Granulomatous Lymphoproliferative Disorders

Granulomatous Slack Skin and Lymphomatoid Granulomatosis

Pamela Gangar, MD, Sangeetha Venkatarajan, MD, MBA*

KEYWORDS

- Lymphomatoid granulomatosis • Granulomatous cutaneous T-cell lymphoma
- Granulomatous mycosis fungoides • Granulomatous slack skin
- EBV-positive lymphoproliferative disorder

KEY POINTS

- Granulomatous cutaneous T-cell lymphomas (CTCL) are rare and present a diagnostic challenge.
- Granulomatous mycosis fungoides and granulomatous slack skin, the 2 most common types of granulomatous CTCL, display overlapping histologic findings, but differ clinically by circumscribed areas of pendulous lax skin seen in granulomatous slack skin.
- Recent studies have suggested that the prognosis of granulomatous mycosis fungoides is worse than that of classic mycosis fungoides.
- Lymphomatoid granulomatosis is a rare Epstein-Barr virus driven lymphoproliferative disease.
- Therapeutic options include oral corticosteroids, rituximab, interferon-α, and combined chemoimmunotherapy, and are based on the histologic grading of the lesion.

GRANULOMATOUS CUTANEOUS T-CELL LYMPHOMA

Introduction

Granulomatous cutaneous T-cell lymphoma (CTCL) is a rare entity. Approximately 2% of all cutaneous lymphomas involve granulomatous infiltrates.[1–3] The most common types of granulomatous CTCL are granulomatous mycosis fungoides (GMF) and granulomatous slack skin (GSS) (**Table 1**).[4]

GMF is an entity distinct from GSS. GMF is a rare histopathologic variant of mycosis fungoides (MF) characterized by a prominent granulomatous infiltrate.[5] The term GMF was coined by Ackerman and Flaxman in 1970.[6] GSS is recognized by the World Health Organization and European Organization for Research and Treatment of Cancer classification for cutaneous lymphomas as 1 of 3 subtypes of mycosis fungoides.[7] GMF and GSS display overlapping histologic findings, but differ clinically by circumscribed areas of pendulous lax skin seen in GSS.[8]

Etiopathogenesis

The pathogenesis of granulomatous CTCLs is unknown. Histologically, GMF and GSS show

Disclosures: The authors do not have any financial disclosures or conflicts of interest.
MD Anderson Cancer Center, Department of Dermatology, 1400 Pressler Street FCT11.6074, Houston, TX 77030, USA
* Corresponding author.
E-mail address: Sangeetha.venkatarajan@gmail.com

Dermatol Clin 33 (2015) 489–496
http://dx.doi.org/10.1016/j.det.2015.03.013
0733-8635/15/$ – see front matter

Table 1
Clinical results and outcomes in the literature: granulomatous mycosis fungoides and granulomatous slack skin

Clinical and Therapeutic Data from a Series of 19 Patients with Granulomatous Cutaneous T-Cell Lymphoma

Patient No.	Stage	Therapy	Treatment Response	Outcome/Follow-Up (years)
Granulomatous Mycosis Fungoides				
1	IB	IFN, PUVA	PR	AWD/8
2	III	IFN, chemo	SD	DOD/1
3	IA	CS, MC, RT, IFN	CR	ACR/20
4	IB	CS, MC	PR	AWD/6
5	IIB	RT, chemo	PR	DOD/2
6	IB	PUVA, RT	PD	DOD/1
7	IA	Imiq, IFN, PUVA, RT	CR	ACR/6
8	IA	Chemo	SD	AWD/1
9	IVA	Chemo	CR	AWD/4
10	IIA	Pred	PD	AWD/5
11	IA	PUVA, IFN	PR	AWD/4
12	IA	PUVA, RT, IFN	PD	DOD/9
13	IA	CS, PUVA, IFN, ret	SD	AWD/7
14	IB	PUVA, IFN, RT, chemo	PD	DOD/1
15	IA	CS, IFN, ret, RT	PD	DOD/5
Granulomatous Slack Skin				
16	IA	PUVA, ret, IFN	PR	AWD/10
17	IA	NA	NA	AWD/16
18	IA	Excision, CS, MC, PUVA, IFN	PD	AWD/15
19	IA	Excision, carmustine	PR	AWD/28

Abbreviations: ACR, alive with complete remission; AWD, alive with disease; chemo, chemotherapy; CR, complete tumor regression; CS, topical corticosteroids; DOD, died of disease; IFN, interferon-α; imiq, imiquimod; MC, mechlorethamine hydrochloride; NA, not available; PD, progressive disease; PR, partial tumor regression; pred, oral prednisone; PUVA, psoralen/UV-A light therapy; ret, retinoids; RT, radiotherapy; SD, stable disease.

Adapted from Kempf W, Ostheeren-Michaelis S, Paulli M, et al. Granulomatous mycosis fungoides and granulomatous slack skin: a multicenter study of the Cutaneous Lymphoma Histopathology Task Force Group of the European Organization for Research and Treatment of Cancer (EORTC). Arch Dermatol 2008;144(12):1610.

overlapping findings and cannot be discriminated by histologic examination alone. Typically, GMF has an atypical lichenoid $CD4^+CD8^-$ lymphocytic infiltrate with interstitial histiocytes and/or perivascular granulomas with concomitant eosinophils and multinucleated giant cells.[9] Sarcoidal granulomas are also commonly encountered.[8] Tuberculoid, periadnexal, and granuloma annulare–like patterns are occasionally seen.[9]

Classic histologic features of GSS include dense diffuse dermal infiltrate of atypical, irregular, and convoluted lymphocytes that may extend to the subcutaneous tissue.[10] In the dermis, diffuse multinucleate giant cells and numerous histiocytes, which exhibit prominent elastophagocytosis and lymphophagocytosis, are observed.[10] The multinucleated giant cells show 20 to 30 nuclei in the periphery of the cytoplasm.[11] Loss of elastic fibers usually correlates with the extent of the granulomatous infiltrate, and is a universal finding in GSS.[10] In the past, elastolysis involving the full thickness of the dermis was thought to be pathognomonic for GSS.[5] However, a more recent study showed loss of elastic fibers in both patients with GSS and patients with GMF.[8]

Clinical Presentation

The clinical presentation and skin manifestations of GMF are similar to those of classic MF, and patients may present with patches, plaques, tumors, erythroderma, poikilodermatous patches, and granuloma annulare–like lesions.[9] GMF may coexist with classic MF lesions.[11] Unlike GSS, patients with GMF present without pendulous skin folds, and extracutaneous spread is common.[8]