Cutaneous granulocytic sarcoma and Koebner phenomenon in a context of myelodysplastic syndrome

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INTRODUCTION

Granulocytic sarcoma (GS) is also known as *myeloid sarcoma* or *chloroma* because of its green hue caused by myeloperoxidase (MPO). This disease involves the localization of myeloblasts or immature myeloid cells to an extramedullary site. GS has been described at numerous anatomic sites, but cutaneous GS (CGS) is uncommon. Although CGS is rare, it is clearly associated with myeloid disorders, such as acute myeloid leukemia, myeloproliferative neoplasms, and myelodysplastic syndromes (MDSs). CGS may herald acute transformation, and it is associated with a poor prognosis.[1-3] However, the mechanism underlying the specific migration of myeloblasts to the skin remains uncertain. In 2008, Kawakami et al[4] presumed that transforming growth factor—beta 1 (TGF-β1) released by hematopoietic cells within the cutaneous extramedullary hematopoiesis could play a role in the onset of such skin lesions.[4]

We report a case of a patient with MDS presenting with 2 CGSs that developed consecutively at traumatized skin sites, suggestive of the Koebner phenomenon (KP). Immunohistochemical (IHC) analysis confirmed the expression of TGF-β1 on myeloblasts and fibroblasts that had infiltrated the CGSs but also showed the expression of its specific receptor (TGF-β1R), suggesting a role for this cytokine in cutaneous tropism and the pathogenesis of the KP.

Abbreviations used:

CGS:	cutaneous granulocytic sarcoma
GS:	granulocytic sarcoma
IHC:	immunohistochemistry
KP:	Koebner phenomenon
MDS:	myelodysplastic syndrome
MPO:	myeloperoxidase
PG:	pyoderma gangrenosum
TGF-β1:	transforming growth factor-beta 1
TGF-β1R:	transforming growth factor-beta 1 receptor

CASE REPORT

A 77-year-old man was admitted to our dermatology department with fevers and a 1-month history of a hematoma on the left thigh, evolving in an indurated necrotizing ulcerative plaque (Fig 1). MDS was diagnosed 18 months prior (refractory anemia with excess blasts I, normal molecular cytogenetics, trisomy 8 in the tumoral clone), which was treated with norethandrolone. A complete blood count on admission showed hemoglobin at 8.2 g/dL (normal ranges, 12.4-14.9 g/dL), platelet level at 28 G/L (normal ranges, 150-400 G/L), a leukocytosis count at 5.8 10^3/mm^3 (normal ranges, 4-10.10^3/mm^3) but with circulating blast cells, and a C-reactive protein level of 117 mg/L (normal, <6 mg/mL). Bone marrow analysis confirmed qualitative abnormalities of the

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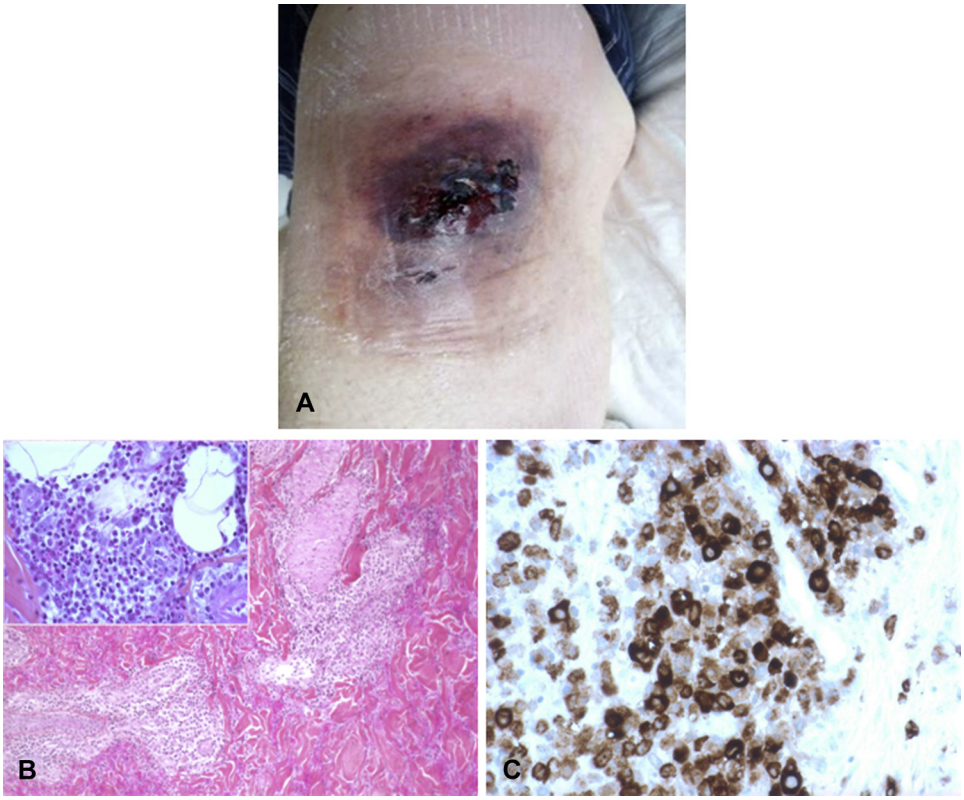

Fig 1. A, Lesions on the left thigh at the site of the hematoma. **B**, Biopsy of the infiltrated necrotizing ulcerative plaque derived from the hematoma showed infiltration of hematopoietic cells within the GS. (Hematoxylin-eosin stain; original magnification ×100; inset, ×400.) **C**, IHC for MPO (1/300) showed the presence of numerous myeloblasts. (Original magnification, ×400).

trilineage, with myeloblasts constituting 7% of the nucleated bone marrow cells.

A culture of the lesion found numerous *Staphylococcus aureus* colonies, but no other organisms were identified. Histopathologic examination of skin biopsies found a dense infiltration of blast cells with round, not lobulated nuclei and scant cytoplasm. The phenotype of myeloblasts was characterized by various immunostains ($CD45^+$, MPO^+, $MiB1^+$, $CD15^+$, $CD99^+$, and $CD68^+$ and $CD34^-$, $CD33^-$, $CD4^-$, and $CD117^-$) allowing the diagnosis of CGS (Fig 1, *B* and *C*). A supplementary IHC analysis found that TGF-ß1 and its specific receptor, TGF-ß1R, were highly expressed in immature hematopoietic cells and dermal fibroblasts within the GS (Fig 2, *A* and *B*). The cutaneous lesion had completely resolved 3 weeks after the resolution of fevers, and the blood count normalized after treatment with antibiotics (cloxacillin for 18 days, 1 g 3 times per day). Skin biopsy results confirmed the complete regression of the GS.

Several days later, complete excision of a squamous cell carcinoma located on the cheek was performed. No myeloblasts were observed by histologic examination of this lesion. However, during the wound healing process (10 days after surgery), a second GS was identified as a purple plaque that had infiltrated and ulcerated around the surgical wound (myeloblasts identified as $CD45^+$, MPO^+, $MiB1^+$, and $CD34^-$; Fig 3). Similar to the first GS detected, expression of TGF-ß1 and TGF-ß1R was observed on myeloblasts and dermal fibroblasts within the GS (Fig 2, *C* and *D*). Complete and spontaneous regression of the lesion was observed 3 weeks later.

Eighteen months later, the patient was still alive and had received chemotherapy treatment, which had been initiated after his GS episodes (3 rounds of cytarabine/mitoxantrone) but did not cure his MDS. Cutaneous surgery was avoided, and no skin lesions were observed. No additional GS was diagnosed.

DISCUSSION

We describe 2 episodes of CGS that occurred after trauma (hematoma and cutaneous surgery) in the context of MDS. The differential diagnosis included pyoderma gangrenosum (PG) and aleukemic leukemia cutis. PG, the most common