# Calciphylaxis, Early Identification and Management: A Report of 2 Cases

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#### Introduction

Calciphylaxis, or calcific uraemic arteriolopathy (CUA), is a life-threatening calcification of arterioles leading to necrotic infarcts of the skin and subcutaneous tissue (panniculus adiposus) with a high potential to progress to bacterial sepsis and death.

The prevalence of CUA has been reported to be approximately 4.1% in patients with end-stage renal disease (ESRD), with the reported incidence increasing over the past 10 years<sup>1,2,3</sup>. This painful condition causes significant morbidity and has a one-year cause-specific mortality rate exceeding 50%<sup>2</sup>.

**Risk factors** include ESRD, hyperparathyroidism, female sex, Caucasian ethnicity, obesity, diabetes mellitus, time on dialysis, systemic corticosteroid use, hypoalbuminaemia, and corrected calcium phosphorus product >4.4 mmol<sup>2</sup>/L<sup>2</sup> <sup>2,3,4</sup>.

Here, we present two cases.

## **Patient Profiles**

Patient 1 is a 57 year old Caucasian male with end-stage renal disease (ESRD) secondary to autosomal dominant polycystic kidney disease (ADPKD), and a dialysis vintage of 2 years. He was on peritoneal dialysis and taking calcitriol and calcium acetate. He was on warfarin for hypercoagulability.

His serum albumin level averaged 39 g/L in the six months before diagnosis, was 39 g/L at time of diagnosis, and averaged 44 g/L in the nine months following diagnosis. At time of diagnosis, adjusted calcium phosphorus product was 4.9 mmol<sup>2</sup>/L<sup>2</sup>. His CUA was diagnosed clinically.

Patient 2 is a 47 year old Caucasian female with ESRD secondary to ADPKD, and a dialysis vintage of 1.5 years. Six months prior to diagnosis of CUA, she had severe hyperphosphataemia and underwent parathyroidectomy. Prior to diagnosis she was on calcitriol and calcium acetate. She was on warfarin for a venous thrombosis.

Her serum albumin level averaged 38 g/L in the six months before diagnosis, was 16 g/L at time of diagnosis, and averaged 23 g/L in the six months following diagnosis. At time of diagnosis, adjusted calcium phosphorus product was 4.7 mmol<sup>2</sup>/L<sup>2</sup>.

Her CUA started with 2 months of painful nodules involving her breasts, abdomen, and thighs. At this time, CT scanning was negative for calcification or ulceration of the soft tissue. Once she developed ulceration, her CUA was confirmed by biopsy.

### Patient 1





**Month 0:** The patient exhibits painful violaceous plaques on the calves and thighs, with livedo reticularis rash on surrounding skin. He has several lesions on the right thigh and two on the left thigh which are erythematous raised plaques of irregular shape.

Treatment: He was started on sodium thiosulphate with haemodialysis.





**Month 2:** A left shin lesion is erythematous with central necrosis of approximately 6 cm in diameter (left photo). A lesion on the right thigh has progressed to blistering and necrosis with eschar formation (right photo).

**Treatment:** He is admitted to the hospital for pain control and daily dialysis with sodium thiosulphate.





**Months 3-4:** The left lateral lower leg wound exhibits diminishing eschar, and is mostly closed (left photo). The left posterior lower leg wound is healing slowly due to painful ulceration over 1 cm deep (not shown). The right thigh lesion shows necrosis with eschar formation (right photo). Induration around the lesions has decreased.

**Treatment:** Continued serial debridement, and use of calcium alginate and silver-impregnated hydrating foam dressings for antimicrobial effect and exudate management.





**Month 5:** The right thigh wound shows minimal yellow slough. Overall, exudates have diminished. All wounds continue to improve (right photo).

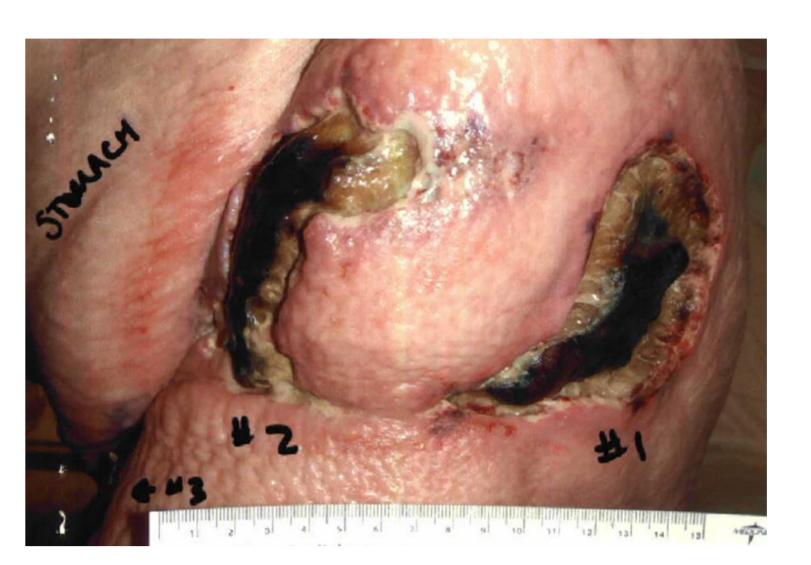
**Treatment:** Wound swabs were sent for culture which was negative for infection. Gentle debridement was continued.

Month 9: An open area on the anterior surface of the left lower leg is pink at the base with some yellow slough and granulation tissue (left photo).

**Treatment:** Silver-impregnated absorbent foam dressings were used to help draw moisture away from the wound. Dialysis with sodium thiosulphate was continued until month 11 when all wounds had closed.

#### Patient 2





**Month 2:** After two months of painful subcutaneous nodules and despite treatment with sodium thiosulphate, these ulcerative lesions developed on the left anterior, lateral and posterior hip, and on the right posterior hip. They are deep with central necrosis. The largest is over 20 cm in diameter. Biopsy revealed thickened vascular walls with areas of calcification, and calcification involving the adipose soft tissue, consistent with CUA.





**Month 3:** The necrotic lesions have stopped expanding. There is surrounding erythema and induration. The patient has severe pain, even with only clothing touching the lesions. She is losing weight and culture grows methicillin-resistant staphylococcus aureus.

**Treatment:** The patient was admitted to hospital for nocturnal tube feeding and wound care with gentle debridement and started on vancomycin for several weeks.





**Month 4:** Wounds show increased exudate, purulence, and sloughing. Eschar is forming. Infection is resolving.





**Month 5:** Granulation tissue is forming in most wounds. Infection has resolved. **Treatment:** Wound vacuum use was avoided due to pain. The patient continued wound care at home.





**Month 6:** The wounds are healing. Enterobacter and candida were cultured. **Treatment:** Wound care nurses applied silver sulfadiazine cream and a trypsin-based debriding cream daily. The patient continued on dialysis six times per week with sodium thiosulphate.

#### Discussion

Patient 1 underwent the following treatments: He was taken off calcitriol and calcium acetate. Cinacalcet was started for control of hyperparathyroidism. Warfarin was changed to low-molecular weight heparin. The patient was counselled extensively to reduce phosphorus intake and improve nutrition, and to encourage adherence to his medical regimen. In addition to intensive wound care, he was converted from peritoneal dialysis to haemodialysis and continued on sodium thiosulphate for nearly 11 months until his wounds healed.

Patient 2 underwent the following treatments: She had had a recent parathyroidectomy. Calcitriol and calcium acetate were changed to cinacalcet and sevelamer. Warfarin was stopped. The patient was given prednisone for one month, and two doses of pamidronate. She was counselled to reduce phosphorus intake, and later she was started on nocturnal tube feeds, and supplemented with cyanocobalamin (B12), alpha-tocopherol (E), and zinc. Intensive wound care was performed with consultation from plastic surgery. Sodium thiosulphate was incorporated into the patient's dialysis treatment. The wounds were healing, however, during month six she was re-admitted to hospital with sepsis and died.

**In conclusion**, the progression of CUA wounds highlights the need for rapid response when early signs appear. Skin biopsy can confirm clinical suspicion but is not without risk of infection and ulceration<sup>3,5</sup>.

At this time, there are no prospective randomised controlled studies relating to CUA of which we are aware. Research is limited to observational and retrospective studies<sup>3</sup>. Future research is needed to improve diagnosis and treatment of this devastating condition.

## **Literature Cited**

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