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Case Report

Penile calciphylaxis: a case report and literature review

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ABSTRACT

Calciphylaxis is a rare and severe vascular disorder characterized by calcification of small vessels, leading to tissue ischemia and necrosis. It predominantly affects patients with end-stage renal disease (ESRD) and is associated with high mortality. This case report describes a 54-year-old male with ESRD on haemodialysis, diabetes mellitus, hypertension, and secondary hyperparathyroidism, who presented with intense penile pain and whitish discoloration of the glans. Despite initial supportive measures, the patient progressed to wet necrosis of the penis and prepuce, accompanied by acute testicular pain and signs of incipient necrotizing fasciitis. Empirical antibiotic therapy and analgesia were initiated, but the condition worsened, necessitating total penectomy with cystostomy due to extensive necrosis. Postoperative complications included surgical site infection, gastric ulcers, and acral necrosis, culminating in refractory septic shock and multiorgan failure, leading to death. In conjunction with this case, we review the existing literature to contextualize its findings, summarize diagnostic and therapeutic challenges, and highlight gaps in evidence. This case underscores the aggressive nature of penile calciphylaxis, its diagnostic dilemmas, and the limited therapeutic options available. Early recognition and multidisciplinary management are crucial, though prognosis remains poor.

Keywords: Calciphylaxis, Penile injuries, Haemodialysis, Hyperparathyroidism, Nephropathy

INTRODUCTION

Calciphylaxis, also known as calcific uremic arteriolopathy, is a severe vascular disorder characterized by calcification of cutaneous arterioles, micro thrombosis, and painful tissue necrosis. Although predominantly associated with end-stage renal disease (ESRD) and dialysis, it can occur in non-uremic patients (15–20% of cases).[1-3]

Its incidence varies geographically, from 1 case per 10,000 dialysis patients in Japan to 35 per 10,000 in the United States. Risk factors include secondary hyperparathyroidism, hyperphosphatemia, autoimmune disorders, type 2 diabetes mellitus, certain medications such as warfarin and systemic steroids, hypercoagulability, hypoalbuminemia and female sex.[4-6] Cutaneous lesions progress in two phases: from indurated inflammatory plaques, livedo reticularis and/or livedo racemosa, laminar erythema, and pruritus in the first phase, to non-healing necrotic ulcers with black eschar in the second phase, located in adipose areas (thighs, abdomen) or acral regions (penis, fingers).[5-7]

Lesions are classified as proximal (chest, abdomen, thighs, areas with more adipose tissue, penis), associated with higher mortality (63%), and distal (extremities, particularly between the ankle and calf), with a relatively better prognosis (mortality of 23–32%).[2,8-10] Pathophysiology involves an imbalance between pro-calcifying factors and vascular calcification inhibitors. The mechanisms include calcium-phosphorus deposits in

arterioles, osteoblastic transformation of smooth muscle cells, deficiency of natural inhibitors such as fetuin-A and matrix Gla protein, and hypercoagulability associated with protein C/S deficiency or warfarin use. In non-uremic patients, inflammation and oxidative stress play a key role.[6,9,11-15]

Diagnosis combines clinical criteria, skin biopsy (contraindicated in penile cases due to necrosis risk), and imaging such as X-rays or CT scans.[11,16,17] Differential diagnosis includes gangrene from peripheral vascular disease, vasculitis, and warfarin-induced necrosis.[4,16]

Management is multidisciplinary and includes pain control with opioids, metabolic management (normalizing Ca/P/PTH, discontinuing warfarin), therapies such as sodium thiosulfate (STS), bisphosphonates, and hyperbaric oxygen therapy.[7,10,18] Wound care involves selective debridement and specialized dressings, avoiding glucocorticoids.[12,15,19]

In severe cases, parathyroidectomy or penectomy is considered.[17,20,21] The prognosis is poor, with a mortality rate of 45–80%, primarily due to sepsis. Poor prognostic factors include proximal lesions, hypoalbuminemia, and diabetes.[9,13] Survival improves with early diagnosis and STS, reducing the annual mortality rate to 40%.[22]

CASE REPORT

A 54-year-old male patient with a history of type 2 diabetes mellitus and systemic arterial hypertension, both of 20 years' duration, under treatment with insulin glargine, losartan, and acetylsalicylic acid at antiplatelet doses.

He also had end-stage chronic kidney disease (CKD) on haemodialysis for over a decade, hypothyroidism (TSH fluctuating between 5.08–9.33, free T3 1.40–1.83, total T4 88.28–122.50), mixed dyslipidemia, a history of ischemic stroke with right motor sequelae, vitamin D deficiency (9.7 ng/ml), and secondary hyperparathyroidism (PTH 200 pg/ml, with calcium levels of 6.4 mg/dl and phosphorus 6.0 mg/dl, peaking at 7.1 mg/dl for both), chronic smoking, and social alcohol use.

He was admitted on 04/19/24 due to intense penile pain associated with whitish discoloration of the glans. He was managed with supportive measures and pain control, continuing his dialysis program during hospitalization; he was discharged after maximum benefit was achieved once the pain crisis resolved a week later.

However, he returned to the emergency department on 17th May 2024 presenting with wet necrosis of the penis and prepuce, along with acute testicular pain and clinical signs suggestive of incipient necrotizing fasciitis

Empirical management with broad-spectrum antibiotics and analgesia was initiated, integrated into the established therapeutic regimen for comorbid conditions. Physical examination revealed distal necrosis of the glans, scrotal edema with hyperaemia, and abdominal pain on palpation in the epigastrium and mesogastrium, without signs of organomegaly.

On 21st May 2024, a total penectomy with cystostomy was performed due to extensive penile necrosis.

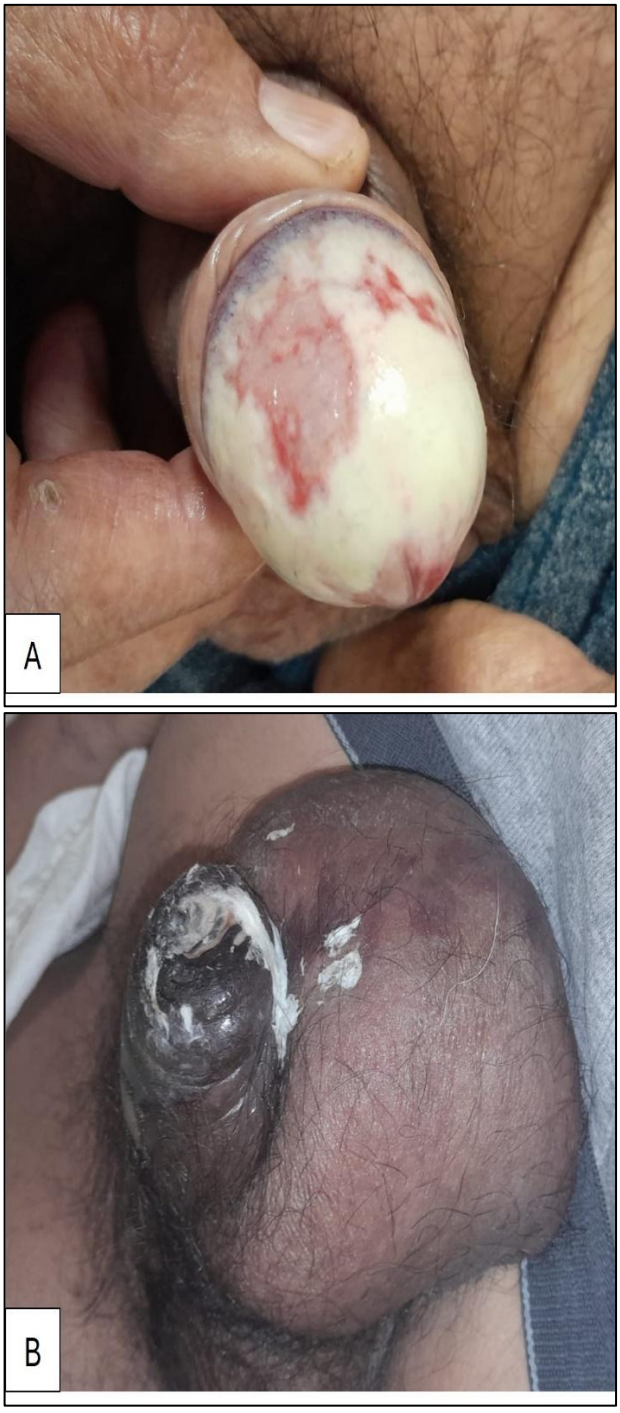

Figure 1: (A) Initial presentation, with pale discoloration of the glans. (B) Progression to wet necrosis of the glans and prepuce, with foul-smelling exudate.

On 28th May 2024, surgical debridement was performed due to surgical site infection. On 05/30/24, gastric ulcers (Forrest IIc-III) were identified via endoscopy.

The clinical course was complicated by severe postoperative pain, grade I-II sacral/gluteal ulcers, acral necrosis in the left upper extremity, and sepsis. On his 20th day of hospitalization, he died due to refractory septic shock and multiorgan failure.

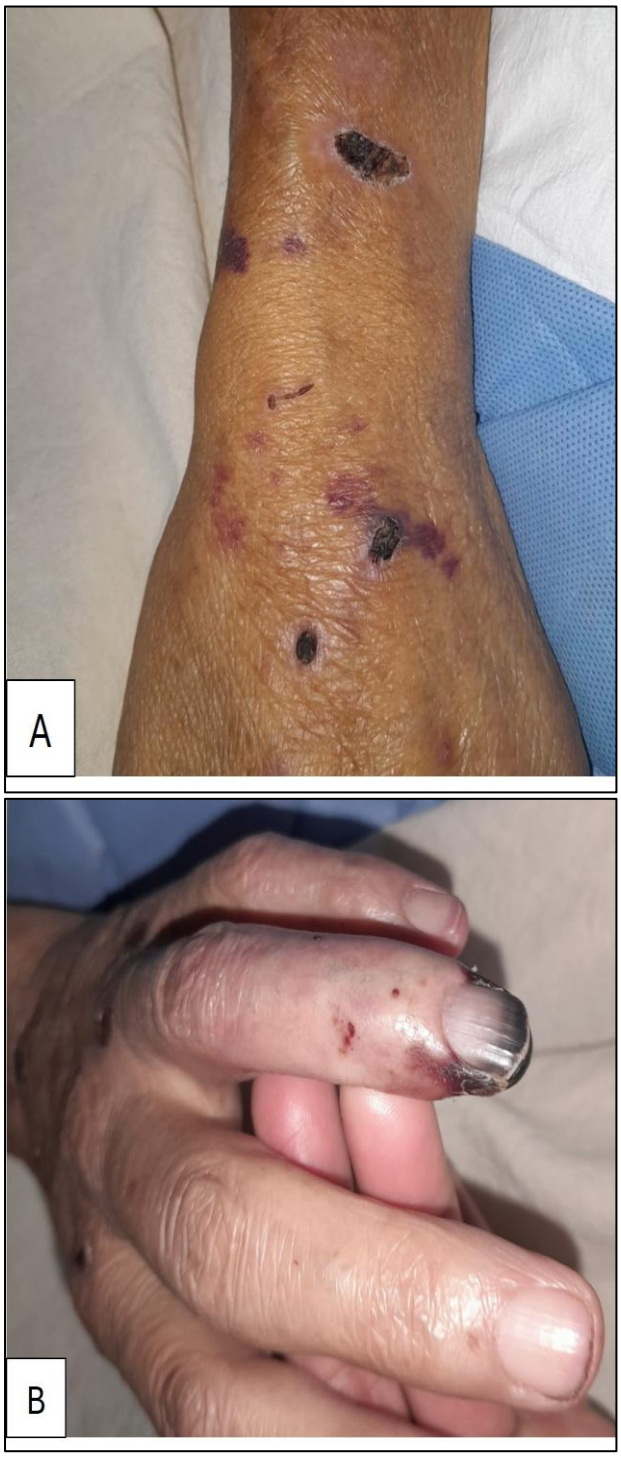

Figure 2: (A) Presence of necrotic eschars on extremities. (B) Acral necrosis in the ring finger.

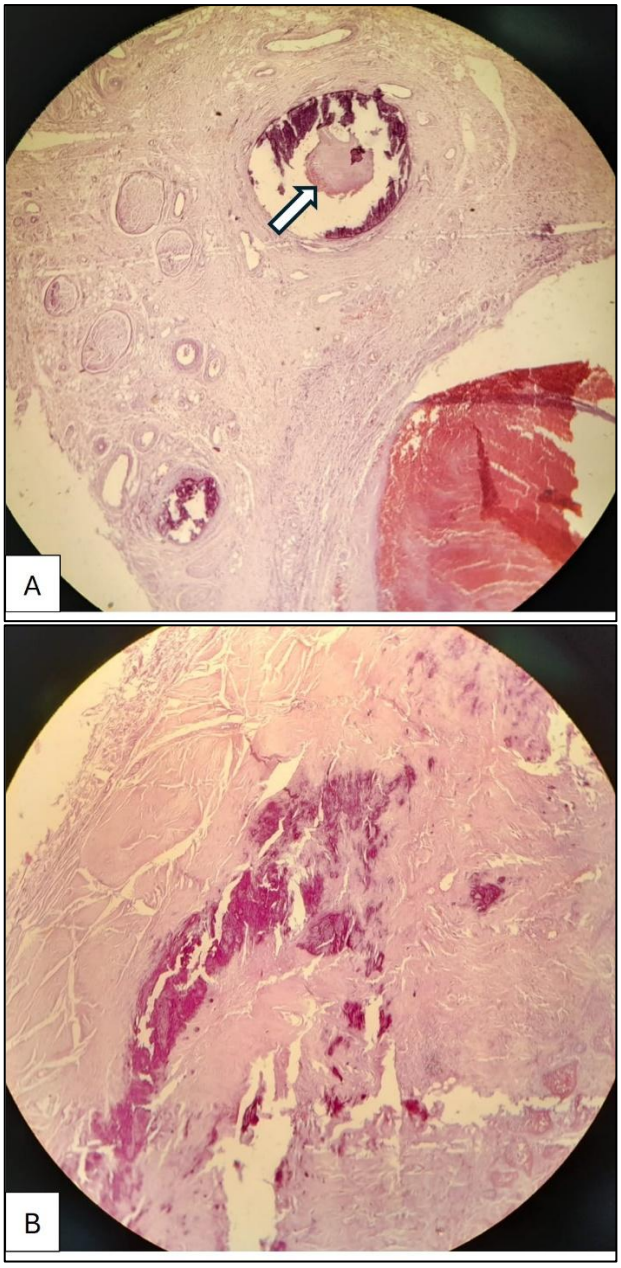

Figure 3: Hematoxylin-eosin staining of the penectomy specimen. (A) Arteries with circumferential calcium deposits in the intima, one of them with a recent thrombus (arrow). (B) Interstitial calcium deposits in the ischiocavernosus muscle tissue.

DISCUSSION

Penile calciphylaxis, although rare (6% of cases, ≈1% in ESRD, has a limited number of reported cases, with a mortality rate of 64–69% at 3–6 months (mean of 2.5) and is associated with ESRD, diabetes, and warfarin use.[20-25] It presents with ischemic necrosis of the glans (93%) or penile body, with lesions varying in morphology from violaceous, dark, whitish, or yellowish plaques to erosion, ulceration, and gangrene, accompanied by intense pain and a high risk of infection.[24] Extragenital lesions may occur in up to half of cases, most commonly affecting the distal

extremities and associated with higher mortality.[25] In a case-control study by Gabel et al, statistically significant differences were found characterizing penile calciphylaxis compared to other calciphylaxis patients, including a higher prevalence of end-stage renal disease (100%), hyperparathyroidism (87%) with a mean PTH level of 261 pg/ml, and markedly higher mortality (mean of 3.1 vs. 24.7 months).[24]

Infection of ulcers and sepsis are common causes of death in these patients. Although diagnosis is often clinical, a high index of suspicion is necessary when these manifestations cannot be explained by another etiology.[1,23]

The presented case illustrates the typical clinical and evolutionary characteristics of penile calciphylaxis, a rare but devastating manifestation of calcific uremic arteriolopathy. The patient, with a history of end-stage chronic kidney disease (ESRD), type 2 diabetes mellitus, secondary hyperparathyroidism, and vitamin D deficiency, had multiple risk factors described in the literature, such as metabolic comorbidities and the chronic proinflammatory state associated with prolonged dialysis.[2,3,8,9] The clinical course, marked by progressive penile necrosis, refractory pain, and septic complications, aligns with previous studies.[20,23-25]

A relevant particularity in this case was the relatively low calcium-phosphorus product (49 mg^2/dl^2), in contrast to studies such as Karpman et al, where values above 70 mg^2/dl^2 were significantly associated with penile calciphylaxis.[20] This discrepancy highlights the pathophysiological heterogeneity of the disease and reinforces the notion that mineral metabolism abnormalities, although important, are not the sole determinant in the development of proximal lesions, as noted by Verdalles et al and other authors.[2,8,12,13] As to the PTH levels, parathyroidectomy may be beneficial in cases with severe hyperparathyroidism with levels above 800-1000 pg/ml, which was not indicated in this case; however, its use is controverted, as it usually does not improve prognosis.[8] Additionally, the rapid progression to extensive necrosis and sepsis underscores the aggressiveness of penile involvement. Although surgical management is controversial, in cases with extensive penile necrosis or infection, penectomy may be considered to reduce morbidity and improve survival.[17] In this case total penectomy was required as a rescue measure for uncontrolled infection and severe pain refractory to analgesics, like what was described by Yang et al.[21]

Other notable aspects included the atypical or infrequent morphology of the initial lesions on the glans, appearing as intense pale discoloration, unlike what has been reported in other studies, such as Gabel et al, as well as the presence of extragenital and visceral lesions (gastric ulcers, extremity involvement, and acral necrosis), consistent with literature reporting multisystem involvement in up to 50% of cases and associated with higher mortality.[24,25] The coexistence of incipient necrotizing fasciitis added complexity to management, emphasizing the need for a multidisciplinary approach integrating nephrology, urology, infectious diseases, and palliative care.[3,18,26]

The lack of favorable response to the implemented therapeutic management reflects the limitations of available therapies.[1,27] This case also illustrates the diagnostic challenges in penile calciphylaxis, where biopsy is contraindicated and diagnosis relies on clinical and imaging findings.[17,26,28]

CONCLUSION

Calciphylaxis is a serious condition with high mortality and limited effective therapeutic options, especially in its penile variant. This case highlights the importance of maintaining a high index of suspicion in patients with ESRD (end-stage renal disease) and painful necrotic lesions, even in the absence of severe calcium-phosphorus metabolism abnormalities. It also underscores the atypical presentation of penile lesions associated with this clinical entity. Keeping these characteristics in mind allows for an early diagnosis, enabling timely multidisciplinary management focused on metabolic control, prevention, and aggressive treatment of infectious complications, especially considering the high mortality rate in these patients. However, the lack of consensus in treatment guidelines and the scarcity of robust clinical trials limit the standardization of therapies.

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REFERENCES

1. Chiriac A, Grosu OM, Terinte C, Perţea M. Calcific uremic arteriolopathy (calciphylaxis) calls into question the validity of guidelines of diagnosis and treatment. J Dermatolog Treat. 2019;31(5):545-8.
2. Cucchiari D, Torregrosa JV. Calciphylaxis in patients with chronic kidney disease: A disease which is still bewildering and potentially fatal. Nefrologia. 2018;38(6):579-86.
3. García-Lozano JA, Ocampo-Candiani J, Martínez-Cabriales SA, Garza-Rodríguez V. An Update on Calciphylaxis. Am J Clin Dermatol. 2018;19(4):599-608.
4. Gómez de la Fuente E, Vicente FJ, Álvarez JG, Naz E, Palencia SI, Pinedo F, et al. Calcifilaxis en pacientes dializados. Actas Dermosifiliogr. 2004;95(3):178-82.
5. Hayashi M. Calciphylaxis: diagnosis and clinical features. Clin Exp Nephrol. 2013;17(4):498-503.
6. Munar MA, Alarcón A, Bernabéu R, Morey Gascó J, Losada P, Antón E, et al. A propósito de un caso de lesiones cutáneas y calcifilaxis. Nefrologia. 2001;21(5):501-4.

7. Polaina Rusillo M, Sánchez Martos MD, Biechy Baldan MM, Liebana Cañada A. Calcifilaxis. Semin Fund Esp Reumatol. 2009;10(4):124-7.
8. Verdalles Guzmán U, De La Cueva P, Verde E, García de Vinuesa S, Goicoechea M, Mosse A, et al. Calcifilaxis: complicación grave del síndrome cardio-metabólico en pacientes con Enfermedad Renal Crónica Terminal (ERCT). Nefrologia. 2008;28(1):32-6.
9. Nigwekar SU, Kroshinsky D, Nazarian RM, Goverman J, Malhotra R, Jackson VA, et al. Calciphylaxis: Risk Factors, Diagnosis, and Treatment. Am J Kidney Dis. 2015;66(1):133-46.
10. Rodríguez-Villarreal I, Callejas R, Sánchez M, Laso N, Gallar P, Ortega O, et al. Calcifilaxis o arteriolopatía urémica calcificante: combinación de tratamientos. Nefroplus. 2010;3(3):39-44.
11. Jeong HS, Dominguez AR. Calciphylaxis: Controversies in Pathogenesis, Diagnosis and Treatment. Am J Med Sci. 2016;351(2):217-27.
12. Rodríguez Weber FL, Cano Aguilar LE. Calcifilaxis. Acta Med Grupo Angeles. 2020;18(1):50-60.
13. Nigwekar SU, Thadhani R, Brandenburg VM. Calciphylaxis. N Engl J Med. 2018;378(18):1704-14.
14. Wu J, Chen L, Dang F, Zha P, Li R, Ran X. Refractory wounds induced by normal-renal calciphylaxis: An under-recognised calcific arteriolopathy. Int Wound J. 2022;20(4):1262-75.
15. Zhou Y, Chen Y, Yin G, Xie Q. Calciphylaxis and its co-occurrence with connective tissue diseases. Int Wound J. 2022;20(4):1316-27.
16. Jiménez-Gallo D, Ossorio-García L, Linares-Barrios M. Calcinosis Cutis and Calciphylaxis. Actas Dermosifiliogr. 2015;106(10):785-94.
17. García Morúa A, Gutiérrez García JD, Arrambide Gutiérrez JG, Gómez Guerra LS. Calcifilaxis de pene: nuestra experiencia en 5 años y revisión de la literatura científica. Actas Urol Esp. 2009;33(9):984-90.
18. Kodumudi V, Jeha GM, Mydlo N, Kaye AD. Management of Cutaneous Calciphylaxis. Adv Ther. 2020;37(12):4797-807.
19. Rrapi R, Chand S, Gabel C, Ko L, Moore KJ, Steele D, et al. Early diagnosis and intervention of calciphylaxis leading to rapid resolution. JAAD Case Rep. 2021;13:65-70.
20. Karpman E, Das S, Kurzrock EA. Penile Calciphylaxis: Analysis of Risk Factors and Mortality. J Urol. 2003;169(6):2206-9.
21. Yang TY, Wang TY, Chen M, Sun FJ, Chiu AW, Chen YH. Penile calciphylaxis in a patient with end-stage renal disease: a case report and review of the literature. Open Med. 2018;13(1):158-63.
22. Torre AC, Bastard DP, Diehl M, Rosa-Diez G, Volonteri V, Mazzuoccolo LD, et al. Calcifilaxis, factores de riesgo, tratamiento y evolución estudio retrospectivo de 39 pacientes. Medicina (B Aires). 2023;84:196-205.
23. El-Taji O, Bondad J, Faruqui S, Bycroft J. Penile calciphylaxis: a conservative approach. Ann R Coll Surg Engl. 2020;102(2):36-8.
24. Gabel C, Chakrala T, Shah R, Danesh MJ, Dobry AS, Garza-Mayers AC, et al. Penile calciphylaxis: A retrospective case-control study. J Am Acad Dermatol. 2021;85(5):1209-17.
25. Wipattanakitcharoen A, Takkavatakarn K, Susantitaphong P. Risk factors, treatment modalities, and clinical outcomes of penile calciphylaxis: systematic review. World J Urol. 2023;41(11):2959-66.
26. Zillioux JM, Geisenhoff A, Gray M. Management of Penile Calciphylaxis. J Wound Ostomy Continence Nurs. 2018;45(6):536-9.
27. Wen W, Portales-Castillo I, Seethapathy R, Durant O, Mengesha B, Krinsky S, et al. Intravenous Sodium Thiosulphate for Calciphylaxis of Chronic Kidney Disease. JAMA Netw Open. 2023;6(4):2310068.
28. Cimmino CB, Costabile RA. Biopsy Is Contraindicated in the Management of Penile Calciphylaxis. J Sex Med. 2014;11(10):2611-7.

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