

# Granulomatous Slack Skin with an unusually aggressive course due to the subsequent development of a CD30-positive Large Cell Lymphoma

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## Abstract

**Objective:** To report a case of Granulomatous Slack Skin with an unusually aggressive course.

**Clinical Presentation and Histopathology:** The patient presented with soft tissue masses accompanied by pendulous lax skin in the upper thighs and the left inguinal region. The clinical findings and the dermal infiltration by CD3+/CD4+ small lymphoid cells led to the diagnosis of Granulomatous Slack Skin. Three years later the bone marrow was infiltrated by a CD30+ Large Cell Lymphoma which resulted in patient's death.

**Conclusion:** This case of Granulomatous Slack Skin presents a fatal course due to the development of a CD30+ Large Cell Lymphoma.

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## Introduction

Granulomatous slack skin (GSS) is a very rare subtype of Cutaneous T-cell lymphomas (CTCL) [1-10]. In the World Health Organization–European Organization for Research and Treatment of Cancer (WHO-EORTC) classification for cutaneous lymphomas, GSS is considered a distinct subtype of mycosis fungoides (MF) [1]. GSS is often associated with preceding or subsequent lymphoproliferations, including MF, Hodgkin lymphoma (HL) or other CD30 positive lymphoproliferations [1, 2]. GSS has a slowly progressive course and a fatal outcome is rare [1-5]. We report a case of GSS with an unusually aggressive course due to the development of a CD30 positive Large Cell Lymphoma which occurred 3 years after the initial diagnosis of GSS and resulted in patient's death.

## Case report

A 41-year-old man presented with a 1-year history of growing asymptomatic soft tissue masses accompanied by pendulous lax skin in the upper thighs bilaterally and the left inguinal region. Magnetic Resonance Imaging confirmed the soft tissue masses (18.6x18x12 cm and 16x14.8x11 cm) and showed bilateral enlargement of inguinal lymph nodes.

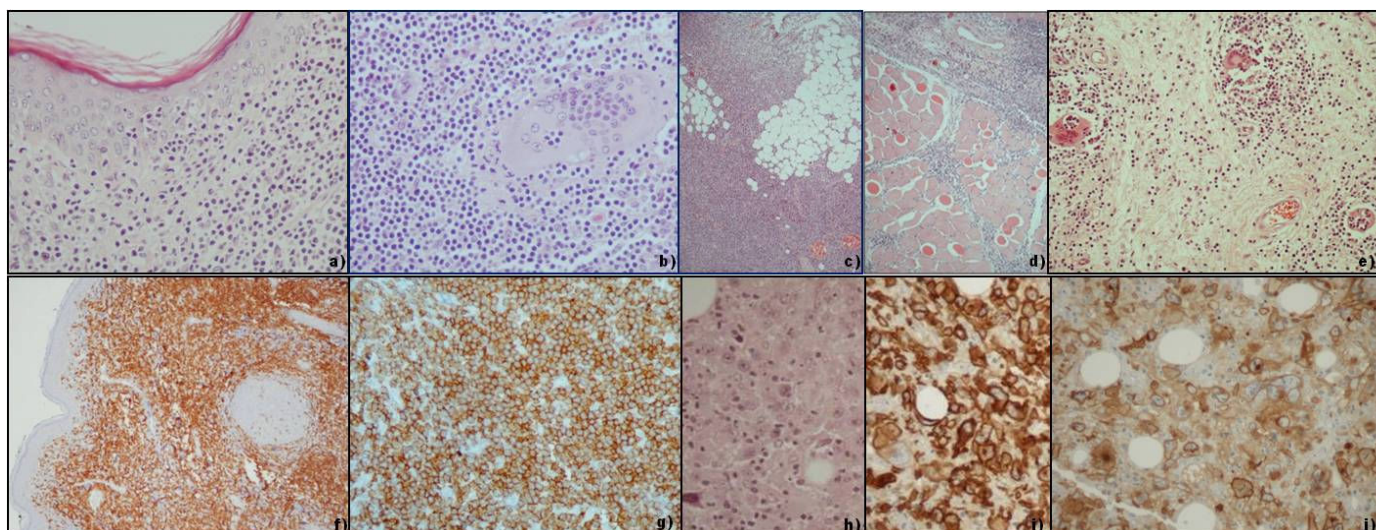
The tissue was fixed in 10% buffered formalin and processed as usual for paraffin embedding. Immunostainings were performed on the Ventana Benchmark autostainer (Ventana Medical Systems, Inc, Tucson AZ) on paraffin embedded sections using the Ventana diaminobenzidine tetrahydrochloride kit according to the manufacturer's instructions. The following antibodies were used: CD2, CD5 and CD7 (CELLMARQUE), CD30, CD45RO, CD43, BCL6, CD68, TIA1 and PD1 (DAKO), CD20 and CD8 (Biogenex), CD10 (Leica, Novocastra), Ki67, (Biocare), and CD3 and CD4 (Spring).

Histological examination of skin biopsy specimens revealed diffuse infiltration of the dermis, subcutis and the excised segment of skeletal muscle by small to medium-sized lymphocytes with slight pleomorphism and scattered large lymphoid cells (Figure). Multinucleated giant cells with intracytoplasmic lymphocytes but no epithelioid cell granulomas or prominent epidermotropism of lymphocytes were observed (Figure). Destruction of elastic fibers was demonstrated by Van Gieson staining. Immunohistological examination of skin biopsy specimens revealed that the small to medium-sized lymphoid cells were CD2+, CD3+, CD4+, CD5+, CD7+, CD8-, TIA1-, Bcl6-, CD10- and PD1- (Figure). CD68 immunostaining was observed in macrophages and multinucleated giant cells, CD30 immunostaining was detected in a few large lymphoid cells and MIB1 (Ki67) immunostaining was found in 10-15% of lymphoid cells (Figure). On the basis of the aforementioned clinical, histological and immunohistochemical findings, the diagnosis of GSS was made.

Histological examination of one removed inguinal lymph node and the bone marrow biopsy showed no infiltration by lymphoma. The patient responded poorly to six months treatment with bexarotene which is an activator of retinoid X receptors. Two years after the initial diagnosis of GSS histological and immunohistochemical examination of a skin biopsy from inguinal region revealed the same picture of GSS and bone marrow biopsy exhibited no infiltration by lymphoma. Three years after the initial diagnosis of GSS the patient presented with fever, weight loss, and generalized lymphadenopathy. Histological and immunohistochemical examination of the bone marrow revealed a diffuse infiltration by a CD30+, CD3+, CD4+, CD8-, CD25+, TIA1- and ALK1- Large Cell Lymphoma

(Figure). The patient received four cycles of CHOP (Cyclophosphamide, Hydroxydaunorubicin [Adriamycin], Oncovin, Prednisone) and a cycle of

ESHAP (Etoposide, Solu-Medrol, High-dose Aracytin, Cisplatin) chemotherapy but he did not respond to treatment and died.



*Figure 1: Massive and diffuse infiltration of the dermis (a, b), subcutis (c) and the excised skeletal muscle (d) by small to medium-sized lymphocytes. Focal epidermotropism of lymphocytes (a). Area with less prominent infiltration where lymphoma cells surround multinucleated giant cells with intracytoplasmic lymphocytes (e). Immunohistochemical detection of CD2 (f) and CD3 (g) in lymphoid cells. Massive and diffuse infiltration of the Bone Marrow by large lymphoid cells (h). Immunohistochemical detection of CD30 (i) and CD3 (j) in large lymphoid cells which infiltrate the Bone Marrow. (Magnifications: a, b, h, i and j X400, c and d X40, e and f X200).*

## Discussion

The differential diagnosis of GSS includes Granulomatous Mycosis Fungoides (GMF) which is the most common form of granulomatous CTCL [2, 3]. A prominent granulomatous reaction has been defined as the presence of a granulomatous component exceeding 25% of the dermal infiltrate and, besides GMF and GSS, may also be observed in other CTCL such as subcutaneous panniculitis-like and small/medium pleomorphic T-cell lymphoma as well as in primary cutaneous B-cell lymphomas such as follicle center lymphoma and diffuse large B-cell lymphoma, leg type [2, 3]. Since patients with GMF and GSS

display overlapping histologic features the diagnosis of GSS should be restricted to those patients presenting clinically pendulous lax skin lesions [2, 3].

The diagnosis in granulomatous CTCL is challenging in cases with predominant granuloma formation in the absence of nuclear atypia or epidermotropism of neoplastic cells [2, 3]. Indeed, in 7/23 cases of cutaneous B and T-cell lymphomas with a prominent granulomatous reaction (22 primary and 1 secondary cutaneous lymphomas exhibiting T-cell phenotype in 21 cases and B-cell phenotype in the remaining 2 cases) a misdiagnosis of granulomatous dermatitis preceded the correct diagnosis for a

period of time variable between 1 and 216 months [3]. Thus, the authors suggested that sequential biopsies and complete phenotypic and molecular genetic analyses should be carried out in cases of "unusual" granulomatous dermatitis [3]. Detection of a neoplastic T-cell clone may be useful for differentiating granulomatous CTCL from granulomatous dermatitis since clonal rearrangement of T-cell receptor (TCR) genes were detected by Polymerase Chain Reaction in 14/15 GMF and 4/4 GSS [2] and in 9/9 GMF and 2/2 GSS [3].

Trisomy 8 and a reciprocal translocation t(3;9)(q12;p24) have been reported in GSS [4, 8]. The t(3;9)(q12;p24) in GSS was not associated with involvement of the JAK2 gene which is located at chromosome band 9p24 and had been found to be amplified in HL and mediastinal diffuse large B-cell lymphoma [8]. Further studies

are required to gain insight into the molecular pathogenesis of GSS.

GSS has a slowly progressive course and a fatal outcome is rare [1-5]. Our case exhibits an unusually aggressive course due to the development of a CD30 positive Large Cell Lymphoma which occurred 3 years after initial diagnosis and resulted in patient's death.

## **Conclusion**

We report a case of GSS with an unusually aggressive fatal course due to the development of a CD30 positive Large Cell Lymphoma which occurred 3 years after initial diagnosis of GSS and resulted in patient's death.

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