Granulomatous slack skin presenting as diffuse poikiloderma and necrotic ulcers, with features of granulomatous vasculitis and response to oral prednisone, acitretin, and oral psoralen plus ultraviolet light therapy—A case report

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Key words: acitretin; granulomatous slack skin; granulomatous vasculitis; poikiloderma; necrotic ulcers; prednisone; psoralen plus ultraviolet light therapy.

INTRODUCTION

Granulomatous slack skin (GSS), a rare variant of mycosis fungoides, is characterized clinically by bulky, pendulous skin folds on flexural areas and histologically by elastolytic granulomatous infiltrates of clonal T cells.[1-9] The monoclonal rearrangement of the T-cell receptor β and γ genes can be demonstrated by polymerase chain reaction in most cases.[6,7,10,11]

The clinical course of GSS is slow and complex, often becoming a diagnostic challenge especially in its early stages. GSS may be confused with leprosy or cutaneous tuberculosis especially if occurring in endemic areas like the Philippines.[12-14]

The prognosis of GSS is influenced by the development of lymphoproliferative concomitant diseases such as Hodgkin disease, non-Hodgkin lymphoma, and acute myelogenous leukemia as evidenced in 50% of reported cases.[5-9]

We report a case of a 43-year-old Filipino man with GSS initially diagnosed as cutaneous tuberculosis. To date, there are only about 50 cases of GSS reported in literature with features of large vessel involvement reported in only 4 cases and necrobiotic changes reported in 1 case.[3,5-7,12,15-22]

Abbreviations used:

GSS: granulomatous slack skin
PUVA: psoralen plus ultraviolet A therapy

CASE REPORT

A 43-year-old Filipino man presented with an indurated mass on the right breast 12 years before consult. The lesions gradually enlarged over 2 years followed by erythema and the appearance of slowly enlarging pendulous indurated masses on the left breast and lower abdominal fold. Initially, cutaneous tuberculosis was diagnosed based on a biopsy finding of granulomatous dermatitis, and the patient was treated 3 times with full courses of antituberculosis medications, without improvement.

Over the next few years, diffuse erythema developed with areas of induration on the neck with reticulated violaceous and hypopigmented patches with atrophy and telangiectasia. Prominent engorged veins with punched out necrotic ulcers were noted associated with severe skin pain.

At the time of consult, the patient presented with more bulky and indurated sagging skin folds on the inframammary areas and lower abdominal fold

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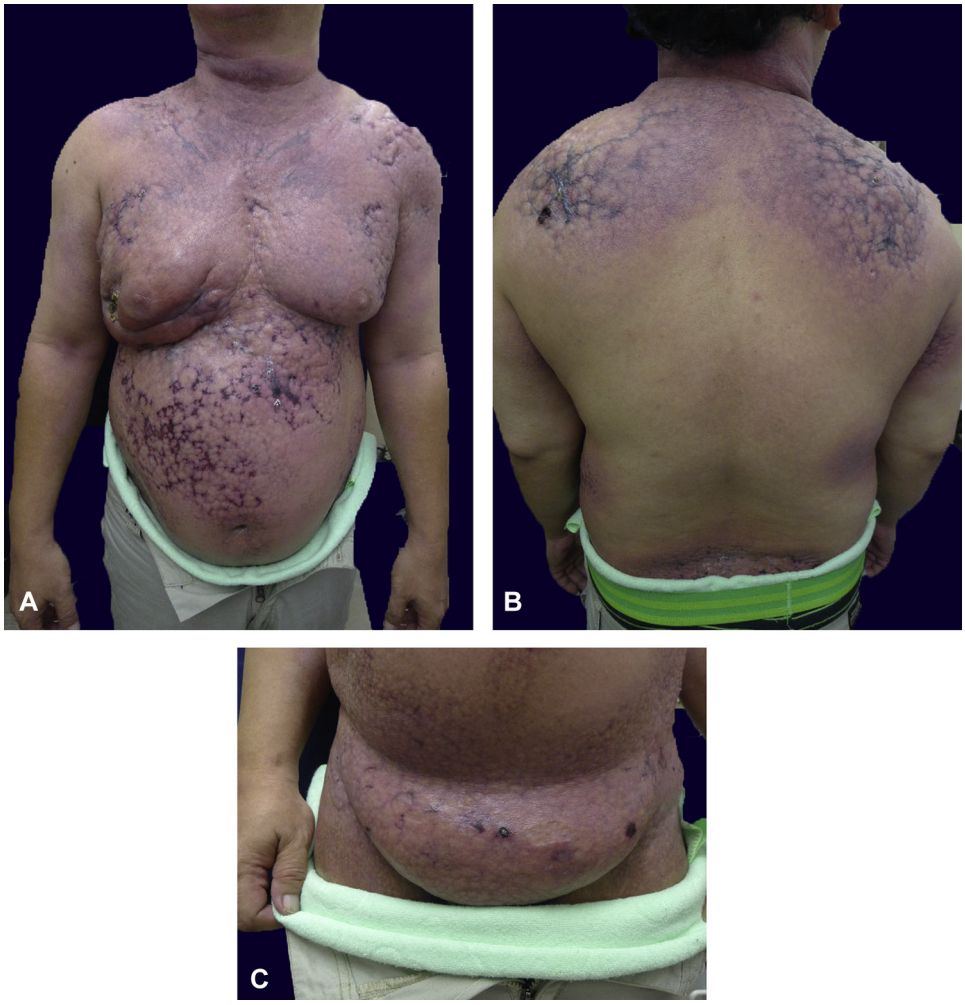

Fig 1. Diffuse erythema with areas of induration and reticulated violaceous and hypopigmented patches with atrophy, telangiectasia, and prominent engorged vessels with punched-out ulcer areas of necrosis on the neck, chest, and abdomen (**A**); symmetrically on the scapulae, flanks, sacral and gluteal areas (**B**), with bulky and indurated sagging skin folds on the inframammary and lower abdominal folds (**C**).

(Fig 1). A series of skin biopsies found nodular-to-diffuse infiltrate of lymphocytes and histiocytes around dilated telangiectatic blood vessels with granulomas composed of lymphocytes, histiocytes, Touton, Langhans, and foreign body—type giant cells throughout the dermis (Fig 2); granulomatous vasculitis of small- to medium-sized vessels seen as fibrin deposition and swollen endothelial cells infiltrated by lymphocytes, histiocytes, and giant cells (Fig 3); and broad areas of sclerotic collagen within the reticular dermis.

Verhoeff Van Gieson elastic tissue stain and immunohistochemical stains showed absence of elastic fibers (Fig 4), elastophagocytosis and a phenotype of $CD3^+$, $CD4^+$, $CD8^-$, $CD45RO^+$, $CD5^-$, $CD7^-$, $CD20^-$, and $CD30^-$ (Fig 5) compatible with the histologic picture of granulomatous slack skin. These findings and the characteristic clinical appearance led to the diagnosis of GSS.

To rule out a possible tuberculosis or fungal infection, acid-fast bacilli and periodic acid—Schiff stains and a fungal culture were done. Acid-fast bacilli and fungal elements were not found. Sputum acid-fast bacilli and culture, purified protein derivative skin test, and a chest radiograph were all normal.

Workup for other systemic diseases was done. Screening for antiphospholipid antibody syndrome and systemic lupus erythematosus were negative. Sarcoidosis was considered by rheumatology service because of the appearance of indurated plaques and telangiectasia and a finding of granulomas on biopsy. The patient was treated with oral prednisone, 45 mg/d, with note of marked decrease

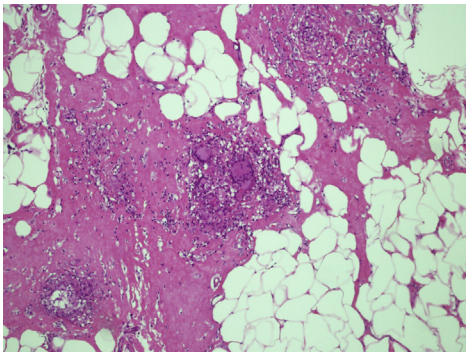

Fig 2. Excision biopsy from the lower abdominal fold. Numerous granulomas composed of lymphocytes, histiocytes, and large multinucleated giant cells, with at least 40 nuclei show phagocytosis of lymphocytes (emperipolesis) pathognomonic of granulomatous slack skin. (Hematoxylin-eosin stain; original magnification: ×100.)

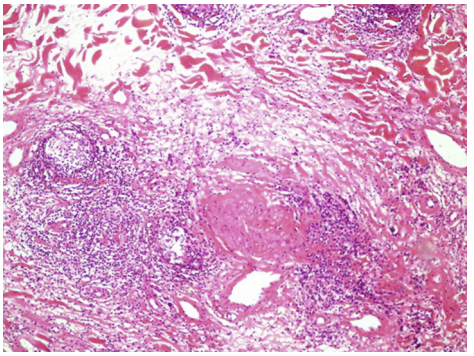

Fig 3. Granulomatous vasculitis of small- to medium-sized vessels are seen as fibrin deposition and swollen endothelial cells infiltrated by lymphocytes, histiocytes, and giant cells. (Hematoxylin-eosin stain; original magnification: ×40.)

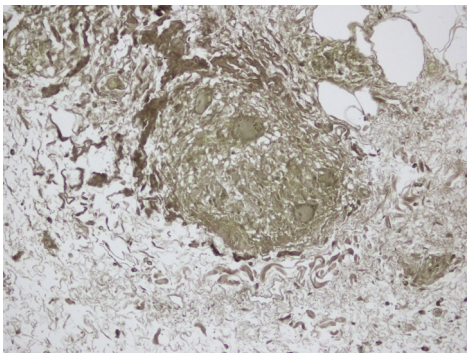

Fig 4. Stringy elastic fibers stained dark brown. Absence of elastic fibers in infiltrative area, some elastic fibers scattered in the periphery. Fragmented elastic fiber inside giant cell pertaining to elastophagocytosis. (Verhoeff Van Gieson elastic tissue stain; original magnification: ×40.)

in truncal violaceous erythema, telangiectasia, decrease in engorgement of veins, and a decrease in the appearance of ulcers after a month; however, the pendulous folds and indurated plaques remained (Fig 6). Prednisone was slowly tapered over 10 months.

The patient was then referred to hematology and oncology services and his disease was staged as IIA (T2, N1-2, M0). Bone marrow aspiration biopsy, flow cytometry with a comprehensive lymphoma panel, and right cervical lymph node excision biopsy found no evidence of lymphoma. tuberculosis culture was negative as was mycobacterium tuberculosis DNA polymerase chain reaction.

Further tests on T-cell clonality found monoclonal rearrangement of the T-cell receptor γ genes, further confirming diagnosis of GSS. Additional diagnostic workup found no evidence of visceral involvement.

The patient's liver enzymes increased 3-fold after only 2 doses of intravenous methotrexate, so the treatment was discontinued. He was started on acitretin, 30-mg tablet, with psoralen plus ultraviolet A therapy (re-PUVA) twice a week. The patient showed a significant decrease in induration and sagging of the skin folds, further improvement of lesions characterized by faint poikiloderma, less engorgement of vessels, and no recurrence of necrotic ulcers within 5 weeks of treatment (Fig 7). Because of a phototoxic reaction described as diffuse erythema on the trunk with severe skin pain, acitretin had to be discontinued, and the patient was instead maintained on PUVA therapy and topical corticosteroids. PUVA and topical corticosteroid therapy is currently ongoing with no recurrence of necrotic ulcers.

DISCUSSION

The initial skin manifestations of GSS are violaceous indurated plaques with atrophy, which transform into bulky, excessive skin folds, which enlarge slowly over several years.[1-4,23] In rare cases, erythematous patches with poikiloderma have been described. A rare variant characterized by either vessel involvement or necrobiotic changes as seen in our patient has been described in previous literature.[3,5-9,20-22,24]

We present an extremely rare variant of GSS with the following features: (1) widespread poikiloderma and engorged veins with concomitant ulcers caused by the small- to medium-sized vessel granulomatous vasculitis evident on biopsy (Fig 3), with response to oral prednisone (Fig 6) and (2) necrobiotic changes also seen on biopsy. A diagnosis of cutaneous tuberculosis was initially considered, and a differential diagnosis of leprosy was included, as both diseases are endemic in the Philippines and because

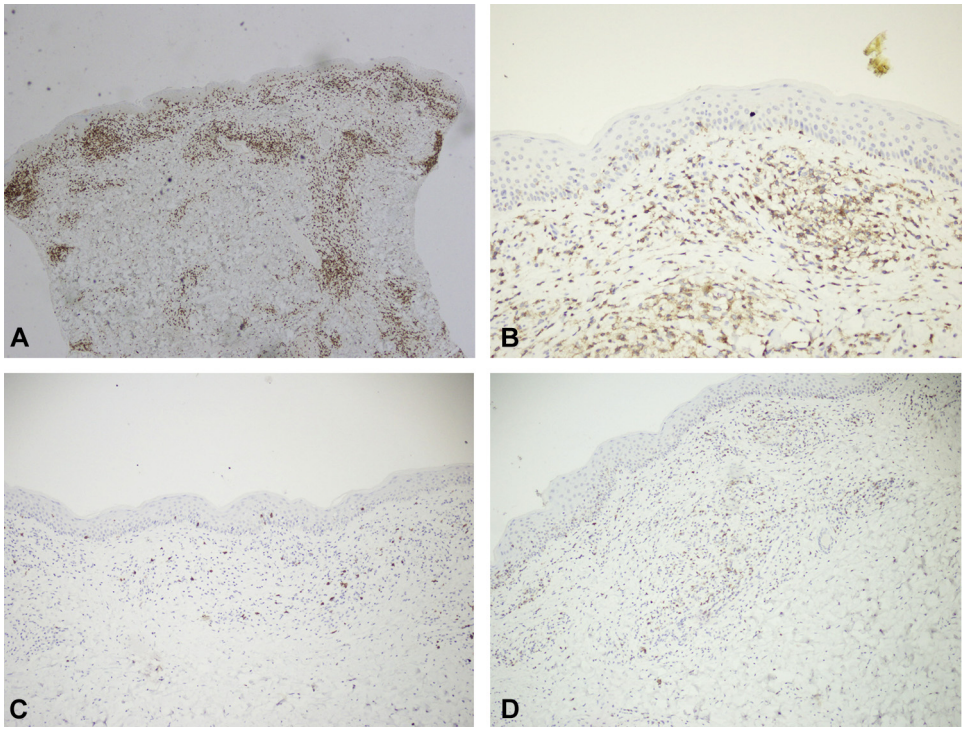

Fig 5. CD3 stain, pan T-cell marker: Most dermal infiltrating mononuclear cells stain positively (**A**). CD4 stain, pan T-cell marker: most infiltrating cells stain positively (**B**). CD8 stain, cytotoxic T-cell: few to some (less than 25%) stain positively (**C**). CD7, stain rare to few staining of mononuclear cells (relative loss) (**D**).

of the following: the presence of indurated plaques and ulcerations clinically and histopathologic features of epithelioid histiocytes, Langhans giant cells, and tuberculoid granulomas. Both diseases were ruled out.

Our patient exhibited unusual skin lesions progressing over a long period eventually leading to the typical presentation of granulomatous slack skin with bulky folds in the inframammary area and abdomen.[3,6,7,16-19] This case is unusual and unique because of the presence of widespread poikiloderma interspersed with engorged veins and multiple necrotic ulcers on the trunk, symmetrically distributed on diffusely indurated plaques, giving it a cobblestone appearance (Fig 1).[3,6,7,15-21] These findings correlate with the histologic findings of nodular-to-diffuse infiltrate of lymphocytes, histiocytes, Langhans and foreign body type giant cells around dilated telangiectatic blood vessels and lymphocytes, histiocytes, and giant cells into the wall of small- to medium-sized vessels—features seen in granulomatous vasculitis. Areas of extensive collagen degeneration (necrobiotic changes) were also evident in the reticular dermis.[3,6,7,10,11,13,20,21,25,26]

The pronounced poikiloderma and engorged veins remarkably improved, and the ulcers completely healed when systemic corticosteroids were given. We postulate that the ulcers appeared because of the granulomatous vasculitis defined as a pathologic process caused by the destruction of vessels by granulomatous infiltrate, therefore leading to ulceration, rather than caused by a direct tumor invasion.[6,22]

There is good evidence that re-PUVA is effective for clearing skin lesions, particularly in early stages of the disease, and long-term remissions have been reported.[2,27-33] Our patient exhibited a significant decrease in size and induration of the folds and a decrease in indurated plaques on the neck and trunk and further clearance of poikiloderma with re-PUVA. He is currently maintained on oral PUVA plus topical corticosteroid therapy. Currently, his condition is controlled with no recurrence of necrotic ulcers.

CONCLUSION

GSS is a common mimicker of inflammatory and infectious skin disease.[1,2,12,13,18,19,25,26,34] It has a slow progressive course, and diagnosis is often delayed. The presence of bulky skin folds with

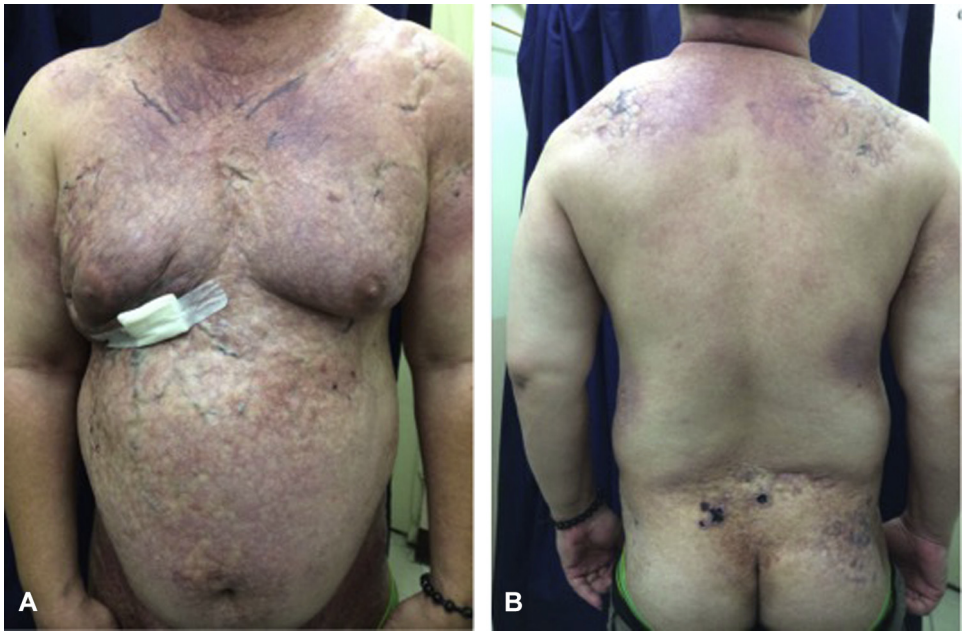

Fig 6. After 1 month of prednisone, 45-mg tablet. Marked decrease in violaceous erythema and telangiectasia, decrease in engorgement of veins, and a decrease in the appearance of ulcers on the trunk (**A** and **B**).

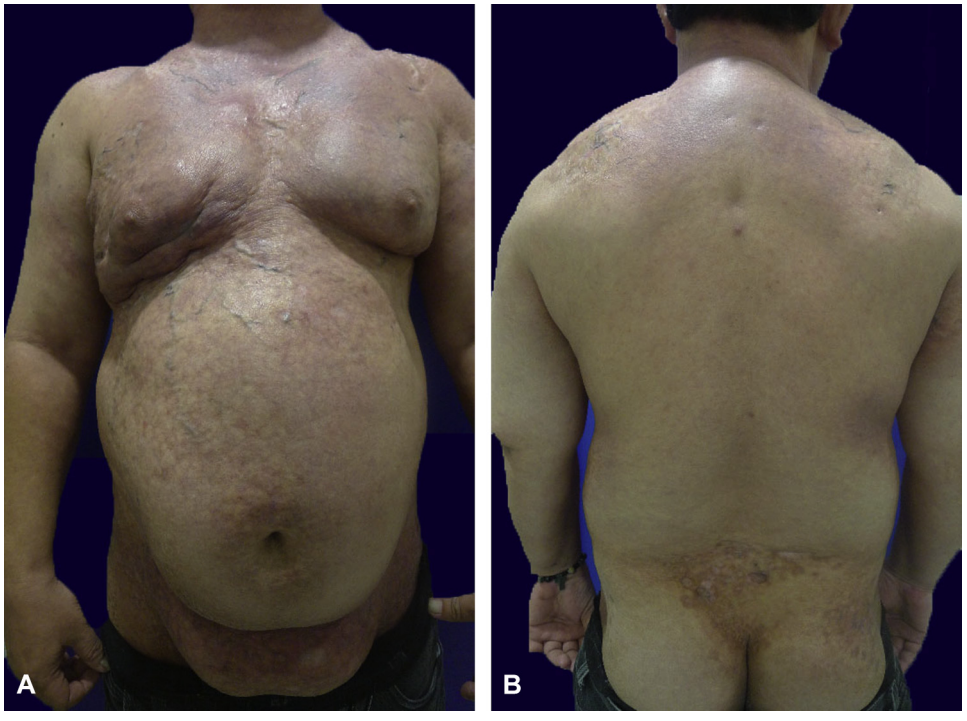

Fig 7. Twenty-fifth session of re-PUVA therapy; 44 days off prednisone. Further decrease of erythema on trunk with fading reticulated patches and significant decrease in induration and sagging of the skin folds with no recurrence of necrotic ulcers (**A** and **B**).

diffuse erythema should give one a high index of suspicion of GSS and should warrant further histopathologic studies with specific immunohistochemical stains.[6,7,10,11,35-37]

Because of the paucity of cases, there is no standard of treatment yet. Our patient continues to respond to oral PUVA and topical corticosteroids and is being monitored closely.[2,27,28,29-33]

Future plans include multiple biopsies and a close follow-up with the oncology service. Oral PUVA will be continued once a week for a year, tapered to every other week in the following year, further tapered to every third week for a year, and every fourth week for the fifth year before the disease is categorized as being in remission. Re-PUVA therapy will be revisited if there is a recurrence of necrotic ulcers or worsening of skin lesions. A repeat biopsy will be done once the poikiloderma and ulcers are no longer evident to assess for a complete response to treatment.

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