

Ocular manifestations of Hansen's disease

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Abstract. A detailed ophthalmic evaluation including slitlamp biomicroscopy, measurement of corneal sensitivity using Cochet and Bonnet aesthesiometer, Schirmer's test and Goldmann applanation tonometry was carried out in 89 patients of Hansen's disease attending the leprosy clinic with or without ocular symptoms and willing to undergo eye evaluation. Thirty-one patients had lepromatous leprosy (8 with erythema nodosum leprosum), 56 patients had borderline disease (13 with reversal reactions) and 2 had tuberculoid disease. In addition to the well documented changes of lagophthalmos (6.7%), uveitis (7.3%) and cataracts (19%), we noted prominent corneal nerves in 133 eyes (74.7%), beaded corneal nerves in 19 eyes (10.7%), corneal scarring in 10 eyes (5.6%), corneal hypoaesthesia in 51 eyes (28%) and dry eye in 18 eyes (13%). Beaded corneal nerves and/or stromal infiltrates occurred mainly in the lepromatous group (75%). Ocular hypotony (IOP less than 12 mm Hg) was not seen more frequently in Hansen's as compared to age and sex matched controls with refractive errors or cataracts (33.7%, vs. 37.8%, $p=0.33$). Our study highlights the primary corneal involvement with corneal neuropathy as the predominant feature of Hansen's disease.

Introduction

Leprosy is a systemic disease caused by the organism mycobacterium leprae, an acid fast bacillus. In a recent report, World Health Organization estimated 250,000 blind people in a total of 10–12 million leprosy patients, world wide. Most of the ocular complications of leprosy are sight threatening and can be prevented if timely treatment is given.

Ridley and Jopling classify leprosy into 5 groups with a spectrum of high cellular immunity and low bacterial counts (tuberculoid - TT) at one end to low cellular immunity and high bacterial counts (Lepromatous-LL) at the other end. There are three intermediate forms; Borderline Lepromatous (BL), Borderline tuberculoid (BT) and Borderline Borderline (BB). For therapeutic purposes the smear positive LL, BL and BB are also called multi bacillary disease (MB) and the smear negative TT and BT are termed as paucibacillary disease (PB). Two types of reactions are described in leprosy, Erythema nodosum leprosum (ENL) is seen in lepromatous leprosy and Reversal reactions (RR) is seen in borderline leprosy.

In this report we present the ocular findings in patients with Hansen's disease wherein detailed ophthalmic evaluation including corneal sensation by Cochet and Bonnet aesthesiometer, intra ocular pressure by Goldmann applanation tonometer, Schirmer's test, slit lamp biomicroscopy and fundus evaluation were carried out.

Patients and methods

The patients in this study attended the Dhoolpet Leprosy Research Center in Hyderabad. All patients attending the clinic for out-patient care, with or without eye complaints and who were willing to undergo a comprehensive eye examination were included in the study.

Disease assessment. The disease status of each patient was assessed at Dhoolpet Leprosy Research Center before referral for eye examination. This comprised complete history, clinical examination and bacteriological tests, including skin smears and skin biopsy where indicated. The age and sex of patient, out-station address, date of diagnosis, disease classification, both clinically and bacteriologically, treatment history and current clinical status were recorded. Biopsy confirmation was available in most cases.

Ophthalmological assessment. Each patient underwent a complete ophthalmic evaluation. After recording the best corrected visual acuity and the adnexal anomalies, Schirmer's test was carried out on the unanaesthetised eye. Wetting of less than 12 mm of the Schirmer's strip after 5 min was taken as evidence of dry eye. Corneal sensation of the pupillary area was assessed by the Cochet and Bonnet aesthesiometer and was recorded as the length of the filament which elicited a blink response. The sensation was considered normal if the length of the filament was between 60 and 40 mm, reduced if the length was between 39 and 20 mm and absent if the length was less than 20 mm. Detailed slit lamp biomicroscopy of the anterior segment was carried out, followed by Goldmann applanation tonometry. Dilated lens and fundus evaluation completed the ocular examination.

Results and observations

Patient demographics and disease status. Of the 89 leprosy patients in this study, 69 (77.5%) were male and 20 were female (22.5%). Thirty-one patients had lepromatous leprosy (8 with erythema nodosum leprosum) and 56 patients had borderline disease (13 with reversal reaction). Of these, 34 patients had PB disease and 55 had MB disease. Age of the study population ranged between 12 and 81 years with a mean age of 37.4 years. Mean duration

Table 1. Summary of ocular findings in Hansen's disease

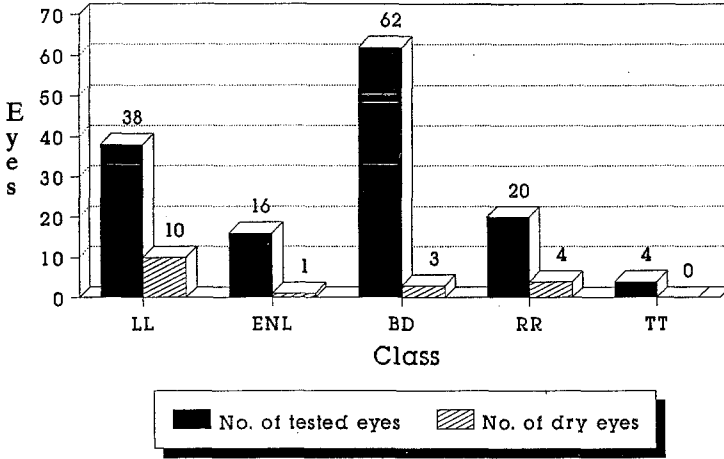
	LL (46 eyes)	EN (16 eyes)	BD (8 eyes)	RR (26 eyes)	TT (4 eyes)	Total (178 eyes)
<i>Findings</i>						
<i>Adnexa</i>						
Madriasis	30	8	16	3	2	59
Lagophthalmos	-	-	10	2	-	12
<i>Cornea</i>						
Prominent 'N'	30	16	67	16	4	133
Beaded 'N'	9	9	-	1	-	19
Infiltrate	8	4	8	1	-	21
Scarring	2	-	7	1	-	10
Reduced Sensation	11	4	26	7	2	50
<i>Iridocyclitis</i>						
Acute	1	-	1	-	-	2
Healed	6	-	4	1	-	11
<i>Cataract</i>						
Senile	4	-	16	2	-	22
Complicated	8	2	2	0	-	14

of leprosy was 7.7 years in lepromatous patients and 3.3 years in borderline patients. Of the two tuberculoid (TT) patients, one was newly diagnosed and the other diagnosed 4 years ago. Fifty-one patients (58%) had been diagnosed as having leprosy within the last 3 years.

Ocular findings. The ocular findings with respect to disease class are summarized in Table 1.

Visual acuity. Initial testing revealed that 20 (11.2%) eyes had a vision less than 6/60 and refraction failed to improve the acuity of 10 eyes (5.6% of total eyes tested) which were thus socially blind. In five of these, the poor vision could be attributed to Hansen's disease, by way of complicated cataract, healed iridocyclitis or corneal stromal scarring. In 4 eyes senile cataract accounted for the poor vision and the 10th eye had anisometropic amblyopia.

Adnexal findings. Brow madarosis (partial or extensive) was the most common finding, occurring in 59 (33.1%) eyes. Though noted in all classes, it was predominantly a feature of lepromatous disease, accounting for 38 (64.4%) of affected eyes.



Total no. of tested eyes: 140;
 Total no. of dry eyes: 18.

Fig. 1. Dry eye by disease class.

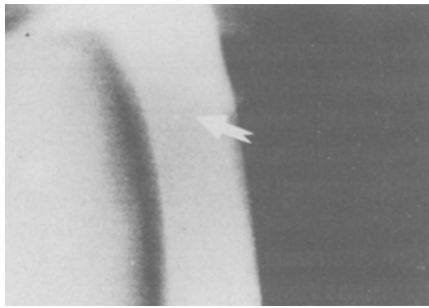


Fig. 2. Beaded corneal nerve.

Lagophthalmos was noted in 12 (6.7%) eyes, in 3 of which, there was, in addition, an ectropion of the lower lid. All of these 12 eyes were of borderline disease with 2 of them in reversal reaction patients. Seven eyes were managed conservatively and 5 were advised surgery. Schirmer's test was performed in 140 eyes. Dry eye was detected in 18 eyes (12.9%), the condition being most common in LL patients (Fig. 1). In addition, 5 of these eyes had superficial punctate keratitis.

Corneal changes. Corneal changes were a common finding among the study population. Prominent corneal nerves were observed in 133 (74.7%) eyes, there being no significant variation between disease class. Corneal nerve beading (Fig. 2) occurred in 19 (10.7%) eyes. A finding termed 'stromal

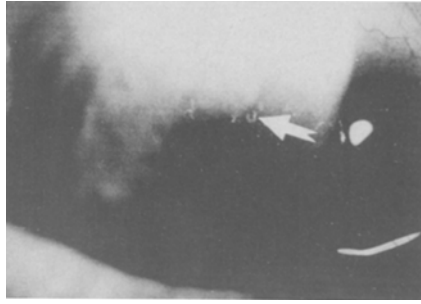


Fig. 3. Superficial corneal infiltrate.

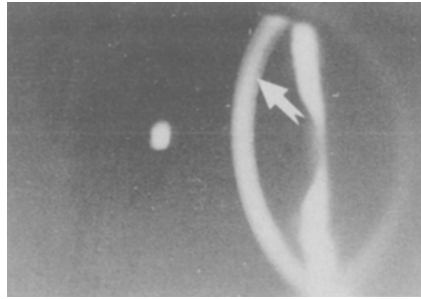


Fig. 4. Deep corneal infiltrate.

infiltrates' or avascular keratitis was documented in 21 eyes. They were of 2 distinct types; the first in the anterior stroma, close to the limbus in the superonasal, superotemporal or 6 o'clock position, of granular appearance and with ill-defined margins (Fig. 3); and the second occurring in the posterior stromal layers of the cornea, positioned more centrally and larger in extent (Fig. 4). The presence of corneal beaded nerves and corneal stromal infiltrates was analysed independently and together with respect to disease class and are depicted in Figs. 5 and 6. These findings were found to be more common in the LL group with or without ENL as compared to others, as well as more common in the multibacillary disease as compared to paucibacillary disease. Scarring secondary to Hansen's disease was observed in 10 (5.6%) eyes. In 5 of these eyes, it could be attributed to exposure keratitis secondary to lagophthalmos; in the remaining 5, the aetiology was healed stromal keratitis (Fig. 7). The presence of corneal hypoaesthesia (absent or reduced) was noted in a total of 50 (28.7%) eyes. The data was analysed with respect to paucibacillary and multibacillary disease status. There appeared to be no significant difference between classes, hyposensation occurring in 26.5% of paucibacillary and 29.0% of multibacillary groups. The incidence of ocular

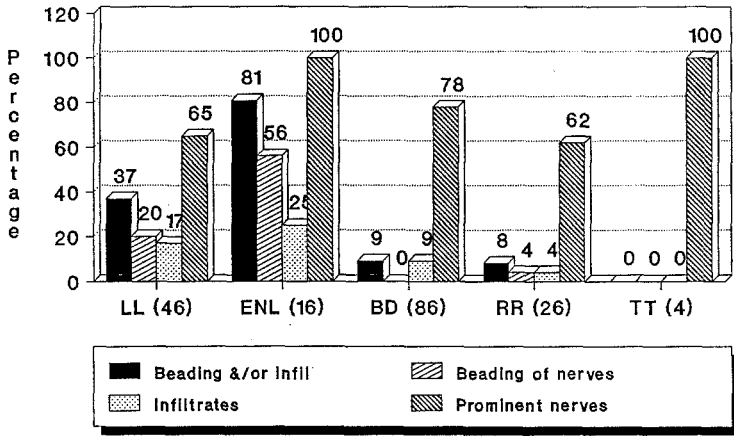


Fig. 5. Corneal stromal and innervational findings by disease class.

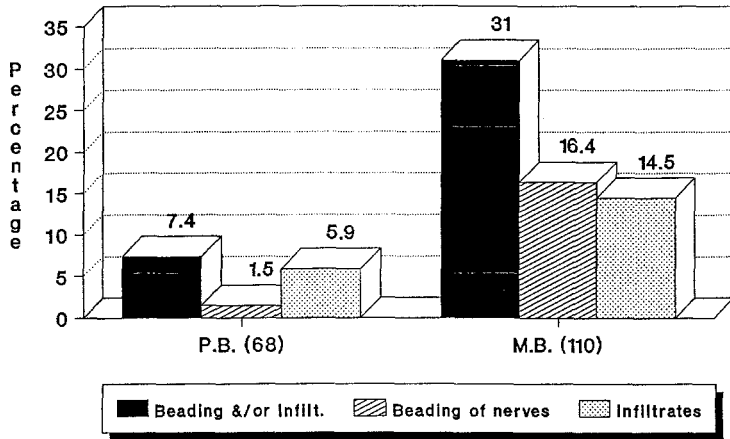


Fig. 6. Corneal stromal and innervational findings by disease class.

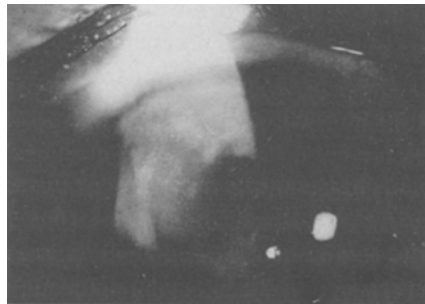


Fig. 7. Corneal scarring.

Table 2. Corneal sensation and anterior segment pathology

	Corneal Sensation / mm		
	Reduced (0-39)	Normal (40-60)	Total
Eyes:	49	125	174
<i>Pathology</i>			
Lagophthalmos	7 (14.3%)	5 (4%)	12
Prominent corneal nerves	38 (77.4%)	91 (72.8%)	129
Beaded corneal nerves	4 (8.2%)	15 (12%)	19
Stromal infiltrates	8 (16.3%)	13 (10.4%)	21
Scarring (due to H.D)	4 (8.2%)	6 (4.8%)	10
<i>Iridocyclitis</i>			
Acute	1 (2%)	1 (0.8%)	2
Healed	6 (12.2%)	5 (4%)	11
Cataract	16 (32.7%)	18 (14.4%)	34
Social blindness	10 (20.4%)	10 (8%)	22

morbidity in relation to corneal hypoaesthesia was analysed and is depicted in Table 2.

Uveitis. Acute iridocyclitis was a rare finding in the study, being detected in only 1 eye each of 2 patients, both of whom had been released from treatment, one borderline patient, 3 months, and one lepromatous patient, 18 months previously. The manifestations of healed iridocyclitis were evident in 11 eyes, with 6 (54.5%) being of LL and 5 (45.5%) of BD with one of them being in reversal reaction. The patients accounting for 5 eyes had been released from treatment, for another 5 eyes, the patients were currently receiving multibacillary multidrug treatment, and the patient in reversal reaction was receiving steroids.

Cataract. Cataracts were detected in 34 eyes (19.1%). Of these, 12 were complicated cataracts, 20 were senile cataracts and 2 were congenital anterior sutural cataracts.

Posterior segment. No abnormalities of the posterior segment were in evidence, except for 1 lepromatous female patient who had advanced cupping of the right optic disc, secondary to open angle glaucoma.

Intra ocular pressure. Evaluation was made of the effect of Hansen's disease on intraocular pressure (IOP). The incidence of hypotony (IOP less than, or equal to, 12 mm of Hg) in the MB and PB disease was compared with that of a control population—provided by a group of age and sex matched individuals, also examined during the same period and were diagnosed as having either cataract or refractive error. There was no significant difference between the 2 populations (33.7% vs. 37.8%). The incidence of hypotony in the multibacillary disease (32.7%) as compared to paucibacillary group (32.3%) was also not significantly different. Further the mean IOP in the multibacillary disease did not differ significantly as compared to the paucibacillary group (13.16 mm Hg and 13.79 mm Hg, respectively).

Discussion

The study comprised a comprehensive ocular evaluation of 89 Hansen's patients. Only 2 patients were classified as having tuberculoid disease. This may be explained by the fact that the cellular immune defences are well developed at this end of the spectrum, with minimal dermatological manifestations and a much shorter duration of treatment than required for lepromatous disease type. Hence tuberculoid patients present less often and attend for a shorter period of time than lepromatous or borderline patients.

The ocular findings have been recorded as adnexal changes, corneal changes, uveitis, cataract, posterior segment abnormalities and intraocular pressure.

When any finding, regardless of severity, was reviewed with respect to disease class, it is found that in all classes, most patients had some ocular finding and that there was little difference between disease types. However, when severe and potentially sight threatening eye lesions, such as iridocyclitis were reviewed with respect to disease class it was apparent that they were more common amongst lepromatous patients (Table 1). The association of lepromatous disease with severe ocular morbidity must be appreciated in order to achieve early recognition and prevention of potentially sight threatening lesions.

The reported extent of social blindness in Hansen's patients varies from study to study, with the prevalence of visual acuity of 6/60 or worse in 1 or both eyes being reported as high as 33% [1].

In our study 11.2% of tested eyes presented with an acuity of 6/60 or less, but in a significant proportion vision could be improved by refraction, leaving only 5.6% of eyes socially blind because of leprosy. This low level of ocular morbidity may be attributed to the fact that all of our patients were either receiving treatment, or had been released from treatment and were attending for follow-up examination and care.

Of the adnexal findings, loss of lateral third of the eye brow was most prevalent and occurred especially amongst lepromatous patients. Though not detrimental to sight, it is important to realise that this disfigurement allows recognition of the leprosy patient, and with the persisting social stigma of the disease, will prevent his reintegration into the community.

Lagophthalmos was a finding amongst borderline and reversal reaction patients. The sequelae of such ocular affection was noted in a proportion of affected eyes, namely ectropion and scarring secondary to exposure keratitis, by which vision may be impaired. Lagophthalmos is caused by nerve damage secondary to reversal reaction in a patient with facial patch or because of the bacillary load [4] in the multi bacillary disease. To explain the weakness of orbicularis oculi muscle causing the lagophthalmos one study (Dastur et al., 1966) postulated that the mycobacteria entered the malar skin through the sensory fibres of the trigeminal nerve, by which route they could infiltrate the cutaneous branches of the facial nerve with which they are in close proximity. In our study, 5 of the 12 affected eyes showed normal corneal sensation indicating that disease mediated damage to the facial nerve can occur independently of the trigeminal nerve.

Dry eye was a finding in 12.9% of tested eyes and was particularly seen in lepromatous patients (Fig. 1).

Lagophthalmos and corneal hypoaesthesia, which are part of the Hansen's ocular disease spectrum, may aggravate the compromised corneal metabolism and result in corneal infections or scarring.

Corneal findings included prominence and beading of corneal nerves, stromal infiltrates, scarring and disturbance of corneal sensation. Prominent corneal nerves showed no significant variation with disease type. It might even be true that this finding is not specific to Hansen's as it is present in significant numbers in normal population also. Corneal nerve beading and stromal infiltrates were noted in high proportions of LL and ENL populations. If analysed together, with the assumption that the process giving rise to the beaded nerves may also give rise to the stromal infiltration, the prevalence is much higher in LL and ENL groups as well as multiple bacillary disease compared to paucibacillary disease. We can only conjecture as to the pathogenesis of these findings. Mycobacterium leprae is a neurotropic bacterium with a predilection for the cooler parts of the body such as the anterior segment of the eye. The association of these findings with patients at the lepromatous end of the spectrum in which cellular immunity is poorly developed and damage is mediated by unchecked bacillary multiplication support the concept that direct bacillary infiltration of the corneal structures as the pathogenesis of the corneal changes. This is supported by the electron microscopic finding in the corneas of experimentally infected armadillos, of numerous bacilli in the ker-

atocytes, macrophages and Schwann cells of myelinated and unmyelinated axons [2].

It is reasonable to assume that the infiltrates observed may be at one end of the spectrum of stromal changes, at the other end of which is the avascular scarring observed in 5 eyes. The observation of anterior stromal and Pre-Descemet's infiltration in some patients and scarring at the same location in others would lend support to this possibility. Prospective evaluation of the patients with avascular keratitis may confirm this sequence of the events.

The frequency of corneal hypoaesthesia was compared between multibacillary and paucibacillary categories of patients. No significant association of hypoaesthesia with disease type was apparent (Fig. 9).

Karacorlu et al. noted that anterior segment pathology was a more frequent finding amongst patients with hypoaesthetic corneas [3]. This is supported in our study, in which, lagophthalmos occurred 3.5 times, Hansen's related scarring 2 times, healed iridocyclitis 3 times and acute iridocyclitis 2.5 times more frequently in hypoaesthetic eyes as compared to eyes with normal sensation (Table 2).

Acute iridocyclitis was in evidence in 2 eyes and healed iridocyclitis in 11 eyes. Both eyes with acute and 5 eyes with healed uveitis were free from active disease both clinically and bacteriologically. This means that ocular morbidity is an on going process even after release from treatment and calls for prolonged follow-up of these patients to avoid blindness in Hansen's secondary to iridocyclitis. The aetiology of this acute iridocyclitis has been postulated as a result of erythema nodosum leprosum, while chronic iridocyclitis has been proposed consequent to disintegrating muscle fibres secondary to iris denervation [4, 5]. Both postulates may be applicable to our patients.

Cataractous changes of lens, senile, complicated as well as congenital were observed. Where indicated, the patients were advised surgery.

Lewallen et al. reported the occurrence of hypotony in a Hansen's population as compared to controls [6]. The prevalence of hypotony (defined as an IOP less than or equal to 12 mm Hg) was not found to be significantly greater in the present study population as compared to age matched controls with refractive error or cataract. Further comparison of mean IOP as well as incidence of hypotony in multibacillary versus paucibacillary groups did not reveal any significant difference (13.79 mm Hg versus 13.16mm Hg).

To conclude, this study documents in addition to the well known ocular changes in leprosy, corneal nerve beading and avascular corneal stromal infiltrates as early corneal changes in Hansen's patients without ocular symptoms. These findings were seen predominantly in the multibacillary disease. Better

understanding of their pathogenesis is essential to prevent corneal blindness in leprosy.

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