Necrobiotic Xanthogranuloma Associated With a Benign Monoclonal Gammopathy

Anne E. Burdick, MD, MPH; Jany Sanchez, MD; George W. Elgart, MD

Necrobiotic xanthogranuloma (NXG) is a disorder characterized by indurated, yellow-red nodules or plaques, primarily involving the face and, less frequently, the trunk and extremities. NXG may be associated with paraproteinemia, multiple myeloma, and hypertension. Histologically, xanthogranulomatous features with hyaline necrosis or necrobiosis are present. No first-line treatment has been established. This disease is a chronic process, and a patient's prognosis depends on the degree of extracutaneous involvement and the presence of visceral malignancies. We describe a patient with typical cutaneous and histologic findings of NXG with an associated monoclonal gammopathy.

Cutis. 2003;72:47-50.

Case Report

A 57-year-old Hispanic woman presented to the Jackson Memorial Hospital Dermatology Clinic in Miami, Florida, with a 7-year history of progressive darkening of the skin on her upper body and eyes with associated burning pain. Her medical history was significant for hepatic cirrhosis of unknown etiology. Current medications included bumetanide and spironolactone. Physical examination of the face revealed a well-defined, red-brown, indurated plaque involving the periorbital region bilaterally (Figure 1). There were confluent, well-demarcated, atrophic yellow-brown plaques with red-orange borders and central telangiectasia on the upper back, chest (Figure 2), and arms. The lesions were not ulcerated. The physical examination also revealed hepatomegaly and an abdominal hernia. Results of laboratory studies revealed normal values of chem-7, calcium, phosphorus, bilirubin, fasting lipids, a complete blood count, and platelets. The patient's aspartate aminotransferase and alanine aminotransferase levels were elevated at 117 U/L (reference range, 15–37 U/L) and 54 U/L (reference range, 15–37 U/L), respectively. Her alkaline phosphatase level also was elevated at 362 U/L (reference range, 50–136 U/L), as was her erythrocyte sedimentation rate at 36 mm/h, (reference range, 0–15 mm/h). Results of antimicrosomal antibody, rheumatoid factor, antinuclear antibody, and serological tests for viral hepatitis were negative. Serum protein electrophoresis revealed the presence of a monoclonal peak with hypoalbuminemia. Immunoprotein electrophoresis showed a paraprotein peak in the κ-globulin fraction of IgG.

Results of biopsies of the cheek and back revealed marked epidermal atrophy with a band of foamy cells in the dermis (Figure 3). Palisading granulomas were present with relatively acellular foci surrounded by histiocytes. Giant cells were present, while cholesterol clefts were absent (Figure 4). These features were interpreted as a xanthogranuloma with focal necrobiosis.

A complete bone survey showed collapse of multiple thoracic and lumbar vertebral bodies with extensive osteopenia. Results of an abdominal ultrasound demonstrated a slight increase in echogenicity of the liver, as well as a 1.5-cm echogenic area in the spleen, thought to represent a hemangioma. The patient was subsequently referred to a hematologist/oncologist for further evaluation, including a bone marrow aspirate smear and biopsy, which showed xanthogranulomata within the medullary tissue and increased plasma cells. Results of special stains for acid-fast bacilli and fungal organisms were negative. Immunostains demonstrated numerous plasma cells containing λ-immunoglobulins and a few cells with κ-immunoglobulins. These findings correlated with the monoclonal IgG-λ serum immunoglobulin peak. No evidence of malignancy was demonstrated; therefore, no treatment was recommended.

Accepted for publication October 9, 2002.

From the Department of Dermatology and Cutaneous Surgery, University of Miami School of Medicine, Florida.
Reprints: Anne E. Burdick, MD, MPH, Department of Dermatology and Cutaneous Surgery, University of Miami School of Medicine, 1600 NW 10th Ave, RMSB 2023A, Miami, FL 33136 (e-mail: aburdick@med.miami.edu).

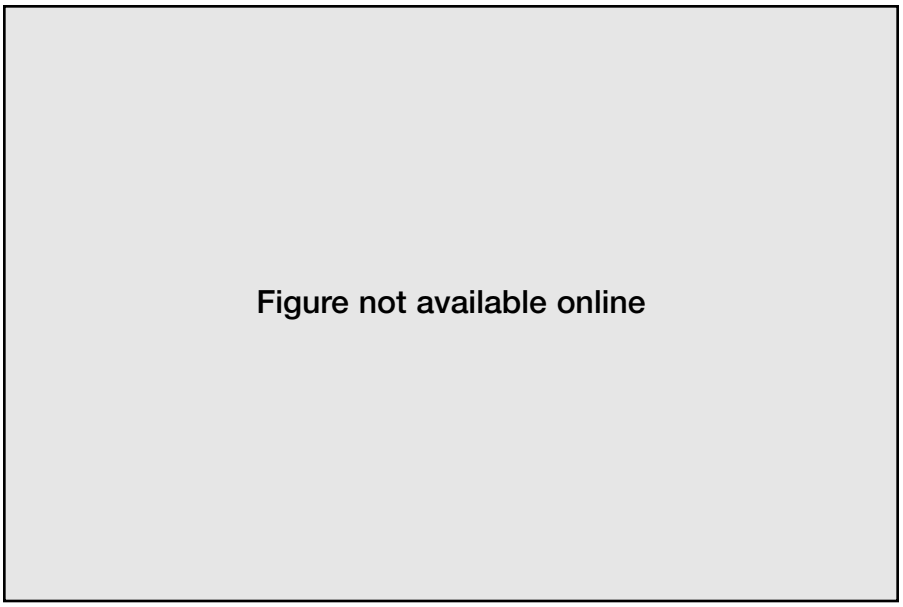

Figure 1. Periorbital indurated red-brown plaques.

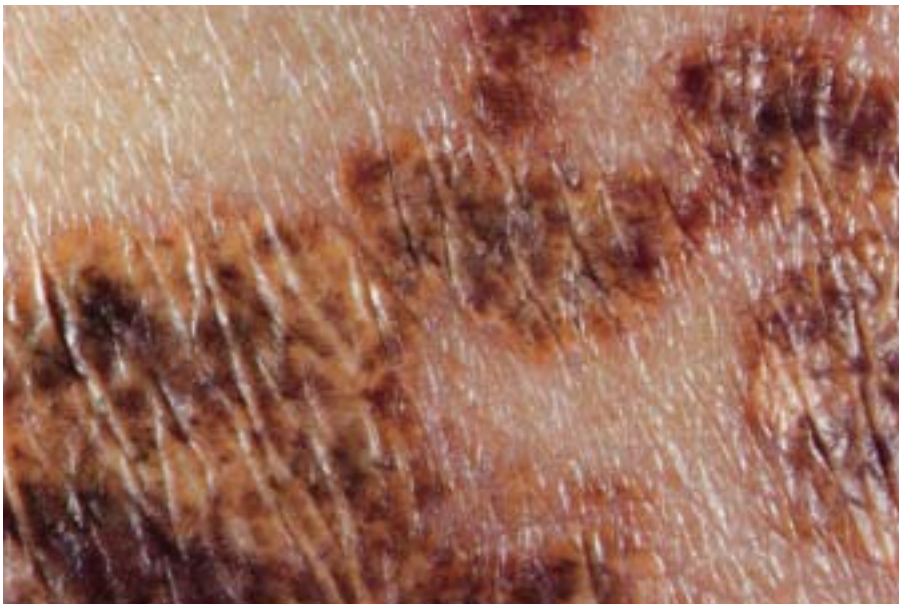

Figure 2. Atrophic yellow-brown plaques on the chest.

Comment

Kossard and Winkelmann[1] first described necrobiotic xanthogranuloma (NXG) in 1980 with a report of 8 patients who presented with distinct cutaneous and subcutaneous xanthomatous plaques with frequent ulcerations and atrophy. Paraproteinemia and lymphoproliferative disease were common associated findings. Approximately 50 additional cases have been reported since that time. The pathogenesis of NXG is unclear. The lesions usually consist of firm papulonodules that enlarge into well-demarcated, indurated yellow-red plaques that may show atrophy with telangiectasias or areas of ulceration. Although most patients are asymptomatic, some report pain or burning sensation.[2] A total of 85% of reported cases have periorbital involvement.[3] Oral mucosal erosions are sometimes present. Hepatosplenomegaly also has been noted in approximately 20% of patients.[3] NXG may be associated with multiple myeloma, hypertension, neuropathy, neoplastic syndrome, arthropathy, primary biliary cirrhosis, and Graves' disease. Onset usually occurs between 50 and 70 years of age, with the same rate of incidence for men and women.[3]

Monoclonal gammopathies consist of identical immunoglobulin proteins formed by the clonal proliferation of plasma cells. These gammopathies may occur in association with multiple myeloma,

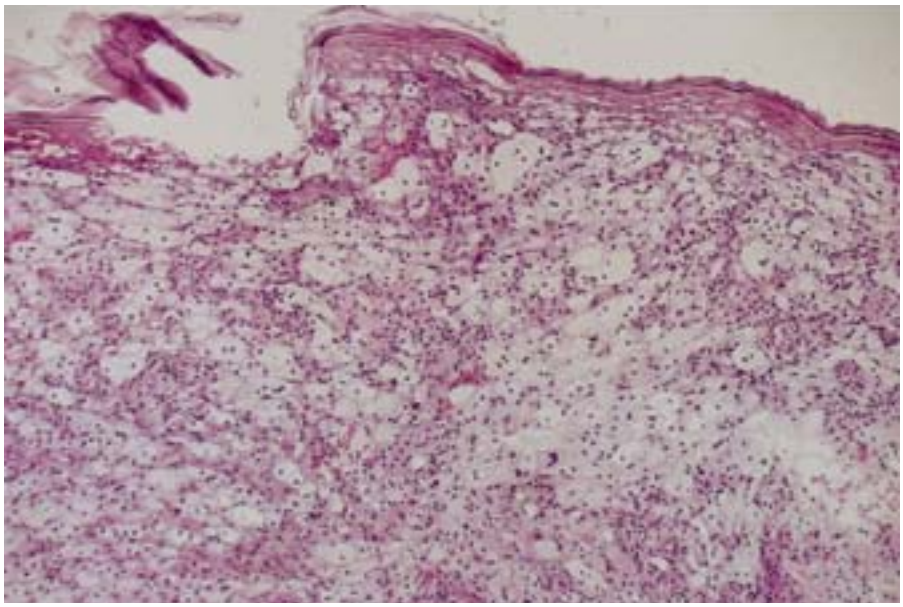

Figure 3. Epidermal atrophy with foamy cells in the dermis (H&E, original magnification ×10).

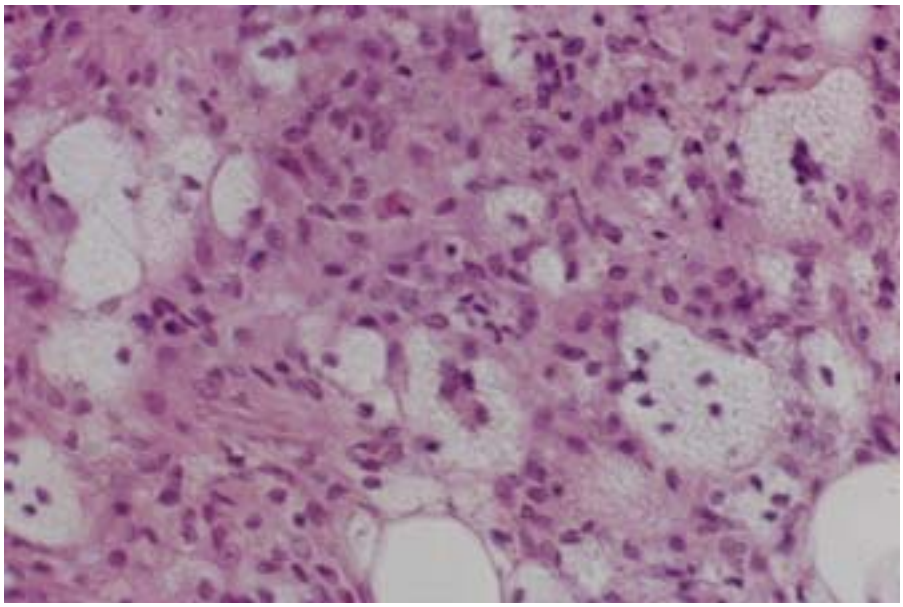

Figure 4. Giant cells with palisading granulomas (H&E, original magnification ×40).

macroglobulinemia, cryoglobulinemia, amyloidosis, or lymphoma, or as an isolated finding. It is estimated that nearly 80% of patients with NXG display an IgG monoclonal gammopathy in which the κ light chains are more prevalent than the λ light chains.[3]

Although an association between NXG and paraproteinemia is well accepted, the underlying pathologic mechanisms remain unclear. Several patients have developed giant cell granulomas of pulmonary or myocardial tissues, suggesting a predilection for granuloma formation in NXG.[4]

Histopathologic findings of NXG are distinctive, with histiocytes and giant cells forming palisading xanthogranulomas seen in conjunction with zones of necrobiotic connective tissue. Both Touton and foreign body giant cells are found within these distinct zones. The necrobiotic regions frequently contain cholesterol crystals, though this was not evident in our patient. Surrounding regions often reveal many bizarre multinucleated giant cells. These characteristic findings, along with the presence of lymphoid nodules, allow histologic distinction of NXG from necrobiosis lipoidica diabeticorum, which may appear clinically similar.[5]

NXG is a chronic process for which the prognosis depends on the degree of extracutaneous involvement, the presence of visceral malignancies

(ie, multiple myeloma), as well as proper wound care if erosions occur. Although no first-line therapy has emerged, treatment options for NXG include low-dose alkylating agents such as chlorambucil[3] and melphalen,[6] radiation therapy,[3] plasmapheresis,[2] and recombinant interferon alfa-2b.[7] Temporary remissions of skin lesions have been obtained with plasmapheresis and radiation therapy.[2]

REFERENCES

1. Kossard S, Winkelmann RK. Necrobiotic xanthogranuloma with paraproteinemia. *J Am Acad Dermatol*. 1980;3:257-270.
2. Finelli LG, Ratz JL. Plasmapheresis: a treatment modality for necrobiotic xanthogranuloma. *J Am Acad Dermatol*. 1987;17:351-354.
3. Mehregan DA, Winkelmann RK. Necrobiotic xanthogranuloma. *Arch Dermatol*. 1992;128:94-100.
4. Daoud MS, Lust JA, Kyle RA, et al. Monoclonal gammopathies and associated skin disorders. *J Am Acad Dermatol*. 1999;40:507-535.
5. Le AV, Fenske NA. An unusual granulomatous disease in the elderly. *Arch Dermatol*. 1997;133:1303-1304, 1306-1307.
6. McGregor JM, Miller J, Smith NP, et al. Necrobiotic xanthogranuloma without periorbital lesions. *J Am Acad Dermatol*. 1993;29:466-469.
7. Venencie PY, Le Bras PL, Toan ND, et al. Recombinant interferon alfa-2b treatment of necrobiotic xanthogranuloma with paraproteinemia. *J Am Acad Dermatol*. 1995;32:666-667.