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Case Report

Calciphylaxis of the breast, mimicking advanced breast cancer with skin involvement☆

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ABSTRACT

Calciphylaxis, also known as calcific uremic arteriolopathy, is a condition most commonly seen in patients with End-stage Renal Disease. The pathophysiology of the condition is related to an elevated calcium-phosphate product. It associated with extensive calcification, especially of the media of arterioles. It most commonly presents with skin manifestations, especially in the abdomen. However, when it occurs in the breast, it can mimic an advanced breast malignancy. We report a case of a 34-year-old female who presented with an extensive lesion to the breast, initially thought to be a long-neglected breast carcinoma. However, it was ultimately diagnosed as calciphylaxis of the breast, and radiologic imaging (particularly ultrasound and mammography) were crucial in making the diagnosis. We make the case of the importance of radiologic imaging in diagnosing this condition.

Introduction

Calciphylaxis is a rare condition associated with extensive calcification, especially of the media of arterioles. It is most commonly seen in patients with End-stage Renal Disease. Skin findings include livedo reticularis and a cord-like thickening, while late stages can show necrotic lesions that often cause significant pain.

Calciphylaxis of the breast is a rare manifestation. It can present with pain or a palpable mass. The overlying skin changes can often be mistaken for a malignant breast lesion. Radiologic imaging, including ultrasound and mammography, are important in making this distinction. Here, we present a case report of calciphylaxis manifesting as a breast lesion mimicking advanced breast cancer.

Case report

Our patient was a 34-year-old female with a past medical history significant for mitral valve stenosis status post mitral valve replacement and receiving anticoagulation with

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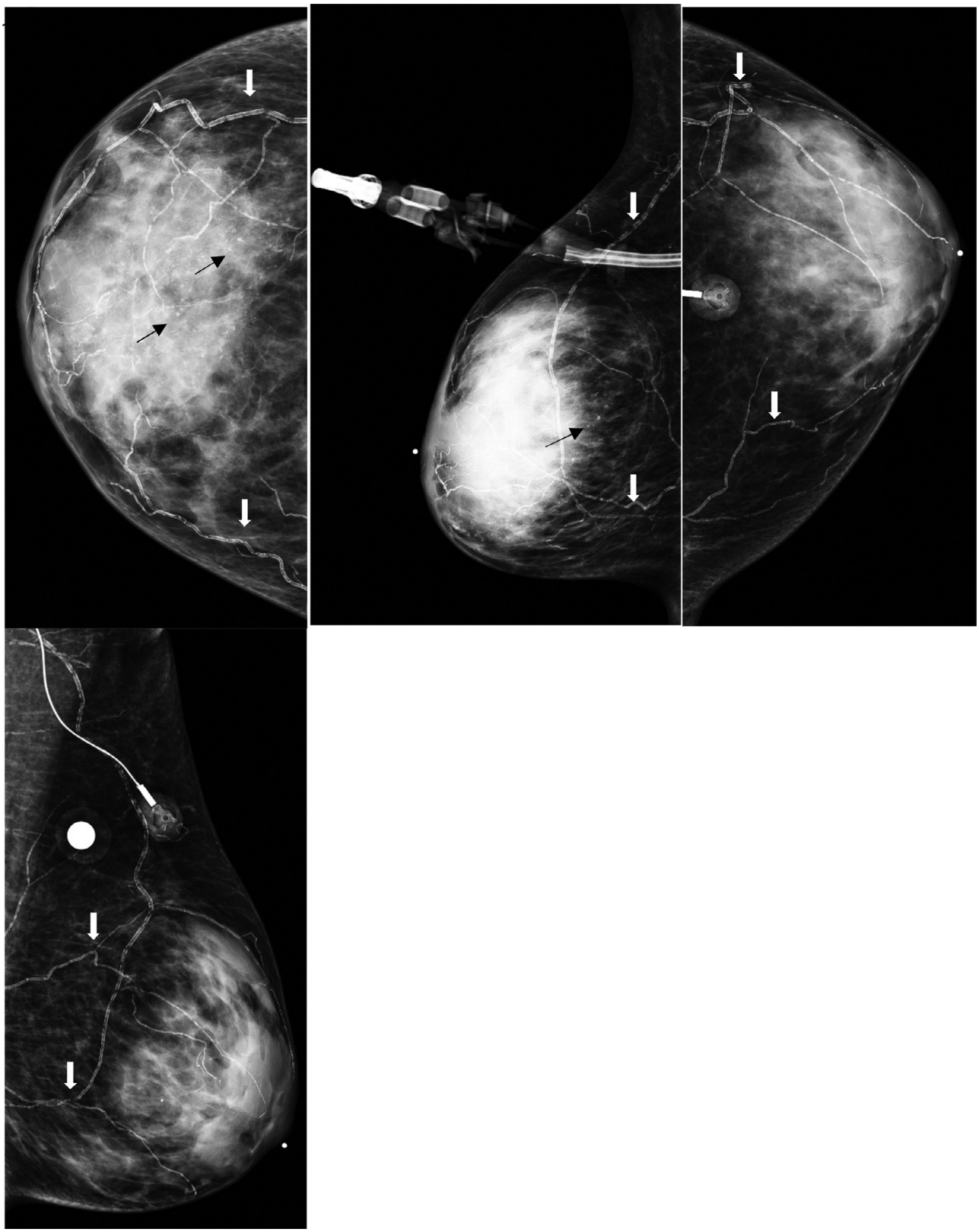

Fig. 1 – A-D. Diagnostic bilateral mammogram. Right craniocaudal (A) and mediolateral oblique (B) views demonstrate extensive vascular calcifications (block arrows). Additional less distinct calcifications throughout the right breast (line arrows), asymmetric when compared with the left (C-D). A right-sided dialysis catheter (B) and left-sided cardiac monitoring leads (C-D) project over the breasts.

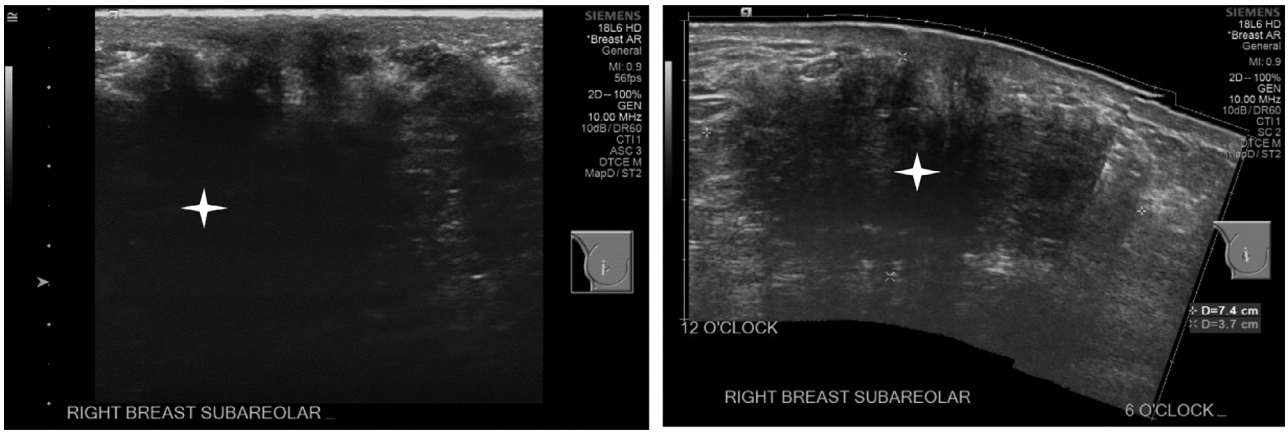

Fig. 2 – A-B. Right breast ultrasound. Ill-defined hypoechoic mass with indistinct margins is identified in the subareolar region, extending to the nipple, measuring 7.4 x 3.7 x 7.3 cm (star).

warfarin who presented to the Emergency Department from the anticoagulation clinic with a supratherapeutic International Normalized Ratio of 7. She had a history of Type 1 Diabetes Mellitus and ESRD and received hemodialysis. In the Emergency Department, she was also found to be in diabetic ketoacidosis with an acute kidney injury and complained of right breast pain. The patient said she was seen at an outside hospital 10 days prior, for which she was given antibiotics for her breast pain. On physical exam, a tender, firm, immobile mass at the 8 o'clock position of the right breast with overlying skin ulceration, erythema, scabbing, blistering, and peeling was noted. There was no associated axillary lymphadenopathy. Labs at the time of admission were notable for calcium 8.8 (8.6-10.6), phosphorus 6.8 (2.5-4.5), blood urea nitrogen 105 (6-20), and creatinine 6.89 (patient's baseline was approximately 6.30). Surgical Oncology was consulted, who recommended a diagnostic mammogram and a breast ultrasound for evaluation of a possible breast abscess versus Paget's disease of the breast.

A bilateral diagnostic mammogram was performed but was limited, due to the patient's limited physical ability to be positioned optimally. Extensive vascular calcifications were identified bilaterally (Figs. 1A and D). Additional indeterminate somewhat amorphous calcifications were seen throughout the right breast; however, the patient was unable to tolerate magnification views for further characterization, due to pain. The right breast demonstrated asymmetric, slightly increased density diffusely when compared with the contralateral breast. No discrete mass was identified in the right breast mammographically, likely due to the extreme right breast density. A complete right breast ultrasound showed a suspicious irregular, hypoechoic mass with indistinct margins in the subareolar region and extending to the nipple, measuring 7.4 × 3.7 × 7.3 cm (Figs. 2A and B). Within the right axilla, a lymph node with mild cortical thickening was noted (Fig. 3) but was unchanged when compared with a previous ultrasound. On direct clinical inspection, the breast demonstrated diffuse hardening and extensive overlying skin ulceration. The nipple was significantly eroded. The breast had the appearance of an advanced, neglected malignancy with skin involvement. The patient underwent an ultrasound-guided core-needle biopsy of the right breast mass (Fig. 4). The biopsy was negative for malignancy, instead showing focal intramural vascular calcification associated with fibrinoid change, fibrin thrombi, stromal fibrosis with extensive hyalinization, fat necrosis, and focal stromal dystrophic appearing calcifications, raising the possibility of calciphylaxis. As warfarin is contraindicated in calciphylaxis, it was discontinued and enoxaparin 60mg daily was started, per recommendations from Cardiology.

Unfortunately, the patient passed away four months later. She developed multiple subdural hematomas and experienced cardiac arrest following intubation in the operating room for planned percutaneous endoscopic gastrostomy tube placement.

Discussion

Calciphylaxis, also known as calcific uremic arteriolopathy, is a rare phenomenon described first by Selye. It is characterized by microcalcification and occlusion of small vessels within the dermis and subcutaneous tissues with subsequent skin and soft tissue necrosis. Skin manifestations can show a livedo reticularis pattern that can progresses to plaques, nodules, and necrotic ulcerations. It is most often seen in patients with ESRD with subsequent secondary hyperparathyroidism, especially those undergoing dialysis [1]. It has been reported that up to 4% of patients undergoing dialysis have calciphylaxis. Rarely, it has been seen in primary hyperparathyroidism or humoral hypercalcemia of malignancy [2]. Rare cases of calciphylaxis without any evidence of renal or parathyroid disease has also been reported [2]. In addition, warfarin is thought to be a risk factor. While the exact pathogenesis is unknown, it could be related to a Matrix GLA protein (MGP), an extracellular matrix protein that inhibits calcification of arteries [3]. Matrix GLA protein (MGP) activity is activated by vitamin K dependent carboxylation, and this may be the mechanism by which vitamin K inhibitors increase the risk of calciphylaxis. Calciphylaxis carries a poor prognosis, with mortality rates estimated as high as 60% [4], often due to infection of the ulcers.

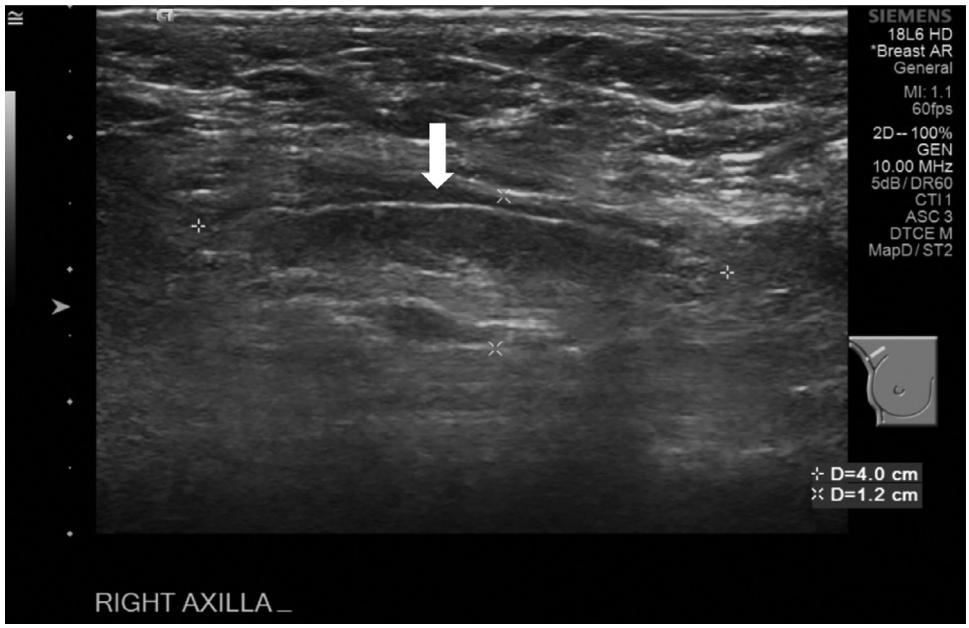

Fig. 3 – Lymph node with mild cortical thickening (arrow).

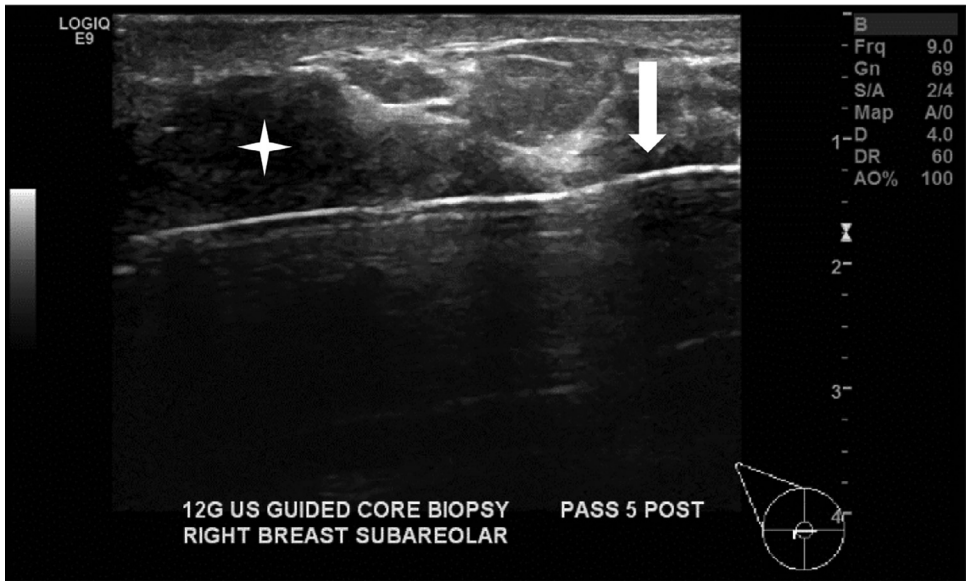

Fig. 4 – Ultrasound-guided core needle biopsy. A core biopsy needle (arrow) is seen traversing the suspicious right breast mass (star).

The exact pathogenesis of calciphylaxis is unclear. The most commonly accepted mechanism posits that calciphylaxis is a hypersensitivity reaction that progresses through three phases [2]: sensitization, the so-called "critical period," and cutaneous calcinosis. Sensitization typically occurs with elevated parathyroid hormone levels, particularly in the setting of ESRD. The "critical period" is a latent period during which a certain "challenging agent" ultimately produces vascular calcification. Regardless of the ultimate cause, calciphylaxis is almost always seen in the presence of elevated calcium-phosphate product.

Calcium deposition in calciphylaxis commonly occurs in the skin, most commonly on the thigh and abdomen. A cord-like thickening of vessels can be seen [5]. In the breast, it can mimic inflammatory breast cancer with peau d'orange skin changes. Patients can present with complaints of lumpiness, a palpable mass, and intense breast pain [6]. A thorough workup, consisting of diagnostic mammography and breast sonography should be pursued. Mammography can be normal initially, but later in the disease course can show extensive arterial calcifications [6] and scatted microcalcifications [7]. Parenchymal distortion and spiculation can be seen, though

not as commonly. Smaller arteries can become visible. Breast ultrasound can demonstrate a pattern reminiscent of fat necrosis, with hypoechoic focal lesions and posterior acoustic shadowing throughout the breast [1], with hyperechoic changes in the surrounding fat [6]. Differential diagnoses based on imaging include fat necrosis, phlegmon and/or abscess, warfarin induced skin necrosis, vasculitides, and malignancy [8]. In general, tissue biopsy is typically pursued as a next step, as some of these findings can overlap with those of invasive breast malignancies. On histology, calciphylaxis shows thrombi, mural calcification, fibroblastic intima proliferation of the arterioles, and obliteration of the intima. Some authors argue that mammography and sonography are sensitive modalities to diagnose calciphylaxis [9], without the need for biopsy. This is especially important to consider because wound healing in ESRD is impaired, and histology can be inconclusive due to patchy calcification patterns. Biopsy can result in non-healing infections and sepsis [1]; it is therefore important to assess whether biopsy is necessary.

It is recommended that patients with ESRD who subsequently develop breast inflammation and necrosis be evaluated for calciphylaxis. Some authors argue that any patient with ESRD who presents with new indeterminate breast calcifications should undergo core needle biopsy. While no formal guidelines exist [5], management of calciphylaxis should include a multidisciplinary team. Sodium thiosulfate, hyperbaric oxygen, anticoagulation, and appropriate wound care have been proposed as temporary treatments for calciphylaxis [6,8]. Some authors suggest total parathyroidectomy (especially if calcium-phosphate product is greater than 55 mg/dL and PTH level is greater than 300 pg/mL[5]), with mastectomy if symptoms persist. Others suggest the use of calcimimetic agents first due to the risks of parathyroidectomy, with surgery reserved for refractory cases [10]. Calciphylaxis recurrence after parathyroidectomy has been reported [4].

Learning points for this case include recognizing calciphylaxis as a cause of an ulcerating lesion of the breast, especially in a patient with ESRD. Calciphylaxis can mimic an advanced breast malignancy with direct skin invasion and tissue sampling is indicated to exclude the possibility of cancer.

Patient consent

Not available as the patient has passed away.

REFERENCES

[1] Bukhman R, Scheri RP, Selim MA, Baker JA. Sonography in the identification of calciphylaxis of the breast. J Ultrasound Med 2010;29(1):129–33. doi:10.7863/jum.2010.29.1.129.

[2] Mastruserio DN, Nguyen EQ, Nielsen T, Hessel A, Pellegrini AE. Calciphylaxis associated with metastatic breast carcinoma. J Am Acad Dermatol 1999;41(2 II):295–8. doi:10.1016/s0190-9622(99)70368-3.

[3] Luo G, Ducy P, Mckeet MD, Pinero GJ, Loyer, E, Behringer RR, Karsenty, G. Spontaneous calcification of arteries and cartilage in mice lacking matrix GLA protein.

[4] Bonilla LA, Dickson-Witmer D, Witmer DR, Kirby W. Calciphylaxis mimicking inflammatory breast cancer. Breast J 2007;13(5):514–16. doi:10.1111/j.1524-4741.2007.00475.x.

[5] Hall DJ, Gentile LF, Duckworth LV, Shaw CM, Singhal D, Spiguel LRP. Calciphylaxis of the breast: a case report and literature review. Breast J 2016;22(5):568–72. doi:10.1111/tbj.12632.

[6] Elghobashy M, Vaquas S, Elshafie M, Kaneri S, Shaaban AM. Novel insights from research practice unusual presentation of mammary calciphylaxis in a patient on long-standing renal dialysis established facts. 2020. doi:10.1159/000508537.

[7] Koratala A, Ejaz AA, Mohandas R. Calciphylaxis of the breast: a rare metabolic complication of kidney disease. 2016. doi:10.1136/bcr-2016.

[8] Novotny AG, Simpson AB, Kral MA, et al. Calciphylaxis of the postmenopausal female breast: an uncommonly encountered mimic of carcinoma. 2017. doi:10.1155/2017/4541620.

[9] Buscher K, Gabriëls G, Barth P, Pavenstädt H. Breast pain in a patient on dialysis: a rare manifestation of calcific uraemic arteriolopathy. 2015. doi:10.1136/bcr-2014-207946.

[10] Nigwekar SU, Sprague SM. We do too many parathyroidectomies for calciphylaxis. Semin Dial 2016;29(4):312–14. doi:10.1111/sdi.12502.