

Clinico-pathological correlations of macular lesions in leprosy, using a new histological grading system

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Abstract

In macular forms of pauci-bacillary (PB) leprosy as the dermal infiltrate is less, greater precision in evaluation is needed both for diagnosis, and for assessment of the efficacy of treatment. With this in view, a new numerical grading system on a scale from 0-4, with intervening decimals, was recently published to describe each specific pathology of the dermal nerves and appendages. This retrospective study of smear negative macular lesions, has utilized this grading system for comparison and follow up.

Fifteen new patients with PB macular leprosy (TT, BT) were divided into two groups – Group A without deformity (ten patients), and Group B with deformity (five patients). All the patients had pre-treatment scalpel biopsies. In the pre-treatment biopsies in Group B the average grade of dermal granuloma was 1.3 compared to 0.5 in Group A. Two patients in Group A who were given daily Rifampicin and Dapsone for five and six months respectively, showed marked reduction in the infiltrate. In many biopsies a linear serpiginous infiltrate (horizontal) was present in the superficial dermis.

This new grading system is useful for quantifying the dermal pathology in PB macular leprosy, for comparison of duration of treatment, or evaluation of newer drugs in studies, and for assessing resolution of the lesion by the pathologist.

Keywords: Macular leprosy (PB), Histological grading, Dermal granuloma, Neural infiltrate and destruction, Linear serpiginous infiltrate.

Introduction

The treatment of leprosy was revolutionized in 1982 with the introduction of multi drug therapy (MDT), when a fixed duration MDT of six months was proposed for Pauci bacillary (PB) leprosy in Control Programmes.¹ However, the ideal treatment for an OPD leprosy patient would be till full clinical and histological resolution of the lesions, rather than fixed duration MDT.²⁻⁵ In macular leprosy TT / BT, the histology does not usually correlate⁶ with the Ridley – Jopling classification,⁷ as the infiltrate and granuloma are quite scanty. Hence, greater care and precision are required for evaluation.

In this regard, a new numerical grading system from 0-4 with intervening decimals was recently published, to depict the quantum of infiltrate around specific appendages and dermal nerves.⁸ The present study has utilized this grading system for comparing two groups of PB macular leprosy patients — ten patients in Group A (without deformity), and five patients in Group B (with deformity). In Group B, the dermal granuloma was 1.3 compared to 0.5 in Group A. This grading system can be utilized for comparative studies, resolution of the histology and efficacy of treatment in macular forms of PB leprosy (TT / BT).^{3,5,9}

Materials and Methods

Fifteen new patients with bacteriologically negative (PB) form of macular leprosy were included in this study. All the patients belonged to the TT / BT spectrum, and had skin smears, and pre-treatment scalpel biopsies. Careful records were maintained with charting of the lesions, measurements, and clinical photographs. Indeterminate leprosy was excluded. This was a

retrospective study. All the patients had smear negative macular lesions.

The patients were divided into two groups: Group A consisted of ten new patients without any deformity, and Group B consisted of five patients with deformities. Post-treatment biopsies were studied only in two patients from Group A, who received PB MDT with daily rifampicin for five to six months.

Grading System Used: A numerical description of the dermal pathology was adopted with a grade of 0 – 4, with intervening decimals, to describe the quantum of infiltration or destruction of the specific dermal appendage or nerve^[8]. Each specific pathology was evaluated in detail, and assigned a grade in one of nine categories. This grading was used to describe the degree of infiltration of the basal cell layer (BC), the amount of granuloma in the papillary dermis (subep. Gr.), for length and thickness of the linear serpiginous infiltrate (LSI) in the upper dermis (serpiginous--Latin: serpere—to creep), density of the deep dermal infiltrate (DDI), and density of the dermal granuloma. The degree of infiltration or destruction of the hair follicles, including sebaceous glands, arrectores pilorum muscles, sweat glands, and dermal nerves were also evaluated and graded separately. In this grading system, 0 indicates no infiltration or destruction, 1 indicates 25% infiltration or destruction, and 2 – 4 indicates 50% to 100% infiltration or destruction. In case the individual grade was expressed as a range, then it was made average before comparison, e.g. a range of 2-3 (50% to 75%) would become 2.5 (about 62.5%). For comparison of two different groups e.g. pre treatment biopsies of Group A (without deformities) and Group B (with deformities),

the grades for each category were totalled up, and the average grade was calculated. The average grade could result in odd decimal figures e.g 0.4, 1.3 and 1.7.

This system is a detailed equivalent of the pictorial histopathology seen under the microscope.

Illustrations: These were all 35 mm transparencies (slides-- clinical photographs and photomicrographs, taken with a film camera), which have been scanned for the digital format.

Results and Discussion

Ten new patients without deformity, and five new patients with deformity had their biopsies studied in detail. All the patients had skin lesions, which were hypopigmented and anaesthetic/ hypoanaesthetic, and many macules were five to ten cm in diameter. The margins were usually well defined, and the hair was diminished in most cases.

Three patients in Group A had TT (one macule), three had BT (more than two macules), and four cases had TT/BT (two macules). In Group B (with deformity) one patient had TT (one macule) and four patients had BT (more than two macules). There were seven males and three females in Group A, with an age range of 10-48 years. In Group B there were four males and one female, with an age range of 20- 60 years. The duration of leprosy was less than five years in eight patients of Group A, and four patients of Group B.

Peripheral Nerves: All the patients in Group B had thickened peripheral nerves, and loss of sensation on the hands and feet. On the other hand, none of the patients in Group A had thickened nerves or loss of sensation of the hands and feet.

Deformities in Group B: One patient had a deformity index (DI) of Grade 1, and four patients had a DI of Grade 2 (claw hand).

Table 1 shows the comparison of the pre-treatment dermal pathology in Groups A and B. The dermal granuloma and the sub epidermal granuloma were more in those with deformity (Group B)-- 1.3 (about 30% infiltration) compared to 0.5 in Group A (about 12.5% infiltration). The average values for infiltration of appendages and nerves were similar in Group A and B, but the LSI (linear serpiginous infiltrate) was more in Group A--1.5 (37.5% than in Group B--1.1 (a bit more than 25%).

Table 2 shows the comparison of pre and post treatment biopsies in two patients who had received daily Rifampicin and Dapsone for five and six months respectively. There was significant reduction of the infiltrate around the nerves and appendages in the post treatment biopsies, and also in the sub epidermal and dermal granulomas. However, there was no reduction of the infiltration of the basal cell layer, or of the LSI.

Some details of the Illustrations

Case 1 was one of the two patients shown in Table 2. He was given daily Rifampicin and Dapsone for five months, before his repeat biopsy (Figs. 1-5).

Case 3 was not a new patient, and was not included in Table 1 of this study. He had BT leprosy, with bilateral claw hands. He had taken MB MDT for eight months outside, before his biopsy was performed here, which showed that his nerve was heavily infiltrated (Fig. 6).

This new grading system could have various applications such as ascertaining resolution of the lesion in individual cases, in order to stop MDT.^{3,5} It can also be used in research projects to evaluate newer drugs causing faster clearance of the infiltrate.^{3,8,9} In addition, the pathologist could utilize parts of this grading system when describing repeat skin biopsies during treatment, such as, the infiltrate around sweat glands has reduced from 3 (75%) to 1 (25%), and the AP muscle from 2 (50%) to 0.5 (about 12.5%). It is hoped that this new grading system could be further improved in the future.

A characteristic feature found in many biopsies was a linear, serpiginous infiltrate usually present in the superficial dermis, and sometimes in the mid dermis⁸ which was slow to disappear with treatment. In many pre treatment, and some post treatment biopsies, (Figs. 3 & 5, 6) the nerve was found to be heavily infiltrated and, almost unrecognizable (Fig. 6) (Tables 1-2), thereby justifying the term Tuberculoid (macular) of the Madrid classification.¹¹ In this study, the nerves were carefully examined, as in PB leprosy the only proof of leprosy is the infiltration and destruction of the nerves. In the same vein as William Boyd's excellent dictum "Rheumatic fever licks the joints but bites the heart", it can be stated that "Leprosy licks the skin but bites the nerve".⁸ In the patients with deformities (Group B), the dermal granuloma was more than that seen in Group A (Table 1). Moreover, it is possible that those with more granuloma are more liable to have deformities (Table 1). Even though this sample was small, it does indicate a trend, which may need further corroboration.

Some limitations of this grading system are that it is time consuming, and subject to some inter-observer variation. In some cases, the grade can only be expressed as a range (e.g. 1.5-2.0), which then has to be averaged for comparison (1.75). Moreover, all the appendages or nerves may not be seen in each repeat biopsy, and so it may be difficult to compare. It is essential to take deep biopsies so as to include the nerves and deeper appendages.

It is to be remembered that the OPD antileprosy treatment in a tertiary care center, or in private practice, should be individualized and there should be no obligation to give a fixed duration therapy as in Control Programmes run by paramedical workers, and where facilities for smears and skin biopsies are not available.

Rifampicin is usually given once a month in both PB and MB MDT regimens.¹ However, certain authors have mentioned that Rifampicin could also be used daily.¹²

Rifampicin is also used daily in the US National Hansen's Disease Programme.⁴ It is of interest that the patient given daily Rifampicin for five months showed dramatic improvement in the infiltration and destruction of the nerves, as well as infiltration around the sweat glands (Table 2) (Figs. 2&4, 3&5). The fixed duration MDT in PB leprosy has been shown to be inadequate in bringing about resolution of the infiltrate in many cases after six months.^{3,5,14,15} It was said to be a compromise between the ideal treatment and practicality.^{2,3,5} Moreover, other authors have shown that the WHO PB MDT is not superior to Dapsone monotherapy for clinical and histological improvement at six months.^[15] Hence, it is necessary to treat for a longer period in OPD

cases,^{4,5} as was previously done with Dapsone Monotherapy.^{5,16} It may even be necessary to use newer drugs.^{3,10} It would be better to individualize each case, and to bring about clinical and histological regression of the lesions,^{3,5} in order to obtain a cure, and to avoid a relapse.

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Table 1: Comparison of the Pre-treatment Dermal Pathology of the two groups) (Group A& B)

| Dermal pathology | Group A (without deformity) Ten Patients (16 biopsies) Average Grade | Group B (with deformity) Five patients(seven biopsies) Average Grade |
|-----------------------------------|--|--|
| BC [†] | 0.5 | 0.6 |
| Subep. Gr. ‡ | 0.2 | 0.8 |
| LSI § | 1.5 | 1.1 |
| DDI | 0.8 | 1.0 |
| Dermal granuloma | 0.5 | 1.3 |
| Hair Follicle Infiltrated | 1.4 | 1.1 |
| Destroyed | 0 | 0 |
| Arrectores Pilorum Infiltrated | 1.4 | 1.7 |
| Destroyed | 0.9 | 1.1 |
| Sweat Glands Infiltrated | 2.0 | 2.0 |
| Destroyed | 1.0 | 1.1 |
| Nerves Infiltrated | 2.4 | 2.6 |
| Destroyed | 2.3 | 2.5 |
| | (Nerves were seen in ten biopsies of seven patients) | (Nerves were seen in six biopsies of five patients) |

Abbreviations used:

[†] BC —Basal cell layer is infiltrated (reached)

[‡] Subep Gr. — Subepidermal granuloma

[§] LSI— Linear serpiginous infiltrate (horizontal) (serpiginous– Latin: serpere– to creep)

|| DDI— Density of deep dermal infiltrate

Table 2: Pre-treatment & Post –treatment Biopsies after five and six months of daily Rifampicin and Dapsone in two patients (Group A–without deformity)

| Dermal pathology | Case I Pre-treatment | Case 1 Post-treatment | Case 2 Pre-treatment | Case 2 Post treatment |
|------------------|-------------------------|--------------------------|-------------------------|--------------------------|
| BC | 0.25 | 0.25 | 0.75 | 0.40 |
| Subep. Gr. | 0 | 0 | 1.75 | 0 |
| LSI | 1.5 | 0.75 | 2.0 | 2.0 |
| DDI | 1.25 | 0.4 | 1.75 | 0.5 |
| Dermal granuloma | 1.0 | 0 | 1.75 | 0 |
| Hair Follicle | | | | |

| | | | | |
|--------------------|-----|------|-----|------|
| Infiltrated | 0.5 | 0.25 | 1.5 | 1.5 |
| Destroyed | 0 | 0 | 0 | 0 |
| Arrectores Pilorum | | | | |
| Infiltrated | 1.0 | 0.5 | 2.0 | 2.5 |
| Destroyed | 1.0 | 0 | 2.0 | 1.5 |
| Sweat Glands | | | | |
| Infiltrated | 3.5 | 0.5 | 3.0 | 2.0 |
| Destroyed | 1.0 | 0 | 1.5 | 2.0 |
| Nerves | | | | |
| Infiltrated | 2.5 | 1.0 | 2.0 | 2.0 |
| Destroyed | 2.0 | 0.5 | 3.0 | 0.5* |

*In Case 2 the nerve which was unrecognizable in the pretreatment biopsy, became recognizable in the post treatment biopsy after six months.



Fig. 1: Case 1, (TT / BT) – Two hypopigmented, anaesthetic hairless macules on forearm. (pre-treatment) (Table 2)

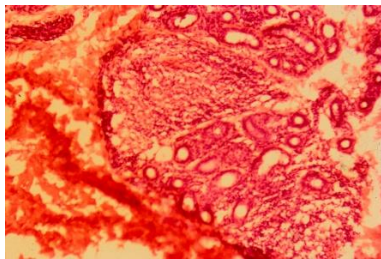


Fig. 2: Case 1, Granuloma around sweat glands, infiltrated 3.5, destroyed 1.0 (H & E x 100) (pre-treatment)

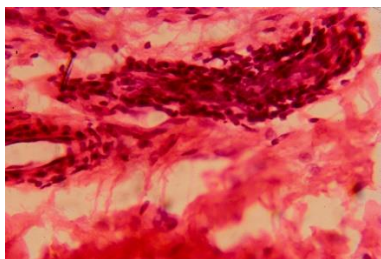


Fig. 3: Case 1, pre-treatment – adjacent nerve, infiltrated 2.5, destroyed 2.0 (H & E x 400) (also seen in Fig. 2)

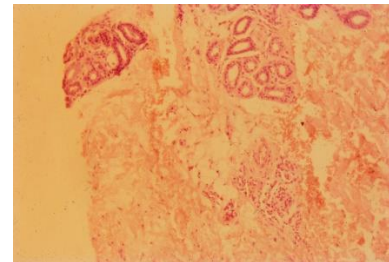


Fig. 4: Case 1, post-treatment five months. Sweat glands infiltrated 0.5, destroyed 0 (H & E x 100)

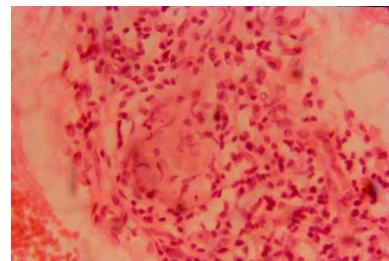


Fig. 5: Case 1, post-treatment five months – nerve in transverse section, infiltrated 1.0, destroyed 0.5 (H & E x 400)

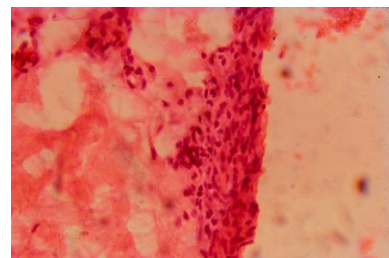


Fig. 6: Case 3, First biopsy after MB MDT eight months – nerve, infiltrated 3, destroyed 3 (H & E x 400)

Conclusion

As the infiltrate in macular leprosy is quite scanty, a numerical grading system from 0-4 was recently published to depict the infiltrate around dermal appendages and nerves. This study found that five PB patients with deformity had a dermal granuloma of Grade 1.3 compared to 0.5 in ten patients without deformity. Also, two patients without deformity had marked reduction of infiltrate after five to six months of

daily Rifampicin. This system can be used by the pathologist to quantify the improvement after treatment, and by the research worker for comparative studies of treatment duration, or after use of newer drugs.

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