

Silent Iritis in Treated Bacillary Negative Leprosy¹

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In lepromatous (LL) leprosy the iris and ciliary body are known to be common sites of infection with *Mycobacterium leprae* (³). Although they are infiltrated with lymphocytes, plasma cells and macrophages packed with acid-fast bacilli (AFB) (²), clinically there are no obvious signs of inflammation. During erythema nodosum leprosum (ENL), an acute iridocyclitis characterized by intense pain, edema, hyperemia of the eye, turbid aqueous, and keratotic precipitates can occur (¹). There is also a silent phase of chronic asymptomatic iridocyclitis which persists with occasional attacks of ENL in some LL patients even 25 years after the patients' bacterial index (BI) had become negative (personal observations, CKJ). It has been suggested that the iris might be a site in which *M. leprae* would survive long after skin smears have become negative (⁵).

In this study we plan to evaluate the prevalence of silent iritis by examining iris specimens from resolved skin-smear-negative leprosy patients and to study their histopathologic appearance compared to that of normal individuals.

MATERIALS AND METHODS

Cataract operations are regularly performed in leprosy and nonleprosy patients in the Purulia Leprosy Home and Hospital, West Bengal, India. During surgery an iridectomy is invariably done. Specimens of iris removed during iridectomy of clinically inactive and skin-smear-negative leprosy patients were obtained. Similarly available iridectomy specimens from normal people

served as controls. The iris tissues soon after removal were fixed in 10% buffered neutral formalin, processed for paraffin sections, cut into 5- μ m sections, stained with hematoxylin and eosin (H&E) and a modified Fite's stain (⁴), and examined with a light-microscope. The H&E sections were examined for evidence of inflammation and other histopathologic changes. The sections stained with the modified Fite's stain were examined for AFB under an oil immersion lens.

Patients were clinically classified according to the Ridley-Jopling classification. The age, sex, duration of disease, and history of antileprosy therapy were recorded. Skin smears were checked to confirm that they were negative for AFB.

Iris biopsies from 59 patients with adequate clinical and laboratory records and 16 controls were available for study (Table 1). There were 40 males and 19 females among the patients and 9 males and 7 females among the controls. The ages of the patients were between 45 and 82 years (mean 59.3 years) and the controls were between 50 and 80 years (mean 60.5 years). Of the 59 patients, 33 were classified as polar lepromatous (LL) leprosy, 16 as borderline lepromatous (BL), 1 as midborderline (BB), 8 as borderline tuberculoid (BT) and 1 as pure neural (PN) leprosy.

RESULTS

On histopathological examination of the 16 control iris specimens, there were very few scattered lymphocytes, and there was no evidence of inflammation in any of them. However, almost all of them showed evidence of atrophy and several small blood vessels had thick hyalinized walls. Of the 33 LL patients, 20 showed varying degrees of inflammatory reaction in addition to signs of atrophy. The inflammatory infiltrate consisted of lymphocytes, plasma cells, mast cells and macrophages. Many of the macrophages were packed with melanin

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TABLE 1. *Iritis in inactive leprosy.*

Patient classification	Male	Female	Avg. age (yrs.)	Iritis	Absence of iritis	Total no.
LL	24	9	60.8	20	13	33
BL	12	4	62.8	3	13	16
BB	0	1	50.0	—	1	1
BT	4	4	55.6	1	7	8
PN	0	1	55.0	—	1	1
Total	40	19	59.3	24	35	59
Control	9	7	60.5	—	16	16

pigment (Fig. 1). In one patient there was a dense focal collection of lymphocytes (Fig. 2). Although in some specimens there were occasional eosinophils and neutrophils, they were far too few to be considered as evidence of acute inflammation. Small blood vessels with thick hyalinized walls, as seen in the controls, were present in some (Fig. 3). Specimens from the other 13

LL patients showed evidence of atrophy but no inflammation. Of the 16 BL patients 3 showed similar inflammatory changes as described above and 13 were free from inflammation. The specimens from all 8 BT patients except 1, the one BB patient, and the 1 PN patient showed only evidence of atrophy but no significant inflammatory changes.

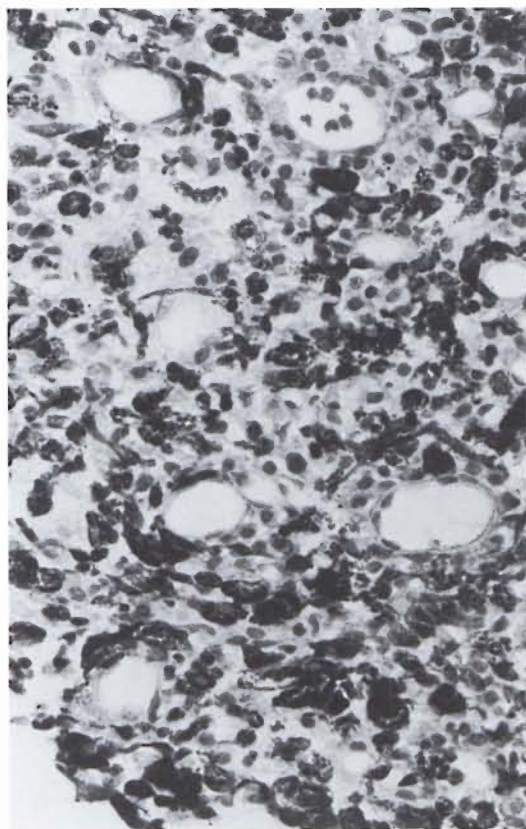


FIG. 1. Photomicrograph of iris showing marked infiltration with lymphocytes, plasma cells, mast cells and melanophages (H&E $\times 400$).

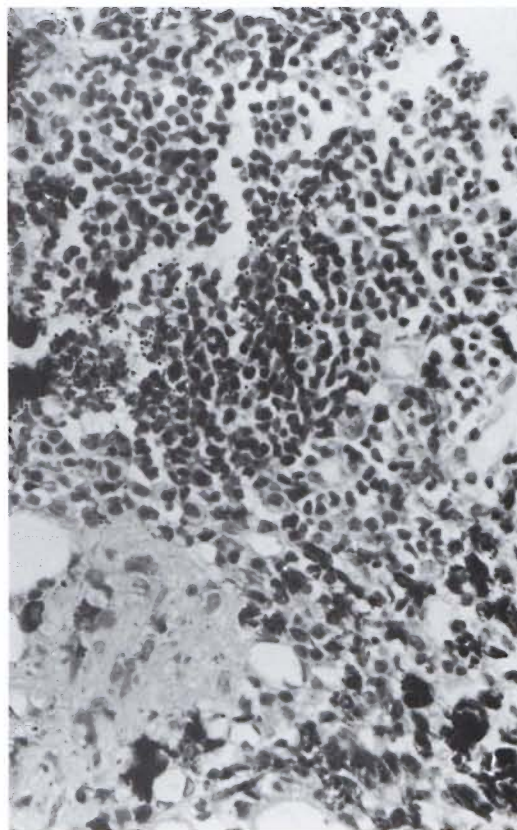


FIG. 2. Photomicrograph showing dense collection of lymphocytes in the iris (H&E $\times 400$).

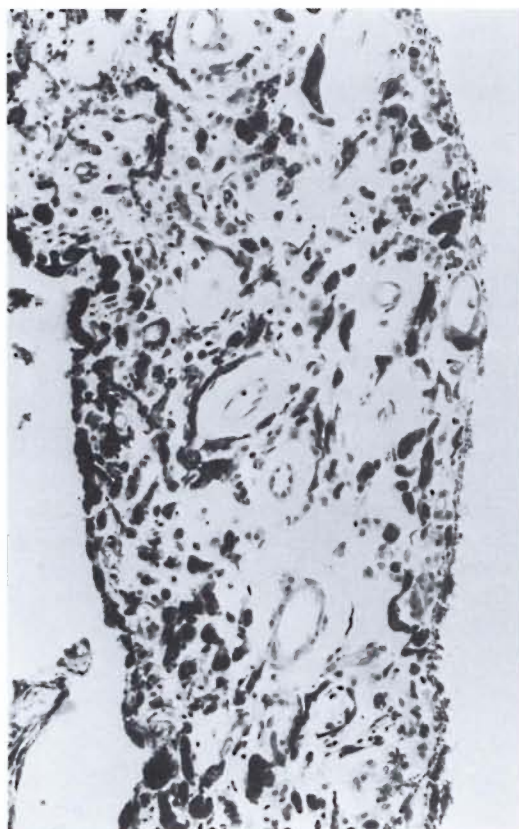


FIG. 3. Photomicrograph of iris showing presence of several small blood vessels with thick hyalinized walls (H&E $\times 400$).

Since the overwhelming majority of iritis was found in LL patients further analysis was done only on LL patients. The average duration of the disease of 20 LL patients who had iritis was 31.5 years; that of the 13 who did not have iritis was 29.7 years. The duration and type of therapy given to the 20 LL patients who had iritis was: 5 (25%) had only dapsone for periods varying from 5 to 15 years with an average of 6.8 years; 12

(60%) had only multidrug therapy (MDT) as recommended by the World Health Organization (WHO) for multibacillary (MB) patients (⁶) for 2 years and 3 (15%) had dapsone for periods varying from 8 to 22 years (mean 17.3 years) followed by MDT for 2 years (Table 2). The duration and type of therapy given to the 13 LL patients who had no iritis was: 1 (7.7%) had only dapsone for 8 years; 9 (69.2%) had only MDT for 2 years; and 3 (23.1%) had dapsone for periods varying from 8 to 25 years (mean 12.7 years) followed by MDT for 2 years (Table 2).

DISCUSSION

The average age of the normal controls with cataract in this study was 60.5 years, that of all leprosy patients was 59.3 years, and that of only LL patients was 60.8 years. It is apparent that the age incidence of cataract in leprosy patients, and especially in lepromatous patients, is not significantly different from that of controls. Therefore, it is reasonable to suggest that leprosy, particularly lepromatous disease, may not contribute significantly to the development of cataract. However, it must be noted here that all of the leprosy patients in this study had "mature" cataracts and therefore might have had the cataracts for a long time.

Of the 59 iris specimens examined, 24 (40.7%) had signs of asymptomatic chronic or silent iritis. Of these 24, 20 were from the 33 LL patients (60.6%), 3 from the 16 BL patients (18.8%), and 1 from the 8 BT patients (12.5%). It is obvious that a significant number (46.9%) of MB patients, especially those belonging to the LL group (60.6%), had chronic iritis. There was evidence of persistent inflammation after they were clinically and bacteriologically declared disease arrested. It is interesting that

TABLE 2. Duration of antileprosy therapy of LL patients with and 13 without iritis.

Classification	MDT only	Dapsone only	Dapsone + MDT	Total
LL with iritis	12 (2 yrs.)	5 (5 to 15 yrs.)	3 (dapsone 8 to 22 yrs. + MDT 2 yrs.)	20
LL without iritis	9 (2 yrs.)	1 (8 yrs.)	3 (dapsone 8 to 25 yrs. + MDT 2 yrs.)	13
Total	21	6	6	33

no stainable organisms were detected in the iris specimens. The persisting inflammation might be due to lingering bacterial antigens, possibly including some solid-staining bacilli which were far too few to be detected in a light-microscopic study. It would be interesting to look for *M. leprae* and its antigens using immunologic and polymerase chain reaction (PCR) techniques. Since there were no stainable organisms in the light-microscopic study, it is highly unlikely that there would be enough viable *M. leprae* in the iris to initiate a relapse. However, the antigens persisting in a significant amount were adequate to maintain a chronic inflammation. It must be mentioned here that of the 20 LL patients with pathologic evidence of chronic iritis only one had chronic iritis clinically which was controlled by treatment but he continued to have flare ups post-operatively. Therefore, lepromatous patients, although they may be pronounced cured or disease arrested after 2 years of MDT, should be monitored for eye complications especially if at any time previously they had had iritis clinically.

The presence of chronic inflammation in one BT patient is difficult to explain. From the records we find that he was treated with dapsone for 20 years followed by MDT for 2 years and, therefore, it is possible that there might be a clerical error in the entry. The other possibility is that this patient was one among the "occult multibacillary patients" in whom although the skin smears were negative antigens of *M. leprae* might persist in the skin, peripheral nerves and even in the iris.

The numbers studied are too small to derive definite conclusions on the presence of iritis in relation to the duration and type of drugs the patients received. However, it appears that iritis was more common among those who received only dapsone. Further, the duration of treatment seems to have no significant effect on the persistence or disappearance of iritis. MDT given only for 2 years was found to have the same effect in controlling iritis as prolonged administration of antileprosy drugs such as dapsone or dapsone followed by MDT.

SUMMARY

Iridectomy specimens from 59 leprosy patients who had adequate medical records

of whom 33 belong to the lepromatous (LL) leprosy variety and 16 normal controls were studied histopathologically. All patients were bacteriologically negative and had received dapsone followed by multidrug therapy (MDT), or MDT only, or only dapsone for varying periods. It was found that leprosy, particularly lepromatous disease, did not significantly decrease the age of formation of cataract. Of the 33 LL patients studied 60.6% had silent iritis. The duration of treatment had no obvious influence on the persistence of iritis. Treatment with only 2 years of MDT for LL patients did not significantly increase the prevalence of persistent silent iritis compared to those who received other types of antileprosy therapy for long periods. It is pointed out that chronic iritis is a serious complication that continues even after the patient is declared clinically and bacteriologically cured, especially in patients who had a history of chronic iritis clinically.

RESUMEN

Se hizo el estudio histopatológico de los especímenes de iridectomía tomados de 59 pacientes con lepra que contaban con expedientes médicos adecuados de los cuales 33 correspondieron a pacientes lepromatosos (LL). Se incluyeron además 16 especímenes de individuos normales. Todos los pacientes fueron bacteriológicamente negativos y habían recibido dapsona y después poliquimioterapia (PQT), o sólo la PQT, o sólo la dapsona, esta última administrada por periodos variables de tiempo. Se encontró que la lepra en general y la lepra lepromatosa en particular, no disminuyeron la edad de aparición de cataratas. De los 33 pacientes LL estudiados, en el 60.6% de los casos se detectó iritis silente. La duración del tratamiento no tuvo una influencia obvia sobre la persistencia de la iritis. El tratamiento por sólo 2 años con PQT de los pacientes LL no aumentó significativamente la prevalencia de la iritis silente persistente ya que ésta fue similar a la observada en los pacientes sujetos a otros tratamientos antileproso durante periodos más prolongados de tiempo. Se hace notar que la iritis crónica es una complicación seria que continúa apareciendo en los pacientes aun después de que estos han sido declarados clínica—y bacteriológicamente curados.

RÉSUMÉ

On a étudié en histopathologie des échantillons d'iris de 59 malades de la lèpre qui avaient des dossiers appropriés, et dont 33 appartenaient à la variété de la lèpre lépromateuse, et également de 16 témoins normaux. Tous les patients étaient négatifs en bactériologie et avaient reçu de la dapsona suivie par

une polychimiothérapie (PCT), ou une PCT seule, ou de la dapsone seule pour différentes durées. On a trouvé que la lèpre, particulièrement la maladie lépromateuse, n'a pas réduit de manière significative l'âge de formation de la cataracte. Parmi les 33 patients LL étudiés, 60.6 % avaient un iritis à bas bruit. La durée du traitement n'avait pas d'influence évidente sur la persistance de l'iritis. Le traitement avec seulement deux ans de PCT pour les patients LL n'a pas augmenté significativement la prévalence de l'iritis persistant à bas bruit, par comparaison à ceux qui ont reçu d'autres types de traitements anti-lèpre pour de longues périodes. Il est souligné que l'iritis chronique est une complication sérieuse qui continue même après que le patient ait été déclaré cliniquement et bactériologiquement guéri, particulièrement chez ceux qui avaient une histoire clinique d'iritis chronique.

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