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Case report

PENILE CALCIPHYLAXIS

ORNELA D. PIÑERO, PATRICIA A. FERNÁNDEZ PARDAL, MAURO CORINGRATO, LUCILA MARCHETTA, LARA MAROTTE, VIVIANA LEIRO

Unidad de Dermatología, Hospital de Infecciosas Francisco J. Muñiz, Buenos Aires, Argentina

Postal address: Ornela D. Piñero, Unidad de Dermatología, Hospital de Infecciosas Francisco J. Muñiz, Uspallata 2272, 1282 Buenos Aires, Argentina
E-mail: ornela-p@hotmail.com
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Abstract

Calciphylaxis is a rare, highly mortal disease, typically diagnosed in patients with end-stage renal disease. This disorder usually presents as necrotic ulcers in acral or adipose areas. Penile necrosis due to calciphylaxis is an uncommon condition with a poor prognosis. Few cases have been described in the literature. We present the case of a 45-year-old male with a history of type 2 diabetes and chronic renal failure on dialysis, who developed painful necrotic ulcers on the glans, had altered phosphocalcic metabolism, and was found to have calcium deposits on imaging studies. Treatment with intravenous sodium thiosulfate was initiated, resulting in favorable evolution.

Key words: calciphylaxis, calcific arteriolopathy, penile ulcer, chronic kidney disease

Resumen

Calcifilaxis peneana

La calcifilaxis es una enfermedad rara, de elevada mortalidad, diagnosticada generalmente en pacientes con enfermedad renal terminal. Este trastorno se presenta típicamente como úlceras necróticas en áreas acrales o adiposas. La necrosis de pene secundaria a calcifilaxis es una entidad poco frecuente que conlleva mal pronóstico. Existen pocos reportes en la literatura. Se presenta el caso de un varón de 45 años con antecedentes de diabetes tipo 2 e insuficiencia renal crónica en diálisis, que desarrolló úlceras necróticas dolorosas en glande, presentaba alteración del metabolismo fosfocálcico y se constató en estudios de imágenes depósito de calcio. Se inició tratamiento con tiosulfato de sodio endovenoso, con evolución favorable.

Palabras clave: calcifilaxis, arteriolopatía calcificante, úlcera peneana, enfermedad renal crónica

Calciphylaxis or calcifying uremic arteriolopathy represents 1 to 4% of dermatological symptoms in patients on dialysis, and is associated to high mortality[1]. Penile disease is even less common (6% of patients with calciphylaxis) and its mortality rates reach up to 70% at 6 months. Calciphylaxis occurs due to calcification of the dermal microvasculature and thrombosis with necrosis of the affected tissue due to ischemia. This disease is more common in patients with end-stage chronic kidney disease, where phosphocalcium metabolism is altered and hyperparathyroidism is also present[2-4].

It is clinically characterized by erythematous-violaceous plaques with a retiform appearance

which later progress to intensely painful necrotic ulcers mainly in acral or fatty areas[2,5,6].

Diagnosis is based on clinical manifestations along with patient history, laboratories values, imaging studies and histological findings[7]. However, diagnosis can be complex as it may mimic other conditions. Image studies shows calcium deposits and reduction of blood flow (X-ray, computerized tomography, ultrasonography and Doppler ultrasound). Histology shows calcification of the middle layer and the internal elastic lamina of small and medium-sized vessels of the dermis and subcutaneous cellular tissue, with intimal hyperplasia, subintimal fibrosis, intraluminal thrombus, inflammation and necrosis[6].

Therapy is multimodal, it should include management of the ulcers (antibiotics, advanced wound healing, surgical debridement of necrotic tissue, hyperbaric oxygen therapy, vasodilators), modification of precipitating factors (normalizing parathyroid hormone levels –PTH- and avoiding calcium, vitamin D, iron, and the use of warfarins and glucocorticoids, since they would be associated with a higher risk to develop calciphylaxis), and inhibition of the calcification process. Sodium thiosulfate could act as an antioxidant, vasodilator and calcium chelator. The dose is 25g The recommendation is to continue the medication for at least two months after complete healing of the ulcer[8,9].

Clinical case

A 45-year-old man was examined for penile dermatosis of 3 months duration, for which he had been administered numerous antibiotic schemes without improvement. The patient's medical record described smoking, type 2 diabetes, high blood pressure, and chronic kidney failure for which he had been on peritoneal dialysis for 2 years.

Upon physical examination, two large ulcers were observed in the genital region, on approximately 80% of the surface of the glans, with circinate and erythematous edges and a bottom covered by whitish necrotic fibrin tissue, accompanied by intense pain (Fig. 1A). The patient did not have inguinal lymphadenopathy, and denied previous episodes of similar characteristics or risk factors for sexually transmitted infections.

The main presumptive diagnoses were chronic genital herpes and calciphylaxis due to his history of chronic renal failure on dialysis.

Laboratory tests included, as relevant data, the following values: hematocrit 28.7%, hemoglobin 9.5 g/dL, urea 204 mg/dL, phosphorus 7.7 mg/dL, (normal value up to 4.5 mg/dL), calcium 8.7 mg/dL, (normal value up to 10.2 mg/dL), PTH 797 pg/mL, (normal value up to 88 pg/mL), and non-reactive serologies for hepatitis C, hepatitis B, HIV and syphilis (CMIA). Tzanck cytodiagnosis and PCR for herpes 1 and 2 in the lesion were negative. Pelvic X-ray revealed scattered calcifications in the soft tissue of the affected site (Fig. 1B).

The diagnosis of penile calciphylaxis was reached with these findings.

Renal replacement treatment was switched to hemodialysis, and intravenous sodium thiosulfate was started at a dose of 25 g (diluted in 100 ml of physiological solution), administered in one hour, three times a week, after hemodialysis. The phosphorus in his diet was also restricted and was prescribed phosphorus binders.

The patient's evolution was favorable with full re-epithelialization of the ulcers three months after starting treatment (Fig. 2); which continued for six months without relapses.

Discussion

Penile calciphylaxis is a very rare condition and requires rapid recognition and management of the disease because of the high mortality. It must be suspected in patients undergoing dialysis. In a systematic review that included 121 patients with penile calciphylaxis, 79% of the cases were on hemodialysis and 11% on peritoneal dialysis like the one here presented. The others, had chronic kidney disease and weren´t on dialysis treatment. Penile calciphylaxis usually occurs between 24 to 96 month, since starting dialysis; our patient had been on peritoneal dialysis for 24 months. Clinically, it presents with black or white necrosis or ulcers in the glans and almost half of the patients have extragenital lesions most common seen in distal extremities[10].

The definitive diagnosis for calciphylaxis are the histological findings[6]. However, it should be considered that biopsies in areas with terminal circulation (like genital area) and concomitant vascular involvement may have a high risk of progressive necrosis, superinfection and delay

Figure 1 | A: Two large ulcers on glans, with circinate and erythematous edges and a bottom covered by whitish necrotic fibrin tissue, accompanied by intense pain. B: Pelvic X-ray revealed scattered calcifications in the soft tissue of the affected site

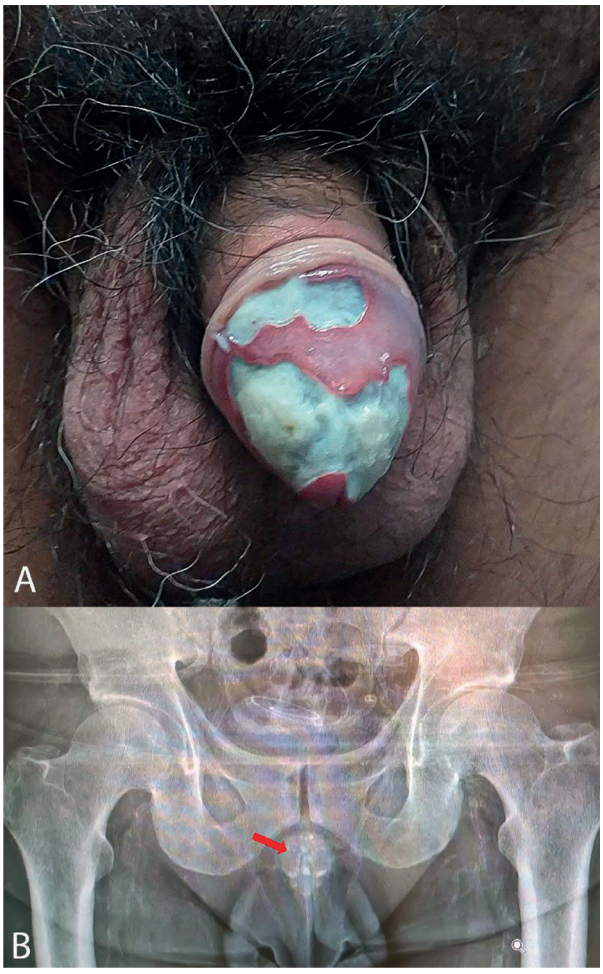
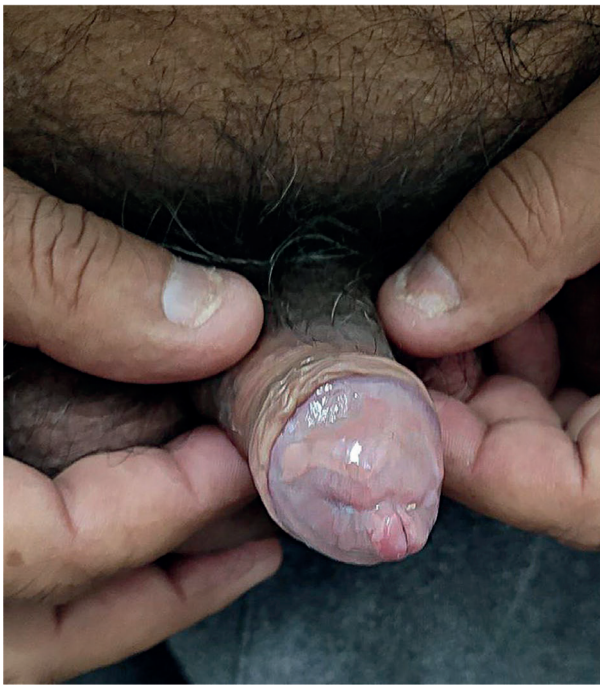


Figure 2 | The genital ulcers healed after three months of starting treatment



wound healing[6,10]. Hence, penile calciphylaxis is typically diagnosed using clinical suspicion and imaging studies that demonstrate calcification and/or reduction of blood flow of the penile vessels[6,11,12]. In this patient, the clinical suspicion and the laboratory and radiologic findings allowed us to reach the calciphylaxis diagnosis in few days, and he experienced pain relief within the first weeks of sodium thiosulfate treatment and complete resolution of the condition by the third month of treatment. However, some authors[10,12] didn´t find any benefits in clinical outcomes in patients with penile calciphylaxis with different farmacologic and surgical treatments. Aggressive surgical interventions (debridement or partial/total penectomy) didn´t improve mortality rates and may lead to progression of the lesion, superinfection and delay wound healing. Despite sodium thiosulfate was proposed to be a calcium and phosphate chelator, antioxidant and induce vasodilation, didn´t show a benefit in mortality and wound healing rates.

Penile calciphylaxis is a rare form of calciphylaxis with poor prognosis. In this case the diagnosis was made fast with the clinical suspicious, the laboratories abnormalities and the X-ray. The patient had very good results to sodium thiosulfate treatment and correction of phospho-calcium metabolism.

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Conflict of interest: None to declare

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