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Metaplastic Bone Formation in the Subcutaneous Nodule of a Patient with Mixed Connective Tissue Disease

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Cutaneous ossification is a rare phenomenon in collagen diseases, despite the rather frequent occurrence in these diseases of dystrophic calcinosis. We observed metaplastic woven bone formation associated with calcification in biopsy material obtained from a 49-year-old woman suffering from mixed connective tissue disease together with multiple subcutaneous indurations. This is the first case of the presence of metaplastic bone formation in a patient with mixed connective tissue disease. ***Key words: cutaneous ossification; collagen disease.***

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Cutaneous ossification is uncommon in collagen disease, although calcinosis cutis is occasionally seen in diseases such as scleroderma and dermatomyositis. We report the first case of cutaneous ossification observed in a patient with mixed connective tissue disease (MCTD).

CASE REPORT

A 49-year-old Japanese female was referred to us by one of the internists of our hospital concerning multiple subcutaneous indurations in her flanks and buttocks that had gradually enlarged during 1 year. She had been treated with oral prednisone 5 mg daily for 12 years since 1983 under the diagnosis of MCTD because of the presence of Raynaud phenomenon, sausage-shaped fingers with ulceration of the fingertips, and a slight sclerotic change of the distal part of the forearms. She showed an exceedingly high titer (1:163,840) of circulating extractable nuclear antigen, being positive for anti-ribonucleoprotein antibody (1:1,280) and negative for Sm antigen. Serum antinuclear antibodies were positive (1:2,560) with a speckled pattern, but anti-DNA antibodies were negative. She also had a history of total thyroidectomy and radiotherapy for a papillary carcinoma of the thyroid gland in 1990. On physical examination, there were ill-defined, irregularly-shaped, rock-hard subcutaneous nodules around her upper arms, waist, and buttocks, where she did not recall any special preceding trauma or hemorrhage. She had kept showing low (7.8–8.6 mg/dl) serum calcium and high (4.1–5.0 mg/dl) serum phosphorus levels (normal range: 8.6–10.5 mg/dl, 2.4–4.2 mg/dl, respectively). Her serum levels of alkaline phosphatase had tended to be lower during her clinical course (53 to 164, normal 112–330 IU/l).

Under a clinical diagnosis of calcinosis cutis, we performed skin biopsy from the induration of the left buttock. The specimen stained with hematoxylin and eosin revealed a polymorphous mass of bone in the dermis and subcutaneous tissue (Fig. 1) together with calcium deposition around the bony tissue, confirmed by von Kossa's reaction (data not shown). The bony tissue contained some lacunae-like structures but no detectable osteocytes, osteoclasts or Haversian canals. Polarized-light view examination of the bony area (Fig. 1, arrows) showed a clear criss-cross pattern of woven bone formation (Fig. 2).

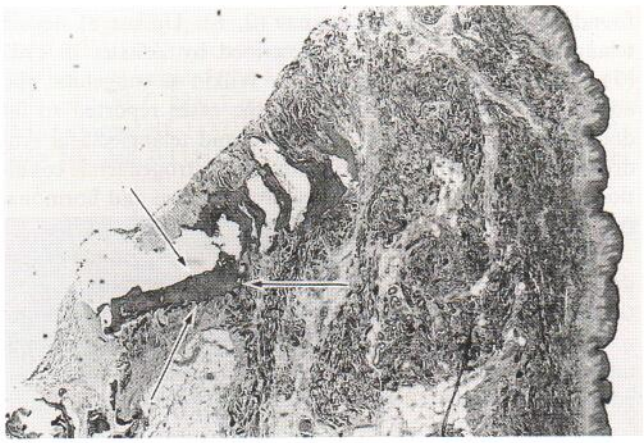

Fig. 1. Histopathologic findings. In the deep dermis there are irregularly shaped masses of bone (hematoxylin and eosin, magnification ×12.5).

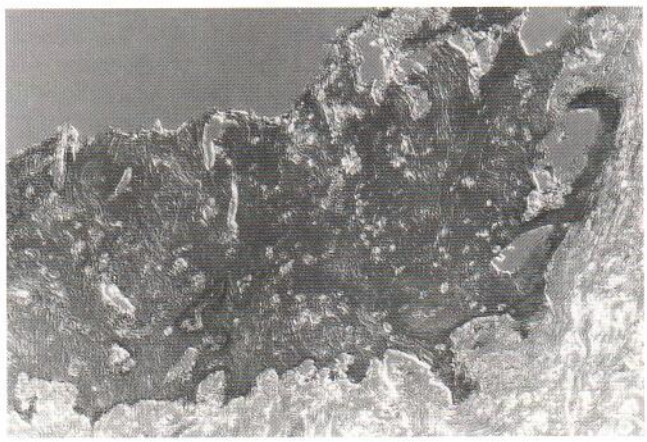

Fig. 2. Polarized-light view of the area in Fig. 1 indicated with *arrows*. Bony tissues were displayed by the criss-cross pattern of collagen fibers (×125).

DISCUSSION

This patient is the first case of MCTD in which ossification was found in the dermis. Cutaneous ossification itself is a relatively unusual event. Burgdorf & Nasemann (1) found only 35 cases of bone formation out of 20,000 skin biopsies. Although there were 3 cases of cutaneous ossification secondary to non-neoplastic conditions, i.e. 2 cases of trauma and one of pyogenic granuloma, they found no cases of cutaneous ossification secondary to autoimmune connective tissue disease. In another study reported by Roth et al. (2), 213 out of 366 cases of secondary ossification were associated with non-

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neoplastic conditions. Again there were only 2 cases secondary to autoimmune connective tissue disease, i.e. one with dermatomyositis (3) and another one with scleroderma (4). Despite two subsequent cases of morphea (5, 6), there has been no report on the presence of bony tissue associated with MCTD in the literature.

As to the histogenesis of cutaneous ossification, the tissue induction theory has long been accepted, according to which fibroblastoid mesenchymal cells are activated to differentiate into bone-forming cells (2). In our case, we think that immune-mediated inflammatory reactions in the dermis due to MCTD and abnormal balance of the serum calcium and phosphorus level might have been responsible for the production of calcinosis and for the appearance of osteoblastoid mesenchymal cells, capable of differentiating into bone-forming cells.

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