Original Article

Description of a Proposed Simple Semi-objective Histological Scale for the Assessment of Dermal Melanophages in Inflammatory Skin Diseases

Rajiv Sharad Joshi
Department of Dermatology, P. D. Hinduja Hospital, Mumbai, Maharashtra, India

Abstract

Background: Dermal melanophages are a common histopathological finding in several inflammatory skin diseases and may be seen even in clinically normal-looking skin. Clinically hyperpigmented and hypopigmented conditions as well as nonpigmented lesions show melanophages which cannot always be correlated with the clinical appearance of the lesion biopsied. No literature exists to help assess the significance of dermal melanophages in inflammatory diseases and correlate their presence with the pathophysiology of the disease biopsied. Methodology: This is a retrospective study of 100 skin biopsies in patients with brown skin, which had mentioned dermal melanophages in the histopathological report. A simple-to-use semi-objective scale (score of 3–10) was used to assess the score of the dermal melanophages. This was done by a dermatopathologist who was blinded to the clinical and histopathological diagnoses. A correlation of the dermal melanophage score was attempted with the clinical/histological diagnoses and known pathogenesis of the diseases. Results: A variety of skin diseases were included in this study which could be broadly grouped into hypopigmented (10 cases, average scores 4), nonpigmented interface diseases (20 cases, average score 6.66), miscellaneous nonpigmented dermatosis (17 cases, average scores 5.3), and hyperpigmented (53). The hyperpigmented group was subdivided into those that were known to show predominantly epidermal melanin (13 cases, average score 4.58) and those who have predominantly dermal melanin following interface dermatitis (29 cases, average score 8.67) and dermal melanosis without interface dermatitis (11 cases, average score 6.18). Conclusions: This scale can be used to determine the significance of dermal melanophages in inflammatory skin diseases. Scores >6 suggest hyperpigmentary conditions due to the presence of dermal melanophages. Low scores of 3–5 are not significant and are seen in epidermal hypermelanoses, hypopigmented conditions, and other varied nonpigmented dermatoses.

Keywords: Dermal melanophages, dermal melanoses, epidermal hypermelanoses, frictional melanosis, idiopathic eruptive macular pigmentation, lichen planus pigmentosus

INTRODUCTION

Dermal melanophages in the upper dermis are commonly seen in many inflammatory skin diseases. Not only clinically hyperpigmented conditions but also hypopigmented and nonpigmented lesions show the presence of melanophages which cannot always be correlated with the clinical appearance of the skin lesions. Several hypopigmented lesions do show melanophages as do some cases of vitiligo. However, the common understanding is that in clinically hyperpigmented lesions, especially dermal melanoses, melanophages are found in the upper dermis in great abundance. Most clinical studies and even histopathology reports mention only the presence of dermal melanophages without any quantification of the amounts of melanin in the dermis.

How then does one assess whether the presence of melanophages in a given condition is significant or not? No published literature addresses this issue, and this study is an attempt to quantify dermal melanophages using a simple, easy-to-use semi-objective histological scale and validate it...
using it in various conditions in which dermal melanophages were seen on histological examination.

**Methodology**

This is a retrospective study in which a semi-objective scale was applied to evaluate dermal melanophages. One hundred consecutive biopsies of various inflammatory skin diseases in patients of brown skin that had mentioned the presence of melanophages in the dermis in the histopathology report were retrieved and studied by a dermatopathologist who was blinded to the clinical and histopathological diagnoses. A numerical score using the scoring system was assigned to each biopsy. One hundred cases studied were analyzed based on their clinical appearance and histological diagnoses into three broad groups. Group 1 was clinically hyperpigmented lesions, Group 2 was clinically hypopigmented lesions, and Group 3 was a miscellaneous group which included diseases as diverse as vesiculobullous diseases, psoriasis, and lichen planus. The group with hyperpigmented lesions was subdivided into those with dermal melanosis and those with predominantly epidermal hypermelanosis. The dermal melanotic conditions were divided further into those with interface dermatitis with dermal melanosis and frictional/photomelanosis and dermal amyloid deposition with dermal pigmentation.

**Description of the scale for evaluation of dermal melanophages**

Three parameters were considered:

1. **Grade (visualization of melanophages at various magnifications)**
   - Grade 3: More than half of the melanophages in the section seen at low power, i.e., ×40 magnification [Figures 1 and 2].
     - Grade 2.5: Few melanophages seen at ×40
     - Grade 2: More than half of the melanophages seen at ×100 [Figures 3 and 4]
     - Grade 1.5: Few melanophages seen at ×100
     - Grade 1: Melanophages seen only at high magnification, i.e., ×400 [Figure 5]

2. **Distribution of melanophages**
   - Melanophages seen focally, i.e., <25% of the upper dermis: Score 1
   - Melanophages seen locally, i.e., between 25% and 50% of the upper dermis: Score 2
   - Melanophages seen over many areas but <75% of the upper dermis: Score 3
   - Melanophages seen throughout the upper dermis: Score 4.

3. **Size and color of melanophages**
   - Small-sized melanophages: 1
   - Medium-sized lightly pigmented: 1.5
   - Medium-sized darkly pigmented: 2
   - Large darkly pigmented (few): 2.5
   - Large darkly pigmented: 3.

Using this scale, the score would range from a minimum of 3 to a maximum of 10.
Results

A variety of skin diseases were included in this study which could be broadly grouped into hypopigmented (10 cases, average score 4), nonpigmented interface diseases (20 cases, average score 6.66, miscellaneous nonpigmented dermatosis (17 cases, average score 5.3), and hyperpigmented (53). The hyperpigmented group was subdivided into those that were known to show predominantly epidermal melanin (13 cases, average score 4.58) and those who have predominantly dermal melanin following interface dermatitis (29 cases, average score 8.67) and dermal melanosis without interface dermatitis (11 cases, average score 6.18).

High scores of 8–10 were seen in dermal melanoses that are associated with interface changes such as lichen planus pigmentosus, fixed drug eruption, and pigmenting lichen planus and pigmented discoid lupus erythematosus (DLE). These were considered to be significant as interface dermatitis is associated with incontinence of melanin and presence of numerous melanophages in the papillary dermis.

Intermediate scores of 6 and 7 were seen in frictional and macular amyloidosis where the numbers of melanophages as well as size and grade are lower than in the above group.

Low scores of 3–5 were considered insignificant and were seen in epidermal hypermelanotic conditions such as acanthosis nigricans and idiopathic eruptive macular pigmentation (IEMP) as well as in hypo- and de-pigmented conditions and varied nonpigmented skin diseases.

Table 1 gives the breakup of the cases with the diagnoses, number of cases, and average melanophage score for each diagnosis.

Figure 6 gives the average score of clinically hyperpigmented conditions.

Discussion

Finding of melanophages in the upper dermis in inflammatory diseases is common and may be seen even in normal skin. Melanophages have been described in clinically normal facial skin of patients with melasma.\textsuperscript{[1,2]} What if any is the relevance of finding melanophages in the dermis. How does one assess and quantify their presence and relate them to the clinical appearance of the lesions and the known pathophysiology of the disease. Most biopsy reports just mention the presence of melanophages in the upper dermis without much information regarding their number, size, degree of pigmentation or distribution in the dermis.

Two recent studies of lichen planus pigmentosus in Indian patients have attempted to grade the dermal melanophages seen in their patients but without any comparison with other inflammatory dermatoses. The presence of melanophages was seen in all cases in both the studies, and in the first study, Sharma et al.\textsuperscript{[3]} categorized melanophages as mild (<10 melanophages/high power field ($\times400$ magnification), moderate (10–20 melanophages/high power field, and severe (more than 20 melanophages/high power field). There was no attempt to quantify the total presence of melanophages in the biopsy. In the second study, Bhat et al.\textsuperscript{[4]} just classified melanophages as conspicuous and nonconspicuous.

The scale we have described is a simple semi-objective histological scale for the quantification of dermal melanophages that takes into account three factors. The grade is the visualization of melanophages at various magnifications which records the overall extent and melanization of the melanophages. Larger and more darkly pigmented melanophages can be seen at lower magnifications and are significant reflecting the pathophysiology of the disease. The distribution quantifies the extent and number of melanophages, and the size and degree of melanization are the microscopic evaluation of the melanophages focally at high power. The range of scores is from 3 to 10. A drawback of this scale is that even if a single small poorly pigmented melanophage is present in the sections as is often seen in
Assuming that more the quantum of melanophages in the dermis more hyperpigmented, the lesion would be clinically, we attempted to correlate the dermal melanophage scores with the clinical appearance of the lesions biopsied and also correlate with the known pathophysiology of the condition. Thus, hyperpigmented conditions that are known to have prominent dermal melanophages should score high on the described scale, and those hyperpigmented conditions that are primarily due to epidermal hyperpigmentation should have lower scores.

Clinically hyperpigmented conditions such as lichen planus pigmentosus, fixed drug eruption, and pigmenting lichen planus and pigmenting DLE which are interface dermatitis and are known to have numerous dermal melanophages (pigment incontinence) had high scores of 8–10, with an average score of 8.67. On the other hand, active lesions of lichen planus and DLE which were clinically not hyperpigmented had lower scores with an average of 6.66, reflecting fewer melanophages and more inflammatory infiltrate.

Frictional melanoses and macular and lichen amyloidosis show dermal melanophages without interface changes. This clinically hyperpigmented group had lower average scores of 6.18. This lower score may be attributed to the larger number of lichen amyloidosis cases which had low scores because of localized dermal melanophages.

Hypermelanoses, on the other hand, which are known to have predominantly epidermal hyperpigmentation (brown color clinically and accentuation of pigment on Wood’s lamp examination) and include acanthosis nigricans, Becker’s nevus, and IEMP, showed very low scores of 4.58 which was comparable to 4.05 for hypopigmented lesions such as

**Table 1: Number of cases, range of scores, mean and median scores of various diseases**

| Number | Diagnosis                  | Number of cases | Range      | Average score | Median score* |
|--------|----------------------------|-----------------|------------|---------------|---------------|
| 1      | LP pigmentosus             | 24              | 8-10       | 8.65          | 8.5           |
| 2      | Pigmenting LP/DLE          | 4               | 7.5-10     | 9             | 9             |
| 3      | FDE                        | 1               | NA         | 8             | NA            |
| 4      | Frictional melanosis       | 6               | 6-9        | 7.67          | 7             |
| 5      | Cutaneous amyloid          | 5               | 3-7        | 4.4           | 4             |
| 6      | Acanthosis nigricans       | 4               | 3-6        | 4.5           | 4             |
| 7      | IEMP                       | 2               | 3          | 3             | 3             |
| 8      | Becker’s melanosis         | 3               | 3-7.5      | 4.83          | 4             |
| 9      | Acropigmentation of dohi   | 1               | NA         | 3             | NA            |
| 10     | Morphea                    | 3               | 5.5-7      | 6             | 5.5           |
| 11     | Postinflammatory (hypopig) | 6               | 3-5.5      | 4.25          | 4             |
| 12     | Vitiligo                   | 3               | 3-5        | 3.67          | 3             |
| 13     | Pityriasis lichenoides chronica | 1          | NA         | 4             | NA            |
| 14     | LP                         | 19              | 4-9.5      | 6.73          | 7             |
| 15     | DLE                        | 1               | NA         | 4             | NA            |
| 16     | Photodermatitis            | 2               | NA         | 6             | NA            |
| 17     | Spongiotic dermatitis      | 3               | 4-5.5      | 4.67          | 4.5           |
| 18     | Psoriasis                  | 3               | 5-8        | 6.33          | 6             |
| 19     | Pemphigus                  | 1               | NA         | 6.5           | NA            |
| 20     | Bullous pemphigoid         | 2               | NA         | 5.5           | NA            |
| 21     | Parapsoriasis              | 3               | 5-6        | 5.33          | 5             |
| 22     | Solar elastosis            | 1               | NA         | 4.5           | NA            |
| 23     | Prurigo                    | 1               | NA         | 3             | NA            |
| 24     | Verruca vulgaris           | 1               | NA         | 4             | NA            |

*When even number of cases were present the median was the number before the center of the distribution of scores. LP: Lichen planus, DLE: Discoid lupus erythematosus, FDE: Fixed drug eruptions, IEMP: Idiopathic eruptive macular pigmentation, NA: Not available

**Figure 6: Average scores of clinically hyperpigmented conditions**

clinically normal skin or in a depigmented condition like vitiligo, the score would still be 3.
vitiligo, pityriasis lichenoides chronica, and postinflammatory hypopigmentation, suggesting that these conditions do not have significant dermal melanophages. Even other nonpigmented conditions such as psoriasis and vesiculobullosous diseases such as pemphigoid and pemphigus had higher average values of 5.3.

Thus, our scale for estimation of dermal melanophages appears to correlate well with the known clinical and histopathological findings in various inflammatory diseases with high scores for dermal melanoses and low scores for epidermal hypermelanotic conditions.

Scores of 8–10 may be considered as significant and indicate the presence of numerous heavily pigmented dermal melanophages that contribute to slaty-gray or dark brown-black pigmentation seen clinically. Scores of 3–5 are nonsignificant and the small poorly pigmented focaly distributed dermal melanophages may be considered as incidental. An intermediate score of 6 and 7 needs clinicopathological correlation and may be seen in frictional melanoses.

There are two clinical situations where application of this scale would be of use.

1. Epidermal hypermelanotic conditions such as IEMP where there is prominent epidermal melanin with papillomatosis and minimal or absent melanophages in the upper dermis. In the past, inclusion of the presence of dermal melanophages as one of the diagnostic criteria for IEMP has created confusion as several cases that appear to be dermal melanoses have been included under IEMP and it has been suggested that presence of significant dermal melanophages should be against the histopathological diagnosis of IEMP. A recent paper reiterated this and suggested the use of the histological scale described here for assessing whether the presence of dermal melanophages was significant or not in diagnosis of IEMP. Our study had two cases of IEMP whose average score was 3 which was less than the average of three cases of vitiligo whose average score was 3.67. This strength the contention that dermal melanophages are not seen in IEMP and if seen are very few, small, and of no diagnostic consequence being less in number and extent than even in a depigmented condition such as vitiligo.

2. Slaty-gray melanoses such as lichen planus pigmentosus, Riehl’s melanosis, ashy dermatosis, and fixed drug eruptions necessarily show high scores of dermal melanophages (8–10). Large plaque parapsoriasis and morphea may also at times show several melanophages in the upper dermis and may be confused with the above conditions both clinically and histologically. In the absence of active interface changes, a high dermal melanophages score helps in confirming the diagnosis of slate-gray melanoses, and on the other hand, a low score is a pointer against the diagnosis.

The limitations of this study are the following:

a) This proposed histological scale needs to be validated by different observers with evaluation of interobserver variation and repeatability of the scores. b) By itself, the score of dermal melanophages does not always correlate with the clinical perception of pigmentation of the lesion that is biopsied and several hypo- to normo-pigmented lesions also demonstrate a dermal melanophage score albeit a lower score. Therefore, a study that includes correlation between the clinical appearance and histological melanophage scores will further add to the validity/utility of this proposed score.

Conclusions

We describe a simple to use (with some practice it takes <30 s to assign a score) semi-quantitative histological scale for the assessment of dermal melanophages in inflammatory skin diseases. This scale can be used to determine the significance of dermal melanophages in inflammatory skin diseases. High scores of 8–10 are significant and are seen in melanoses that follow interface dermatitis. Other dermal melanotic conditions such as frictional melanosis and macular amyloidosis have intermediate scores of 6–7. Low scores of 3–5 are not significant and are seen in epidermal hypermelanoses, hypopigmented conditions, and other varied nonpigmented dermatoses.

Further studies are desirable to establish the validity of this scale which would test the repeatability, interobserver variance, and correlation with the clinical perception of skin color.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Kang WH, Yoon KH, Lee ES, Kim J, Lee KB, Yim H, et al. Melasma: Histopathological characteristics in 56 Korean patients. Br J Dermatol 2002;146:228-37.
2. Grimes PE, Yamada N, Bhawan J. Light microscopic, immunohistochemical, and ultrastructural alterations in patients with melanoma. Am J Dermatopathol 2005;27:96-101.
3. Sharma VK, Gupta V, Paahadiya P, Yedi KK, Arava S, Ramam M, et al. Dermoscopy and patch testing in patients with lichen planus pigmentosus on face: A cross-sectional observational study in fifty Indian patients. Indian J Dermatol Venereol Leprol 2017;83:656-62.
4. Bhat RM, Mathanda TR, Jayaprakash CS, Dandakeri S. Clinical, histopathological characteristics and immunohistochemical findings in lichen planus pigmentosus. Indian J Dermatol 2017;62:612-7.
5. Sanz de Galdeano C, Léauté-Labrèze C, Bioulac-Sage P, Nikolic M, Taieb A. Idiopathic eruptive macular pigmentation: Report of five patients. Pediatr Dermatol 1996;13:274-7.
6. Joshi RS, Rohatgi S. Idiopathic eruptive macular pigmentation: A critical review of published literature and suggestions for revision of criteria for diagnosis. Indian J Dermatol Venereol Leprol 2015;81:576-80.
7. Joshi R. Idiopathic eruptive macular pigmentation in an Indian male. Indian Dermatol Online J 2018;9:64-5.