Difficulty with clinical differentiation between two markedly similar urological presentations: balanitis xerotica obliterans vs. penile calciphylaxis

Romelio Carangan DO, PGY2

Kettering Health Dayton Internal Medicine Residency Program

Abstract

A nonsmoking 67-year-old Hispanic male PMH significant for end-stage renal disease on peritoneal dialysis (PD) secondary to hypertension and coronary artery disease presented to the emergency room originally for shortness of breath found to have white hypo-pigmented lesions on glans penis for the past six weeks. Urology diagnosed the patient with balanitis xerotica (BXO) and was started on topical triamcinolone. Penile culture grew *Candida albicans* and *Candida glabrata*. Despite adequate treatment, the patient's condition was devolving. Infectious Disease trialed anti-fungal medications and topical steroids without improvement. Urology ultimately diagnosed the patient with penile calciphylaxis (PC) and patient underwent a dorsal slit procedure with significant improvement.

Introduction

Balanitis xerotica obliterans (BXO) is defined as a chronic atrophic dermatitis of the penile foreskin and glans penis. The etiology of this condition remains unknown and seems to be more common in patients that are uncircumcised and/or have comorbid diabetes mellitus. It does seem most cases are infectious in nature, with candida species accounting for about 40% of cases.

Calciphylaxis (calcific uremic arteriolopathy) is a very serious disorder in which there is initial vascular obstruction leading to ischemia of the skin and necrosis. It involves dysregulation in calcium, phosphate, and PTH levels. This is much more common in individuals with end-stage renal failure (ESRD) who are on hemodialysis (HD). Proposed diagnostic criteria for calciphylaxis includes all 3 of the following clinical criteria or 2 of the clinical criteria plus positive histology on biopsy: ESRD on hemodialysis or the glomerular filtration rate <15 mL/min/1.73 m^2, presence of 2 or more treatment-resistant painful ulcers associated with purpura, and treatment-resistant painful ulcers located on trunk, limbs, or penis with associated purpura.

Obesity, being uncircumcised, and other edematous conditions such as nephrotic syndrome tend to lead to increased risk of BXO (2) while dialysis-dependent ESRD is more associated with a higher risk of penile calciphylaxis (11). In a retrospective study performed by Fekete et al (1), they found that patients with diabetes, obesity, uncircumcision, and Hispanic populations had a much higher risk of developing BXO.

Two large cross-sectional studies cited that the prevalence of BXO is between 0.0014% and 0.07% (5). As for penile calciphylaxis, the prevalence of this disease is about 6%, but carries up to an 80% mortality rate (11).

Case

67-year-old Hispanic male DNR-CC PMH significant for monoclonal gammopathy of undetermined significance (MGUS), ESRD on PD, secondary hyperparathyroidism, and insulin-dependent type 2 diabetes mellitus, presented to KHED on 8/13/2024 for weakness & hypotension after missing 2 days of dialysis found to volume overloaded. Admitted to ICU and the following specialties consulted the same day.

Nephrology: Started patient on PD with UF goal 2 L discussing possible need to convert to HD.

Urology: Diagnosed patient with BXO based on clinical presentation **(Figure A)** and comorbidities. Started patient on topical triamcinolone & fluconazole after penile drainage cultures grew *Candida albicans* & *Candida galbrata*

8/17/2024 - Patient started becoming more uncomfortable and pain progressed with recurrent intermittent bouts of bradycardia and hypotension. Concern for patient not improving on PD due to developing ileus treated with nasogastric tube, but patient refusing some treatments and goals of care were not clear. The following specialties were consulted:

Palliative Care: Changed CODE STATUS from DNR-CC to DNR-CCA (Yes to intubation, dialysis, surgery)

Vascular Surgery: Recommended HD catheter placement given lack of clinical improvement on PD, which was eventually placed via femoral access.

8/23/2024 - PD resumed after 2 rounds of HD and ileus resolving.

9/03/2024 - **Infectious Disease consulted** as there was lack of improvement of BXO despite topical steroids and antifungals **(Figure B**). Diagnosed patient with severe adherent *Candida balanitis* with acquired phimosis. Trialed IV micafungin & miconazole cream. Blood cultures still showed no growth to date.

9/11/2024 - **Urology reconsulted** given continual progression of penile lesions despite maximal therapy for BXO. Patient's wife revealed penile lesions were present for over 6 weeks. **A new diagnosis of penile calciphylaxis** was made. Patient received sodium thiosulfate (STS) therapy and eventually underwent dorsal slit procedure with marked improvement in his lesions.

Interestingly though, when biopsy was performed, it showed marked inflammation and foci of necrosis **but was negative for calcification of vessels (a requirement for diagnosis).**

Images

Figure A – Initial diagnosis of BXO started on topical triamcinolone and fluconazole. Eventually, started on micafungin as lesions were progressing.

Figure B – Lesions progressed to grayish white plaques completely covering glans penis despite above therapy. Thus, another urological consult put in and patient diagnosed with penile calciphylaxis.

Conclusion

Based solely on clinical history, our patient was statistically more likely to have presented with BXO, yet his condition improved with the treatment for PC. Although penile calciphylaxis was the second diagnosis after failed improvement on antifungal agents for BXO, biopsy was negative for vascular calcifications, and it remained unclear what the diagnosis was.

This case sheds light on the similarities between two very rare painful conditions with regards to their risk factors, clinical presentation, physical exam, and histopathological findings. Given the very high mortality rate associated with these two conditions, further studies are warranted to develop diagnostic criteria that can better elucidate the two conditions.

References

1) Adler K, Flores V, Kabarriti A. Penile calciphylaxis: A severe case managed with partial penectomy. Urol Case Rep. 2020 Oct 16;34:101456. doi: 10.1016/j.eucr.2020.101456. PMID: 33102133; PMCID: PMC7578200.
2) Barrisford, G. W. (2024). Balanitis in Adults. UpToDate. Retrieved September 24, 2024 from https://www.uptodate.com/contents/balanitis-in-adults?search=balantis%20adult&source=search_result&selectedTitle=1%7E36&usage_type=default&display_rank=1#H2904629949
3) De Luca DA, Papara C, Vorobyev A, Staiger H, Bieber K, Thaçi D, Ludwig RJ. Lichen sclerosus: The 2023 update. Front Med (Lausanne). 2023 Feb 16;10:1106318. doi: 10.3389/fmed.2023.1106318. PMID: 36873861; PMCID: PMC9978401.
4) Fekete GL, Schwarzkopf-Kolb D, Brihan I, Boda D, Fekete L. Balanitis xerotica obliterans: An observational, descriptive and retrospective clinical study. Exp Ther Med. 2022 May;23(5):361. doi: 10.3892/etm.2022.11288. Epub 2022 Mar 31. PMID: 35493424; PMCID: PMC9019671.
5) Fergus KB, Lee AW, Baradaran N, Cohen AJ, Stohr BA, Erickson BA, Mmonu NA, Breyer BN. Pathophysiology, Clinical Manifestations, and Treatment of Lichen Sclerosus: A Systematic Review. Urology. 2020 Jan;135:11-19. doi: 10.1016/j.urology.2019.09.034. Epub 2019 Oct 9. PMID: 31605681.
6) Kasai T, Washida N, Muraoka H, Fujii K, Uchiyama K, Shinozuka K, Morimoto K, Tokuyama H, Wakino S, Itoh H. Penile calciphylaxis in a patient on combined peritoneal dialysis and hemodialysis. CEN Case Rep. 2018 Nov;7(2):204-207. doi: 10.1007/s13730-018-0327-0. Epub 2018 Mar 28. PMID: 29594982; PMCID: PMC6181884.
7) Kyriakis KP, Emmanuelides S, Terzoudi S, Palamaras I, Damoulaki E, Evangelou G. Gender and age prevalence distributions of morphea en plaque and anogenital lichen sclerosus. J Eur Acad Dermatol Venereol. 2007;21:825–826. doi: 10.1111/j.1468-3083.2006.01954.x.
8) Lipinski M, Sahu N. Hyperbaric Oxygen Therapy Improving Penile Calciphylaxis. Cureus. 2020 Jul 14;12(7):e9190. doi: 10.7759/cureus.9190. PMID: 32818121; PMCID: PMC7426662.
9) Misakyan N, Abu-Shanab A, Shah S. Penile Calciphylaxis: A Successfully Treated Case. Cureus. 2024 Feb 24;16(2):e54824. doi: 10.7759/cureus.54824. PMID: 38529436; PMCID: PMC10962866.
10) Neill SM, Tatnall FM, Cox NH. Guidelines for the management of lichen sclerosus. Br J Dermatol. 2002;147:640–649. doi: 10.1046/j.1365-2133.2002.05012.x. British Association of Dermatologists.
11) Nigwekar, S. U., Thadhani, R. I. (2024). Calciphylaxis (calcific uremic arteriolopathy). UpToDate. Retrieved September 24, 2024 from https://www.uptodate.com/contents/calciphylaxis-calcific-uremic-arteriolopathy?search=penile%20calciphylaxis&source=search_result&selectedTitle=1%7E150&usage_type=default&display_rank=1#H2270362372
12) Sandhu G, Gini MB, Ranade A, Djebali D, Smith S. Penile calciphylaxis: a life-threatening condition successfully treated with sodium thiosulfate. Am J Ther. 2012 Jan;19(1):e66-8. doi: 10.1097/MJT.0b013e3181e3b0f2. PMID: 20634681.
13) Wipattanakitcharoen A, Takkavatakarn K, Susantitaphong P. Risk factors, treatment modalities, and clinical outcomes of penile calciphylaxis: systematic review. World J Urol. 2023 Nov;41(11):2959-2966. doi: 10.1007/s00345-023-04611-9. Epub 2023 Oct 2. PMID: 37782324.