Plasma cell myeloma with immature plasma cells in the skin arising within the areas of chronic stasis dermatitis

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INTRODUCTION

Skin involvement in plasma cell myeloma (PCM) occurs in <1% of cases and often portends a poor prognosis.[1] We present an unusual case of skin involvement in PCM, with immature neoplastic plasma cells arising within the areas of chronic lower-extremity venous stasis dermatitis.

CASE REPORT

A 69-year-old-man with a history of PCM presented with a chief complaint of "firm bumps on the legs." His medical history was remarkable for chronic, bilateral, lower-extremity edema, hypertension, diabetes mellitus type II, right common femoral vein stent placement, and PCM (IgA kappa subtype). His PCM was diagnosed 5 months prior to his presentation to the dermatology department. His initial bone marrow biopsy was consistent with plasma cell leukemia involving 90% of the bone marrow and 36% circulating plasma cells in the peripheral blood. Positron emission tomography/computed tomography at baseline showed no fluorodeoxyglucose-avid bone lesions. He was initially treated with hyperfractionated cyclophosphamide, carfilzomib, and dexamethasone, and he achieved a response with near normalization of his serum IgA level. Four months later, he was noted to have an increase in his serum IgA level, with a subsequent bone marrow biopsy with persistent PCM. He was then admitted for chemomobilization with cyclophosphamide-based therapy, followed by autologous stem cell collection with plans for an autologous stem cell transplant following a preparative regimen of busulfan and melphalan.

Abbreviations used:

CD: cluster of differentiation
PCM: plasma cell myeloma

On presentation, he had 2+ lower-extremity edema bilaterally with hyperpigmented patches on the bilateral aspects of the shins and inner ankles. Within the hyperpigmented patches were many firm, pink, 0.5-1−cm papules (Fig 1). A biopsy of the papules showed a compact stratum corneum and dense, diffuse, superficial, and deep dermal infiltrates of atypical immature plasma cells (Fig 2), which stained positively for cluster of differentiation (CD)138 and CD43. In situ hybridization studies revealed monoclonal kappa-positive cells (Fig 2). Deeper portions of the biopsy showed lipomembranous changes.

DISCUSSION

Plasma cell neoplasms of the skin can present as solitary, extraosseous lesions (plasmacytomas) or lesions secondary to PCM. The secondary lesions are typically due to a direct extension from an underlying focal bony involvement and rarely spread through the blood and lymphatics. Although most secondary cutaneous plasmacytomas occur after an established diagnosis, they may be the

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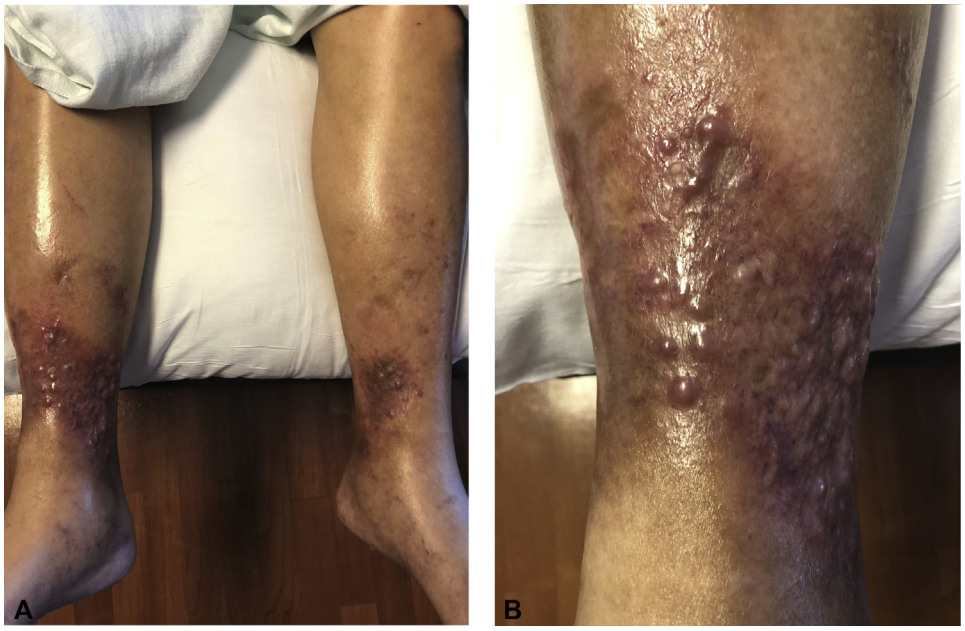

Fig 1. **A**, Bilateral aspects of the lower legs with many firm pink papules within hyperpigmented patches. **B**, Lower portion of the right leg with many firm pink papules within hyperpigmented patches.

initial manifestation of an underlying disease. The skin and soft tissue make up 14%-30% of plasma cell neoplasms and are more associated with IgA- and IgD-producing myelomas, which is consistent with this patient's increase in the serum IgA level.[1,2] The appearance and location of the lesions may vary, but they are often violaceous nodules—few in number—on the trunk. This patient's cutaneous findings, immunohistochemical studies, underlying PCM, and initial positron emission tomography/computed tomography scan ruling out skeletal lesions pointed toward a hematogenous spread of PCM.

The patient's lesions were confined to areas of pre-existing, long-standing hyperpigmentation caused by chronic venous stasis dermatitis on the lower portion of both legs.[3] To our knowledge, this is the first report on PCM with immature plasma cells occurring in the areas of stasis dermatitis. Although the hyperpigmentation could have resulted from an alternative source of inflammation or even from the atypical plasma cell infiltrate, we believe that it is better explained by venous stasis dermatitis. The distribution of the hyperpigmentation, previous history of hypertension and lower-extremity swelling, and lipomembranous changes seen in the biopsy all support the diagnosis of venous stasis dermatitis. This unique presentation could be linked to the pathophysiology of chronic venous insufficiency, in which damaged valves in the veins are incompetent, building up pressure and fluid in the lower extremities. The pooled fluid can leak into the skin, causing chronic inflammation. Previous reports have suggested that high-dose chemotherapy may select for tumor cell subclones that express chemokine receptor type 4, which responds to inflammatory cytokines released from a traumatized tissue.[4] It is possible that this patient's long-established history of chronic venous insufficiency and stasis dermatitis provided a cytokine environment that potentiated circulating plasma cells to localize to the skin. Alternatively, previous reports have asserted a pathophysiologic mechanism of scar tissue acting as an attachment for tumor cells.[5] Some develop scarring in stasis dermatitis, although it is difficult to ascertain if that is the case in this patient. Scar tissue can also alter the lymphatics and blood vessels, providing a conduit for skin involvement by malignant plasma cells.[5]

The tissue or bone-marrow biopsies of plasmacytomas show a dense infiltration of plasma cells. Histologic findings can be classified as well differentiated (grade I), moderately differentiated (grade II), or poorly differentiated based on plasma cell morphology.[6] It is impossible to differentiate primary plasmacytomas from systemic plasmacytomas based on the histology alone as they stain for the same biologic markers. Immunohistochemically, plasma cell neoplasms exhibit the expression of CD79a and CD138 and variable expression of VS38c and CD43, which is consistent with our

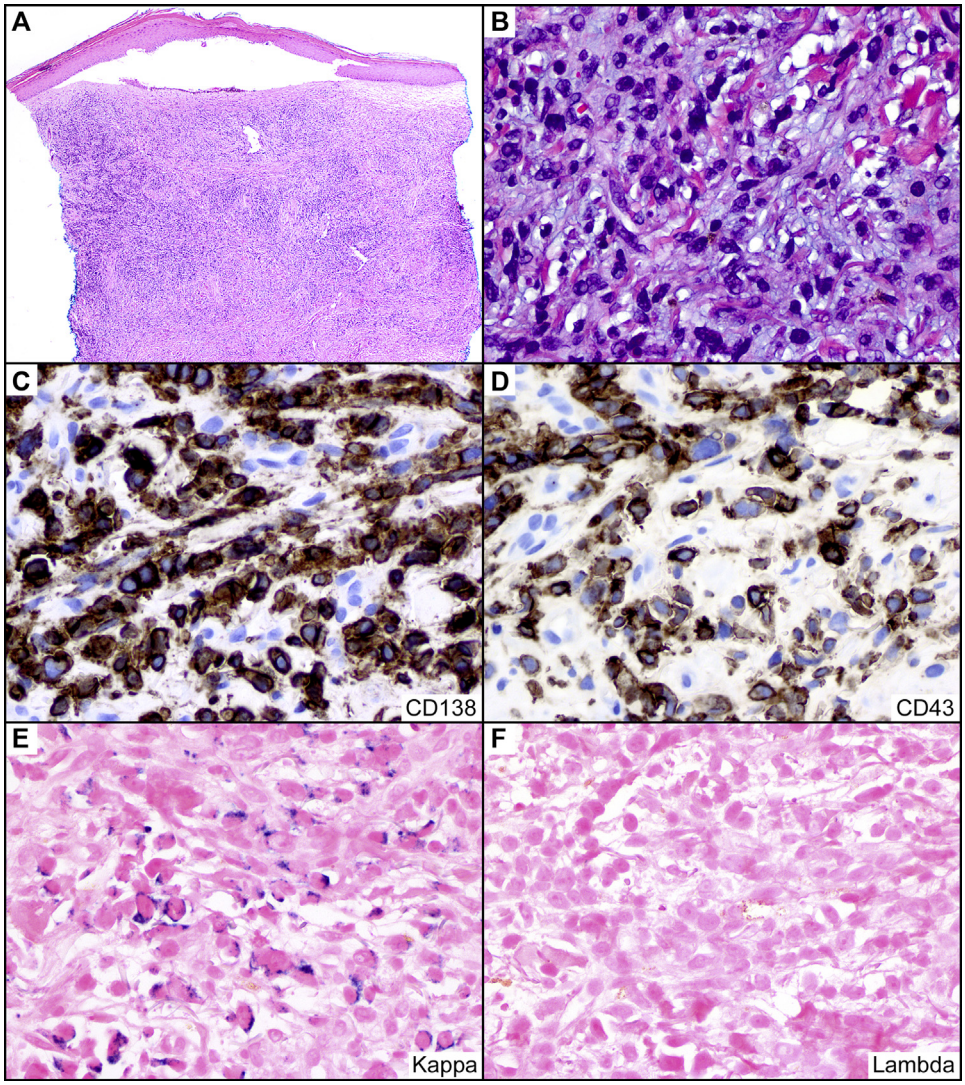

Fig 2. A, Skin involvement by PCM with dense, diffuse infiltrate of atypical plasma cells (hematoxylin-eosin stain; original magnification: ×20). **B**, PCM composed of immature tumor cells exhibiting atypical, hyperchromatic, irregular nuclei (Hematoxylin-eosin stain; original magnification: ×400). **C-D**, PCM tumor cells were positive for CD138 and CD43 (Immunohistochemistry, anti-CD138; original magnification: ×400; anti-CD43; original magnification: ×400). **E-F**, Kappa and lambda in situ hybridization studies revealed a monoclonal population of kappa-positive cells (in situ hybridization, anti-kappa; original magnification: ×400; anti-lambda; original magnification: ×400.) *CD*, Cluster of differentiation; *PCM*, plasma cell myeloma.

patient's presentation and immunohistochemical studies.[7]

For primary solitary plasmacytomas, radiation therapy or surgery can be beneficial. For systemic disease, treatment is aimed at the underlying PCM. This patient underwent stem cell collection with plans for an autologous stem cell transplant once the collection was completed. Unfortunately, the prognosis for those with cutaneous involvement of multiple myeloma is poor—the mean survival time after the development of cutaneous plasmacytomas was only 8.5 months in a previous study.[3] Dermatologists and oncologists should be aware of this unusual presentation to provide appropriate counseling and treatment, given the short mean survival time.

Cutaneous plasma cell neoplasms are a rare consequence of PCM, and their appearance bodes a poor prognosis. This unique presentation of PCM appearing within the areas of stasis dermatitis highlights the variability of cutaneous presentations and suggests that the pathophysiology of stasis dermatitis may have contributed to the developing

skin involvement by PCM. Dermatologists have a unique role in identifying cutaneous plasma cell neoplasms, which is exceptionally important for patients in whom these neoplasms may present as the first visible signs of the underlying PCM.

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