

Granulomatous slack skin syndrome: Report of a unique case

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Abstract

Granulomatous slack skin syndrome is a rare variant of cutaneous T-cell lymphoma (mycosis fungoides). It is characterized clinically by redundant skin folds, which show a predilection towards flexural areas such as the axilla and the groin. Histologically, it shows a granulomatous T-cell infiltrate and loss of elastic tissue. It has an indolent but progressive course; and is usually refractory to treatment. We report a unique case of slack skin syndrome, sparing the classical sites with rapid and unusual involvement of non-intertriginous areas.

Key words: Granulomatous, mycosis fungoides, slack skin

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Introduction

Primary cutaneous lymphomas very rarely display granulomatous features (2%) and these include granulomatous slack skin syndrome and granulomatous mycosis fungoides. Granulomatous slack skin syndrome is a rare variant of cutaneous T-cell lymphoma, with approximately fifty cases reported in literature so far.^{1,2} It is characterized by the gradual development of erythematous plaques and redundant skin folds in intertriginous and flexural areas.¹ We report a unique case of granulomatous slack skin syndrome, sparing the classical sites with a rapid and unusual involvement of non-intertriginous areas.

Case Report

A 60-year-old woman presented with a 1-year history of multiple pigmented asymptomatic lesions involving the lower part of the trunk and bilateral lower limbs. Over a period of 5 months, the lesions progressively increased in size and some lesions showed laxity of the overlying skin. On examination, sharply demarcated pigmented plaques with fine scales were seen predominantly on the left lower abdomen, buttock, thigh, shin, ankle and a part of the right leg [Figure 1].

The intertriginous areas such as axilla and groin were normal. The lax skin on the left thigh and right leg appeared like atrophic poikilodermatosus plaques [Figure 2a and b]. The basic

investigations were within normal limits; except for a mild increase in serum calcium levels. Serum protein immunotyping showed absence of monoclonal gammopathy. Immunofluorescence was negative for autoantibodies. Computerized tomography of the chest, abdomen and pelvis showed shotty pulmonary, mesenteric and retroperitoneal lymph nodes; however fine needle aspiration cytology/biopsy could not be done as the patient did not give her consent.

Skin biopsy from the affected sites revealed diffuse granulomatous infiltrates composed of lymphocytes and histiocytes and giant cells [Figure 3a]. Lymphocytes showed atypical changes with single-cell epidermotropism [Figure 3b]. The infiltrates were seen throughout the entire dermis and extending up to the subcutis [Figure 4a and b]. Numerous multinucleated giant cells (more than 40 nuclei) scattered throughout the dermis, showed evidence of emperipoleisis and elastophagocytosis [Figure 5a]. Elastica van Gieson staining revealed reduced or absent elastic tissue in dermis [Figure 5b]. Immunohistochemistry showed CD3 and CD4 positivity and reduced CD7 and CD8 expression [Figure 6a-d]. Based on the above clinicopathological findings, we made a diagnosis of granulomatous slack skin syndrome, which is a variant of mycosis fungoides. The patient was started on psoralen and ultraviolet A therapy. Since the clinical response was not satisfactory, the patient was referred to oncology department for further management and follow-up.

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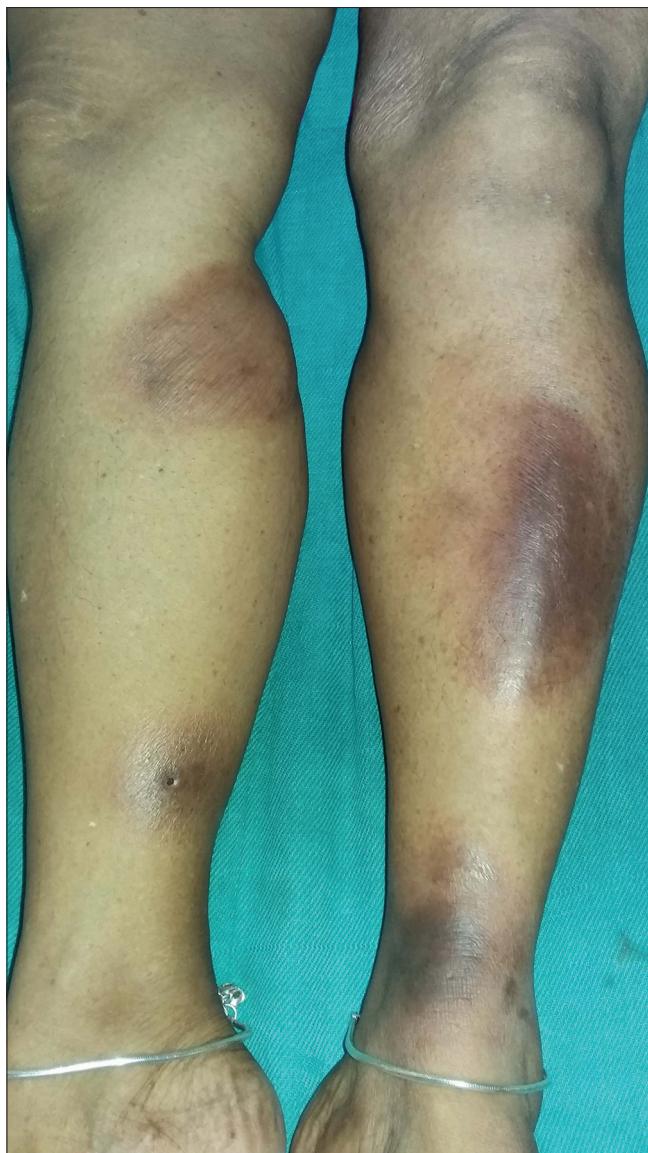


Figure 1: Well-defined, hyperpigmented, indurated plaques

Discussion

The term “granulomatous slack skin syndrome” was coined by Ackerman in 1978.³ It is an extremely rare subtype of cutaneous T-cell lymphoma with a slight male preponderance.⁴ The common clinical presentation includes the appearance of sharply demarcated painless, poikilodermatous, indurated plaques and patches, predominantly involving the axilla and the inguinal regions; but can be quite variable at initial presentation. The size increases slowly and progressively within a few years, leading to redundant folds of loose skin, whereas lesions in nonintertriginous regions tend not to undergo this transformation.⁵ Our case, in contrast to the above findings, involved the nonintertriginous areas and lacked the typical feature of redundant skin folds. The development of skin lesions in our case was very rapid in contrast to the observations made by van Haselen *et al.*⁶ and Kempf *et al.*¹ where the disease had an indolent slow and progressive course. The extracutaneous manifestations of the disease can rarely involve organs such as spleen, lymph node and lung.⁷



Figure 2a: Skin laxity in the right leg

This condition is histologically characterized by the presence of diffuse granulomatous infiltrates composed of lymphocytes and histiocytes, throughout the entire dermis and sometimes the subcutaneous tissues as well. The granulomas are noncaseating in nature. The lymphocytes show pleomorphic, hyperchromatic and irregular nuclei. In the dermis, numerous multinucleated giant cells phagocytosing lymphoid cells (emperipoleisis) and elastic fibers (elastophagocytosis) are seen. The giant cells have nuclei arranged either as Langhans type cell or of foreign body type. The reduced or absent elastic tissue is demonstrated in van Gieson staining. In immunohistochemistry, lymphocytes typically stain positive for CD3 and CD4 along with a negative or reduced staining for CD7 and CD8.⁷ All the above findings were documented in our case.

The exact etiology of this condition is presently unknown. A chromosomal translocation involving *t(3;9) (q12; p24)* has been described. The rearrangement of T-beta cell receptor gene is seen in molecular analysis. In approximately 50% of the patients, an



Figure 2b: Skin laxity in the left thigh region

association with Hodgkin's disease, non-Hodgkin's lymphoma or mycosis fungoides is observed.⁶

Hermes *et al.* hypothesized that the granuloma formation in this condition may be the result of antigenic status of the atypical lymphocytes and/or elastic fibers.⁸ Some researchers consider these granulomatous reactions associated with malignancies as peculiar hypersensitivity response to malignant cells, or to some persistent infection, while others consider it as protective phenomenon with a good prognosis.⁹ Granulomatous mycosis fungoides is a close differential diagnosis of granulomatous slack skin syndrome. Even though they share overlapping histologic features, LeBoit *et al.* had identified certain pathological features to distinguish between the two [Table 1].¹⁰ Generalized cutis laxa is differentiated from granulomatous slack skin syndrome by its frequent facial skin involvement and flexural sparing. In anetoderma, lesions are usually smaller with random distribution and there is no association with systemic elastolysis.

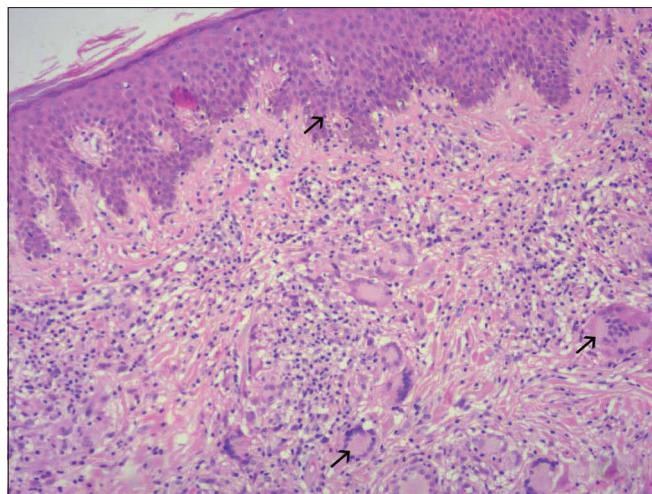


Figure 3a: Diffuse granulomatous dermal infiltrates composed of atypical lymphocytes and giant cells (H and E, $\times 200$)

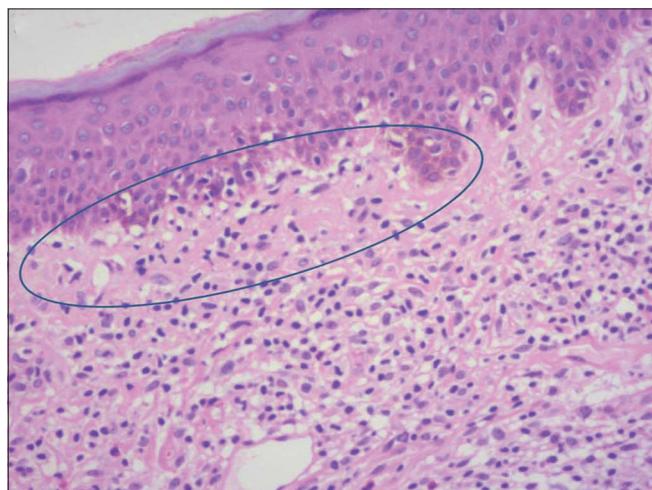


Figure 3b: Focal epidermotropism of atypical lymphocytes (H and E, $\times 200$)

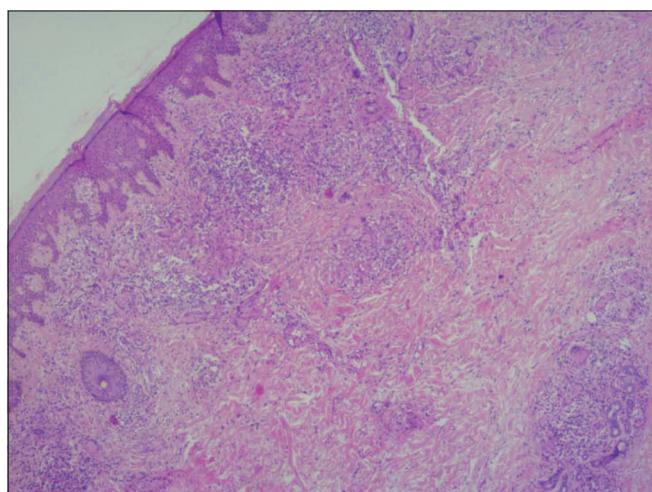


Figure 4a: Deep dermal granulomas (H and E, $\times 100$)

Mid-dermal elastolysis also mimics slack skin syndrome, but the wrinkling is of crinkle type and there is no tendency to develop into pendulous folds. Furthermore, early lesions of granulomatous slack

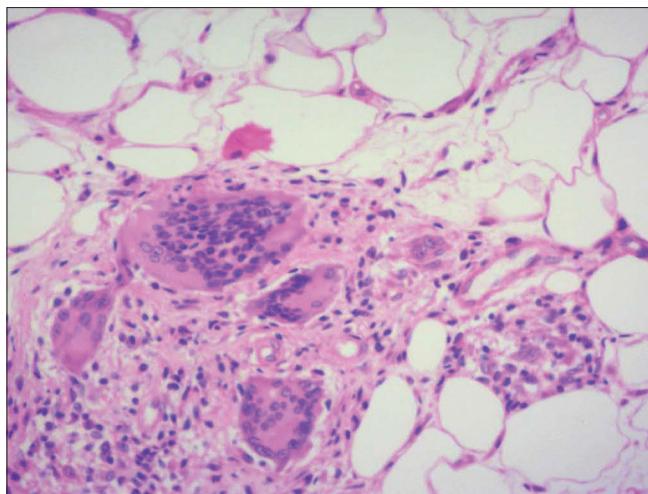


Figure 4b: Infiltrates extending up to subcutis (H and E, $\times 400$)

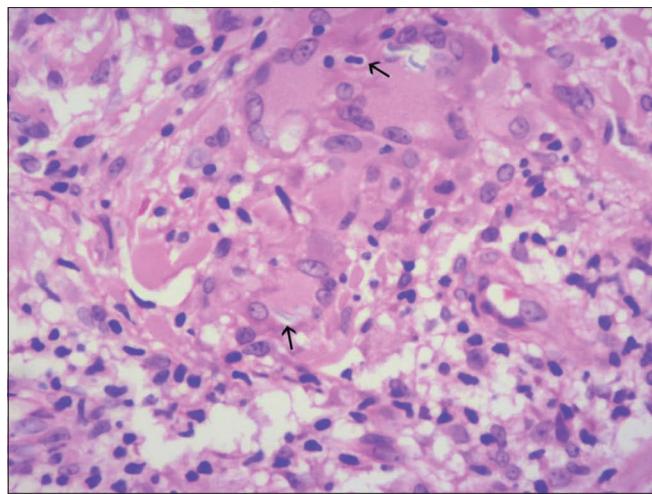


Figure 5a: Multinucleated giant cells showing emperipoleisis and elastophagocytosis (arrows) (H and E, $\times 400$)

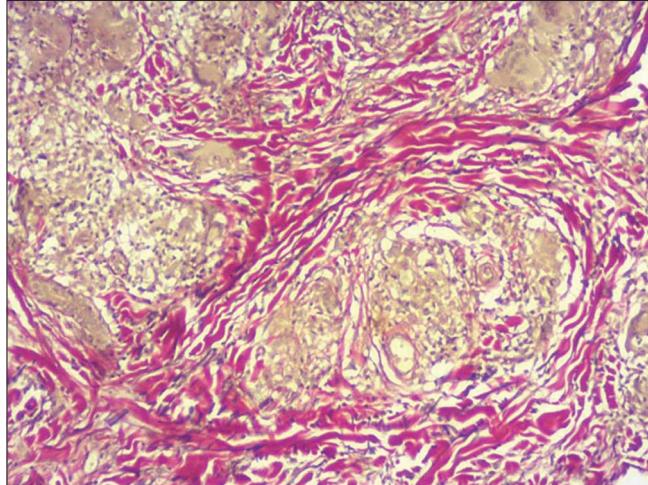


Figure 5b: van Gieson staining showing reduction in elastic fibers ($\times 100$)

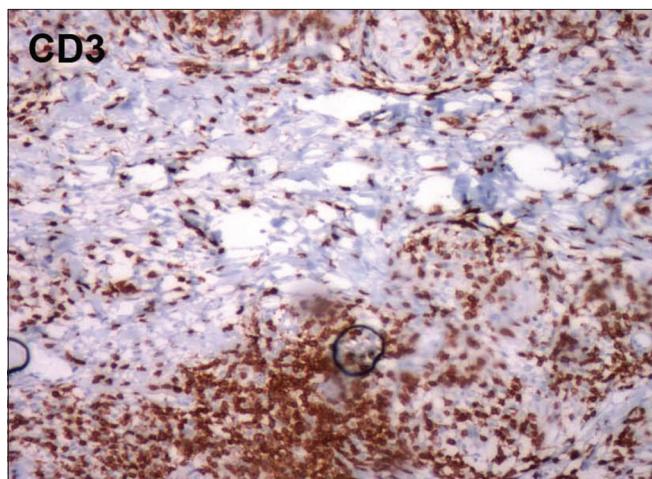


Figure 6a: Immunohistochemistry showing CD3 positivity ($\times 100$)

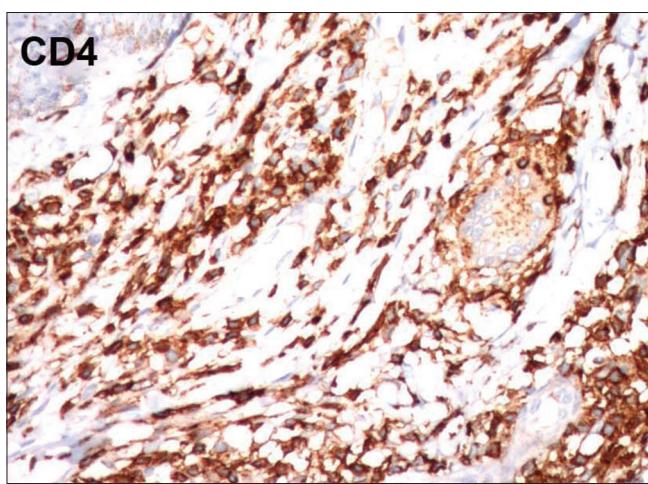


Figure 6b: Immunohistochemistry showing CD4 positivity ($\times 100$)

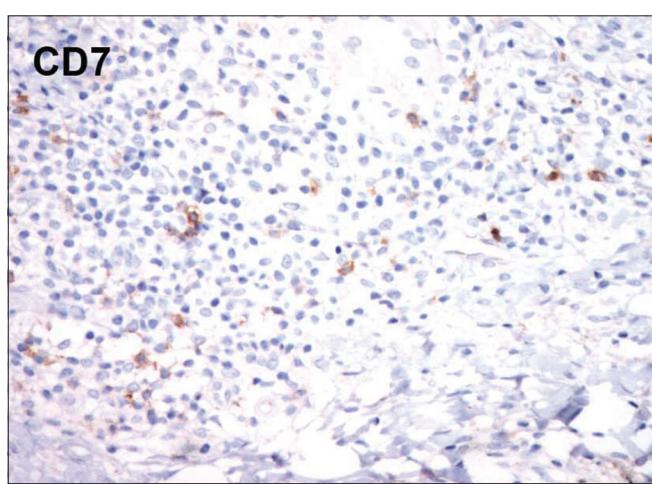


Figure 6c: Immunohistochemistry showing reduced staining for CD7 ($\times 100$)

skin may mimic patches and plaques of classical mycosis fungoides.⁶ A case of granulomatous slack skin, mistaken for leprosy and treated with dapsone and rifampicin has also been described.⁹

There is no standard treatment protocol for this condition and the choice of a particular regimen will entirely depend on the stage of the disease. The treatment options include topical nitrogen mustard,

Table 1: Granulomatous slack skin versus granulomatous mycosis fungoides

Features	GSS	Granulomatous MF
Clinical	Very rare form of CTCL	Most common form of granulomatous CTCL
Histopathology	Clinically featured by bulky skin folds in flexural areas Even distribution of giant cells and granuloma Abundance of giant cells, many of them with more than 40 nuclei per cell Elastophagocytosis and lymphophagocytosis are characteristic Subcutis may be involved Less pronounced nuclei atypia of lymphocytes	Nodules and plaques similar to that of classical MF Patchy in distribution Some giant cells with 5-10 nuclei per cell Pautrier's microabscesses is characteristic Subcutis usually spared More pronounced atypical lymphocytes
Treatment and prognosis	No standard protocol. Topical, systemic and phototherapy can be tried singly or in combination 5-year survival rate is 100%	Early systemic therapy is required 5-year survival rate is 66%

GSS: Granulomatous slack skin, CTCL: Cutaneous T-cell lymphoma, MF: Mycosis fungoides

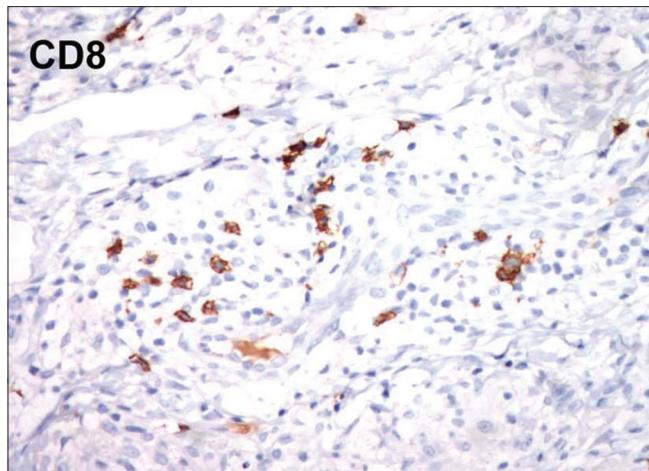


Figure 6d: Immunohistochemistry showing reduced staining for CD8 ($\times 100$)

psoralen and ultraviolet A, corticosteroids, retinoids, radiotherapy, interferon alpha, poly-chemotherapy (Cyclophosphamide, doxorubicin, vincristine and prednisolone- CHOP) and total skin electron beam irradiation, which can be employed either in isolation or in a multimodal setting.⁴ However, none of these appears to provide sustained satisfactory clinical outcomes. The surgical treatment of excising the redundant skin for esthetic and functional improvement has a high relapse rate.¹ Even though the 5-year disease-specific survival of this condition is close to 100%, its association with lymphoproliferative disorders warrants a lifelong close follow-up.²

Conclusion

Our case contributes to the further understanding of this rare condition. In addition, we were unable to find any previous reports of granulomatous slack skin syndrome rapidly involving the nonintertriginous areas, sparing the classical sites.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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