



Inflammation and infection

## Penile calciphylaxis, infrequent complication with bad prognosis: a case report

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### ABSTRACT

68-years-old man with end-stage-renal-disease (ESRD) and obesity presented with painful penile lesion: necrotic glans, extended till the penile base with the exposition of corpora cavernosa. Laboratory testing were normal and was afebrile so subsequently discharged with antibiotic therapy and medications. Clinical evaluation was suggestive for penile calciphylaxis, confirmed by seeing arterial calcifications at CT. Patient died one month later. Penile calciphylaxis is a rare life-threatening condition characterized by vascular calcification and fibrosis of medium and small arteries which causes an obstructive vasculopathy and tissue necrosis. Normalization of metabolic parameters, antibiotics, topical enzymatic debridement agents are recommended, considering the poor outcome.

### 1. Introduction

Penile calciphylaxis or calcific uremic arteriolopathy, is a rare and life-threatening syndrome characterized by the occlusion of micro vessels in the subcutaneous adipose tissue and dermis of the penis. The global prevalence rate of calciphylaxis is estimated to be between 1 and 4.1% of patients with ESRD.<sup>1,2</sup> An increase in incidence, may be due to an actual increase or increased awareness of the disorder. It causes intense pain and tissue necrosis, prognosis is poor (<1 year).

### 2. Case presentation

A 68-years-old man presented to ER for the worse of a penile lesion with mild local pain. He was on chronic dialysis for ESRD and suffered of obesity, atrial fibrillation, and hypertension. He was also affected by long-COVID for 21 days. Laboratory tests were negative for infection signs, PCR 77mg/L, WBC 8,2 10<sup>9</sup>/L, calcium 2,37 mmol/L. Glans was necrotic but was not frankly compatible with Fournier's gangrene. The necrosis extended from penile bulb till the meatus with the exposition of corpora cavernosa without any clear distinction between penile shaft and glans that appeared totally necrotic. The smell was pungent, and the surface of glans had an increased consistence (Fig. 1). It was suggestive for penile calciphylaxis. The patient was discharged with antibiotic therapy and indication for daily medications. In the following weeks many cutaneous ulcers appeared, and the necrosis got worse. 18 days later he presented again because of the presence of larvae on cutaneous lesions. At the beginning of the second hospitalization (Ca 2.56 mmol/L, P 2,76 mmol/L) plastic surgeon suggested only daily medications. After

further 10 days a CT was performed showing prostatic abscess (14 × 10mm), another abscess on the dorsal portion of penis (50 × 26 × 13) with bubbles and initial spondylodiscitis extended till iliopsoas-muscle. Moreover, penile arterial calcifications are pathognomonic for penile calciphylaxis (Fig. 2). The antibiotic therapy was adequate based on isolation of bacteria (urine-culture, skin, and central-venous-catheter). Next days succeeded a sudden worsening of hemodynamic situation and exitus exceeded 31 days after the diagnosis.

The pathological evaluation was suggestive for septic shock and multiorgan failure.

### 3. Discussion

Penile calciphylaxis is a rare form of penile gangrene and is often a complication of end-stage renal disease (ESRD).<sup>1,2</sup> The underlying mechanism is thought to be related to vascular calcifications and fibrosis of the intima of medium and small arteries, leading to an obstructive vasculopathy and eventually, tissue necrosis.<sup>1</sup> Calciphylaxis is particularly rare because of the important vascular network of penis.<sup>3-5</sup> Calciphylaxis is not only limited to patients with ESRD, it has been reported also in patients with earlier-stages-renal-disease, acute kidney injury, or prior receipt of kidney transplant. Additionally, cases have been reported in patients without any known kidney problems.<sup>3</sup> Risk factors include obesity, diabetes mellitus, increased phosphate, and calcium serum levels, as well as overuse of calcium and vitamin D supplements, leading to PTH suppression and adynamic bone, which may exacerbate extra-skeletal calcium deposition.<sup>3,5</sup> Probably a triggering event is even necessary, i.e., physical trauma.<sup>5</sup> Our patient had a recent leg trauma,

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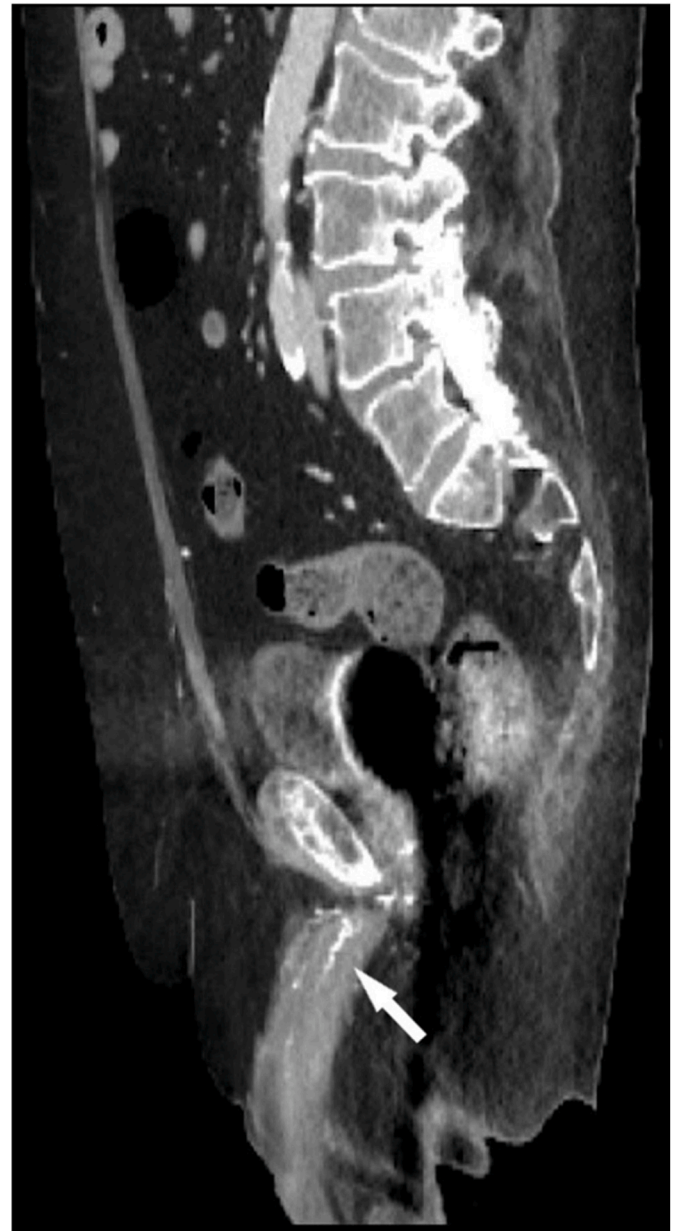
**Fig. 1.** Clinical presentation of the patient's penis. The necrosis causes the exposition of corpora cavernosa. There isn't any distinction between penile shaft and glans. This is suggestive for penile calciphylaxis.

developed an ulcer, and he was COVID+. The underlying process is due to ossification of the arteriolar media layer muscle which is related on the expression of the fibroblast-growth-factor.<sup>3</sup> It causes calcification and fibro intimal hyperplasia in small arteries and arterioles with micro thrombosis.<sup>2</sup> Calcified narrow vessels caused ischemia in long term. The final occlusion can be supported by thrombosis endothelial injury.<sup>1,3</sup> Diagnosis is supported by biopsy or imaging. Penile biopsy has the high risk of inadequate wound healing, infection, and sepsis, but it might be necessary in the atypical presentation. In our case the diagnosis was clinical, and the penile arteries showed calcification areas at CT. Penile calciphylaxis has a bad prognosis and patients suffer from huge penile pain.<sup>3</sup> The overall mortality is probably underestimated at 64%, with a mean time to death of 2,5 months. The poor outcomes and potentially fatal ending must be considered in decision making. Despite other penile gangrene, the benefit of aggressive surgical approach is controversial.<sup>3</sup>

Non-invasive methods such as normalization of metabolic parameters (sodium thiosulfate, parathyroidectomy), antibiotics, analgesia, topical enzymatic debridement agents, agents which improve blood flow are recommended. Partial or complete penectomy may be necessary in more extensive lesions with wet gangrene or intolerable pain.<sup>3</sup> Hyperbaric oxygen camera could help tissue revascularization<sup>3</sup> and should be considered in patients with high risk of sepsis and to improve the QoL (pain and flow) as palliative treatment.

Multidisciplinary setting with plastic surgeons is important. In our case, according to literature, we decided for a conservative approach.

In literature there is not statistic significative difference between surgical approach (radical penectomy or local debridement) and non-invasive treatments. More studies are necessary to establish their efficacy.<sup>2</sup> Hypercalcemia and hyperphosphatemia should be corrected, and the intake of calcium and vitamin-D stopped. Systemic therapy, however, doesn't arrest the necrosis progressions. This area becomes a fertile culture medium for bacteria. Our patient was colonized by *P. Vulgaris* and *S. Epidermidis*.<sup>3</sup> An early therapy with sodium thiosulfate had reported off label success in uremic and non-uremic patients. It is an antioxidant and vasodilator that reduces pain and sometimes also allows



**Fig. 2.** Calcification at CT examination. It shows prostatic and penile abscess, the dorsal penile one has bubble in it. We can also see small penile arteries with calcifications (arrow).

regression of subcutaneous calcification acting as adipocyte calcifications prevention. A complete resolution in patients with ESRD has been achieved with kidney transplantation. The most common cause of death is sepsis.<sup>3</sup>

#### 4. Conclusion

Penile calciphylaxis is a rare expression of systemic syndrome that occurs mostly in ESRD. The diagnosis is clinical, supported by imaging. Our patient was paucisymptomatic, maybe secondary to a neurovascular disease due to his comorbidities such as diabetes mellitus. Prognosis is dramatic: very high mortality rate in few weeks. There are several treatment approaches, but there are not survival differences between them. So, we performed a conservative approach with daily medication and antibiotics therapy. Multidisciplinary setting including urologists, plastic surgeons, radiologists, and nephrologists is mandatory to choose

the proper treatment for each case.

## References

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