

SHORT COMMUNICATION

Treatment of Skin Calcifications with Intra-lesional Injection of Sodium Thiosulphate: A Case Series

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Accepted Aug 4, 2015; Epub ahead of print Aug 10, 2015

Skin calcifications can describe several conditions, including dystrophic calcification (DC) and lesions containing calcium. DC is defined as pathological calcification of the dermis with accumulation of calcium apatite crystals and normal calcium/phosphorus metabolism. DC may also be located in the subcutaneous tissue and deeper around muscles and joints. DC is associated with some autoimmune diseases, including dermatomyositis, lupus erythematosus, mixed connective tissue diseases and systemic sclerosis (SSc) (1). DC is present in up to 72% of SSc patients who are anti-centromere antibody positive (2). Nephrogenic systemic fibrosis (NSF) is a debilitating and painful disease with progressive fibrosis of the skin and joints that develops in some renal impaired patients after exposure to gadolinium-based contrast agent (3). A recent study (Personal communication, Anne Braae Olesen) indicates that gadolinium gathers in the dermis in clusters with a polycrystalline structure containing calcium and phosphorous and may cause calcifications and ulcerations of the skin.

DC can be symptomatic and complicated by pain, ulceration and infection, and thereby have a great impact on activities of daily living and quality of life (4). The most common locations for DC are the extensor surfaces of the extremities in relation to joints and sites of repeat trauma, for example on the palmar and plantar surfaces of the hands and feet.

Treatment of DC is difficult; there is a lack of effective treatments. There are several case reports on different medical treatments with no convincing results (5). Surgical interventions may be necessary, although wound-healing is often prolonged and may result in

scarring in patients with autoimmune diseases, for example SSc (5).

In 2004 a case report of successful treatment of systemic calciphylaxis, a calcific uraemic arteriopathy resulting in progressive cutaneous necrosis, with sodium thiosulphate was published and more case reports have followed (6). Intravenous sodium thiosulphate is associated with an increased risk of serious side-effects. However, some case reports suggest that sodium thiosulphate as either a topical dressing or intra-lesional injections in DCs with or without ulcers is effective with few or no side-effects (7–11). The mechanism of action of sodium thiosulphate is unclear, but it involves chelation of calcium into calcium thiosulphate salts, which increases the solubility of calcium up to 100,000 times (6).

We report here a case series of 6 consecutive patients with calcifications due to SSc or NSF who were treated successfully with intra-lesional injections of sodium thiosulphate, 150 mg/ml.

METHODS

From July to December 2014 we consecutively identified 5 SSc patients with disabling DC's and 1 NSF patient with severe fibrosis and ulcerations. All patients were women (mean age 63 years, age range 49–71 years). The SSc patients were all anti-centromere antibody positive. The lesions were located on extensor sites of the extremities and fingertips and more of them were complicated with ulceration and severe pain (up to a visual analogue (VAS) score of 9). The patients were treated with intra-lesional injections of sodium thiosulphate, 150 mg/ml, in the base of the calcification. The primary endpoint of treatment was partial or total remission of the lesions. The patients were evaluated by the same clinician, who measured the

Table I. Descriptive data for the 6 cases treated with sodium thiosulphate

Diagnosis/ age, years	Localization	Size of calcinosis mm	Treatment	Sodium thiosulphate, mg Mean (range)	Complications	Size (mm)/ reduction (%) week 4	Size (mm)/ reduction (%) week 12
SSc/59	Fingertip	3	Single injection	12.5	No	0/100	0/100
SSc/59	Knee	70	Repeated injection every week for 4 weeks	57.5 (12.5–87.5)	Infection followed injection in week 2	30/57	5/93
SSc/65	Fingertip	6	Repeated injection every week for 4 weeks	37.5 (25–62.5)	Transient pain associated with injection	3/50	2/67
SSc/71	Anterolateral side of lower left leg	80	Repeated injection every week for 4 weeks	150 (100–275)	No	50/38	10/80
SSc/74	Elbow	4	Single injection	30	Transient pain associated with injection	1/75	0/100
NSF/49	Buttocks	75 85	Repeated injection every week for 3 weeks (both)	120 (60–150)	Transient pain associated with injection	30/60 35/59	Lost to follow-up

SSc: systemic sclerosis; NSF: nephrogenic systemic fibrosis.

size of the calcifications in weeks 4 and 12. Calcifications on the fingertips of less than 5-mm diameter were treated with a single injection of sodium thiosulphate, 150 mg/ml. More widespread calcifications complicated with ulcerations were treated with repeated injections every week for 4 weeks.

RESULTS

A total of 8 lesions on the extremities in 6 female patients were treated with a total of 21 injections of sodium thiosulphate for up to a 4-week period, using doses ranging from 12.5 to 275 mg at each treatment (Table I). The clinical response was evaluated at weeks 4 and 12. The size of the lesions were, on average, reduced by 67% by week 4 and by 90% by week 12. Complete remission was obtained in 50% of patients by week 12 and 80% remission was achieved in the remaining 50% by week 12 compared with baseline lesion size before treatment. Furthermore, the patients all reported improvement in pain and disability. The patient with NSF died shortly after the third treatment due to complications (acute gastric bleeding) related to a gastroscopy. The procedure was evaluated and no suspicions were raised of a link between sodium thiosulphate treatment and the episode that led to death.

Most patients reported transient pain related to the injection site. One cutaneous infection in relation to a lesion complicated by ulceration was treated with oral antibiotics. Fig. 1 illustrates a 59-year-old woman with SSc with a DC complicated by ulceration on her right knee before and after 4 weeks of treatment.

DISCUSSION

In this case series we observed convincing results with total and/or partial reduction of the calcifications. Furthermore, the patients reported less pain and disability in the treated areas compared with before treatment. No severe side-effects were observed, but one infection developed in a treated area. Although the treatments were performed in highly selected patients we suggest that intra-lesional injection with sodium thiosulphate, 150 mg/ml, may be considered in severe and/or ulcerated lesions before surgery or if doctor-initiated amputation is planned.

Injection with sodium thiosulphate, should be performed by physicians who are familiar and trained in this procedure. Further studies, with a randomized controlled clinical trial, are needed to qualify these



Fig. 1. Patient before treatment (left) and after weekly repeated injections for 4 weeks (right).

observations and to answer important questions concerning relevant doses and treatment intervals.

The authors declare no conflicts of interest.

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