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CASE REPORT

Simultaneous Penile Gangrene and Testicular Infarction Secondary to Calciphylaxis in a Uremic Patient

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We report here a 46-year-old man with end stage renal disease (ESRD) secondary to type 2 diabetes, who had been on hemodialysis for 5 years. He had a painful glans lesion for 1 week. Five days later, he also complained of right testicular pain. Computed tomography of the pelvis demonstrated calcification of both penile arteries. Scrotal sonography revealed right testicular infarction. He received partial penectomy and right orchiectomy because of progressive lesions and intractable pain. Pathologic examination revealed testicular and penile tissue with necrotizing inflammation accompanied by multifocal calcification in the tunica media, compatible with calcinphylaxis. This is the first report to document simultaneous penile gangrene and testicular infarction secondary to calciphylaxis.

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1. Introduction

Calciphylaxis, also called calcific uremic arteriolopathy, is a small-vessel vasculopathy with medial calcification, intimal fibrosis and thrombosis resulting in ischemia and necrosis of the skin, subcutaneous fat, visceral organs, and skeletal muscle. Clinical manifestations include painful, violaceous skin lesions that may progress to chronic ulcers, tissue necrosis and gangrene, and can ultimately lead to amputation, sepsis, and death.[1] Calciphylaxis is an uncommon systemic disease occurring in 1–4.1% of the hemodialysis population.[1,2] It is sometimes observed in patients with end-stage renal disease (ESRD) and secondary hyperparathyroidism, but is known to occur in the absence of renal or parathyroid disease.[3] Since the first description by Ivker et al.[4] in 1995, only 37 cases have been documented to date in the literature concerning penile gangrene or necrosis due to calciphylaxis.[5] However, to the best of our knowledge, simultaneous penile gangrene and testicular infarction have not been reported previously. This report emphasizes the etiology, clinical presentation and management in an extremely rare case.

2. Case Report

A 46-year-old man had ESRD secondary to type 2 diabetic nephropathy and had been on hemodialysis for 5 years. He was also being treated for hypertension and coronary arterial disease. He suffered a painful glans lesion for 1 week before coming to our emergency room. History showed no trauma and no indication of sexual disease. Physical examination revealed that the prepuce was phimotic with purulent discharge. There was no evidence of inguinal lymphadenopathy. Balanoposthitis was suspected,

and a dorsal slit was made and empiric antibiotics were given. Five days later, the wound was healing poorly and the patient also complained of right scrotal pain. Scrotal sonography showed right testicular infarction (Figure 1). Pelvic computed tomography revealed significant calcification of the patient's bilateral penile arteries and bilateral spermatic cord. Plain films of the hand and leg also showed calcification of adjoining vessels (Figure 2). Laboratory results showed a calcium level of 9.8 mg/dL (normal, 8.4–10.2 mg/dL), phosphorus level of 4.1 mg/dL (normal, 2.3–4.7 mg/dL), and parathyroid hormone (PTH) level of 27.5 pg/mL (normal, 14–72 pg/mL). The penile lesion became gangrenous (Figure 3) and the pain was not relieved by medication, so the patient received right orchiectomy, partial penectomy and suprapubic cystostomy. The patient had a daily urine output of 200 mL, and the remaining penile shaft was shorter than 1 cm. He might have had difficulty in voiding. Therefore, we performed suprapubic cystostomy for urinary diversion.

Pathologic examination revealed penile and testicular tissue with necrotizing inflammation (Figure 4) accompanied by multifocal calcification in the vascular wall (Figure 5) compatible with calciphylaxis. The patient was discharged with a favorable condition. After 14 months, he succumbed to acute myocardial infarction.

3. Discussion

The etiology of calciphylaxis is still not well known. This condition is caused by the accumulation of calcium salts in the tunica 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.[5] This leads to decreased organ perfusion and, later, infarction. Most patients with calciphylaxis have ESRD on hemodialysis, which may also lead to high levels of calcium, phosphorus, and PTH. In those cases not associated with ESRD, there is often primary or tertiary hyperparathyroidism, or other causes of hypercalcemia.[2] Laboratory values can be helpful in determining the diagnosis of calciphylaxis. The calcium-phosphate product is elevated in up to 80% of patients with calciphylaxis, and PTH is also

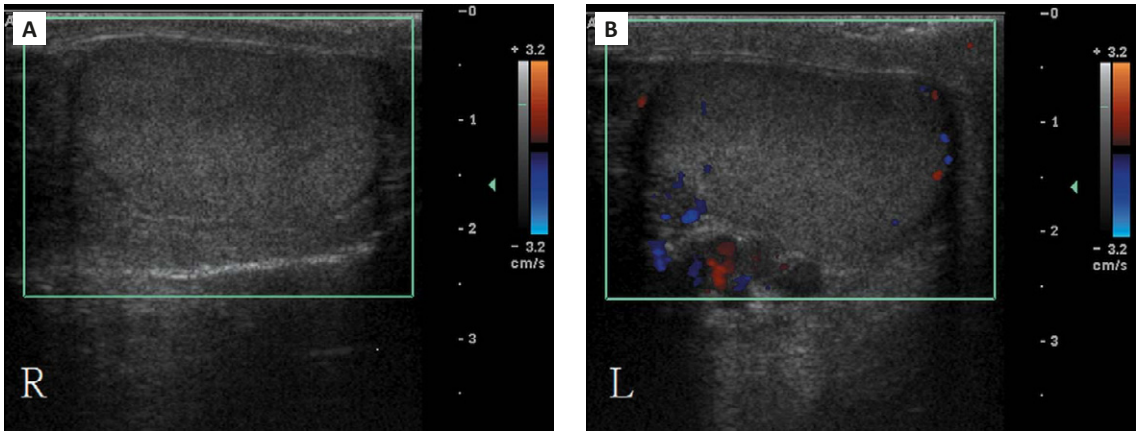

Figure 1 (A, B) Color duplex sonography shows normal sizes of both testes. (A) Vascular flow was not observed in the right (R) scrotum but (B) was observed in the left (L).

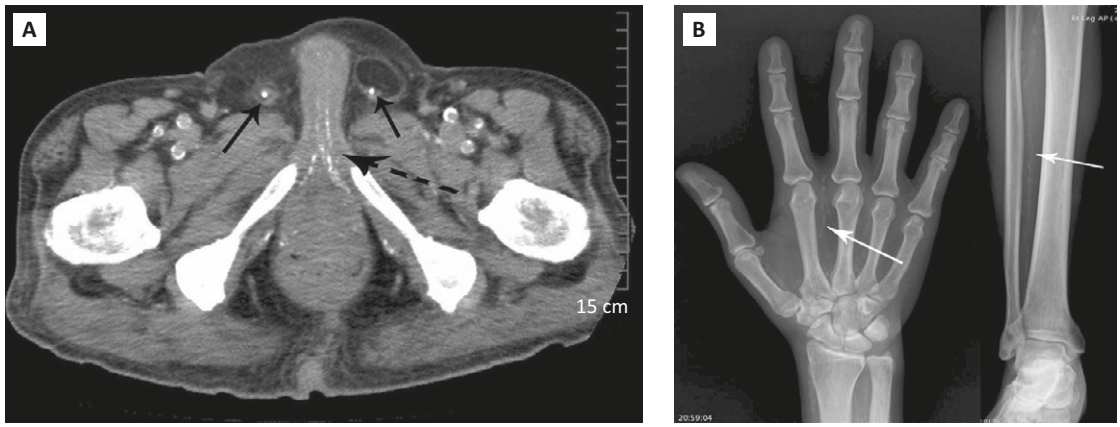

Figure 2 (A) Pelvic computed tomography demonstrates calcification of both penile arteries (dotted arrow) and the arteries (arrows) in the bilateral spermatic cord. (B) Plain films of the hand and leg show calcification of accompanying vessels (arrows).

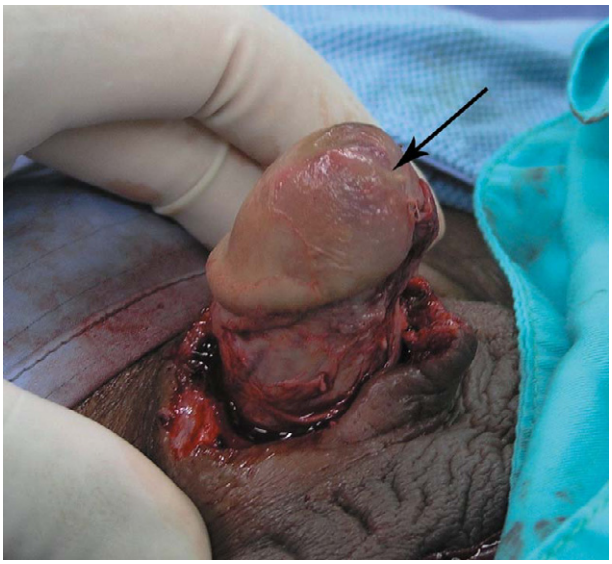

Figure 3 Violaceous lesion at the glans (arrow). Only mild hemorrhage occurred after retracting the penile skin.

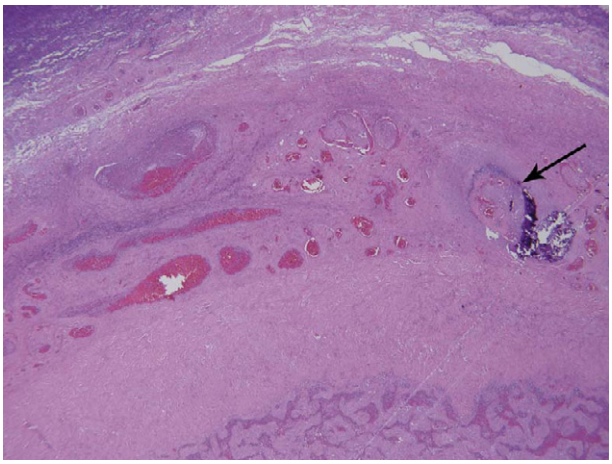

Figure 4 Penile tissue with gangrenous changes, covered by purulent exudates. An artery with prominent calcification and almost total luminal occlusion (arrow) was also found (hematoxylin and eosin, 40×).

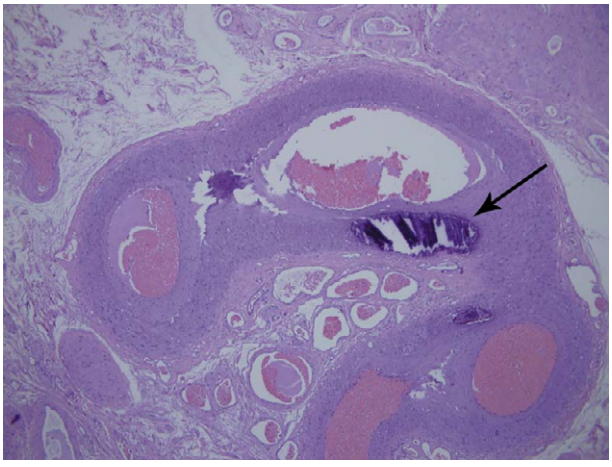

Figure 5 Tissue at the spermatic cord shows vascular congestion and calcification (arrow) involving the tunica media (hematoxylin and eosin, 40×).

often elevated. However, normal serum levels of the calcium–phosphate product or PTH do not preclude the diagnosis of calciphylaxis.[6]

Our case had type 2 diabetes with ESRD and had been on hemodialysis for 5 years. He suffered from a progressive penile purulent lesion and rapid gangrene within 2 weeks. This led to right testicular infarction without spermatic cord torsion. His laboratory data, including calcium, phosphorus and PTH levels were normal, but imaging, symptoms and histology indicated calciphylaxis. This condition is different from diabetic vasculopathy, which has pathologic change mainly in the tunica intima, including endothelial dysfunction, reduced vascular compliance and atherosclerosis.

The blood supply for the penis and testes is distinct. The arterial supply of the testes comes from three arteries, all within the spermatic cord (testicular, deferential and cremasteric arteries).[7] Sampaio et al.[8] found that fetal testes are always supplied by at least two arteries and nearly 80% have more the three arteries. Previously reported testicular infarctions have been related to testicular torsion, with all arteries compromised at the same time. This implies that testicular infarction is not a common condition and occurs only if all three vessels are compromised. Therefore, simultaneous infarction of the penis and testes is considered to be extremely rare, unless it involves systemic calciphylaxis. All of these arteries supplying the right testis were calcified and compromised in our case.

The clinical presentation of calciphylaxis often begins with skin mottling, and tender, painful violaceous lesions on the distal extremities. Lesion progression may result in necrosis, gangrene, amputation, sepsis, and death.[2] Weenig et al.[9] reported that the estimated 1-year cause-specific survival rate for calciphylaxis is 45.8%. Karpman et al.[10] reviewed 34 cases of penile calciphylaxis and documented that the overall mortality rate associated with this disease is 64%, with a mean time to death of 2.5 months. Most deaths are caused by wound superinfection and sepsis. Our patient had initial penile infection and lateral gangrene, in spite of local debridement and wound care. This condition led to the decision to perform a partial penectomy to prevent complications such as sepsis from developing.

Conventional treatment for calciphylaxis is multidisciplinary. It includes reduction of serum phosphate and calcium levels using intensified hemodialysis protocols. Other treatment options include parathyroidectomy, aggressive wound care, analgesia, hyperbaric oxygen, surgical debridement, and amputation. Successful treatment of recurrent calciphylaxis with intravenous sodium thiosulfate has been reported, but this involved cutaneous lesions not genital lesions.[11]

Survival is better in patients who undergo parathyroidectomy (75%) compared with local debridement or

penectomy alone (28%).[10] Parathyroidectomy is the definitive surgical treatment for calciphylaxis,[2] because it decreases PTH levels, and consequently hypercalcemia and elevated calcium phosphate products are blocked. It can have dramatic results, with immediate relief of pain and healing of lesions. Our patient had normal PTH levels and no adenoma of the parathyroid gland, and therefore, parathyroidectomy was not considered.

In conclusion, simultaneous penile gangrene and testicular infarction secondary to calciphylaxis in ESRD is a rare condition. It is important to be aware of patients with ESRD who present with characteristic genital lesions, including penile gangrene and testicular infarction. Aggressive surgical intervention and wound care is the key to reducing the mortality rate.

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