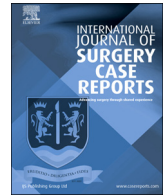


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# Penile gangrene from calciphylaxis is salvageable with intravenous sodium thiosulfate and early total parathyroidectomy

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## ABSTRACT

Penile gangrene is a rare but fatal complication of calciphylaxis in end-stage renal disease (ESRD). To date, there are no guidelines on its management, and outcomes are generally poor with high mortality rate. We present a case of a diabetic patient with ESRD presenting with dry gangrene of the glans penis due to calciphylaxis and successfully treated with intravenous sodium thiosulfate (STS) and early total parathyroidectomy. We further analysed existing literatures on cases that utilized STS in the treatment of penile calciphylaxis.

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## 1. Introduction

Penile gangrene is a rare complication of calciphylaxis in end-stage renal disease (ESRD). It rarely occurs as the penis has a rich vascular network. It has high rates of morbidity and mortality, potentially resulting in sepsis and death [1,2]. We present a case of a diabetic patient with ESRD presenting with dry gangrene of the glans penis due to calciphylaxis and successfully treated with intravenous sodium thiosulfate (STS) and early total parathyroidectomy.

## 2. Case presentation

A 60-year-old Chinese gentleman with a background history of ESRD secondary to diabetes mellitus presented with a penile lesion that gradually enlarged over a few days. He had been on peritoneal dialysis (PD) for three years and was recently diagnosed with tertiary hyperparathyroidism three months ago (adjusted calcium level 2.66 mmol/L, phosphate 1.9 mmol/L, parathyroid hormone level 94.1 pmol/L).

On presentation, there was a 2 cm by 2 cm necrotic patch over the dorsal glans, with a white sloughy circumference (Fig. 1). He had no fever or penile discharge. No other gangrenous lesions were found elsewhere. There were no signs of Fournier's gangrene.

A computed tomography (CT) scan of the pelvis showed extensive calcification of the seminal vesicles and vas deferens, and atherosclerosis of the vessels (Fig. 2). Punch biopsy of the necrotic patch over the glans penis showed acute inflammation and calcification of vessels consistent with calciphylaxis. The patient was started on prophylactic antibiotics and intravenous sodium thiosulfate (STS) 25 g three times a week during dialysis for two months.

The necrotic penile patch was monitored closely and dressed over the next few weeks and there was no extension or worsening of the disease nor any signs of infection. Subsequent laboratory tests at one month of treatment showed that the adjusted serum calcium level fell from 2.30 mmol/L to 2.19 mmol/L. The necrotic patch sloughed off without complication and the penile lesion healed fully by the second month on review (Fig. 1). An early total parathyroidectomy was performed thereafter. On follow-up at one year, the patient remained well with no further recurrence of penile gangrene or calciphylaxis.

## 3. Discussion

Calciphylaxis, or calcaemic uremic arteriolopathy (CUA), describes disseminated calcification involving small vessels and skin necrosis. Painful cutaneous purpuric lesions are predominantly found on the extremities. The pathophysiology of calciphylaxis is raised calcium-phosphate product, most frequently in ESRD patients with tertiary hyperparathyroidism, leading to calcium-phosphate precipitation in tissues. This process can occur in the media of small arteries or arterioles resulting in narrowing of the artery lumen and hence cutaneous ischemia and necrosis [3]. Penile gangrene as a result of calciphylaxis rarely occurs but has

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Fig. 1. Penile gangrene before and after treatment with intravenous sodium thiosulfate.



Fig. 2. Computed tomography scan of the pelvis prior to treatment (arrows point to calcifications of the pudendal and penile vessels).

a high mortality of 64–69 % [1]. Clinical diagnosis may be delayed as the calcium level may be normal or only mildly elevated at the time of presentation and the condition may be mistaken for other mimics such as balanitis. Such a scenario has been reported in a case report by Gaillet et al., with resultant mortality [4].

The use of radiological investigations is suggested when diagnosis is unclear [5]. Useful investigations include computed tomography (CT) scan of the pelvis to visualize penile vessels, doppler ultrasound of the penis to investigate the patency of blood flow, and magnetic resonance imaging (MRI) of the pelvis to investigate the extent of tissue destruction.

While skin biopsy helps to confirm the diagnosis of calciphylaxis, several articles urge to avoid biopsy of penile lesions due to poor healing of the biopsy wound and higher risk of infection [5,6]. For our patient, a simple punch biopsy with minimal tissue sample was performed to confirm the diagnosis so as to guide further treatment. We conclude that skin biopsy should only be considered in patients whose clinical diagnosis is equivocal and if the biopsy would change the management of such patients. We advocate for punch biopsy rather than excision biopsy when necessary, as in the case of our patient.

There are no existing guidelines for the management of such patients despite the lethality of this condition. Treatment include pain management, local debridement, wound care, and penectomy [2]. Majority of cases found in literature had surgical debridement or penectomy done and few were treated conservatively without surgery. Cimmino et al. [5] reported poorer outcomes in patients treated more aggressively with surgery: 71.4 % (5 of 7 cases) treated initially with penectomy progressed to require further resection or death and 33.3 % (2 of 6 cases) treated with debridement progressed

to require further interventions. There was however no mention regarding the severity of gangrene or the presence of infection in each case as patients requiring more aggressive therapy may have inherently more severe disease, Karpman et al. [1] and Yang et al. [2] reported no statistically significant difference in the mortality rate of patients receiving penectomy (50 % and 42.9 %) versus local debridement (68 % and 52 %) in a review of 34 and 50 cases respectively.

In the recent decade, there has been a rise in the use of STS, an antioxidant and calcium-chelating agent, in the treatment of calciphylaxis after it was first successfully used to treat calciphylaxis more than 10 years ago. While there is a lack of clinical trials supporting its efficacy, one clinical trial (non-randomized) [7], one systemic review [8], several cohort studies and case series [9] have demonstrated good clinical outcomes including prompt reduction in pain, improvement in calcium, phosphate and parathyroid hormone homeostasis and better healing of skin lesions. The proposed mechanisms of action of this drug include calcium-chelation, enhanced calcium solubility and inhibition of vascular calcification, antioxidant and vasodilatory properties [10]. All these play a role in recanalization of the calcified vessels. In terms of adverse effect profile, it is relatively safe and well tolerated with the most serious complication being that of biochemical abnormalities, particularly metabolic acidosis and hypernatremia [9]. However, as the vast majority of the target population are ESRD patient on dialysis, this complication can be mitigated by giving STS therapy with dialysis.

Specific to penile calciphylaxis, a literature search revealed only six reported cases that used STS. Four cases were used in combination with surgical interventions including debridement and/or penectomy as the initial form of treatment; three out of the four

patients survived at the time of reporting [11–13] while one out of the four patients was readmitted a week later for urosepsis and demised [14]. The fifth case was a patient with initial good recovery of penile lesion but subsequently readmitted for wet gangrene of the penis four weeks later due to poor wound care [15]. The last case was that of delayed diagnosis and hence delayed use of STS as the patient was treated initially with dermocorticoids as for balanitis, resulting in progression of necrosis and demise two months later [4]. Overall, the first five cases demonstrated good initial recovery of the penile lesion with sodium thiosulfate although two patients had re-presentation with infectious complications.

Our patient had good resolution of penile gangrene and calciphylaxis with early administration of STS and early parathyroidectomy to prevent recurrence. This is in contrast with the poor outcomes reported in majority of patients diagnosed with penile calciphylaxis, likely attributed to delayed diagnosis, lack of control of calciphylaxis and overly aggressive surgical debridement of the penile gangrene resulting in wound complications. This case study raises confidence in the use of STS to treat penile calciphylaxis. Its mechanism of action could be related to its overall ability to improve patency of calcified blood vessels via calcium-chelation and calcium-solubilization, inhibition of vascular calcification and vasodilation. However, further high-quality research is needed to support the efficacy of STS.

#### 4. Conclusion

Our patient was fortunate to survive and not require any surgery to the penile lesion – we attribute this to early STS administration and early parathyroidectomy to treat the calciphylaxis as well as the penile gangrene. Knowledge about this condition is insufficient now and delayed diagnosis may result in detrimental effects. With advancements in therapies, awareness of complications of calciphylaxis and the promising role of STS combined with parathyroidectomy, the prognosis of penile calciphylaxis will likely be improved with early intervention.

#### Declaration of Competing Interest

The authors report no declarations of interest.

#### Funding

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#### Ethical approval

This case report is exempted from ethical approval in our institution.

#### Consent

Anonymity has been kept and no patient identifier or information that may compromise patient confidentiality was released in

this paper. Photographs were taken with informed consent from the patient.

#### Author contribution

Geraldine Lei Yanlei, Cheryl Hern Qi Chong: Drafting of case report.

Tay Kon Voi: Critical revision of case report.

Thomas Ho: Critical revision of case report.

#### Registration of research studies

Not applicable.

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#### References

- [1] E. Karpman, S. Das, E.A. Kurzrock, Penile calciphylaxis: analysis of risk factors and mortality, *J. Urol.* 169 (6) (2003) 2206–2209.
- [2] T.-Y. Yang, T.-Y. Wang, M. Chen, F.-J. Sun, A.W. Chiu, Y.-H. Chen, Penile calciphylaxis in a patient with end-stage renal disease: a case report and review of the literature, *Open Med. (Wars)* 13 (2018) 158–163.
- [3] F. Llach, The evolving clinical features of calciphylaxis, *Kidney Int. J.* 63 (2003), S122–S4.
- [4] A. Gaillet, Y. Luque, Penile calciphylaxis, *Urology* 140 (2020) e8–e9.
- [5] C.B. Cimmino, R.A. Costabile, Biopsy is contraindicated in the management of penile calciphylaxis, *J. Sex. Med.* 11 (10) (2014) 2611–2617.
- [6] S.U. Nigwekar, R. Thadhani, V.M. Brandenburg, Calciphylaxis, *N. Engl. J. Med.* 378 (18) (2018) 1704–1714.
- [7] S.U. Nigwekar, S.M. Brunelli, D. Meade, W. Wang, J. Hymes, E. Lacson Jr., Sodium thiosulfate therapy for calcific uremic arteriopathy, *Clin. J. Am. Soc. Nephrol.* 8 (7) (2013) 1162–1170.
- [8] T. Peng, L. Zhuo, Y. Wang, M. Jun, G. Li, L. Wang, et al., Systematic review of sodium thiosulfate in treating calciphylaxis in chronic kidney disease patients, *Nephrology (Carlton)* 23 (7) (2018) 669–675.
- [9] P. Bourgeois, P. De Haes, Sodium thiosulfate as a treatment for calciphylaxis: a case series, *J. Dermatolog. Treat.* 27 (6) (2016) 520–524.
- [10] W.C. O'Neill, K.I. Hardcastle, The chemistry of thiosulfate and vascular calcification, *Nephrol. Dial. Transplant.* 27 (2) (2012) 521–526.
- [11] A. Ahmad, A. Albaghli, A. Michael, K. Refaat, M. Omar, A. Ibrahim, et al., A rare case of multiorgan calciphylaxis in a patient with stage 5 chronic kidney disease, *Case Rep. Urol.* 2018 (2018), 9603680.
- [12] G. Sandhu, M.B. Gini, A. Ranade, D. Djebali, S. Smith, Penile calciphylaxis: a life-threatening condition successfully treated with sodium thiosulfate, *Am. J. Ther.* 19 (1) (2012) e66–8.
- [13] M. Morrison, M. Merati, J. Ramirez, H.C. Cha, A. LaFond, Penile calciphylaxis diagnosed with computed tomography, *J. Eur. Acad. Dermatol. Venereol.* 30 (2) (2016) 352–353.
- [14] E. Sarkis, Penile and generalised calciphylaxis in peritoneal dialysis, *BMJ Case Rep.* 2015 (2015), bcr2014209153.
- [15] J.M. Zillioux, A. Geisenhoff, M. Gray, Management of penile calciphylaxis: a case study, *J. Wound Ostomy Continence Nurs.* 45 (6) (2018) 536–539.

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