

Slack Skin Syndrome with Granulomatous Involvement of the Lungs: A Case Report and Literature Review

Ramya Vangipuram², Casey Wang^{1,3*} and Madeleine Duvic¹

¹Division of Internal Medicine, Department of Dermatology, The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA

²Texas Tech Health Science Center School of Medicine, Lubbock, TX, USA

³The University of Texas M.D. Anderson Cancer Center, 1515 Holcombe Blvd, Unit number: 1452, Houston, TX 77030, USA

*Corresponding author: Wang C, The University of Texas M.D. Anderson Cancer Center, 1515 Holcombe Blvd, Unit number: 1452, Houston, TX 77030, Tel: (713)745-1918; E-mail: cwang4@mdanderson.org

Received date: April 1, 2015; Accepted date: October 20, 2015; Published date: October 28, 2015

Copyright: © 2015 Wang C, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Granulomatous slack skin syndrome is a rare variant of mycosis fungoides characterized by the development of pendulous skin folds in the intertriginous regions. It has an indolent but progressive course and is usually refractory to treatment. Extra-cutaneous involvement is rare. We report a unique case of slack skin syndrome coexisting with a progressive granulomatous lung disease.

Keywords:

CTCL; Slack skin; Cutis laxa; Sarcoidosis; Mycosis fungoides

Introduction

Granulomatous slack skin (GSS) syndrome is a rare variant of the cutaneous T-cell lymphoma (CTCL) mycosis fungoides (MF), with fewer than 100 cases reported. Initial presentation varies but commonly includes indurated, poikilodermatous, and sharply demarcated patches and plaques, and tends to involve the groin and axilla. GSS has an indolent but progressive course, and is generally therapy resistant. Granulomatous mycosis fungoides can result in slack skin syndrome, characterized by the appearance of hanging folds of skin in the intertriginous areas. Extra-cutaneous involvement in granulomatous slack skin syndrome is rare, with only 2 case reports of extra-cutaneous dissemination. We report a unique case of granulomatous lung involvement in a patient with granulomatous slack skin syndrome, complicated by pulmonary hypertension.

Report of a Case

A 50-year-old Caucasian female presented with a 10 year history of pruritic erythematous papules on her inner thighs followed by rapid development of lax skin in the inguinal folds. The lesions were unresponsive to topical and intralesional steroids. A past lesional skin biopsy of her left thigh revealed an atypical lymphoid infiltrate with both focal epidermotropism and with extension into the subcutaneous tissue which contained numerous multinucleated giant cells forming granulomas, consistent with granulomatous mycosis fungoides with slack skin syndrome. Prior to her presentation, she had been treated with local electron beam radiation and responded partially. She also had received psoralen-UVA (PUVA) therapy, oral bexarotene in combination with topical nitrogen mustard, Intron A, and gemcitabine over the next eight years, all with disease progression.

The patient also developed a persistent cough and worsening exertional dyspnea five years after her diagnosis. Pulmonary function testing revealed obstructive lung disease, and computed tomography

(CT) scan of the chest showed pulmonary hypertension, ground-glass infiltrates, and bronchiectasis. Bronchial brushings were negative for malignant cells, viral inclusions, acid-fast bacilli, and fungal elements. Laboratory studies revealed an elevated angiotensin converting enzyme and beta 2 microglobulin. Peripheral blood flow cytometry was negative for an aberrant T-cell population. The patient underwent an open-lung wedge biopsy which showed diffuse non-necrotizing granulomas without hyaline sclerosis. She was treated with systemic steroids over four years for possible pulmonary sarcoidosis. Her symptoms worsened with attempted steroid tapering, and she was intolerant of methotrexate.

Because the patient gradually developed new skin lesions, the patient was referred to our clinic to discuss treatment options. Physical exam revealed pendulous lax skin bilaterally in the groin along with many hyper-pigmented and erythematous papules distributed on the upper extremities, back forehead, and in the axilla. Skin in the axilla was atrophic though not pendulous (Figure 1).



Figure 1: Granulomatous slack skin syndrome characterized by the development of hyper-pigmented and erythematous papules (A-B) that later transform into pendulous folds (C).

Immunohistochemistry revealed the lymphocytes to be predominantly CD3 positive cells. In addition, a high CD4:CD8 ratio of 8:1, reduced CD7 expression, and negative CD8 expression were also consistent with mycosis fungoides (Figures 3A-3D). Orcein stain showed a reduction in elastic fibers, consistent with slack skin syndrome. Repeat CT of the chest showed progression of ground-glass opacities in the right lung apex, chronic multilobar bronchiectasis with

catrization atelectasis, cardiomegaly and dilated pulmonary artery compatible with pulmonary hypertension.

Punch biopsies of the left forearm and left lower back showed an atypical lymphoid infiltrate with epidermotropism and granulomatous dermal inflammation (Figure 2).

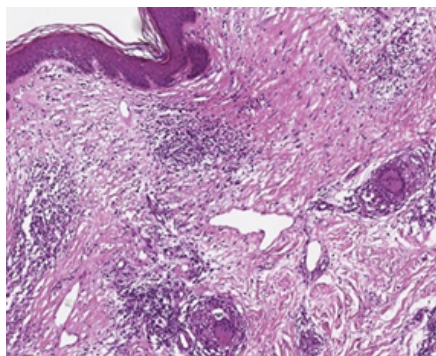


Figure 2: Punch biopsy of L forearm shows an atypical lymphoid infiltrate with multinucleated giant cells, deep granulomas. H&E. 40X.

Further invasive workup such as additional lung biopsies or bronchoscopic studies was not pursued because the previous studies were unremarkable. The patient continued treatment with maintenance 10 mg daily prednisone therapy, topical steroids, and bronchodilators combined with inhaled steroids. Six months later, the patient has progressive disease in her lungs but no new skin lesions.

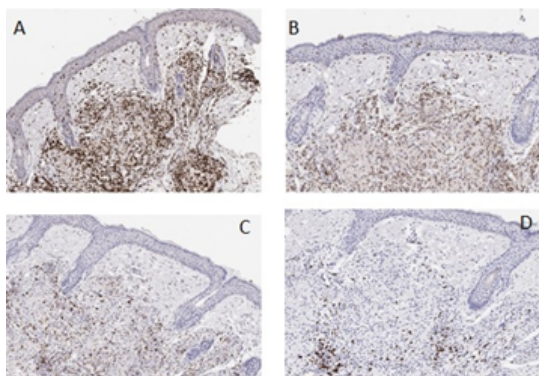


Figure 3: Immunohistochemistry shows lymphoid infiltrate to be positive for CD3 (A) and CD4 (B) expression with reduced CD7 expression (C) and negative for CD8 (D). 40X.

Discussion

Granulomatous cutaneous T-cell lymphomas are rare and include granulomatous mycosis fungoides and granulomatous slack skin syndrome [1]. Clinically, granulomatous MF lesions are similar to erythematous patches and plaques typical of MF. The distinguishing feature of GSS is the development of pendulous skin folds in the intertriginous regions, resembling cutis laxa [1,2]. Skin lesions in the nonintertriginous regions tend to not undergo this transformation, which is the result of elastophagocytosis by histiocytic giant cells [1-3].

Histologically, granulomatous MF and GSS have overlapping features except the loss of elastin, which is present in GSS. The atypical infiltrate can be diffuse, nodular, perivascular or periadnexal. Epidermotropism is often not prominent or absent [1]. The pattern of granulomatous inflammation seen on histology can resemble sarcoidosis, granuloma annulare, and infectious granulomas [2]. This patient exhibits typical cutis laxa-like changes in her inguinal region and to a lesser extent axilla, which combined with the histology showing abundant multinucleated giant cells, deep granulomas, and atypical infiltrate with focal epidermotropism meet the criteria for GSS. The reduction in elastic fibers in the skin biopsy corroborates this diagnosis.

The unique feature of this patient's case of GSS is her coexisting granulomatous lung involvement. Extracutaneous involvement in GSS and granulomatous MF is rare and only previously described in two case reports. There is one GSS case reporting lymph node, liver and spleen involvement [4]. A case of granulomatous MF with lung and thyroid involvement has been reported, but without a lung biopsy [5]. Lung involvement in CTCL is uncommon and often discovered incidentally on autopsy. In one retrospective study, lung involvement was present in 6 out of 710 patients with confirmed CTCL over a 9-year period. 122 of the 710 patients had pulmonary radiographic abnormalities. In this population, the radiological appearance of the cancer was most commonly either a solitary nodule or multiple progressing nodules. Although these patients had few respiratory symptoms, the lung involvement by CTCL carried a poor outcome [6]. This patient's presentation is distinct because her lung disease is slowly progressive and characterized by infiltrative lesions on CT scan.

Other possible etiologies that may contribute to the patient's pulmonary findings include radiation induced lung disease given her multiple radiation treatments, reactive granulomatous conditions, cryptogenic infection, and sarcoid-lymphoma-syndrome. However, the progressive nature of the lung disease evidenced on repeat CTs suggests that radiation-induced scarring is not the sole factor. Infectious studies were unremarkable, and there are no clinical or historical elements that favor reactive conditions such as hypersensitivity or autoimmune disease. The patient's loosely packed non-necrotizing granulomas without hyaline sclerosis are inconsistent with sarcoidosis, although angiotensin-converting enzyme (ACE) level and beta 2 microglobulin are elevated. Notably, an association between granulomatous MF and increased serum level of angiotensin-converting enzyme has been previously reported [4,7]. Furthermore, elevated beta-2-microglobulin is nonspecific and can be seen in non-granulomatous CTCL [8]. Sarcoid-lymphoma-syndrome, first described in 1965, is a well-known phenomenon characterized by the occurrence of sarcoid-like granulomas most commonly observed in patients with Hodgkin disease [1,9]. Although the exact nature of the association between sarcoidosis and lymphomas is unclear, there is some evidence to suggest that sarcoidosis may be a paraneoplastic process of lymphoma or can serve as a prognostic factor [10]. Because the patient's lung pathology is histologically inconsistent with sarcoidosis, it likely represents lung involvement by granulomatous CTCL.

References

1. Kempf W, Ostheeren-Michaelis S, Paulli M, Lucioni M, Wechsler J, et al. (2008) Granulomatous Mycosis Fungoides and Granulomatous Slack Skin: A Multicenter Study of the Cutaneous Lymphoma Histopathology Task Force Group of the European Organization for Research and Treatment of Cancer (EORTC). *Arch Dermatol* 144: 1609-1617.

2. Shah A, Safaya A (2012) Granulomatous slack skin disease: a review in comparison to mycosis fungoides. *J Eur Acad Dermatol Venereol* 26: 1472-1478.
3. Goldsztajn KO, Troupe BM, Ribeiro-Lenzi ME, Cuzzi T, Ramos-e-Silva M (2012) Granulomatous slack skin: Histopathology diagnosis preceding clinical manifestations by 12 years. *J Dermatol Case Rep* 6: 108-112.
4. Liu J, Jin H, Liu Y, Zhang H, Fang K, et al. (2005) Granulomatous slack skin with extracutaneous involvement. *Arch Dermatol* 141: 1178-1179.
5. Gomez de la Fuente E, Ortiz PL, Vanaclocha F, Rodriguez-Peralto JK, Iglesias L (2000) Aggressive granulomatous mycosis fungoides with clinical pulmonary and thyroid involvement. *Br J Derm* 142: 1026-1029.
6. Baser S, Onn A, Lin E, Rodolfo MC, Duvic M (2007) Pulmonary manifestations in patients with cutaneous T-cell lymphomas. *Cancer* 109: 1550-1555.
7. Metzler G, Schlagenhauff B, Krober SM, Kaiserling E, Schaumburn-Lever G, et al. (1999) Granulomatous mycosis fungoides: report of a case with some histopathologic features of granulomatous slack skin. *Am J Dermatopathol* 21: 156-160.
8. Hassel JC, Meier R, Joller-Jemelka H, Burg G, Dummer R (2004) Serological immunomarkers in cutaneous T cell lymphoma. *Dermatology* 209: 296-300.
9. Bichel J, Brincker H (1965) Treatment of pruritus in Hodgkin's disease and in reticulum cell sarcoma. *Scand J Haematol* 2: 85-90.
10. Goswami T, Siddique S, Cohen P, Cheson BD (2010) The sarcoid-lymphoma syndrome. *ClinLymphoma Myeloma Leuk* 10: 241-247.