

What Is Your Diagnosis?



A 62-year-old woman who was obese with idiopathic thrombocytopenic purpura; a history of diabetes mellitus, hypertension, and acute renal insufficiency; recent treatment with high-dose (2 mg/kg) glucocorticosteroids; and sepsis presented with ulcers on the thighs and buttocks after being transferred in a patient lift. The ulcers had developed in areas of pressure corresponding to placement in the patient lift.

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The Diagnosis: Calciphylaxis

Calciphylaxis is a rare disorder that most commonly affects patients with impaired renal failure. Calciphylaxis, known as calcific uremic arteriopathy,^{1,2} involves calcification of small- and medium-sized blood vessels,³ which may lead to necrosis of the dermis, subcutaneous tissue, muscles, fascia, and internal organs.^{4,6} Calciphylaxis usually occurs in fatty areas such as the calves, thighs (Figure 1), abdomen, and buttocks.^{3,7,8} Although calciphylaxis most commonly is associated with severe renal disease,^{1,3} pharmacologic agents such as glucocorticoids, high-dose vitamin D, warfarin, iron salts, insulin injections, calcium-based phosphate binders, and chemotherapeutic agents also may precipitate this condition.^{9,10} Diagnostic biopsies typically reveal fat necrosis, inflammation, and associated small vessel calcification (Figures 2 and 3).

Our patient may have been predisposed to calciphylaxis due to her history of obesity, diabetes mellitus, and hypertension, and recent high-dose (2 mg/kg) glucocorticosteroid treatment. Five months prior to the current presentation, the patient was admitted to the hospital for treatment of sepsis with high-dose glucocorticoids for presumed idiopathic thrombocytopenic purpura. She also developed several ecchymotic regions on her skin at that time. Additionally, she developed acute renal insufficiency resulting from septic shock that improved over several weeks. Interestingly, 2 months after full recovery of her renal function, which was marked by normal creatinine levels and glomerular filtration rate, she developed a violaceous rash over the thighs and buttocks in the distribution of the straps from a patient lift that was used to transfer her from a bed into a wheelchair while residing at a physical rehabilitation facility. In the time after recovery of renal function, the eruption progressed to necrosis over 2 weeks in the areas of skin that came into contact with the lift's straps. The patient's renal function and parathyroid hormone, ionized calcium, phosphate, and vitamin D levels were all within reference range at the time of diagnosis.

On biopsy, characteristic findings established the diagnosis of calciphylaxis. Furthermore, the pattern of ulceration in pressure areas associated with the patient lift indicated that infection was not the precipitating event. A von Kossa stain highlighted the calcium deposition in small blood vessels in areas of panniculitis (Figure 4). Atherosclerosis may be



Figure 1. Nonhealing skin ulcers secondary to calciphylaxis on the thigh.

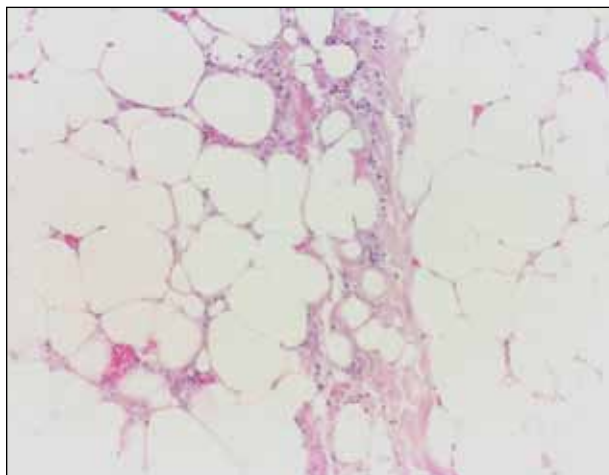


Figure 2. Necrosis within adipocyte lobules was evident and a neutrophilic inflammatory response was noted (H&E, original magnification $\times 100$).

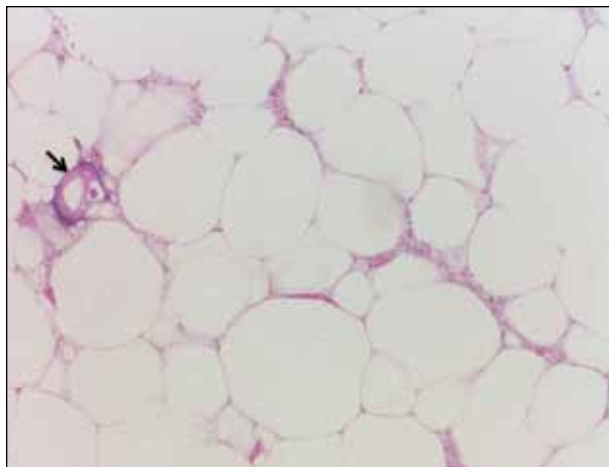


Figure 3. Calcification (arrow) of small blood vessels was evident in areas of panniculitis (H&E, original magnification $\times 400$).

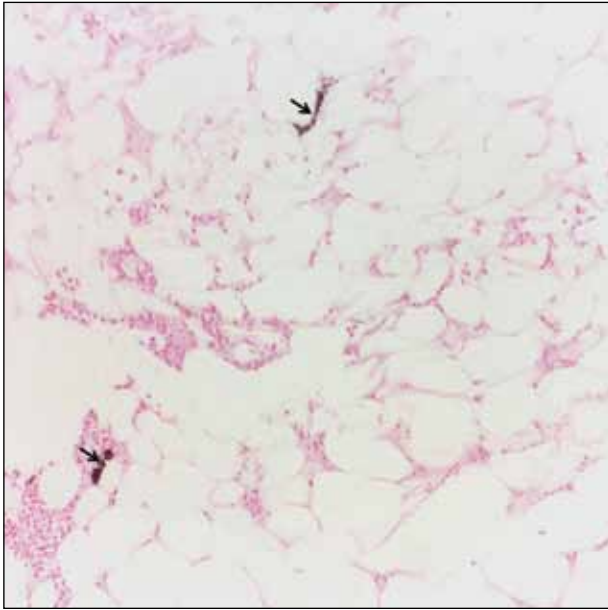


Figure 4. Calcification (arrows) of small blood vessels in areas of panniculitis was highlighted on von Kossa staining (original magnification $\times 100$).

associated with vascular calcification but does not involve acute small blood vessel calcification, and other ulcerative disorders in the differential diagnosis (eg, pyoderma gangrenosum) would not be associated with small vessel vasculitis.

Treatment of calciphylaxis must be individualized. It is important to treat any underlying disease and remove any precipitating factors. In the case of severe renal disease, a multidisciplinary approach typically is necessary.³ Correction of serum calcium and phosphate levels, rapid and safe rehydration, dialysis, and intravenous bisphosphonates all may be needed in patients with chronic kidney disease.¹¹ Surgical management of the nonhealing necrotic skin lesions via surgical debridement and skin grafting has been reported to improve overall morbidity and survival rates.¹² For patients with calciphylaxis from hyperparathyroidism, parathyroidectomy has been used but has demonstrated minimal effects on survival rates.⁹ Currently, there is no standard therapy in place for treatment of calciphylaxis but several are under investigation. Most notably, sodium thiosulfate, an inorganic salt that promotes dissolution of calcium deposits by chelating calcium, has shown rapid improvement when other treatments have failed.¹³⁻¹⁶ In patients with marginal decreases in blood flow and ischemia of skin, hyperbaric oxygen therapy has been found to resolve cutaneous ulcers of calciphylaxis.^{17,18} Patients with renal disease who develop calciphylaxis have benefited from

treatment with cinacalcet, a calcimimetic that lowers parathyroid hormone levels and improves calcium phosphorus metabolism in patients undergoing dialysis.^{13,14}

Our patient was treated with 2 weeks of broad-spectrum antibiotics along with extensive wound care and vacuum-assisted closure of surgically debrided tissue on her thighs and buttocks. Glucocorticoid therapy was rapidly tapered. Three months after the initial presentation, the patient was placed in outpatient wound care with evaluation for hyperbaric oxygen therapy.

Calciphylaxis is a rare condition with a high mortality rate, most often due to septicemia from secondary infection of skin lesions.¹⁹ The exact pathogenic mechanisms are vague but may be the result of several precipitating factors.¹⁰ Local wound care and therapeutics should be used synergistically and individualized for each patient with calciphylaxis.

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