Successful treatment of calcinosis cutis of fingertip in the setting of CREST syndrome with topical 20% sodium thiosulfate

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INTRODUCTION

Calcinosis cutis (CC) is a rare chronic process characterized by deposition of insoluble calcium salts in the skin and subcutaneous tissues. There are 5 subtypes of CC: dystrophic, metastatic, idiopathic, iatrogenic, and calciphylaxis.[1] Dystrophic calcinosis is the most common type of CC and is seen in association with autoimmune connective tissue diseases such as systemic sclerosis, dermatomyositis, lupus erythematosus, and lupus panniculitis. CC is thought to occur as a result of chronic local tissue injury and is a common complication of systemic sclerosis especially the limited form (CREST syndrome: calcinosis, Reynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia), affecting approximately 25% of these patients.[2] It usually presents as subcutaneous nodules in fingers or areas of pressure such as elbows, knees, or ischial tuberosities and might be associated with pain, soft tissue swelling, ulcers, or deformities, which may lead to functional limitations. There may be a toothpaste-like material protruding from the skin, predisposing to infection.[3] Treatment of CC is difficult and challenging, and there is no consensus on the suggested treatments. Because CC is a rare condition, there is a significant absence of controlled clinical trials on its treatment and, the available data for all suggested therapies are generally reported in case reports or small case series.[4] Sodium thiosulfate (STS) is an inorganic salt, which increases calcium solubility and has been reported to be helpful in treating calcinosis.[2,3] Here we report a case of CC of the fingertip in the setting of CREST syndrome that responded to treatment with topical STS 20%.

Abbreviations used:

CC:	calcinosis cutis
CREST:	calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, telangiectasia
STS:	sodium thiosulfate

CASE REPORT

The patient is a 67-year-old woman with limited scleroderma (CREST syndrome) for 20 years. She presented to our clinic with a very painful and ulcerated lesion on the tip of the right index finger for more than 6 months. Physical examination found a 3- × 3-mm ulcer with extrusion of a little stony hard white material associated with significant tenderness. We also noticed some scaling around this lesion (Fig 1). Based on history and physical examination, CC was diagnosed by a dermatologist. In this patient, antinuclear antibody and anticentromere antibody were positive, whereas anti−topoisomerase I (anti−Scl-70) antibody was negative. She was on treatment with sucralfate, ranitidine, and omeprazole for acid reflux and amlodipine for Raynaud phenomenon. Sildenafil was added to her treatment regimen later in her next follow-up visit. For the treatment of CC, the patient was started on topical STS 20% in petrolatum base. The patient was instructed to apply the medication 3 times a day and cover it with a bandage whenever possible, especially during night. She tolerated the medication well without any significant adverse effect. After almost 2 months of treatment, her severe pain was relieved, and 3 months after initiation of treatment,

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Fig 1. Calcinosis cutis of index finger tip presented as a painful ulcer with extrusion of a hard, white material before treatment.

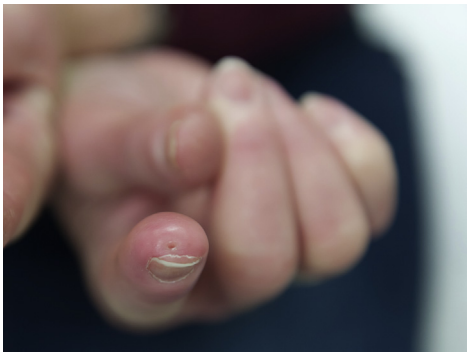

Fig 2. Resolution of calcinosis cutis of index finger tip after treatment with topical 20% sodium thiosulfate.

her calcinosis lesion was resolved with a 1- × 1-mm residual pitted atrophic scar (Fig 2). Finally, after more than 3 years, in her last visit in August 2019, the site of previous CC was well healed and associated with a very small hyperkeratotic papule.

DISCUSSION

Dystrophic type of CC can frequently occur in the setting of scleroderma and CREST syndrome. The pathophysiology of dystrophic calcification is not well understood. Several mechanisms including chronic inflammation, vascular hypoxia, recurrent trauma, and abnormalities in bone matrix proteins have been proposed.[3]

General therapeutic measures for treatment of CC consist of improving blood circulation to the extremities; avoiding stress, cold exposure, and trauma; antibiotics covering streptococci and staphylococci for superinfection and acetaminophen, nonsteroidal anti-inflammatory agents, and even opioids for pain relief.[3] Although no drug has been proven effective in clinical trials, current treatment modalities include warfarin, bisphosphonates, minocycline, calcium channel blockers (mostly diltiazem), ceftriaxone, aluminum hydroxide, probenecid, intravenous immunoglobulin, biologic agents such as infliximab and rituximab, intralesional corticosteroid, extracorporeal shock wave lithotripsy, curettage, surgical excision, and carbon dioxide laser. The type of treatment being used (systemic vs topical or medical vs surgical) depends on the severity and distribution of the lesions.[3,4]

STS in forms of intravenous, intralesional, and topical has also been studied as treatment for CC.[3,5,6] Three mechanisms of action have been proposed for STS: increased calcium solubility (through its chelation effect for cations that produces soluble calcium thiosulfate complexes), vasodilatation, and antioxidant effect that restores endothelial cell function.[7]

There are previous reports of successful use of topical STS for the treatment of CC. In 2008, Wolf et al[8] reported a case of a leg ulcer with dystrophic calcification that was successfully treated with topical 10% STS solution.[8] Bair and Fivenson[9] reported 2 cases of ulcerative dystrophic calcinosis refractory to multiple topical treatments that had excellent responses to topical 25% STS compounded in zinc oxide. García-García et al[7] also reported an iatrogenic case of CC in a 6-year-old boy who was treated with 10% topical STS. Complete resolution of lesions was achieved after 6 months, with no local or systemic adverse effects. In July 2019, Ma et al[10] reported a series of 28 patients with CC associated with underlying autoimmune connective tissue diseases treated with topical 25% STS compounded in zinc oxide ointment. In their experience, of 28 patients with CC, 19 had clinical improvement of their CC, 7 had no response, and 2 had unknown response. In their report, 3 patients experienced adverse events: 2 had skin irritation and the third had pain with application.[10]

Here we also reported successful treatment of superficial CC of a fingertip in a patient with CREST syndrome, and based on our experience we think topical STS can be considered an effective treatment modality for patients with limited numbers of superficial CC in the setting of autoimmune connective tissue diseases. However, it is necessary to evaluate the efficacy and safety of this treatment option by conducting controlled clinical trials in future studies.

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