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## Letter

## Hyperbaric oxygen treatment as a therapeutic option for penile calciphylaxis



Dear Editor,

We present a rare case of penile calciphylaxis, a rare complication and a life-threatening condition affecting patients with end-stage renal disease (ESRD) undergoing dialysis. It is characterized by necrosis due to calcification of the penile arterioles and it is associated with a poor prognosis and a high mortality rate [1]. Informed consent was obtained from the patient for both clinical treatment (per institutional ethical guidelines) and publication of relevant data, and refusal of publication consent did not affect clinical care.

Our patient was a 60-year-old man who presented with suspected mycosis and necrosis of the glans, experiencing worsening pain in the glans over the past 15 days. His medical history was significant for ESRD requiring hemodialysis, secondary to type I membranoproliferative glomerulonephritis, with overlapping diabetic nephropathy and cyclosporine-induced nephropathy. Additionally, he had a history of a heart attack treated with percutaneous transluminal coronary angioplasty, hypertension, atrial fibrillation, severe chronic obstructive pulmonary disease, and a liver transplant following cirrhosis post-hepatitis.

His physical examination revealed multiple ulcers and necrosis of the glans. A systemic infection was ruled out because laboratory tests revealed a white blood cell count 6240/ $\mu$ L (normal range 4000–11 000/ $\mu$ L) and C-reactive protein 42.3 mg/L (normal value <5.0 mg/L). To prevent the progression of the infection, empirical antibiotic therapy with ceftriaxone 1 g per day for 10 days was administered.

Penile color Doppler ultrasound (PDU) revealed extensive calcification of the cavernosal, helical, and dorsal arteries of the penis. Furthermore, after contrast-enhanced ultrasound (CEUS), the corpora cavernosa appeared markedly

hypovascularized, while the glans showed partial vascularization. Penile calciphylaxis was postulated (Fig. 1).

The CT scan revealed extensive calcifications of the aortic wall, iliac arteries, and pudendal arteries, and the notably reduced caliber of the prostatic, cavernosal, dorsal, and terminal branches of the glans arteries.

Laboratory tests revealed serum calcium 7.74 mg/dL (normal 8.50–10.50 mg/dL), serum phosphate 7.86 mg/dL (normal 2.50–4.50 mg/dL), and parathyroid hormone 418.8 pg/mL (normal 11.0–73.0 pg/mL). Blood tests for cryoglobulins, complement component 3, and complement component 4 ruled out cryoglobulinemia and supported the diagnosis of penile calciphylaxis.

Prior to surgery, we opted for daily hyperbaric chamber treatments to minimize post-surgical complications. Clinical improvement was noted within 72 h, leading us to postpone surgery. By the time of discharge, after 9 days, our patient was stable, with physical examination showing early re-epithelialization of the glans. Our patient completed eight hyperbaric chamber sessions, and a subsequent urological exam showed a grey-necrotic flap with underlying signs of re-epithelialization, confirming resolution of the glans necrosis. Our patient reported persistent tactile sensitivity, though it was initially painful. Six months later, our patient died of cardio-respiratory arrest during dialysis treatment. Autopsy revealed extensive destructive fibrous-calcific arteriosclerosis, confirming systemic calciphylaxis.

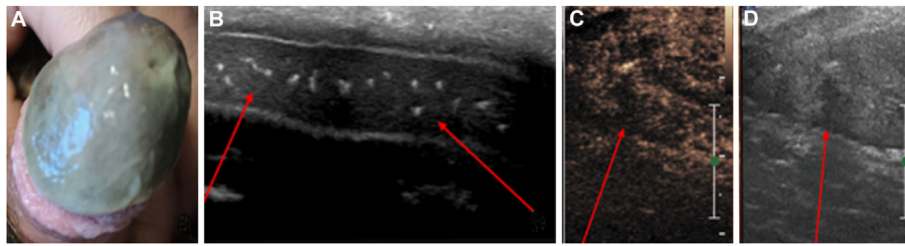
Calciphylaxis is a rare and severe complication of ESRD characterized by painful skin lesions that can progress to necrosis, eventually requiring penectomy [2]. The pathophysiology of calciphylaxis involves calcification, fibrointimal hyperplasia, and thrombosis of the microvessels in the subcutaneous adipose tissue and dermis, often leading to necrosis [1].

Penile calciphylaxis is rare due to its rich vascular network, and the prognosis is poor, with an overall mortality rate of 64% and a mean time to death of 2.5 months [3].

The diagnosis and management of penile calciphylaxis are challenging, and there is no consensus on appropriate treatment. A positive history of ESRD, combined with the finding of necrotic lesions of the glans during physical

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**Figure 1** Penile calciphylaxis clinical appearance. (A) The first clinical examination: multiple ulcers and necrosis of the glans; (B) Penile color Doppler ultrasound showing the characteristic “pearl necklace” appearance (red arrows); (C) Contrast-enhanced penile color Doppler ultrasound image (the red arrow indicates the markedly hypovascularized corpora cavernosa after contrast administration); (D) Non-contrast penile color Doppler ultrasound image (the red arrow indicates the hypoechoic and markedly hypovascularized corpora cavernosa).

examination, raises clinical suspicion of penile calciphylaxis. A CT scan confirms the diagnosis.

In our case, the PDU finding of calcifications in the penile arteries supported the diagnosis of penile calciphylaxis before tomographic evidence of diffuse arterial calcification. PDU is easy to perform and useful for assessing the local status of corpora cavernosa and corpora spongiosa before surgery [4].

Furthermore, based on our experience, we utilized CEUS to enhance the evaluation of peripheral tissues. While a biopsy of skin lesions remains the gold standard for diagnosis [3], current literature advises against penile biopsy due to the increased risk of infection and potential development of wet gangrene [1].

The management of penile calciphylaxis remains a topic of debate, but it primarily focuses on local wound care, pain control, and maintenance penile blood flow. Treatment options are highly limited and include medical approaches such as normalizing metabolic parameters, administering sodium thiosulfate infusions, providing wound care to prevent infection, using agents to enhance perfusion, and employing hyperbaric oxygen therapy to promote wound healing. Surgical options include debridement, partial penectomy, and revascularization surgery [3].

Hyperbaric oxygen therapy is an innovative approach for treating penile calciphylaxis, though it should be regarded as an off-label therapy. This treatment uses high-pressure oxygen to enhance oxygen delivery to the affected tissue [5]. Current literature contains only a few cases of penile calciphylaxis treated with hyperbaric oxygen therapy. Vassa et al. [6] reported complete resolution of pain and skin ulcers in a patient with bilateral lower extremity calciphylaxis after 38 sessions of hyperbaric oxygen therapy. Similarly, Dean et al. [7] and Podymow et al. [8] described favorable outcomes using this therapy for calciphylaxis treatment. Lipinski and Sahu [5] documented a case of slow resolution of penile ulceration following multiple hyperbaric oxygen treatments. In our case, hyperbaric oxygen therapy resulted in a gradual improvement of the necrotic lesions and could be administered on an outpatient basis.

In conclusion, penile calciphylaxis is a rare and severe complication of ESRD that presents with significant clinical

challenges, including high morbidity and mortality. This case underscores the importance of early and accurate diagnosis through imaging modalities such as PDU and CEUS, which are invaluable in assessing the extent of vascular calcification and guiding management decisions.

In this case, hyperbaric oxygen therapy emerged as a promising alternative to surgery, showing a notable improvement in necrotic lesions and facilitating wound healing. Although this therapy is still considered off-label, it demonstrated efficacy in reducing complications and improving patient outcomes, supporting its potential role in the management of penile calciphylaxis.

Despite the advances in diagnostic and therapeutic approaches, the prognosis for penile calciphylaxis remains poor, and further research is needed to establish standardized treatment protocols. This case highlights the need for continued exploration of innovative therapies and emphasizes the importance of individualized care strategies to improve patient survival and quality of life in the face of this challenging condition.

## Author contributions

*Study concept and design:* Maria Barbiero, Andrea Piasentin.

*Data acquisition:* Michele Bertolotto, Michele Rizzo.

*Data analysis:* Maria Barbiero, Andrea Piasentin.

*Drafting of the manuscript:* Maria Barbiero, Andrea Piasentin.

*Critical revision of the manuscript:* Andrea Piasentin, Michele Bertolotto, Michele Rizzo, Giovanni Liguori.

## Conflicts of interest

The authors declare no conflict of interest.

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