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Bilateral Breast Necrosis: A Rare Presentation of Calciphylaxis

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Background	An 81-year-old woman with multiple comorbidities presented with bilateral central breast necrosis.
Summary	Our patient is an 81-year-old woman with multiple comorbidities who presented to the clinic after an alleged left breast spider bite resulting in superficial necrosis. She was managed with outpatient local wound care. She then developed analogous right breast necrosis. Punch biopsy of the breast necrosis was suggestive of calciphylaxis. Breast imaging was unremarkable. She was empirically started on sodium thiosulfate and underwent debridement of the necrosis. Culture from breast wound fluid yielded pseudomonas. Pathologic evaluation of the breast eschar revealed changes likely secondary to calciphylaxis. She continued on antibiotics and cinacalcet. Due to her worsening overall status, she transitioned to home hospice and expired.
Conclusion	Calciphylaxis is a rare cause of breast necrosis. Our case highlights the importance of this entity in the differential diagnosis to encourage prompt recognition and treatment.
Key Words	breast necrosis; calciphylaxis; breast pain

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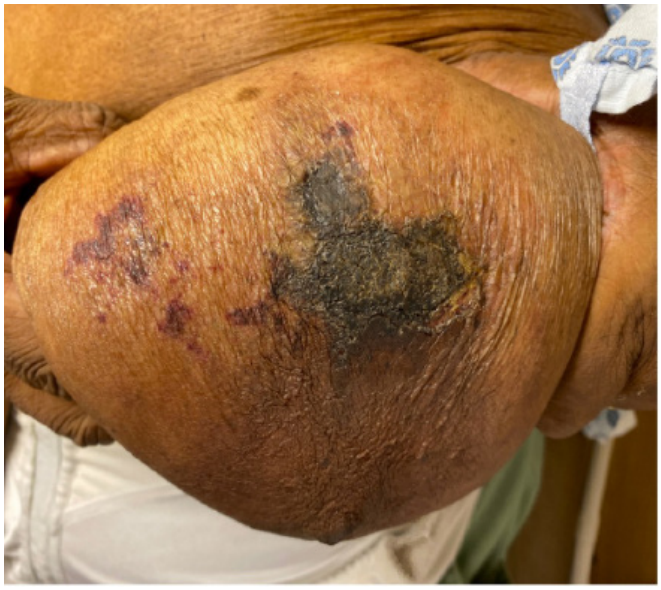
Case Description

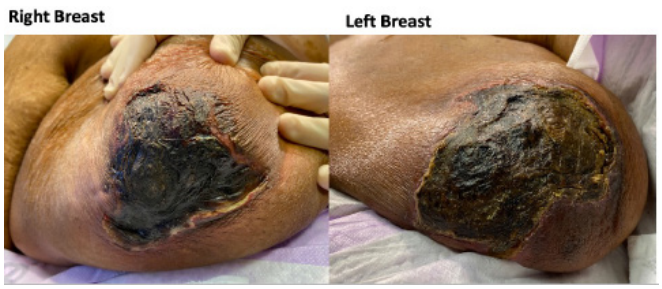
An 81-year-old woman with multiple comorbidities, including stage IV CKD, hypertension, morbid obesity, diabetes, hypoalbuminemia, secondary hyperparathyroidism, meningioma (causing vasogenic edema, midline shift), and atrial fibrillation (on warfarin), presented to the clinic after a self-reported left breast spider bite resulting in superficial necrosis (Figure 1).

Figure 1. Left Breast Necrosis at Presentation in Breast Clinic. Published with Permission



The patient had no history of prior breast problems. She was initially managed with outpatient local wound care over the course of four months. She then developed analogous right breast necrosis (Figure 2), worsening pain (breast and lower extremities), and altered mental status, requiring admission.

Figure 2. Bilateral Breast Necrosis, 4 Months After Initial Presentation. Published with Permission



Dermatology was consulted and was concerned about a diagnosis of calciphylaxis. Her home warfarin was discontinued. Additional 2–3 cm crusted plaques coalesced with minimal surrounding erythema identified on the left calf. Punch biopsy of the breast necrosis was nondiagnostic, but some peri-vasculature calcium was noted, potentially suggestive of calciphylaxis. Mammogram was not tolerated by the patient, and the whole breast ultrasound was unremarkable. A nuclear medicine bone scan was also potentially suggestive but not definitive for breast calciphylaxis. Laboratory studies were consistent with hypercalcemia (peak serum calcium 11.3) and hyperparathyroidism (PTH 165). Her phosphorus was within normal limits (3.6) on admission but notably elevated in the two weeks before admission (7.1). She was empirically started on sodium thiosulfate, resulting in acidosis and no improvement in calcium levels, thus was discontinued after two doses. Due to a rising white blood cell count, broad-spectrum antibiotics were started, and debridement was attempted. Culture from her right breast wound fluid yielded pseudomonas; antibiotics were tailored based on susceptibility. Pathologic evaluation of the left breast eschar revealed gangrenous necrosis and focal elastotic calcific deposits, potentially representing changes secondary to calciphylaxis. She was treated with cinacalcet 30 mg, which was up-titrated to 60 mg. In addition, calcitonin was given once during admission, with a subsequent reduction in her ionized calcium. Her calcium on discharge was 9.4. Due to her worsening overall status and other ongoing chronic medical conditions, she transitioned to home hospice and expired.

Discussion

Calciphylaxis is an infrequent complication found in 1% to 5% of patients with ESRD. It has also been described in patients with active malignancy, alcohol liver disease, and connective tissue diseases.[1,2] Breast-specific calciphylaxis is an even rarer entity, with only a few case reports in the literature.[2-4] The proposed pathogenesis is excess calcium and phosphate deposits in the subcutaneous fat and dermis arterioles resulting in luminal narrowing and progressive fibrosis and thrombosis, which causes local ischemia, infarct, and necrosis.[1,5] Unfortunately, there is a high one-year mortality rate, up to 80%. Several risk factors have been defined, including female gender, Caucasian race, obesity, hypertension, diabetes, dialysis duration of greater than six years, chronic inflammation, hyperparathyroidism, hypoalbuminemia, hypercoagulable state, vitamin D

administration, corticosteroids, vitamin K antagonist, and advanced age.[3,4,6] Vitamin K deficiency (as seen with Vitamin K antagonists like warfarin) de-activates a calcification inhibitor secreted by vascular smooth muscle cells.[5] Our patient had several of these risk factors. The differential diagnosis includes warfarin-induced skin necrosis, vasculitis, antiphospholipid syndrome, cholesterol embolization, and cellulitis.[7]

The diagnosis is mainly clinical; however, adjunct tests can facilitate or confirm the diagnosis, including skin biopsy, ultrasound, mammography, X rays, or a three-phase technetium ^{99m}Tc-methylene diphosphonate bone scan. If a biopsy is performed, the characteristic histologic features include vessel wall calcifications, subintimal fibroplasia, and intraluminal thrombosis found in dermal and subcutaneous fat blood vessels. Sometimes, calcifications can also be found outside the vessels within the tissue.[5]

There are no randomized trials or standard treatment guidelines for breast calciphylaxis. The treatment is centered around symptom control and improving the underlying conditions. Wound management is critical to symptom control. High-quality wound care is essential to avoid delayed complications and the potential for more radical surgery. Surgical debridement is contraindicated in a stable noninfected wound covered with dry eschar. However, debridement may be necessary if the wound becomes significantly infected or an abscess is present.[3] A mastectomy may even be warranted depending on the depth and size of the infection. Hyperbaric oxygen has been described to facilitate healing in areas of limited skin necrosis.[4] This is a painful condition, so multimodal pain management is recommended. Antibiotics may be warranted in situations of infection or sepsis. Optimizing underlying conditions such as improving nutrition, normalizing calcium and phosphate levels, intensifying dialysis frequency, and stopping vitamin K antagonists, steroids, and vitamin D use helps halt vessel wall calcification progression.[2] For patients with hyperparathyroidism, phosphate binders or parathyroidectomy may be considered.[3] Lastly, there are some opportunities to reverse vessel wall calcification. Sodium thiosulfate is an antioxidant used in acute calciphylaxis.[8] It causes vasodilatation and increases the solubility of the calcium-phosphate deposits. It has an efficacy rate of 67 to 84% with many side effects. Metabolic acidosis, like this patient had as a result of the drug, occurs in approximately 7.8% of patients.[9] It is mainly used in IV forms but can also be injected directly at lesion borders.[9] Vitamin K administration is an investigational approach also to help reverse vessel wall calcification.[5]

Our case underscores the importance of early recognition and treatment of this disease entity. The patient's initial unilateral presentation and report of a spider bite at the pathologic site seemed plausible. However, the continued expansion of the necrosis over time with worsening whole breast pain eventually prompted further investigation, including breast imaging and punch biopsy, to rule out underlying malignancy or other diagnoses. Once she developed bilateral necrosis and showed other signs of decline, a multidisciplinary approach was undertaken, which led to her subsequent diagnosis and treatment for breast calciphylaxis. Unfortunately, her overall declining health, including a meningioma causing vasogenic edema, midline shift, and mental status changes, ultimately led to the family's decision to transition to hospice and eventually the patient's death.

Conclusion

Calciphylaxis is a rare cause of breast necrosis. We present an interesting case with a prolonged course and rapid decline once the disease significantly progressed and other comorbidities became life-limiting.

Lessons Learned

Breast necrosis is a rare entity, and calciphylaxis should be on the differential diagnosis, especially in a patient with multiple comorbidities and renal dysfunction. This may facilitate earlier recognition and optimization of underlying conditions and prompt treatment.

References

1. Halasz CL, Munger DP, Frimmer H, Dicorato M, Wainwright S. Calciphylaxis: Comparison of radiologic imaging and histopathology. *J Am Acad Dermatol*. 2017;77(2):241-246.e3. doi:10.1016/j.jaad.2017.01.040
2. Novotny AG, Simpson AB, Kral MA, et al. Calciphylaxis of the Postmenopausal Female Breast: An Uncommonly Encountered Mimic of Carcinoma. *Case Rep Pathol*. 2017;2017:4541620. doi:10.1155/2017/4541620
3. Hall DJ, Gentile LF, Duckworth LV, Shaw CM, Singhal D, Spiguel LR. Calciphylaxis of the Breast: A Case Report and Literature Review. *Breast J*. 2016;22(5):568-572. doi:10.1111/tbj.12632
4. Verstappen EMJ, Maaskant-Braat AJG, Scheltinga MR. Bilateral breast calciphylaxis in a patient who survived earlier extensive tissue necrosis 5 years previously: A case report. *Int J Surg Case Rep*. 2018;48:22-25. doi:10.1016/j.ijscr.2018.04.035

5. Chang JJ. Calciphylaxis: Diagnosis, Pathogenesis, and Treatment. *Adv Skin Wound Care*. 2019;32(5):205-215. doi:10.1097/01.ASW.0000554443.14002.13
6. McCarthy JT, El-Azhary RA, Patzelt MT, et al. Survival, Risk Factors, and Effect of Treatment in 101 Patients With Calciphylaxis. *Mayo Clin Proc*. 2016;91(10):1384-1394. doi:10.1016/j.mayocp.2016.06.025
7. Westphal SG, Plumb T. Calciphylaxis. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; August 8, 2022.
8. Shen G, Huang R, Liu B, Kuang A. Sodium Thiosulfate in the Treatment of Lung and Breast Calciphylaxis: CT and Bone Scintigraphy Findings. *Clin Nucl Med*. 2017;42(11):893-895. doi:10.1097/RLU.0000000000001837
9. Peng T, Zhuo L, Wang Y, et al. Systematic review of sodium thiosulfate in treating calciphylaxis in chronic kidney disease patients. *Nephrology (Carlton)*. 2018;23(7):669-675. doi:10.1111/nep.13081