

Case Report

Penile Necrosis in End-Stage Renal Disease

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Penile necrosis in the form of dry gangrene in end-stage renal disease (ESRD) is a rare but devastating condition that usually has a grim prognosis. Treatment may be either surgical or conservative, and is usually dictated by the patient's general condition, in addition to symptoms such as pain and urinary obstruction. Herein, we report 3 additional cases of penile necrosis in ESRD.

Case Reports

Case 1— The first patient (IB) was a 52-year-old man with chronic liver disease, type II diabetes, and ESRD. He had been on hemodialysis for 1 year when he developed a 4-cm superficial ulcer on the medial aspect of his left foot, and an exudative ulcer on the ventral aspect of his penis proximal to the glans. Initially, the lesion on the foot was considered a diabetic ulcer and the penile lesion was thought to be a drug eruption. The penile lesion progressed despite wound care with dressings, and the patient also began to experience severe pain. As a result, a urology consult was obtained 1 week after presentation. Physical examination revealed a circumcised penis with a 2-cm necrotic ulcer involving the ventral portion of the sulcus coronarius and the glans. At this stage, laboratory studies showed serum calcium 6.8 mg/dL (normal: 8.4-10.2 mg/dL), phosphorus 9.6 mg/dL (normal: 2.7-4.5 mg/dL), and parathyroid hormone (PTH) 0.98 ng/mL (normal: 0.01-0.07 ng/mL). Pelvic arteriography demonstrated extensive atherosclerosis of both the internal iliac and the internal pudendal arteries, but no occlusion. The penile lesion was debrided and a urethral catheter was inserted. The penile lesion progressed despite debridement and the patient continued to suffer severe pain that was not responsive to narcotic analgesics. Partial penectomy was performed in the second week after presentation. Five days after surgery, the patient developed multiple ecchymotic and superficial necrotic lesions on both legs. His general condition continued to deteriorate, and he died 3 weeks after initial appearance of the penile ulcer. Histopathological examination of the partial penectomy specimen revealed atherosclerosis of the medium-sized arteries and intraluminal

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calcification of the small arteries and arterioles ([Figure 1](#)). There was also extensive calcification of the corporal bodies and the tunica albuginea.

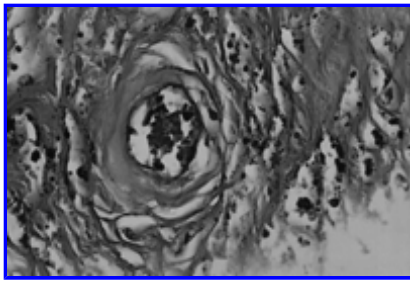


Figure 1. Slide of partial penectomy specimen from case 1 shows intraluminal thrombus and calcification in a small artery. Hematoxylin and eosin stain, magnification 200x.

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Case 2— The second patient (YK) was a 51-year-old man who had amyloidosis secondary to familial Mediterranean fever and ESRD. He had been on hemodialysis for 9 years when he developed a painful necrotic lesion on the glans of his circumcised penis. A few weeks after detection, the lesion had progressed to involve the entire glans. The patient also had a necrotic ulcer in the left inguinal area and painful subcutaneous lumps on both shoulders and both elbows. Laboratory testing revealed serum calcium 9.15 mg/dL, phosphorus 6.3 mg/dL, and PTH 0.42 ng/mL. The penile and inguinal lesions were debrided. A pelvic arteriogram showed irregularity and stenosis of the internal iliac arteries due to atherosclerosis. The left and right penile arteries were both patent but showed irregular contours. The distal segments of the dorsal and cavernosal arteries were obliterated. Severe calcification was noted in the walls of the penile, dorsal penile, and cavernosal arteries ([Figure 2](#)).

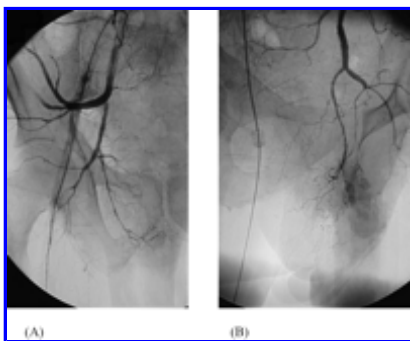


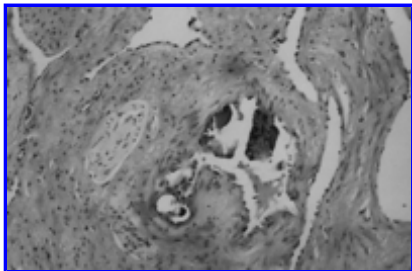
Figure 2. Pelvic arteriogram from case 2 shows patent penile artery with irregular contours, and obliteration of the distal segments of the dorsal and cavernosal arteries **(A)** on the right and **(B)** left.

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Despite wound care with wet dressings and repeated debridement, the necrotic lesions progressed and the patient developed severe pain that was unresponsive to narcotic analgesics. Partial penectomy was performed 2 weeks after initial debridement. The wound healed well, and the patient went home 5 days after the operation. Eight months later, he required amputation of the first, second, and third fingers of his right hand. Ten months after penile resection, the necrotic lesion in his left

inguinal area had progressed and another necrotic ulcer had developed in the right inguinal region. He also had painful nodules affecting both shoulder and both elbow joints. Biopsies of these revealed a diagnosis of pseudotumoral chondrocalcinosis. By this stage, the patient's serum calcium and phosphorus levels had risen to 11.2 mg/dL and 8.53 mg/dL, respectively. He died 1 year after partial penectomy. Histopathological examination of the partial penectomy specimen showed calcification of the tunica media, luminal obliteration in the small arteries due to intimal hyperplasia, and intraluminal calcium deposits. The tunica albuginea also exhibited calcification, and atherosclerosis was noted in the small arteries within the corporal bodies ([Figure 3](#)).



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Figure 3. Atherosclerotic calcification of a small artery within the corpus cavernosum in case 2. Hematoxylin and eosin stain, magnification 200x.

Case 3— The third individual (HC) was a 56-year-old man who had type II diabetes, hypertension, and ESRD. He had been on hemodialysis for 1 year when he was referred to our urology department for a painful penile lesion. One year before presentation, the patient had developed a 2-cm dry necrotic ulcer below the lateral malleolus of his left foot and necrosis of multiple phalanges. He had since had his left foot, left distal arm, and the second and third fingers of his right hand amputated. In the urologic evaluation, physical examination revealed a circumcised penis with a 5-cm necrotic area on the ventral aspect just proximal to the frenulum. Testing showed serum calcium 8.4 mg/dL, phosphorus 3.7 mg/dL, and PTH 0.36 ng/mL. A pelvic arteriogram demonstrated extensive atherosclerosis in all branches of the internal iliac arteries, and total occlusion of the penile branches of both pudendal arteries ([Figure 4](#)). The patient was scheduled for a left below-the-knee amputation, and debridement of the penile lesion was performed in the same session. However, after debridement the necrosis progressed to involve all of the glans and the penile shaft, and the pain became severe and unresponsive to narcotic medication. Consequently, partial penectomy was performed the following week. The penile stump healed poorly and became infected despite vigorous wound care. The stump and the infected scrotal tissues were further debrided, and a cystostomy tube was placed. The patient's general condition deteriorated and he died because of sepsis 3 months after the penile lesions first appeared. Histopathological examination of the partial penectomy specimen revealed extensive atherosclerosis of the medium-sized arteries.

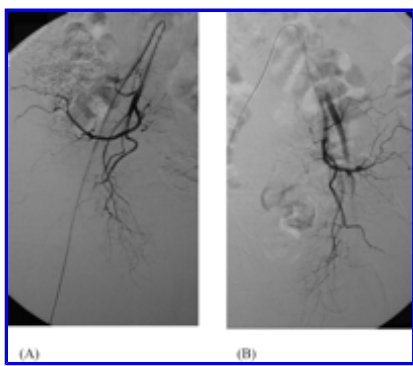


Figure 4. Pelvic arteriogram from case 3 shows total occlusion of the penile branch of the pudendal artery (**A**) on the right and (**B**) left.

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Comment

Vascular calcification (VC) is a well-known condition associated with ESRD. In 1 study of patients on long-term hemodialysis, the authors observed radiological evidence of vascular calcification in 39% of the patients at the start of dialysis, and found that this increased to 92% and that severity progressed over 10 years ([Goldsmith et al, 1997](#)). Another investigation revealed that 19% of male patients on maintenance hemodialysis show calcification of the penile artery on plain x-ray films ([Dalal et al, 1992](#)).

Calciophylaxis is a rare but frequently fatal condition in patients with chronic renal failure. It is characterized by calcification of subcutaneous arterioles and infarction of the adjacent subcutis and skin, which are considered primary and secondary lesions, respectively ([Janigan et al, 2000](#)). The pathogenesis of this condition is still not clear, and no single laboratory test is diagnostic. Instead, the diagnosis is made on the basis of the clinical scenario and is supported by histological findings. The primary lesion is caused by the accumulation of calcium salts in the media of small arteries and arterioles in response to a challenging agent in a hypersensitive environment. Subsequently, the intima becomes thickened by loose connective tissue and this narrows the lumen. Infarcts of the subcutis and skin occur secondarily, and are responsible for the initial clinical manifestations of the syndrome. Before the skin ulcerates, the infarctions confer a firm, lumpy, plaquelike character to the subcutis. This then progresses to painful violaceous lesions and hemorrhagic mottling of the skin. Variations in the distribution of the secondary lesions are used to identify subtypes of the condition. Typical lesions that develop in the skin of the breasts, lower abdominal wall, and upper thighs are classified as the proximal form, whereas those on the legs or arms (or both) are categorized as the distal variant. Some patients may show both of these patterns of distribution. Patients with necrosis of the hands, fingers, feet, toes, or penis are classified as having acral gangrene variants. However, acral gangrene and atherosclerotic gangrene may occur simultaneously, and are difficult to clinically distinguish because the lesions may be similar in both.

In a recent review, 34 cases were identified in the literature ([Karpman et al, 2003](#)). Many of these individuals also have other systemic illnesses, such as diabetes, coronary artery disease, chronic obstructive pulmonary disease, amyloidosis, chronic liver disease, and malignancy. Most patients have elevated serum calcium-phosphorus product, and elevated serum PTH values. A trial of conservative treatment with meticulous wound care with or without circumcision may be appropriate for some patients since resolution of the lesions or autoamputation have been reported. The

indications for surgical resection are pain or urinary obstruction or both. Survival time for the patients with available data ranged from less than 1 month to 12 months. Patients who underwent parathyroidectomy seemed to have better outcomes with respect to both penile necrosis and survival.

Wood and co-workers introduced the term "penile calciophylaxis" in 1997 ([Wood et al, 1997](#)). From that date on, all case reports have referred to penile necrosis in ESRD as penile calciophylaxis. However, some of these patients did not exhibit the characteristic skin lesions and histopathologic findings of calciophylaxis. It is probable that some of these patients who were reported to have penile calciophylaxis actually exhibited penile necrosis due to the VC that is very common in ESRD.

Two of our three patients had calciophylaxis. One of these men (case 1) had the distal type, with lesions on his legs, and the other (case 2) had the proximal type, with lesions on his lower abdomen and in the inguinal areas. The latter patient also exhibited ischemic necrosis of multiple phalanges. Our third patient had multiple ischemic necrotic lesions of the extremities together with penile necrosis. Two of the cases (cases 2 and 3) also featured obliteration of the arteries of the penis. These findings indicate that penile necrosis was caused by calciophylaxis in case 1, and by occlusion due to VC in case 3. In case 2, both of these factors contributed to the patient's condition.

It is unclear whether the penile necrosis that occurs in patients with and without calciophylaxis results from the same or 2 different pathological processes. We believe that penile necrosis is a consequence of ischemia caused by accelerated VC in ESRD, and that, in some patients, calciophylaxis is a contributing factor that triggers or exacerbates this situation. Thus, the term "penile calciophylaxis" is inaccurate in most cases, and should no longer be used. Instead, this condition should be identified as "penile necrosis in ESRD," and contributing factors such as diabetes or calciophylaxis should be mentioned as additional issues. Adopting this system would prevent any further confusion of terminology.

Penile necrosis in ESRD is frequently a poor prognostic sign. A trial of conservative treatment may be appropriate according to the patient's general condition and symptoms. Surgical resection is reserved for patients with severe pain, infection, or obstruction, and for those that do not respond well to conservative measures. Wound infection and disruption can be problematic after surgical resection despite meticulous wound care. Parathyroidectomy should be considered in patients with elevated serum PTH.

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