INTERNATIONAL JOURNAL OF LEPROSY

Volume 69, Number 3
Printed in the U.S.A.
(ISSN 0148-916X)

INTERNATIONAL JOURNAL OF LEPROSY
and Other Mycobacterial Diseases

VOLUME 69, NUMBER 3 SEPTEMBER 2001

Distinct Histopathological Patterns in Single Lesion Leprosy Patients Treated with Single Dose Therapy (ROM) in the Brazilian Multicentric Study[1]

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Histomorphological studies from skin biopsies have contributed substantially to the diagnosis and the classification of well-established leprosy which comprises a spectrum of forms, ranging from paucibacillary (PB) tuberculoid to multibacillary (MB) lepromatous types ([2, 12, 16, 25]). At the tissue level, the morphological assessment of granuloma formation, the indication of cutaneous nerve inflammation and the presence of intracellular acid-fast bacilli (AFB) allow the differentiation between the diversity of host immune responses to *Mycobacterium leprae*. The extent of local cellular immune response to *M. leprae* has been related to protective and immunopathologic responses ([11, 19]).

In the context of leprosy endemic countries, histomorphology of skin biopsies mainly has been applied for research ([3, 22]). For public health purposes, leprosy case ascertainment is based on clinical description and the presence of AFB in slit-skin smears yielding the microbiological classification of MB and PB. The clinical classification categorizes PB patients into those with a single lesion or with 2 to 5 skin lesions for operational and treatment purposes (World Health Organization. Recommended surveillance standards. WHO/CDS/CSR/ISR/ 99.2; 1999). A single skin lesion has been considered the

[1] Received for publication on 17 April 2001. Accepted for publication in revised form on 23 July 2001.

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earliest clinical manifestation of leprosy ([6, 10, 20]). This clinical entity may be unstable, spontaneously healing or progressing to any form in the disease spectrum ([2, 5, 18, 21]).

Recently, the single-dose therapy of rifampin, ofloxacin and minocycline (ROM) trial for single skin lesion PB (SSL-PB) patients without nerve involvement has raised issues related to case definition and their immunopathology ([9, 28]). Few histopathological studies on early leprosy have been published ([1, 7, 13, 27]) and, to our knowledge, there is no previous report of the morphological features of single lesion patients in the context of the Brazilian endemicity. Since 1997, a cohort of single lesion patients have been monitored after ROM therapy. The study design and the baseline epidemiological and immunological results were described in a previous report ([14]).

In this paper, we aim to describe the histomorphologic features of skin biopsies of single lesion leprosy patients recruited in a single lesion multicentric study. The features of the cellular inflammatory infiltrates and the presence of nerve involvement and AFB were used to categorize SSL-PB biopsies into different histopathological groups. Identification of homogenous groups of patients according to these histologic features may add some insight into the diagnosis and the prognosis in early leprosy.

MATERIALS AND METHODS

The study participants were recruited at six outpatient clinics located in four Brazilian states in the Northeast (Amazonas and Rondonia states), Southeast (Rio de Janeiro state) and Center-West (Goiás state) between October 1997 and December 1998. Detection rates ranged from 7.0 to 8.4 per 10,000 inhabitants in the highly endemic regions (Center-West and North) to 1.5 per 10,000 in the Southeast region (Brasil, Ministério da Saúde, 1998) at the beginning of the study.

Each site enrolled between 45 and 80 SSL-PB patients over a 1-year period. Clinical examination, the Mitsuda test (cutoff point for positivity ≥5 mm) and IgM anti-PGL-I serology (positive samples OD ≥0.2) were performed at baseline. Details of the study design and the baseline profile of SSL-PB patients treated with ROM therapy were described in a previous report ([14]). Briefly, baseline results showed predominance of adults with a median lesion size of 5.1 cm (95% CI 4.6–5.6), 75.0% were Mitsuda positive (≥5 mm) and 17.3% were seropositive for anti-PGL-I IgM antibodies. All patients had at least moderate sensory loss assessed by monofilaments, without disability. The inclusion criteria were: newly diagnosed, single lesion, untreated leprosy patients characterized by a hypopigmented or erythematous lesion with or without infiltration, definite sensory loss, without thickened nerves. All SSL-PB cases had negative slit-skin smears. Patients were excluded if a subsequent histopathology reading was consistent with MB leprosy forms (BB, BL or LL types) according to Ridley and Jopling criteria. Children younger than 7 years, pregnant women and known HIV seropositives were not enrolled in the SSL-PB cohort.

Prior to ROM therapy, all recruited patients had a standard 4-mm punch skin biopsy taken from a lesion for histopathological study. The biopsies were fixed in 10% buffered formalin, processed for paraffin sections and stained with hematoxylin and eosin (H&E) and Fite-Faraco for AFB. In order to identify homogenous histopathological categories among single lesion PB patients, the features of the cellular inflammatory infiltrates, nerve involvement and the presence of bacilli were analyzed in the skin biopsies. Using these characteristics, lesions were classified into five histomorphological groups: a) well-circumscribed epithelioid cell granuloma (Group 1); b) less-circumscribed epithelioid cell granuloma (Group 2); c) mononuclear inflammatory infiltrate permeated with epithelioid cells (Group 3); d) perivascular/periadnexal mononuclear inflammatory infiltrate (Group 4), and e) minimal or no morphological alteration detected (Group 5).

The finding of AFB in single lesion skin biopsies was considered to be a definitive diagnosis of leprosy. Leprosy was considered highly probable in the presence of cutaneous nerve involvement and/or an epithelioid granuloma (Groups 1 and 2) among clinically suspected leprosy patients in highly endemic areas. The presence of mononuclear inflammatory infiltrates, with or without epithelioid cells, was considered to be probable leprosy (Groups 3 and 4). In addition, for comparison purposes we have

TABLE 1. *Recruited single-skin lesion paucibacillary leprosy patients (SSL-PB) for the multicentric Brazilian study.*

Locale/exams	Findings
Regional health centers in three endemic regions	
Clinical and microbiology	299 patients screened
	278 potentially eligible for ROM[a] therapy with available skin biopsy
Coordinator Center	
Histomorphologic evaluation of skin biopsies	259 PB[b]/possible leprosy case patients treated with ROM
	7 MB[c] leprosy excluded
	12 other skin diseases excluded

[a] Rifampin, ofloxacin and minocycline.
[b] PB = Paucibacillary.
[c] MB = Multibacillary.

applied these criteria to the Ridley and Jopling classification.

To avoid potential biases introduced by multicenter recruitment, all skin biopsies were processed or reviewed by one pathologist with expertise in dermatopathology, without the knowledge of the patient's clinical classification, at the Pathology Laboratory in the Coordinator Center (Federal University of Goiás, Central Brazil). In order to assess inter-observer variation, 14.7% (N = 38) of the biopsy samples were re-scored blindly by another experienced pathologist (National Hansen's Disease Center, U.S.A.) considering histologic features only, without knowledge of the results of the Fite-Faraco staining.

Written informed consent was obtained from all participants, and the project was approved by each regional and by the National Ethical Committee Board (CONEP-Brazilian Ministry of Health).

Descriptive statistics were applied to evaluate the morphological groups stratified by settings. Exploratory data analysis was used to describe Mitsuda and anti-PGL-I values. The chi-squared test was applied to evaluate differences among proportions. McNemar's chi-squared test was also applied to compare the frequency of discordant pairs between pathologists; p values lower than or equal to 0.05 were regarded as significant.

RESULTS

Two-hundred-seventy-eight (93.0%) out of 299 patients had a skin biopsy available, and they were considered potentially eligible for ROM therapy according to the dermato-neurological exam and negative slit-skin smear bacteriology test (Table 1). Among excluded cases, seven single lesion patients were diagnosed as BL or LL leprosy types (MB) by the histopathological exams. Of these seven MB cases, most had a low bacterial index (BI 1+) and only one had a high bacillary load (BI 4+) according to Ridley's logarithmic scale ([24]). All of the MB cases were adults, ages ranging from 27 to 56 years, six were males and none had a BCG scar. Additionally, 12 cases were also excluded from the SSL-PB cohort due to other skin diseases such as: 2 cutaneous leishmaniasis, 2 pityriasis alba, 2 foreign-body reactions, 1 granuloma annulare, 1 morphea, 1 pityriasis versicolor, 1 insect bite, 1 cutaneous amyloidosis, and 1 eczematous dermatitis. In addition to these cases, six other biopsies were considered unsuitable for analysis. Therefore, 259 patients had skin lesions with histomorphological features compatible with PB leprosy.

The main characteristics of the histopathologic sections of skin biopsies are described below.

Group 1. Well-circumscribed epithelioid cell granulomas, with well-differentiated epithelioid cells, encompassed by a dense mantle of mononuclear inflammatory cells, mainly lymphocytes. These infiltrates were present as a single or multiple granulomas with defined limits and were around neurovascular bundles and/or periappendageal. Langhans' giant cells occasionally were present. Dermal nerve bundles sometimes

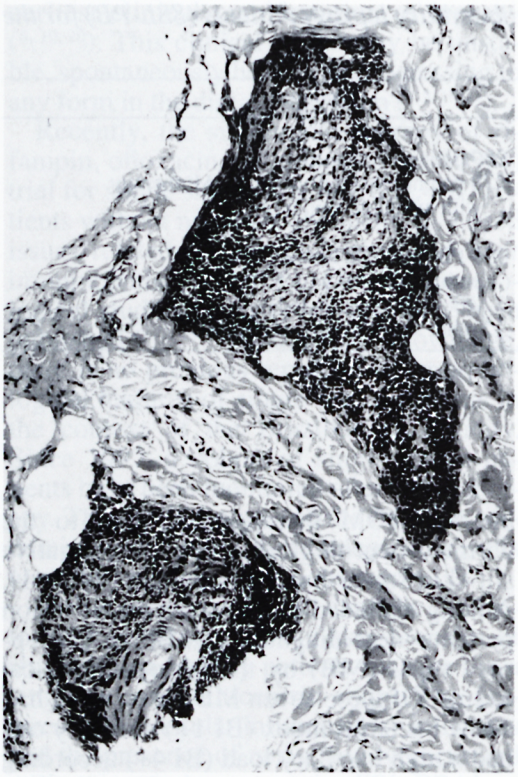

FIG. 1. Group 1: Well-circumscribed epithelioid cell granulomas, with well-differentiated epithelioid cells, encompassed by a dense mantle of mononuclear inflammatory cells, mainly lymphocytes (H&E ×125).

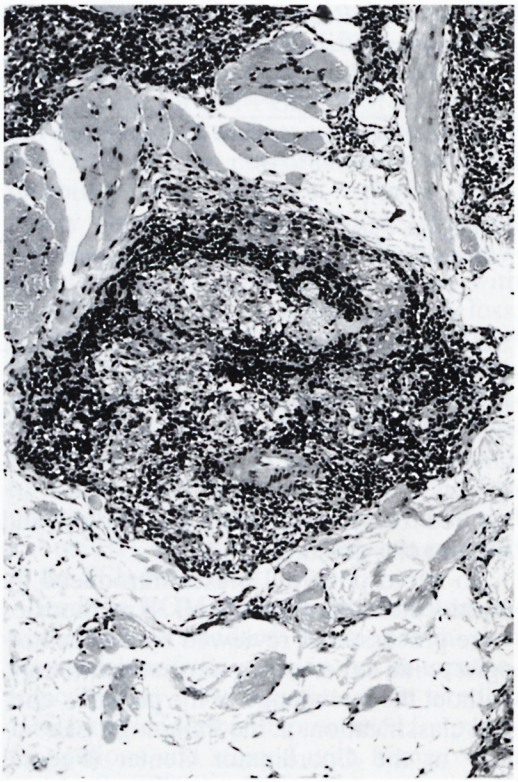

FIG. 2. Group 2: Histopathologic sections of skin biopsies presented less-circumscribed epithelioid cell granulomas, with well-differentiated epithelioid cells permeated by macrophages with vacuolated cytoplasm. The mantle of mononuclear cells was not well formed (H&E ×250).

were absent (completely destroyed or obliterated) or surrounded by dense lymphocyte cuffs. Nerve involvement was observed in 51.7%. Rare AFB were found in only one case (1.1%) (Fig. 1).

Group 2. The histopathologic sections of skin biopsies presented less-circumscribed epithelioid cell granulomas, with well-differentiated epithelioid cells permeated by macrophages with vacuolated cytoplasm. The mantle of mononuclear cells was not well formed. AFB were scanty but were found in 21.4% of the cases. Nerve involvement was represented typically by lymphocytes and macrophages obliterating the dermal nerve and was observed in 62.5% of the samples within this group (Fig. 2).

Group 3. The histopathologic sections of skin biopsies showed moderate mononuclear inflammatory infiltrates permeated with less-differentiated epithelioid cells, mainly perivascular and periadnexal. AFB were detected in 9.7% of the biopsies, and nerve involvement was observed in 71.0% (Fig. 3).

Group 4. The histopathologic sections of the skin biopsies showed mild/moderate mononuclear inflammatory infiltrate, mainly around neurovascular bundles and periadnexal. Nerve involvement was observed in 20.5%, and AFB were found in only one case (Fig. 4).

Group 5. The histopathologic sections of the skin biopsies showed mild mononuclear inflammatory infiltrate, represented mainly by lymphocytes, localized around superficial and deep dermal vessels recalling what is sometimes observed in normal skin biopsies. Neither nerve involvement nor AFB was observed.

The five histopathological groups described within the studied cohort of SSL-PB leprosy cases were categorized as follows: 33.6% (N = 87) of the biopsies repre-

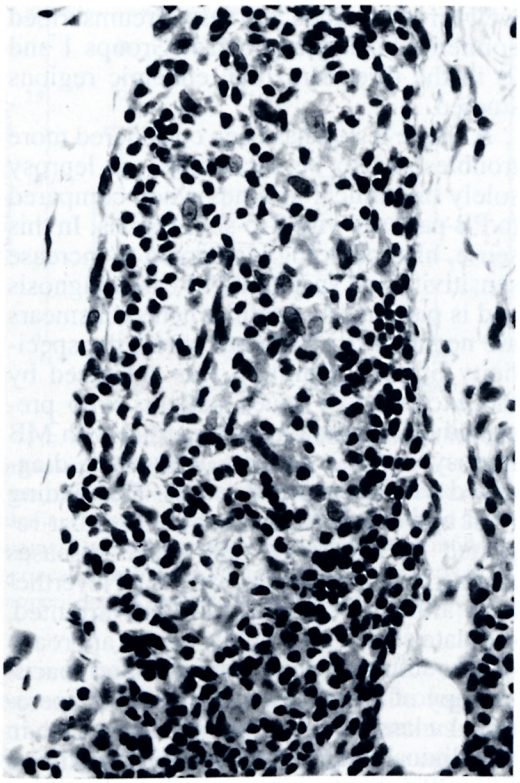

FIG. 3. Group 3: Histopathologic sections of skin biopsies showed moderate mononuclear inflammatory infiltrates permeated with less-differentiated epithelioid cells, mainly perivascular and periadnexal (H&E ×250).

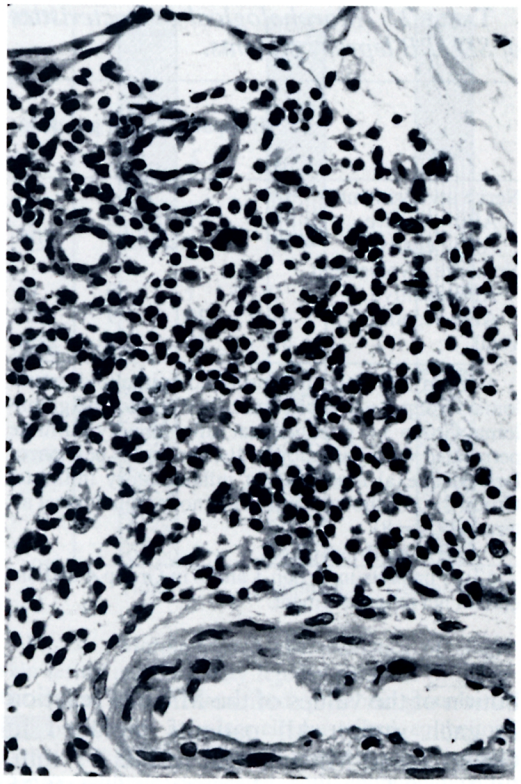

FIG. 4. Group 4: Histopathologic sections of skin biopsies showed mild/moderate mononuclear inflammatory infiltrate, mainly around neurovascular bundles and periadnexal (H&E ×250).

sented well-circumscribed epithelioid cell granuloma (Group 1); 21.6% (N = 56) less-circumscribed epithelioid cell granuloma (Group 2); 12.0% (N = 31) were described as mononuclear inflammatory infiltrate permeated with epithelioid cells (Group 3), and 29.7% (N = 77) had perivascular/periadnexal mononuclear inflammatory infiltrate (Group 4). Minimal/no morphological alteration in the skin was detected in only eight (3.1%) SSL-PB patients categorized as Group 5, who were considered leprosy by clinical parameters. For simplified comparison, Group 1 could correspond to TT forms, Groups 2 and 3 to the BT forms in the Ridley and Jopling classification and Group 4 was considered as indeterminate leprosy.

When different histopathological sections were examined independently by two pathologists, 30 out of 38 specimens were considered compatible with leprosy and one was not considered leprosy, yielding 81.6% (95% CI 65.7–92.3) of overall agreement. There was no statistically significant difference in the comparison of the proportions in paired analysis (Fisher, p = 0.15). There was close agreement between pathologists in the ascertainment of the SSL-PB leprosy diagnosis, indicating reproducible criteria used and good quality control.

Table 2 shows the distribution of skin/nerve involvement concomitant with the presence of bacilli stratified into the five histopathological groups described. The overall percentage of nerve involvement was 49.8% (N = 127) and in 17 patients (6.7%) rare AFB were found mainly coexisting with nerve involvement. AFB mainly were detected within lesions representing the less-circumscribed epithelioid cell granuloma (Group 2). There was no statistically significant difference in the frequency of nerve involvement among the groups.

The box plots in Figure 5 show the distri-

TABLE 2. *Morphological characteristics of SSL-PB leprosy patients.*

	Histopathological groups[a]			
	1	2	3	4
Nerve involvement				
AFB[b] positive	1	11	3	1
AFB negative	43	24	19	25
No nerve involvement				
AFB positive	0	1	0	0
AFB negative	41	20	9	49
Total	85[c]	56	31	75[c]

[a] Group 1 = Well-circumscribed epithelioid granuloma; Group 2 = less-circumscribed epithelioid granuloma; Group 3 = mononuclear inflammatory infiltrate permeated with epithelioid cells; Group 4 = perivascular/periadnexal mononuclear inflammatory infiltrate; Group 5 = not shown; minimal or no morphological alteration (N = 8).

[b] AFB = Acid-fast bacilli.

[c] Two patients in Group 1 and 2 in Group 4 had uncertain nerve involvement.

bution of the values of the Mitsuda reaction in each group. All patients included in Group 1 had Mitsuda test results >3 mm, 89.3% of them strongly positive (cutoff ≥5 mm). In contrast, 23.6% of the patients assembled as Group 4 had negative Mitsuda reactions. There was a statistically significant association between a positive Mitsuda test and patients classified as Group 1 (χ^2 = 16.0, DF = 3, $p < 0.05$). Variables related to age, sex, household contact, BCG scar, time of perceived lesion and lesion size were not statistically significantly different among the groups. Anti-PGL-I IgM serology was predominantly negative, ranging from 70% to 84%, without any association with the five histopathological groups. In all sites, approximately one third of the SSL-PB biopsies had skin lesions presenting well-circumscribed epithelioid cell granulomas (Group 1) (Fig. 6).

DISCUSSION

Our data clearly show that SSL-PB leprosy patients recruited in a multicentric study presented histomorphology readings comprising the whole PB leprosy spectrum but also a few MB cases, despite being diagnosed as a single clinical entity for treatment purposes. These results indicate a histomorphological heterogeneity among SSL-PB patients, with predominance of well-circumscribed and less-circumscribed epithelioid cell granulomas (Groups 1 and 2) in the three Brazilian endemic regions studied.

A single lesion has been considered more troublesome to be ascertained as leprosy solely on clinical grounds when compared to PB patients with 2–5 skin lesions. In this sense, histopathology is known to increase sensitivity and specificity of case diagnosis and is particularly useful when skin smears are negative ([21, 22]). In our study, the specificity of case definition was enhanced by the exclusion of seven patients who presented histopathology compatible with MB leprosy and 12 patients who were diagnosed with other skin diseases. This finding is in agreement with other studies that reported MB leprosy and other diseases among monolesion patients ([7, 21]). Nevertheless, although some caution is warranted, our data support the public health approach of the clinical manifestation and bacilloscopy of single lesion patients for operational classification, already discussed in the clinical and immune baseline profile of SSL-PB patients in a previous report ([14]).

We have attempted to develop histopathological criteria by which subgroups within the PB portion of the leprosy spectrum may be recognized. The main premise was that the five-part immune classification ([25]) was conceived to categorize the whole spectrum of leprosy disease and some difficulties were reported when applying this system to PB and the early lesion ([4]). This baseline histopathology evaluation, even when performed among newly diagnosed SSL-PB patients, cannot determine with any certainty the duration of illness or how early the cases are. In this sense, a time dimension should be considered when analyzing the immunopathologic spectrum of leprosy, and changes in histopathology may occur during clinical evolution ([26]).

In the majority of the readings, an inflammatory infiltrate, nerve involvement and/or the finding of AFB were found. AFB were detected in only a small percentage of the biopsies (6.7%). These findings are in concordance with previous experience that AFB are rarely detected in skin biopsies of PB patients, which makes it difficult to confirm the diagnosis of leprosy by the detection of bacilli alone ([6, 11, 12, 23]). Therefore,

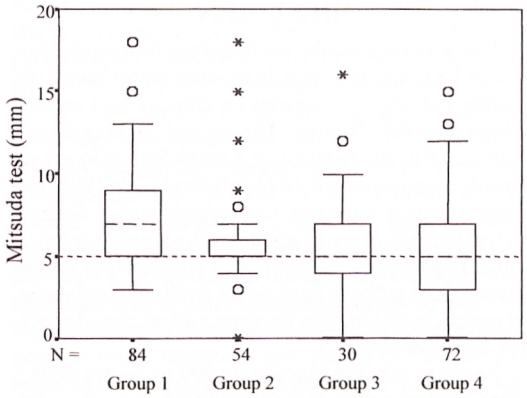

FIG. 5. Mitsuda test distribution among different groups of paucibacillary leprosy patients. ----cut-off (mm); Group 1 = Well-circumscribed epithelioid granuloma; Group 2 = less-circumscribed epithelioid granuloma; Group 3 = mononuclear inflammatory infiltrate permeated with epithelioid cells; Group 4 = perivascular/periadnexal mononuclear inflammatory infiltrate.

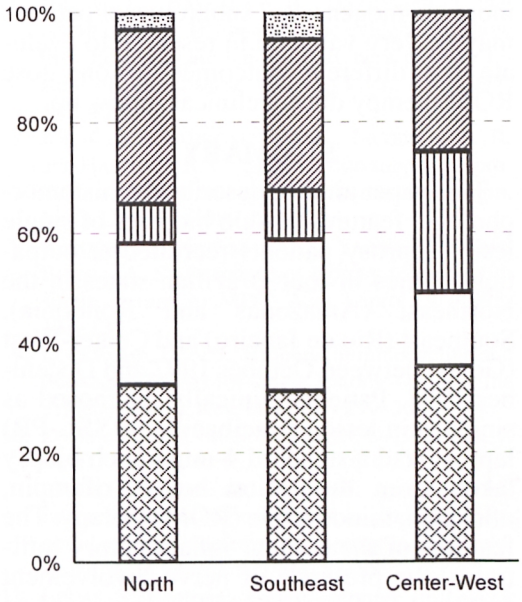

FIG. 6. Morphological characteristics of single skin lesion paucibacillary leprosy patients. ▨ = Group 1 = Well-circumscribed epithelioid granuloma; ▨ = Group 2 = less-circumscribed epithelioid granuloma; ▨ = Group 3 = mononuclear inflammatory infiltrate permeated with epithelioid cells; □ = Group 4 = perivascular/periadnexal mononuclear inflammatory infiltrate; ⊠ = Group 5 = minimal or no morphological alteration.

perineural inflammation and/or the presence of AFB detected by histopathology in granulomatous and non-granulomatous skin lesions, obtained from clinically suspected patients, have been considered highly probable for or definitive of leprosy, respectively.

By these criteria, half of the skin biopsies in our study were considered TT or BT leprosy. Interestingly, AFB were detected mainly in the less-circumscribed epithelioid granulomas or mononuclear inflammatory infiltrates (Groups 2 and 3) considered BT in the Ridley and Jopling ([25]) classification. A possible explanation is that effective cell-mediated immunity (CMI) leads to the formation of well-circumscribed granuloma (Group 1) which restrain *M. leprae* multiplication at the tissue level ([17, 19, 30]). In this study, a diagnosis of probable leprosy was made when histomorphological features of granulomatous and non-granulomatous inflammation were associated with a clinical diagnosis of leprosy by experts in an endemic region, considering that there is no independent "gold standard" for early disease ([12]).

Most of the recent leprosy literature refers to early/single-lesion leprosy as an indeterminate form of the disease which may progress to either pole of the spectrum ([5, 10, 11, 21, 29]). Our study reveals that almost 70% of patients with a single lesion had histopathological findings compatible with the TT or BT forms, independent of the Brazilian region. This suggests that a substantial portion of monolesion patients may be classified as TT or BT rather than indeterminate, although it is not possible at this point to identify those who might have the potential to downgrade to other borderline types. This finding is in agreement with studies conducted in India ([8, 13, 15, 27]) before the implementation of ROM therapy. Notably also, our results showed some correlation of the histologic findings with the Mitsuda response, and no correlation with the serologic status of the patients. These observations are consistent with earlier studies of PB disease, and have significance for efforts in developing skin tests or better serologic tests to aid in the early diagnosis of leprosy.

Finally, the different histomorphological profiles among SSL-PB patients demonstrated the heterogeneity of the local cellular immune response. The identification of

more "homogeneous" subgroups of patients may be very valuable in research to evaluate the different outcomes to one-dose ROM therapy during clinical follow up.

SUMMARY

This paper aims to describe the histomorphologic features of skin biopsies of single lesion leprosy patients recruited at outpatient clinics in four Brazilian states in the Northeast (Amazonas and Rondonia), Southeast (Rio de Janeiro) and Center-West (Goiás) between October 1997 and December 1998. Patients clinically diagnosed as single skin lesion paucibacillary (SSL-PB) leprosy had a standard 4-mm punch biopsy taken from the lesion before rifampin, ofloxacin, minocycline (ROM) therapy. The features of the cellular inflammatory infiltrates, the presence of nerve involvement and acid-fast bacilli (AFB) were used to categorize SSL-PB biopsies into different histopathological groups. Two-hundred-seventy-eight (93.0%) out of 299 patients had a skin biopsy available. Seven single lesion patients were diagnosed as BL or LL leprosy types (MB) by the histopathological exams and 12 cases were excluded due to other skin diseases. Therefore, 259 patients had skin lesions with histomorphological features compatible with PB leprosy categorized as follows: 33.6% (N = 87) of the biopsies represented well-circumscribed epithelioid cell granuloma (Group 1); 21.6% (N = 56) less-circumscribed epithelioid cell granuloma (Group 2); 12.0% (N = 31) were described as mononuclear inflammatory infiltrate permeated with epithelioid cells (Group 3), and 29.7% (N = 77) had perivascular/periadnexal mononuclear inflammatory infiltrate (Group 4). Minimal/no morphological alteration in the skin was detected in only 8 (3.1%) SSL-PB patients categorized as Group 5, who were considered to have leprosy by clinical parameters. SSL-PB leprosy patients recruited in a multicentric study presented histomorphology readings comprising the whole PB leprosy spectrum but also a few MB cases. These results indicate heterogeneity among SSL-PB patients, with a predominance of well-circumscribed and less-circumscribed epithelioid cell granulomas (Groups 1 and 2) in the sites studied and the heterogeneity of local cellular immune response.

RESUMEN

Este estudio describe los hallazgos histomorfológicos de las biopsias de piel de lesiones únicas en los pacientes con lepra, reclutados en clínicas de 4 estados brasileños del Noreste (Amazonas y Rondonia), Sureste (Rio de Janeiro), y Centro-Este (Goias) de Brasil, entre octubre de 1997 y diciembre de 1998. Las biopsias de estos pacientes se tmaron antes y después del tratamiento con rifampina, ofloxacina y minociclina. Las biopsias se clasificaron en diferentes grupos histológicos sobre la base de los infiltrados celulares, la presencia de afección nerviosa y el número de bacilos ácido-resistentes.

Se contó con 278 biopsias de 299 pacientes (93%). Siete lesiones únicas se diagnosticaron como lepra BL o LL multibacilar (MB) y 12 casos se descartaron debido a otras afecciones de la piel. Las restantes 259 biopsias correspondieron a lesiones compatibles con lepra paucibacilar: 33.6% (N = 87) de las biopsias mostraron granulomas de células epitelioides bien circunscritos (Grupo 1); 21.6% (N = 56) tuvieron granulomas epitelioides menos circunscritos (Grupo 2): 12.0% (N = 31) mostraron infiltrados inflamatorios mononucleares con algunas células epitelioides infiltrantes (Grupo 3), y 29.7% (N = 77) tuvieron infiltrado mononuclear inflamatorio perivascular/perianexal (Grupo 4). Sólo 8 pacientes (3.1%) con lesiones únicas de la lepra mostraron ausente o mínima alteración de la piel. Los pacientes paucibacilares (PB) con lesiones únicas, incluidos en el estudio multicéntrico, presentaron características que abarcaron todo el espectro de la lepra paucibacilar, aunque también hubieron algunos casos multibacilares. Los resultados indican heterogeneidad histomorfológica entre los pacientes PB con lesiones únicas, con predominio de granulomas de células epitelioides más o menos circunscritos (Grupos 1 y 2), y heterogeneidad de la respuesta celular local.

RÉSUMÉ

Cet article vise à décrire les caractères histo-morphologiques de biopsies cutanées provenant de patients non-hospitalisés souffrant de lésion unique de lèpre, recrutés à partir de cliniques situées dans quatre états bréziliens du nord-est (Amazonas et Rondonia), sud-est (Rio de Janeiro) et centre-ouest (Goias) entre octobre 1997 et décembre 1998. Préalablement au traitement associant la rifampine, l'orofloxacine et la minocycline (ROM), les patients diagnostiqués cliniquement comme lésion cutanée unique paucibacillaire (SSL-PB) eurant leur lésion prélevée à l'aide d'un trocard 'punch' de 4 mm. Les caractères de l'infiltrat cellulaire inflammatoire, la présence de nerfs lésés et de bactéries acido-alcoolo-résistantes (AAR) furent utilisés pour regrouper les biopsies SSL-PB dans plusieurs ensembles histopathologiques.

Deux cent soixante dix-huit (93,0%) parmi 299 patients présentaient une biopsie exploitable. Sept lésions uniques de patients furent diagnostiquées comme de type BL et LL (multibacillaire; MB) par l'examen histopathologique et 12 cas furent exclus à cause de

maladies intercurrentes. Ainsi 259 patients eurent des lésions cutanées avec des caractères histomorphométriques compatibles avec une lèpre paucibacillaire (PB), qui furent regroupées comme suit: 33,6% (N = 87) des biopsies présentaient des granulomes épithélioïdes bien circonscrits (groupe 1); 21,6% (N = 56) des granulomes épithélioïdes moins bien circonscrits (groupe 2); 12,0 (N = 31) furent décrits comme des infiltrat de cellules mononucléées parsemés de macrophages épithélioïdes (groupe 3), et 29,7% (N = 77) avaient un infiltrat périvasculaire et/ou périannexiel de cellules mononucléées (groupe 4). Des altérations morphologiques minimes ou absentes de la peau ne furent observées que chez 8 (3,1%) des patients SSL-PB, qui furent classés dans le groupe 5, car considérés comme hanséniens sur des critères et paramètres cliniques.

Les patients hanséniens SSL-PB recrutés pour cette étude multicentrique ont présenté des aspects histopathologiques comprenant non seulement l'ensemble du spectre de la lèpre PB, mais aussi de rares cas MB. Ces résultats indiquent un aspect histomorphologique hétérogène des patients SSL-PB, avec une prédominance de granulomes épithélioïdes bien et moins bien circonscrits (groupes 1 et 2), accompagné d'une hétérogénéité e la réponse locale immune à médiation cellulaire.

Acknowledgment. We thank the members of the Leprosy Study Group (Dr. Sylvana Castro Sacchetim, Dr. Silmara Navarro Pennini, Dr. Ana Lúcia Osório Maroclo Souza, Dr. Ilma M. Silva, Dr. José Augusto C. Nery, Dr. Flávia Pretti) for their assistance. We thank Dr. Thomas P. Gillis and Dr. Euzenir Sarno for helpful suggestions on the manuscript. This study was partially sponsored by PAHO, the Brazilian Ministry of Health and FUNAPE-Federal University of Goiás in 1998. This investigation received financial support from the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) ID number 981007.

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