

A case of necrobiotic xanthogranuloma without paraproteinemia presenting as a solitary tumor on the thigh

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A 82-year-old Korean woman had had a 6-month history of an asymptomatic, flat, hard, red to brown tumor on her right thigh. This lesion had been slowly enlarging with an advancing margin. She had noted gradually developing pain associated with necrosis and ulceration on the lesion. Examination revealed a solitary, 8 × 7.5 cm, yellow to dark red, telangiectatic tumor with multiple areas of punched out ulceration and a peripheral elevated yellowish margin on the right inner upper thigh (Fig. 1). No clinically similar lesions on the periorbital area or other sites were seen. Histologic examination revealed a massive palisading granulomatous infiltration with several layers of extensive bands of necrobiotic zone in the entire dermis and deep subcutaneous tissue (Fig. 2a). In the granulomatous infiltrate in the dermis and subcutis, many various-shaped, some bizarre, angulated, foreign-body type multinucleated giant cells, many Touton giant cells, and a few Langhans giant cells were found to be scattered (Fig. 2b). There were numerous xanthomatized histiocytes. Dense infiltration of lymphoplasmic cells was seen in the periphery of the granuloma and perivascularly. Conspicuous granulomatous panniculitis composed of lymphoplasmic cells, polymorphonuclear cells, foam cells, and Touton and foreign-body giant cells was also seen. However, cholesterol clefts and lymphoid follicles were not seen. Subcutaneous septae were widened by necrobiotic change and fibrosis with thrombosed large vessels. Gram, Gomori-methenamine silver and acid-fast stains were negative. The necrobiotic areas were positive to alcian blue. Laboratory investigation revealed elevated white blood cell counts, anemia and elevated erythrocyte sedimentation rate. The following parameters were within the normal range: lipids, glucose, renal and liver function tests, serum complements, serum immunoglobulins, cryoglobulins and antinuclear antibodies. The findings of chest X-ray, skull X-ray and electrocardiography were normal. Serum electrophoresis and serum immunoelectrophoresis revealed no abnormality. The patient was diagnosed as having necrobiotic xanthogranuloma without paraproteinemia. She was treated with oral steroid (0.5–0.6 mg/kg) and NSAIDs for 1 month with partial improvement of pain and the lesion ceased to enlarge. In the following 1 year of follow-up, with only intermittent NSAIDs, her lesion did not progress and there were no signs of systemic involvement or new skin lesions.

Discussion

Necrobiotic xanthogranuloma (NXG) is a rare xanthomatous disorder with distinct clinicopathological findings. There are less than 80 reported cases, including a large series analyzed by Mehregan *et al.*,¹ in the English literature.^{1–10} NXG usually presents with two or more indurated yellow-red papules, nodules, or plaques sometimes with ulceration.^{1,2} The most common sites are the periorbital area, followed by the trunk, face, arms, upper thighs, legs, shoulders, and buttock.^{1–5} Histologically, necrobiotic areas and palisading granulomatous inflammation with xanthomatous histiocytes are characteristic.^{2,6,7} NXG can be differentiated from

necrobiosis lipoidica diabetorum (NLD) by a more dense infiltrate with a greater proportion of foamy histiocytes, Touton giant cells and angulated giant cells and a wider, deeper band of necrobiosis.^{8,9} In our case of NXG, numerous xanthomatous cells and an absence of diabetes helped the differentiation from NLD. Most cases of NXG are in periorbital lesions^{1–4} and it is associated with paraproteinemia in up to 80% of cases.^{1–4} The deposition of immunoglobulin/lipid complexes might lead to a xanthogranulomatous reaction of NXG.^{2,3} A small proportion of patients subsequently developed myeloma.^{1,4} Leukopenia is common, and cryoglobulinemia and abnormalities of complements can be detected.^{1–5} NXG can be associated with malignancy^{1,4,8} and can involve



Figure 1 (a) A solitary, red to brown plaque with multiple ulcerations and a peripheral elevated yellowish margin on the inner upper thigh

internal viscera such as the lungs, heart and liver.⁵ As in our case, some 20% of patients with NXG do not have paraproteinemia and cases of NXG with neither paraproteinemia nor significant laboratory abnormality have been reported.^{1,7,9} Another clinically similar case to ours was recently reported in a 60-year-old white woman who presented with a solitary plaque on the buttock without paraproteinemia, leukopenia or systemic lesions.⁷ This and our case could represent a solitary variant of NXG without paraproteinemia. However, paraproteinemia may pre- or post-date the appearance of skin lesions by up to 10 years.^{4,8} NXG with paraproteinemia can be resistant to various treatments with such as chemotherapies, plasmapheresis, radiotherapy or interferon α and can have a fatal outcome as a result of the subsequent hematolymphoid malignancy or myeloma.^{4,8} A recent report showed that

recalcitrant NXG with paraproteinemia responded to pulsed high-dose oral dexamethasone plus oral prednisolone.¹⁰ The skin lesions of our patient did not progress with only NSAIDs for the following 1 year without any systemic upset. For improved survival, aggressive treatments such as cytotoxic agents and high-dose steroids may not be appropriate in our elderly patient. Our case had no malignancy, periorbital involvement or systemic involvement, which indicate main morbidity of NXG. However, the absence of paraproteinemia and systemic involvement at presentation does not mean that the patient will not eventually develop them. Periodic examinations for the rest of the patient's life are mandatory to detect the development of associated malignancy.

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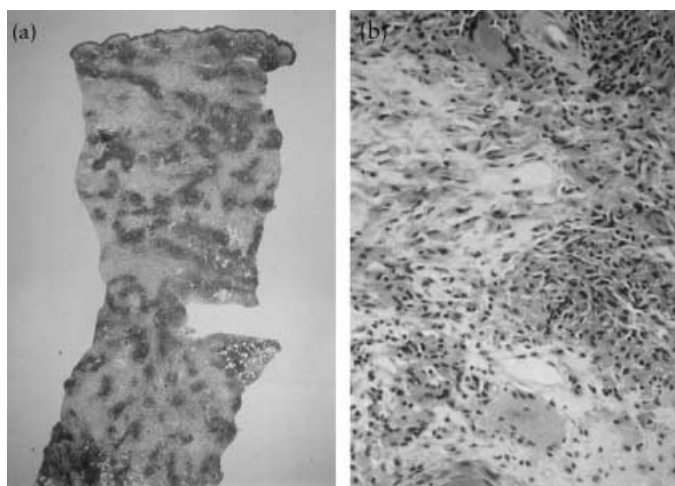


Figure 2 (a) A dermal and subcutaneous massive xanthogranulomatous infiltrate with zonal necrobiosis of collagen ($\times 20$). (b) Prominent infiltrate of xanthomatized histiocytes and giant cells with perivascular lymphoplasmic cells (H&E, $\times 100$)

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Cameo

Anaphylaxis due to burdock

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A 53-year-old Japanese man, with a history of developing urticaria (once after consuming mackerel and 10 times after consuming boiled burdock, carrot, curry, and rice), presented with redness over his entire body and dyspnea 1 h after eating boiled burdock. Physical examination revealed a low blood pressure of 64/29 mmHg and stridor, together with striking redness of the whole body; he was diagnosed to be in anaphylactic shock.

He recovered from the anaphylactic shock with subcutaneous injection of epinephrine (1 mg) and an intravenous drip of lactate Ringer's solution containing hydrocortisone (100 mg) and dexamethasone (8 mg).

Laboratory examination and skin prick test were performed 3 weeks after his first visit. The total immunoglobulin E (radioimmunosorbent test) level was 190 IU/mL, and specific immunoglobulin E for mackerel and carrot was found to be negative. Skin prick test was performed on the volar forearm with burdock, carrot, and turmeric after he had not taken any medication for 1 week. It was also conducted in normal healthy persons at the same time. A skin prick was made with a PRICK-LANCETTER® (made in Sweden) using 1% histamine chloride solution and 0.9% saline solution as positive (3+) and negative (–) controls, respectively. For skin prick tests, burdock and carrot were employed in their boiled and raw conditions. Turmeric powder was diluted to 1% and 10% in petrolatum. Skin prick tests were judged according to the recommendations of the European Academy of Allergy and Clinical Immunology (Shono M. The skin test learned in Finland. *Hifubyō-Shinryō* 1999; **25** (3): 255–269; Bernstein IL. Proceedings of the task force on guidelines for standardizing old and new technologies used for the diagnosis and treatment of allergic diseases. *J Allergy Clin Immunol* 1988; **82**: 487–526). The results of the skin prick tests (Table 1) were positive for raw and boiled burdock and carrot, but negative for turmeric (Fig. 1). Two normal healthy controls showed negative responses to all substances.

This is the first case report of anaphylaxis due to burdock.

Discussion

There have been scattered case reports of anaphylactic-type food allergy to vegetables, e.g. celery, peanuts, and carrot,^{1–3} but none on anaphylaxis due to burdock. Burdock (*Arctium lappa*), which belongs to the Compositae (Asteraceae) family,

is a biennial plant. Its carrot-like root is commonly cooked and eaten in Japan. As far as we know, only one other case of allergy to burdock has been reported.⁴ This involved contact dermatitis to burdock, and no immediate-type allergy has been documented in the past. The reason for this may be that burdock is not eaten in Western countries.

Table 1 Results of skin prick test

	Wheal size (mm)	Score
Boiled burdock	3 × 4	(3+)
Boiled carrot	3 × 3	(3+)
Raw burdock	3 × 4	(3+)
Raw carrot	3 × 3	(3+)
1% turmeric diluted with petrolatum	0 × 0	(-)
10% turmeric diluted with petrolatum	0 × 0	(-)
1% histamine chloride	4 × 4	(3+)
Normal saline	—	(-)

Our case developed anaphylaxis after eating burdock, demonstrating immediate-type allergy by skin prick test. We do not believe that the so-called pseudo-allergen contained in burdock played a role in this case, because skin prick tests in two other normal individuals were negative. We also found immediate-type hypersensitivity to carrot in our case. Thus, our patient might develop urticaria by ingesting carrot only. It is not clear whether there are common antigenic substances or allergic cross-reactivity between burdock and carrot.

Although specific immunoglobulin E antibody for burdock is not available commercially, we checked the patient's immediate-type allergy to burdock by skin prick test. It was detected in both the boiled and raw condition. There was no significant difference in skin reactivity between raw and boiled burdock. From these results, we believe that the antigenic substance of burdock is heat-stable. Skin prick test can examine food in the edible state, and can judge the responses quantitatively using positive (histamine) and negative (saline) controls.

Recently, it has come to our attention that burdock root is used as an ingredient in herb tea or folk medicines in Western countries. Therefore, it is possible that similar cases may arise world-wide.

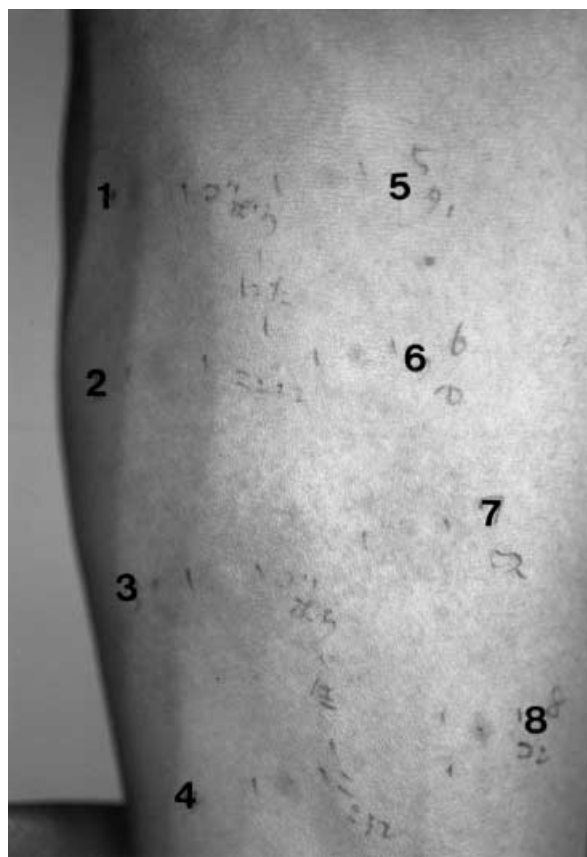


Figure 1 Skin prick tests performed on the flexor surface of the forearm (left: 1, boiled burdock; 2, boiled carrot; 3, raw burdock; 4, raw carrot; right: 5, 1% turmeric; 6, 10% turmeric; 7, histamine chloride; 8, normal saline)

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