

Calciophylaxis: Beating the Odds

José Mário Bastos ¹, Joana Medeiros ¹, Johanna Viana ¹, Catarina Oliveira Silva ¹, Maria Joao Rocha ²

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1. Nephrology, Unidade Local de Saúde de Braga, Braga, PRT 2. Nephrology, Unidade Local de Saúde de Matosinhos, Porto, PRT

Corresponding author: José Mário Bastos, jmsbastos33@gmail.com

Abstract

Calciophylaxis is an obliterative vasculopathy characterized by ischemic cutaneous necrosis secondary to the calcification of small- and medium-caliber blood vessels. This condition poses a significant therapeutic challenge and is often associated with poor outcomes.

We report the case of a 59-year-old man who had been on renal replacement therapy for 28 years and presented with a painful necrotic ulcer on his left leg, which progressively worsened over three weeks. A skin biopsy confirmed the diagnosis of calciophylaxis. The treatment approach included intensified hemodialysis, optimization of mineral and bone disorder management, treatment of secondary bacterial infection, intravenous sodium thiosulfate infusion, chemical and surgical debridement, and partial-thickness skin grafting. This comprehensive strategy resulted in complete wound healing within three months.

This case highlights the importance of early diagnosis and a multidisciplinary approach in managing calciophylaxis, a rare condition associated with a highly unfavorable prognosis.

Categories: Plastic Surgery, Dermatology, Nephrology

Keywords: calciophylaxis, chronic kidney disease, hemodialysis, partial-thickness skin grafting, sodium thiosulfate

Introduction

Calciophylaxis, also known as calcific uremic arteriolopathy, is a rare and life-threatening obliterative vasculopathy characterized by ischemic skin necrosis due to the calcification and occlusion of small- and medium-sized blood vessels. This vascular calcification leads to luminal narrowing and thrombosis, resulting in reduced blood flow, tissue ischemia, and subsequent skin necrosis [1]. Although it is most commonly observed in patients with end-stage renal disease (ESRD) undergoing dialysis, calciophylaxis can also occur in earlier stages of chronic kidney disease (CKD), after kidney transplantation, and, rarely, in individuals with normal kidney function [1,2]. The condition is associated with a poor prognosis, with a one-year mortality rate reaching up to 80% in patients with CKD [3].

Numerous risk factors have been associated with calciophylaxis, including disturbances in calcium-phosphate metabolism, obesity, diabetes mellitus, female sex, white race, vitamin K deficiency, and prolonged use of calcium-based phosphate binders or vitamin D supplements [1,3]. Additionally, patients often present with elevated parathyroid hormone (PTH) levels, hyperphosphatemia, and a deficiency of natural inhibitors of calcification, such as fetuin-A and matrix Gla protein [2, 4]. However, not all affected individuals display these abnormalities, highlighting the multifactorial and poorly understood pathogenesis of this condition [4].

The clinical presentation is typically characterized by painful, ischemic skin lesions that frequently progress to necrosis, increasing the risk of infection and sepsis [3]. Given its dismal prognosis and limited therapeutic options, calciophylaxis underscores the critical need for early recognition and a multidisciplinary approach to treatment [4].

Case Presentation

A 57-year-old male presented to the emergency department with a three-week history of a painful ulcer that appeared spontaneously on the back of his left lower leg and was progressively increasing in size. He denied fever, chills, or any other systemic symptoms.

The patient had a 28-year history of ESRD, managed with two kidney transplants that lasted a total of 11 years, along with 17 years of hemodialysis, including periods between the two transplants and following the second transplant. His medical history was notable for secondary hyperparathyroidism, treated with etelcalcetide (5 mg three times per week) and alfacalcidol (0.5 mcg three times per week), as well as paroxysmal atrial fibrillation managed with long-term anticoagulation using warfarin.

On physical examination, the patient was afebrile, with a blood pressure of 135/77 mmHg and a heart rate of 75 beats per minute. He presented with a necrotic ulcer approximately 4 cm in diameter on the back of his

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left lower leg (Figure 1). There were no signs of cellulitis or systemic infection at the time of presentation. Cardiopulmonary and abdominal examinations were unremarkable.



FIGURE 1: Necrotic lesion at admission.

Necrotic ulcer approximately 4 cm in size on the posterior left lower leg, with a central black eschar and an erythematous border, consistent with ischemic necrosis and calciphylaxis.

Laboratory results at admission are summarized in Table 1.

Parameter	Result	Units	RR
Parathyroid hormone (PTH)	393.58	pg/mL	10-65*
Serum calcium	9.2	mg/dL	8.3-10.6
Phosphate	4.0	mg/dL	2.4-5.1
C-reactive protein (CRP)	3.5	mg/L	<5.0

TABLE 1: Laboratory results at admission.
*For patients with chronic kidney disease (CKD) on hemodialysis, the target PTH range is approximately 2-9 times the upper limit of the normal range (ULN).
RR, reference range

Given the clinical presentation and the patient’s history, calciphylaxis was suspected, and the patient was admitted under the care of the nephrology team. A skin biopsy confirmed the diagnosis, revealing vascular calcification and thrombosis in small- and medium-sized arterioles, accompanied by tissue necrosis. Non-calcium-based phosphate binders (sevelamer) were initiated, and the calcimimetic therapy (etelcalcetide) was continued. Hemodialysis was intensified to four sessions per week to optimize metabolic control and fluid balance. Warfarin was replaced with enoxaparin adjusted to renal function, and alfacalcidol was discontinued.

On the fifth day of hospitalization, the patient developed signs of local infection around the ulcer, including erythema, warmth, and swelling. Laboratory tests showed a leukocytosis of 13,600/μL with 10,200 neutrophils/μL and a C-reactive protein (CRP) of 115 mg/L. Empiric antibiotic therapy with vancomycin and meropenem was initiated to target possible Gram-positive and Gram-negative pathogens. Blood cultures and a swab of the lesion were collected but yielded no microbial growth. Antibiotic therapy was continued for 14 days, leading to the resolution of the inflammatory signs.

Intravenous sodium thiosulfate therapy was started on the seventh day of hospitalization, at a dose of 25 grams three times weekly after dialysis. Early involvement of the Plastic Surgery team facilitated both chemical debridement with silver sulfadiazine and surgical debridement to remove necrotic tissue and promote wound healing. Although the patient was listed for hyperbaric oxygen therapy, the wound began to show significant improvement before this intervention could be initiated.

By the 41st day of hospitalization, a partial-thickness skin graft was harvested from the ipsilateral thigh and successfully applied to the wound bed. The patient continued to demonstrate gradual improvement, achieving complete wound healing and being discharged on the 47th day of hospitalization. At the one-month outpatient follow-up consultation, the lesion was fully healed, with no signs of recurrence or complications (Figure 2).



FIGURE 2: Calciphylaxis lesion at the one-month follow-up consultation.

Healed lesion on the posterior left lower leg at the one-month follow-up, showing complete wound closure with residual scarring and no evidence of active infection or recurrence.

Discussion

Calciphylaxis, or calcific uremic arteriolopathy, is a rare but life-threatening condition that primarily affects patients with ESRD undergoing dialysis. Despite advancements in understanding the disease, calciphylaxis remains associated with a poor prognosis, with mortality rates reported to range between 50% and 80% within the first year, largely due to complications such as sepsis and delayed wound healing [5,6]. Furthermore, calciphylaxis carries a significant risk of recurrence, particularly in patients with ongoing inflammation or inadequate control of underlying risk factors, such as hyperparathyroidism and elevated calcium-phosphorus product levels [7].

This case underscores the importance of identifying risk factors and implementing early interventions in patients at high risk for calciphylaxis. The patient's long-standing ESRD, having been on renal replacement therapy (RRT) for 28 years, coupled with secondary hyperparathyroidism and chronic warfarin use, placed him in a high-risk category. Warfarin is a known contributor to calciphylaxis due to its inhibition of vitamin K-dependent proteins, such as matrix Gla protein, a critical inhibitor of vascular calcification. Its replacement with enoxaparin may have mitigated further progression of vascular calcification. The lower extremities, particularly the legs, are common sites for calciphylaxis lesions due to reduced vascular reserve, ischemic predisposition, and increased susceptibility to chronic microtrauma, all of which exacerbate tissue necrosis in these regions [5-7].

Management of calciphylaxis requires a multidisciplinary approach addressing both systemic and local factors contributing to disease progression. Sodium thiosulfate was initiated as part of the therapeutic regimen. Although its precise mechanism of action is not fully understood, sodium thiosulfate is thought to reduce vascular calcification by chelating calcium, enhancing its solubility, and mitigating oxidative stress. It has also been associated with improvements in pain and wound healing in patients with calciphylaxis [8,9].

Optimization of mineral and bone metabolism was another cornerstone of this patient's management. Sevelamer was introduced to reduce phosphorus while minimizing further calcium overload. Since the calcium-phosphorus product is one of the main risk factors for the onset and progression of calciphylaxis, it was used even with normal serum phosphorus levels, effectively reducing the product without ever causing hypophosphatemia. Etelcalcetide was continued to address secondary hyperparathyroidism, without raising the phosphate or calcium levels. These interventions are essential in controlling the calcium-phosphate balance and preventing vascular calcification and subsequent tissue necrosis [5,10].

Secondary bacterial infection of necrotic ulcers is a common and serious complication of calciphylaxis [11]. In this case, the development of local signs of infection, including erythema, swelling, and elevated inflammatory markers, prompted the timely initiation of broad-spectrum antibiotics. The absence of microbial growth in blood cultures and lesion swabs highlights the challenge of identifying causative organisms in such cases [6,11]. Nonetheless, early and effective antimicrobial treatment was crucial in resolving the infection and preventing systemic complications.

The involvement of the Plastic Surgery team was decisive in achieving a successful outcome. Early debridement, both chemical and surgical, was essential to create an optimal environment for wound healing. Chemical debridement with silver sulfadiazine not only controlled bacterial colonization but also facilitated autolytic debridement by maintaining a moist wound bed. Surgical debridement further ensured the removal of nonviable tissue. A partial-thickness skin graft, harvested from the ipsilateral thigh, was successfully applied to the prepared wound bed. This intervention accelerated wound closure and minimized the risk of long-term complications such as chronic infection or limb dysfunction. The early collaboration with plastic surgery points to the importance of integrating specialized surgical care into the management of calciphylaxis, particularly for large or refractory wounds [5,12].

Conclusions

This case highlights the role of early recognition and a multidisciplinary approach in the management of calciphylaxis, a condition that poses significant therapeutic challenges. A combination of systemic therapy, advanced wound care, and surgical interventions was key to achieving a positive outcome in this patient. Continued research is necessary to enhance treatment protocols and improve survival rates for those affected by this rare but severe disease.

With a treatment plan guided by the latest literature and a close collaboration with the plastic surgery team, complete therapeutic success was achieved. This case underscores the importance of maintaining a high index of suspicion and providing timely interventions for a disease that, although rare, is frequently associated with poor outcomes.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: José Mário Bastos, Joana Medeiros, Maria Joao Rocha , Johanna Viana, Catarina Oliveira Silva

Acquisition, analysis, or interpretation of data: José Mário Bastos, Joana Medeiros

Drafting of the manuscript: José Mário Bastos, Johanna Viana, Catarina Oliveira Silva

Critical review of the manuscript for important intellectual content: José Mário Bastos, Joana Medeiros, Maria Joao Rocha

Supervision: José Mário Bastos, Maria Joao Rocha

Disclosures

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References

- Seethapathy H, Brandenburg VM, Sinha S, El-Azhary RA, Nigwekar SU: Review: update on the management of calciphylaxis. *QJM*. 2019, 112:29-34. [10.1093/qjmed/hcy234](https://doi.org/10.1093/qjmed/hcy234)
- Weenig RH, Sewell LD, Davis MD, McCarthy JT, Pittelkow MR: Calciphylaxis: natural history, risk factor analysis, and outcome. *J Am Acad Dermatol*. 2007, 56:569-79. [10.1016/j.jaad.2006.08.065](https://doi.org/10.1016/j.jaad.2006.08.065)
- Hayden MR, Goldsmith DJ: Sodium thiosulfate: new hope for the treatment of calciphylaxis. *Semin Dial*. 2010, 23:258-62. [10.1111/j.1525-139X.2010.00738.x](https://doi.org/10.1111/j.1525-139X.2010.00738.x)
- Nigwekar SU, Zhao S, Wenger J, Hymes JL, Maddux FW, Thadhani RI, Chan KE: A nationally representative study of calcific uremic arteriolopathy risk factors. *J Am Soc Nephrol*. 2016, 27:3421-9. [10.1681/ASN.2015091065](https://doi.org/10.1681/ASN.2015091065)
- Nigwekar SU, Thadhani R, Brandenburg VM: Calciphylaxis. *N Engl J Med*. 2018, 378:1704-14. [10.1056/NEJMra1505292](https://doi.org/10.1056/NEJMra1505292)
- Brandenburg VM, Kramann R, Rothe H, et al.: Warfarin-related nephropathy and vascular calcification: clinical relevance. *Kidney Int*. 2014, 85:1006-14. [10.1038/ki.2013.366](https://doi.org/10.1038/ki.2013.366)
- Gaisne R, Péré M, Menoyo V, Hourmant M, Larmet-Burgeot D: Calciphylaxis epidemiology, risk factors, treatment and survival among French chronic kidney disease patients: a case-control study. *BMC Nephrol*. 2020, 21:63. [10.1186/s12882-020-01722-y](https://doi.org/10.1186/s12882-020-01722-y)
- Wyne K: How can the poor outcomes for diabetic dialysis patients be improved? . *Semin Dial*. 2004, 17:194-5. [10.1111/j.0894-0959.2004.17305.x](https://doi.org/10.1111/j.0894-0959.2004.17305.x)
- Cozzolino M, Magagnoli L, Ciceri P, Conte F, Galassi A: Effects of a medium cut-off (Theranova®) dialyser on haemodialysis patients: a prospective, cross-over study. *Clin Kidney J*. 2021, 14:382-9. [10.1093/ckj/sfz155](https://doi.org/10.1093/ckj/sfz155)
- Joseph AK, Abbas LF, Chong BF: Treatments for disease damage in cutaneous lupus erythematosus: a narrative review. *Dermatol Ther*. 2021, 34:e15034. [10.1111/dth.15034](https://doi.org/10.1111/dth.15034)
- Mazhar AR, Johnson RJ, Gillen D, Stivelman JC, Ryan MJ, Davis CL, Stehman-Breen CO: Risk factors and mortality associated with calciphylaxis in end-stage renal disease. *Kidney Int*. 2001, 60:324-32. [10.1046/j.1523-1755.2001.00803.x](https://doi.org/10.1046/j.1523-1755.2001.00803.x)
- Lajoie C, Ghanemi A, Bourbeau K, Sidibé A, Wang YP, Desmeules S, Mac-Way F: Multimodality approach to treat calciphylaxis in end-stage kidney disease patients. *Ren Fail*. 2023, 45:2256413. [10.1080/0886022X.2023.2256413](https://doi.org/10.1080/0886022X.2023.2256413)