A unique case of calcinosis in a patient with systemic sclerosis treated with spinal cord stimulation

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ABSTRACT

Systemic sclerosis (SSc) is a complex autoimmune disease presenting with a wide organ-manifestation. One out of three patients with SS is affected by calcinosis, i.e. the deposition of apatite in soft tissue. The association between digital ulcers and calcinosis suggests a role of tissue hypoxia and inflammation in its pathogenesis. Treatment of SSc related ulcers and calcinosis includes immunosuppressive agents, autologous haematopoietic stem cell transplantation, calcium channel blockers, phosphodiesterase 5 inhibitors iloprost or bosentan. Different reports provided promising results about the effect of spinal cord stimulation in the management of digital ulcers, in terms of pain relief and improvement in microcirculation. None of these reports describe the possibility to retrieve calcinosis around the epidural catheter or the pulse generator. The present case report describes a unique case of calcinosis distributed around the pulse generator in a patient with SSc and digital ulcers.

Introduction

Systemic sclerosis (SSc), also called scleroderma, is a complex autoimmune disease that presents with a wide organ-manifestation. Multiple organ fibrosis is described, involving the skin but also vasculature and internal organs such as lung, heart, kidneys.[1] Typically, early symptoms include Raynaud's phenomenon, gastrointestinal reflux and itching.[2] Raynaud's phenomenon affects 96% of patients with systemic sclerosis, and it is associated with distressing physical symptoms, impaired function, body image dissatisfaction and reduced health-related quality of life.[3] Moreover, it can promote the development of peripheral ulcers, involving hands and feet, but also ankle, elbows, forefeet.[2] It is supposed that the pathogenesis of systemic sclerosis is multifactorial, involving genetic and environmental factors, that cause an imbalance between cellular proliferation and remodelling in various cell line, including fibroblasts, endothelium, lymphocytes.[1] The key driver seems to be an increased level of endothelin, that promotes excessive vasoconstriction, triggering tissue hypoxia. The subsequent vasoconstriction stimulated by hypoxia further enhances cytokines production, fibroblasts activation and platelet aggregation, thus promoting the fibrotic stage.[4] Moreover, one out of

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Key words: systemic sclerosis; calcinosis; spinal cord stimulation.

Key points:
- Systemic sclerosis (SSc), also called scleroderma, is a complex autoimmune disease that presents with a wide organ-manifestation.
- One out of three patients with SSc is affected by calcinosis.
- Calcinosis could be localised even around implantable devices, such this unique case describes.

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three patients with SSc is affected by calcinosis, i.e. the deposition of apatite in soft tissue.[5] The pathogenesis of calcinosis is still under investigation, but the association between digital ulcers and calcinosis suggests a role of tissue hypoxia and inflammation, that can trigger calcification by regulation ATP production, phosphate liberation, and calcium transport and concentration.[6]

Treatment of SSc related ulcers and calcinosis has improved over years, and now includes immunosuppressive agents, autologous haematopoietic stem cell transplantation, dihydropyridine calcium channel blockers (especially nifedipine), then phosphodiesterase 5 inhibitors iloprost or bosentan.[7] Moreover, non-pharmacologic approaches have been suggested such as digital sympathectomy and botulinum toxin injections.[8,9] Recently, different reports provide promising results about the effect of spinal cord stimulation in the management of digital ulcers, both in terms of pain relief and on improvement in microcirculation.[10-12] However, none of these reports describe the possibility to retrieve calcinosis even around the epidural catheter or the pulse generator.

The present case report describes a unique case of calcinosis distributed along the course of the extension and the pulse generator in a patient with SSc and digital ulcers.

Case Report

The selected patient was 45-year-old women, who was diagnosed SSc in 1994, basing on the American College of Reumatology criteria for SSc.[13] She presented a long history of Raynaud's phenomenon, skin thickening of both hands, proximal to metacarpophalangeal joints, digital tip ulcers involving both toes and the third, fourth and fifth fingers of both hands, and a proximal involvement of trunk and legs. She presented severe osteoporosis. Moreover, she showed evolving pulmonary fibrosis and pulmonary hypertension. She was treated with bosentan 125 mg twice a day, methotrexate, prednisone 10 mg, oxycodone 60 mg/day and amitriptiline 10 mg/day with no pain control and with no improvement in digital lesions. Therefore, the patient underwent a trial of spinal cord stimulation with a single octopolar catheter (Vectris™ SureScan® MRI 1x8, Medtronic, Minneapolis, MN, USA) midline positioned at C3-C4 in 2017 in a different Pain Clinic, and the pulse generator (RestoreAdvanced™ SureScan MRI Medtronic, Minneapolis, MN, USA) was allocated in a subcutaneous pocket in the supragluteal right region.

She reported a significant reduction of pain, an increased function, and an improvement of wound healing. The stimulation pattern was stabilised at amplitude of 2 V, frequency of 80 Hz pulse with of 200 microseconds with an efficient pain control, so that the patients stopped her medication for pain control. The patient was then referred to our Pain Unit in December 2023 since the pulse generator has expired and a replacement was deemed necessary.

At physical inspection, the patient present diffuse calcinosis alongside all the subcutaneous extension, till the cervical entrance of the catheter (Figure 1). An echographic exam of the lumbar and dorsal region showed diffused calcinosis surrounding the extension (Figure 2).

She did not complain of pain or other symptoms, excluding the loss of paraesthesia elicited by the spinal cord stimulation and the mounting of burning pain at extremities.

Therefore, the patient underwent under local anaesthesia to the replacement of the pulse generator. At surgical incision, calcium deposition was evident also in the subcutaneous pocket, where the pulse generator was allocated (Figure 3), surrounding and completely covering the generator and the extension near the generator (Figure 4). A careful removal of hydroxyapatite depositions was performed, in order to free the extension, and

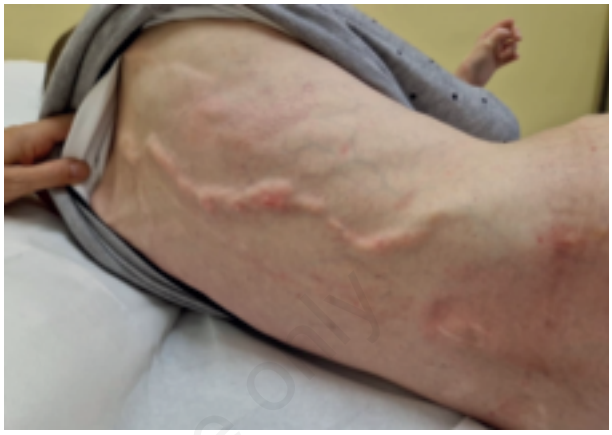

Figure 1. At physical inspection, the patient presents diffuse calcinosis alongside all subcutaneous extension from the catheter to the pulse generator.

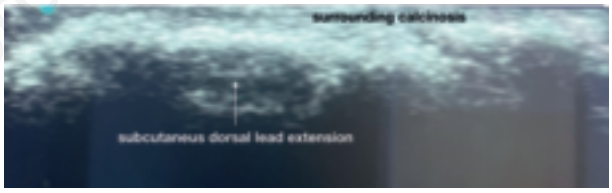

Figure 2. An echographic exam of the lumbar and dorsal region of the patient showed diffused calcinosis surrounding the extension.

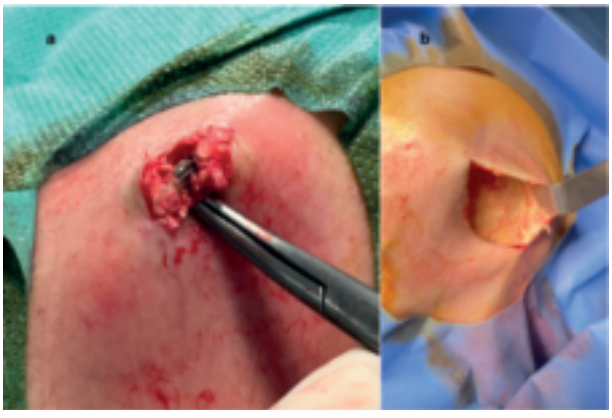

Figure 3. At surgical incision, calcium deposition was evident also along extension course (a), and in the subcutaneous pocket, where the pulse generator was allocated (b).

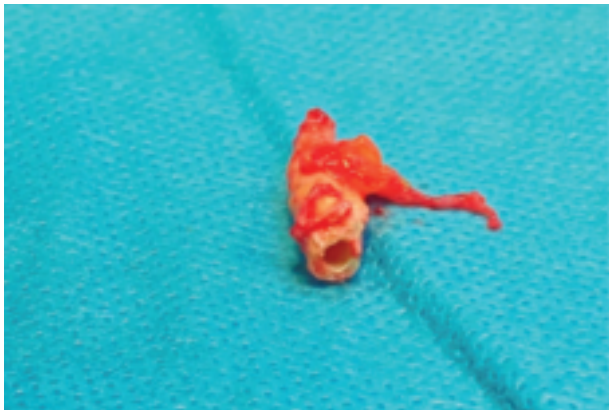

Figure 4. The cylindric shape of calcium deposition around the distal end of the extension.

the new generator was connected. Fortunately, no impedance increase was retrieved, and the intra-operative test was successfully completed. The stimulation was reprogrammed, ensuring an adequate paresthetic coverage.

The patients then returned home with no complications, with the suggestion to come back to check the system every three months.

Discussion

To our knowledge, this is the first case of a diffuse calcinosis in a patient suffering from SSc and digital ulcers, that is located not at the extremities as usually described, but alongside the course of an implantable device.

The beneficial effect of spinal cord stimulation in Raynaud's phenomenon has been reported both in term of pain reduction and better perfusion.[10-12,14] The proposed mechanisms involve the activation of inhibitory (GABA-ergic or cholinergic) interneurons in the spinal dorsal horn thus reducing the excitability of spinal second order neurons,[12,14] the increase of cutaneous blood flow by antidromic activation of afferent fibres in the dorsal roots, the inhibition of efferent vasoconstrictor sympathetic activity, and the suppression of nociceptive transmission via descending inhibitory pathways.[16] The present report further confirms the beneficial effect of spinal cord stimulation to treat digital ulcers and related pain in SSc.

Anyway, no one of these papers describe the occurrence of calcinosis around the pulse generator nor the extension. We could argue that the surgical insult related to the positioning of the catheter and the generator may have triggered an inflammatory state, that, in turn, could have stimulated calcium deposition. In addition, the possibility of repeated microtrauma over time since this lady was extremely thin has maybe triggered the activation of phosphate cascade. As a matter of fact, repetitive microtrauma is often associated with calcinosis.[17] Moreover, the patient presented long disease duration and osteoporosis, that have been recently independently associated with apatite deposition.[7] Surprisingly, no other evidence of calcinosis was retrieved by physical inspection, nor at extremities where ulcers were evidenced in previous years, nor in other body sites.

The patients did not complain of any other symptom that could suggest the presence of calcinosis at the spine, that is described in literature, involving the facet joints, or even the spinal cord,[19] so no other imaging exams were undertaken. Fortunately, no impedance increase was retried at control and no loss of stimulation were perceived by the patient, so we could argue that apatite deposition did not alter the function of the device.

The patient received the implant in another centre and was referred to our centre only later, when the pulse generator expired, and a replacement was required. Therefore, we could only argue that a spinal cord stimulator was chosen over a dorsal root ganglion stimulator at the time due to technical difficulties with the dorsal root ganglion (DRG) implant, that the multiple locations of pain and ulcers influenced the decision to use a spinal cord stimulation rather than DRG stimulation.

In conclusion, the present report describes a unique case of a rare deposition of apatite alongside the pulse generator and the extension of a cervical epidural lead, in a patient that underwent spinal cord stimulation to control pain and digital ulcers related to SSc, with no other signs of calcium deposition in soft tissue or near long bones or vertebrae. Fortunately, in this patient it resulted in no malfunction or any other adverse events (like extension fracture or impedance alteration). Moreover, the risk of skin ulcers around the calcinosis should always be considered, therefore a careful monitoring of all the implant should be done over time.

Calcinosis is as a potential complications of spinal cord implant in SSc patients. Further evidence is needed to explain its pathogenesis in this subset of patients.

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