

Case report

Extensive soft tissue calcification (calcinosis universalis) in systemic lupus erythematosus

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SUMMARY A 21-year-old woman with long-standing systemic lupus erythematosus developed extensive calcification of the soft tissues of the thoracic and abdominal walls and extremities early in her illness, and these calcifications gradually disappeared over the course of her disease. The extent of this calcinosis and apparent spontaneous regression are unusual events in systemic lupus erythematosus.

Soft tissue calcification is commonly associated with progressive systemic sclerosis and with dermatomyositis (Muller *et al.*, 1959a, b). It is less commonly found in systemic lupus erythematosus (SLE). Only few cases of SLE with associated soft tissue calcification have been reported (Keats, 1961; Coltoiu *et al.*, 1968; Kabir and Malkinson, 1969; Savin, 1971; Dubois, 1974; Powell *et al.*, 1974; Quismorio *et al.*, 1975; Budin and Feldman, 1975). No effective therapy for calcification is known, though temporary benefit has been reported with the use of chelating agents and with diphosphonate. No cases of spontaneous remission have been reported to date.

The purpose of this paper is to report an additional case of SLE associated with extensive soft tissue calcification of the extremities and the abdominal and thoracic walls. Our observation of the disappearance of the calcification in this patient following long term observation and treatment for SLE is discussed.

Case report

A 29-year-old woman was noted to have SLE at age 12 when she was initially admitted to hospital for arthritis of both hands, a maculopapular erythematous rash in the malar distribution, and posterior

cervical, submandibular, and inguinal adenopathy. Anaemia, high erythrocyte sedimentation rate, hyperglobulinaemia, positive LE cells, and abnormal Addis count were also noticed on that admission. Many symptoms were observed during the following 7 years including recurrent arthritis, Raynaud's phenomenon, buccal mucosal ulcerations, perforated nasal septum, alopecia, pericardial effusion, membranous glomerulonephritis, and Coombs positive haemolytic anaemia. Prednisone 75 mg daily was started initially, and the joint symptoms cleared.

In the following 4 years she was on prednisone continuously, doses varying from 5 to 80 mg a day depending on the activity of her disease process. Three years after the first symptom of SLE at the age of 15, calcinosis of the arms, legs, axillae, chest, back, buttocks, and abdominal wall was observed (Figs 1 and 2). Biopsy of the skin from the arm revealed dystrophic calcification. At the age of 16 treatment was switched to azathioprine 150 mg a day. At the age of 18 while on azathioprine the patient developed an aplastic crisis, and the drug was discontinued. Subsequently she had several flares of disease activity which were marked by high fever, lymphadenopathy, pericarditis, arthritis, and myalgias. In addition she suffered from severe leg ulcers. At the age of 20 during the last year of her life she was on prednisone 25–100 mg daily and azathioprine 100 mg daily. Because of seizures which had been observed she was also on hydantoin 300 mg daily. During that year a remarkable reduction of soft tissue calcification was noted (Fig. 3). The patient suddenly

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Fig. 1 X-ray of left leg, lateral view, showing soft tissue calcification.

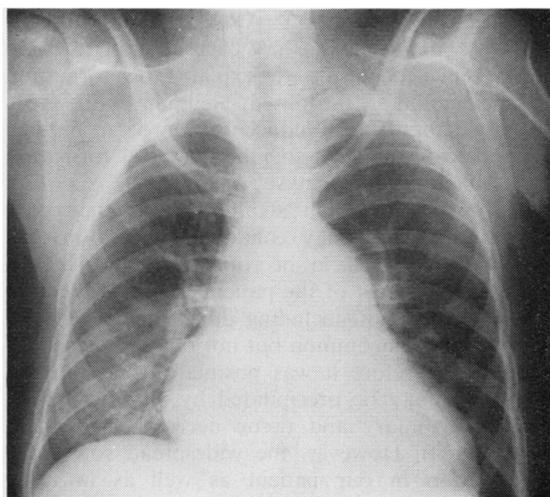


Fig. 3 Anteroposterior view of chest when patient aged 20, showing no calcification.

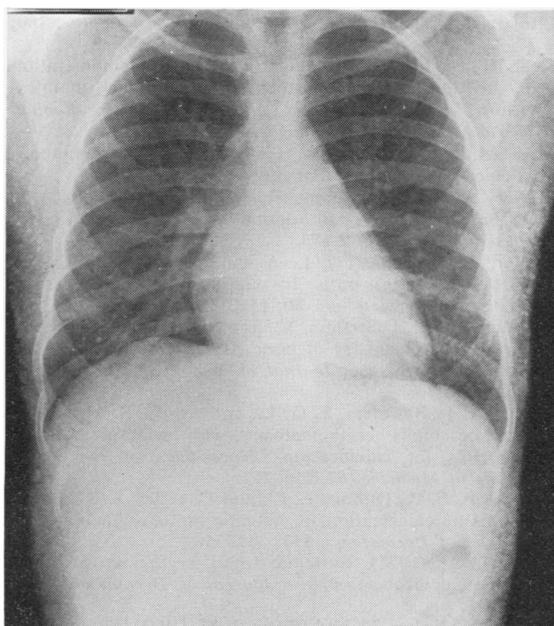


Fig. 2 Anteroposterior view of the chest at the age of 15 years showing extensive calcification of the soft tissue of the thoracic wall and abdomen.

died from an acute myocardial infarction when she was 21 years old.

During all investigations the serum calcium, phosphorus, and alkaline phosphatase levels were normal. Renal insufficiency was never present.

Discussion

Calcinosis circumscripta and calcinosis universalis are terms commonly used in the literature. When calcium deposits are few and localised to the extremities or the joints, the condition is called calcinosis circumscripta. Generalised calcification involves subcutaneous tissues and fibrous tissues of muscles and tendons and is referred to as calcinosis universalis. These are only descriptive terms and are unrelated to the aetiology of the calcifications. The calcifications which occur in patients with progressive systemic sclerosis tend to be small and localised in the hands, feet, knees, and hips (Muller *et al.*, 1959a, b), whereas those of dermatomyositis/polymyositis are more extensive and can be observed in muscles, tendons, skin, and subcutaneous tissues (Muller *et al.*, 1959a, b; Herd and Vaughan, 1964). Calcification of the skin or subcutaneous tissue of the forearms, fingers, buttocks, thighs, legs, knees, and ankles is rarely reported in patients with SLE (Dubois, 1974). These calcifications can mimic those seen in either progressive systemic sclerosis or dermatomyositis. Extensive calcifications of the thoracic and abdominal wall as noted in our patient, who obviously fulfils the preliminary American

Rheumatism Association (ARA) criteria for SLE (Cohen *et al.*, 1971), has not been described before.

Several mechanisms to explain the formation of calcification are proposed. Neuman *et al.* (1951) suggested that a small concentration of an organic phosphate is sufficient to inhibit crystal formation and alkaline phosphatase can remove such an inhibitor. Indeed, high alkaline phosphatase concentration, which may enhance calcification, has been demonstrated in necrotic tissue (Moss and Urist, 1964). Most of the patients with calcification of the soft tissues, including ours, had in addition leg ulcers, an uncommon but not rare manifestation of SLE. Therefore it was postulated that the calcifications may be precipitated by chronic inflammation or injury and tissue necrosis (Moss and Urist, 1964). However, the widespread soft tissue calcification in our patient as well as in those described by Quismorio *et al.* (1975) suggest that this factor is not the primary one in the pathogenesis of the calcifications. Moreover, our patient began to suffer from leg ulcers 3 years after the calcification had been noted, and therefore tissue injury due to ulcers cannot be the cause for calcification in our case.

Another explanation for soft tissue calcification is a pressure phenomenon producing ischaemia (Powell *et al.*, 1974). However this is not the case in our patient, since she had the calcifications also in the chest and abdominal walls.

Fleish and Neuman (1961) showed that polyphosphate compounds can inhibit calcium phosphate precipitation, and they postulated that alkaline phosphatase may cause inactivation of these compounds. Pyrophosphates have the ability to prevent calcification of normal collagen either by inhibiting spontaneous precipitation from solution or by binding to the surface of collagen fibres at the site of calcium-phosphate-hydroxyapatite crystals and thus preventing further growth of the crystals.

The treatment of calcinosis has been disappointing. Diphosphonate, a related compound to pyrophosphate, chelating agents, probenecid, and phosphate binding agents have been used for prevention and dissolution of calcifications (Herd and Vaughan, 1964; Weiss *et al.*, 1971; Dent and Stamp, 1972).

Soft tissue calcification was noted in our patient while she was on steroid therapy. It gradually disappeared during a period of 1 year when she continued with steroid treatment. It is difficult to attribute that response to steroids, since they were reported to be unsuccessful in the treatment of calcinosis (Herd and Vaughan, 1964), and since the patient was on this medication when calcifications

initially appeared. We assume that spontaneous dissolution occurred in our patient, though such a phenomenon has never been reported.

References

- Budin, J. R., and Feldman, F. (1975). Soft tissue calcifications in systemic lupus erythematosus. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine*, **124**, 350-364.
- Cohen, A. S., Reynolds, W. E., Franklin, E. G., Kulka, J. P., Popes, M. W., Shulman, L. E., and Wallace, S. L. (1971). Preliminary criteria for classification of systemic lupus erythematosus. *Bulletin of the Rheumatic Diseases*, **31**, 643-648.
- Coltoiu, A. L., Mataesu, G., and Diaconu, J. (1968). Systemic lupus erythematosus calcifying polymyositis and ascitic cirrhosis. *Romania Medical Review*, **21**, 29-32.
- Dent, E. C., and Stamp, T. C. B. (1972). Treatment of calcinosis circumscripta with probenecid. *British Medical Journal*, **1**, 216-218.
- Dubois, E. L. (1974). Clinical picture of systemic lupus erythematosus. *Lupus Erythematosus, a Review of Current Status of Discoid and Systemic Lupus Erythematosus and their Variants*, 2nd edn., p. 232. University of Southern California Press: Los Angeles.
- Fleish, H., and Neuman, W. W. (1961). Mechanisms of calcification: role of collagen, polyphosphates, and phosphatase. *American Journal of Physiology*, **200**, 1296-1300.
- Herd, J. K., and Vaughan, J. H. (1964). Calcinosis universalis complicating dermatomyositis. Its treatment with EDTA. Report of two cases in children. *Arthritis and Rheumatism*, **7**, 259-271.
- Kabir, D. L., and Malkinson, F. D. (1969). Lupus erythematosus and calcinosis cutis. *Archives of Dermatology*, **100**, 17-22.
- Keats, T. E. (1961). The collagen diseases: A demonstration of the nonspecificity of their extrapulmonary manifestations. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine*, **86**, 938-943.
- Moss, M. J., and Urist, M. R. (1964). Experimental cutaneous calcinosis. *Archives of Pathology*, **78**, 127-134.
- Muller, S. A., Winkelmann, R. K., and Brunsting, L. A. (1959a). Calcinosis in dermatomyositis. *Archives of Dermatology*, **79**, 669-673.
- Muller, S. A., Brunsting, L. A., and Winkelmann, R. K. (1959b). Calcinosis cutis: Its relationship to scleroderma. *Archives of Dermatology*, **80**, 15-21.
- Neuman, W. F., DiStefano, V., and Mubryan, B. J. (1951). The surface chemistry of bone. III. Observations on the role of phosphatase. *Journal of Biology and Chemistry*, **193**, 227-236.
- Powell, R. J., Bywaters, E. G. L., and Ansell, B. M. (1974). Systemic lupus erythematosus with widespread subcutaneous fat calcification. *Proceedings of the Royal Society of Medicine*, **67**, 215-217.
- Quismorio, F. P., Dubois, E. L., and Chander, S. B. (1975). Soft tissue calcification in systemic lupus erythematosus. *Archives of Dermatology*, **111**, 352-356.
- Savin, J. A. (1971). Systemic lupus erythematosus with ectopic calcification. *British Journal of Dermatology*, **84**, 191-192.
- Weis, I. W., Fisher, L., and Phang, J. M. (1971). Diphosphonate therapy in a patient with myositis ossificans progressiva. *Annals of Internal Medicine*, **74**, 933-936.