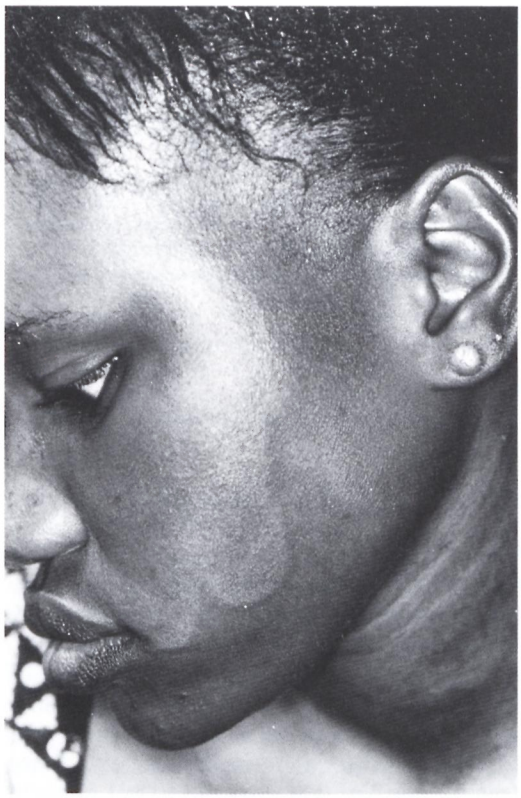

FIG. 3. Same lesion than Figure 1 two weeks after the bleaching practice was stopped. Frank hypochromia can be easily seen.

related to leprosy through voluntary lightening of contiguous healthy skin, and typical cutaneous features could only be seen after the bleaching practice was stopped. We believe that hiding the signs of leprosy strongly contributed to the important delay of diagnosis as observed, with consecutive severe and irreversible nerve damage. We are not aware of any other reported cases with such consequences of the use of BPs. Nevertheless, owing to today's huge extent of uncontrolled BP use and the wide availability of skin-lightening products, similar cases might be seen.

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Uveitis Seen in the Long Clinical Course of Leprosy

TO THE EDITOR:

Frequent occurrence of the anterior uveitis (UV) in leprosy patients is a well-known fact ([1]). However, we cannot find enough explanation for the details of these uveal inflammations. From our experiences in leprosy patients, most UV develops as chemotherapy is progressing effectively, or perhaps even after a bacteriological cure. In this report, we studied the relationship between the development of UV and the immunological status of leprosy to explore the possible pathogenesis of UV seen throughout the long clinical courses of leprosy patients.

Seven cases that suffered from UV were studied. They were composed of 6 cases of

TABLE 1. *The shift of bacterial index (BI) and other symptoms accompanied each episode of uveitis (UV).*

Cases	Age/[a] Sex	BI before chemotherapy	First UV		Second UV		Third UV	
			BI	Other sympt.[b]	BI	Other sympt.	BI	Other sympt.
LLs1	36/M	5	5	RR[c]	1	RR	0[d]	Nothing
LLs2	64/F	5	5	T2R[e]	1	Neuritis (RR)	0 (10 y)[f]	Neuralgia
LLs3	53/F	6	6	T2R	0 (6 y)	Nothing	0 (16 y)	Neuralgia
LLs4	58/M	6	6	T2R	0 (4 y)	Neuritis (RR)		
LLs5	59/M	5	1	Neuritis (RR)	0 (16 y)	Neuritis (relapse)		
LLs6	63/F	5	1	T2R	0 (2 y)	Neuritis (RR)		
BL	60/F	3	0 (2 y)	RR	0 (7 y)	RR		

[a] Age at the first visit to our clinic.
[b] Other symptoms that accompanied each episode of UV.
[c] Reversal reaction.
[d] BI (0) was found when the third UV developed.
[e] Type 2 reaction.
[f] The number of years from having a negative BI.

sub-polar lepromatous leprosy ([13]) (LLs; LLs1–LLs6) and one case of borderline lepromatous leprosy (BL). At our first examination one BI case was 36 years old and the others ranged from 53 to 64 years old. Most of the follow-up periods were more than 40 years, except one case (LLs1) of 6 years. No cases had a history of diabetes or tuberculosis (TB). The diagnosis of LLs was based on their clinical records that suggested downgrading from the borderline group, i.e., positive lepromin reaction, annular skin eruption of leprosy, and reversal reaction (RR). Most RRs were confirmed by the authors' direct examination. The ophthalmologists made the diagnosis of UV with slit-lamp examination. In our situation, patients can request a doctor's examination whenever they need one.

One case (LLs1) received a multibacillary (MB) regimen of World Health Organization/multidrug therapy (WHO/MDT) for 2 years, followed by dapsone and minocycline (DDS+MINO) for another 2 years. All the other 6 cases received various regimens composed of dapsone (DDS), clofazimine (CLF), rifampin (RFP), thiambutosine (Ciba) and other anti-tuberculosis (anti-TB) drugs for the treatment of leprosy. These regimens were not the same as WHO/MDT, and, in most cases, the dosage of each drug was smaller than that used in WHO/MDT.

Out of 6 cases that had not been treated with WHO/MDT, four cases (LLs2, 3, 5 and BL) had on-going UV at our first examination and received further treatment with various CLF-containing regimens. Before the additional treatment, prednisolone (PSL) of 20 mg was also tried with the second UV case of BL and the third case of UV, LLs2 and LLs3. Before proceeding, patients were well informed and they provided us additional consent to receive these treatments. We were unable to get consent for these treatments from two cases.

The shift of bacterial index (BI) of skin-smear throughout the follow-up period was tracked. Other clinical signs, such as leprosy reactions and neuritis, were also investigated through their available clinical records. The record of "neuritis" was used when the cause of "neuritis" was not mentioned. If only nerve tenderness was documented without detail, it was expressed as "neuralgia".

During the follow-up period of 7 cases, 3 cases had 3 episodes of UV and 4 cases had 2 episodes. The maximum BIs recorded before treatment and during each episode of UV are shown in Table 1, along with leprosy reactions and/or neuritis/neuralgia as seen during each episode.

The BI before treatment of all 6 LLs was 5 or 6. Out of these, four cases (LLs1–LLs4) also presented a high BI when they had their first UV episode. However, at their second attack, the BI was very low or zero. In another two cases (LLs5 and LLs6), the BI at their first UV episode was very low and was zero at the second attack. On the other hand, the case of BL already had a BI of 0 when her first UV episode de-

TABLE 2. *Regimens for additional treatment given to the four cases and their efficacy.*

Cases	Drugs[a] used and period of treatment	Interval[b] of negative BI	Efficacy of re-treatment
LLs2	LVFX[c] + CLF[d] for 2 y[e]	16 y	Not effective
LLs3	LVFX + MINO[f] + CLF for 1 y	17 y	Not effective
LLs5	RFP[g] + CLF for 1.5 y	23 y	Effective
BL	MINO + CLF for 2 y	8 y	Effective?[h]

[a] Detail (dosage and interval) of each regimen is omitted.
[b] Period from having negative BI to the start of re-treatment.
[c] Levofloxacin.
[d] Clofazimine.
[e] Year(s).
[f] Minocycline.
[g] Rifampicin.
[h] The efficacy was not clear because of occasional administration of prednisolone.

veloped. At the third UV episode, all three cases had a BI of 0.

In all 17 episodes of UV seen in our 7 cases, 4 episodes developed following type 2 reactions (T2R). On the other hand, 8 episodes were accompanied with reversal reactions (RR) or neuritis that was considered to be relevant to RR. Another 2 episodes developed without any other symptom when the BI was decreasing (the third UV of LLs1) or 6 years after getting a negative BI (the second UV of LLs3). The third UV of LLs2 and LLs3 was seen long after getting negative BIs along with refractory neuralgia. Based on the clinical records, the severity of UV that was accompanied by T2R was higher than the other UV episodes and the most UV was seen with neuritis or when neuralgia was chronic and of low grade.

The CLF-containing regimens given to the 4 cases and their efficacy are shown in Table 2, along with the interval period from having a negative BI to the start of another treatment. It was effective in one case (LLs5), having apparent improvement of refractory UV and neuritis. In the case of BL, some efficacy of CLF was noticed in the UV and neuritis. In this case, occasional PSL was also given to abate the neuritis, so that it is difficult to know the true efficacy of re-treatment with chemotherapy. In another two cases, neither PSL nor re-treatment with chemotherapy gave any apparent efficacy to the UV or the neuritis/neuralgia.

Of the 17 episodes of UV seen in 7 leprosy patients having high bacterial loads, 4 episodes were seen during T2R, when their BI was still very high. For a long time, it has been accepted that acute UV is a manifestation of T2R ([8, 9]). However, after the introduction of WHO/MDT, T2R became rare in the clinical course of leprosy ([6]). Our case of LLs1 is one example of such cases.

In our study, the most episodes developed during RR or the restorative phase of cell-mediated immunity against *Mycobacterium leprae* as shown in the shift of BI in Table 1. High bacterial load with immunological instability can be a risk factor for recurrent RR and may bring about uveal inflammation as one of the clinical manifestations of RR. Because isolated tissue involvement in leprosy reaction is not uncommon in the case of neuritis ([12]), localized inflammatory changes of RR based on the local immunity may also occur inside uveal tissue. The report indicating that RR can cause low-grade iritis ([14]) may support our findings.

We experienced one case (LLs5) that developed UV in the process of probable relapse. In some LL cases, the eye may continue to harbor antigen, or perhaps even living organisms, long after the completion of appropriate chemotherapy ([3, 7]). Since there was no active symptom other than UV and neuritis with the second UV episode of LLs5, the residual bacilli that had been kept in his particular nerves and uveal tissue, the most favorite sites of bacilli, might have multiplied leading to relapse.

The pathogenesis of chronic UV seen during the quiescent periods of LLs2 and LLs3 is difficult to explain. We can only present the following speculations: a) Tissue destruction caused during the active phase can remain as residual autonomic nerve dysfunction and secondary muscle atrophy. The fragile tissues may be more

prone to cause inflammatory reaction that brings about a chronic low-grade inflammation ([1, 4, 5]). b) Some antigenic substances such as residual bacterial antigens may cause persistent and recurrent inflammation ([15]). In a previous study, we reported that insufficient bacterial clearance could be a risk factor for chronic UV ([10, 11]). c) Autoimmunity could be involved in the cause of long-standing chronic UV, because of its endogenous nature without active infection ([2]).

Many subjects related to UV seen in leprosy patients are still to be studied. Close observation of each case for lengthy periods is mandatory to study the true magnitude of ocular leprosy and to prevent additional disability. More study from the viewpoint of the immunological status of leprosy may help gain additional understanding of the inflammation of uveal tissue as seen in the long clinical course of leprosy.

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