Granulomatous slack skin: case report with electron microscopic features

Bo Wang[1,2] MD PhD, Jie Zheng[2] MD, Hong-Wei Wang[3] MD

Affiliations: Department of Dermatology, University of Michigan, Ann Arbor, Michigan, USA, [2]Department of Dermatology, Ruijin Hospital, School of Medicine, Shanghai Jiaotong University, Shanghai, China, [3]Department of Dermatology, Huadong Hospital, Shanghai Medical College, Fudan University Shanghai, China

Corresponding Authors: Bo Wang MD PhD, 1910 Taubman Center, University of Michigan, 1500 East Medical Center Drive, Ann Arbor, Michigan 48109-5314, Email: makiwang@umich.edu; Hong-Wei Wang MD, 221 West Yan An Road, Shanghai, 200040, China, Tel: 86-21-62483180, Email: hongweiwang2005@aliyun.com

Abstract

Granulomatous slack skin (GSS) is a rare subtype of mycosis fungoides. It usually presents as slowly evolving, erythematous, slack plaques that usually involve folds of lax skin. Herein, we report a case of GSS and we show electron microscopy examination. Atypical T cells with convoluted and cerebriform nuclei, lymphophagocytosis, and elastophagocytosis are key features of GSS under electron microscopy.

Keywords: granulomatous slack skin, cutaneous T cell lymphoma, electron microscopy

Introduction

Granulomatous slack skin (GSS) is a rare cutaneous T cell lymphoma (CTCL) affecting all age groups. According to the WHO/EORTC classification in 2005, GSS is a subtype/variant of mycosis fungoides (MF) with slowly evolving, erythematous, slack plaques that usually involve folds of lax skin, especially in the groin and axilla [1]. Herein, we present a patient with characteristic clinical and pathological presentations of GSS with a detailed description of electron microscopic (EM) findings.

Case Synopsis

A 30-year-old man presented to the dermatology clinic in 2003 for evaluation of longstanding widespread erythematous patches for 16 years. In 1987, the patient noticed the initial involvement in the left popliteal fossa; the findings were described as skin-colored nodules with diameters 1-3cm. The lesions then slowly grew in size and number over the next decade. New plaques and papules appeared on the neck, extremities, and trunk. The color evolved from skin-colored to erythematous and purplish. Lesional skin became pendulous and atrophied. The patient reported no obvious accompanying symptoms other than occasional pruritus. He denied any significant past medical history; family history was non-contributory. He was treated for presumed sarcoidosis with topical and oral corticosteroid; no improvement was noticed.

Upon physical examination, well-demarcated erythematous and purplish papules and plaques were observed on the left chest, lower back, buttocks, and all extremities (**Figure 1A**, **B)**. Lax skin was found in intertriginous areas such as the axillary, popliteal, and gluteal regions. Infiltrative erythematous papules were also observed on the dorsal neck. Lymph node enlargement and hepatosplenomegaly were not observed. Other review of systems was negative.

Histopathological examination from a skin biopsy revealed dense dermal and subcutaneous infiltrates with lymphocytes, histiocytes, and multinucleated giant cells (**Figure 1C**, **D)**. Atypical lymphocytes with irregular nuclei were found in the dermis without obvious epidermotropism. No significant alteration

was noticed in the epidermis. Immunohistochemistry showed that T cells were positive for CD3, CD4, and CD5; CD7 and CD8 were not found. PCR from the lesion biopsy showed a clonal rearrangement of TCR Vγ1-8. Weigert elastic stain showed mild decrease and irregular arrangement of elastin fibers, which further supports the diagnosis of GSS (not shown). Electron microcopic examination of lesional skin showed detailed features of multinucleated giant cells, atypical lymphocytes, and extracellular spaces. Multiple T lymphocytes with convoluted and cerebriform nuclei were observed under EM (**Figure 1E)**. Increased numbers of lysosomes and mitochondria were found in most macrophages, correlating with their increased activity (**Figure 1F)**. These activated macrophages were in close contact with lymphocytes and elastin fibers, potentially facilitating subsequent lymphophagocytosis and elastophagocytosis (**Figures 1G, H)**. We observed fragmented elastin fibers (appearing as amorphous material) in macrophages (**Figure 1G)**. Other laboratory testing including LDH, β2-microglobin and flow cytometry were within reference range. Flow cytometry analyses of blood and bone marrow, as well as bone marrow biopsy, were within normal range, excluding hematological involvement. Given the typical clinical manifestations and pathological features, the patient was diagnosed with GSS. Owing to the cost of phototherapy, the patient chose oral acitretin 30mg daily as monotherapy. Lesion appearance and body involvement remained unchanged for 10 years before he was lost to follow-up.

Discussion

Granulomatous slack skin is an extremely rare type of CTCL and was categorized as a subtype/variant of MF in the 2005 WHO/EORTC classification [1, 2]. It was previously classified as a peripheral T cell lymphoma (PTCL). Compared to aggressive PTCL, GSS is clinically indolent with a disease specific 5-year survival of 100% according to recent case reports [3, 4].

The diagnosis of GSS is based on consideration of both clinical manifestations and pathological features. Clinically, GSS typically starts with erythematous plaques that evolve slowly to skin laxity and atrophy, most commonly in intertriginous areas. The differential diagnosis includes acquired/secondary skin laxity and atrophy related to drug and sunlight exposures and inflammatory disorders. However, these disorders rarely present as annular lesions in intertriginous skin and generally, no sign of inflammation can be observed. Histopathologically, GSS presents with non-caseating granulomas with macrophagic and lymphocytic infiltrations. The distinction between

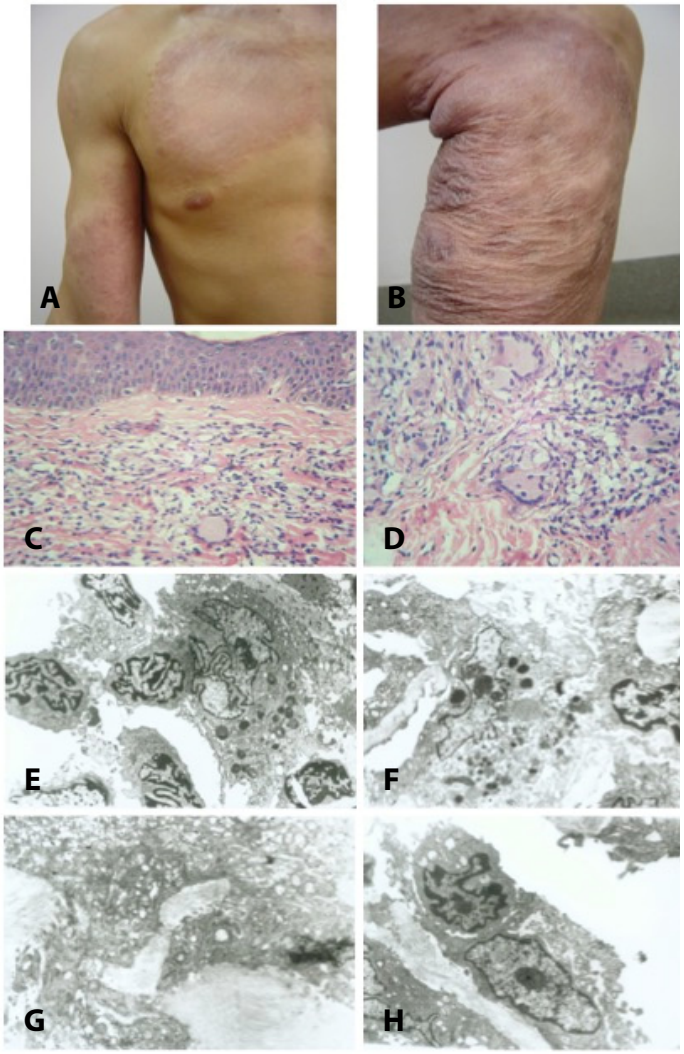

Figure 1. ***A)*** *Erythematous plaques on right chest and right arm.* ***B)*** *Erythematous plaques and skin laxity can be observed on left leg.* ***C)*** *Confluent lymphocytic infiltration and multi-nucleated giant cell in dermis. H&E, 100×.* ***D)*** *Multi-nucleated giant cells and collagen fibers in dermis. H&E, 200×. Electron microscopy:* ***E)*** *T lymphocytes with convoluted and cerebriform nuclei;* ***F)*** *Macrophages with increased lysosomes;* ***G)*** *Fragmented elastin fibers within dermis, elastin fiber appears as amorphous mass;* ***H)*** *Macrophage in close contact with elastin fibers and lymphocyte.*

GSS and granulomatous MF (GMF) can be challenging with merely pathological analysis [3, 5]. Elastophagocytosis occurs only in GSS and not GMF. However, it is rare finding in GSS and often missed by pathologists. Elastophagocytosis causes decreased or absence of elastic fibers in the dermis and results in clinically apparent skin laxity. Thus, elastophagocytosis is both a pathological feature and a key player in GSS pathogenesis. Herein, we innovatively used EM to visualize this phenomenon and provided EM as an alternative modality for diagnosing GSS. Elastin fiber appears as an amorphous mass under EM. We observed fragmented elastin fibers in macrophages, indicating elastophagocytosis. These findings correlate with the disorganized elastin fibers observed in the Weigert elastic stain.

Owing to its rarity, there is no consensus on GSS treatment. Numerous successful treatment options were reported including topical and systemic corticosteroid, interferon-α, radiotherapy, retinoid, narrow-band UVB, and PUVA [6]. Because of the cost, our patient refused to receive phototherapy. Oral acitretin 30mg daily as monotherapy stabilized disease progression. The course of our patient is consistent with the common stable clinical course and favorable disease outcome of GSS. As discussed above, GSS enjoys a favorable clinical prognosis without extracutaneous involvements. An adverse clinical outcome mainly depends on development of secondary lymphoproliferative diseases. According to limited available reports, close to half of GSS patients eventually developed Hodgkin disease, non-Hodgkin lymphoma, MF, and leukemia [5]. Thus regular follow-up is crucial to screen for development of these conditions. Our patient did not develop lymphoproliferative disorders over 10 years of follow-up.

Conclusion

Granulomatous slack skin is a rare form of CTCL and has clinical chronicity. Our case is a pathology-proven GSS with longstanding involvement of multiple body sites. Using electron microscopy, we observed several features of GSS lesions: atypical T cells with convoluted and cerebriform nuclei, lymphophagocytosis, and elastophagocytosis. We believe EM may serve as an alternative diagnostic modality, especially for differentiating GSS from granulomatous MF.

Potential conflicts of interest

The authors declare no conflicts of interests.

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