Biopsy Is Contraindicated in the Management of Penile Calciphylaxis

Cara B. Cimmino, MD and Raymond A. Costabile, MD

Department of Urology, University of Virginia, Charlottesville, VA, USA

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ABSTRACT

Introduction. Calciphylaxis, a rare obliterative small vessel vasculopathy associated with diabetes mellitus (DM), end-stage renal disease (ESRD), portends a poor prognosis. Because penile involvement is rare, agreement on appropriate diagnosis and management is unclear.

Aim. To determine the role and effect of penile biopsy for diagnosis and management of penile calciphylaxis.

Methods. Medical records of three penile calciphylaxis patients from our institution were evaluated. Data collected included age, history of DM, ESRD, and hemodialysis (HD) status, serum calcium (Ca), Ca × phosphorous product (C × P), parathyroid hormone (PTH), performance of biopsy, presence of non-penile cutaneous lesions, intervention, survival, and time from diagnosis to death. PubMed Search for relevant publications from 1995 to 2012 was performed to identify case reports of penile calciphylaxis that provided the same clinical data obtained from the 3 patients from our institution.

Main Outcome Measures. Clinical evidence for outcomes in patients with penile calciphylaxis after biopsy of penile lesion compared to those without biopsy.

Results. A total of sixteen patients were identified in the literature and in our institution with clinical data of interest. Overall, 10/16 (62.5%) patients identified with penile calciphylaxis had a penile biopsy, and 7/10 (70%) experienced disease progression, while only 3/10 (30%) stabilized. Mean time to death in this patient population was short, approximately 6.5 months, regardless of type of intervention.

Conclusion. Based on the results of our study, we argue that conservative measures should be employed as first line therapy for penile calciphylaxis. More importantly, secondary to likely resultant progression of necrosis, penile biopsy is not only unnecessary for diagnosis of penile calciphylaxis, but is also harmful and contraindicated.
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Key Words. Penile Biopsy; Penile Calciphylaxis; Penile Calcific Uremic Arteriolopathy

Introduction

Calcific uremic arteriolopathy, or calciphylaxis, is an obliterative small vessel vasculopathy characterized by medial calcification of small arteries and arterioles. This vascular calcification leads to luminal narrowing of the artery, resulting in cutaneous necrosis and ulceration. The distribution of these dermatologic lesions has been described as proximal (involving the face, trunk, genitalia, or buttocks), or distal (extremities) [1]. Patients with proximal calciphylaxis have a mortality rate of 63–80%, while those with distal lesions have a mortality rate of approximately 23% [2–4]. Because penile involvement is rare, agreement on its appropriate diagnosis and management is not clear.

Diagnosis of penile calciphylaxis can be made on the basis of clinical history and physical examination, laboratory studies and imaging, demonstrating calcification of penile and pelvic arteries with Computerized tomography (CT) scan or radiographs. Some studies have reported the use of penile lesional biopsy to confirm the diagnosis and rule out other vascular, infectious, or malignant causes. After our experience with 3 recent patients,

and a review of reported cases in the literature, we would propose that diagnosis of penile calciphylaxis is best done with analysis of clinical parameters, and the risk of penile biopsy outweighs potential benefits.

Case Histories

Over the past 5 years, three patients presented to our single institution, ultimately diagnosed with penile calciphylaxis. Given the low incidence of this disease, we were encouraged to report our findings.

Patient 1

A 62-year-old male with history of end stage renal disease (ESRD) secondary to diabetic nephropathy, on hemodialysis (HD) for 3 years prior to presentation, was referred to the Urology Department after a transfer of care between facilities for a 3 month history of painful, necrotic ulcers on the distal penis and scrotum. He was voiding per urethra without difficulty. On examination, the patient was circumcised with swelling of the penile shaft and scrotum. The glans was nodular and hard with several black necrotic lesions. Several small necrotic lesions were noted on the scrotal skin as well. Mild tenderness was noted on penile and scrotal exam. No evidence of erythema, crepitus or purulent drainage was noted.

On presentation, his serum calcium (Ca) was 9.0 mg/dL, Calcium × Phosphate product (C × P) was 75.6 mg^2/dL^2, and parathyroid hormone (PTH) was not recorded. The patient's Ca and phosphorous levels were tightly controlled by Nephrology via regular hemodialysis. The patient was managed with narcotic pain control, local wound care, and debridement of the penile and scrotal lesions as needed on an outpatient basis. A pain management consult was eventually called for assistance with the patient's pain control regimen. One year after initial presentation, the patient underwent amputation of two right toes secondary to osteomyelitis. During the following year the patient required several hospitalizations for infected foot ulcers and osteomyelitis requiring surgical debridement and washout. He was followed regularly by Urology, during which time his penile and scrotal lesions remained stable, but did not resolve. He did not require biopsy or surgical intervention for his penile lesion. He ultimately expired 22 months after presentation secondary to complications from osteomyelitis and overwhelming sepsis.

Patient 2

A 38-year-old male with history of Type I insulin-dependent diabetes mellitus (DM), congestive heart failure (CHF), and ESRD on HD, who presented to the emergency room with complaints of a painful blister at the tip of his penis. He first noticed this lesion 2 weeks prior to presentation, however, the blister "popped" and developed into an open ulcer, which was tender to palpation. He initially presented to an outside facility where a biopsy of the lesion was performed. His pain increased after this intervention, as did the area of ulceration. He then transferred his care to our facility.

At this point the patient complained of pain with voiding secondary to irritation of the lesion when contacted by urine, but denied difficulty emptying his bladder. He denied any fever, chills, nausea or vomiting. He denied any other concurrent lesions elsewhere on his body, however on exam it became apparent that he had two previous toe amputations and one current necrotic toe. Physical examination demonstrated a 1 cm ulceration on the lateral aspect of the glans penis, with an area of eschar. He was circumcised, but had some redundant foreskin which did not appear involved. The urethral meatus was patent and visible, though in close proximity to the edge of the lesion. Scrotal exam was normal. The patients laboratory studies revealed calcium level of 8.7 mg/dL, but a phosphorous, C × P product and PTH were not obtained.

As there was no evidence of infection the patient was managed with wound care and pain control with Tramadol. He was seen one month later for persistent pain and was given narcotic pain medication, the eschar was carefully debrided at that time as well. Management continued with conservative wound care, pain control and debridement for the next six months. The wound stabilized, and improved somewhat, though it failed to completely resolve. The patient discontinued his Urology follow-up after approximately 3 months of care and was lost to follow-up.

Patient 3

A 49-year-old male with history of DM, ESRD on HD, and peripheral vascular disease, admitted to the vascular surgery service for amputation of a gangrenous left fifth toe. On admission a small soft ulcer was noted on the tip of his penis. After 3 days this lesion became painful necrotic, and hard to the touch. The Urology service was notified to evaluate the lesion at this time. On exam the patient was