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Diffuse eruptive ulcerated plaques

Shamir Geller, MD^{1,*}, Melissa Pulitzer, MD², and Patricia L. Myskowski, MD¹

¹Dermatology Service, Department of Medicine, Memorial Sloan-Kettering Cancer Center and Weill Cornell Medicine, New York, NY, USA

²Department of Pathology, Memorial Sloan-Kettering Cancer Center and Weill Cornell Medicine, New York, NY, USA

Keywords

cutaneous lymphoma; cytotoxic; aggressive epidermotropic cytotoxic CD8+ T-cell lymphoma

Clinical Findings

A woman in her 90s presented to our clinic with pruritic widespread ulcerated papules and plaques that had rapidly developed within the previous ten days. A 3-year history of a pruritic eczematous rash was reported. The patient complained of fatigue and a 20 lb weight loss within the past year. No fevers, chills or night sweats were noted. Her medical history was significant for asthma and chronic back pain. Medications included ventolin and lorazepam. She had taken no new medication prior to the onset of rash. Physical examination revealed numerous erythematous papules and plaques with central necrosis on her neck, back, breasts, arms, abdomen and thighs (Figure 1). No patches or tumors were seen. No involvement of the oral mucosa was noticed. Palpation revealed no evidence of adenopathy. Two punch biopsies were performed on the patient's upper back skin.

Histopathological and Other Findings

Two punch biopsies were performed on the patient's upper back skin (Figure 2a). Histological examination demonstrated dermal and epidermal infiltration by atypical lymphocytes that were strongly and diffusely positive for CD3, CD7, CD8 (Figure 2b) and TIA-1, while negative for CD4, CD30, CD20, CD56, CD25, EBER-*ish*. Tumor cells were T-cell receptor chain (TCR) $\alpha\beta/\gamma\delta$ double-negative with absent TCR- β and TCR- δ immunohistochemical staining. Polymerase chain reaction (PCR) showed the presence of monoclonal TCR-gamma gene rearrangements in the skin. Flow cytometric analysis identified an abnormal T-cell population with normal expression of CD3 and CD7, loss of CD2, dim CD8 and CD45, and no CD4, CD56 or CD30. No abnormal mature B- or T-cell

*Corresponding author: Shamir Geller, MD, Dermatology Service, Memorial Sloan Kettering Cancer Center, 16 East 60th Street, New York, NY 10022, USA, Tel: (646) 888 6032, shamirgeller@gmail.com.

DR. SHAMIR GELLER (Orcid ID : 0000-0003-1206-1057)

ORCID: 0000-0003-1206-1057

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populations were detected on peripheral blood flow cytometry. A positron emission tomography (PET) scan revealed widespread cutaneous FDG-avid foci and multiple mildly FDG-avid nonspecific axillary, sub-pectoral, inguinal and neck lymph nodes.

Diagnosis

Primary cutaneous aggressive epidermotropic cytotoxic CD8+ T-cell lymphoma (PCAECyTCL)

Clinical Course

Treatment with systemic gemcitabine and liposomal doxorubicin was complicated by a hypersensitivity reaction to doxorubicin and cardiac ischemia. Thereafter low dose gemcitabine was given alone. This achieved partial response with persistent asymptomatic non-necrotic stable plaque disease. Unfortunately, the patient died six months after her diagnosis.

Discussion

We report the case of a generally healthy female in her 90s with a 3-year history of an eczematous rash and the acute rapid appearance of diffuse ulcerating plaques. Based on the clinicopathological features, PCAECyTCL was diagnosed and systemic chemotherapy was initiated promptly. PCAECyTCL is a rare cutaneous cytotoxic T-cell lymphoma, representing <1% of all cutaneous T-cell lymphoma (CTCL) cases.¹ Extensive proliferation of CD8+ cytotoxic T-cells in the epidermis that results in keratinocyte necrosis and ulceration is characteristic for this cutaneous lymphoma subtype and is associated with an aggressive and progressive disease course and poor response to therapy.^{2,3} It usually affects mid-aged and elderly patients, presenting as multiple papules, plaques and tumors with central necrosis and hemorrhagic crust that appear abruptly, rapidly spread on the trunk and the limbs,^{2,4,5} and possibly disseminate to internal organs.³ The tumor cells in PCAECyTCL have a CD3+/CD4-/CD8+/CD45RA+ phenotype and express cytotoxic molecules: TIA-1, granzyme B and perforin.^{3,5}

Differentiating PCAECyTCL from other types of CTCLs that demonstrate a CD8+ cytotoxic T-cell phenotype can be histologically challenging. The neoplastic cells in mycosis fungoides (MF), while typically CD4+/CD8-, may less commonly be CD4-/CD8+. These cases can easily be distinguished from PCAECyTCL with knowledge of the patient's clinical presentation and temporal progression of the disease. Unlike PCAECyTCL, MF has a gradual and prolonged evolution of patches, plaques and possible late-onset tumors that can become ulcerated. In most cases MF is an indolent cutaneous lymphoma and CD8 positivity is associated with a favorable prognosis compared to classical CD4+ MF. Immunophenotypically, CD8+ MF is more likely to show loss of CD7 and CD45RO positivity compared to PCAECyTCL which tend to retain CD7 and show CD45RA positivity. The differential diagnosis of cutaneous CD8+ lymphocytic infiltrate also includes the aggressive cutaneous lymphomas: extranodal NK/T cell lymphoma and primary

cutaneous gamma delta T-cell lymphoma, as well as the indolent CD8+ Lymphomatoid papulosis (type D LyP).

PCAECyTCL can be misdiagnosed clinically as inflammatory dermatoses such as erythema multiforme or pityriasis lichenoides et varioliformis (PLEVA/Mucha-Haberman disease). Histology, immunohistochemistry and molecular studies can help to distinguish these conditions. However, the recognition of the clinical possibility of PCAECyTCL may be the critically defining factor in some cases, as PLEVA may also present as a CD8+, monoclonal, ulcerating disorder.

PCAECyTCL patients have a poor prognosis, with a 5-year survival rate of 32% (median survival: 12 months).² No significant survival advantage was found for any of the treatment modalities used, including systemic chemotherapy, however allogeneic hematopoietic stem cell transplantation (HSCT) resulted in prolonged partial or complete remissions in some cases,² supporting additional reports on complete response after allogeneic and autologous HSCT in PCAECyTCL.

Overall, this case highlights the importance of careful and expedited integration of clinical, histopathologic, immunophenotypic and molecular findings in patients who present with features that might suggest an aggressive cytotoxic cutaneous lymphoma.

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Figure 1. Diffuse erythematous plaques and papules with focal central necrosis and black crust on the thighs (a) and on the chest and arm (b). Biopsy site is marked with a black triangular sticker.

Figure 2.

Hematoxylin-eosin staining of skin biopsy shows atypical lichenoid and deep diffuse pan-dermal and epidermotropic lymphocytic infiltrate (a, x200). CD8 stain diffusely highlights the neoplastic T-cells in the epidermis (b, x200).