UVEITIS IN LEPROSY PATIENTS WHO GOT INACTIVE CONDITION IN PRE-WHO/MDT ERA

Sir,

Among the various ocular diseases caused by leprosy, complications of the uveal tissue are considered to be the leading courses of blindness.[1] Apart from uveitis relating to active leprosy, the occurrence of uveal inflammation long after the disease becomes inactive as defined by standard criteria is also well known.[2] In Japan leprosy has almost been eradicated, but doctors frequently see the inflammatory conditions in anterior chambers of leprosy patients even though their disease has long been quiescent.[3] Our study examined the cases of on-going uveitis in patients whose leprosy had been quiescent for more than 10 years.

Patients and methods

In April 1995, 598 cases (mean age: 70·8 years) were registered in our hospital (Tama-Zenshoen, Tokyo, Japan). They were Japanese and Koreans therefore having the same ethnic origin. They were composed of 341 cases of lepromatous leprosy (LL), 217 cases of borderline leprosy (B) and 36 cases of tuberculoid leprosy (TT). Of 598, we excluded all 36 cases of TT, 4 cases of under 40 years and 1 active pulmonary tuberculosis. In the residual 557 cases, 416 cases (244 of LL, 172 of B) could attend at both the dermatological and ophthalmological clinics during the years from January 1993 to April 1995. Based on the annual medical examination, any other diseases which can cause uveitis, such as sarcoidosis, Behçet disease, toxoplasmosis, Harada's disease and adult T cell leukemia/lymphoma have not been found in these registered cases.

Of the 416, 69 cases had positive skin smears for AFB or any active skin lesions during the past 10 years. As for all remaining 347 cases (mean age: 71.0 years), the leprosy condition was inactive for more than 10 years bacteriologically and dermatologically. All these 347 were treated before current regimens as WHO/MDT were adopted in Japan, and most of them received dapsone (DDS) monotherapy.

Among the 347, 69 cases (mean age: 68.0 years) were found to have uveitis based on the inflammatory findings such as flare, cells or keratic precipitates in their anterior chamber. Some of them had irregular pupils and posterior synechiae also. Binocular phthisis was found in 24 cases (mean age: 78.8 years). Some of these were suspected to have been caused by acute or insidious uveitis from their medical records. However, we could not clarify the reliable histories of each phthisic eye (blindness, loss of light perception) for all 24 patients. Fifty cases (mean age: 76.7 years) had corneal disorders which were composed of corneal opacity and/or corneal ulcer. For these 50, there was no evidence of uveitis so far as the views of their anterior chambers were available using slit-lamp, but on the other cases the examinations of their anterior chambers were difficult because of their severe corneal opacity. The remaining 204 cases (mean age: 70·2 years) had neither uveitis nor corneal disorders. Anesthetic cornea and other ocular diseases of conjunctiva, sclera, lens and posterior part of eyeball were not examined in this study. The leprosy classification in each group of 347 cases is summarized in Table 1.

Table 1. Results of ophthalmological examination of 347 cases

Type of leprosy	No. of cases	Binocular phthisis	Corneal* disorder	Uveitis (group 1)	Disease free† (group 2)
LL	188	20	30	45	93
BL	68	2	17	19	30
BB	43	2	3	4	34
BT	48	0	0	1	47
Total	347	24	50	69	204
Mean age	71·0	78·8	76·7	68·0	70·2

*No uveitis was found so far as the views of their anterior chambers were available using slit-lamp. In the other cases the examination of anterior chamber was difficult because of their severe corneal opacity.

†Neither uveitis nor corneal disorder was found.

In the 69 with uveitis (group 1) and the 204 with neither uveitis nor corneal problems (group 2), we conducted the following studies: (1) the types of leprosy were compared; (2) 52 cases of group 1 and 56 cases of group 2 consented to undergo the gonioscopic examination of the limbic area for the search of iris pearls; and (3) serum samples of all cases of group 1 and group 2 were taken at the time of each ophthalmological examination, and IgG and IgM fractions of the Mycobacterium leprae (ML)-specific

anti-phenolic glycolipid-I (PGL-I) antibody were measured by ELISA. The procedure was basically the same as that described elsewhere using NT-P-BSA.[4] The titer was considered positive at ≧0.08 OD for PGL-I-IgG and ≧0.380 OD for PGL-I-IgM. The seropositivity of the PGL-I-IgG and/or PGL-I-IgM were deemed positive for the anti-PGL-I antibody.

The significance of differences was calculated from 2×2 contingency tables using Yete's test.

Results

1 The comparison of the prevalence of uveitis between the two groups by type of leprosy is shown in Table 2. Uveitis was found significantly more often in LL (32·6%) and BL (38·8%) cases than in BB (10·5%) or BT (2·1%) cases.

2 Iris pearls were found in 19 of the 52 (36·5%) cases of group 1 and in none of the 56 of group 2

Table 2. Prevalence of uveitis by type of leprosy, comparison between the two groups

	No. of cases (%)	group 1 case (%)	group 2 case (%)
LL	138 (100)	45 (32·6)	93 (67·4)
BL	49 (100)	19 (38·8)	30 (61·2)
BB	38 (100)	4 (10·5)	34 (89·5)
BT	48 (100)	1 (2·1)	47 (97·9)

Significant difference was found between;
LL and BB; $p < 0{\cdot}05$
LL and BT; $p < 0{\cdot}0001$
BL and BB; $p < 0{\cdot}05$
BL and BT; $p < 0{\cdot}0001$

Table 3. Detection of iris pearls in group 1 and group 2

	group 1 cases with iris pearls /all examined (%)	group 2 cases with iris pearls /all examined (%)
LL	14/33 (42·4)	0/38 (0)
BL	5/17 (29·4)	0/10 (0)
BB	0/2 (0)	0/8 (0)
Total	19/52 (36·5)	0/56 (0)

(Table 3). They were recognized as small round white particles usually on the surface of iris near the limbus.

3 The seropositivity results of the anti-PGL-I antibody assay are shown in Table 4. The rates of seropositivity in group 1 were higher than those of group 2 for all types of leprosy, and a significant difference was found for BL cases. For BB and BT, the number of cases were too small to be statistically evaluated.

Discussion

Among 347 cases without TT, aged more than 40 years old and keeping inactive condition of leprosy for more than 10 years, we found 69 cases (19·9%) of on-going uveitis.

It is generally accepted that intraocular involvement occurs often in LL, less often in BL, and never in tuberculoid leprosy. However, some recent reports show that BB and BT cases can also develop uveitis.[1,6] In our study, although the rates of uveitis in LL and BL were significantly higher than those in BB and BT, some BB and BT cases were also found to have uveitis. Noteworthy is the high rate of uveitis in our BL cases (38·8%), even higher than in LL cases (32·6%), though significant difference was not seen.

Chronic iritis is believed to be neuroparalytic to the small nerve of the iris from its early stage, particularly affecting autonomic supply.[7] In recent reports discussing postural changes in intraocular pressure, patients with immunologically unstable leprosy showed significant postural changes compared to patients with immunologically stable leprosy.[8] Other reports discussing 'pupil cycle time' also show that all LL, BL and BT leprosy cases involve conditions affecting the autonomic nerves.[9] If the

Table 4. Results of anti-PGL-I antibody assay*

	group 1 seropositive cases/total (%)	group 2 seropositive cases/total (%)
LL	28/45 (62·2)	47/93 (50·5)
BL	19/19 (100)†	5/30 (16·7)†
BB	2/4 (50·0)	9/34 (26·5)
BT	1/1 (100)	4/46 (8·7)
Total	50/69 (72·5)	65/204 (31·9)

*At least one of the two antibodies, PGL-I-IgG and PGL-I-IgM, was positive by ELISA.

†$p < 0·0001$.

autonomic dysfunction and the bacterial load during the active phase of leprosy can be assumed to account for the development of uveitis, they may explain the high rates of uveitis in the BL cases of our study.

We found iris pearls in 19 cases (36·5%) of 52 of group 1 but none in 56 of group 2 with close examination using gonioscopy. Since the iris pearls often change their locations,[10] repeated examinations of anterior chamber might increase the prevalence of iris pearls. Although iris pearls are miliary lepromas staying for years in iris stroma,[11] some small iris pearls, however, are calcified and do not respond to systemic therapy.[10,11] Further study of the relationship between the iris pearls and another factors like duration of active leprosy or the chemotherapy which had been administered during their active phase is currently undertaken seeking the etiology and character of these iris pearls.

The serological responses to ML-specific PGL-I antigen have been used to complement the clinical evaluation of leprosy patients.[12,13] From our results, comparing the seropositive rates between the two groups, the rates of positive cases in group 1 were higher than those in group 2 for all types of leprosy, and a significant difference was found for BL. B-group leprosy is immunologically unstable, and BL patients can develop both types of leprosy reaction.[14] Before modern treatment, the feasibility of reactions in B-group patients may have led to lower levels of chemotherapy and therefore inadequate bacterial clearance resulting in high levels of ML-specific antibodies. Our results may indicate the past history of insufficient chemotherapy especially in BL cases with uveitis. Further study on the more cases of BB and BT is needed to better understand the uveitis in B-group leprosy. The seropositivity of all our

cases, independent of uveitis, may also indicate the manner of formation of ML-specific antibodies of the cases who were treated in pre-MDT era.

The follow-up observation of all our cases hereafter might throw light on a part of uveitis-related tragedy which can occur on the patients who have already anesthetic limbs. We are also expecting to share our findings on the B-group leprosy with more other cases of the same or different ethnic groups. Long-term follow-up studies of the ocular diseases in the cases treated by WHO/MDT are also of great interest for the study on the relationship between the uveitis and the chemotherapy.

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