Published in final edited form as:

Arch Dermatol. 2009 March ; 145(3): 299–302. doi:10.1001/archdermatol.2008.596.

Isolated Benign Primary Cutaneous Plasmacytosis in Children:

Two Illustrative Cases

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Abstract

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 sequelae.

Cutaneous plasmacytoma is an extramedullary collection of monoclonal plasma cells seen in myeloma, which typically occurs in bone. Extramedullary plasmacytomas are rare. They can be seen in the skin in multiple myeloma and in POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin abnormalities). Primary cutaneous plasmacytosis is a rare skin disorder that is thought to be a benign proliferation of mature plasma cells in the skin, producing solitary dark brown to purplish cutaneous plaques with papules and nodules. The diagnosis is based on histologic findings, the presence of a polyclonal population of plasma cells, and negative results from a diagnostic workup for systemic disease.^{1–3} The age of onset is mainly between 20 and 62 years. The disorder is

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Financial Disclosure: None reported.

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.

rare in children. Most of the cases reported are in adults of Japanese descent. Results from a study of 5 adults with cutaneous plasmacytosis were negative for human herpes virus 8.⁴

In adults, the cutaneous lesions can be associated with lymphadenopathy, hypergammaglobulinemia, and an increased serum interleukin 6 level.¹ Occasionally, adult cases are accompanied by anemia, fever, and interstitial pneumonia. Multiple lesions in adults may precede the onset of leukemia.¹ If an individual has extracutaneous manifestations along with the cutaneous lesion, the disorder is then termed *systemic plasmacytosis*, and an evaluation for an underlying systemic condition is indicated.⁵

We present 2 cases of isolated primary cutaneous plasmacytosis in children with infiltrates of mononuclear cells and many polyclonal plasma cells in plaques on the lower extremity. Neither patient had systemic disease, and the lesions have been present for 3 to 12 years. We suggest that the disorder represents a benign reactive process of unknown etiology in children.

REPORT OF CASES

CASE 1

A white, female adolescent aged 15 years presented for the evaluation of an asymptomatic lesion on the skin of the left anterior tibia that developed in childhood. The lesion initially began at age 4 years as 3 to 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 (Figure 1A) 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 gammopathy were normal. Her antinuclear antibody titer was 1:80, with a speckled pattern, and her IgE level was elevated at 0.277 U/ μ L (normal value, <0.115 U/ μ L), 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).^{1–3} 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.^{6–8} Therapy with intralesional corticosteroids has reduced interleukin 6 levels and produced improvement in a few individuals with plasmacytosis.⁹

The immune system of infants and children is different qualitatively and quantitatively from that in adults. For instance, benign disorders in which idiopathic cutaneous 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 lymphoid hyperplasia.

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.¹ 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.¹⁰ 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.

Acknowledgments

Funding/Support: Anita Gilliam is supported by grants R01 AR 049284 from the National Institutes of Health (NIH), National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) and P30-AR 39750 from the NIH NIAMS Case Skin Diseases Research Center.

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Figure 1. Clinical presentation. A, Case 1: A white female adolescent aged 15 years with a 12-year history of a linear dark reddish-brown, violaceous plaque containing some papules and nodules on the left anterior leg. B, Case 2: A white male child aged 7 years with a 2-year history of a cluster of dark reddish-brown papulonodules on the right anterior leg.

Figure 2.

Routine hematoxylin-eosin histopathologic examination of the lesions in Figure 1. Both biopsy specimens showed dense superficial infiltrates of mononuclear cells with numerous plasma cells in the papillary and upper reticular dermis (A and B, case 1; C and D, case 2). No atypia of the infiltrating cells was present. Results from ancillary studies showed a polyclonal process in both cases (A and C, original magnification $\times 10$; B and D, original magnification $\times 40$).

Table**Plasma Cells in the Skin**

Category/Disease	Histologic Findings
Malignant condition	
Cutaneous plasmacytoma	Large collection of monoclonal plasma cells
Marginal zone B-cell lymphoma, follicle center B-cell lymphoma	Plasma cells sprinkled around periphery of germinal center formations
Skin cancers	Plasma cell infiltrates in association with epithelial malignant conditions; Kaposi sarcoma
Autoimmune disease	
Lupus erythematosus and scleroderma	Sprinkling of plasma cells in predominantly lymphohistiocytic infiltrates
Infection	
Bacterial, fungal, mycobacterial, treponemal	Plasma cells and neutrophils, clues to cutaneous infection
Other	
Plasmacellularis vulvitis and balanitis (Zoon)	Sheets of polyclonal plasma cells in bandlike infiltrates under epithelium
Primary cutaneous plasmacytosis	Collections of polyclonal plasma cells in the upper dermis
Nodular amyloidosis	Nodules of cellular material and plasma cells around fat lobules, adnexa, and vessels
Cutaneous Rosai-Dorfman disease	Sheets of plasma cells in dense nodular infiltrates with emperipolesis
Inflammatory conditions	Plasma cells in infiltrates in the scalp and mucosa