Penile calciphylaxis: a conservative approach

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ABSTRACT

Penile calciphylaxis or calcific uremic arteriopathy is a rare urological condition often associated with patients undergoing renal dialysis for end-stage renal disease. The majority of cases are associated with systemic calciphylaxis. The pathophysiology, diagnosis and management of penile calciphylaxis as an individual entity has brought little attention. The rates of comorbidity and mortality of these patients are often particularly high. Early diagnosis and a multidisciplinary approach are therefore essential. We report a case of penile calciphylaxis in a 59-year-old man with end-stage renal failure on haemodialysis who was successfully managed conservatively.

KEYWORDS

Penis – Calciphylaxis – Penile disease

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Background

Calciphylaxis, also known as calcific uremic arteriopathy, is a life-threatening condition often characterised by severe obstructive vasculopathy with the calcification of arteries eventually resulting in tissue necrosis. Studies have shown that the underlying process is that of ossification of the arteriolar media muscle layer and is heavily dependent on the expression of the fibroblast growth factor-23.¹ Its presence in patients with chronic kidney disease is approximately 1–4% in those on dialysis. Risk factors include warfarin use, obesity, hyperphosphataemia, hypercalcaemia and haemodialysis. Areas commonly affected include the thighs, buttocks and distal phalanges.

Penile calciphylaxis is extremely rare, due to the abundant vascular network of the penis. There are only 51 reported cases, recording a mortality of up to 69% at six months.² Diagnosis is often clinical, although calciphylaxis can be confirmed through biopsy, which is not encouraged because of the high risk of inadequate wound healing, wound infection and sepsis.³ Management is often supportive, with a low threshold to manage conservatively if there are no overt signs of infection or gangrene present. This involves normalisation of calcium and phosphate levels, analgesia, local wound care and antibiotics if necessary. Debridement, partial and complete penectomy may be necessary in more extensive lesions with wet gangrene or in patients with intolerable pain.²

Case history

A 59-year-old man was admitted under the renal physicians with raised C-reactive protein, necrotic lesions on his

limbs and a lesion on his penis. He was reviewed by the urology team. An extensive past medical history consisted of end-stage renal failure secondary to diabetes. He was on haemodialysis, with a failed transplant 20 years previously (chronic antibody mediated rejection) and parathyroidectomy. Additionally, he suffered from peripheral vascular disease, dilated cardiomyopathy, atrial fibrillation (on warfarin) and congestive heart failure. On examination he had dry gangrene across his thumb with fluctuance up to the interphalangeal joint (Fig 1) and a tracking necrotic appearance of his left calf (Fig 2). On examination of his genitalia there was an obvious well-circumscribed lesion on an oedematous glans penis with overlying exudate (Fig 3). His perineum showed no evidence of disease, nor were there any palpable lymph nodes.

His blood analysis demonstrated a white cell count of $14.4 \times 10^9/l$ (normal range $4–11 \times 10^9/l$), haemoglobin 98 g/l (range 13–170 g/l), C-reactive protein 183 mg/l (range 0–5 mg/l), creatinine 578 mmol/l (range 59–104 mmol/l), calcium 1.81 mmol/l (range 2.2–2.6 mmol/l), phosphate 1.34 mmol/l (0.8–1.5 mmol/l) and parathyroid hormone 2.65 pmol/l (1.48–7.63 pmol/l). Liver tests were normal and his HbA1c was 68 mmol/mol with a body mass index of 28.1 kg/m^2 . Wound swabs demonstrated only mixed floral growth. Computed tomography demonstrated widespread arterial calcification with significant calcified plaques in the right common iliac arteries, internal iliac arteries and their branches, causing significant stenosis (Figures 4–6). Additional findings were of atrophic kidneys bilaterally as well as in the transplanted kidney.

The vascular surgeons organised a high pressure angioplasty for the left superficial femoral artery with excellent angiographic results. The patient was then started on dual

Figure 1 Dry gangrene across the left thumb.

Figure 2 Necrotic appearance of the left calf.

Figure 3 Penile lesion with overlying exudate.

Figure 4 Significant calcification at the bifurcation of the right common iliac artery and proximal internal iliac artery.

Figure 5 Calcification at the right internal iliac artery.

Figure 6 Calcification of left internal pudendal artery.

antiplatelet therapy for six weeks followed by single-agent therapy for life.

We discussed the patients' case at our urology multidisciplinary team meeting and sought advice from a regional andrology centre. We managed the penile lesion conservatively as there was no evidence of wet gangrene, nor was there any significant amount of pain attributed to it. The lesion was dressed daily and his calcium, phosphate and renal function were monitored, while also undergoing his normal haemodialysis regimen. The patient was discharged three weeks later and six months on he is currently doing well.

Discussion

Penile calciphylaxis is rare and there have only been 51 cases described in the literature.² Our patient's clinical diagnosis was based on characteristic clinical presentation, radiological findings and exclusion of other similar conditions. A tissue biopsy was deemed inappropriate owing to the lack of evidence and associated complications.⁵ There is no gold standard in the definitive management of patients with penile calciphylaxis, and multiple approaches have been described.

Karpman *et al* reviewed 34 cases of penile calciphylaxis and reported that survival was independent of the type of local treatment for the penile lesions, with no statistical significance in patients receiving partial/total penectomy or local debridement/wound care.⁴ Similarly, Yang *et al* reviewed 50 cases of penile calciphylaxis receiving either partial/total penectomy or local debridement/wound care and demonstrated mortality rates of 42.9% and 52%, respectively ($P = 0.54$).²

Parathyroidectomy has also been suggested. However, the benefit of this procedure for survival is not clear, although it could relieve pain and expedite wound recovery. Our patient had a normal parathyroid hormone level as he had undergone parathyroidectomy 20 years ago. Yang *et al* reported mortality rates of 33% and 60% in patients undergoing parathyroidectomy after calciphylaxis and those without parathyroidectomy, respectively ($P = 0.18$).² This is in contrary to Karpman *et al*, who suggested that parathyroidectomy may improve survival.⁴

Sodium thiosulfate has demonstrated reassuring results in treating calciphylactic cutaneous lesions, with 52% resolution in a retrospective study.⁵ Its role as a relatively potent antioxidant has distinctively been related to a prompt reduction in pain and its chelating properties are associated with regression of subcutaneous calcifications. In the context of penile calciphylaxis, three patients have been reportedly managed with sodium thiosulfate, with two patients surviving.²

More novel treatments include femoral artery–dorsal penile vein bypass and hyperbaric oxygen therapy. Hyperbaric oxygen therapy works through increasing oxygen delivery to tissues and seems to promote cutaneous lesions healing through angiogenesis, fibroblastic growth and collagen expression; however, these two patients died within one month.²

Conclusions

Penile calciphylaxis is a rare and potentially fatal condition which requires a detailed and meticulous approach with early recognition. We have managed a patient with penile calciphylaxis conservatively with a good outcome. Despite this, there is no consensus regarding the ideal treatment for these patients and therefore management should be determined on a case by case basis.

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