

Histopathological study of ocular erythema nodosum leprosum and post-therapeutic scleral perforation: A case report

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Leprosy is a chronic granulomatous disease caused by *Mycobacterium leprae*, clinically present either as tuberculoid, borderline or lepromatous type. Erythema nodosum leprosum (ENL) is an acute humoral response in the chronic course of lepromatous leprosy. Although very severe ENL reactions are known in systemic leprosy, such severity is rare in ocular tissues. A leprosy uveitis patient suffered from a severe form of post-therapeutic ENL reaction which resulted in perforation of the globe at the site of preexisting subconjunctival leproma. Painful blind eye was enucleated. Histopathological study revealed infiltration of numerous polymorphs and macrophages packed with acid-fast bacilli in the conjunctiva, cornea, ciliary body, ora serrata and sclera. A profuse influx of neutrophils on a background of macrophages packed with *M. leprae* confirmed the ocular ENL reaction. This case is reported to alert the ophthalmologists to a rare ocular complication of ENL.

Key words: Leprosy, ocular erythema nodosum leprosum, scleral perforation

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Leprosy is a chronic granulomatous infection caused by *Mycobacterium leprae*. Depending on the immunological status of the patient, the disease clinically presents either as tuberculoid, borderline or lepromatous type. Erythema nodosum leprosum (ENL) is an acute inflammatory reaction that results out of an exaggerated humoral response. This complicates the chronic course of lepromatous leprosy. Histopathological changes of ENL reactions of skin, nerves, lymph nodes and joints have been reported earlier.¹⁻⁴ Such studies are rare in ophthalmology because of the difficulty in obtaining biopsy from the inflamed eye. A leprosy patient, on starting multi-drug therapy (MDT), developed severe systemic and ocular ENL reaction and perforation of the globe. We report a histopathological study of ocular ENL.

A 42-year-old male lepromatous leprosy (LL) patient refused MDT after one month of treatment initiation because of severe ENL and he was lost for follow-up. After 15 years, he developed pain in his left eye. On general examination, patient had trophic ulcers in the fingers and toes. His vision was 20/20

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in his right eye and 2/200 in the left. Intraocular tension was normal in both eyes. He had bilateral chronic anterior uveitis, the left eye showed a conjunctival leproma near 5 o'clock position of limbus and an iris granuloma. Hypopyon was seen in the anterior chamber which revealed positive acid-fast bacilli (AFB) on 5% Ziehl-Nielsen staining.⁵ After 20 days of standard MDT, (rifampicin 600 mg first day of every month, clofazimine 50 mg/day, and dapsone 100 mg/day) and 40 mg oral prednisolone started by the dermatologist, the patient became febrile. Multiple tender ulcers with elevated necrotic base and serosanguinous discharge appeared all over the body and he developed severe excruciating pain in his left eye. The left eye was congested, a scleral perforation and iris prolapse were seen at the previous site of leproma [Figure 1]. Anterior chamber showed 4+ inflammatory cells and a blood-tinged hypopyon. Left eye had no light perception. After informed consent, enucleation was performed to alleviate the pain in the blind left eye. The patient was referred back to the dermatologist for additional steroids for ENL.

The enucleated eye was fixed in 10% buffered formalin. Several 5µ thick sections were cut and stained with hematoxylin and eosin (H and E) and modified Fite's stain.⁶ Gross examination of the enucleated eyeball showed a marked disruption of the normal architecture of the eyeball [Figure 2]. Histopathological findings are discussed in four major sites including leproma [Figure 2A,B], ciliary body, ora serrata, posterior choroid [Figure 2C,D,E] and the sclera [Figure 3]. The leproma infiltrated into the ciliary body along the choroid and slightly beyond the ora serrata resulting in disruption of conjunctiva, sclera, cornea and the ciliary body. Perforation of the eyeball was noted at the limbus near the leproma. Descemet's membrane was seen fragmented [Figure 2A], iris tissue was seen prolapsing. Hematoxylin and eosin staining revealed inflammatory cells infiltrating the conjunctival epithelium forming micro-abscesses. The limbal leproma was composed of numerous polymorphs and macrophages, plasma cells and lymphocytes. The ciliary body and choroid also showed lymphocytes and macrophages with foamy cytoplasm. Modified Fite's stain for AFB revealed heavily loaded *Mycobacterium leprae* inside the macrophages in the conjunctival epithelium, leproma, cornea, iris, ciliary body, ora serrata and sclera. Some of the bacilli were solid staining and many were granular. The choroidal blood vessels were dilated. Significantly, a large number of polymorphs were



Figure 1: Scleral perforation and iris prolapse: Inset showing trophic ulcer and extensive tissue loss

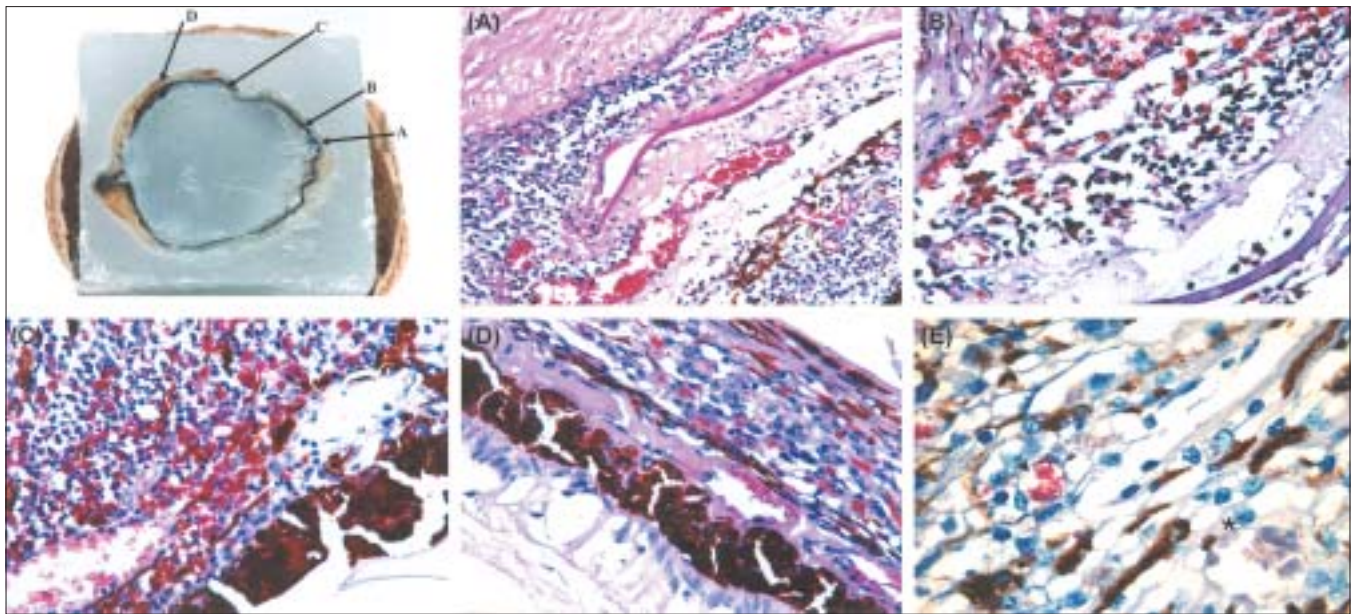


Figure 2: Enucleated eyeball with marked disruption of architecture of the eyeball. The cornea, conjunctiva and sclera are partly destroyed. Labels, a, b, c, and d represent the sites of cytological analysis shown in subsequent figures. (A) Section at limbus (Site "a" of fig 2 H&E) Leproma infiltrates anterior segment, shows numerous polymorphs, macrophages, plasma cells and lymphocytes. A disrupted Descemet's membrane seen with micro-abscesses. Iris is distorted and filled with lymphocytes (x200). (B) Section at limbus (site "a" of fig 2 - Modified Fite's stain) *Mycobacterium lepra* seen inside as well as outside the macrophages. Descemet's membrane is fragmented. Conjunctival epithelium shows micro-abscesses and ulcerations (x400). (C) A fragmented ciliary body is seen with pigment dispersion (site "b" of fig 2). It is surrounded by plasma cells and foamy macrophages which are loaded with lepra bacilli. The blood vessel is much dilated (Modified Fite's x400). (D) Section at the ora serrata (site "c" of fig 2) shows intact retina, free of inflammatory cells. Significantly, a large layer of macrophages loaded with bacilli and polymorphs is infiltrating the choroid. Choroidal blood vessels are dilated (Modified Fite, x400). (E) (Site "d" of fig 2) Red-colored bacilli inside macrophage (Arrowhead) adjacent to faint pink RBCs inside capillaries (Asterisk). Few bacilli-filled macrophages and more of polymorphs in the posterior choroid. The architecture of macrophages in the posterior segment is preserved (Modified Fite's, x1000)

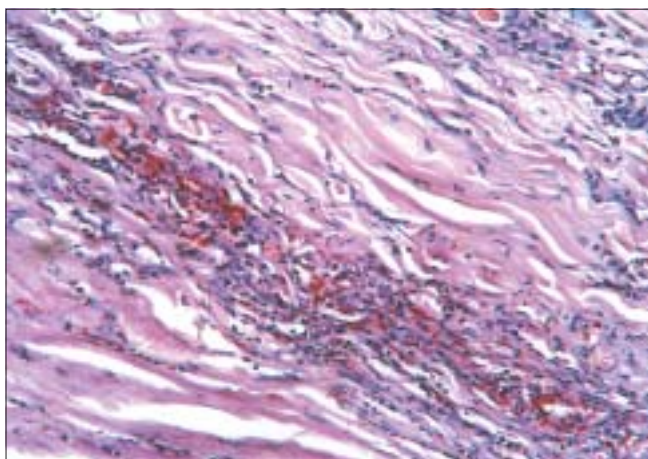


Figure 3: Bacilli-filled macrophages and more of polymorphs in the sclera (Modified Fite's, x200)

seen infiltrating the choroid. However, when compared to the anterior segment, there were lesser macrophages loaded with bacilli in the posterior choroid [Figure 2E]. No organisms were present anywhere in the retinal layer although macrophages in the choroid were packed with AFB.

Discussion

Polar lepromatous leprosy is the anergic form of the disease characterized by marked lack of cell-mediated immunity

against leprosy. Macrophages become foamy in which *Mycobacterium leprae* continue to grow and multiply and are transported to all parts of the body. The bacilli invade the anterior segment of the eye and cause chronic uveitis. Our patient had old keratic precipitates, iris atrophy and 2-mm hypopyon in the anterior chamber. As reported earlier, the anterior chamber aspirate revealed plenty of AFB on Ziehl-Nielsen staining confirming the clinical diagnosis of leprosy uveitis.⁵

The course of the disease is dependent mainly upon the individual's immunologic response to the bacilli. Erythema nodosum leprosum is an acute and exaggerated immunological reaction in the chronic course lepromatous leprosy, it can be very severe and prove fatal.¹⁻⁴ Severe ENL is termed as erythema necroticans when it presents as pustular or ulcerated lesions.¹ Patients with lepromatous disease and a bacterial index of >4+ were reported to be at significantly increased risk, the usual triggers associated with ENL reaction include intercurrent illness or anti-leprosy treatment.⁷ Even though our patient received moderate doses of steroids in addition to MDT, he developed severe necrotic systemic ENL.

Histopathologically, ENL or Type 2 reaction is characterized by an influx of neutrophils on a background of lepromatous granuloma in contrast to Type 1 reaction which depict granulomas comprising of epithelioid cells, lymphocytes and Langhans giant cells.⁸ The infiltration of neutrophils is specific to lepromatous ENL while it is lymphocyte infiltration in erythema nodosum of other causes.⁹ Chaudhary reported a

case of lepromatous ENL with a very high leucocyte count in the peripheral blood and he named it as a myeloid leukemoid reaction.¹⁰ In our patient, in addition to macrophages, numerous polymorphs with and without *Mycobacterium leprae* were seen in almost all layers except the retina. Perforation of the globe with influx of neutrophils during the generalized ENL reaction confirmed ocular ENL.

Leprosy is a challenging disease to manage because of patient's varying immune response. This report depicts a case of histopathologically confirmed severe ENL that resulted in post-therapeutic perforation of the globe. This case is reported to alert the ophthalmologists to the peculiar ocular complication of ENL when a patient is treated with highly bactericidal drugs.

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