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Treatment of calcinosis cutis with sodium thiosulfate therapy

To the Editor: Calcinosis cutis (CC) is a rare cutaneous condition defined by abnormal depositions of insoluble calcium salts in the skin and subcutaneous tissue.[1] Finding effective and safe treatments for these calcified lesions has been a known challenge among dermatologists. A variety of therapies have been reported, with limited success, including the treatment of CC with the use of warfarin, bisphosphonates, minocycline, intralesional corticosteroids, surgical excision, and carbon dioxide laser therapy.[2]

Sodium thiosulfate (STS) has been attempted as a CC treatment and demonstrated successful in a small number of reported cases.[3,4] Exhibiting characteristics of a potent antioxidant and vasodilator, STS aids in the dissolution of calcium deposits and provides rapid resolution of pain.[5] This retrospective analysis evaluated the efficacy of using STS therapy to treat patients with CC. Here we examine 80 CC lesions treated with 1 of the 3 variations of STS treatment: topical, intradermal, and intravenous.

Patients who were prescribed topical STS were advised to apply topical STS serum, compounded 50:50 with petrolatum or Eucerin (Beiersdorf AG, Hamburg, Germany) ointment, twice daily until complete dissolution of calcinosis. Intradermal STS injections were performed using undiluted 12.5 g (50 mL) STS in doses of 0.1 to 1 mL. Injections were provided once every 3 weeks until dissolution of the calcinosis was observed or the patient discontinued therapy. Intravenous STS was administered to 2 patients who presented with exophytic and innumerable large tumoral calcifications.

Response to treatment for STS regimens was determined by clinical examination performed by the attending physician. Success rate was graded in a binary manner of (1) complete response to treatment and dissolution of calcium deposit or (2) failure to entirely resolve CC lesion.

Success rates of STS treatment regimens for various sizes of CC lesions treated are summarized in Table I. Topical STS therapy completely resolved all of the 53 CC lesions examined that were less than 0.2 cm in size. CC lesions that fell between the ranges of 0.2 to 0.3 cm and of 0.3 to 0.5 cm had reduced success rates of 78% and 20%, respectively, when treated with topical STS. Intradermal STS injections were a successful therapeutic regimen for all calcifications that measured 2.0 cm or less in size, with a success rate of 100%. However, intradermal STS injections failed to resolve any calcinosis lesions greater than 2.0 cm in size. Intravenous STS failed to resolve the exophytic and tumoral CC lesions.

Of the 3 STS therapies examined in this study, we recommend intradermal injections as a novel treatment to safely and effectively resolve microscopic and small CC lesions (Fig 1). Topical STS could also

Table I. Success rates of calcinosis cutis lesions treated with topical, intradermal, or intravenous sodium thiosulfate therapy

Sodium thiosulfate therapy	Size of lesion, cm	Number of lesions	Success rate, %
Topical sodium thiosulfate	<0.1	41	100
	0.1-0.2	12	100
	0.2-0.3	4	78
	0.3-0.5	5	20
Intradermal sodium thiosulfate	<0.5	10	100
	0.5-2.0	3	100
	>2.0	3	0
Intravenous sodium thiosulfate	…	2	0

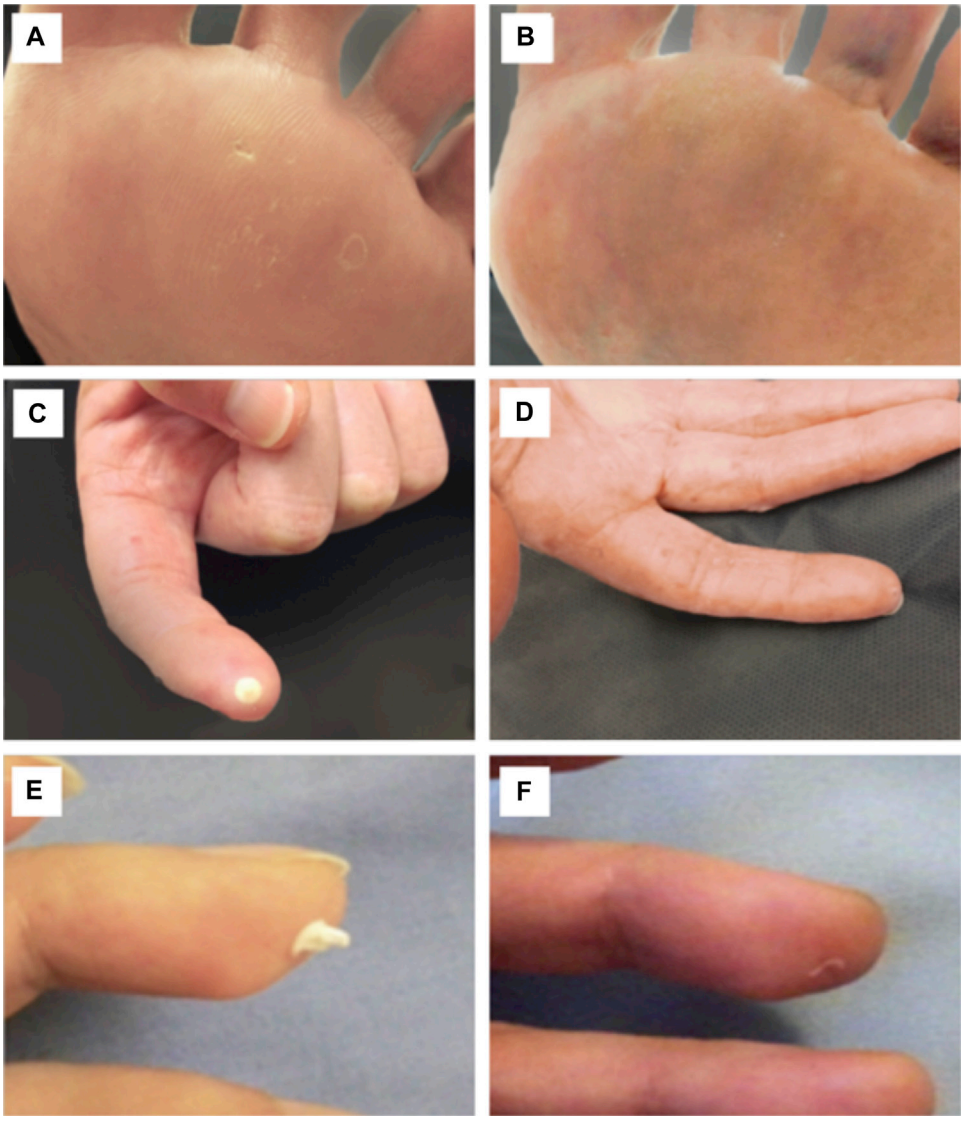

Fig 1. Calcinosis cutis lesions (**A**, **C**, and **E**) before and (**B**, **D**, and **F**) after sodium thiosulfate therapy.

be used to successfully treat microscopic calcifications less than 0.2 cm in size. Intravenous STS therapy is not an ideal form of treatment for patients with CC due to its low efficacy and practicality.

Future investigations should aim to more precisely understand the mechanism of STS and optimize current STS treatment regimens for CC. Given the success of intradermal STS therapy in this study, developments of prospective, controlled, multisite studies would be beneficial to confirm treatment efficacy and optimize procedures for the most effective intradermal delivery, including ideal dosing concentrations and frequency of injections.

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Characterizing dupilumab facial redness in children and adolescents: A single-institution retrospective chart review

To the Editor: Dupilumab facial redness (DFR) is an adverse event characterized by new-onset or paradoxical flaring of facial dermatitis reported in approximately 10% of patients receiving dupilumab.[1] Unlike dupilumab ocular surface disease (DOSD), DFR was not reported in dupilumab clinical trials.[1] Although dupilumab has been approved for the treatment of atopic dermatitis in children as young as 6 years, no dedicated studies have been performed to determine whether DFR occurs at similar rates in children and adults. A total of 225 patients were included in the 2 published retrospective chart reviews describing DFR, only 9 of whom are children.[1,2] Here, this study aims to characterize DFR in the pediatric population.

The University of Connecticut Health Center medical records were queried for all patients younger than 18 years who were prescribed dupilumab. Patients were excluded if they were taking dupilumab for a nondermatologic diagnosis, had not yet taken their prescribed dupilumab, or had no follow-up visits since initiating dupilumab. Patients were categorized as prepubertal or postpubertal based on the average ages of puberty (10 years in girls and 11.5 years in boys).[3] This segmentation was performed because one explanation for DFR is that it is a seborrheic dermatitis-like process, which presumably occurs more frequently in postpubertal children.[1,4] This protocol was approved by the University of Connecticut Health Center institutional review board.

Table I. Patient demographics

Variable	Patients with DFR, n (%)	Patients without DFR, n (%)	*P* value
Sex			>.99
Female	4 (31)	9 (69)	
Male	3 (27)	8 (73)	
Age, y			.63
≤10	1 (17)	5 (83)	
11-15	3 (27)	8 (73)	
16-18	3 (43)	4 (57)	
Puberty			.62
Prepubertal	1 (14)	6 (86)	
Postpubertal	6 (35)	11 (65)	
Dosing frequency			.69
Every 1 week	1 (50)	1 (50)	
Every 10 days	0 (0)	1 (100)	
Every 2 weeks	6 (33)	12 (67)	
Every 4 weeks	0 (0)	3 (100)	
Treatment duration, mo			.33
≤6	2 (20)	8 (80)	
7-12	4 (50)	4 (50)	
>12	1 (17)	5 (83)	
Ocular symptoms			.29
No	6 (26)	17 (74)	
Yes	1 (100)	0 (0)	

DFR, Dupilumab facial redness.

We identified 24 children receiving dupilumab (Table I). All children were prescribed dupilumab for treatment of AD. Overall, 7 of 24 (29%) children had documented worsening or new-onset facial dermatitis after starting dupilumab, 2 of whom had documented neck involvement (29%). DFR occurred more frequently in postpubertal children compared to prepubertal children (35% and 14%, respectively; $P = .63$), and there was a higher incidence of DFR with increasing age (17%, 27%, and 43% for ≤10 years, 11-15 years, and 16-18 years, respectively; $P = .63$). Although trends were apparent, they did not achieve statistical significance. Sex, dosing frequency, and dupilumab dosage were not significantly associated with DFR based on chi-square analysis. Additionally, although anecdotal reports have associated DFR with DOSD, only 1 patient (4%) with DFR experienced DOSD in our study (statistical test, $P = .29$).

Our findings suggest that DFR occurs in children and may occur more frequently in postpubertal children. This finding could be explained by a seborrheic dermatitis−like etiology of DFR with interleukin 4 receptor blockade facilitating a T helper