Acta Derm Venereol 2001; 81: 42–44

CLINICAL REPORT

Granulomatous Slack Skin: A Distinct Disorder or a Variant of Mycosis Fungoides?

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About 75% of cutaneous lymphomas belong to the group of T-cell lymphomas. Mycosis fungoides is the most common entity in this group. Granulomatous slack skin is a rare form of cutaneous T-cell lymphoma closely related to mycosis fungoides. We present here a patient with areas of lax skin for several years who developed a generalized erythroderma with associated immunoactivation and a deterioration in his general condition. This report discusses clinically and histologically the differential diagnoses, namely granulomatous slack skin and granulomatous mycosis fungoides, and suggests that these 2 disorders are only variants in the broad spectrum of a single disease. ***Key words: cutaneous T-cell lymphoma; elastolysis; erythroderma.***

(Accepted October 30, 2000.)

Acta Derm Venereol 2001; 81: 42–44.

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Granulomatous slack skin (GSS) is a very rare form of cutaneous T-cell lymphoma closely related to mycosis fungoides. The first case of GSS was clinically described by Bazex et al. (1) and the disease was first called granulomatous slack skin by Ackerman (2). Thirty-seven patients have been described with GSS in the literature, 34 of these being described in a Table by Van Haselen et al. (3).

Clinically GSS is mostly characterized by circumscribed areas of pendulous asymptomatic skin, mainly in the groins, axillae and abdomen. Initially, indurated plaques often occur which transform into bulky, excessive skin folds. In rare cases only erythematous scaly patches or macules resembling poikiloderma vasculare atrophicans occur initially.

Histopathology shows a granulomatous infiltrate with giant cells and atypical lymphocytes (hyperchromatic and pleomorphic cells with large cerebriform nuclei), epidermotropism and elastolysis (2, 4). In early lesions only a dense infiltrate of mononuclear cells (lymphocytes, monocytes, eosinophils, macrophages) may be present. In long-standing lesions the disappearance of elastic fibres is a primary feature. Clonality of the T-cell receptor ß- or γ-gene has been proven in 13 patients.

The association of GSS with other preexisting or subsequent lymphoproliferative disorders such as Hodgkin's disease, non-cutaneous non-Hodgkin's lymphoma or mycosis fungoides is about 50% (3).

The present report describes a unique case of GSS, which presented with areas of lax skin associated with persisting generalized erythroderma.

CASE REPORT

A 68-year-old Caucasian male presented to the Department of Dermatology, University of Innsbruck in February 1998 with a generalized pruritic erythroderma accompanied by an indolent lymph node enlargement in the groins. Additionally the patient reported a history of photosensitivity. Clinical examination showed excessive skinfolds predominantly on the back and upper arms (Figs. 1A and B). The patient suffered from reduced appetite, weight loss, weakness and sweating during the night.

Histopathological examination of a skin biopsy showed, under a hyperkeratotic psoriasiform epidermis, perivascular and interstitial dermatitis with lymphocytes and histiocytes, including some focal giant cells and scattered eosinophils and plasma cells. The infiltrate was irregularly distributed and revealed lymphohistiocytic cells with hyperchromatic and pleomorphic nuclei. These lymphocytes also showed epidermotropism, predominantly in the basal layer. Giant cells, some with phagocytosis of elastic fibres, were visible (Fig. 2). The papillary dermis showed wiry bundles of collagen fibres in an irregular arrangement. An elastica–van Giesson stain confirmed areas of elastolysis in the upper-to-middle dermis (Fig. 3). Immunohistochemistry revealed that the neoplastic cells were of T-lineage (CD45+ , UCHL1+ , L26-) and the giant cells showed reactivity with the histiocytic marker CD68. Electron microscopy detected histiocytes and lymphocytes with cerebriform nuclei. Southern blot analysis of a skin biopsy showed a polyclonal rearrangement; suggested further biopsies to produce more material were forbidden by the patient. Histology of an inguinal lymph node revealed a non-specific inflammation and no specific infiltrate. Bone marrow histology showed no specific infiltration and no other organ involvement could be found by imaging procedures.

Routine laboratory tests showed initially leukocytosis of 14.6×10^9/l (normal range $4.0–10.0 \times 10^9$/l) with associated lymphopenia. The blood sedimentation rate was elevated to 48 mm in the first hour. Other routine laboratory parameters (liver function tests, electrolytes, total serum protein, blood urea nitrogen, serum creatinine, bilirubin) were within normal ranges. Semi-thin sections of peripheral blood were negative for Sezary cells. Serum immunoactivation parameters such as interleukin-2 receptor (16.8 ng/ml [normal 0–4.8 ng/ml]), neopterin (17.3 nmol/l [0–10.0 nmol/l]) and beta-2-microglobulin (2.5 mg/l [0.7–1.9 mg/l]) were elevated. High values of interleukin-6 (27.3 pg/ml [0–3.0 pg/ml]) and tumour necrosis factor-α (30.1 pg/ml [0–20.0 pg/ml]) were found. Angiotensin-converting enzyme was normal and α1-antitrypsin was slightly elevated (216 mg/dl [90–200 mg/dl]).

Treatment was started with a systemic corticosteroid (20 mg methyl prednisolone/day) in combination with chlorambucil (2 mg/day). After 4–5 weeks, remission of erythroderma and relief of pruritus were observed, in association with a better general condition and a normalization of immunoactivation parameters. The appearance of the excessive skin folds remained unaffected. No more enlarged lymph nodes were palpable. The systemic corticosteroid dosage was reduced and chlorambucil was continued at the same dosage for 1.5 years. At present the patient is free of recurrence with this therapy.

 ISSN 0001-5555

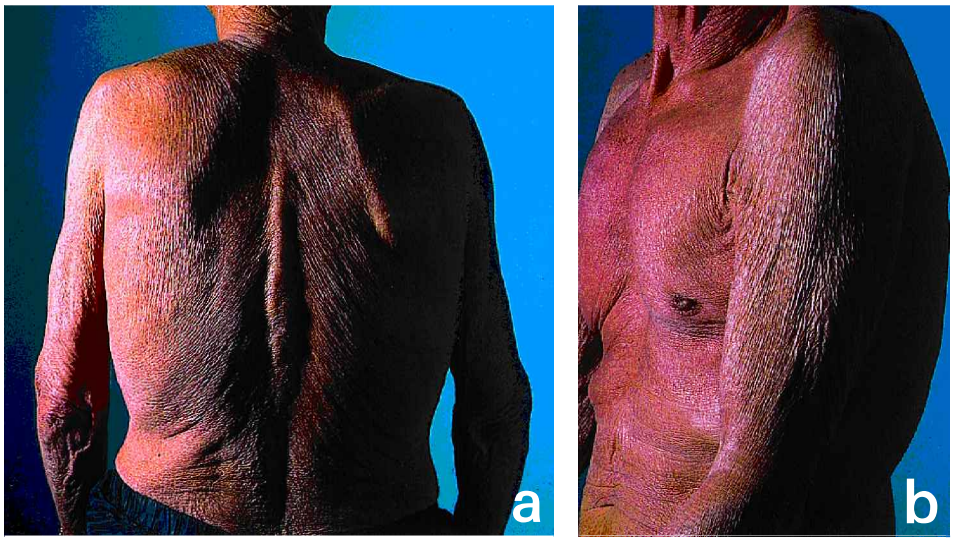

Fig. 1. (a) Back and (b) arm showing erythrodermatic and atrophic skin in addition to lax skin folds.

DISCUSSION

The literature reports 37 cases of GSS, all with the typical features of lax or pendulous skin. Our case of GSS is the first who initially, in addition to surplus skin folds, presented with erythroderma. His general condition was poor, with a loss of appetite, weight loss, sweating and weakness and the immunoactivation parameters were markedly elevated. Owing to this clinical appearance our first differential diagnoses were Sezary's syndrome or erythrodermatic mycosis fungoides. However, histopathology and electron microscopy demonstrated features typical of GSS or granulomatous mycosis fungoides. According to LeBoit et al. (4) the main feature differentiating these 2 disorders is the phagocytosis of elastic fibres in GSS, which does not occur in granulomatous mycosis fungoides. According to this definition our case should be categorized as GSS, because of evident elastolysis. In contrast to LeBoit et al. (4), however, Ackerman (2) proposed that the histological findings of GSS represent only one manifestation of mycosis fungoides and he describes GSS as a "misnomer" for this condition.

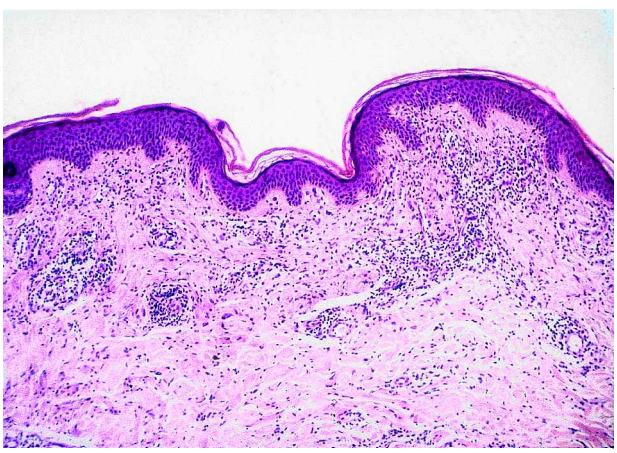

Fig. 2. Skin biopsy from the back showing an irregular infiltrate of lymphohistiocytic cells with some giant cells. The basal layer shows areas of epidermotropism (haematoxylin and eosin staining; original magnification × 100).

In an ongoing study at our clinic we used the elastica – van Giesson stain to look for elastolysis in cases of mycosis fungoides and also in patients with Sezary's syndrome. A reduction in the number of elastic fibres could be detected in 33% of these patients (manuscript in preparation). These findings confirm Ackerman's theory that GSS is a variant of the broad spectrum of mycosis fungoides.

Recently another group (5) described a case with an overlap between granulomatous mycosis fungoides and GSS. The patient showed clinically the picture of granulomatous mycosis fungoides in the tumour stage and had some histopathological findings similar to those of GSS.

No standard therapy exists for GSS. A wide variety of modalities such as azathioprine (6), chlorambucil (7), polychemotherapy (1, 8, 9), topical and systemic steroids (10), surgical excision (11), radiotherapy, PUVA (12) and combination therapy have been used. No single option resulted in complete remission.

The rational of our therapy was based on the observation that chlorambucil can alleviate GSS, as reported by Helm et al. (7), and on the fact that chlorambucil in combination with systemic corticosteroids is very effective in patients

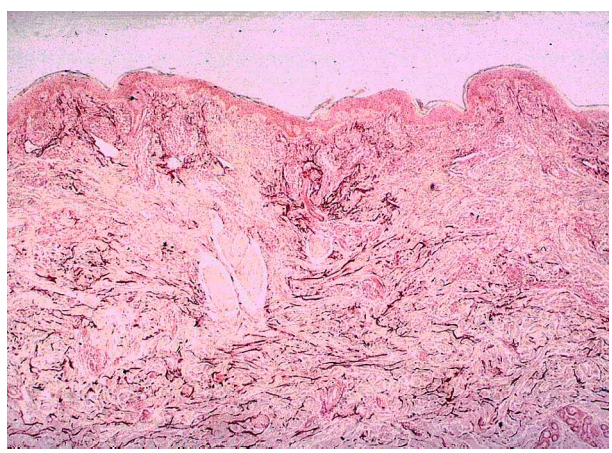

Fig. 3. Elastica – van Giesson stain showing absence of elastic fibres in the upper-to-middle dermis (original magnification × 100).

with Sezary's syndrome, who also have erythroderma and pronounced immunoactivation. Photochemotherapy was ruled out because of the patient's history of photosensitivity. The good response to this therapy is in concordance with the observation of Van Haselen et al. (3), who also observed that treatment options similar to those given to patients with mycosis fungoides or Sezary's syndrome are effective in GSS.

In summary, our case of GSS with erythroderma and the case of Metzler et al. (5) of granulomatous mycosis fungoides with histological features of GSS show an overlap between the clinical and histological pictures of these 2 diseases, suggesting that they are different expressions of the same disease, namely mycosis fungoides.

REFERENCES

1. Bazex A, Dupré A, Christol B. Maldie de Besnier-Boeck-Schaumann chalazodermique? Bull Soc Fr Dermatol Syph 1968; 75: 448–450.
2. Ackerman AB. Mycosis fungoides. In: Ackerman AB, ed. Histologic diagnosis of inflammatory diseases, 2nd edn. Philadelphia, PA: Williams & Wilkins, 1997: 838–856.
3. Van Haselen CW, Toonstra J, Van der Putte SJC, Van Dongen JJM, Van Hees CLM, Van Vloten WA. Granulomatous slack skin. Report of three patients with an updated review of the literature. Dermatology 1998; 96: 382–391.
4. LeBoit PE, Zackheim HS, White CR Jr. Granulomatous variants of cutaneous T-cell lymphoma: the histopathology of granulomatous mycosis fungoides and granulomatous slack skin. Am J Surg Pathol 1988; 12: 83–95.
5. Metzler G, Schlagenhauff B, Krober SM, Kraiserling E, Schaumburg-Lever G, Lischka G. Granulomatous mycosis fungoides: report of a case with some histopathologic features of granulomatous slack skin. Am J Dermatopathol 1999; 21: 156–160.
6. Balus L, Bassetti F, Gentili G. Granulomatous slack skin. Arch Dermatol 1985; 121: 250–252.
7. Helm KF, Cerio R, Winkelman RK. Granulomatous slack skin: A clinicopathological and immunhistochemical study of three cases. Br J Dermatol 1992; 126: 142–147.
8. Mouly F, Baccard M, Cayuela JM, Jansen F, Verola O, Flageul B, et al. Cutaneous T-cell lymphoma associated with granulomatous slack skin. Dermatology 1996; 192: 288–290.
9. Balus L, Manente L, Remotti D, Grammatico P, Bellocci M. Granulomatous slack skin: Report of a case and review of the literature. Am J Dermatopathol 1996; 18: 199–206.
10. LeBoit PE. Granulomatous slack skin. Dermatol Clin 1994; 12: 375–389.
11. Noto G, Pravata G, Micelli S, Arico M. Granulomatous slack skin: Report of a case associated with Hodgkin's disease and a review of the literature. Br J Dermatol 1994; 131: 275–279.
12. Tsang WYW, Chan JKC, Loo KT, Wong KF, Lee AW. Granulomatous slack skin. Histopathology 1994; 25: 49–55.