Cutaneous Plasmacytosis Limited to the Extremities in a White Patient: An Unusual Clinical Picture

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Cutaneous plasmacytosis is an uncommon disease characterized by a cutaneous polyclonal plasma cell infiltrate usually associated with polyclonal hypergammaglobulinemia. It has predominantly been found in Japanese patients and it is rare in white patients. Clinically, this condition manifests as multiple red to dark brown skin lesions that mainly are located on the trunk. We report the case of a 66-year-old white woman who presented with reddish brown to violaceous macules and plaques restricted to the extremities. The histopathologic findings, laboratory data, and systemic studies led us to the diagnosis of cutaneous plasmacytosis.

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The presence of a plasma cell infiltrate in the skin may be secondary to a neoplastic or inflammatory process, or it may be isolated with a monoclonal or polyclonal cellular proliferation. Benign polyclonal plasma cell proliferation in the absence of underlying diseases represents a rare disorder known as plasmacytosis. Two variants have been described: (1) involvement restricted to the skin, or cutaneous plasmacytosis[1]; and (2) systemic plasmacytosis, defined as an infiltration of more than 2 organs (eg, skin, lymph nodes, bone marrow, lung).[2] However, differentiating between the 2 variants is sometimes complicated because systemic involvement could be occult in patients with cutaneous plasmacytosis.[3]

Cutaneous plasmacytosis has been described almost exclusively in Asian patients.[4-7] It clinically manifests as multiple red to dark brown macules, plaques, or nodules that often are associated with polyclonal hypergammaglobulinemia. The skin lesions can be distributed over the body, though the trunk is involved in almost all patients.[4,7] The most common manifestation of extracutaneous involvement is superficial lymphadenopathy, which occurs in approximately 60% of cases.[8] The majority of patients are asymptomatic, though those with systemic involvement (systemic plasmacytosis) may have constitutional symptoms such as fatigue, weight loss, and fever. Histopathologically, the cutaneous lesions are characterized by dense perivascular infiltrates of mature plasma cells without atypia in the dermis.[4-8]

We report a case of cutaneous plasmacytosis in a white patient with an unusual clinical picture.

Case Report

A 66-year-old white woman presented in April 2004 with a 2-year history of cutaneous lesions on the right upper limb and lower extremities. The lesions were asymptomatic and had slowly enlarged since then. She was in otherwise good health and was not taking any medications. There was no family history of similar eruptions. Dermatologic examination revealed large reddish brown to violaceous macules and plaques involving the extensor side of the right upper limb as well as the anterior and posterior aspects of both legs (Figure 1). No other lesions were present on the skin or mucosae. The superficial lymph nodes, liver, and spleen were not palpable.

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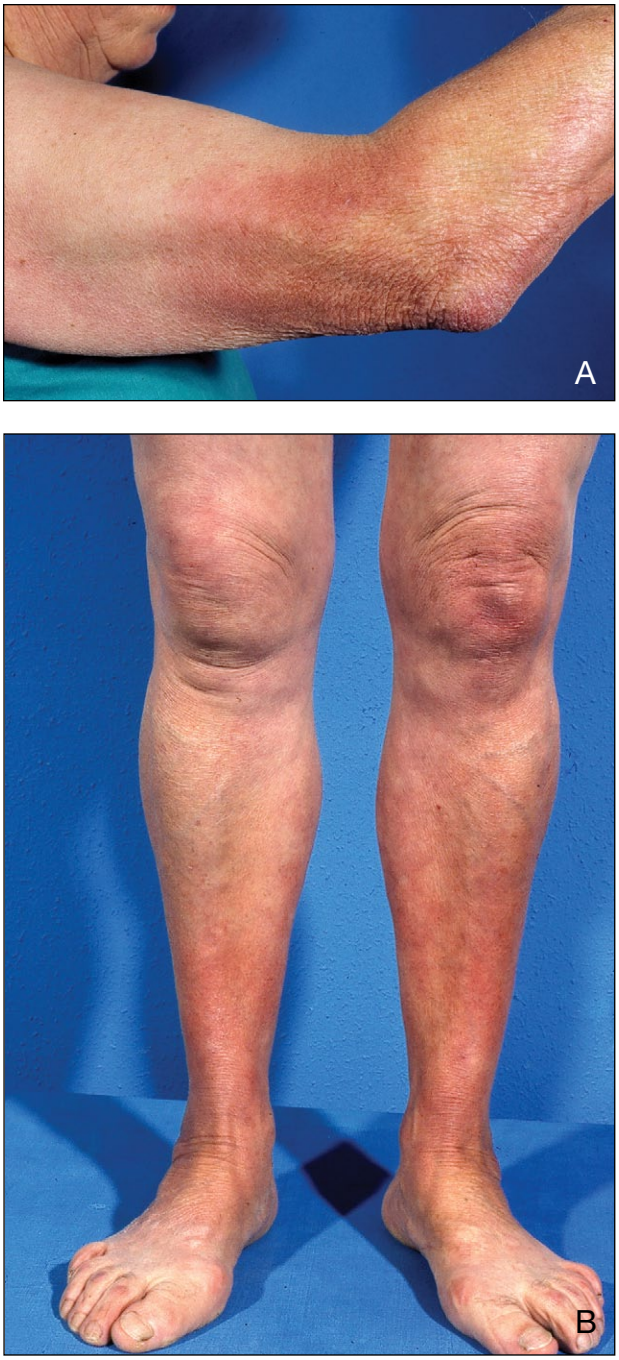

Figure 1. Large reddish brown to violaceous macules on the right upper limb (A). The lower extremities also were involved (B).

Two biopsy specimens from the right arm and right leg lesions were taken. The histopathologic results were similar. There were dense perivascular and periadnexal infiltrates in the superficial and deep dermis (Figure 2A) composed predominantly of mature plasma cells and small lymphocytes (Figure 2B). Immunohistochemical phenotyping of the infiltrate was performed. The cells were mostly plasma cells ($CD138^+$)(Figure 3) and showed polyclonal reactivity for κ and λ immunoglobulin light chains. The small lymphocytes were $CD20^+$. There also were scattered $CD5^+$ T lymphocytes. Immunohistochemical staining for the Lna-1 (latent nuclear antigen 1) antigen of human herpesvirus 8 was negative. Polymerase chain reaction analysis showed no evidence of a clonal immunoglobulin heavy chain gene rearrangement.

Laboratory investigations revealed no abnormalities in the complete blood cell count with differential; the erythrocyte sedimentation rate was slightly elevated at 39 mm/h (reference range, 0–20 mm/h). Chemical analyses showed hyperproteinemia (8.7 g/dL; reference range, 6.0–8.0 g/dL) with an increased γ-immunoglobulin level at 2 g/dL (reference range, 0.5–1.2 g/dL). Serum immunoelectrophoresis revealed polyclonal hypergammaglobulinemia with an IgG level of 2360 mg/dL (reference range, 734–1486 mg/dL), IgM of 326 mg/dL (reference range, 56–159 mg/dL), and IgA of 221 mg/dL (reference range, 49–401 mg/dL). Urinalysis was normal and repeated examinations did not reveal Bence Jones protein in the urine. Results of serologic tests for syphilis, hepatitis B and C viruses, human immunodeficiency viruses 1 and 2, antinuclear antibodies, and antinative DNA antibodies were all negative. Radiographs of the chest and whole body computed tomographic scans did not reveal systemic involvement. Bone radiography showed no signs of myeloma. Examination of bone marrow aspiration was normal with 2% mature plasma cells.

A diagnosis of primary cutaneous plasmacytosis was made. The patient initially was treated with topical corticosteroids and then with the topical calcineurin inhibitors tacrolimus ointment 0.1% and pimecrolimus cream 1%, though only a slight improvement was observed. The patient was followed over 4 years. The cutaneous lesions remained stable and she did not develop lymphadenopathy or other signs of systemic involvement. A new biopsy specimen (December 2007) of persistent lesions showed histopathologic features similar to the findings of the original biopsies. Immunohistochemical staining and immunoglobulin heavy chain polymerase chain reaction studies on the skin biopsy showed no evidence of clonality.

Comment

Our patient was diagnosed with primary cutaneous plasmacytosis based on the following: (1) polyclonal dermal hyperplasia of mature plasma cells (polyclonality was confirmed immunohistochemically because of the coexistence of both κ and λ immunoglobulin light

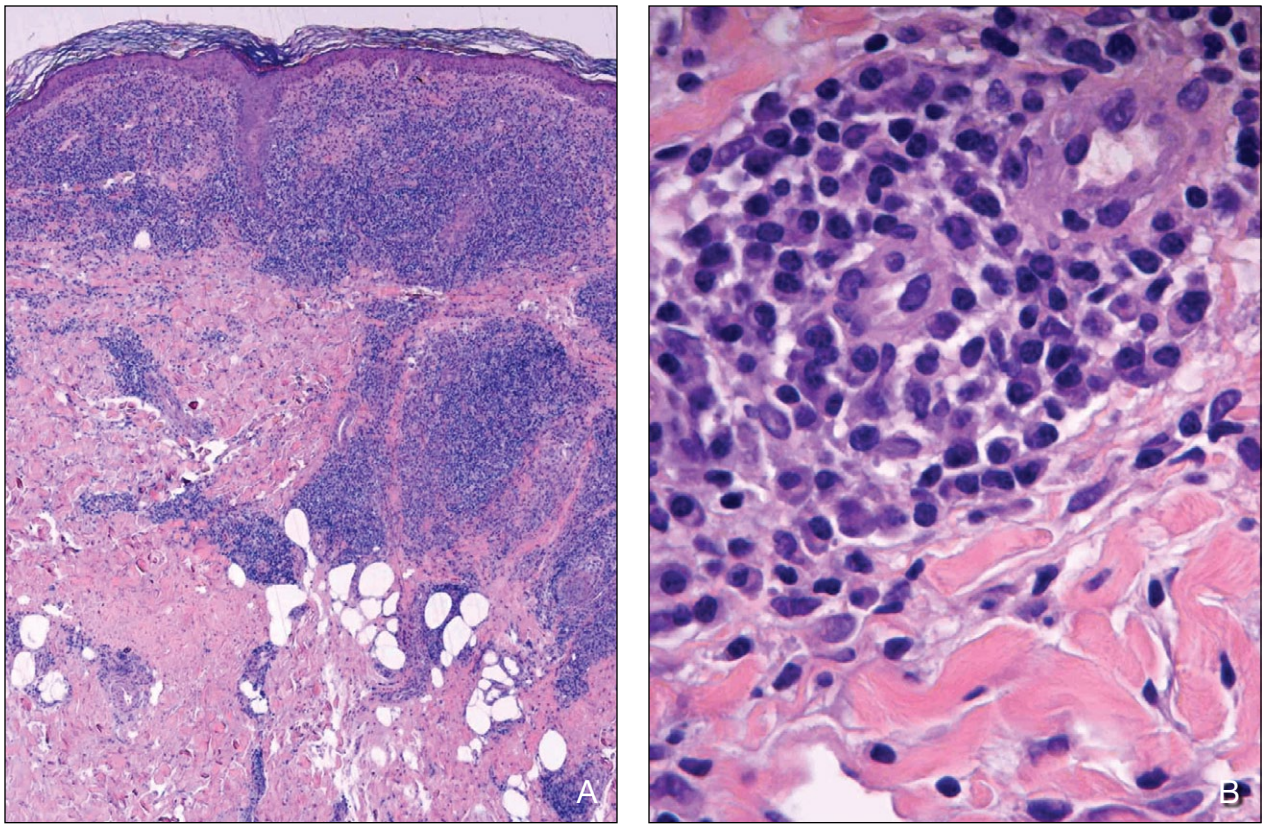

Figure 2. Dense perivascular and periadnexal infiltrate in the superficial and deep dermis (A)(H&E, original magnification ×25). High-power view revealed an infiltrate composed predominantly of mature plasma cells (B)(H&E, original magnification ×400).

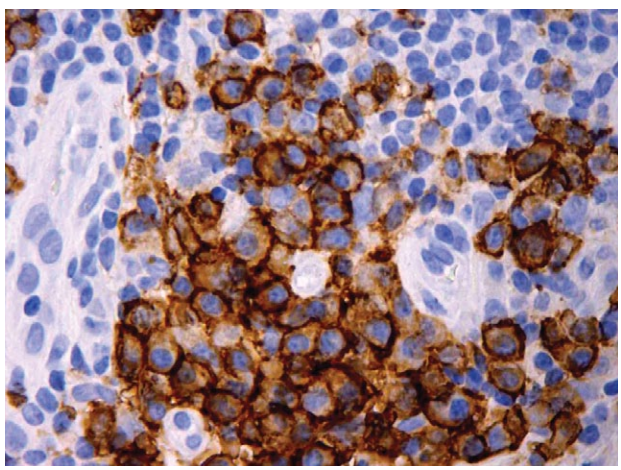

Figure 3. Immunohistochemical phenotype of the infiltrate showed a preponderance of mature plasma cells ($CD138^+$)(original magnification ×400).

chains); (2) polyclonal hypergammaglobulinemia; (3) absence of involvement of any other organ or system; and (4) exclusion of other diseases that may be associated with primary or secondary infiltration of plasmacytes in the skin.[4-9] The presence of mature plasma cells without mitotic figures, atypia, or light chain restriction; the normal findings in the examination of bone marrow aspirate; and the absence of either monoclonal paraprotein in blood and urine or Bence Jones protein excluded the diagnosis of multiple myeloma and cutaneous plasmacytoma. The lack of evidence for a clonal B-cell population in the original and persistent skin lesions excluded the diagnosis of a primary cutaneous marginal zone B-cell lymphoma. Other diseases causing dermal proliferation of plasma cells such as several chronic infections as well as chronic inflammatory and collagen vascular diseases were ruled out because in these conditions the plasma cell infiltration is a secondary feature and other clinical, laboratory, and microscopic findings are present.[5,9]

A review of the literature concerning this condition and a comparison of our case with those previously reported emphasize that cutaneous plasmacytosis has been described essentially in Japanese and other Asian patients, and it is rare in white patients; according to a PubMed search of articles indexed for MEDLINE using the term *cutaneous plasmacytosis*, only 7 well-documented cases of cutaneous plasmacytosis or systemic plasmacytosis with cutaneous involvement have been described in white

Cutaneous Plasmacytosis in White Patients

Reference	Sex/ Age, y	Location of Cutaneous Lesions	Hypergammaglobulinemia	Lymphadenopathy
López-Estebaranz et al[9]	M/40	Face, neck, trunk, upper limbs	+	+
Carey et al[10]	M/78	Neck, trunk, upper limbs	+	+
Cerottini et al[11]	M/90	Trunk, lower limbs	+	−
Aricò and Bongiorno[12]	F/7	Trunk	−	−
Martin et al[13]	M/55	Trunk	−	+
Hafner et al[14]	M/75	Face	−	−
Present case	F/66	Right upper limb, lower extremities	+	−

Abbreviations: M, male; +, present; −, not present; F, female.

patients to date including our patient (Table).[9-14] It may be worth noting that 3 of these cases (including ours) were described in Spain.[9,13] All of the patients except one[14] had an eruption on the trunk and some also had the face or limbs affected. Only 1 patient had isolated cutaneous plasmacytosis of the face.[14] In this context, our case is unique and distinctive because cutaneous plasmacytosis was restricted to the extremities.

The etiology of cutaneous and systemic plasmacytosis remains uncertain. It has been speculated that the condition may be a reactive plasmacytic disorder (ie, an overreaction to an unknown agent).[3,13] The predominance in a geographic area such as Asia suggests that a primary infectious cause could be responsible.[15] On the other hand, increased serum levels of IL-6, a cytokine that induces the terminal differentiation of activated B cells into immunoglobulin-producing cells, have been detected in patients with cutaneous plasmacytosis.[16,17] The evidence of a close link between plasma IL-6 level and disease activity suggests that this cytokine might play an important role in the pathogenesis of cutaneous plasmacytosis,[17] similar to its role in other plasmacytic disorders such as Castleman disease. However, a possible association with human herpesvirus 8, which is frequently detected in Castleman disease, has not been established in cutaneous plasmacytosis.[18]

The treatment of this disease is difficult. Several therapies have been used with variable degrees of success including topical, intralesional, and systemic corticosteroids; topical tacrolimus[19] and pimecrolimus[14]; topical psoralen plus UVA[20]; radiotherapy; and photodynamic therapy.[21]

In most cases, the clinical course of cutaneous plasmacytosis is chronic and benign with a favorable prognosis. Nevertheless, there have been a few cases of an aggressive clinical course with plasmacytosis showing systemic involvement.[2-5,7] Uhara et al[7] reported that serum immunoglobulin (IgG) levels greater than 5000 mg/dL and plasma cell counts into the bone marrow greater than 6.9% (reference range, 1.6%–4.5%) are parameters associated with a more severe clinical outcome. Although a benign course is characteristic, a long-term close follow-up of patients is mandatory because of the possibility of systemic progression or malignant transformation.

ADDENDUM

After the manuscript was accepted for publication, 3 cases of pure cutaneous plasmacytosis in white patients were reported: 2 in children (an adolescent

girl aged 15 years and a boy aged 7 years)[22] and 1 in a woman (aged 78 years).[23]

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