Calcinosis cutis in the setting of severe COVID-19 infection

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INTRODUCTION

A growing body of data is unveiling the role of skin in understanding the pathophysiologic changes of COVID-19.[1-3] Common cutaneous morphologies of COVID-19 include pernio-like lesions; eruptions that can be urticarial, macular, vesicular, or papulosquamous; and retiform purpura.[1,3] Limited data exist on whether dystrophic calcification—the deposition of insoluble calcium salt in cutaneous and subcutaneous tissue, which has been previously linked to multiple underlying triggers, including infectious, connective tissue–related, endocrinologic, and malignant etiologies—may be a cutaneous manifestation of COVID-19.[4,5] We present a case of dystrophic calcification in the setting of a complex case involving COVID-19 and renal failure as a potential cutaneous manifestation of the disease.

Abbreviation used:

STS: sodium thiosulfate

CASE REPORT

A 51-year-old man with a history of type 2 diabetes mellitus, hypertension, and hyperlipidemia was admitted for acute respiratory distress syndrome in the setting of COVID-19. His hospital course was complicated by the development of a dramatic post–COVID-19 inflammatory response syndrome, marked by high fevers, leukemoid reaction, acute renal failure requiring initiation of renal replacement therapy, deep venous thrombosis and pulmonary embolism requiring initiation of heparin, and pneumoperitoneum.

On hospital day 89 of admission, the dermatology team was consulted regarding a lesion on the right upper arm of unknown duration. Per the patient, the lesion was occasionally tender to palpation but otherwise asymptomatic. The lesion presented with indurated pink-yellow linear columns of coalescing papules arising from an inferior central plaque with an overlying angulated eschar spanning most of the right upper arm (Fig 1).

The patient's chemistries and electrolytes were within the normal range, with the exception of a blood urea nitrogen concentration of 87 mg/dL and a phosphorous concentration of 5 mg/dL. The erythrocyte sedimentation rate was 44 mm/h. Bloodwork was negative for antinuclear antibody.

Two 5-mm punch biopsies were performed at the superior and inferior aspects of the lesion (Fig 1). Biopsy samples showed necrotic changes with extensive calcium deposition involving the dermis and subcutis (Fig 2). These findings and the involvement of vascular walls raised a differential diagnosis of calciphylaxis, Monckeberg medial calcific sclerosis of vessels, or extensive dystrophic calcinosis. The inferior biopsy site also demonstrated thrombus formation within areas of necrosis on pathology. After the skin biopsies, necrotic tissue formed around the sites, consistent with pathergy (Fig 1).

Initial treatment involved wound care with collagenase to the eschar, emollient to all other parts of the lesion, and a covering with petroleum jelly–impregnated gauze. Sodium thiosulfate (STS),

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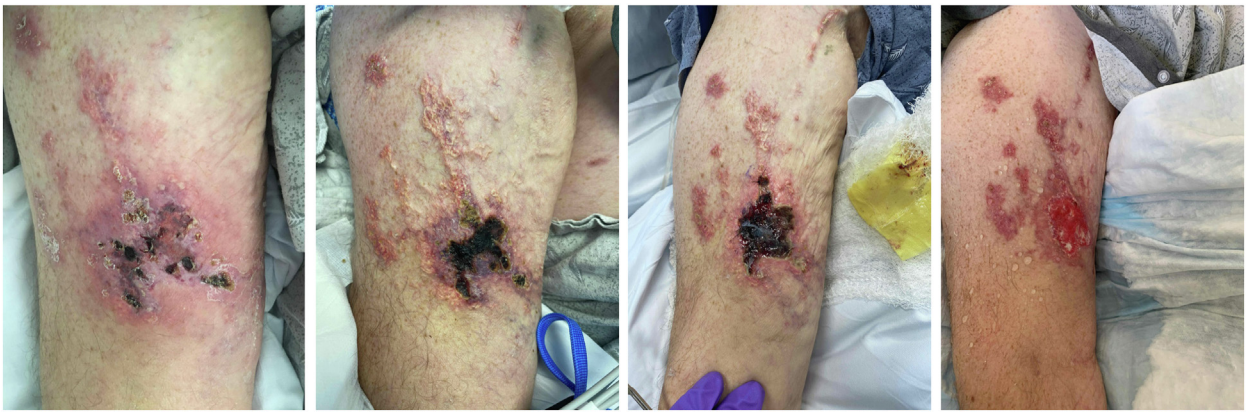

Fig 1. Progression and pathergy of a right upper extremity lesion after biopsy.

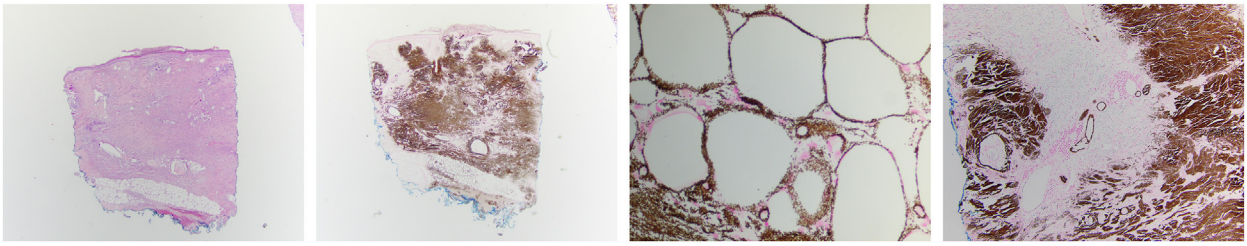

Fig 2. Histopathology of the biopsy sample. *Left* to *right*: Hematoxylin and Eosin stain; Von Kossa stain of superior biopsy site indicating calcium deposition involving dermis and subcutis; Higher magnification Von Kossa stains in the subsequent two panels.

an inorganic salt that increases calcium solubility, has been reported to be helpful in treating calcinosis.[6] Given its potential to induce hypotension, STS was held until the patient's blood pressure stabilized. Once initiated, 25 g of STS in 0.9% sodium chloride was administered over the course of 60 minutes during dialysis sessions 3 times a week for a total of 5 doses. Significant improvement in lesion size was noted with the use of STS, with diminishment of necrotic tissue and no further progression of the lesions (Fig 1).

DISCUSSION

We present a unique case wherein dystrophic calcification arose in the setting of COVID-19 complicated by acute renal failure, systemic inflammatory response, and a prothrombotic diathesis. Calcinosis typically develops as yellow-white papules, plaques, or nodules with possible tissue necrosis or ulceration.[7] In this case, the lesion was largely necrotic with surrounding pink-yellow columns of papules. The combination of examination findings, biopsy results, and pathergy provided clinicopathologic correlation to support a diagnosis of calciphylaxis or dystrophic calcinosis cutis, and the clinical response to STS was in keeping with the observation of its effectiveness in these conditions.[6]

Five subtypes of calcinosis cutis are classically recognized: dystrophic, metastatic, calciphylaxis, idiopathic, and iatrogenic. Dystrophic calcinosis cutis, the most common form, occurs secondary to local tissue damage driven by trauma, infection, or connective tissue disorders.[8] Metastatic calcinosis cutis occurs secondary to systemic calcium and phosphate abnormalities.[9] Calciphylaxis involves calcification of small- and medium-sized vessels and is often associated with chronic renal failure and a need for hemodialysis.[8,10] Iatrogenic calcinosis cutis occurs from administration of calcium- or phosphate-containing solutions that induce precipitation of calcium salts.[11,12]

Regarding the differential between calciphylaxis and dystrophic calcinosis cutis, in this case, components of the clinical picture and biopsy provide support for both potential etiologies. Findings in favor of calciphylaxis include ulceration, thrombus formation, and the clinical picture of renal failure secondary to post—COVID-19 inflammatory response syndrome. However, the extensive spread of calcification, the rope-like pattern of calcium deposition seen on pathology, and the known inflammation secondary to COVID-19 favor dystrophic calcinosis. The exact cause of dystrophic calcification in this patient may be multifactorial, including the recent infection and its associated inflammatory state, the development of acute renal failure, and the exposure to anticoagulant agents in the setting of thromboembolism—all of which may

contribute to the complex process of calcium regulation and homeostasis.

Though cases of morbilliform; urticarial, purpuric, macular erythematous; and vesicular lesions associated with COVID-19 have been more commonly described,[4] dystrophic calcification may be another cutaneous manifestation associated with COVID-19, particularly when associated with a significant concomitant systemic inflammatory reaction.

Given the challenge of treating dystrophic calcification, therapy often prioritizes minimizing symptoms and alleviating functional limitations rather than completely resolving cutaneous calcification.[13] As such, simultaneous treatment of potential underlying conditions is imperative.[14] The preferred initial therapy for dystrophic calcification is often STS, a medication with cation-chelating properties allowing for soluble calcium thiosulfate complex formation.[6] Our observations suggest that clinicians should consider the possibility of dystrophic calcification arising in the setting of severe COVID-19 and acute renal failure, and provide support for the use of STS as a potential treatment option in this clinical context.

Conflicts of interest

None disclosed.

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