Ocular erythema nodosum leprosum: An immunohistochemical study

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Episcleritis, scleritis, and anterior uveitis are common clinical manifestations of ocular leprosy. Erythema nodosum leprosum (ENL) is an acute, exaggerated systemic immunological reaction that complicates the course of this chronic indolent disease. We present an ocular immunohistochemical study of severe form of ENL involving even the ciliary body and choroid resulting in the perforation of the globe on the initiation of anti-leprosy therapy. We used CD-3, CD-68, S-100, and CD-20 for immunohistochemistry. It revealed plenty of CD-3-positive T-cells and CD-68-positive macrophages and a few S-100 and CD-20-positive cells. The inflammatory exudates stained positive for IgG and IgM. The diagnosis was ocular ENL.

**Key words:** Eye, immunohistochemistry leprosy, ocular erythema nodosum leprosum

Patients with lepromatous leprosy lack cell-mediated immunity, which is protective in nature. Humoral immune reaction is not protective and results in erythema nodosum leprosum (ENL), an acute and exaggerated immunological reaction. Humoral immune reaction results in maximum tissue damage in some patients, even steroids fail to stop immune reaction in some patients. We present immunohistochemical features of ENL as a result of severe ocular humoral immune reaction and ocular perforation.

**Case Report**

A 40-year-old male patient presented to an ophthalmologist with complaints of pain and redness in his left eye for 2 months. The patient produced documented evidence of histopathologically confirmed polar lepromatous leprosy (LL) diagnosed 15 years back. However, he stopped taking the drugs after one month as he suffered from recurrent episodes of erythema nodosum leprosum (ENL) following the treatment. According to him he never went for a follow-up to the leprosorium thereafter. He attended eye hospital after 15 years of initial systemic diagnosis. His vision was 20/20 in his right eye and 20/400 in the left. On general examination, the patient had severe malformation of fingers and toes of both the hands and both the legs [Fig. 1]. He also had multiple trophic ulcers and hypopigmented skin lesions. The left eye showed a lepoma near the 5-o-clock position of the limbus. Hypopyon and inflammatory cells were noted in the anterior chamber. After 20 days of standard WHO multibacillary multidrug therapy and 40 mg oral corticosteroids, the patient developed excruciating pain in his left eye and multiple tender skin ulcers with serosanguinous discharge. There was no light perception in the left eye. A scleral perforation was seen at the previous site of the lepoma [Fig. 2]. After written informed consent, enucleation of the left eye was performed to alleviate the pain, and the globe was stored in paraffin block. The patient was referred back to leprasorium for control of systemic ENL.

Institutional review board approval was obtained [RES2005017BAS] to study pathogenesis of leprosy infection. Histopathologic examination of the globe was performed after staining with hematoxylin and eosin to study the inflammatory cells. Modified Fite’s stain was used...
to stain the acid-fast bacilli. The patient’s globe was also studied immunohistochemically with CD-3, CD-68, CD-20, IgG, and IgM as well as S-100. Macroscopic examination of the globe showed perforation of the eye ball. An iris prolapse was noted near the limbal leproma. Histopathology revealed infiltration by acute inflammatory cells and macrophages in the disrupted cornea, conjunctiva, and sclera. The leproma of the limbus was composed of numerous viable and necrotic leukocytes, macrophages, lymphocytes, and scattered plasma cells. Several macrophages had foamy cytoplasm, and some were granular. Surprisingly, even the ciliary body showed inflammation along the choroid and slightly beyond ora serrata. Lepra stain revealed the presence of numerous lepra bacilli within the histiocytes in the anterior segment involving the sclera, iris, and ciliary body [Fig. 3]. Similarly, several bacteria were noted within the long ciliary nerve in the choroid. However, the choroidal tissue surrounding the nerve showed only
chronic inflammatory cell infiltration. The retina showed the absence of inflammatory cells and lepra organisms. CD-3 was 4+ positive. Similarly, CD-68 was 4+ positive. CD-20 revealed trace cells to 1+ positive. IgG and IgM were trace positive and S-100 cells were few. The sclera was perforated, and the wound contained necrotic iris tissue [Fig. 4]. The diagnosis was ocular ENL.

**Discussion**

Polar LL is the widespread anergic form of the disease where there is a lack of cell-mediated immunity against leprosy. Without the assistance of "T" lymphocytes, macrophages ingest *M. leprae* and they cannot digest them. Macrophages become foam cells inside which *M. leprae* continue to grow and multiply and are transported to various parts of the body in the bloodstream.\(^1\) This makes LL, a disseminated disease, which is found in all parts of the body. Similarly in our patient, plenty of lepra bacilli were seen even in the aqueous fluid on aspiration and modified Fite’s staining, which we published previously.\(^2\) There was a subconjunctival leproma near the limbus. On histopathology, massive collections of macrophages containing large numbers of acid-fast lepra bacilli were seen in the hypopyon.\(^3\)

ENL is an acute inflammatory response in LL.\(^1-7\) ENL reaction is characterized by an influx of neutrophils at the site of leprosy lesions. The histologic changes of ocular tissue observed in this study were similar to those observed in the skin lesions of ENL. The infiltrate contained CD-68-positive macrophages and CD-3-positive lymphocytes, and exudates made up of IgG.\(^7-10\)

**Conclusion**

The mechanism for the development of ENL appears to be the release of bacterial antigen and an exaggerated immune response, which is mediated by immune complex formation and generation of tumor necrosis factor (TNF)-α. The immunohistochemical findings of the present case support the exaggerated immune response with the presence of large numbers of CD-3-positive T- cells and deposits of IgG. Since ENL is an exaggerated immunologic process, higher dose systemic corticosteroids could have prevented these reactions.\(^10\) Some patients may need only oral steroids, some need intravenous steroids, and some may need even immunosuppressives like methotrexate or even thalidomide. Our patient was unwilling for any further medication.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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