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Combined 12-Month WHO/MDT MB Regimen and *Mycobacterium w.* Vaccine in Multibacillary Leprosy: A Follow-Up of 136 Patients[1]

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The World Health Organization (WHO) recommended multidrug therapy (MDT) to overcome the problem of drug resistance and to introduce an effective and practible regimen for treatment of leprosy in 1982 ([32]). Since the data on limiting MDT to two years in multibacillary (MB) leprosy, rather than continuing until skin smears negativity, were favorable, the WHO study group in 1994 recommended that all MB patients be given the standard WHO/MDT MB regimen for 24 months fixed duration therapy (FDT) ([33]). The MDT regimens have proved to be highly effective and are well tolerated by the patients ([31]). Some reports had indicated earlier that even after 2 years of continuous MDT highly bacilliferous BL/LL cases continue to be smear positive with about 9% to 16% of them harboring viable bacilli ([11, 25]), resulting in higher rates of relapses ([6, 14, 27]). However, the available data from several field studies, carried out in different parts of the world, have reported very low relapse rates in MB patients (<1%) with the standard WHO/MDT MB (FDT) regimen given for 24 months ([31]). However, from the operational point of view, the duration of MDT was still too long, especially for MB leprosy. With 15 years of experience and encouraging information on the clinical use of MDT, the WHO Expert Committee on Leprosy concluded at its last meeting in 1997, that it is possible to further shorten the duration of its MDT regimen for MB leprosy to 12 months without significantly compromising its efficacy ([7, 31]). This has been well accepted by almost all the leprosy control programs of the major endemic countries, and is being actively implemented. However, information regarding the efficacy and safety of the shortened MB regimen (12 months) is very limited at present. In cases treated with MDT MB (whichever regimen), the dead bacillary antigens and viable persisters lead to immunological complications, such as recurrent reactions and late relapses, respectively. Recently some leprosy workers have reported that immunotherapy with *Mycobacterium w.* (*M. w.*) vaccine resulted in rapid killing and faster clearance of *M. leprae;* thereby minimizing risk of relapses and possibly reactions ([10, 21]).

We have been practicing MDT MB (the 12-month regimen) at the Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India, according to the WHO guidelines. Additionally, all multibacillary patients with BI ≥2 are also given immunotherapy with the *M. w.* vaccine. In this study, patients treated with the 12-month MDT MB regimen and the *M. w.* vaccine, and having been followed up for more than two years, are analyzed with the aim of defining the course of progress and studying relapses, if any.

MATERIALS AND METHODS

Our hospital is a tertiary care institute catering to a large population of northern India, but it is located in a very low endemic zone for leprosy. A large proportion of cases attending the leprosy clinic of the institute consist of the migrant population from major endemic states of the country, like Bihar and Uttar Pradesh. In this study,

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TABLE 1. *Bacterial load and clinical classification of patients.*

Bacteriological index	LL	BB/BL	BT[a]	Total
>4	39	19	0	58
3.1–4	19	13	0	32
2.1–3	9	26	3	38
≤2	0	0	8	8
Total	67	58	11	136

[a] Downgrading (appearance of new lesions at distant sites, lesion of varied morphology, facial lesions, breaking down of borders, involvement of nerves in more than one limb, etc.)

previously untreated, smear-positive MB patients with a BI ≥2 were included. The group consisted of active LL, BL, BB and few BT patients. All patients with a BI ≥2 were given WHO/MDT MB for 12 months and were additionally given the *Mycobacterium w.* vaccine. The first dose of the vaccine was 1×10^9 bacilli in 0.1 ml physiological saline (0.85% NaCl), and subsequent doses contained half the number of bacilli (5×10^8). A total of 4 doses were given intradermally over the deltoid region at 3-month intervals. Clinically, patients were diagnosed and classified according to the Ridley-Jopling classification ([8]) and each diagnosis was confirmed in all the patients by histopathology. During and after MDT treatment, activity of the disease was routinely assessed clinically and skin-slit smears were taken every 6 months from the same four sites studied initially in all patients. The biopsy was also repeated from the same sites after 6 and 12 months of starting treatment for histopathologic evaluation. Whenever fresh lesions were suspected, these sites were included for smears. The biopsy results were compared in respect to the clearance of dermal granuloma(s), consisting of lymphocytes, epithelioid cells, giant cells, macrophages and foam cells in variable proportions depending upon the type of leprosy and also by measuring the estimated reduction in granuloma fraction (GF) (i.e., the fraction of dermis occupied by the granuloma(s) and the clearance of acid-fast bacilli).

Reactions. Type 1 reaction (reversal reaction) was diagnosed by noting visible changes in the existing or new lesions in the form of erythema, swelling (edema), the presence of a subjective feeling of warmth, tingling sensations and/or local tenderness associated with or without constitutional symptoms. Type 2 reaction was diagnosed on the basis of presence of constitutional symptoms of varying degrees, such as fever, aches, joint pains, bony tenderness with characteristic evanescent lesions of erythema nodosum leprosum (ENL) associated with or without a specific organ involvement, such as the eye, the testes, or the kidney. Only neuritis was diagnosed by the presence of tenderness in the nerves (thickened or not) in the absence of any evidence of inflammation in the leprosy lesions. Whereas, a tenderness of nerves in the presence of inflamed skin lesions of type 1 reaction or type 2 reaction was considered to be part of the reaction.

Relapse. In the present study, a relapse was defined as an increase of at least 2 log units of the BI over the previous value at a progressively active site with or without appearance of new lesions.

RESULTS

Out of 164 patients who took regular treatment, 11 left for their place of work or home state and were advised to get regular follow-up at any treatment center. Of the remaining 153 patients available to us, 17 were lost to follow up in between due to migration and other causes not related to the study. A total of 136 patients, having been followed-up for at least 2 years or more, were included in the analyses. Seventy-seven out of 136 patients had completed 3 years follow-up. Of these 136 cases, 92 were males and 44 were females. The age of the patients varied from 6 years to 77 years (mean 34 ± 11.3 years) and they had the disease for periods varying from 3 months to 7 years (mean 1.9 ± 1.4 years). Their disease classification and initial BI is shown in Table 1.

Fall in BI. The mean of the average BI before starting treatment was 3.6 ± 1.3. Among 136 patients, 11 patients were diagnosed with BT leprosy. Clinically, all 11 patients were downgraded from the BT spectrum (appearance of new lesions at distant sites, lesions of varied morphology, facial lesions, breaking down of borders, nerve involvement in more than one limb, etc.), though none had classical morphological lesions of or had reached the BB/BL spec-

TABLE 2. *Skin-slit smear status at the end of 2 and 3 years.*

Bacterio-logical index	At 2-year follow-up (N = 136)		At 3-year follow-up (N = 77)	
	No. of patients	Smear negativity	No. of patients	Smear negativity
>4	58	5 (8.6%)	24	13 (54.2%)
3.1–4	32	1 (31.3%)	20	15 (75%)
2.1–3	38	31 (81.6%)	28	25 (89.3%)
≤2	8	8 (100%)	5	5 (100%)

trum according to the Ridley-Jopling classification ([8]). Of them, 3/11 had BI of 2.1–3.0, whereas in the remaining 8/11, the BI recorded was 2. At the end of a 2-year follow-up, a total of 54 patients out of the 136 (39.7%) had become smear-negative. A larger proportion of patients, 39/46 (84.8%) with BI of ≤3 had become smear negative, whereas, only 10/32 (31.3%) patients with a BI of 3.1–4.0 and 5/58 (8.6%) highly-bacillated patients having an initial BI of >4 had become smear-negative at the end of 2 years. All BT patients with a BI of 2 became smear-negative at the end of 2 years. Out of the 77 patients who were available for follow up at 3 years, 30/33 (90.9%) patients with a BI of ≤3, 15/20 (75%) patients with BI of 3.1–4.0 and 13/24 (54.2%) patients having an initial BI of >4, respectively, had attained smear negativity (Table 2). We did not observe treatment failure or a stationary BI in any patient.

Lepra reactions. Reactions occurred more frequently after 6 months of therapy. Subsequently, the incidence decreased gradually and the same trend continued in the follow up period. Table 3 shows the frequency of episodes of reversal reaction (RR), erythema nodosum leprosum (ENL) and neuritis-only and the time of their occurrence in relation to the treatment in these

TABLE 3. *Reactions during and after MDT + the M. w. vaccine.*

MDT (months)	Type 1 reactions	Type 2 reactions	Neuritis only
0–6	6.3%	2.7%	2.5%
6–12	13.4%	6.3%	2.8%
Follow-up			
1st year	5.9%	5.0%	1.8%
2nd year	4.3%	2.5%	0.1%
After 2nd year	0.7%	1.2%	0%

TABLE 4. *Details of relapses.*

Period of follow up	No. of patients	Initial BI[a]	Person-years follow up	Relapses	
				Number	Rate/ 100 patient years
2 years	136	>4	272	1	0.36
3 years	77	>4	231	2	0.86

[a] BI—bacterial index.

136 patients. Over a period of time, the frequency of occurrence of reactions decreased gradually; however, they continued to occur even two years after release from treatment (RFT). The frequency of RRs was observed to be higher among patients in the borderline group (BT, BB, BL), whereas, the majority of ENL reactions were observed in LL, followed by BL, cases.

New deformities. The overall deformity rate, according to the WHO criteria before starting MDT, was 26.5%. More deformities involved hands (17.6%) than of the other sites. During the course of MDT and thereafter in follow up 4.6% and 1.3% of the patients developed new deformities, or an increase in the existing grade of deformities respectively.

Leprosy in children. Of a total 136 patients, 6 were children. Their mean age was 11.4 ± 2.1 years (range 6 years–14 years). One child had a grade II deformity of the left hand, and a history of household contact was present in two children.

Relapses. Three relapses (2 in LL and 1 in BL) occurred in patients having an initial BI of >4. One patient relapsed in the second year and the other 2 relapsed in the third year of follow up (Table 4) and were successfully treated with a reintroduction of the same MDT MB regimen.

Drug reactions. Five patients developed a dapsone hypersensitivity reaction. Out of these five patients, three had classical clinical features of dapsone hypersensitivity, like exfoliative dermatitis, hepatitis, lymphadenopathy and fever, whereas the remaining two had only features of hepatitis (elevated liver enzymes and jaundice). Three patients had rifampin-induced urticaria and one manifested a flu-like syndrome.

Local ulceration healing with scar formation and regional lymphadenopathy were the

only local reactions to the vaccine seen in 47/136 (34.5%) patients. No systemic complications related to the vaccine were noted.

Histopathological changes. All the patients showed a gradual reduction of granuloma fraction. No definite granuloma or solid staining AFB was identifiable in the biopsy specimens taken at 12 months after therapy. Other important findings noted were a reduction in the population of both foam cells and macrophages, the appearance of epithelioid cells in some patients and an increase in the number of lymphocytes and plasma cells in the granuloma(s).

DISCUSSION

Multidrug therapy (MDT) has been successful in the treatment of leprosy with a rapid killing of the bacilli. With two years of the MDT MB regimen, the relapse rates reported were as low as 0.77% ([31]). On basis of this and other available information, WHO reduced the recommended length of treatment from 24 months to 12 months ([7, 31]), though the wisdom of this changed regimen has been questioned by some workers ([28, 30]).

BI fall. The rate of decline in BI in multibacillary patients treated with MDT is similar in most reported series and is in the range of 0.57 to 1.01 log unit/year ([17]). Accelerated decline of BI in patients given the *Mycobacterium w.* vaccine suggests that its addition to the MDT upgrades the cell-mediated immunity to a significantly higher level, aiding faster clearance of bacilli than reported in patients receiving MDT alone. Katoch, *et al.* ([10]), and Sharma, *et al.* ([21]), also observed a more rapid fall in the BI and killing of viable bacilli using the *Mycobacterium w.* vaccine. The observations of Mukherjee, *et al.* ([15]), Talwar, *et al.* ([26]), and Zaheer, *et al.* ([34]), regarding the early clearance of dead bacilli are similar and this indicates the benefits of immunotherapy with the *M. w.* vaccine.

Lepra reactions. There is a wide variation in the frequency of ENL reactions experienced by leprosy patients in different parts of the world with 31% of multibacillary cases afflicted with reactions in Brazil ([16]), 19% in Nepal ([13]), and 5.3% in Ethiopia ([18]). The incidence of ENL appears to have fallen with the introduction of MDT, possibly due to the combined rapid bactericidal effect of rifampin and the anti-inflammatory effect of clofazimine in suppressing ENL ([1]). In the present study, there was no increase in the frequency of ENL reactions observed as compared to the reported figures in the past for patients who were not given the *M. w.* vaccine ([13, 16, 18]). This has been attributed to the immunomodulating effect of the *M. w.* vaccine ([26]). Similar findings of no noticeable increase in the frequency of ENL reactions have been reported by Katoch, *et al.* ([10]), Sharma, *et al.* ([22]), and Zaheer, *et al.* ([36]), with the use of the *M. w.* vaccine. The rationale for immunotherapy with the *M. w.* vaccine is to boost cell-mediated immunity (CMI), thereby resulting in a faster clearance of bacillary antigens and so reduce chances of the immune complexes formation required for ENL reactions.

There are apprehensions concerning theoretical reasons that immunotherapy, due to an upgrade of CMI, might increase the incidence of reversal reactions and neuritis. The incidence of reversal reactions in MB patients treated with MDT alone is reported to vary from 9% to 41% in hospitalized patients ([12, 19]). In almost all the earlier studies, though there is an apparent increase in the reversal reactions in patients treated with the *M. w.* vaccine as compared to the group given MDT alone, in none did it reach statistical significance ([4, 9, 10, 36]). The incidence of reversal reactions we observed is comparable to the figures reported in the studies where *M. w.* vaccine was administered as part of immunotherapy. Sharma, *et al.* ([22]), observed type 1 reaction (mild in most cases) to occur more frequently, especially in those labelled as LL in the vaccine treated group. However, this difference was not significant on correction of the p value for the number of variables. Overall the *M. w.* vaccine did not precipitate reactional states and neuritis more frequently, compared to the incidence with MDT alone. It has also been reported earlier that the incidence of neuritis in patients given immunotherapy (*M. w.*) is rather less, or almost similar, as compared to the patient group treated with MDT alone ([9, 10, 22, 24]). In another study from our institute, De Sarkar, *et al.* ([4]), observed that the differences in the incidence of neuritis and reversal reactions in the patient group treated with MDT alone and

the group treated additionally with the *M. w.* vaccine was not statistically significant.

New deformities. Several studies have noted a steady fall in the deformity rate among new cases following the introduction of MDT since the 1980s ([2]). The worldwide disability rates among leprosy patients have varied from 16% to 50% ([5]). It has been reported that patients, during treatment with MDT and thereafter, can have further progression of their existing deformities due to an increased incidence of reactions and neuritis, especially in those with a higher degree of impairment at the beginning of therapy ([20]). In our study, the deformity rate before starting MDT was 26.5%, whereas during the MDT and the follow-up period, an additional 5.9% of the patients developed a new or an increase in the grade of their existing deformities. Immunotherapy with *M. w.* did not precipitate neuritis or deformities more than those reported with MDT alone. Similar observations have been made regarding immunotherapy with the *M. w.* vaccine by Sharma, *et al.* ([23]), and with BCG + killed *M. leprae* by Convit, *et al.* ([3]).

Relapse. The occurrence of relapse in patients with a high BI and their satisfactory response to the same regimen indicates that the relapses were as a result of persistence of drug-sensitive organisms, due to insufficient treatment. However, the overall relapse rate (Table 4) was comparable to that reported with the standard MDT MB regimen (FDT for 24 months) ([31]). More recently, a higher figure for relapse on longer follow up has been reported from some centers, especially in patients with a very high initial BI ([6, 14]). In our patients, relapse was also seen in only the highly bacillated (≥4) group of patients. Although the duration of follow up in our patients was limited, a rapid decline in BI and faster clearance of bacilli is expected to continue as a result of immune enhancement with the *M. w.* vaccine and the probable risk of relapses should be less on longer follow up, compared to those who are given MDT alone. Significantly, 11 of our BT patients were smear-positive and required treatment with the MDT MB regimen. However, in the control program, where slit-skin smears are not done and patients are treated based on the number of lesions alone, such cases are likely to be under-treated.

Drug reactions. In patients with dapsone hypersensitivity, apart from symptomatic treatment, MDT without dapsone was reintroduced, and it was well tolerated. Other minor side effects to MDT were successfully managed, either by temporarily withdrawing the drug or with a short course of systemic steroids. Local ulceration due to vaccine healing with scar formation and accompanying regional lymphadenopathy are the already known local reactions noted in one-third of the patients. The ulceration healed in 3–4 weeks. No systemic complication related to the vaccine was noted.

Histopathological changes. A reduction in bacterial load, an absence of viable bacilli, changes in the cellular composition of the granuloma(s) from lower to higher spectrum, and a reduction in the granuloma fraction observed in all of our patients reflects the MDT and possible upgradation of CMI following vaccination.

In the previous similar studies with the *M. w.* vaccine, MDT was given for two years or until smear negativity ([9, 10, 21, 22, 24, 29, 34, 35]). The results of this study, though with a shorter follow up, indicate that the relapse rates after shortened WHO/MDT MB regimen (12-month) combined with the *M. w.* vaccine are still at a level which is low enough to be acceptable in the leprosy elimination program. WHO/MDT MB regimen (12-month) combined with immunotherapy with the *M. w.* vaccine is well tolerated, does not increase the incidence of reactions, neuritis and deformities, and helps in faster clearance of dead bacilli and so a reduction in the incidence of ENL in the post-MDT period. We found the shortened (12-month) MDT MB regimen plus the *M. w.* vaccine for multibacillary patients to be effective and safe. Seemingly, it has tremendous operational advantages, and we should be prepared to treat fewer relapses in the post-elimination era, as they occur. However, a long-term follow-up of a larger number of patients will settle the issue of safety and efficacy of the shortened MDT MB regimen and the place of the *M. w.* vaccine in immunotherapy of multibacillary patients.

SUMMARY

A total of 136 patients with BI ≥2 having been followed up for at least 2 years or more were included in the analyses. Seventy-seven out of 136 patients had completed

three years follow up. All patients were given WHO/MDT MB regimen for 12 months and additionally 4 doses of *Mycobacterium w.* vaccine at 3-month intervals. The age of the patients varied from 6 to 77 years (mean 34 ± 11.3 years) and they had the disease varying from 3 months to 7 years (mean = 1.9 ± 1.4 years). The mean of the BI before starting treatment was 3.6 ± 1.3. At the end of 2 years follow-up, a total of 54 patients out of the 136 (39.7%) had become smear-negative. A larger proportion of patients, 39/46 (84.8%) with BI of ≤3 had become smear-negative, whereas, only 10/32 (31.3%) patients with BI between 3.1 to 4 and 5/58 (8.6%) highly bacillated patients having initial BI >4 had become smear-negative at the end of 2 years. Out of the 77 patients who were available for follow up at 3 years, 30/33 (90.9%) patients with BI of ≤3, 15/20 (75%) patients with BI between 3.1 to 4 and 13/24 (54.2%) patients having initial BI >4, respectively, had attained smear negativity. Reactions occurred more frequently after 6 months of therapy and over a period of time their frequency gradually decreased, however, they continued to occur even two years after RFT. During the course of MDT and thereafter in follow up 4.6% and 1.3% of the patients developed new deformities or an increase in the existing grade of deformities, respectively. Three relapses (2 in LL and 1 in BL) occurred in patients having initial BI of >4. One patient relapsed in the second year and the other two relapsed in the third year of follow up and were successfully treated with reintroduction of the same MDT MB regimen. Local ulceration healing with scar formation and regional lymphadenopathy were the only local reactions to the vaccine seen in 47/136 (34.5%) patients. All the patients showed histopathological improvement in the form of a gradual reduction of granuloma fraction. Although the results of this limited period follow up are satisfactory, a long-term follow-up in larger number of patients will settle the issue of safety and efficacy of shortened MDT MB regimen and the place of immunotherapy with *M. w.* vaccine in multibacillary patients.

RESUMEN

Se hizo un análisis sobre la evolución de 136 pacientes bacilíferos (IB ≥2) a lo largo de más de 2 años de seguimiento. Setenta y siete de los 136 pacientes habían completado 3 años de seguimiento. Todos los pacientes habían recibido durante 12 meses la terapia recomendada por la OMS para la lepra multibacilar (WHO/MDT MB), y 4 dosis adicionales de la vacuna con *Mycobacterium w.,* a intervalos de 3 meses. La edad de los pacientes estuvo entre los 6 y 77 años (media = 34 ± 11.3 años) y la duración de la enfermedad, entre los 3 meses y los 7 años (media = 1.9 ± 1.4 años). La media del IB antes de iniciar el tratamiento fue de 3.6 ± 1.3. Al final del segundo año de seguimiento, 54 de los 136 pacientes (39.7%) habían llegado a ser baciloscopicamente negativos. La proporción de los pacientes que habían alcanzado la negatividad baciloscópica hacia el final del segundo año de seguimiento fue más alta en los pacientes con un IB = 3 (39/46 u 84.8%) que entre los pacientes con un IB entre 3.1 y 4 (10/32 o 31.3%), o mayor de 4 (5/58 u 8.6%). De los 77 pacientes en los que el seguimiento pudo hacerse hasta los 3 años, 30 de 33 pacientes con un IB = 3 (90.9%), 15 de 20 pacientes con un IB entre 3.1 y 4 (75%), y 13 de 24 pacientes con un IB >4 (54.2%), habían alcanzado la negatividad baciloscópica. En cuanto a las reacciones de la lepra, éstas ocurrieron más frecuentemente después de los primeros 6 meses de terapia, y aunque su frecuencia disminuyó gradualmente de manera considerable, continuaron ocurriendo aun después de dos años de tratamiento con RF. Durante el curso de la poliquimioterapia, y durante el seguimiento, algunos pacientes desarrollaron nuevas deformaciones (4.6%), o mostraron un agravamiento de las deformaciones ya existentes (1.3%). Tres recaídas (2 en LL y 1 en BL) ocurrieron en pacientes con IB iniciales >4. Un paciente recayó en el segundo año de seguimiento y los otros dos en el tercero, pero todos ellos fueron tratados exitosamente con la misma terapia MDT MB. La aparición de úlceras locales que curaron espontáneamente dejando solo una cicatriz y el desarrollo de linfadenopatía regional, fueron las únicas reacciones adversas de la vacuna *M. w.* observadas en 47 de los 136 pacientes (34.5%). Todos los pacientes mostraron mejoría histopatológica manifestada en la forma de una reducción local de la fracción granuloma. Aunque los resultados de este periodo limitado de seguimiento fueron satisfactorios, un seguimiento a un plazo más largo, y con un mayor número de pacientes, podría darnos información definitiva sobre la seguridad y eficacia de la poliquimioterapia acortada recomendada para la lepra multibacilar (MDT MB) y sobre la utilidad de la vacuna *M. w* en el tratamiento de los pacientes multibacilares.

RÉSUMÉ

Un population totale de 136 patients hanséniens présentant un index bactérioscopique (IB) supérieur ou égal à 2 (IB ≥2) et un suivi clinique d'au moins 2 années fut sélectionnée pour ces analyses. Soixante dix sept de ces 136 patents avaient complétés trois ans de suivi. Tous les patients ont été traités par une

polychimiothérapie recommandée par l'OMS pour les patients multibacillaires (OMS/PCT MB) et par 4 doses de *Mycobacterium w.* administrées à intervalles de 3 mois. L'âge des patients était compris entre 6 et 77 ans (âge moyen ± déviation standard 34 ± 11,3 ans) et ils ont eu la maladie pendant une durée variant de 3 mois à 7 ans (moyenne de 1,9 ± 1,4 ans). L'IB moyen avant traitement était de 3,6 ± 1,3. A la fin du suivi de deux ans, 54 patients parmi 136 (39,7%) étaient devenus négatifs au test du suc dermique. Une plus grande proportion de patients avec un IB ≤3, soit 39/46 (84,8%), étaient devenus négatifs au test du suc dermique, tandis que seulement 10/32 (31,3%) patients avec un IB entre 3,1 et 4 et 5/58 (8,6%) patients avec un fort index (IB >4) étaient devenus négatifs au test du suc dermique au terme des 2 années de suivi. Parmi les 77 patients qui avaient été suivis pendant 3 ans, 30/33 (90,9%) patients avec un IB ≤3, 15/20 (75%) patients avec un IB compris entre 3,1 et 4 et 13/24 (54,2%) patients ayant un IB initial >4 avaient atteint un statut négatif au test du suc dermique. Les réactions adverses apparurent plus fréquemment après 6 mois de traitement puis leur fréquence diminua graduellement. Cependant, elles continuèrent d'apparaître même au terme de 2 années après RFT. Durant la PCT et ensuite pendant le suivi, 4,6% et 1,3% des patients ont développé, soit une nouvelle difformité, soit une augmentation du grade de la difformité déjà existante, respectivement. Trois rechutes (2 de forme LL et 1 de forme BL) apparurent chez des patients ayant un IB initial >4. Un de ces patients a rechuté dans la seconde année et les 2 autres ont rechuté dans la troisième année de suivi ; ils furent traités avec succès en ré-introduisant le même traitement PCT MB. Des ulcérations locales avec la formation de cicatrices et des lymphadénopathies régionales furent les seules réactions locales au vaccin; elles furent observées chez 47/136 (34,5%) des patients. Tous les patients ont montré une amélioration histopathologique en terme de réduction progressive de la fraction granulomateuse. Bien que ces résultats concernant une période de suivi limitée soient satisfaisants, un suivi à plus long terme sur un nombre plus élevé de patients permettra de régler la controverse entourant l'efficacité et la sécurité du traitement raccourci PCT MB, ainsi que la place de l'immunothérapie au vaccin *M. w.* chez les patients multibacillaires.

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