Case report

Tumoural calcinosis of the spine in the course of systemic sclerosis: report of a new case and review of the literature

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ABSTRACT

We report here a case of a 62-year-old Caucasian woman, suffering from diffuse cutaneous systemic sclerosis (SSc), who developed a tumoural calcinosis (TC) localised in the left side of the neck around the cervical spine that caused severe pain and motion impairment, without involvement of regional neurological structures. A review of the literature on this issue (based on PubMed database) allowed us to identify 35 previously described cases of TC in para-vertebral area in the course of SSc. The main characteristics of these patients have been summarised.

Case report

A 62-year-old Caucasian woman was referred to our Scleroderma Clinic and Rheumatic Disease Unit in January 2012. A diagnosis of diffuse cutaneous systemic sclerosis (dcSSc) was formulated by the presence of typical skin involvement, Raynaud's phenomenon, puffy hands, typical nailfold videocapillaroscopic aspects, hand arthritis, antinuclear antibodies (title 1/320, speckled pattern), with positivity for anti-Scl70 (anti-topoisomerasi I) antibodies. A patient's complete clinical work-up demonstrates that the disease was in an active phase with diffuse involvement of the skin (modified Rodnan Skin score = 20), hand arthritis, and interstitial lung disease showed by the presence of ground glass opacities in the chest HRCT, and associated with a slight reduction of diffusion capacity for carbon monoxide. Signs of cutaneous calcinosis were absent at the diagnosis. Plasmatic and urinary phosphorus and calcium levels, renal function tests and plasma parathyroid hormone level were all within the normal limits. Treatment with daily small dose steroids, weekly methotrexate (15 mg), and monthly infusion of iloprost was then introduced.

A year later, the patient referred once again to our Unit**,** because of the presence of severe neck pain that was accompanied by the appearance of a large lateral cervical lump. The clinical examination confirmed the presence of a round firm mass sited in the left side of the neck. No neurological signs indicating impairment of spinal cord or nerve roots were observed. The plain radiograms showed the presence of a massive cervical calcified mass. The neck computed tomography (Fig. 1) confirmed the presence of coarse calcified poly-lobed, confluent mass, with well-defined margins, adjacent to the articular processes of from 4th to 6th cervical vertebras.

A biopsy of the lesion was carried out. The surgeon who performed the biopsy described the material excised as looking like "milk of calcium" or "toothpaste". The histological analysis demonstrated that the lesion was constituted by amorphous calcified tissue (Fig. 2), without any evidence of neoplastic or inflammatory cells. A diagnosis of tumoural calcinosis (TC) secondary to SSc was finally made. The patient underwent a successful surgical excision of the lesion. At the follow-up work-up, one year later, she does not show any new evident lesion in the computed tomography of the neck.

Review of the literature and discussion

We report here an additional case of TC developed in the course of SSc and localised in the neck close to the cervical spine, causing severe local pain and motion impairment of the neck without any compression of the adjacent neurological structures. The absence of any neurological sign, despite the fact that the calcified mass was very close to the nerve roots emerging from the left C4-C5 and C5-C6 foramina, could be

explained with the consistency of the lesion content that was described as a toothpaste by the surgical operator, and so not dense enough to cause any damage of the near neurological structures and the consequent symptoms.

Calcinosis is often observed in patients with SSc, and namely in those suffering from the limited cutaneous (lc) variant of the disease (1). Its presence also characterises the SSc variant known as CREST syndrome (2), where C of the acronym stands for calcinosis. In most of the patients calcified areas are quite small and localised under the skin in characteristic areas such as distal phalanges, posterior surface of the elbow and anterior side of the knee, and more rarely in other sub-cutaneous areas of arms and legs (1).

The mechanisms of calcium deposition and tissue calcinosis are far from being completely clarified. It has been suggested that tissue hypoxia**,** due to reduced vascular perfusion caused by SSc-related micro-vascular bed impairment, may drive an inflammatory reaction, and namely an activation of macrophages, and an unbalanced local production of different soluble mediators that induces increased cellular calcium uptake with consequent cellular necrosis**,** and in many cases local accumulation of calcium (3). Similar mechanisms of tissue hypoxia may be responsible for bone resorption, with consequent formation of osteolytic areas that may be or not accompanied by calcium deposition in the surrounding soft tissues. Osteolysis is a well-known skeletal feature in SSc (4)**,** and acro-osteolysis, with resorption of distal phalanges, is the most common presentation of this process, occurring in 40-80% of patients (5). However, other sites of the skeleton can be involved in the osteolytic process, including distal radius, ulna, ribs, mandible, distal clavicle and spine (6).

Larger calcification masses, defined as TC, are rarely observed in SSc, and have also been described in other autoimmune systemic diseases, such as systemic lupus, and mixed connective tissue disease. The pathological conditions where secondary TC has been reported are listed in Table I (7).

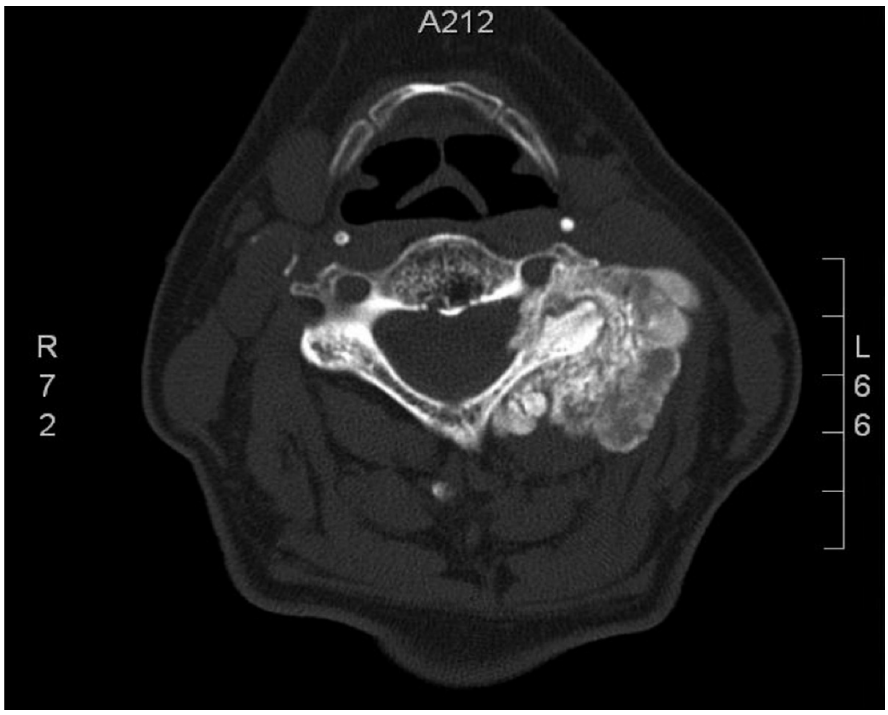

Fig. 1. Computed tomography of the patient's neck, showing in the left side a calcified poly-lobed, partly confluent mass, with well-defined margins, adjacent to the articular processes of the 4th and the 6th cervical vertebras, with an extension in the context of regional muscle floor, cranially, caudally, and laterally. The mass in its cranial extension had a transverse maximum diameter 29x33 mm, while it reached the largest transverse diameter (44x25 mm) at the level of the 5th cervical vertebra. The coarse ossification with lateral development was located in the context of the muscle bellies of spinalis colli, multifidus, and longissimus cervicis. The calcification caused partial commitment of the left C4-C5 and C5-C6 foramina.

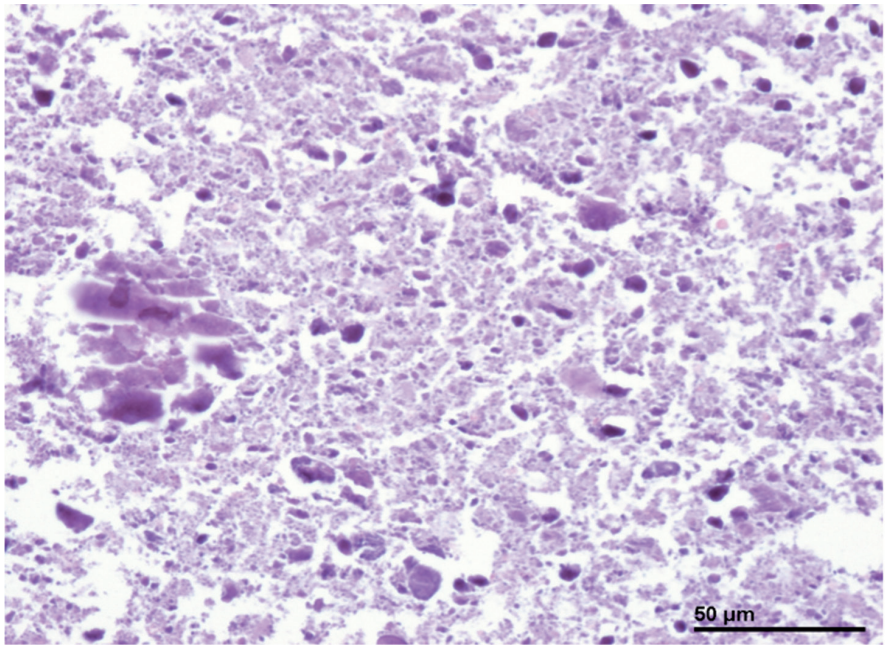

Fig. 2. The histological picture (20x) of the biopsy material drawn from the lesion highlights only the presence of amorphous calcified material.

Taking into account only the TC localised near the spine, we performed a review of the literature using the search terms "tumoural calcinosis", "calcinosis", "cervical spine", "thoracic spine", "lumbar spine", "spine", and "systemic sclerosis (scleroderma)" in Pubmed® database. We considered the papers

Table I. Secondary forms of tumoural calcinosis.

Neoplasias
Chronic renal failure
Primary hyperparathyroidism
Hypervitaminosis D
Milk-alkali syndrome
Massive osteolysis
Pseudoxanthoma elasticum
Connective tissue diseases
Systemic sclerosis
Systemic lupus erythematosus
Mixed connective tissue disease

written in English, French and German. The main data, derived from the analysis of 35 case reports published since 1974, are summarised in Table II (8-36). The data collected from our literature review were not exhaustive since the SSc variant that the patients have been suffering from is often not indicated in some reports, and as often there is no mention of the patients' age, or the disease duration. Apart from these limitations, it seems evident that TC of the spine is more frequent in dcSSc than in lcSSc, whilst the contrary is true for calcinosis at all (1). It is worth noting that the appearance of TC is more common in patients with quite long disease duration (mean 9.09 years, range 4–22 years), and with a rather advanced mean age (mean 58.5 years, range 12-74). Only in one case (14) the onset of calcinosis anticipated the diagnosis of lcSSc. Moreover, Dray *et al*. (28) reported the unique case of spine TC in a 12-year-old girl, suffering from a SSc-myositis overlap syndrome. In this case a TC sited in the para-vertebral area, from the 7th cervical to the 9th thoracic vertebra, was incidentally observed in performing lung high-resolution CT scan.

Our case reflects the mean age of the series, but it differs as to an early onset of the lesion since it became evident 19 months after the disease onset, *i.e*. the first episode of Raynaud's phenomenon. The para-vertebral TC is more prevalent in females (32 cases *vs*. 3 in males), in agreement with the commonly reported difference in gender prevalence of SSc. The first case of male affected was reported by Durant *et al*. (17), who performed a retrospective study on a large series of 21 cases of TC of the spine of different origin. This case and another male case reported by Smucker *et al*. (22) share the involvement of the cervical tract of the spine. In this second male case TC was associated with partial erosion of the vertebral arches and joint facets, which called for prompt surgery. In the third male case (27), the TC was localised at the low lumbar tract of the spine and was entrapping the right L4 and L5 nerve roots. The patient had severe abdominal pain, and just a plain radiography of the abdomen led to the discovery of the calcified mass.

As to the prevalent localisation of TC along the spine, the cervical tract of the spine was largely prevalent (26 cases) when compared to thoracic or lumbar parts (3 and 6 cases, respectively). All of the patients with neck involvement complained of local pain and/or limitation of motion. Nineteen out of the 35 patients with TC of the spine showed clear signs of spinal cord compression (14, 15, 29, 30) with Lhermitte's sign (13), weakness in the limbs (11, 20, 23, 26), radiculopathy (12, 21), motor (22) or sensitive dysfunction (8).

Apart from the cases with TC, less extended calcinosis along the spine appears to be more frequent. Ogawa *et al*. described, in a series of 41 patients with SSc where this aspect was specifically investigated on chest computed tomography (37). Out of them, 24 patients showed small calcifications close to the thoracic spine, but only 4 complained of associated neurological manifestations.

Table II. Main data from the literature-derived case reports of TC of the spine in the course of SSc.

Authors	Year	Sex	Age (years)	Diagnosis	Years from disease onset	Localisation	Ref.
Haverbush TJ, *et al*.	1974	F	46	Diffuse	9	C3 – C5	(8)
Meyer E, *et al*.	1987	F	56	Limited	7	L5	(9)
Walden CA, *et al*.	1990	F	62	NA	14	T4	(10)
Bracard S, *et al*.	1991	F	62	Limited	7	C3 – C4	(11)
Schweitzer ME, *et al*.	1991	F	65	NA	10	C3 – C6	(12)
		F	56	NA	NA	C3 – C5	
		F	NA	NA	NA	C	
		F	NA	NA	NA	C	
Arginteanu MS, *et al*.	1997	F	65	NA	5	C1 – C5	(13)
Ojemann JG, *et al*.	1997	F	52	Limited	-1	C	(14)
Ward M, *et al*.	1997	F	62	Diffuse	7	C1 – C3	(15)
		F	53	Diffuse	4	L3 – L5	
Manelfe C, *et al*.	1999	F	74	Diffuse	NA	C3 – C4	(16)
Durant DM, *et al*.	2001	M	48	NA	NA	C3 – C4	(17)
Van de Perre S, *et al*.	2003	F	74	NA	NA	C2 – C7	(18)
Olsen KM	2004	F	75	NA	NA	C2 – C4	(19)
Lima IVS, *et al*.	2005	F	51	Diffuse	22	C4 – T1	(20)
Shibuya S, *et al*.	2006	F	49	NA	7	L3 – L4	(21)
Smucker JD	2006	M	60	NA	NA	C1 – C2	(22)
		F	59	NA	NA	C2 – C5	
		F	73	NA	NA	C3 – C4	
Teng AL, *et al*.	2006	F	59	Limited	NA	C3 – C6	(23)
Nagay Y, *et al*.	2008	F	55	Diffuse	8	L5	(24)
Tuy BE, *et al*.	2008	F	50	NA	2	C2 – C3	(25)
Ogawa T, *et al*.	2009	F	53	Diffuse	10	T4 – T8	(26)
Durant C, *et al*.	2011	M	62	Diffuse	3	L4 – S1	(27)
Dray N, *et al*.	2011	F	12	NA	12	C7 – T9	(28)
Shoji A, *et al*.	20012	F	34	Diffuse	15	C1 – C2	(29)
Weerakoon A, *et al*.	2011	F	60\	Limited	12	L3 – L4	(30)
Bisson-Vaivre A, *et al*.	2013	F	72	Diffuse	5	C1 – C2	(31)
Bluett J, *et al*.	2013	F	64	Diffuse	7	C3 – C4	(32)
Daumas A, *et al*.	2013	F	60	Diffuse	13	C2 – C5	(33)
Onishi S, *et al*.	2013	F	67	NA	10	C	(34)
Nakamura T, *et al*.	2014	F	74	Diffuse	10	C3	(35)
Zenone T, *et al*.	2014	F	66	Limited	10	T	(36)

F: Female; M: Male; Diffuse - Limited: diffuse - limited cutaneous SSc; NA: Not Available; C: cervical; T: thoracic; L: lumbar spine.

In conclusion, the data collected and analysed in this review suggest that calcinosis around the spine and namely TC is quite a rare event, but probably misdiagnosed. The presence of this pathological condition merits to be more carefully investigated in patients with SSc complaining of local pain, sometimes accompanied by the appearance of a palpable tumour-like lesion, or by the presence of neurological signs and symptoms that can be ascribable to local compression of the spinal cord, or nerve roots, or both. An early surgical removal of calcified lesions may prevent more severe and irreversible damages due to compression of the adjacent neurological structures.

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