Images — Penile pain in the setting of end-stage renal disease: An unusual anatomic location for calciphylaxis

Ummah Salma Nisar[1], John C. Cheville[2], Charles D. Sturgis[2]

[1]Liver Transplant Center, Mayo Clinic, Rochester, MN, United States; [2]Anatomic Pathology, Mayo Clinic, Rochester, MN, United States

Cite as: Nisar US, Cheville JC, Sturgis CD. Images — Penile pain in the setting of end-stage renal disease: An unusual anatomic location for calciphylaxis. *Can Urol Assoc J* 2022;16(5):E304-5. http://dx.doi.org/10.5489/cuaj.7618

Published online December 21, 2021

Introduction

Calciphylaxis (also called calcific uremic arteriolopathy) is a rare but serious condition associated with significant calcification of the media of small and medium-sized arteries, primarily affecting the distal extremities.[1] Calciphylaxis is almost always seen in patients with end-stage renal disease who are on dialysis.[1-3] It is sometimes associated with hyperparathyroidism and elevated serum calcium and phosphorus levels.[4]

Penile calciphylaxis is very rare and is associated with a poor prognosis. As the penis contains a rich network of interconnecting vascular channels, diseases of the vessels (such as calciphylaxis), may be associated with serious clinical symptoms. Patients with penile calciphylaxis often present with severe penile pain and necrosis of surrounding skin and subcutaneous tissues.[5]

In this report, we present findings from an adult patient with penile calciphylaxis who underwent penectomy and survived for five weeks after the diagnosis of calciphylaxis was confirmed. Early diagnosis may increase survival time.[6]

Case report

A 60-year-old white man presented to the emergency department with urinary retention and penile pain. His symptoms began 20 days prior, when he presented to outpatient with pain in his digits and penis, with associated skin necrosis. He had a history of coronary artery disease, peripheral vascular disease, and end-stage renal disease maintained on peritoneal dialysis after failed renal transplantation.

Examination confirmed scrotal erythema and edema over necrotic tissue in the glans penis. Labs revealed serum calcium 8.1 mg/dL, elevated serum phosphorus 6.9 mg/dL, elevated parathyroid hormone (PTH) 114 pg/mL, and elevated white blood cells (WBC) 17.2x10^9/L. Imaging was suspicious for superinfection of the penis, with gas identified in the soft tissues.

A suprapubic catheter was placed after consultation with a urologist, followed by partial penectomy with penile and scrotal debridement. Calciphylaxis was clinically/radiologically somewhat favored over Fournier's gangrene due to lack of subcutaneous emphysema and hemodynamically stable state. Gross examination of the penectomy showed gray-blue discoloration, softening, and sloughing of surface layers of tissue with prominent vascular calcifications (Figure 1).

Histologically, extensive necrosis of the central shaft was identified in a roughly triangular shape, with large expanses of corpus cavernosum being extensively degenerated with intravascular and sheet-like calcifications spanning the entirety of tissue, sparing the urethra, corpus spongiosum, and inferior vascular structures (Figure 2). Superficial secondary bacterial overgrowth was noted.

Postoperatively, the patient was managed with supportive care. He died five weeks later at his home under hospice care.

Discussion

Calciphylaxis is a rare condition involving calcification of small and medium arteries and is most commonly encountered in the distal extremities.[1-5] Calciphylaxis is seen in 1–4%[2,3] of patients with end-stage renal disease and has a grim prognosis. Penile involvement is uncommon, with only rare reported cases and small series in the English-language literature.[5-11] Most patients who present with penile calciphylaxis may also have comorbidities, such as atherosclerosis, peripheral vascular disease, diabetes, hypertension, and obesity.[5] Control of these comorbid conditions in patients with end-stage renal disease may diminish the likelihood of developing calciphylaxis.

Patients with penile calciphylaxis typically present with penile pain and necrosis of surrounding skin and subcutaneous tissue. The mean survival after diagnosis is 2.5 months, with maximum survival generally not exceeding six months.[9] Some authors suggest that early diagnosis and interventions may increase survival.[8]

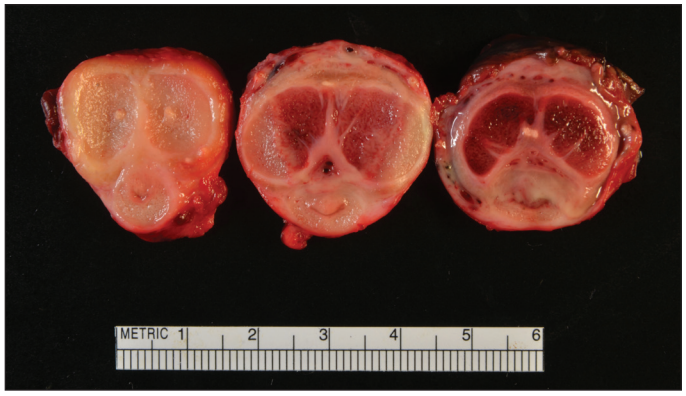

Figure 1. Serially sectioned penectomy specimen with peripherally sloughed skin showing calcification of cavernous arteries (best seen in the left most section) with necrosis of corpora cavernosa and peripheral sparing. Necrosis extends to dorsal aspect of urethra involving corpora spongiosa.

Aberrant serum calcium, phosphorus, and PTH levels seen in patients with penile pain in the setting of end-stage renal disease may suggest a diagnosis of penile calciphylaxis, but serum parameters may, in some instances, fall within normal ranges.

Radiological studies using modalities like Doppler ultrasound, computed tomography, or magnetic resonance imaging (MRI) may contribute to diagnosis.[10] Doppler testing to evaluate the flow in penile blood vessels may be of supplemental value to MRI, which can be helpful in delimiting boundaries between viable and necrotic tissue.[11]

Treatments can be medical, surgical, or both. Medical management may include administration of calcium and phosphate chelators to normalize elevated levels. For cases with associated hyperparathyroidism, cinacalcet administration and/or parathyroidectomy can be considered. Many patients ultimately undergo partial or complete penectomy to avoid further medical decompensation, significant pain, and sepsis.[5] No significant differences in outcomes (mortality rates) are reported between medically and surgically managed patients.

Conclusions

Penile calciphylaxis should be considered in patients with end-stage renal disease who present with ulcers or pain in the penis, particularly the glans. Patients who are being dialyzed and/or who have concomitant diabetes are at greatest risk. The diagnosis can generally be reached using clinical, biochemical, and radiological evaluations. Tissue confirmation may be achieved with biopsy (which has attendant risks) or by examination of penectomy specimens. Penile calciphylaxis in the setting of end-stage renal disease is associated with unfavorable prognosis. Survival is most often measured in weeks to months.

Competing interests: The authors do not report any competing personal or financial interests related to this work.

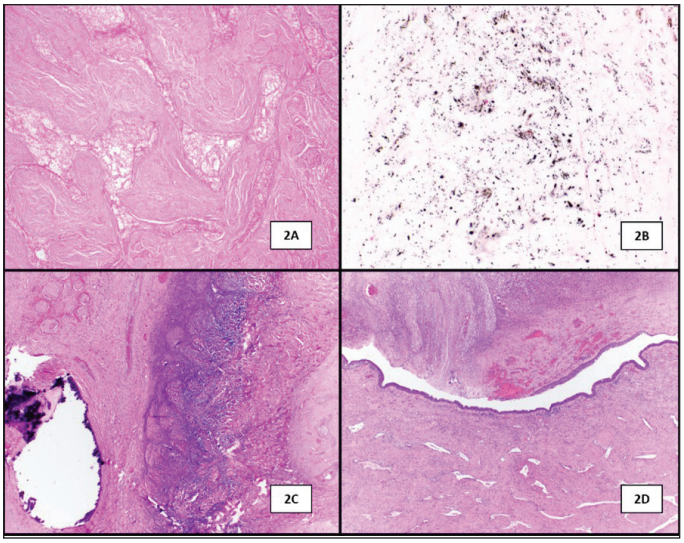

Figure 2. Histology of the penectomy specimen showing complete necrosis of corpora cavernosa (2A, hematoxylin and eosin, 100X) with diffuse granular calcification throughout soft tissues (2B, Von Kossa, 400X). Urethral artery with coarse intimal calcification and necrosis with inflammation intervening between vasculature and corpus spongiosum (2C, hematoxylin and eosin, 40X) dorsolateral corpus spongiosum with necrosis showing relative sparing of urethra proper and inferior soft tissues (2D, hematoxylin and eosin, 40X).

This paper has been peer-reviewed.

References

1. Kent RB 3rd, Lyerly RT. Systemic calciphylaxis. *South Med J* 1994;87:278-81. https://doi.org/10.1097/00007611-199402000-00029
2. Ivker RA, Woosley J, Briggaman RA. Calciphylaxis in three patients with end-stage renal disease. *Arch Dermatol* 1995;131:63-8. https://doi.org/10.1001/archderm.1995.01690130065013
3. Vedvyas C, Winterfield LS, Vleugels RA. Calciphylaxis: A systematic review of existing and emerging therapies. *J Am Acad Dermatol* 2012;67:253-60. https://doi.org/10.1016/j.jaad.2011.06.009
4. Duh QY, Lim RC, Clark OH. Calciphylaxis in secondary hyperparathyroidism. Diagnosis and parathyroidectomy. *Arch Surg* 1991;126:1213-9. https://doi.org/10.1001/archsurg.1991.01410340055008
5. Wood JC, Monga M, Hellstrom WJ. Penile calciphylaxis. *Urology* 1997;50:622-4. https://doi.org/10.1016/S0090-4295(97)00311-7
6. El-Taji O, Bondad J, Faruqui S, et al. Penile calciphylaxis: A conservative approach. *Ann R Coll Surg Engl* 2020;102:e36-8. https://doi.org/10.1308/rcsann.2019.0119
7. Tezuka M, Mizusawa H, Tsukada M, et al. Severe necrosis of the glans penis associated with calciphylaxis treated by partial penectomy. *IJU Case Rep* 2020;3:133-6. https://doi.org/10.1002/iju5.12166
8. Gomes Torres JH, Neves Ribeiro SC, Carvalho de Souza I, et al. Penile necrosis and calciphylaxis. *Urol Case Rep* 2021;39:101770. https://doi.org/10.1016/j.eucr.2021.101770
9. Karpman E, Das S, Kurzrock EA. Penile calciphylaxis: Analysis of risk factors and mortality. *J Urol* 2003;169:2206-9. https://doi.org/10.1097/01.ju.0000064334.85656.a1
10. Morrison M, Merati M, Ramirez J, et al. Penile calciphylaxis diagnosed with computed tomography. *J Eur Acad Dermatol Venereol* 2016;30:352-3. https://doi.org/10.1111/jdv.12764
11. Campbell RA, Alzweri LM, Sopko NA, et al. Penile calciphylaxis: The use of radiological investigations in the management of a rare and challenging condition. *Urol Case Rep* 2017;13:113-6. https://doi.org/10.1016/j.eucr.2017.03.008

Correspondence: Dr. Charles D. Sturgis, Mayo Clinic Pathology, Rochester, MN, United States; Sturgis.Charles@Mayo.edu