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Primary cutaneous plasmacytosis in a woman with previously undiagnosed celiac disease

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Abstract

Cutaneous plasmacytosis has <60 cases worldwide, typically characterized by multiple asymmetric facial and truncal cutaneous nodules and plaques. We describe the case of a 68-year-old woman with erythematous plaques on the feet who had a biopsy showing primary cutaneous plasmacytosis and subsequent workup revealing celiac disease. Our patient's clinical presentation of symmetric plaques on the dorsal feet is previously unreported. Additionally, plasmacytosis occurs predominantly in Japanese patients and men younger than 40. Cutaneous plasmacytosis is hypothesized to be reactive from overreaction to stimuli including trauma, infections, or malignancies. The origin of our patient's reactive process could be related to celiac disease or could be unknown. Plasmacytosis in bone marrow has been reported with celiac disease, but to our knowledge, this is the first report of cutaneous plasmacytosis in a patient with celiac disease.

Keywords: celiac disease, cutaneous plasmacytosis, plasmacytic infiltrate

Introduction

Primary cutaneous plasmacytosis represents a proliferation of benign plasma cells in the skin and is characterized clinically by cutaneous reddish-brown nodules and plaques on the face and trunk. It is rare, with <60 cases reported worldwide. Cases have predominantly been described in middle-aged Asian patients [1]. Cutaneous plasmacytosis has skin-confined disease and polyclonal hypergammaglobulinemia. Systemic plasmacytosis has extracutaneous plasmacytic infiltrates often involving lymph nodes and polyclonal hypergammaglobulinemia, with or without skin involvement. We present a 68-year-old White woman with erythematous plaques on the feet who had a biopsy showing primary cutaneous plasmacytosis and subsequent workup revealing celiac disease (CD).

Case Synopsis

A 68-year-old previously healthy woman presented to Columbia University Irving Medical Center with 8 months of a "band-like rash" on her dorsal feet. She denied travel, new footwear, or product exposure. Her local dermatologist performed patch testing which was negative and prescribed clobetasol 0.05% cream without improvement. A biopsy of the left dorsal foot was possibly indicative of a plasma cell dyscrasia, and she was referred to Columbia University Irving Medical Center for further evaluation.

Upon presentation to Columbia University Irving Medical Center, the patient had symmetric reddish-brown and erythematous plaques on dorsal feet and superficial inguinal lymphadenopathy (**Figure 1A**). Repeat biopsy demonstrated superficial and deep interstitial and perivascular plasmacytic infiltrates with associated fibroplasia that was not patterned. Plasma cells exhibited clock-face chromatin and eccentrically disposed nuclei (**Figure 1B**). There were concomitant germinal centers that exhibited somewhat expansile margins (**Figure 1C**).

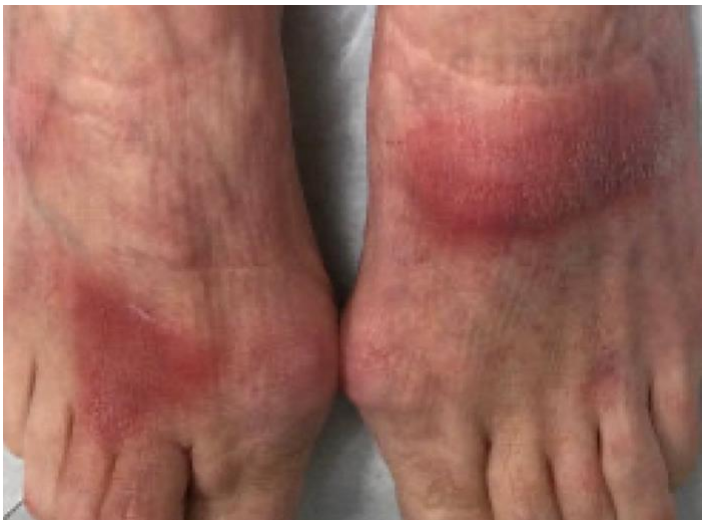

Figure 1A. *Primary cutaneous plasmacytosis. Clinical Image. Bilateral dorsal feet with erythematous plaques before radiation treatment.*

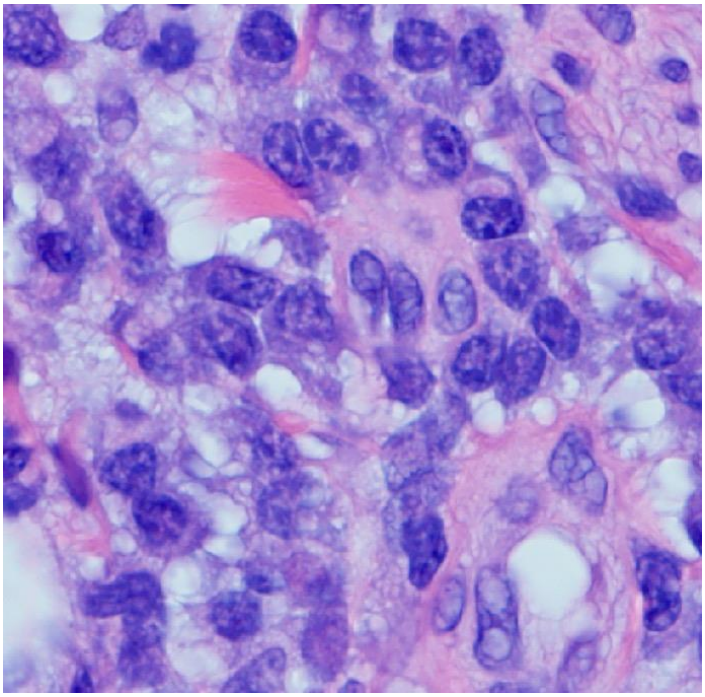

Figure 1B. *Hematoxylin and eosin stain 200x. The biopsy shows a dense well-differentiated plasmacytic infiltrate juxtaposed to a reactive germinal center, the latter highlighted by CD21 (not shown).*

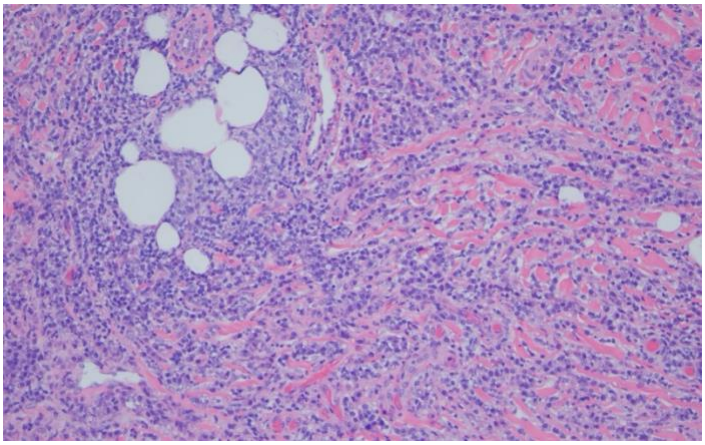

Figure 1C. *Hematoxylin and eosin stain 200x. The benign cytomorphology as characterized by the clock-face chromatin pattern in a round-to-oval nucleus in association with an eosinophilic golgi perinuclear Hof reflective of intracytoplasmic immunoglobulin is exemplified. There are no signs of plasma cell dysplasia*

Immunostaining was performed. The B-cell component was highlighted by *CD20*. Staining for *CD79a* highlighted the extensive plasmacytic infiltrate and positivity in nonplasmacytic B-cells. The germinal center foci were highlighted by B-cell lymphoma 6 but not B-cell lymphoma 2 and demonstrated high *Ki67* proliferation index. *CD21* stain highlighted follicular dendritic cell network and exhibited small foci of dendritic cell lysis. Plasma cells were highlighted by *CD138* and multiple myeloma oncogene 1. There was extensive staining for kappa and lambda with dominance of kappa whereby kappa:lambda ratio was slightly greater than 1:1 by RNA scope in situ hybridization (**Figure 1D,E**). Plasma cells were highlighted by immunoglobulin (Ig) G whereas IgG4 stain was minimally positive. A diagnosis of cutaneous plasmacytosis was rendered, whereby germinal center foci, although somewhat atypical, were not diagnostic of concurrent follicle center lymphoma.

Following pathological diagnosis of cutaneous plasmacytosis, the patient underwent workup for systemic disease with positron emission tomographic

scan showing hypermetabolic skin thickening of dorsal feet, representing lymphocytic infiltration with no other evidence for hypermetabolic malignancy. Bloodwork showed elevated erythrocyte sedimentation rate to 52, serum IgG to 1805 (normal 600-1540), kappa free light chain to 27.4 (normal 3.3-19.4), and lambda free light chain to 33.5 (normal 5.7-26.3). Her gliadin antibody IgA was elevated to 68.6 (normal <15) and tissue transglutaminase antibody IgA was elevated to 43.3 (normal <15). The patient subsequently underwent an intestinal biopsy, which led to her diagnosis of CD.

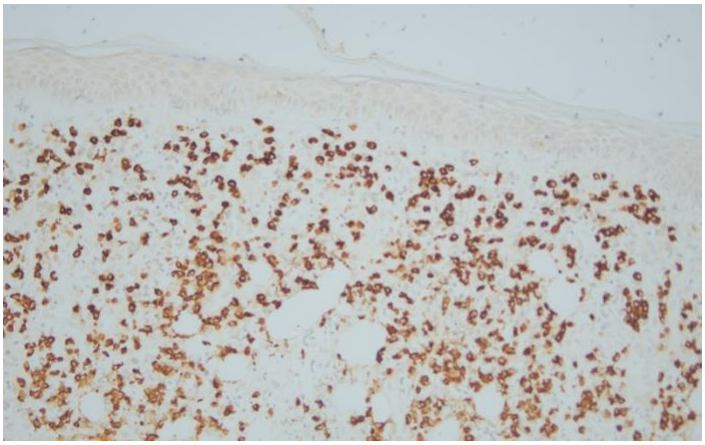

Figure 1D. *Immunohistochemistry. The plasma cells are polytypic; there is no evidence of light chain restriction. DAB Kappa 400x.*

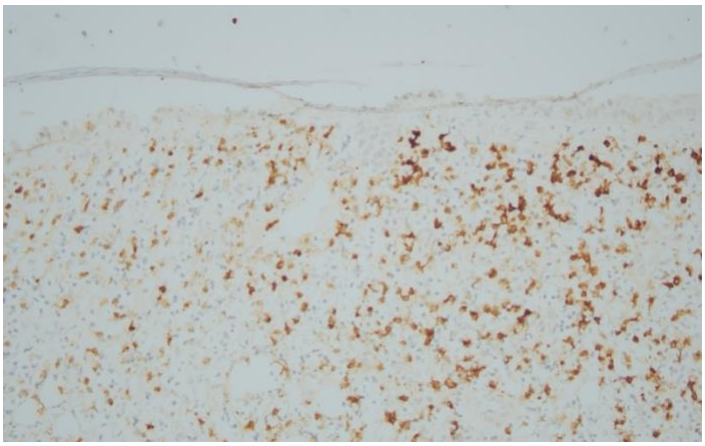

Figure 1E. *Illustrated is kappa and lambda. DAB Lambda 400x.*

Overall, her cutaneous lesions, lymphadenopathy, and polyclonal hypergammaglobulinemia, in the absence of other signs of systemic disease, was consistent with primary cutaneous plasmacytosis.

The patient received localized electron beam radiation with partial response and self-initiated a gluten-free diet. She declined additional therapy.

Case Discussion

Primary cutaneous plasmacytosis is characterized by skin infiltration by polyclonal plasma cells accompanied by hypergammaglobulinemia [2]. Cutaneous plasmacytosis does not have extracutaneous involvement, whereas patients with systemic plasmacytosis frequently have skin involvement and extracutaneous plasmacytic infiltrates involving liver, kidney, spleen, or most commonly, lymph nodes. Although our patient had limited superficial lymphadenopathy, additional workup was negative for systemic plasmacytosis. Given the clinical picture and biopsy-proven plasmacytosis limited to skin with polyclonal hypergammaglobulinemia, the diagnosis of primary cutaneous plasmacytosis was made.

Our patient's clinical presentation is unusual. Cutaneous plasmacytosis has been reported worldwide in <60 cases, and these are typically characterized by multiple asymmetric facial and truncal cutaneous nodules and plaques [3]. Our patient had symmetric plaques on dorsal feet, a previously unreported presentation. Additionally, plasmacytosis occurs predominantly in Japanese patients and men younger than 40 [1], but our patient was a 68-year-old White woman.

Histologically, cutaneous plasmacytosis is characterized by dense perivascular infiltration of polyclonal plasma cells, findings well-exemplified here. There can be reactive germinal centers. Biopsy findings may resemble cutaneous marginal-zone lymphoproliferative disorder. However, discriminating features include light chain restriction amidst plasma cells and characteristic infiltration of benign germinal centers by small monomorphic nonplasmacytic B-cells [4]. With polytypic plasmacytic infiltrate, IgG4-associated disease should be considered. In IgG4-associated disease,

IgG4 to IgG ratio should be greater than 40% with >200 IgG4+ plasma cells per individual high-power-field, an absent feature in our case. Another critical consideration is multicentric Castleman disease, which can exhibit morphology and reddish-brown cutaneous lesions similar to primary cutaneous and systemic plasmacytosis. However, the patient lacked constitutional symptoms, thrombocytopenia, hypercytokinemia including elevated interleukin 6, hepatomegaly, splenomegaly, and clinical features of anasarca seen in patients with thrombocytopenia, anasarca, fever, reticulin fibrosis and organomegaly syndrome [5,6]. Moreover, plasma cell variants of Castleman disease are associated with HIV or human herpesvirus-8. Finally, adenopathy and extensive skin patch overlying a plasmacytoma syndrome is also possible. However, the clinical presentation without an underlying tumor and pathology was more suggestive of cutaneous plasmacytosis.

The clinical course of cutaneous plasmacytosis is chronic, without spontaneous remission [1]. Although most often benign, some cases showed a protracted clinical course, demonstrating need for monitoring. Treatments include topical/intralesional/systemic corticosteroids, tacrolimus, psoralen plus ultraviolet A, radiotherapy, topical photodynamic therapy, and systemic chemotherapy [7,8,9].

Cutaneous plasmacytosis is hypothesized to be reactive from overreaction to stimuli including trauma, infections, or malignancies [4,10]. The stimuli is usually unknown. Here, the origin of the patient's reactive process could be related to CD, although this is speculative, and the link cannot be determined definitively. Plasmacytosis in bone marrow has been reported with CD, but to our knowledge this is the first report of cutaneous plasmacytosis in a patient diagnosed with CD [11]. Although the exact mechanism is unknown, it has been hypothesized that the proliferative response of intestinal mucosal B-cells to gluten-associated food antigen leads to generation of memory B-cells in secondary lymphoid tissues such as mesenteric lymph nodes and Peyer patches, which upon interacting with dendritic cells differentiate into plasmablasts that migrate into bone marrow to become plasma cells, eventuating in hypergammaglobulinemia. One could postulate that these antigenically specific plasma cells and plasmablastic precursors could migrate to skin and other organs based on cross-reactivity between gut-derived antigen and extraintestinal antigen [11]. However, it is also possible that the patient's cutaneous plasmacytosis and CD were merely coincidentally co-occurring.

Conclusion

We describe the unique presentation of a 68-year-old White woman with erythematous plaques on the feet who had a biopsy showing primary cutaneous plasmacytosis and subsequent workup revealing CD. Further investigation into rare presentations of cutaneous plasmacytosis may lead to better understanding of disease pathogenesis.

Potential conflicts of interest

The authors declare the following potential conflicts: Dr Geskin has served as an investigator for and/or received research support from Helsinn Group, J&J, Mallinckrodt, Kyowa Kirin, Soligenix, Innate, Incyte, Trillium, Merck, BMS, and Stratpharma; on the speakers' bureau for Mallinckrodt and Recordati; and on the scientific advisory board for SciTech and Celsyntec.

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