Isolated Benign Primary Cutaneous Plasmacytosis in Children

Two Illustrative Cases

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Background: Plasma cells are normally found in bone marrow and the intestinal tract. They appear in the skin in malignant conditions, autoimmune diseases, infection, and idiopathic and poorly understood disorders such as primary nodular amyloidosis. It is uncommon to find collections of plasma cells in the skin in the absence of these conditions.

Observations: We present 2 cases of cutaneous plasmacytosis, one in a white, female adolescent aged 15 years with an 11-year history of a solitary, asymptomatic, violaceous plaque on the left anterior tibia and the other in a white, male child aged 7 years with a 2-year history of a solitary erythematous plaque on the right anterior tibia. In both patients, infiltration of mature polyclonal plasma cells was confined to an area on the skin with papulonodules. There was no history of previous trauma, malignant conditions, autoimmune disease, or infection in either child.

Conclusion: Although incipient or occult systemic disease cannot be definitively ruled out, the course of these 2 individuals suggests that isolated primary cutaneous plasmacytosis in children is a benign chronic process with no adverse sequela.

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4 small, light-red papules in a linear pattern. Over the course of 11 years, the lesion gradually formed into a single, dark reddish-brown, violaceous plaque containing some papules and nodules. There was some recent enlargement that prompted the visit to a physician. Physical examination revealed an otherwise healthy adolescent girl with a solitary, dark reddish-brown, violaceous plaque measuring 4.5 × 1.9 cm in diameter.

The patient’s medical history included varicella at age 2 months, varicella zoster at age 10 years, and molluscum contagiosum at age 4 years. She also had a history of intestinal _Giardia lamblia_ infection at age 4 years, which occurred before the onset of the skin lesion. The patient is adopted, and her family history of plasmacytosis is unknown.

A 4-mm punch biopsy specimen of lesional skin was submitted for histologic review. Paraffin-embedded, hematoxylin-eosin–stained sections revealed a dense, nodular infiltrate within the upper reticular dermis composed of numerous plasma cells admixed with lymphocytes (Figure 2A and B). A grenz zone was present. A second biopsy specimen showed similar findings. Special immunoperoxidase stains in paraffin sections for immunoglobulin light chains showed a polyclonal process, with a κ to λ ratio of 3:1. Immunoglobulin light chain gene rearrangements also showed a polyclonal process. The histologic differential included primary cutaneous plasmacytosis, cutaneous lymphoid hyperplasia, and reactive plasmacytosis in response to infection, arthropod assault, or trauma. Findings from laboratory studies of serum protein and urine for gammapathy were normal. Her antinuclear antibody titer was 1:80, with a speckled pattern, and her IgE level was elevated at 0.277 U/µL (normal value, <0.115 U/µL), but this had been elevated in the past. A serologic test result was negative for syphilis. A _Borrelia_ serologic test was not performed because there was no history of travel, and Ohio, her home state, is not an endemic area for Lyme disease. Bone scans showed no abnormalities.

Currently, the patient continues to be completely asymptomatic. She is self-conscious about the cutaneous lesion and was treated with pulsed-dye laser for cosmetic purposes with some fading of the violaceous color.

**CASE 2**

A white male child aged 7 years presented with a 2-year history of a red area over the right anterior tibia. Physical examination revealed an otherwise healthy boy with
scaling violaceous papulonodules on the leg (Figure 1B).

His medical history was unremarkable. Results from laboratory studies (antinuclear antibody panel; *Crithidia* test; creatine kinase, aldolase, lactate dehydrogenase, and rapid plasma reagin level measurements; erythrocyte sedimentation rate; urinalysis; and complete blood cell count) were normal, except for a slightly depressed complement 4 level with normal complement 3. A *Borrelia* serologic test was not performed because there was no history of travel, and California, his home state, is not an endemic area for Lyme disease. Cultures of fresh tissue taken from one of the papulonodules were negative for mycobacteria and fungi.

A 4-mm punch biopsy specimen of lesional skin was submitted for histologic review. Paraffin-embedded, hematoxylin-eosin–stained sections revealed a dense, nodular infiltrate within the upper reticular dermis composed of numerous plasma cells admixed with lymphocytes (Figure 2C and D). A second biopsy specimen showed similar findings. Special immunoperoxidase stains in paraffin sections for immunoglobulin light chains and in situ hybridization for immunoglobulin light chains showed a polyclonal process. Immunohistochemical stains for spirochete organisms and Warthin-Starry stains for spirochetes were negative.

### COMMENT

The diagnosis of primary cutaneous plasmacytosis is made by a combination of histologic and clinical findings, a polyclonal plasma cell infiltrate, and studies with negative results for systemic disease such as malignant conditions, autoimmune diseases, or infections (Table). The differential diagnosis for these solitary lesions in both children included cutaneous lymphoma, lupus erythematosus, and nodular amyloidosis (Table), all of which were unlikely in the clinical setting. Benign cutaneous lymphoid hyperplasia with plasma cells was an alternative diagnosis. The chronicity of both lesions and prominence of plasma cells were more consistent with primary cutaneous plasmacytosis.

The etiology of idiopathic plasma cell infiltrates is unknown. One hypothesis is that interleukin 6, which drives B-cell differentiation, is increased in plasmacytosis. Therapy with intralesional corticosteroids has reduced interleukin 6 levels and produced improvement in a few individuals with plasmacytosis. The immune system of infants and children is different qualitatively and quantitatively from that in adults. For instance, benign disorders in which idiopathic cu-
taneous eosinophilic infiltrates occur in infants and children include incontinentia pigmenti, erythema toxicum neonatorum, Ofuji syndrome, and eosinophilic pustular folliculitis. Benign disorders in which idiopathic neutrophilic infiltrates occur in infants and children include transient neonatal pustular melanosis and palmoplantar eccrine hidradenitis. Primary cutaneous plasmacytosis may be another example of localized benign cutaneous infiltrates of immune cells in children that are uncommon in adults. It may be a childhood version of benign cutaneous lymphoid hyperplasia. In the 2 patients described herein, there was no identifiable inciting agent (trauma or local infection) to explain cutaneous eosinophilic infiltrates in the scalp and mucosa.

The course for primary cutaneous plasmacytosis is typically long-term. An aggressive clinical course has been observed in a small number of adults with multiple cutaneous plasma cell infiltrates and extracutaneous manifestations, for which the outcome has been fatal owing to lymphoid interstitial pneumonia, renal failure, or leukemia. We found 1 reported case of primary cutaneous plasmacytosis in a white female child aged 7 years with a 4-year history of polyclonal cutaneous plasma cell infiltrates in a 10-cm plaque on the right axillary and scapular region. The child had type 1 diabetes mellitus but no other systemic disease. Because of the small numbers of individuals with primary cutaneous plasmacytosis and the uncertainty about prognosis, an adult with unexplained multiple cutaneous plasma cell infiltrates should be carefully evaluated and followed up for progression and/or transformation of disease. Our 2 cases of isolated cutaneous plasmacytosis in children are illustrative because (1) the disorder is rare in children and in whites and (2) in both patients there were negative results from an extensive workup for malignant conditions, autoimmune diseases, or infections, causing concern and great expense for the patients and their families. The long course of the lesions and the otherwise good health of both children argue for an idiopathic benign condition in children that may represent a different entity than plasmacytosis in adults, requiring close follow-up and a conservative approach to therapy.

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Author Contributions: All authors had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Gilliam and Mostow. Acquisition of data: Gilliam, Mullen, Oviedo, Bhatnagar, Patton, Rodriguez-Soto, and Mostow. Analysis and interpretation of data: Gilliam, Smith, and Rodriguez-Soto. Drafting of the manuscript: Gilliam, Mullen, and Rodriguez-Soto. Critical revision of the manuscript for important intellectual content: Gilliam, Mullen, Bhatnagar, Smith, Patton, and Mostow. Obtained funding: Gilliam. Administrative, technical, and material support: Gilliam, Oviedo, Smith, and Rodriguez-Soto. Study supervision: Gilliam, Bhatnagar, and Mostow.

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Table. Plasma Cells in the Skin

<table>
<thead>
<tr>
<th>Category/Disease</th>
<th>Histologic Findings</th>
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<tbody>
<tr>
<td>Malignant condition</td>
<td>Large collection of monoclonal plasma cells</td>
</tr>
<tr>
<td>Cutaneous plasmacytoma</td>
<td>Plasma cells sprinkled around periphery of germinal center formations</td>
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<tr>
<td>Marginal zone B-cell lymphoma, follicle center B-cell lymphoma</td>
<td>Plasma cell infiltrates in association with epithelial malignant conditions; Kaposi sarcoma</td>
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<tr>
<td>Skin cancers</td>
<td>Sheets of polyclonal plasma cells in dense nodular infiltrates with emperipolisis</td>
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<tr>
<td>Autoimmune disease</td>
<td>Sheets of polyclonal plasma cells in dense nodular infiltrates with emperipolisis</td>
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<tr>
<td>Lupus erythematosus and scleroderma</td>
<td>Collections of polyclonal plasma cells in the upper dermis</td>
</tr>
<tr>
<td>Infection</td>
<td>Sheets of plasma cells in dense nodular infiltrates with emperipolisis</td>
</tr>
<tr>
<td>Bacterial, fungal, mycobacterial, treponemal</td>
<td>Sheets of polyclonal plasma cells in dense nodular infiltrates with emperipolisis</td>
</tr>
<tr>
<td>Other</td>
<td>Sheets of plasma cells in dense nodular infiltrates with emperipolisis</td>
</tr>
<tr>
<td>Inflammatory conditions</td>
<td>Sheets of plasma cells in dense nodular infiltrates with emperipolisis</td>
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<tr>
<td>Primary cutaneous plasmacytosis</td>
<td>Sheets of plasma cells in dense nodular infiltrates with emperipolisis</td>
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<tr>
<td>Nodular amyloidosis</td>
<td>Sheets of plasma cells in dense nodular infiltrates with emperipolisis</td>
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<tr>
<td>Cutaneous Rosai-Dorfman disease</td>
<td>Sheets of plasma cells in dense nodular infiltrates with emperipolisis</td>
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REFERENCES