OBSERVATION

Two Pediatric Cases of Nonbullous Histiocytoid Neutrophilic Dermatitis Presenting as a Cutaneous Manifestation of Lupus Erythematosus

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Background: Nonbullous neutrophilic dermatoses are seen infrequently in association with lupus erythematosus (LE). A recently described histopathologic variant of Sweet syndrome, to our knowledge, histiocytoid Sweet syndrome (HSS) has not been described in either pediatric or adult patients with LE.

Observations: We describe 2 pediatric patients with nonbullous histiocytoid neutrophilic dermatitis in the setting of LE. One case represents the initial presentation of subacute cutaneous LE, while the other case represents a manifestation of established systemic LE. Both cases demonstrate histopathologic findings of HSS.

Conclusions: We believe that the dermatosis observed in these 2 patients represents a nonbullous histiocytoid neutrophilic dermatosis that is best termed HSS. This entity may represent a distinct and important cutaneous manifestation of LE. Additional study is needed to further elucidate the relationship between neutrophilic dermatitis and LE.

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We describe 2 pediatric patients with nonbullous neutrophilic dermatitis presenting as a cutaneous manifestation of lupus erythematosus (LE). Both cases demonstrated unique histopathologic features that resembled a variant of neutrophilic dermatosis recently coined histiocytoid Sweet syndrome (HSS). However, the clinical presentation of these 2 patients was not typical of conventional Sweet syndrome.

REPORT OF CASES

Case 1

A 9-year-old girl with systemic LE (SLE) presented with a 2-month history of an asymptomatic eruption on the upper and lower extremities. The patient reportedly had experienced a “stomach flu” associated with fever prior to the onset of the eruption. She denied other systemic symptoms. Her medical history was significant for mesangial glomerulonephritis, malar eruption, and atopic dermatitis. Her medications included prednisone, mycophenolate mofetil, hydroxychloroquine, and aspirin, all of which she had been taking for more than 6 months prior to the onset of the eruption.

Physical examination revealed scattered blanching violaceous papules and macules, some of which coalesced into plaques on the palms, arms, thighs, and buttocks. (Figure 1A). She also had erythematos confluent patches on the malar eminences.

Laboratory examinations performed on initial presentation revealed a normal white blood cell count with lymphopenia, hypocomplementemia, and an elevated double-stranded DNA level of 790 IU/mL (normal, <25 IU/mL). Erythrocyte sedimentation rate and C-reactive protein level were also both elevated at 40 mm/h (normal, <15 mm/h) and 9.4 mg/L (normal, <6.3 mg/mL) respectively. (To convert C-reactive protein to nanomoles per liter, multiply by 9.524.)

A skin biopsy specimen revealed an interstitial dermal infiltrate of histiocytelike cells and lymphocytes coupled with segmented neutrophils and scant leukocytoclasis debris. Focal dermal edema was also noted. There was no evidence of vasculitis or vacuolar alteration at the dermoeidermal junction (Figure 1B). A colloidal iron stain showed an increase in dermal mucin. Immunoperoxidase staining revealed that the histiocytelike cells showed avid expression of myeloperoxidase and CD68, suggesting myeloid lineage (Figure 1B, inset). Results for CD20 stain were negative, indicating that B cells were absent. Direct immunofluorescence (DIF) findings were negative for evidence of immunoreactant deposition along the dermoepidermal junction or in the vicinity of blood vessels. How-
ever, the DIF slides did reveal nuclear staining with IgG of keratinocytes, consistent with the positive results of an antinuclear antibody test and the presence of anti–ribonucleoprotein antibodies, which this patient had.

Treatment was initiated with pulsed methylprednisolone and dapsone. The patient responded well to the corticosteroids and experienced a slow but almost complete response to dapsone after 6 months of therapy.

**CASE 2**

A previously healthy 5-year-old girl presented with an asymptomatic facial eruption of several months’ duration. It initially appeared on the ears and eventually spread to involve the nasal bridge and malar cheeks. She had no systemic symptoms. She had received multiple courses of antibiotics for presumed cellulitis, but the eruptions seemed to resolve and recur on average every 3 months regardless of antibiotic treatment.

Physical examination findings revealed well-defined erythematous plaques of the helix, both annular and linear in configuration. There were several arcuate edematous and erythematous plaques with overlying crust extending over the nasal bridge onto the malar cheeks. (Figure 2A).

Initial laboratory examination revealed a normal white blood cell count and normal hemoglobin and complement levels. Findings for anti–Sjögren syndrome antigen B anti-
Neutrophilic dermatoses are commonly seen in association with connective tissue disease, but they are infrequently reported as a manifestation of LE. Bullous SLE is a well-documented but rare neutrophilic dermatosis that manifests as a vesiculobullous eruption in the setting of SLE. Palisaded neutrophilic granulomatous dermatitis (PNGD), also known as interstitial granulomatous dermatitis with arthritis, represents an uncommon condition characterized by a nonbullous symmetric papular eruption and has been described as a manifestation of connective tissue disease, including LE. One case of PNGD in a pediatric patient with LE has been reported. In addition, isolated case reports of pyoderma gangrenosum in association with SLE are described in the literature.

Sweet syndrome and Sweet-like eruptions with histopathologic findings including a diffuse neutrophilic infiltrate and papillary dermal edema have also been described as uncommon manifestations of LE. However, many of the patients with LE who present with these neutrophil-rich eruptions do not meet the diagnostic criteria for classic Sweet syndrome. Gleason et al have postulated that this nonbullous neutrophilic dermatosis, or Sweet-like eruption, is an underrecognized variant of cutaneous LE.

Of interest, the histopathologic findings of all cases of neutrophilic dermatosis in the context of established LE suggested LE. Conversely, the biopsy specimens from patients with no history of LE did not reveal such

### Table. Neutrophilic and Histiocytic Disorders Within the Differential Diagnosis of Nonbullous Histiocytoid Neutrophilic Dermatitis

<table>
<thead>
<tr>
<th>Differential Diagnosis</th>
<th>Morphologic Characteristics and Anatomic Location</th>
<th>Associated Clinical and Laboratory Findings</th>
<th>Associated Disease</th>
<th>Histopathologic Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSS</td>
<td>Erythematous plaques and nodules with no clear distribution</td>
<td>Leukocytosis with neutrophilia, elevated ESR and CRP level</td>
<td>Malignant neoplasms (6 of 41), no associated autoimmune disease</td>
<td>Infiltrate of histiocytoid myeloid cells, confirmed by immunostaining</td>
</tr>
<tr>
<td>Nonbullous histiocytoid neutrophilic dermatitis (includes our 2 cases)</td>
<td>Erythematous and/or violaceous papules, plaques, nodules, and papulovesicles affecting the extremities, trunk, and face</td>
<td>Absent or mild associated systemic symptoms such as malaise and flulike symptoms, few with arthralgias and fever; criteria of Sweet syndrome not established</td>
<td>Remains to be established&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Infiltrate of histiocytoid myeloid cells, confirmed by immunostaining, accompanying neutrophils, nuclear dust, and leukocytoclastic debris</td>
</tr>
<tr>
<td>PNGD and IGDA</td>
<td>Nonbullous, symmetric papular eruption on extensor extremities (PNGD); symmetric erythematous plaques, papules, and linear cords, typically on extremities and trunk (IGDA)</td>
<td>Polyarthralgias and/or arthritis, some with myalgias</td>
<td>Strong association with autoimmune diseases including rheumatoid arthritis, SLE, and other connective tissue disorders associated with immune-complex deposition and autoimmune thyroiditis</td>
<td>Mixed infiltrate of histiocytes, neutrophils, and neutrophil fragments; histiocytes sometimes palisaded around foci rich in neutrophils or around a vasculitis nidus</td>
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<td>Interstitial granuloma annulare</td>
<td>Many clinical variants, often erythematous papules and annular plaques on extremities</td>
<td>None</td>
<td>Possible association with autoimmune thyroiditis, diabetes mellitus (controversial), and AIDS</td>
<td>Interstitial infiltrate of true histiocytes with lymphocytes and dermal mucin, sparse neutrophils, and eosinophils</td>
</tr>
</tbody>
</table>

Abbreviations: CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; HSS, histiocytoid Sweet syndrome; IGDA, interstitial granulomatous dermatitis with arthritis; PNGD, palisaded neutrophilic granulomatous dermatitis; SLE, systemic lupus erythematosus.

<sup>a</sup> Nonbullous histiocytoid neutrophilic dermatitis is the preferred term to describe the cases in the present report.

<sup>b</sup>To our knowledge, the cases in the present report are the first to suggest an association of histiocytoid neutrophilic dermatitis with lupus erythematosus.

body were positive, with the relative antibody titer index higher than 5 (normal, <1). Serologic findings were initially negative for anti–Sjögren syndrome antigen A antibody, antinuclear antibody, and anti–double-stranded DNA.

Histopathologic examination of a skin biopsy specimen from the right ear revealed an interstitial and diffuse dermal infiltrate, including segmented neutrophils, scant leukocytoclastic debris, lymphocytes, and monocytoid cells that resembled histiocytes (Figure 2B). There was a sparse lobular infiltrate of similar composition in the subjacent panniculus. No significant vacuolar alteration was seen. Findings from DIF staining were negative.

A presumed diagnosis of subacute cutaneous lupus erythematosus was made based on the clinical findings and positive Sjögren syndrome antigen B results. The patient was treated with hydroxychloroquine, and the skin lesions resolved. One year later, antinuclear antibody testing was repeated, and the titer was found to be 1:320 with a speckled pattern. Sjögren syndrome antigen A results were also positive at this time, with a value higher than 5 (normal, <1).
findings. Consistent with these reports, the biopsy specimens from our patient 1, who had prior SLE, showed an increase in dermal mucin and nuclear IgG staining on DIF, while the biopsy specimen from patient 2, who did not carry a diagnosis of LE at the time of presentation, did not show findings suggestive of LE.

One of the distinctive aspects of our 2 pediatric LE cases is that the histopathologic findings in both revealed not only interstitial and diffuse infiltrates of segmented neutrophils but also monocytoid cells resembling histiocytes. These histiocytelike cells were confirmed to be of myeloid lineage by positive staining for myeloperoxidase and CD68. In 2005, Requena et al. first coined the term histiocytoid Sweet syndrome, thus expanding the spectrum of histopathologic findings. They described 41 cases of cutaneous lesions consistent with Sweet syndrome in which biopsy specimens showed cutaneous infiltrates, including many histiocytelike cells that were confirmed to be of myeloid lineage by immunohistochemical analysis. Six of the 41 patients had associated malignant neoplasms. None of the patients were children. The course of the disease was similar to that of classic Sweet syndrome, with prompt resolution of the cutaneous lesions after administration of systemic corticosteroid therapy. Chow et al. more recently elaborated on this phenomenon as they reported 6 additional cases of inflammatory skin disease characterized by dermal and/or subcutaneous infiltrates of histiocytoid myeloid cells. Most of their cases did not fulfill the strict criteria for a diagnosis of classic Sweet syndrome, and therefore they referred to this spectrum of observations as “histiocytoid neutrophilic dermatoses and panniculitides.”

Although the histopathologic findings from both of our pediatric patients with LE were consistent with HSS as described by Requena et al., the criteria for a diagnosis of Sweet syndrome were not met by either of our patients. In addition, because the clinical picture of our patients was not typical of classic Sweet syndrome, we do not believe that Sweet-like represents the best descriptive term for these 2 cases. We have chosen the designation nonbullous histiocytoid neutrophilic dermatitis to generally describe the observed cases in this report, which we believe is both descriptive and accurate.

The presence of an interstitial infiltrate of histiocytoid myeloid cells in the setting of connective tissue disease raises a differential diagnosis that includes interstitial granulomatous dermatitis and interstitial granuloma annulare (Table). Intersitial granulomatous dermatitis differs histopathologically from HSS and nonbullous histiocytoid neutrophilic dermatitis in that it is characterized by a mixed infiltrate that includes both histiocytes and neutrophils, with histiocytes sometimes palisaded around foci rich in neutrophils or around a vascular nidus. The clinical morphologic characteristics of interstitial granulomatous dermatitis also differ from those observed in our patients. In interstitial granuloma annulare, the infiltrate is composed of authentic histiocytes rather than histiocytoid myeloid cells, and thus the findings are distinct from HSS nonbullous histiocytoid neutrophilic dermatitis, both histopathologically and immunohistochemically.

In conclusion, we report 2 pediatric cases of a nonbullous neutrophilic dermatitis, a variant of the recently described HSS, presenting as a cutaneous manifestation of LE. We believe that these cases further support the conclusions of Gleason et al. that nonbullous neutrophilic dermatitis should be considered a possible skin manifestation of LE. Moreover, the histopathologic findings of a histiocytoid neutrophilic dermatitis infiltrate may represent an important clue to the diagnosis of LE.

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