Iatrogenic calcinosis cutis from extravasated phosphate-containing solution treated with topical sodium thiosulfate

Catherine B. Xie, PhD,[a] Michal Kidacki, MD, PhD,[b] Nan Ring, MD,[b,c] Gauri Panse, MD,[b,c] and Jonathan Scott Leventhal, MD[b]
New Haven, Connecticut

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INTRODUCTION

Calcinosis cutis (CC) is a condition characterized by aberrant calcium salt deposition within cutaneous and subcutaneous tissue.[1] Iatrogenic CC is caused by extravasation of agents that induce precipitation of calcium salts. We present the case of a patient undergoing chemotherapy, who developed progressive iatrogenic calcification secondary to intravenous phosphate-containing fluid extravasation that was successfully treated with topical sodium thiosulfate (TST) 25% cream that expedited clinical resolution without significant side effects.

Abbreviations used:

CC: calcinosis cutis
TST: topical sodium thiosulfate

CASE REPORT

A 50-year-old woman undergoing etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab chemotherapy treatment for recently diagnosed Epstein-Barr virus-positive large B-cell lymphoma with secondary hemophagocytic lymphohistiocytosis presented with a painful and progressive plaque on her left side of the upper extremity. The area initially appeared as an erythematous tender patch and progressed to a 15-cm × 8-cm chalky, yellow, firm plaque over the next few weeks (Fig 1, *A*). Upon closer investigation, it was discovered that during an admission 4 weeks earlier, the patient experienced extravasation of potassium phosphate fluid into the site through an intravenous catheter placed in the left antecubital fossa. Skin biopsy demonstrated aggregations of homogenous amorphous basophilic material consistent with calcium within the papillary dermis (Fig 2). The epidermis was slightly atrophic with loss of rete ridges but otherwise unremarkable. Serum calcium and phosphate levels and kidney function were within the normal ranges. These findings along with clinical-pathologic correlation were compatible with iatrogenic calcification caused by extravasation of a phosphate-containing agent inducing calcium salt precipitation.

To treat the CC, 25% TST cream compounded in gel base no. 72 (Versapro DS) was chosen. The patient applied the cream to the plaque twice a day for 3 weeks. Scaling and mild erythema with application was reported but did not require cessation of treatment. After dissolution of the overlying yellow-white calcified material following 3 weeks of treatment, she continued to apply mupirocin ointment and silver sulfadiazine 1% cream daily to the site for wound care. Within 2 months, the plaque almost completely resolved, and at the 4-month follow up, the area showed only linear hypertrophic scarring with mild tenderness to palpation (Fig 1, *B*). Of note, she was able to continue her chemotherapy infusion regimen through a right internal jugular vein port without interruption.

DISCUSSION

The etiology of calcium deposition in iatrogenic CC is unclear but likely multifactorial.[1] In this patient,

From the Department of Immunobiology,[a] Department of Dermatology,[b] and Department of Pathology, Yale University School of Medicine, New Haven.[c]
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Correspondence to: Jonathan Scott Leventhal, MD, Department of Dermatology, Yale School of Medicine, 330 Cedar St, New Haven, CT 06520. E-mail: Jonathan.leventhal@yale.edu.

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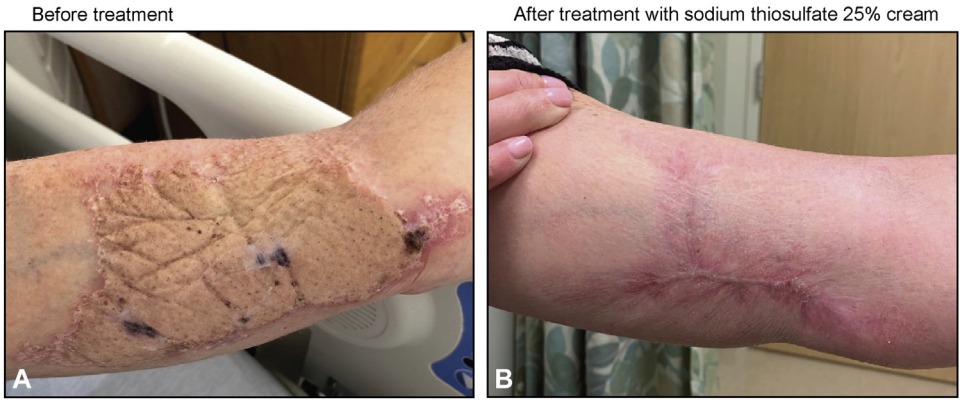

Fig 1. Clinical images showing the treatment response of dystrophic calcinosis cutis to topical sodium thiosulfate therapy. **A**, The patient's left anterior upper extremity shows a thick, calcified, yellow-white plaque with erosions. **B**, Linear hypertrophic scarring without evidence of calcification at the 4-month follow up following a 3-week treatment with 25% topical sodium thiosulfate cream.

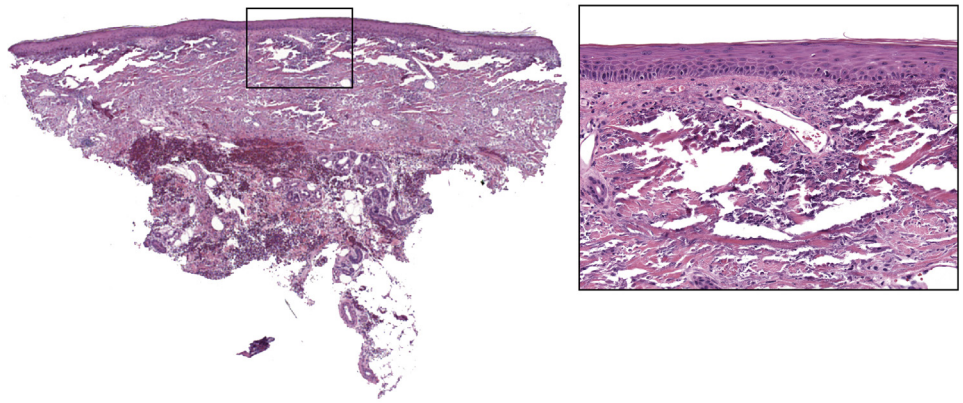

Fig 2. Skin biopsy from the left side of the upper extremity. Hematoxylin-eosin staining shows a diffuse distribution of calcium in the papillary dermis. The inset shows aggregations of homogenous amorphous basophilic material consistent with calcium deposition in dermis. (Hematoxylin-eosin stain; original magnifications: ×20; **inset**, ×200.)

the extravasation of phosphate-containing fluid led to local tissue inflammation and injury, which promoted intracellular calcium release and created a nidus for calcium-phosphate salt precipitation exacerbated by the patient's intense chemotherapy infusions. Chemotherapy extravasation causing CC has been reported[2]; however, the development of this patient's plaque prior to starting etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab chemotherapy makes this less likely.

We report, to our knowledge, the first case of using 25% TST cream to successfully treat a large plaque of iatrogenic CC with expedited clinical resolution by 2 months in comparison with the reported natural time course. Signs of inflammation and calcification typically appear several days after administration of calcium solution, with a mean period between infusion and appearance of clinical lesion of 13 days and a range of 2 hours to 24 days.[3] Less severe cases of iatrogenic CC (<2 cm) tend to gradually resolve in 2 to 6 months, but treatment should be considered due to the variable time course and unpredictable severity.[4] Two previous cases reported on the efficacy of treating smaller iatrogenic CC lesions (<4 cm) using 10% TST with complete resolution ranging from 3 to 6 months.[5,6] Severe presentations of lesions of >4 cm in diameter have required surgical debridement.[7] A variety of therapeutic options for CC have been reported, including bisphosphonates, aluminum hydroxide, diltiazem, colchicine, probenecid, and surgical excision, but there is insufficient data from controlled trials showing efficacy to reach treatment consensus.

Sodium thiosulfate, an intraparenchymal and intravascular calcium chelator, has been used effectively to treat calciphylaxis and recently been

investigated as a treatment for CC. Intravenous sodium thiosulfate has limited efficacy and practicality,[8,9] as its adverse effects necessitate closer monitoring. Intralesional sodium thiosulfate treatment has been found to be more effective at resolving CC lesions measuring <2 cm but not >2 cm, and injection site pain to an intrinsically painful lesion can result in discontinuation of therapy or necessitate analgesic coinjection.[9] TST has been used to treat dystrophic calcification of plaques up to 3 cm × 4 cm with formulations ranging from 10% to 25% with no to minor adverse effects of redness and scaling.[5,6,10] We proceeded with 25% TST rather than intravenous and intradermal therapy, given the practicality, large extent of the lesion, and that our patient was undergoing infusional chemotherapy. Our case demonstrates that 25% TST cream is an effective, well-tolerated, safe, and practical treatment modality for expedited resolution of large plaques of iatrogenic CC.

Conflicts of interest

None disclosed.

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