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Case presentation

Widespread calciphylaxis and normal renal function: no improvement with sodium thiosulfate

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Abstract

Although calciphylaxis generally occurs in patients with chronic renal failure, we present a patient with widespread calciphylaxis in the setting of normal renal function following renal transplant. IV and IL sodium thiosulfate injections were not beneficial in our patient.

Keywords: calciphylaxis, lupus erythematosus, renal transplant, intralesional sodium thiosulfate

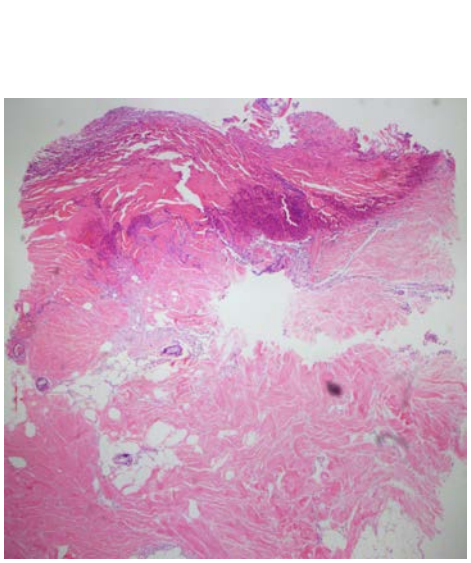
Introduction

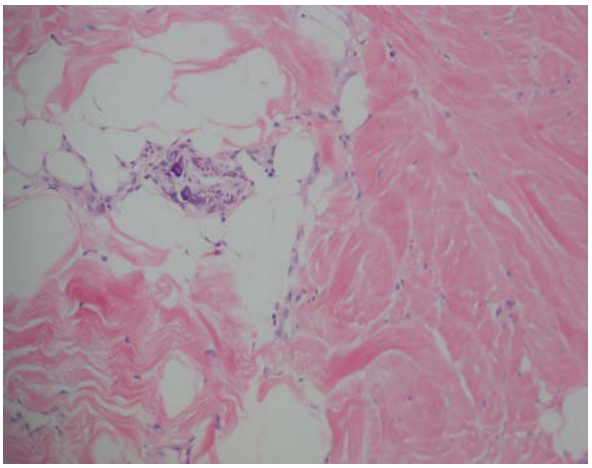
Calciphylaxis usually occurs in patients with chronic renal failure and secondary hyperparathyroidism, although rare cases in the absence of renal failure have been described [1]. Recently, intralesional (IL) sodium thiosulfate has been suggested as a novel treatment for localized calciphylaxis associated with chronic renal disease [2]. We present a patient with widespread calciphylaxis in the setting of normal renal function following renal transplant for which IV and IL sodium thiosulfate injections were not beneficial.

Case synopsis

A woman in her 30s with a history of end-stage renal disease (ESRD) secondary to systemic lupus erythematosus (SLE) was transferred from an outside hospital 7 weeks post donor kidney transplantation. Her transplant was complicated by delayed graft function requiring hemodialysis, but she was discharged a week later on prednisone, tacrolimus, and mycophenolic acid

immunosuppression. One week later she was found to have a faint non-bullous and non-ulcerated eruption. Despite persistent normal renal function, her skin exam progressed and over the ensuing days she developed retiform purpura eventually complicated by cutaneous ulceration and necrosis. Warfarin was stopped and a skin biopsy taken at that time was consistent with calciphylaxis. At the time of transfer to our hospital, her cutaneous exam revealed 2-4 cm retiform purpuric patches with central black eschars distributed on her trunk and extremities. Her kidney function, ionized calcium, phosphorous, antiphospholipid antibodies, and parathyroid hormone were all normal. Given the onset and progression of her rash in the context of normal renal function, a biopsy of a new lesion on her right shoulder was taken and this again showed features consistent with calciphylaxis (Figures 1-3).





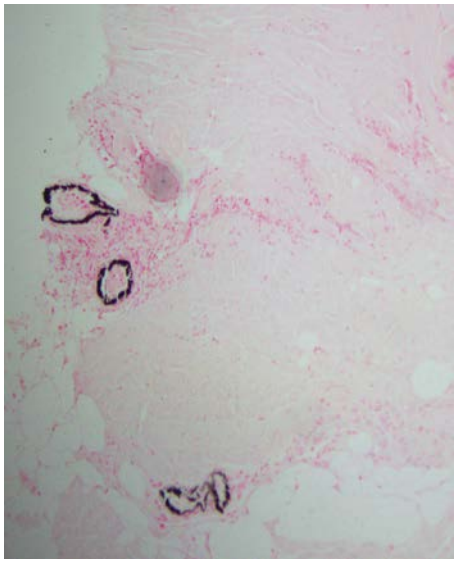
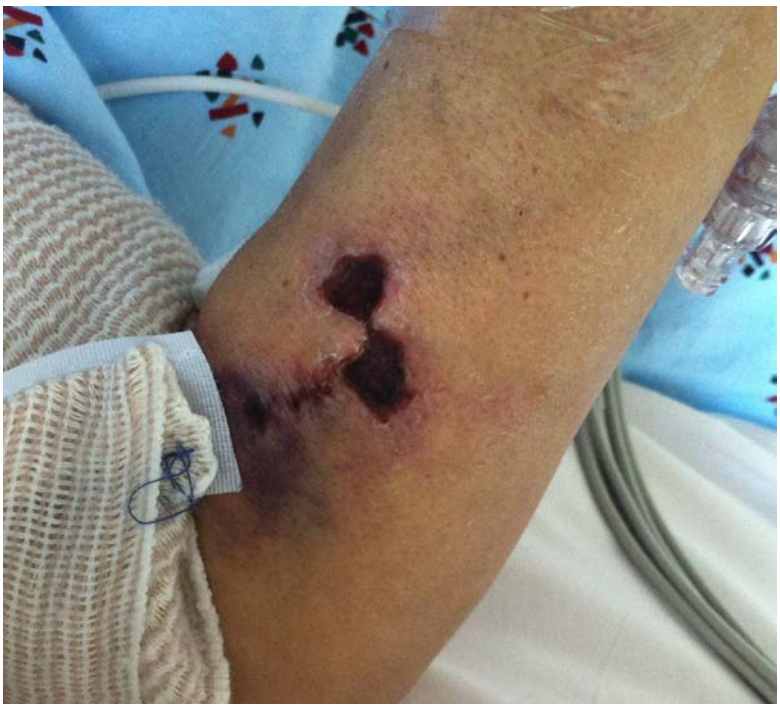


Figure 1. Low power magnification of a biopsy of the right shoulder reveals calcium (blue) in the post-capillary venules (hematoxylin and eosin stain, 4x) **Figure 2.** High power magnification of a biopsy of the right shoulder reveals calcium (blue) in the post-capillary venules (hematoxylin and eosin stain, 10x) **Figure 3.** High power magnification of a biopsy of the right shoulder reveals calcium (black) in the post-capillary venules (von kossa stain, 10x)

Following the initial dermatology consultation, she was started on intravenous (IV) sodium thiosulfate, 25g twice weekly. Since she continued to develop new lesions after one week, a decision was made to increase IV sodium thiosulfate to three times per week and to inject IL sodium thiosulfate (250mg/mL). A total of 4mL was injected into a painful necrotic lesion on the forearm (Figure 4) and 5ml to a newer lesion on the thigh. Injections were performed at 12, 3, 6, and 9 o'clock, approximately 2mm from the lateral edge of skin necrosis. Given a lack of any improvement after two weeks (Figure 5), additional injections were not attempted and instead IV therapy was continued. Unfortunately, the patient continued to decline; lesions progressed onto her face and tongue. She expired two weeks after initial injections were performed.



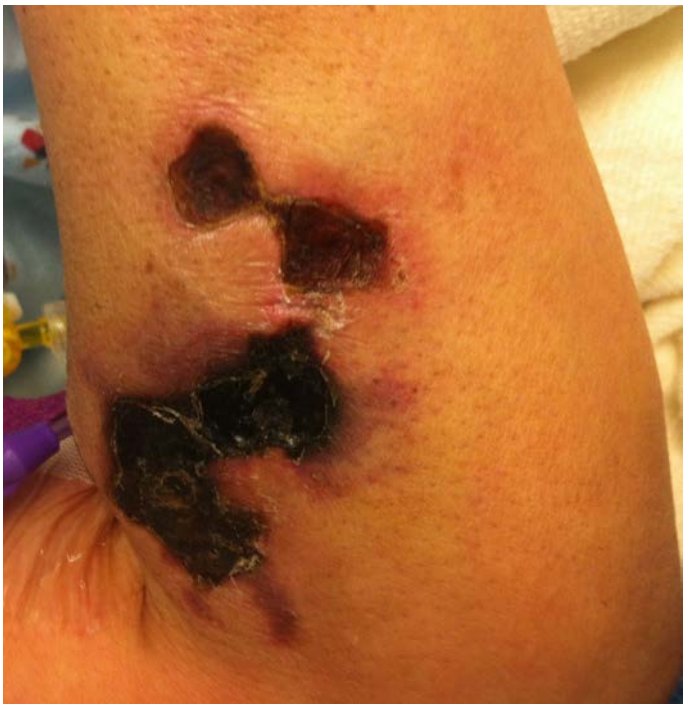


Figure 4. Right proximal forearm lesion 1 day pre-injection. **Figure 5.** Right proximal forearm lesion 8 days post-injection

Discussion

Calciphylaxis is an uncommon, often fatal disorder, characterized by small vessel calcification leading to ischemia, ulceration, and painful tissue necrosis [3]. Although traditionally viewed as a complication of renal failure, cases in nontraditional patients have emerged in recent literature. Uncommon associations have included liver and/or hematologic dysfunction (cirrhosis, hypoalbuminemia, protein C or S deficiency, anticoagulants), malignancy, medications (systemic corticosteroid use, chemotherapy), and metabolic insult (obesity, rapid weight loss, infection) [1]. To our knowledge, the development of calciphylaxis in a patient with normal kidney function following renal transplantation has not previously been reported. The etiology of calciphylaxis in our patient is unclear, though her risk factors include a history of ESRD, and both warfarin and prednisone use. This unique presentation broadens the clinical scope in which calciphylaxis develops.

Sodium thiosulfate may be used to treat calcifying skin conditions. Its action as a chelating agent is thought to convert calcium to soluble calcium thiosulfate, whereas its antioxidant properties may decrease pain [4]. Sodium thiosulfate can improve outcomes when given intravenously for calciphylaxis [5]. It has also been used topically to treat both connective tissue associated calcinosis cutis and familial tumoral calcinosis syndrome [6] and intralesionally for calcinosis secondary to dermatomyositis [7].

Strazzula et al recently proposed that IL sodium thiosulfate may be beneficial for chronic kidney disease patients with localized calciphylaxis [2]. To our knowledge, our case represents the first report of IL treatment for widespread calciphylaxis with normal renal function following renal transplant. Lack of improvement suggests this approach is less effective in systemic, necrotic calciphylaxis. Further investigation is warranted to clarify treatment indications.

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