have normal optic nerve appearance at presentation and they are considered to have retrobulbar optic neuritis. Periocular pain is seen in 90% of cases and may occur before the onset of visual loss, which is mostly unilateral with severity varying between mild to total loss of light perception. A centrocaecal scotoma is typical in optic neuritis and a RAPD is present in the affected eye. However, visual loss, periocular pain and dyschromatopsia, the three most common symptoms, have inconsistent and variable presentation. The study of visual evoked potentials (VEPs), which measure functional changes occurring earlier than anatomical changes and are reversible, is preferred over magnetic resonance imaging (MRI) in the early diagnosis of optic neuritis.[6] Interestingly, our patient presented with single lesion BB leprosy without facial or trigeminal neuritis and optic neuritis of sudden onset.

The pathogenesis of optic neuritis in leprosy is poorly understood. Lee *et al.*[4] suggested that optic neuritis in leprosy resembles post viral immune mediated optic neuritis due to direct viral infection, or to molecular mimicry between viral and neural antigens, or attachment of viral antigen to neural tissues such as the membrane of oligodendrocytes and the myelin sheath. However a Type-1 leprosy reaction, a delayed (Type IV) hypersensitivity reaction which occurs in relation to dead bacilli in dermal macrophages and Schwann cells leading to inflammation of the skin and nerve trunks, is unlikely to manifest in the optic nerve due to the absence of Schwann cells, the primary target for leprosy bacilli.[3] Another possible explanation is that granulomatous inflammation is perhaps itself destructive for the involved tissue as well as for the nerves caught up in the inflammatory process as has been observed in cases of other non-leprous granulomas.[3,7] Dhaliwal *et al.*[8] also described a case of erythema nodosum leprosum and orbital involvement leading to orbital apex syndrome and ocular ischemia i.e. non-arteritic anterior ischemic optic neuropathy (NAION). Occulomotor (3rd), supratrochlear (4th), first branch of trigeminal (5th) and abducent (6th) cranial nerves enter the orbit through the supraorbital fissure while the optic nerve along with the ophthalmic artery enters the orbit via the optic canal. Any inflammation involving the orbital apex will interrupt the nerves in these bony canals leading to ophthalmoplegia, loss of vision and ocular sensations (orbital apex syndrome). Associated inflammatory edema of orbital connective tissue and vasculitis affecting the ophthalmic, posterior (short) cilliary or central retinal arteries (branches of ophthlamic artery), will result in ocular ischemia of posterior segment, manifesting in sudden visual loss. Although dapsone, particularly in high doses (400-800 mg/d), is reported to cause toxic optic neuritis or NAION perhaps from decreased oxygenation as a result of hemolysis, therapeutic doses (100 mg/d) are not considered likely to cause direct retinopathy or optic neuritis.[9,10] The optic neuritis did not deteriorate in our patient despite being continuously on dapsone. His diabetes was well controlled and the features of diabetic retinopathy were absent. Post neuritic optic atrophy is rare in uncontrolled diabetes even if it is long standing and develops insidiously, and occurs mostly in association with other features of diabetic retinopathy.[11] Although it might have been due to other causes,

inflammatory edema of orbital connective tissue or other surrounding structures from Type-1 lepra reaction or due to direct infiltration of vasa nervosa with resultant vascular occlusion (vasculopathy) leading to reduced perfusion and oxygenation (ischemia) of the optic nerve, arteritic anterior ischemic optic neuropathy seems more plausible in our case. The efficacy of systemic steroids in resolution of optic neuritis remains speculative[4] as the visual loss progresses for an average of 7-10 days before recovery begins spontaneously within 2-3 weeks and becomes stabilised over several months.

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