Necrobiotic Xanthogranuloma with Multiple Myeloma and No Periorbital Involvement

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Necrobiotic xanthogranuloma (NXG) is a rare multisystemic disease that manifests as cutaneous inflammatory lesions and has a strong association with paraproteinemia and an increased risk of plasma cell dyscrasias and other lymphoproliferative disorders. Its general skin manifestation is multiple, asymptomatic, indurated nodules or plaques with a yellowish hue which frequently affect the periorbital regions. This case is unusual in that cutaneous lesions developed only at the extremities without periorbital involvement, accompanied by multiple myeloma. (Ann Dermatol (Seoul) 19(1) 22~24, 2007)

Key Words: Multiple myeloma, Necrobiotic xanthogranuloma

INTRODUCTION

Necrobiotic xanthogranuloma (NXG) is a rare disease that manifests as generalized xanthomatous inflammatory skin lesions that are associated with paraproteinemia and other possible lymphoproliferative diseases. It typically presents as indurated yellow-red nodules or plaques, which are often ulcerated, frequently affecting the periorbital regions. Histologically, necrobiotic areas and palisading granulomatous inflammation with xanthomatous histiocytes are typical findings[1]. We report a case of NXG with multiple myeloma in which the NXG developed as subcutaneous nodules and plaques on the extremities, without periorbital involvement.

CASE REPORT

A 66-year-old female presented with five subcutaneous nodules and plaques on her extremities. A physical examination revealed that three on the pretibial area were brownish, hyperpigmented, waxy, indurated plaques and two on the right wrist and thigh were skin-colored, rubbery subcutaneous nodules. The size varied from 1 to 3 cm in diameter (Fig. 1). The lesions were asymptomatic and were detected 7 months ago. The periorbital region was

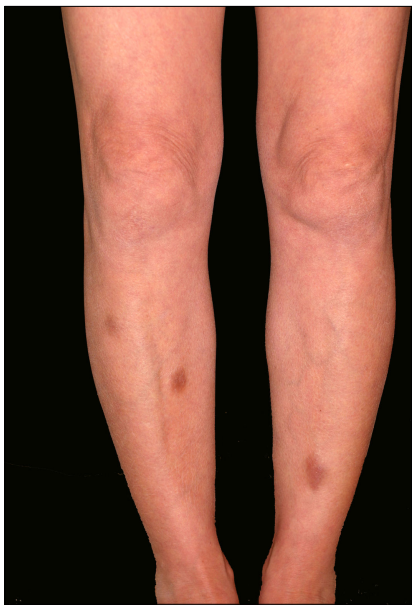

Fig. 1. Brownish, hyperpigmented, indurated plaques on both shins.

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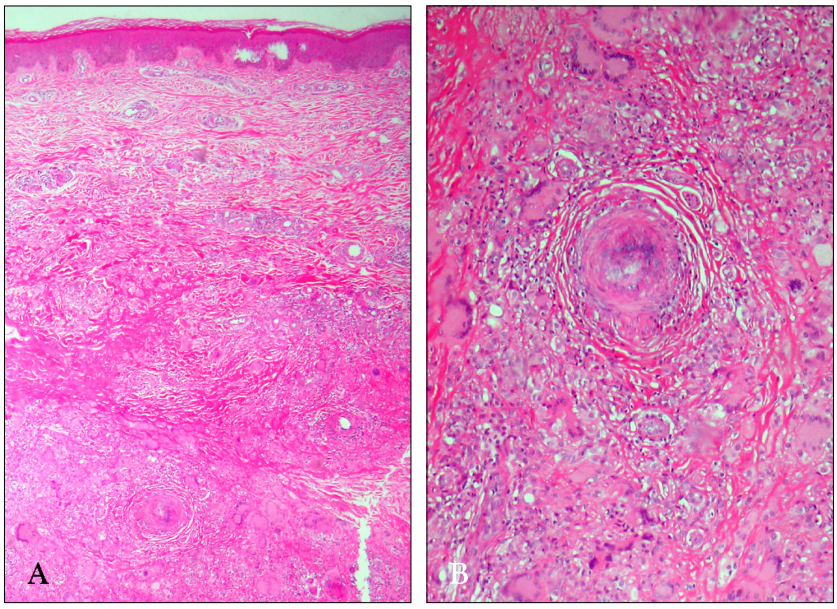

Fig. 2. (A) Xanthogranulomatous infiltrate with zones of necrobiosis, involving the whole dermis (H&E, × 40). (B). Numerous multinucleated giant cells and necrobiosis (H&E, × 200).

not involved. The patient had been investigated for a recent weight loss and generalized weakness 1 month before her visit to our clinic. The hemoglobin level was 6.8 g/dL (normal 14-18). The leukocyte count was 6380/mm^3, with 49.8% polymorphonuclear leukocytes and 37.8% lymphocytes. There were 307,000 platelets/mm^3. The sedimentation rate was 95 mm/hour. The total protein level was elevated at 13.05 mg/dL (normal 6-8) with a low albumin level of 2.62 mg/dL (normal 3-5). Serum and urine protein immunoelectrophoresis revealed monoclonal gammopathy, Ig G kappa type. Bone marrow examination showed 30-40% of cellularity mainly composed of mature and immature plasma cells. The patient was diagnosed as having multiple myeloma. The skin lesions were mildly decreased in size during the first cyclic course of chemotherapy with vincristine (0.4 mg daily), adriamycin (10 mg daily), dexamethasone (40 mg daily). A histology examination of the skin biopsy specimen from the pretibial indurated plaque revealed an orthokeratotic epidermis and a dense granulomatous reaction with areas of severe necrobiosis in the dermis (Fig. 2A). The granulomas were composed of many multinucleated bizarre foreign-body cells, Touton giant cells, foamy histiocytes, epithelioid cells and some lymphocytes (Fig. 2B). Immunohistochemical staining showed some CD 8$^+$ cells in the granulomatous infiltrates but they tested negative to the Lambda and Kappa light chain.

DISCUSSION

In NXG, periorbital involvement is the most frequent finding. The eyelid lesion often resembles xanthelasma, with the exception that they are deep, firm, and indurated on palpation. Mehregan et al.[2] reported that the periorbital region was the most common site of involvement in 39 out of 48 cases they encountered. All cases had multiple lesions, not only the periorbital lesions, but also lesions on the trunk, face, arms, thighs, and lower parts of the legs. However, cases without periorbital presentations, such as in our case, are rare. A review of the relevant literature revealed there to be 12 cases of NXG without periorbital presentation[2-8]. The clinical presentations of those cases were yellowish papules, nodules and plaques that were sometimes ulcerated in any part of the body, with the exception of the periorbital area. Among the 12 cases, 8 cases were accompanied with paraproteinemia and 4 cases showed laboratory abnormalities including cryoglobulinemia, low complement levels, anemia, and leukopenia without evidence of paraproteinemia. NXG is a distinctive form of inflammatory xanthoma and is believed to be a cutaneous marker of systemic disease with serum protein abnormalities, including monoclonal IgG paraproteinaemia. Bone marrow plasmacytosis in these patients are common, but multiple myeloma is rare.

A clinical and histological examination shows that the most important differential diagnosis with NXG

is necrobiosis lipoidica (NL). However, the necrobiotic changes in NXG are more extensive, and extend deeper into the subcutis than NL. A granulomatous reaction with atypical foreign body giant cells and Touton giant cells is a characteristic histological feature. Vasculopathic changes are characteristic of NL cases associated with systemic disease and include luminal thrombosis and granulomatous vasculitis[9]. Cholesterol clefts are more prominent in NXG, whereas lipid deposition is more characteristic of NL[2]. However, the absence of cholesterol clefts does not exclude NXG. Muscardin LM et al.[3] reviewed 41 cases in the literature and found cholesterol clefts in only 19 cases. Other disorders in the clinical differential diagnosis of NXG include xanthelasma, sarcoid, plane xanthoma and xanthoma disseminatum. Especially in the cases of periorbital involvement, xanthelasma should be considered as a differential diagnosis. However the histiocytes and giant cells of NXG lesions are often foamy but, unlike xanthelasma, foam cells do not predominate.

The treatment of NXG is difficult and the course is usually chronic and progressive. Surgical removal is generally not recommended due to the potential of a recurrence. Combinations of melphalan and prednisone, and cyclophosphamide have been reported to be successful. Pulsed high-dose oral dexamethasone, recombinant interferon alpha-2b and plasmapheresis are considered as treatment modalities[10]. In our case, systemic chemotherapy for multiple myeloma had some beneficial effect.

NXG is considered a systemic disease whose development affects internal organs, such as myocardium, the larynx, lungs, intestine and ovaries[2]. Therefore following up the patient with echocardiographic monitoring, hepatic MRI and chest X-ray is recommended. In conclusion, this is the first case histologically showing typical NXG, which did not have the typical presentation of periorbital lesions and accompanying multiple myeloma.

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