JAMA Dermatology Clinicopathological Challenge

Asymptomatic Green-Gray Nodules on the Chest

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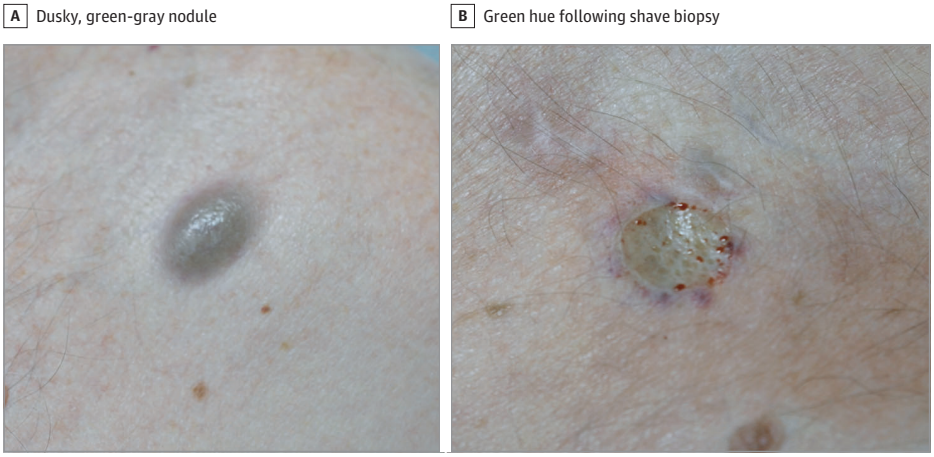

Figure 1. A, Representative dusky, green-gray nodule located on the upper chest. B, A prominent green hue is present at the base of a lesion following shave biopsy.

A man in his 60s presented for evaluation of asymptomatic skin lesions on the chest that had been stable since onset 4 months prior. His medical history was significant for hyperlipidemia, familial polyposis, and acute myelogenous leukemia (AML) for which he had undergone an allogenic hematopoietic stem cell transplant 13 months earlier. Cutaneous examination revealed green-gray nodules and plaques on the left and right upper chest (**Figure 1**). Bilateral cervical, axillary, and inguinal lymph node chains were negative for adenopathy. The patient had not attempted measures to alleviate the nodules and denied experiencing exacerbating factors or pain. Biopsies of the skin lesions were performed.

WHAT IS YOUR DIAGNOSIS?

A. Merkel cell carcinoma

B. Chloroma

C. Blastic plasmacytoid dendritic cell neoplasm

D. Histiocytoid Sweet syndrome

Diagnosis

B. Chloroma

Discussion

Histopathologic findings included a diffuse mononuclear infiltrate with expression of lysozyme and myeloperoxidase (MPO) (**Figure 2**). Additional immunohistochemical staining demonstrated expression of CD34 and was negative for CD4, CD56, and CD123. A myeloid neoplasm sequencing panel was performed on the tissue sample and demonstrated mutations in *DNMT3A*, *IDH1*, *NPM1* (type A), *NRAS*, and *STAG2*, identical to findings noted from the patient's bone marrow biopsy specimen on initial diagnosis. These findings established a diagnosis of chloroma, also known as myeloid sarcoma.

Myeloid sarcoma results from extramedullary leukemic blasts. When occurring in the skin, it is also known as chloroma because of the green hue imparted by diffuse expression of MPO.[1] Myeloid sarcoma presents in patients with a history of AML or myelodysplastic

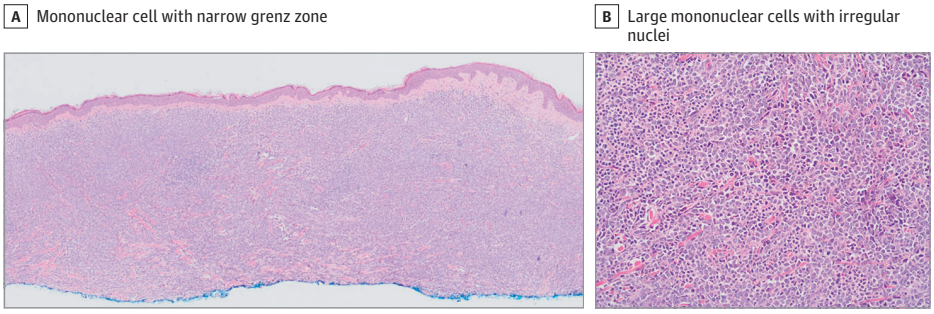

Figure 2. A, Diffuse infiltrate of mononuclear cells with a narrow grenz zone (hematoxylin-eosin, original magnification ×20). B, High-power magnification demonstrates large mononuclear cells with irregular nuclei (hematoxylin-eosin, original magnification ×400).

syndromes or during the blast phase of chronic myeloid leukemia.[2] On rare occasion, skin lesions may be present without prior history of systemic disease or bone marrow involvement.[1] The lesions may occur throughout the body, including the skin and soft tissue.[1] Studies have reported that up to 9% of patients with AML have at least 1 site of myeloid sarcoma.[3] Additionally, there appears to be an association between allogenic hematopoietic stem cell transplant (HCT) and an increased incidence of extramedullary relapse.[4] Extramedullary relapse following HCT most commonly occurs within 12 months to 5 years of transplant.[5]

Histopathologic specimens consist of myeloid cells with granulocytic or monocytic differentiation that infiltrate the dermis and surrounding soft tissue to varying degrees.[3] Immunohistochemical analysis typically demonstrates expression of lysozyme, MPO, and CD34.[6] Additional markers that may be expressed include CD117, CD43, and CD68.[6]

The treatment of myeloid sarcoma depends on an individual's concomitant AML and HCT status and consists of one or more of the following: localized radiotherapy, systemic chemotherapy, donor lymphocyte infusions, and a second HCT.[5] Because the treatment approach depends on the location and extent of disease relapse and whether bone marrow is involved, a diagnosis of myeloid sarcoma should prompt restaging with imaging studies and bone marrow biopsy.[1] Skin-directed radiotherapy may be considered when cutaneous lesions are refractory to chemotherapy or HCT, because control of myeloid sarcoma is paramount to survival.[1] Blast cells contained within the lesions may reseed bone marrow and result in relapse of systemic disease, which contributes to greater morbidity and mortality.[1]

The differential diagnosis for the presented case includes other malignant hematolymphoid infiltrates, particularly blastic plasmacytoid dendritic cell neoplasm (BPDCN). Sweet syndrome and solid tumors characterized by atypical basophilic cells in the dermis, such as Merkel cell carcinoma, are also considerations. A myeloid-derived malignancy of dendritic cells, BPDCN may present with one to several nodular lesions to diffuse plaques on the face, limbs, and trunk, with a characteristic red-brown color and associated lymphadenopathy.[7] Morphologically, the infiltrate of BPDCN consists of mononuclear plasmacytoid cells that may resemble myeloid sarcoma; neoplastic cells express CD4, CD56, and CD123 and, unlike AML, are negative for MPO and lysozyme.[7] Sweet syndrome, also known as acute febrile neutrophilic dermatosis, is characterized by the abrupt onset of multiple tender, edematous papules and nodules with violaceous color accompanied by fever and frequently occurs in the setting of AML. The most common sites of involvement are the upper extremities and trunk, and the lesions are often tender or associated with a burning sensation.[8] Histologic features include a dense infiltrate of neutrophils in the superficial to deep dermis, with prominent papillary dermal edema.[8] In the histiocytoid variant of Sweet syndrome, the dermal infiltrate is characterized by large epithelioid cells resembling histiocytes that represent immature neutrophils.[9] Cutaneous findings in Merkel cell carcinoma include firm, nontender, pink to bluish nodules that present with rapid growth in sun-exposed areas.[10] Histologic analysis demonstrates strands and nests of basophilic nuclei with dispersed chromatin with immunohistochemical expression that includes epithelial markers such as pan-cytokeratin and CK20 in a perinuclear dot pattern and neuroendocrine markers such as chromogranin and synaptophysin.[10]

Myeloid sarcoma, also known as chloroma, involves extramedullary leukemic blasts that occur in individuals with a history of myelodysplastic syndrome, AML, or chronic myeloid leukemia and represents disease relapse. Cutaneous lesions may have a distinctive green-gray hue, imparted by the presence of MPO, which may raise clinical suspicion of the diagnosis. A diagnosis of myeloid sarcoma should prompt restaging with imaging studies and bone marrow biopsy to determine location and extent of disease relapse, which will guide the therapeutic approach.

ARTICLE INFORMATION

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