Open Journal of Clinical & Medical Images

www.jclinmedimages.org

Case Series

Open Access, Volume 3

Massive pseudotumoral calcinosis in patients affected by systemic sclerosis: A case series

Galluzzo Claudio; Spinella Amelia; Testoni Sofia; De Pinto Marco; Amati Gabriele; Oliva Marianna; Mascia Maria Teresa; Sandri Gilda; Giuggioli Dilia*

Scleroderma Unit, Rheumatology Unit, University Hospital of Modena, University of Modena and Reggio Emilia, Modena, Italy.

***Corresponding Author: Giuggioli Dilia**

Scleroderma Unit, Rheumatology Unit, University Hospital of Modena, University of Modena and Reggio Emilia, Modena, Italy.

Email: dilia.giuggioli@unimore.it

Received: Oct 20, 2023

Accepted: Nov 21, 2023

Published: Nov 28, 2023

Archived: www.jclinmedimages.org

Abstract

Background: Pseudotumoral calcinosis (PC) can occur in patients affected by systemic sclerosis (SSc), involving soft tissues, articular and periarticular structures. Here we report a case series of PC in SSc patients presenting pain, articular functional impairment and an overall disability, with a significant reduction of life quality.

Case 1: An 81-year-old woman, with longstanding history of SSc, limited cutaneous subset, complicated by digital ulcers and pulmonary hypertension, presented with severely restricted range of motion of the left shoulder, with progressive impairment, periarticular swelling and pain during movement. Abnormalities of calcium-phosphate metabolism or kidney failure were ruled out. Imaging showed extensive periarticular calcific mass. Because of the aforementioned comorbidities, the patient was only eligible for physiotherapy and eventually targeted lithotripsy.

Case 2: A 41-year-old woman with longstanding history of SSc, diffuse cutaneous subset, complicated by digital ulcers and multiple self-amputations, developed a rapidly spreading periarticular bulk to the left elbow in just a few months, without calcium-phosphate metabolism alterations or kidney failure. Imaging showed multiple low intensity and high calcium content masses with conglomerated features at the articular level. Semifluid content with sclero-necrotic, calcific features was evacuated from the mass, with relapse of the swelling a few days later. A second evacuation of the fluid content was subsequently performed, followed by intralesional steroid injection. The patient referred easing of pain and regained range of motion in the elbow, with no evidence of relapse within months.

Case 3: A 54-year-old woman with a longstanding history of SSc, diffuse cutaneous subset, complicated by digital ulcers and pulmonary fibrosis, complained of painful swelling of the right dorsal region, displaying a cystic area with liquid content at palpation. The presence of PC was previously identified by a chest radiography performed two years earlier, showing a polylobate calcific mass localized in the soft tissue of the dorsal region, in a patient with no evidence of calcium-phosphate metabolism abnormalities or kidney failure. Surgical treatment could not be performed due to the clinical need of strong immunosuppressive therapy.

Conclusion: Currently, there are no recommended therapies to treat PC. Surgery seems to be an effective option for selected patients, while there are no validated treatments for patients not eligible for surgery. The evacuative approach alone seems to be ineffective, whereas the combination of evacuation and intralesional steroid seems to be promising. Thus, further studies exploring also less invasive local approaches are needed to ensure the best and safest therapeutic options for this disabling condition.

Abbreviations: PC: Pseudotumoral calcinosis; SSc: Systemic sclerosis; LcSSc: Limited cutaneous systemic sclerosis; DcSSc: Diffuse cutaneous systemic sclerosis; VAS: Visual analogue scale; BAP: Bone alkaline phosphatase; PTH: Parathormone; TSH: Thyroid stimulating hormone; MRI: Magnetic resonance imaging; MRSS: Modified Rodnan skin score; HAQ: Health assessement questionaire; US: Ultrasounds; CT: Computed tomography; MDCT: Multidetector computed tomography

Background

Systemic sclerosis (SSc) is a connective tissue disease which potentially involves all body structures. Endothelial dysfunction and immune dysregulation are the main features of the disease, leading to an altered fibroblast activity and widespread tissue fibrosis of the skin and internal organs [1]. Cutaneous involvement is classified as limited (lcSSc) and diffuse (dcSSc) cutaneous SSc subsets, according to skin fibrosis extension [2]. Calcinosis is frequently observed in SSc patients and consists of calcium salt deposits in skin and subcutaneous tissues, often complicated with skin ulceration, fistulization and supra-infection [3]. Although the cause of calcinosis formation is unknown, it has been supposed that structural damage, hypovascularity and local tissue hypoxia could contribute to calcinosis formation [4]. Calcific masses larger than 2 cm have been described, and some authors suggested that this should be addressed as pseudotumoral calcinosis (PC) [5]. It is similar to a neoplasm and appears as the result of calcium deposition in the soft tissues around large joints [6]. This manifestation can develop as a primary normophosphatemic, primary hyperphosphatemic or secondary tumoral calcinosis [7]. The most commonly associated conditions of secondary tumoral calcinosis are: chronic renal failure, pseudoxanthoma elasticum, malignancy, sarcoidosis, primary hyperparathyroidism, hypervitaminosis D, milk-alkali syndrome, massive osteolysis, and connective tissue diseases such as scleroderma [7]. Limited data are available on SSc-PC [6]. Prevalence of calcinosis has been estimated to be 18-49% in literature reports [8,9]. The presence of PC in SSc is reported in 3% of cases, often symmetrical and in multiple sites [7], and seems to be more frequent in patients affected by dcSSc than lcSSc [10]. PC affecting para-vertebral and vertebral structures have been described by some authors and can lead to neurological symptoms [11-15]. PC development seems to occur more frequently in patients with long disease duration (mean 9.09 years) and with an advanced mean age (mean 58.5 years) [11]. Below we report a case series of difficult-to-treat PC in SSc patients presenting pain, and articular functional impairment, with significant impact on overall disability and reduction of life quality. PC diagnosis was challenging in these patients due to the presence of a recent bulky lesion which is mandatory to exclude the neoplastic nature of the aforementioned lesion. In addition, investigations should be conducted to rule out other secondary causes of PC. The treatment of PC is challenging as well, not all patients undergo surgery, and treatments are empirical and not evidence-based.

Case series

Case 1: An 81-year-old woman affected by SSc (limited subset) for 14 years, positive anti-PM/SCL75 and PM/SCL100 antibodies, complicated by digital ulcers, mild pulmonary arterial hypertension and dysphagia, presented with severely restricted range of motion of the left shoulder. She complained of progressive impairment (HAQ 2,125), mild periarticular swelling and only mild pain during the shoulder movement over the last few years, visual analogue scale (VAS) pain 5/10. Examinations revealed an impairment of shoulder joint motion, in particular, limitation in forward flexion of shoulders over 45 degrees, limitation in the abduction of the shoulders over 40 degrees. There were no abnormalities involving calcium or phosphate metabolism (Calcium 9.4 mg/dl, Phosphate 3.6 mg/dl, bone alkaline phosphatase (BAP) 7.3 µg/l, 25-hydroxycholecalciferol 31.5 ng/ml, parathormone (PTH) 33,7 pg/l, thyroid stimulating hormone (TSH) 4,37 µIU/ml. The patient's renal function was normal. Imaging investigations were required, X-ray showed a massive periarticular calcific mass (Figure 1). Relatively less extensive calcifications were also present in the right hip (Figure 2) with mild functional impairment. In addition, magnetic resonance imaging (MRI) confirmed the presence of a multitude of small nodular-like calcification surrounding the humeral head (12x11 cm) correlating with the diagnosis of PC (Figure 3). The patient was not eligible for surgery because of the cardio-pulmonary comorbidities, besides there are no currently recommended therapies for PC. The patient is performing physiotherapy, and we are evaluating to perform targeted lithotripsy.

Case 2: A 41-year-old woman affected by SSc for 17 years, positive anti-SCL-70 antibody, developed a rapidly spreading periarticular bulk to the left elbow in a few months. This condition occurred within an advanced subset of vascular systemic disease, modified Rodnan skin score (mRSS) 30, complicated with recurrent digital ulcers and multiple self-amputations, Health assessment questionnaire (HAQ) 1,125. No calcium-phosphate metabolism alterations were found, thyroid and re-

nal function were normal. X-ray examination (Figure 4) showed a large periarticular high-density bulk of the elbow. Subsequently, MRI evaluation (Figure 5) characterized it as multiple low-intensity and high calcium content masses (3x2.1x3,4 cm) with conglomerated features at the articular level (2.8x1.5x5.7 cm) (Figure 2). Contrast enhancement showed inflammatory tissue, although synovial hyperplasia could not be excluded. A biopsy was performed, with evacuation of semifluid content from the mass. A mostly acellular sclero-necrotic calcific material was found. Due to clinical presentation, radiological and histological features, the lesion was considered a PC. After the biopsy, the patient showed temporary benefit for a few weeks, unfortunately the swelling relapsed after a few days. Therefore, a second evacuation of the mass content was performed, followed by intralesional methylprednisolone (40 mg) injection. The patient subsequently referred easing of pain and regained elbow range of motion, with no evidence of relapse within the following months. A highly accurate analysis of radiological pictures revealed other calcific masses along the spine, both at paravertebral level (Figure 6) and projecting inside the spinal canal, despite the patient not complaining of any neurological symptoms.

Case 3: A 54-year-old woman affected by SSc (diffuse subset) for 12 years, positive anti-SCL-70 antibody, complicated by digital ulcers and pulmonary fibrosis, presented with painful swelling of the right dorsal region (VAS 7/10) (HAQ 2,125). Examinations revealed a painful and extensive swelling adhering to the tissue below, displaying a cystic area with liquid content at palpation. The presence of PC was identified for the first time two years before with a chest radiography which showed a polylobate calcific mass (8,8x6,8 cm) localized in the soft tissue of the dorsal region (Figure 7). There were no evident abnormalities involving calcium or phosphate metabolism (Calcium 8.8 mg/dl, Phosphate 3.8 mg/dl, BAP 5.5 µg/l, 25-hydroxycholecalciferol 80.9 ng/ml, PTH 86,5 pg/l). The renal function of the patient was normal. Ultrasound (US) and computed tomography (CT) were also performed in the following weeks and confirmed the presence of polylobate PC having an increased dimension since the previous evaluation (10x9 cm) (Figure 8). Surgical treatment could not be performed due to the clinical need of an aggressive immunosuppressive therapy.

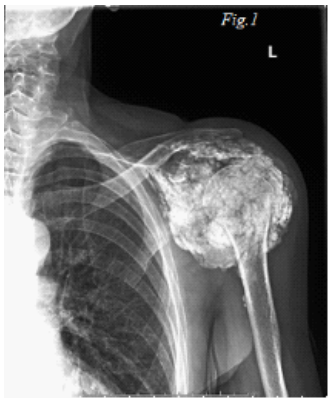

Figure 1: Pseudotumoral calcinosis of the left shoulder, front X-ray.

Discussion

Literature offers limited data on the frequency, distribution and clinical association of calcinosis in SSc [16,17]. The actual occurrence of large calcified masses is even less known. According to the classification proposed by Smack et al. [7], large calcinosis in non-hereditary predisposing conditions can be defined

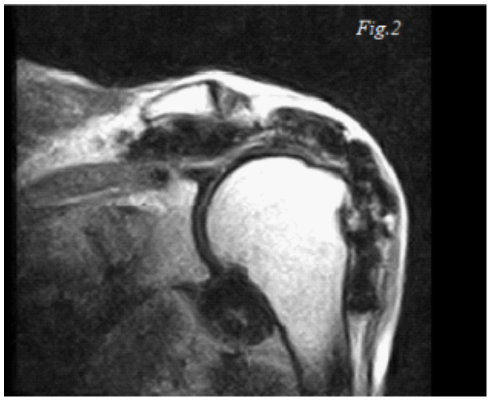

Figure 2: Pseudotumoral calcinosis of the left shoulder, front MRI scan, T1 weighted image.

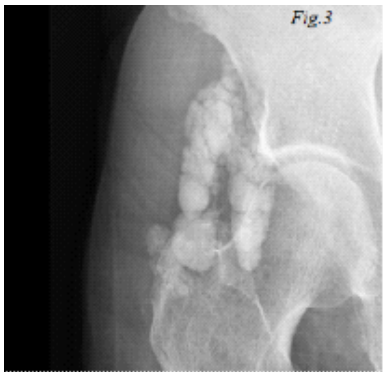

Figure 3: Pseudotumoral calcinosis of the right hip, front X-ray.

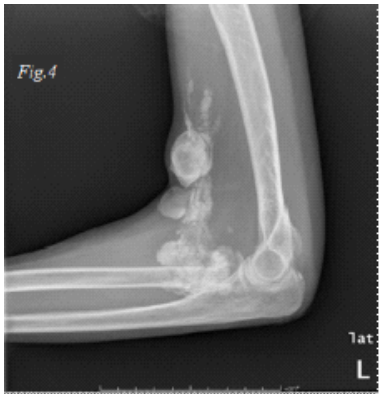

Figure 4: Pseudotumoral calcinosis of the left elbow, lateral X-ray.

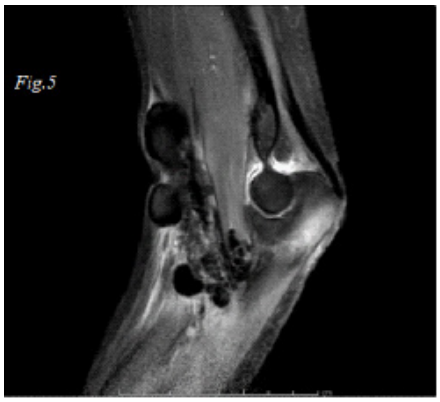

Figure 5: Pseudotumoral calcinosis of the left elbow, lateral MRI scan, T2 weighted image.

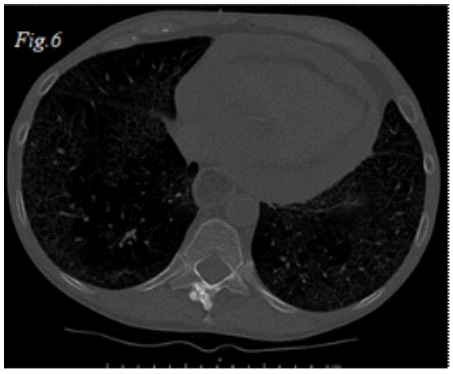

Figure 6: Pseudotumoral calcinosis in paravertebral region, transverse CT scan.

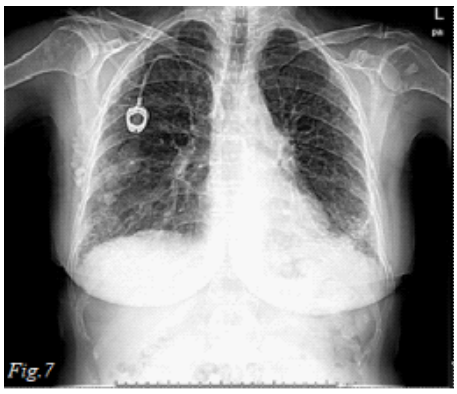

Figure 7: Pseudotumoral calcinosis of the right dorsal region, front X-ray.

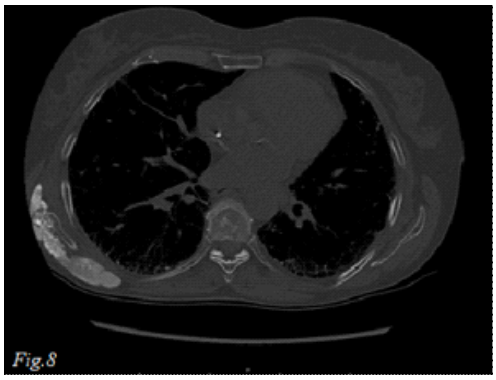

Figure 8: Pseudotumoral calcinosis of the right dorsal region, transverse CT scan.

as "secondary" forms of tumoral calcinosis. As previously introduced, the main causes of secondary forms are chronic renal failure (usually with secondary hyperparathyroidism), primary hyperparathyroidism, hypervitaminosis D, sarcoidosis, hydroxyapatite deposition disease, and connective tissue diseases, such as dermatomyositis or systemic sclerosis. In this regard, some screening tests (i.e. kidney functionality and phospho-calcium metabolism panel) should be performed in SSc patients to exclude other potential causes of calcinosis. The investigation of serum calcium, phosphate, and other plasmatic ions levels, parathormone, vitamin D and antibody screening for rheumatic disease is fundamental [6]. Imaging is essential to perform diagnosis of calcinosis, quantification of disease, disease monitoring and better pathophysiologic understanding. Traditionally, X-rays have been the most frequently used imaging modality for diagnosis; however, advances in US, MRI and CT led to a greater ability to characterize these lesions and surrounding structures [18,19]. Multidetector computed tomography (MDCT) has been described as the most accurate radiological technique to precisely assess location and extent of calcinosis. On the other side, it implies a higher radiation exposure. MDCT may be useful especially in some cases, such as disabling calcinosis, preoperative assessment and treatment follow-up. It also allows to evaluate the calcinosis extent through the dermis, through the bone with erosive changes, intra-articular calcinosis, and it also identifies calcinosis of paraspinal periarticular soft tissues that may involve neural structures to eventually guide diagnostic aspiration [20].

There is no recommended medical therapy for PC to date. Calcium channel blockers, bisphosphonates, warfarin, biologic agents, topical and intralesional sodium thiosulfate injection were tested as treatment of calcinosis cutis, with no clear evidence of efficacy [8]. Moreover, calcium channel blockers and colchicine were proven ineffective in the specific treatment of PC. Colchicine, in particular, showed a mild effect in reducing peri-calcinosis tissue inflammation [5]. Surgery on selected cases is recommended as the only effective treatment for PC so far [5,8]. In literature only Hazen et al. reported in 1982 a case of scleroderma calcinosis resolution after repeated intralesional injections of steroids [21].

Conclusion

PC is a rare manifestation in patients affected by systemic sclerosis. The exact mechanism leading to PC development is not completely clear. A proper diagnostic evaluation of PC (biochemical assessment and imaging techniques) is essential to optimize the diagnosis and facilitate disease monitoring in order to maximize future therapeutic options. We have noticed that radiologists did not signal asymptomatic pseudotumoral calcinosis localized at spinal level at the first imaging evaluation, maybe due to the atypical localization, which has been rarely described in literature [5,22]. On the contrary, clinical evident PC were promptly detected after targeted research, as expected. In our experience, we have observed that an evacuative approach alone does not seem to be effective. The association of fluid content evacuation and steroid injection seems to be more promising, suggesting possible underlying inflammatory mechanisms. Unfortunately, we did not know how to manage effectively our other patients who were not eligible for surgery, and in which fluid evacuation and following steroid injection were not possible to perform for PC morphology or localization. Greater awareness of PC is needed, and its presence should be screened in all patients affected by systemic sclerosis, as it often can be initially asymptomatic, then abruptly lead to relevant clinical condition with pain and functional impairment. More extensive studies, including exploring mini-invasive local approaches, are necessary to ensure the best and safest therapeutic options for this condition, which may compromise patients' quality of life.

Declarations

Ethical approval and consent to participate: Not applicable.

Consent for pubblication: Written informed consent was obtained from the patients for publication of this case report and any accompanying images. A copy of written consent is available for review by editor-in-chief of this journal.

Competing interests: none.

Funding: none.

Authors' contributions: Mascia Maria Teresa conceived the original idea. Galluzzo Claudio and Testoni Sofia wrote the manuscript with support from Spinella Amelia and de Pinto Marco, Amati Gabriele and Oliva Marianna collected the data, edited the images, Giuggioli Dilia and Gilda Sandri supervised the project. All authors contributed to the final manuscript.

Acknowledgements: Not applicable.

References

1. Ferri C, Sebastiani M, Lo Monaco A, Iudici M, Giuggioli D, Furini F, et al. Systemic sclerosis evolution of disease pathomorphosis and survival. Our experience on Italian patients' population and review of the literature. Autoimmun Rev. 2014; 13(10): 1026-34.
2. Giuggioli D, Colaci M, Cocchiara E, Spinella A, Lumetti F, Ferri C. From Localized Scleroderma to Systemic Sclerosis: Coexistence or Possible Evolution. Dermatol Res Pract. 2018; 2018: 1284687.
3. Giuggioli D, Lumetti F, Spinella A, Cocchiara E, Sighinolfi G, Citriniti G, et al. Use of Neem oil and Hypericum perforatum for treatment of calcinosis-related skin ulcers in systemic sclerosis. J Int Med Res. 2019; 48(4): 0300060519882176.
4. Boulman N, Slobodin G, Rozenbaum M, Rosner I. Calcinosis in rheumatic diseases. Semin Arthritis Rheum. 2005; 34(6): 805-12.
5. Zanatta E, Desportes M, Do HH, Avouac J, Doria A, Feydy A, et al. Pseudotumoral calcinosis in systemic sclerosis: Data from systematic literature review and case series from two referral centres. Semin Arthritis Rheum. 2020; 50(6): 1339-47.
6. Freire V, Moser TP, Lepage-Saucier M. Radiological identification and analysis of soft tissue musculoskeletal calcifications. Insights Imaging. 2018; 9(4): 477-92.
7. Smack D, Norton SA, Fitzpatrick JE. Proposal for a pathogenesis-based classification of tumoral calcinosis. Int J Dermatol. 1996; 35(4): 265-71.
8. Valenzuela A, Song P, Chung L. Calcinosis in scleroderma. Current Opinion in Rheumatology. 2018; 30(6): 554-61.
9. Valenzuela A, Baron M, Herrick AL, Proudman S, Stevens W, Rodriguez-Reyna TS, et al. Calcinosis is associated with digital ulcers and osteoporosis in patients with systemic sclerosis: A Scleroderma Clinical Trials Consortium study. Seminars in Arthritis and Rheumatism. 2016; 46(3): 344-9.
10. Hachulla E, Launay D. Diagnosis and classification of systemic sclerosis. Clin Rev Allergy Immunol. 2011; 40(2): 78-83.
11. Sambataro D, Sambataro G, Zaccara E, Maglione W, Vitali C, Del Papa N. Tumoral calcinosis of the spine in the course of systemic sclerosis: report of a new case and review of the literature. Clin Exp Rheumatol. 2015; 33(4 Suppl 91): 175-178.
12. Durant C, Farge-Bancel D. Clinical images: Voluminous ectopic tumoral calcinosis of the spine in systemic sclerosis. Arthritis Rheum. 2011; 63(2): 411.
13. Dray N, Rao AG, Silver RM. Paraspinal tumoral calcinosis in a child with systemic sclerosis/myositis overlap. Pediatr Radiol. 2011; 41(9): 1216-8.
14. Shibuya S, Kawaguchi Y, Arima N, Yamamoto T, Dobashi H, Tokuda M. Tumoral calcinosis in bilateral facet joints of the lumbar spine in scleroderma. Case report. J Neurosurg Spine. 2006; 5(5): 451-4.
15. Liberato ACP, Amaral LLFD, Marussi VHR. Tumoral calcinosis in the lumbar spine secondary to systemic sclerosis: a rare cause of radiculopathy in an adult with advanced disease. BJR Case Rep. 2016; 2(3): 20150435.
16. Koutaissoff S, Vanthuyne M, Smith V, De Langhe E, Depresseux G, Westhovens R, et al. Hand Radiological Damage in Systemic Sclerosis: Comparison with a Control Group and Clinical and Functional Correlations. Seminars in Arthritis and Rheumatism. 2011; 40(5): 455-60.
17. Bartoli F, Fiori G, Braschi F, Amanzi L, Bruni C, Blagojevic J, et al. Calcinosis in systemic sclerosis: subsets, distribution and complications. Rheumatology (Oxford). 2016; 55(9): 1610-4.
18. Hughes M, Hodgson R, Harris J, Porter N, Jackson S, Kirwadi A, et al. Imaging calcinosis in patients with systemic sclerosis by radiography, computerised tomography and magnetic resonance imaging. Semin Arthritis Rheum. 2019; 49(2): 279-82.
19. Mar D, Valenzuela A, Stevens KJ, Chung L, Fairchild RM. A narrative review of imaging in calcinosis associated with systemic sclerosis. Clin Rheumatol. 2021.
20. Freire V, Becce F, Feydy A, Guérini H, Campagna R, Allanore Y, et al. MDCT imaging of calcinosis in systemic sclerosis. Clin Radiol. 2013; 68(3): 302-9.
21. Hazen PG, Walker AE, Carney JF, Stewart JJ. Cutaneous Calcinosis of Scleroderma: Successful Treatment With Intralesional Adrenal Steroids. Archives of Dermatology. 1982; 118(5): 366-7.
22. Rato M, Rocha TM, Bernardo A, Costa L. Pseudotumoral calcinosis of the spine in systemic sclerosis - an atypical location. ARP Rheumatol. 2022; 1(3): 262-3.