

Unusual case of calciphylaxis associated with digital necrosis and penile necrosis

Case Report

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Abstract: Calciphylaxis is a relatively rare disorder associated with calcification of small- and medium-sized blood vessels, progressive ischemic skin necrosis, and ulcerations. This situation is a potentially life-threatening condition seen in patients with endstage renal disease (ESRD). A 64-year-old man with ESRD on dialysis for 6 years was admitted to our clinic with severe pain and partial necrosis of some fingers on his right hand. In addition, the patient had suffered from diabetes for 22 years and had been on insulin therapy for 17 years. His necrotic fingers were amputated. After two months, necrosis on his glans penis developed despite medical management. Penile amputation was performed. In this case report, the patient serves to illustrate the spectrum of complications with which calciphylaxis can be associated.

Keywords: *Calciphylaxis • Penile necrosis • Digital necrosis*

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1. Introduction

Calciphylaxis is a relatively rare disorder associated with the calcification of small and medium sized blood vessels, progressive ischemic skin necrosis, and ulcerations [1]. It has an incidence of 1-4% among patients with end-stage renal failure [2]. The pathogenesis of this disease remains unclear. However, the elevated serum calcium and phosphate concentration are the most responsible factors [3].

Calciphylaxis most frequently affects the lower limbs, particularly the buttocks and thighs [4,5]. Digital necrosis or penile necrosis due to calciphylaxis is a rare entity and only a few cases have been described [6,7] We present a case of calciphylaxis in a rare location where is digital and penile area together.

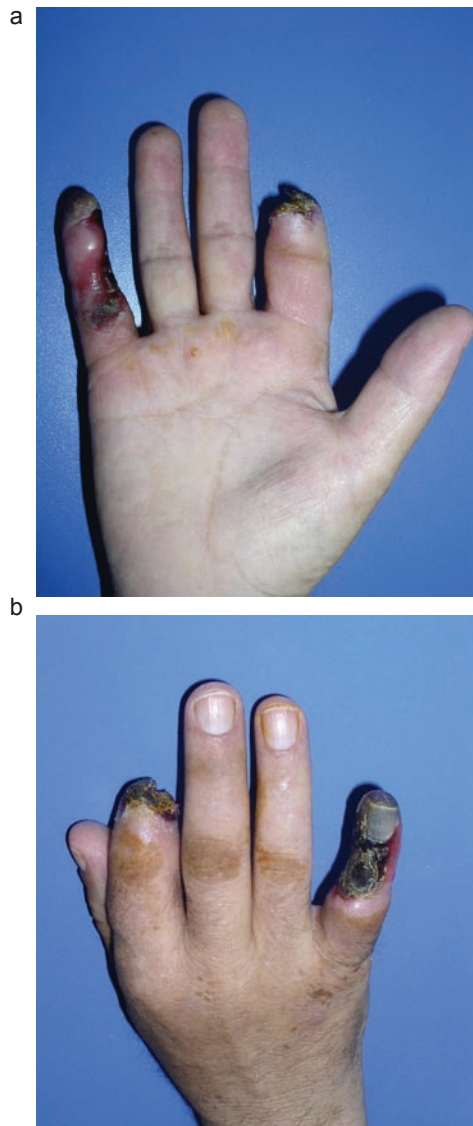
2. Case Report

A 64-year-old man with end stage renal disease (ESRD) admitted to our clinic with pain and necrosis on second and fifth fingers on his right hand.(Figure 1a –1b) At the age of 61 years, the distal part of his second finger had amputated due to a trauma. He had a 22-year history of type I diabetes. At the age of 47 years, insulin therapy had started. At the age of 58 years, hemodialysis therapy had performed to treat end-stage renal failure due to diabetic nephropathy. In the past three years the Ca/P product was persistently higher than 70 mg²/dL², he had hyperphosphatemia and severe hyperparathyroidism. No control could be achieved either with calcitriol or with subtotal parathyroidectomy.

The white blood cell count was 21,300/μl and CRP was 3.36 mg/dl, suggesting inflammatory changes. Serum Ca was 8.5 mg/dl and P was 5.2 mg/dl. HbA1c value was 12.6%, showing poor glycemic control, because Hb was only 10.7 g/dl due to renal anemia by ESRD. Serum total cholesterol and LDL-cholesterol

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Figure 1. Dry necrosis in the right second and fifth fingers.



were normal. Parathyroid hormone was also high (142 pg/ml). Coagulation parameters were normal and HIV serology was negative. Antinuclear antibody and autoantibodies related to angitis were all negative. (Table 1) The laboratory findings of the present patient were not already under control.

After assesment of clinical and laboratory findings, the medical management by nephrologists was started. Calcium carbonate supplements and calcitriol were also discontinued, warfarin was replaced by low molecular weight heparins. The dialysis rate was increased to 4 sessions/week, and from 3 h to 3.5 h/session. biphosphonates was started (sodium etidronate 200 mg/day), which was discontinued since there was no clinical improvement after 10 days on treatment.

Table 1. Laboratory Data on First Admission.

WBC	21300 / μ l	ALT	12 IU/ l	PTH	114 pg / l
RBC	710 x 10 ⁴ / μ l	AST	19 IU/ l	P	5.2 mg/dl
Hb	10.7 g / dl	LDH	255 IU/ l	T. Chol	163 mg/dl
Hct	38.2 %	ALP	415 IU/ l	LDL	89 mg/ dl
MCV	66.2 fl	Cr	12.50 mg/dl	TG	115 mg/ dl
MCH	20.4 pg	BUN	86 g / dl	HbA1c	12.6 %
Plt	39.2 x 10 ⁴ / μ l	Na	142 mg/ l	CRP	3.36 mg/ dl
		K	5.3 mg/ l	ESR	7 mm
		Cl	89 mg/ l		
		Ca	8.5 mg/ l		

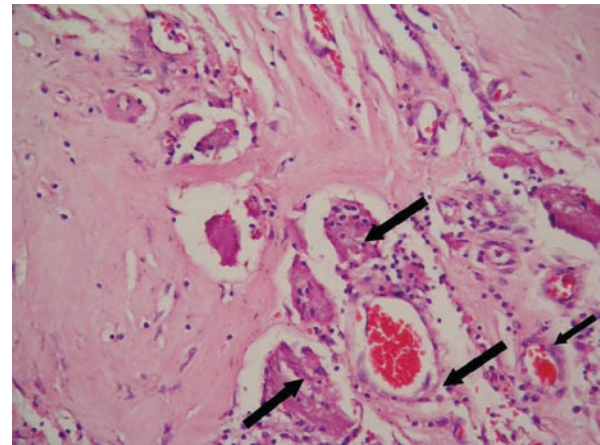
Therefore, surgery was selected for the present patient, because conservative treatment with a vasodilator did not improve his symptoms and continuation of dialysis became difficult due to severe pain. The necrotic second and fifth fingers were amputated. Surgical treatment should be selected with careful consideration of the risk of postoperative aggravation of the systemic condition. Histopathological examination of the fingers revealed advanced arteriosclerosis accompanied by calcification of the tunica intima and tunica media of the digital artery with fibrin deposition. After ten days,the patient was discharged uneventfully. Two months after the surgery, the patient applied again to the emergency service complaining of fever, elevated white blood cell counts and a necrosis of his glans penis.(Figure 2a–2b.) Despite longstanding aggressive medical management by nephrologists, his parathyroid hormone level (PTH) was nearly twice the normal level, 142 pg/mL (reference 12–65 pg/mL), while serum calcium was low at 8.8 mg/ dL (reference 8.9–10.2 mg/dL). Doppler ultrasound of the penis and the iliac vessels revealed a complete lack of flow in the penis. The pain complaint was severe. The patient was consequently taken to the operating room. The penectomy was performed on the 3rd day. The pathological examination revealed hyperplasia of the intimal layer, calcifications in the media with necrotic areas (Figure 3).

Seven days after penectomy, urinary-tract infection with *Pseudomonas aeruginosa* was diagnosed. The patient's overall condition remained poor. At 14 days after penectomy, the clinical and laboratory signs of presepsis were determinated and noted. There were respiratory distress signs. That required immediate intubation and ventilatory support. In subsequent days, sepsis signs came out. He had fever and elevated white blood cell counts. *Pseudomonas aeruginosa* was cultured from the blood in 16.day. The patient died from systemic inflammatory response syndrome (SIRS) at 25. days after penectomy

Figure 2. Penile necrosis.

3. Discussion

The pathogenesis of calciphylaxis disease remains unclear. Hyperparathyroidism, hyperphosphataemia in renal disease patients, vitamin D treatment, calcium salt administration, diabetes mellitus and decreased serum albumin are risk factors for developing calciphylaxis [5-8]. When diabetic nephropathy progresses to end-stage renal failure, the serum phosphate level increases, which causes arteriosclerosis. Furthermore, in patients on dialysis, a high serum phosphate and is possible factor which causes vascular calcification, and a high serum phosphate and calcium level. Calcium begins to deposit in the media of small-sized and medium-sized

Figure 3. Biopsy show the presence of calcifications in the arterioles (arrow). (HE stain, $\times 100$).

vessels [3-5,8]. Subsequently, the affected vessels show endovascular fibrosis, some with thrombosis or calcific occlusion and obliteration. Calcium deposits are generally present in the subcutaneous tissue. The overlying epidermis shows ischemic epidermolysis, often with progressive necrosis.

Calciphylaxis is associated with high levels of morbidity and mortality without specific treatment. The prognosis in Calciphylaxis patients is very poor, with up to 6 months life expectancy after appearance of necrosis [5]. Typically, death occurs due to sepsis, multisystem organ failure, myocardial infarction, pneumonia, or renal failure [8].

The main approach to this condition should be the prevention, through monitoring of calcium levels and appropriate frequency of dialysis sessions. In addition, in these patients it is important to avoid hypotension episodes during dialysis, dialysis hypotension appears to be an important risk factor who promote ischemia of subcutaneous adipose tissue. Concerning the treatment of calciphylaxis, some studies have indicated that parathyroidectomy, low molecular weight heparin, and hyperbaric oxygen are useful for correcting hyperphosphatemia and hypocalcemia, while local treatment includes debridement. Parathyroidectomy is only beneficial in case of very high PTH levels [10]. The parathyroidectomy in calcium phosphate control has been advocated as treatment for calciphylaxis. However, this surgery aggravated the condition, leading to high morbidity and mortality [9]. However, no effective procedure has been established so far.

Our patient carried risk factors like diabetes, ESRD and was found to have an elevated PTH despite medical management. We would like to report the subsequent progress of this patient who was referred by nephrologist when he developed gangrene of his second and fifth

fingers. He was on regular haemodialysis with end-stage renal failure and tertiary hyperparathyroidism. On examination, there were necrosis of the tip of the digits with the phalynx exposed. This required amputation and subsequently healed uneventfully. The underlying cause of fingers necrosis were calcification of the media with intimal hyperplasia and thrombosis of the lumen of digital arteries.

The review of the literature reveals that cases of penile necrosis as a result of calciphylaxis rarely because the penis receives an abundant blood supply from its dorsal and deep arteries and from the urethral artery. The rapid

development of painful, necrotic ulceration of the distal penis is the classic features of penil calciphylaxis. Some investigators advocate the conservative management of penile gangrene. However, surgical intervention may improve their quality of life by preventing or limiting further ischemia and by decreasing pain [8,12].

In conclusion, penile and digital calciphylaxis are a result of medial calcification and fibrosis of blood vessels. The co-morbidity and mortality associated with this disease are extremely high. Surgical intervention may improve their quality of life by limiting further ischemia.

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