Extensive soft tissue calcifications in systemic sclerosis

Sirs,

A 34 year-old female has been affected by diffuse pattern systemic sclerosis (SSc) with anti-Scl70 antibody positivity since 1998; the disease started with the appearance of Raynaud's phenomenon simultaneously with fingers and hands swelling. The clinical picture is characterised by widespread skin involvement (Rodnan skin score 35/51), pulmonary fibrosis with severe restrictive ventilatory defect, multiple flexion contractures of the hand joints complicated by recurrent digital ulcers. Nailfold videocapillaroscopy showed late scleroderma pattern. The patient was initially treated at another Rheumatology Unit with cyclophosphamide, corticosteroid and cyclic infusion of iloprost; cyclophosphamide therapy (total dose 45 g) was followed by permanent amenorrhea. At our Unit the patient continued monthly iloprost infusion and corticosteroid at a low dosage; cyclophosphamide was substituted with azathioprine 100 mg/day. In June 2008 the patient underwent autologous peripheral blood stem cell transplantation obtaining mild amelioration of skin involvement and of general status; pulmonary function test remained stable. In April 2009 the patient complained of low back pain, which was not caused by any traumatic event, and of the appearance of painless protuberance in the right periclavicular region. X-ray showed some large calcifications, one around the right clavicula, one near the transverse process of T12 of 2 cm in diameter, three near the spinous process of L5, the largest one of 5 cm in diameter; moreover a very large calcinotic accumulation surrounded the right femoral neck with a major axis of 12 cm; no signs of erosion of the bones close to the calcinosis were evident. Physical examination showed limitation of the right hip mobility. Volume-rendered images from total-body unenhanced CT showed coarse calcifications in the soft tissues of the right thigh (Fig. 1). Coronal multiplanar reconstructions and transverse images depict coarse calcifications in the soft tissues of the right clavicle and cervical spine (Fig. 2A) and around the spinous process of L5 (Fig. 2B).

Serum concentrations of calcium, phosphorus, parathyroid hormone and alkaline phosphatase were normal. The patient did not present subcutaneous calcific deposits neither on the hands, forearms and prepatellar bursae nor intramuscolar calcifications.

No pharmacological or surgical approach of the calcinosis was proposed to the patient nor histological study of the lesions was performed.

As known, subcutaneous calcinosis is a frequent feature of SSc; more often it complicates the course of limited SSc with anticentromere antibody (1, 2) and may predispose to secondary infection. Calcinosis preferentially develops in the sites of the trauma or near bony prominences (2); the face is seldom involved (3, 4). Calcific deposits are frequently grouped in clusters, of linear or punctuate pattern and are usually ranging in diameter from a few millimeters to a few centimeters. The large compact calcific deposits of the patient here described are very unusual for what regards the sites and, above all, for the large dimensions observed. In SSc it has been rarely described evidence of big calcific masses, sometimes improperly defined as "tumoral calcinosis" (3, 5); in fact this term should be referred to

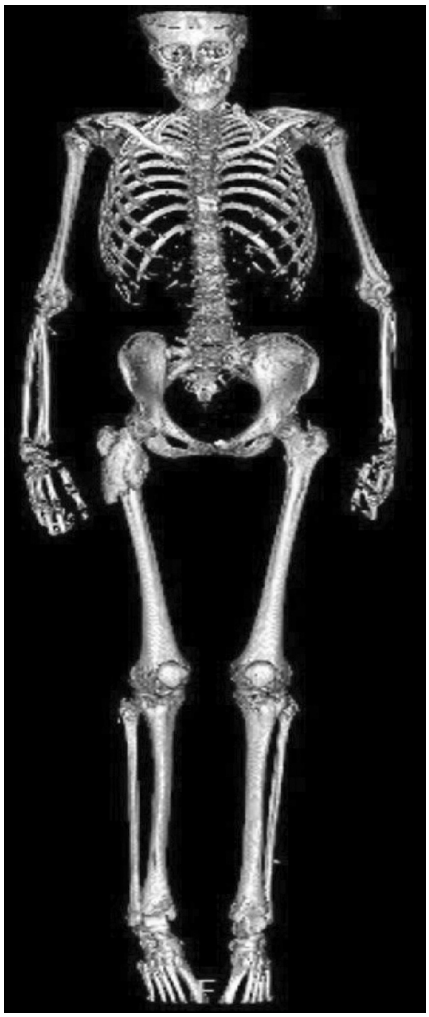

Fig. 1. Volume-rendered images from total-body unenhanced CT show coarse calcification in the soft tissues of the right thigh which measures 60 mm (transverse diameter) x 35 mm (sagittal diameter) x 120 mm (cranio-caudal diameter). Besides, it can be noticed that the calcification slightly displaces the tensor fascia lata muscle anteriorly on one side while the rectus femoris and the sartorius muscles anteromedially on the other side.

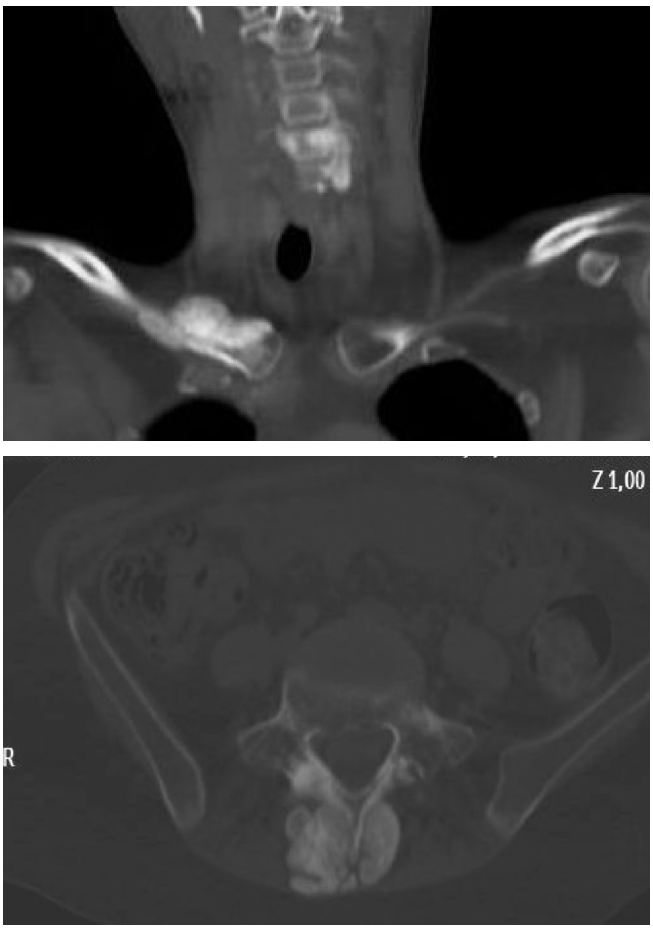

Fig. 2. Coronal multiplanar reconstructions and transverse images depict coarse calcifications in the soft tissues of the right clavicle and cervical spine (**A**) and around the spinous process of L5 (**B**). The calcification surrounding the clavicle measures 51.5 mm (transverse diameter) x 35 mm (sagittal diameter) x 40 mm (cranio-caudal diameter) whereas the calcification near the spinous process of L5 measures 45mm (transverse diameter) x 30 mm (sagittal diameter) x 43 mm (cranio-caudal diameter).

a hereditary condition associated with massive periarticular calcifications (6).

In SSc both paraspinal and infraspinal calcinosis have been reported (7, 8), in some cases complicated by neurological signs due to the narrowing of the spinal canal. Paraspinal and infraspinal calcinosis was associated with regular occurrence of Raynaud's phenomenon, digital ulcers and calcinosis cutis; all these features are present in our patient.

Although calcinosis is more frequently observed in SSc patients with detection of anticentromere antibodies, the positivity of anti-Scl70 antibodies was found in some cases of SSc complicated by large calcific deposits (3, 4, 7).

Tissue calcinosis may be present in different disorders, sometimes in association with hypercalcemia; in the lack of calcium metabolism disorders, calcinosis frequently occurs in damaged or devitalised tissues and is defined as "dystrophic calcinosis", as the soft tissue calcifications of connective tissue diseases (9). Currently, the pathophysiology of the calcinosis remains unclear; as suggested by immunohistochemistry studies (10, 11), bone matrix proteins osteonectin and hypoxia-associated glucose transporter molecule may be involved in this issue.

Yet, no currently approved medical treatment exists; many drugs have been tried such as diltiazem (12), warfarin (13) and minocycline (14) with no convincing results.

P. CARAMASCHI[1], *MD*
I. BAGLIO[2], *MD*
V. RAVAGNANI[1], *MD*
L.M. BAMBARA[1], *Professor of Rheumatology*
D. BIASI[1], *MD*

[1]*Unità di Reumatologia, Dipartimento di Medicina Clinica e Sperimentale, and* [2]*Dipartimento di Scienze Morfologico-Biomediche, Università di Verona, Verona, Italy.*

Please address correspondence and reprint requests to: Dr Paola Caramaschi, Unità di Reumatologia – Istituto di Medicina Interna B, Policlinico G.B. Rossi, P.le Scuro 37134 Verona, Italy
E-mail: paola.caramaschi@ospedaleuniverona.it

Competing interests: none declared.

References

1. ERRE GL, MARONGIU A, FENU P *et al*.: The "scleroderma hand": A radiological and clinical study. *Joint Bone Spine* 2008; 75: 426-31.
2. BOULMAN N, SLOBODIN G, ROZENBAUM M, ROSNER I: Calcinosis in rheumatic diseases. *Semin Arthritis Rheum* 2005; 34: 805-12.
3. CHIKAZU D, MORI Y, SAIJO H *et al*.: A case of tumoural calcinosis in the temporomandibular joint associated with systemic sclerosis. I*nt J Oral Maxillofac Surg* 2008; 37: 190-3.
4. NESTAL-ZIBO H, RINNE I, GLUKMANN M, KAHA H: Calcinosis on the face in Systemic Sclerosis: case report and overview of relevant literature. *J Oral Maxillofac Surg* 2009; 67: 1530-9.
5. MARIE I, DUPARC F, JANVRESSE A, LEVESQUE H, COURTOIS H: Tumoral calcinosis in systemic sclerosis. *Clin Exp Rheumatol* 2004; 22: 269.
6. OLSEN KM, CHEW FS: Tumoral calcinosis: pearls, polemics, and alternative possibilities. *Radio Graphics* 2006; 26: 871-85.
7. OGAWA T, OGURA T, HAYASHI N, HIRATA A: Tumoral calcinosis of thoracic spine associated with Systemic Sclerosis. *J Rheumatol* 2009; 36: 2552-3.
8. OGAWA T, OGURA T, OGAWA K: Paraspinal and infraspinal calcinosis: frequent complications in patients with Systemic Sclerosis. *Ann Rheum Dis* 2009; 68: 1655-6.
9. SAAVEDRA MJ, AMBROSIO C, MALCATA A, MATUCCI-CERINIC M, DA SILVA JAP: Exuberant calcinosis and acroosteolysis. A diagnostic challenge. *Clin Exp Rheumatol* 2009; 27 (Suppl. 54): S55-S58.
10. DAVIES CA, JEZIORSKA M, FREEMONT AJ *et al*.: The differential expression of VEGF, VEGFR-2, and GLUT-1 proteins in disease subtypes of systemic sclerosis. *Hum Pathol* 2006; 37: 190-7.
11. DAVIES CA, JEZIORSKA M, FREEMONT AJ *et al*.: Expression of osteonectin and matrix Gla protein in scleroderma patients with and without calcinosis. *Rheumatology* 2006; 45: 1349-55.
12. VAYSSAIRAT M, HIDOUCHE D, ABDOUCHELI N, GAITZ JP: Clinical significance of subcutaneous calcinosis in patients with systemic sclerosis. Does diltiazem induce its regression? *Ann Rheum Dis* 1998; 57: 252-4.
13. CUKIERMAN T, ELINAV E, KOREM M, CHAJEK-SHAUL T: Low dose warfarin treatment for calcinosis in patients with systemic sclerosis. *Ann Rheum Dis* 2004; 63: 1341-3.
14. ROBERTSON LP, MARSHALL RW, HICKLING P: Treatment of cutaneous calcinosis in limited systemic sclerosis with minocycline. *Ann Rheum Dis* 2003; 62: 267-9.