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A rare but fatal complication of end stage renal disease

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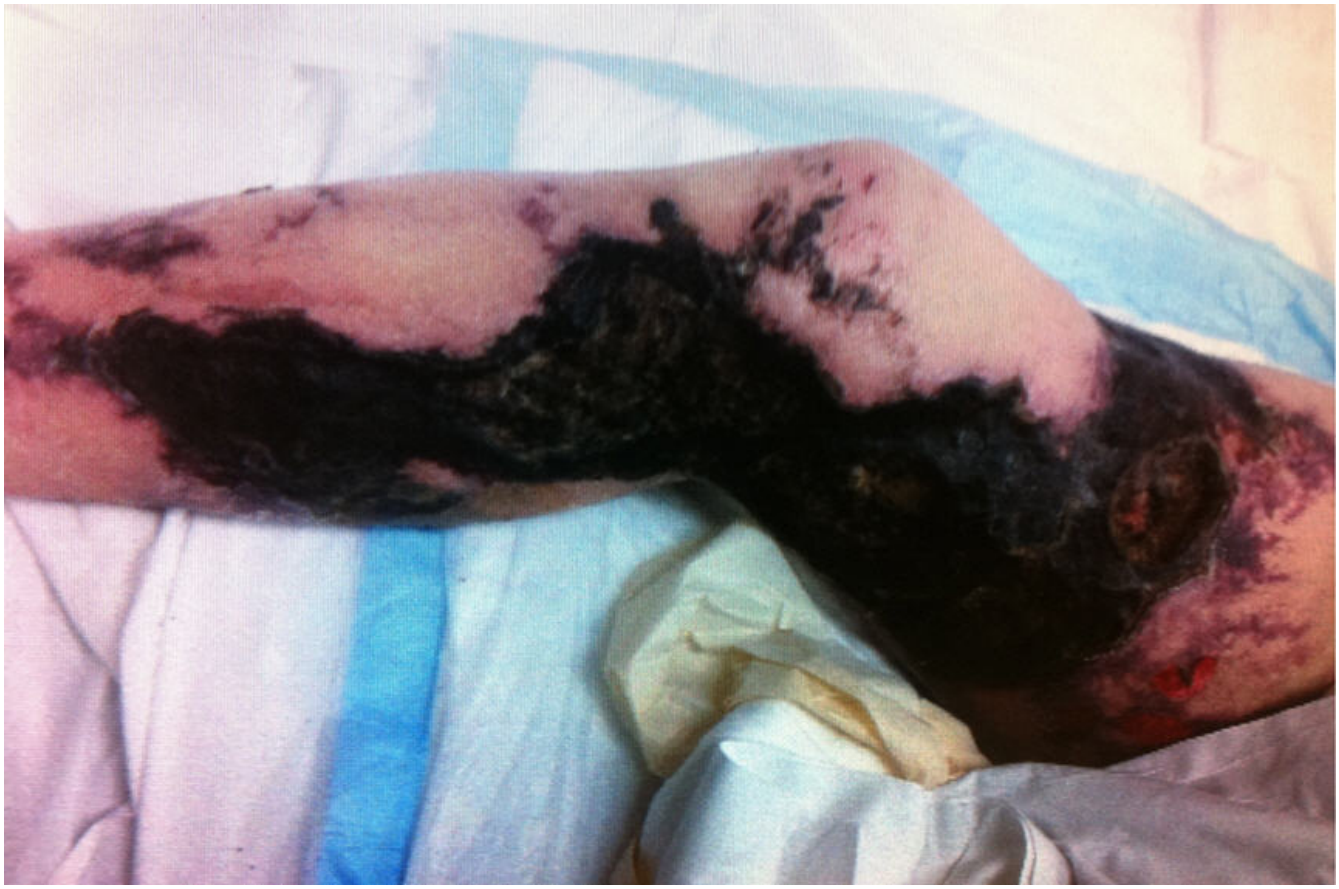
Clinical—A 49-year-old male with end stage renal disease (ESRD) on haemodialysis was referred for further management of painful, extensive bilateral lower extremity ulcerations present for 8 months (Figure 1).

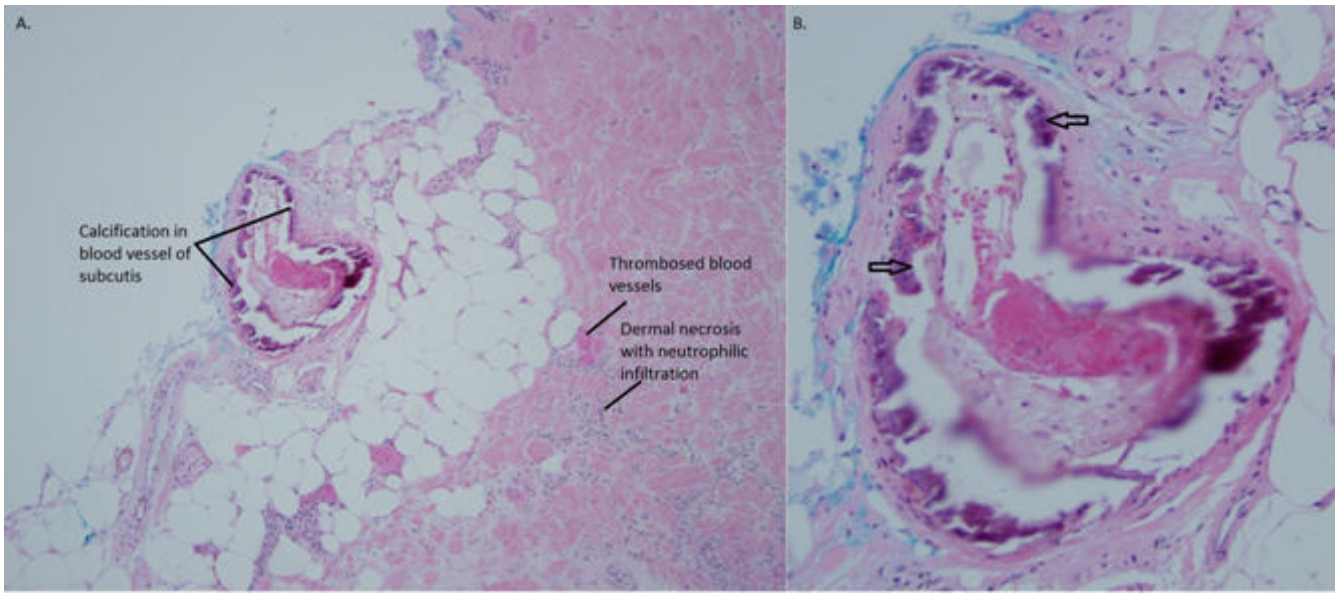
Figure 1. Lower extremity ulceration and overlying eschar



Significant labs were leukocytosis, elevated calcium-phosphorus product (CaxP) of 97.5 mg^2/dl^2 and parathyroid hormone (PTH) level of 3708 pg/ml (10–60).

Biopsy of the cutaneous lesions revealed epidermal and dermal necrosis, thrombosis and calcifications in small blood vessels of subcutis (Figure 2).

Figure 2. (A) Skin biopsy showing dermal necrosis with neutrophilic infiltration, subcutaneous arterial vessel with thrombosis, marked intimal proliferation and near circumferential calcification causing occlusion of the lumen. H&E magnification ×100; (B) Inset showing the thrombosed vessel with circumferential calcification in the vessel wall (black arrows). H&E magnification ×400



What is the diagnosis?

Answer—*Calcific uremic arteriolopathy (CUA).*

Discussion

CUA, also known as calciphylaxis, is a rare life-threatening syndrome of vascular calcification and necrosis that presents in 1% of ESRD patients each year with a prevalence of 4% in patients on dialysis. Risk factors include duration of dialysis, abnormal CaxP, hyperparathyroidism (especially with PTH levels >1000 pg/ml) and use of calcium-based phosphate binders and vitamin D analogues.[1] Other rare causes include obesity, trauma and coagulopathy.

Non-ESRD causes of CUA include primary hyperparathyroidism, vitamin D intoxication, malignancy, multiple myeloma, alcoholic cirrhosis and use of long-term steroid and methotrexate.[2,3]

Increased CaxP can precipitate metastatic calcification in arterioles leading to intimal fibrosis and vascular thrombus causing occlusion with tissue ischemia, necrosis and gangrene. It manifests as violaeous plaques with subcutaneous nodules which progress to necrotic ulcers with eschars and superadded infection. The mortality rate is reported to be as high as 60–80%[1] and the leading cause of death is sepsis. Confirmation of diagnosis is by skin biopsy.

Recommendations for prevention include maintaining phosphorus level <5.5 mg/dL, calcium level <9.6 mg/dL, and a CaxP product <55 mg^2/dL^2. This can be accomplished by low calcium dialysate, dietary protein restriction, using calcium-free phosphorus binders and newer vitamin D analogues. Paricalcitol and doxercalciferol may reduce PTH and calcium concentrations more rapidly than calcitriol.

A multidisciplinary team management with aggressive local wound care, debridement and control of CaxP is required.

Available treatment options include cinacalcet, a calcimimetic which lowers PTH and calcium levels and is indicated in patients where CaxP remains high despite standard therapy[4]. Novel therapeutic options, not well validated include sodium thiosulfate , which increases the solubility of calcium deposits, hyperbaric oxygen, corticosteroids, and bisphosphonates.

The treatment of choice remains early parathyroidectomy[5] which has shown improved wound healing and survival rates versus nonoperative treatment.

Our patient was treated with aggressive wound care, debridement, cinacalcet and sodium thiosulfate. Despite these measures, he succumbed to sepsis and died.

This case illustrates the importance of prevention and early detection of CUA which may facilitate treatment and possibly reduce mortality. Evaluation of skin for breakdown should be part of the routine care of these patients. A diagnosis of CUA should be considered in ESRD patients with a non-healing ulcer.

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