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Case presentation

Tender, necrotic plaques of the glans penis due to calciphylaxis

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Abstract

Calciphylaxis, also known as calcific uremic arteriolopathy, is a rare, but often fatal condition involving vascular calcification that can result in tissue ischemia and cutaneous necrosis. It is most often seen in patients with renal failure among many other occasionally reported etiologies. Below, we present a rare and challenging case of calciphylaxis involving the glans penis and right leg in a man with end stage renal disease on hemodialysis.

Keywords: calciphylaxis, calcific uremic arteriolopathy, penile necrosis

Introduction

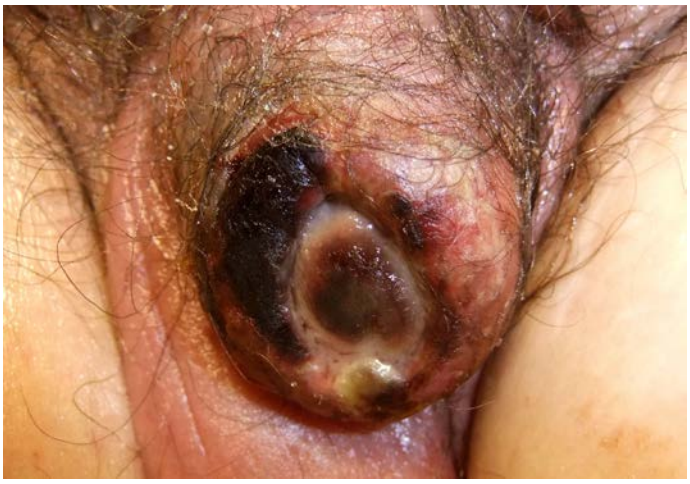
Calciphylaxis, also known as calcific uremic arteriolopathy, is a rare, yet serious condition characterized by vascular calcification resulting in tissue ischemia and cutaneous necrosis [1]. Owing to extensive collateral circulation of the perineum and lower abdomen, calciphylactic necrosis of the penis is very rare with very few cases reported in the literature [2]. We describe a challenging case of calciphylaxis involving the glans penis and right leg in a man with end stage renal disease on hemodialysis.

Case synopsis

A 58-year-old man with a history of end stage renal disease on hemodialysis, peripheral arterial disease, and diabetes mellitus was admitted to the hospital with necrosis of the glans penis and right leg as well as a rash on his right leg. He first noticed tender, erythematous macules on his penis and right leg one month prior to presentation with a rapid progression to the current state. The patient's left leg had been amputated below the knee four months earlier as a result of acute limb ischemia secondary to peripheral arterial disease. He denied any history of recent illness, trauma, fever, or chills.

Upon admission, he was started on morphine for pain and a dermatology consult was requested. Cutaneous examination revealed a 2 cm firm, black, leathery necrotic plaque with surrounding poorly demarcated purpura of the glans penis (Figure 1). A 10 cm

black, necrotic plaque with surrounding retiform purpura was also present on his posterolateral right leg (Figure 2). A 5mm punch biopsy was performed on a violaceous patch on the right leg. The histopathologic findings of the punch biopsy specimen revealed a necrotic epidermis and dermis with dilated blood vessels containing small vascular thrombi (Figure 3). Calcium deposits involving the small and medium sized vessel walls in the deep dermis and the subcutaneous tissue were noted. Von Kossa staining was performed and highlighted the calcium deposits within the vessel walls (Figure 4), confirming a diagnosis of calciphylaxis.



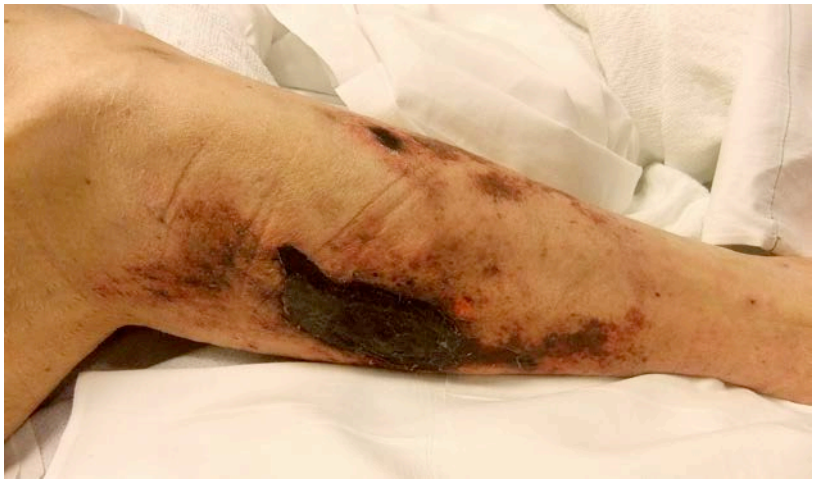
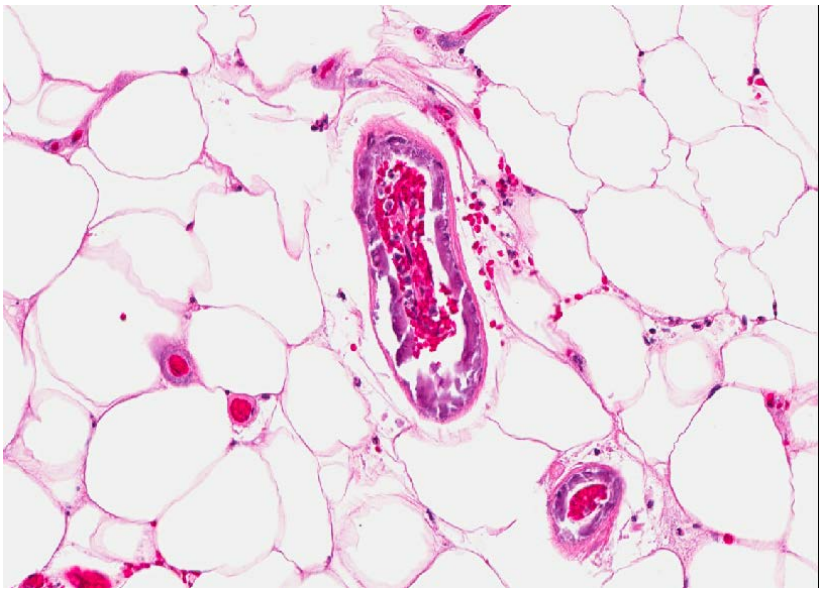


Figure 1. Firm, black, leathery necrosis of the glans penis **Figure 2.** Black, leathery necrosis and tender retiform purpura of the right leg



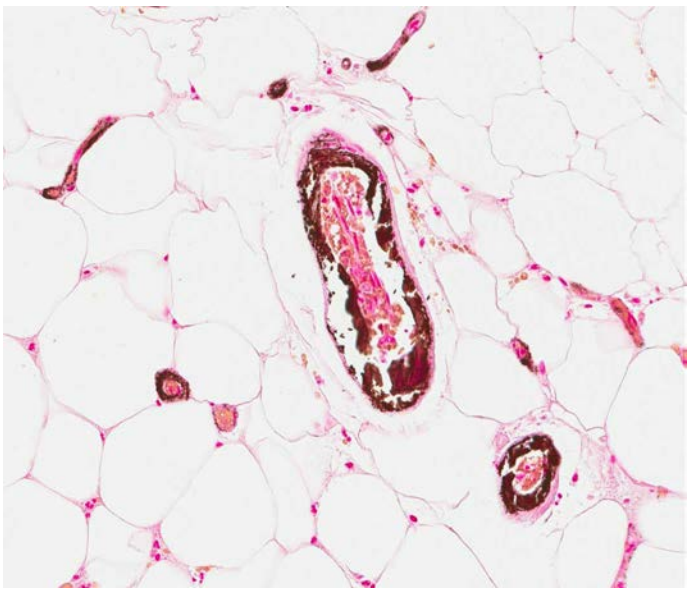


Figure 3. Histopathology reveals dilated blood vessels containing small thrombi and calcium deposits in the vascular walls (H&E, original magnification x14). **Figure 4.** Von Kossa staining highlights the calcium deposits within the small and medium sized vessel walls (Von Kossa, original magnification x14).

Laboratory evaluation revealed normal calcium (9.0 mg/dL), phosphorous (4.1 mg/dL), and corrected-calcium x phosphorous product (39.8 mg^2/dL^2). The parathyroid hormone was found to be elevated (410 pg/mL).

The patient was treated with ongoing hemodialysis, sodium thiosulfate, and hyperbaric oxygen. Ultimately, he succumbed to his disease three months later.

Discussion

The exact pathogenesis of calciphylaxis remains unclear, but it occurs predominantly in those with end stage renal disease undergoing chronic hemodialysis. Other risk factors include female gender, diabetes, obesity, concomitant vascular disease, elevated calcium x phosphate product (CPP), and hyperparathyroidism secondary to nephropathy [1,3]. A CPP greater than 70

mg^2/dL^2 may put patients at an increased risk for vascular calcification, but it is not required for patients to develop calciphylaxis and many patients, as in this case, have a normal CPP [4].

Clinically, patients often present with exquisitely tender, erythematous to violaceous macules and patches that appear in a livedoid pattern, often referred to as retiform purpura. These patches may progress into plaques with central necrosis and black eschar formation [5]. The lower extremities are the most common site for these lesions to occur. Calciphylactic necrosis of the penis is very rare because the penis receives blood from three interconnected arterial pathways: the dorsal artery of the penis, the deep artery of the penis, and the urethral artery [2]. Regardless of location, the morbidity and mortality is significant, with death occurring in more than 50% of patients within one year of diagnosis [6]. Death usually results from septicemia owing to the impaired integrity of the epidermis and dermis.

The differential diagnosis for necrotic lesions of the penis includes Fournier's gangrene, peripheral vascular disease, and calciphylaxis [2]. In this case, the diagnosis was challenging because of the patient's recent history of peripheral arterial disease with limb amputation. However, calciphylaxis was particularly likely given the patient's history of end stage renal disease treated with hemodialysis. All of the items in the differential diagnosis above usually portend a poor prognosis, but it is very important to distinguish between these entities with a thorough history and physical exam to enable the appropriate treatment to be administered as timely as possible.

Although a thorough history and clinical features may be suggestive of calciphylaxis, histopathological examination of a skin biopsy is the gold standard for diagnosis [3]. Calcium deposition in the media of dermal and subcutaneous arterioles is the most common histopathologic feature [3,7]. The Von Kossa stain may be utilized to highlight calcium deposition as seen in the histopathological evaluation of this patient's punch biopsy specimen (Figure 4). Vascular thromboses and cutaneous necrosis is also seen in the majority of patients [7].

A multi-interventional treatment plan is the best approach to managing patients with this challenging disease. Wound care is of utmost importance along with hemodialysis, which may need to be increased if patients are already being dialyzed. More recently, many studies have shown improvement with sodium thiosulfate, generally dosed at 25mg IV post-hemodialysis three times a week [8,9]. Sodium thiosulfate is used to displace calcium ions from vascular deposits by forming calcium thiosulfate, which,ultimately gets excreted by the kidneys or dialyzed [10]. Hyperbaric oxygen therapy has been used to restore tissue PO_2 and thus enhance fibroblast proliferation, collagen production, and angiogenesis in areas of calciphylactic skin ulcers [11].

Calciphylaxis is an uncommon and difficult diagnosis to make and lesions involving the penis are even more rare. When penile lesions are present, infection and arterial disease should be considered in addition to calciphylaxis. Appropriate diagnosis should be made to allow proper treatment to be initiated in a timely manner.

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