“Melanocytic Nests Arising in Lichenoid Inflammation”: Reappraisal of the Terminology “Melanocytic Pseudonests”

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Abstract: Pseudonests or pseudomelanocytic nests represent aggregates of cells and cell fragments, including keratinocytes, macrophages, lymphocytes, and occasional melanocytes. Pseudomelanocytic nests in the setting of lichenoid inflammation can mimic atypical melanocytic proliferations. Several reports documented nonspecific staining of pseudonests with melanoma antigen recognized by T cells-1/Melan-A, which can be detected in the cytoplasm of nonmelanocytic cells. In contrast, nuclear stains, such as MITF and SOX10, avoid this nonmelanocyte cytoplasmic staining. The authors have previously proposed the term melanocytic pseudonests to describe junctional nests with numerous (>2) true melanoma antigen recognized by T cells-1/Melan-A, SOX10, and MITF in a nonmelanocytic lesion with lichenoid inflammation (unilateral lichen planus pigmentosus/erythema dyschromicum perstans). In this study, the authors report another case of this phenomenon arising in a different lichenoid inflammatory dermatitis (lichen planus). The immunophenotype and number of clustered true melanocytes indicate that these dermoepidermal aggregates represent true melanocytic nests and not pseudonests of any type. Therefore, the authors propose the revised terminology of “melanocytic nests arising in lichenoid inflammation” to describe this novel pattern of benign melanocytic reorganization or proliferation in a subset of lichenoid dermatitides. Because this phenomenon can mimic atypical melanocytic proliferations, clinicopathologic correlation is essential for the correct diagnosis.

Key Words: pseudomelanocytic nests, pseudonests, melanocytic pseudonests, lichenoid inflammation

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FIGURE 1. A, Well-circumscribed, violaceous, polygonal, flat-topped papules coalescing into plaques at the site of a previous lower back surgery. B, Similar lesions were also noted on the medial aspect of the foot and ankle. C, Six weeks after high-potency topical steroid use, only postinflammatory hyperpigmentation remains, and erythema of the scar (unrelated to the rash) is unchanged.
INTRODUCTION

Pseudonests or pseudomelanocytic nests represent aggregates of cells and cell fragments that include keratinocytes, macrophages, and lymphocytes, as well as occasional melanocytes. Pseudomelanocytic nests in the setting of lichenoid inflammation can mimic atypical melanocytic proliferations. In contrast, we have previously reported junctional nests with numerous melanoma antigen recognized by T cells-1 (MART-1)/Melan-A–positive, SOX10-positive, and MITF-positive melanocytes in a lesion clinically determined to be unilateral lichen planus pigmentosus (LPP)/erythema dyschroemicum perstans (EDP).¹ In the previous report, we suggested the terms “melanocyte-rich pseudomelanocytic nests” or “melanocytic pseudonests” for this phenomenon. Here, we report another case of the same phenomenon with melanocytic pseudonests arising in lichen planus.

CASE REPORT

A 40-year-old white man with Fitzpatrick skin type II presented with violaceous, polygonal, flat-topped, mildly pruritic papules overlying and adjacent to a scar from an orthopedic procedure to the back 3 months before onset of the rash (Fig. 1A). Simultaneously, similar papules developed on the medial aspects of his feet and ankles (Fig. 1B). No mucosal lesions were present. His medical and family histories were unremarkable for skin cancer or hepatitis, and there were no changes in medications. The clinical impression was lichen planus. Histological findings from a punch biopsy of a back lesion revealed flattened epidermis, basal layer vacuolization with individual necrotic keratinocytes forming a subepidermal cleft, and a dense band-like lichenoid lymphocytic infiltrate with scattered pigment-laden macrophages (Fig. 2). In addition, nests were noted at the dermal–epidermal junction containing numerous (at least 3 or more) MART-1/Melan-A–positive and SOX10-positive melanocytes (Fig. 3). Ten days later, punch biopsy from another back lesion revealed histological changes similar to the original, although definitive junctional nests were not identified possibly because this latter specimen was denuded (Fig. 4). Criteria diagnostic for malignant melanoma in situ were not present in either biopsy specimen. Clinically, there was no evidence for an incidental melanocytic nevus associated with the inflammatory papules biopsied. The clinicopathologic correction in this case was consistent with lichen planus. In support of this diagnosis, after 6 weeks of high-potency topical steroid, the rash was significantly improved with only residual postinflammatory hyperpigmentation (Fig. 1C).

FIGURE 2. Low magnification view shows flattened epidermis, basal layer vacuolization with individual necrotic keratinocytes forming subepidermal cleft and dense, and band-like lichenoid lymphocytic infiltrate with scattered pigment-laden macrophages (hematoxylin and eosin, ×400).

FIGURE 3. Immunoperoxidase staining showing junctional nest-like structures (highlighted by black arrows) with numerous (A) SOX10-positive and (B) MART-1/Melan-A–positive cells (×200).

FIGURE 4. Low magnification view from a different back lesion that also exhibits denuded dermis and underlying dense band-like lymphohistiocytic infiltrate (hematoxylin and eosin, ×100) with scattered MART-1/Melan-A–positive cells at the remaining dermoepidermal junction (highlighted by arrows) (inset) (×200).
DISCUSSION

Pseudonests in the setting of lichenoid inflammation can lead to the misdiagnosis of an atypical melanocytic proliferation. Previous several reports documented nonspecific staining of pseudonests with MART-1/Melan-A, which may detect a combination of few residual melanocytes or melanocytic debris engulfed by macrophages Table 1.2,3 Given that MART-1/Melan-A can be detected in the cytoplasm of non-melanocytic cells including keratinocytes or macrophages, we used nuclear stains, such as MITF and SOX10, to detect melanocytes in nests in a lesion of unilateral LPP/EDP.1 Nicholson and Gerami4 also used MITF and MART-1 to present 2 cases initially misdiagnosed as melanoma in situ as MART-1 positivity in pseudomelanocytic nests but finally diagnosed as fixed drug eruption as a result of failing of positive staining of MITF in pseudomelanocytic nests.

As described in previous case report from our group,1 we again identify junctional nests with aggregates of MART-1/Melan-A–positive and SOX10-positive melanocytes too numerous to be considered pseudomelanocytic nests in a lesion of lichen planus. Recently, Gavino et al5 identified nested aggregates of true melanocytes at the dermoepidermal junction in 4 cases of previously diagnosed as lichen planus-like keratoses. In 70 cases of lichen planus-like keratoses, 4 cases demonstrated an occasional MART-1–positive junctional nest that also revealed MITF positivity.

### TABLE 1. Reported Cases of Pseudomelanocytic Nests or Melanocytic Nests in Lichenoid Inflammation

| Reference                  | Age/Sex | Location        | Clinical Presentation                       | Mel-A | MITF | SOX10 | HMB 45 | S100 |
|----------------------------|---------|-----------------|-------------------------------------------|-------|------|-------|--------|------|
| Maize et al6               | 35/M    | Left temple     | Recent onset of blue-gray macules         | +     | NP   | NP    | –      | –    |
| Beltraminelli et al7       | 60/M    | Checks          | Ill-defined brown grayish pigmentation    | +     | NP   | NP    | –      | –    |
| Beltraminelli et al7       | 59/M    | Forehead        | Irregular, partly confluent, reticulated  | +     | NP   | NP    | –      | –    |
| Beltraminelli et al7       | 52/F    | Infraorbital area | Small scaly plaque of the infraorbital region | +      | NP   | NP    | –      | –    |
| Nicholson and Gerami4      | 39/F    | Along the hair line | New asymptomatic brown macules           | +     | A rare cell | NP   | A rare cell | A rare cell |
| Nicholson and Gerami4      | 76/F    | Periocular area  | Well demarcated hyperpigmented patch      | +     | –    | NP    | –      | –    |
| Silva et al3               | 48/M    | Neck            | Discrete, reticulate, hyperpigmented patch | +     | Numerous cells (≥3) | Numerous cells (≥3) | NP | Focal positive |
| Gavino et al3              | 4 cases but U | U              | U                                         | +     | –    | NP    | –      | –    |
| Boros et al6               | 66/M    | Interdental papilla | Solitary slightly elevated pigmented lesion | –      | –    | NP    | –      | –    |
| Boros et al6               | 61/F    | Hard plate      | Solitary pigmented lesion                 | –     | NP   | NP    | NP     | NP   |
| Present case               | 40/M    | Back, ankles, and feet | Violaceous, polygonal, flat-topped, mildly pruritic papules | +     | NP   | NP    | NP     | NP   |

| Reference                  | CK      | CD68 | CD3 | Tyr | BCL2 | Final Interpretation                      | Interpretation of Nests                  |
|----------------------------|---------|------|-----|-----|------|-------------------------------------------|------------------------------------------|
| Maize et al6               | NP      | NP   | NP  | –   | –    | Favored discoid lupus erythematosus       | Pseudomelanocytic nests                  |
| Beltraminelli et al7       | (+) some cells in nests | NP   | NP  | NP  | NP   | Lichenoid phototoxic reaction            | Pseudomelanocytic nests                  |
| Beltraminelli et al7       | (+) some cells in nests | NP   | NP  | NP  | NP   | LPP                                        | Pseudomelanocytic nests                  |
| Beltraminelli et al7       | (+) some cells in nests | NP   | NP  | NP  | NP   | Pigmented lichenoid keratosis             | Pseudomelanocytic nests                  |
| Nicholson and Gerami4      | Occasional cells | Occasional cells | Occasional cells | NP | NP   | Fixed drug eruption                       | Pseudomelanocytic nests                  |
| Nicholson and Gerami4      | Occasional cells | –    | Occasional cells | NP | NP   | Fixed drug eruption                       | Pseudomelanocytic nests                  |
| Silva et al3               | Occasional cells | NP   | NP  | NP  | NP   | LPP/EDP                                   | Melanocytic proliferation in a lichenoid dermatitis |
| Gavino et al3              | –       | NP   | –   | NP  | NP   | Melanocytic nevi with lichenoid inflammation | Melanocytic nests with lichenoid inflammation |
| Boros et al6               | NP      | (+)  | NP  | NP  | NP   | Chronic mucositis                         | Pseudomelanocytic nests                  |
| Boros et al6               | NP      | (+)  | NP  | NP  | NP   | Melanophages                               | Pseudomelanocytic nests                  |
| Present case               | NP      | NP   | NP  | NP  | NP   | Lichen planus                             | Melanocytic nests arising in lichenoid inflammation |

+ present; – absent; CK, cytokeratin; Mel-A, Melan-A/MART-1; NP, not performed; Tyr, tyrosinase; U, unspecified.
confirming a true melanocytic origin (Table 1). The authors felt that these melanocytic aggregates represented true melanocytic nests and so reclassified the 4 lesions as “benign melanocytic nevi with lichenoid inflammation.” Unlike Gavino et al, our clinical settings of EDP/LPP and lichen planus do not afford a reclassification of these inflammatory lesions to any known melanocytic proliferation. Nevertheless, we feel that these aggregates represent true melanocytic nests and not pseudonests of any type. Therefore, we propose the revised terminology of “melanocytic nests arising in lichenoid inflammation” to describe this novel pattern of benign melanocytic reorganization or proliferation in a subset of lichenoid dermatitides. Because this phenomenon can mimic atypical melanocytic proliferations, clinicopathologic correlation is essential for the correct diagnosis.

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