

## Scintigraphic Demonstration of Calciphylaxis

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We report the case of a 59-year-old woman with end-stage renal disease who presented with bilateral medial calf tenderness and subsequent development of a large necrotic plaque that was proven at biopsy to be calciphylaxis. A radionuclide bone scan contributed to management by helping establish the diagnosis. Calciphylaxis is a highly morbid small vessel vasculopathy encountered in patients on hemodialysis. Early recognition and proper management may improve outcomes.

### Introduction

Calciphylaxis is a highly morbid small vessel vasculopathy encountered in up to 4% of patients with end-stage renal disease on hemodialysis. Patients commonly succumb to sepsis within months of the diagnosis. Early recognition and proper management can result in limb salvage and decreased mortality.

### Case Report

A 59-year-old woman with end-stage renal disease presented initially to our vascular clinic with red streaking at the left medial calf area with tenderness and warmth of the area. She had a past medical history

significant for hypertension and diabetes (leading to her end-stage renal disease), peritoneal dialysis for three years after failing hemodialysis, secondary hyperparathyroidism, obesity, hyperlipidemia, and obstructive sleep apnea.

After ruling out an underlying abscess with ultrasound of the left lower extremity, the patient was treated with oral antibiotics for presumed cellulitis. The pain and size of the lesion progressed over the next two weeks. The patient denied fevers or constitutional symptoms and had no laboratory evidence of infection. After failure of oral antibiotics the patient was admitted for intravenous antibiotics, discharged, and then given another trial of oral antibiotics. The multiple courses of antibiotics included keflex, nafcillin, docloxicillin, and bactrim but there was no improvement in her symptoms.

Approximately one month after initial presentation, the patient was seen in our renal clinic where she complained of ongoing lower extremity pain, now bilateral, with some clear drainage from the left medial calf area. Bilateral tibia-fibula radiographs with focus on soft tissue showed streaky calcifications in the superficial soft tissues (Fig. 1).

The patient was admitted for presumed calciphylaxis and a peripherally inserted central venous line

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Abbreviations: MDP, methylene diphosphonate; Tc, technetium

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was placed with intent to begin therapy with sodium thiosulfate. Dermatology was consulted regarding the now necrotic lesion on her medial left calf. Their exam documented a 14 cm x 8 cm ill-defined indurated tender plaque with distal 3 cm necrotic patch with central clearing at left medial calf area. An incisional wedge biopsy at this site was performed for diagnosis. The right medial calf demonstrated an 8 cm stellate ill-defined bluish very tender patch. No skin lesion was noted at the right medial thigh but there was an area of extreme tenderness, possibly heralding a new/developing lesion.

Given the positive findings on the bilateral tibia/fibular plain films and the clinical concern for calciphylaxis as well as osteomyelitis, a whole body bone scan using 21 mCi Tc-99m-labeled MDP was performed (Fig. 2).

The flow study and blood pool images showed increased activity in the lower legs, left greater than right (not shown). Delayed images showed bilateral diffuse

increased uptake in the soft tissues below the knees. The left lower leg had a photopenic area corresponding to the necrotic wound noted on clinical exam. These findings together with the clinical presentation lead to a radiologic impression of bilateral lower leg calciphylaxis with focal area of necrosis on the left. Note was also made of increased uptake in the skull bilaterally and non-visualization of the kidneys consistent with renal osteodystrophy.

The patient was begun on triweekly sodium thio-phosphate intravenous infusions of 50 g given over 1 hour. The hospital course was complicated by peritonitis and continued wound necrosis at the bilateral medial calf area that eventually required debridement followed by application of a split-thickness autograft from scalp. A multidisciplinary team involving vascular surgery, plastic surgery, nephrology, burn specialists, and family medicine was key to preserving bilateral lower extremities.



Figure 1. 59-year-old woman with calciphylaxis. Anterior-posterior left tibia-fibula radiograph demonstrates increased soft tissue density of the left leg with diffuse fine linear opacities correlating to calcified small vessels seen with calciphylaxis and on this patient's skin biopsy.

## Discussion

Lipoma arborescens is a rare benign lesion, which Our intent in presenting this case is the raise awareness of the soft tissue findings of calciphylaxis on bone scans. Early identification of calciphylaxis can lead to limb salvage. Calciphylaxis affects up to 4% of the dialysis population [1]. Although not common, calciphylaxis is encountered in routine clinical practice across a broad range of specialties. Initial symptoms of pain and erythema can mimic cellulitis and lead to ineffective oral or intravenous antibiotic therapy, as presented in this case. Indurated painful plaques with ulceration and necrosis usually ensue, which in turn can lead to sepsis and death. Early diagnosis requires a high level of suspicion in the high risk population and may be aided by biopsy and bone scan.

The common endpoint of calciphylaxis is calcium deposition and fibrosis in the skin and subcutaneous tissue resulting in ischemia followed by necrosis of the tissue. Although the pathophysiology remains elusive, it is thought that abnormal phosphate/calcium homeostasis seen in dialysis patients leads to characteristic calcium deposition in small dermal and subcutaneous vessels with secondary fibrosis and thrombosis [2], sometimes referred to as a calcific thrombogenic microangiopathy.

Long-term dialysis patients with secondary hyper-

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Figure 2. Tc-99m MDP bone scan shows markedly increased uptake in the skin and subcutaneous tissues of the bilateral calves, most prominent on the left (arrow). A large photopenic defect at the medial calf (arrowhead) correlates with a large necrotic plaque on physical exam. Increased uptake in the skull and non-visualization of the kidneys is consistent with renal osteodystrophy.

parathyroidism are thought to be at highest risk [3], however, calciphylaxis is not limited to this population. Other risk factors include obesity and female gender 3:1. Patients typically present with painful and sometimes ulcerating plaques in the trunk or extremities with the distal lower extremities being the most common site [4,5]. These can begin with a subtle redness and tenderness of a focal small area and progress into a larger area of intense erythema. These lesions are usually hard, and can have regions of violaceous mottling, plaques, and livido reticularis. Later lesions can develop a stellate configuration with purpura and with necrosis can have

a black eschar type appearance [6]. Mortality is approximately 60%, usually from sepsis, and increases to above 80% after ulceration [5] with median survival of as dismal as 9.4 months [7]. Pain associated with the skin and subcutaneous lesions of calciphylaxis can be severe and debilitating. Large doses of analgesics are used and early involvement of a pain consult team is appropriate [3].

Although tissue is necessary for firm diagnosis of calciphylaxis, some practitioners caution that there is a poor likelihood of healing the primary biopsy site [3] and prefer to make the diagnosis on clinical grounds. These clinicians reserve biopsy only for unusual lesions that require exclusion of other possible etiologies. Regardless, consultation with dermatology will lend insight to this issue. Although a bone scan can be helpful in identifying calciphylaxis and possibly in monitoring the course of treatment, it is by no means mandatory and at some centers not routinely used in establishing a diagnosis of calciphylaxis. However, osteomyelitis can be a concern with this clinical presentation and bone scan can serve a dual purpose of ruling out osteomyelitis while demonstrating calciphylaxis.

The case presented here involved family practitioners, vascular surgeons, dermatologists, radiologists, and nephrologists before a final diagnosis was established, thus emphasizing the broad spectrum of specialties encountering patients with calciphylaxis. With better awareness of calciphylaxis as a disease entity, earlier and more effective treatment may ensue.

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