

AMSER Case of the Month

April 2024

29 y.o. Female with Increased Parathyroid Hormone
Related Peptide (PTH-RP)

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Patient Presentation

- 29 y.o. female with hypercalcemia and found to have mildly elevated PTH-RP. Endocrine team concerned for possible breast cancer.
- PMHx: Alcoholic cirrhosis, history of recurrent acute kidney injury requiring hemodialysis, hypertension
- PSHx: S/p liver transplant 9 months ago on tacrolimus for suppression
- FHx: No family history of cancer

Pertinent Labs

- Ca: 10.5 mg/dL (normal 8.6-10.2 mg/dL)
- Albumin: 4.9 g/dL
- PTH within normal limits (10–60 pg/mL)
- PTH-RP: 6.0 pmol/L (female over 18 normal 0.0-3.4 pmol/L)
- Tacrolimus trough: 7 ng/mL
- Creatinine: 1.17 mg/dL (normal 0.50-0.96 mg/mL)
- GFR: 54 mL/min/1.73m² (normal > or = 60 mL/min/1.73m²)

Hypercalcemia & PTH-RP

- Hypercalcemia is when total serum calcium is greater than or equal to 10.5 mg/dL
 - Must be adjusted if albumin is low as 40% of serum calcium is bound to albumin
 - Differential includes PTH-dependent (hyperparathyroidism, FHH, lithium use) and PTH-independent (malignancy, Vitamin D intoxication, granulomatous disease, adrenal insufficiency, medication-associated)
- Parathyroid Hormone (PTH) is a part of the body's calcium homeostasis and can be elevated in conditions such as chronic kidney disease (secondary hyperparathyroidism)
 - Renal Disease → low $1,25(\text{OH})_2\text{D}$ production & decreased phosphate excretion → low calcium gut and renal reabsorption & high phosphate → increased PTH → increased serum Ca^{2+}
- Elevated Parathyroid hormone-related peptide (PTH-RP) in the setting of hypercalcemia is seen in humoral hypercalcemia of malignancy, most commonly secreted in breast, lung, and kidney cancers

Other Imaging Workup

- Due to elevated PTH-RP, the patient underwent full imaging workup for primary malignancy
- Prior Imaging Workup: CT Chest/Abdomen/Pelvis, MRI Abdomen/Pelvis, and Neck US all negative for findings of malignancy.

What Additional Imaging Should We Order?

ACR Appropriateness Criteria

Variant 2:

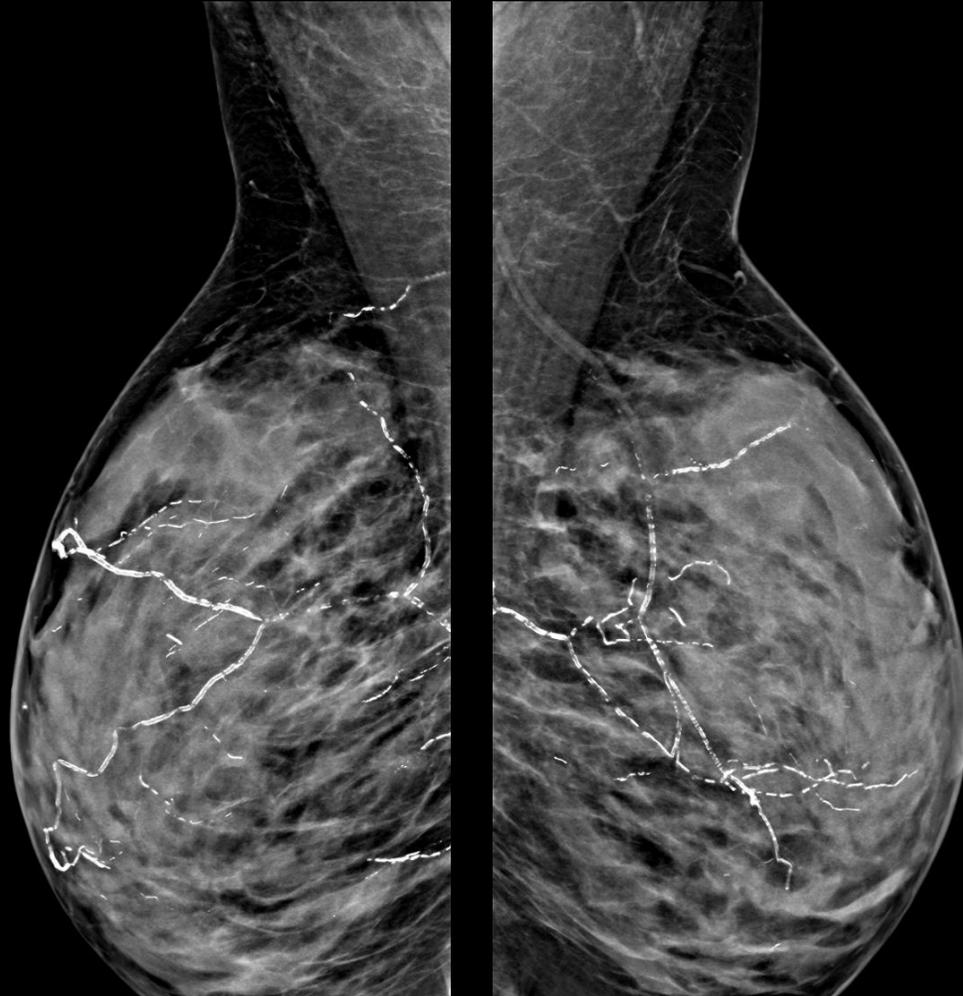
Breast cancer screening. Intermediate-risk women: women with personal history of breast cancer, lobular neoplasia, atypical ductal hyperplasia, or 15% to 20% lifetime risk of breast cancer.

Procedure	Appropriateness Category	Relative Radiation Level
Mammography screening	Usually Appropriate	☢☢
Digital breast tomosynthesis screening	Usually Appropriate	☢☢
MRI breast without and with IV contrast	May Be Appropriate	○
US breast	May Be Appropriate	○
FDG-PET breast dedicated	Usually Not Appropriate	☢☢☢☢
Sestamibi MBI	Usually Not Appropriate	☢☢☢
MRI breast without IV contrast	Usually Not Appropriate	○

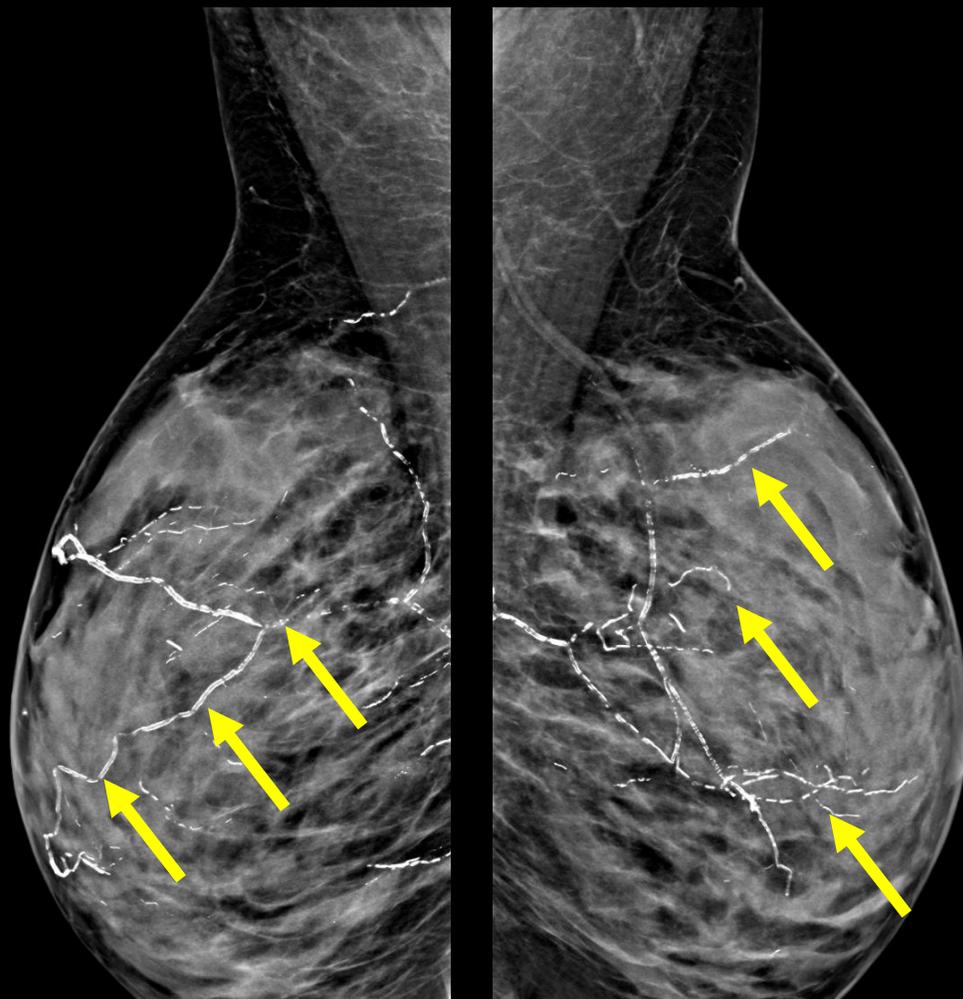


This imaging modality was ordered by the Endocrine physician as the patient was undergoing complete malignancy workup due to elevated PTH-RP. While screening mammograms would not typically begin until 40, workup was warranted due to elevated PTH-RP.

Findings Unlabeled - MLO Images

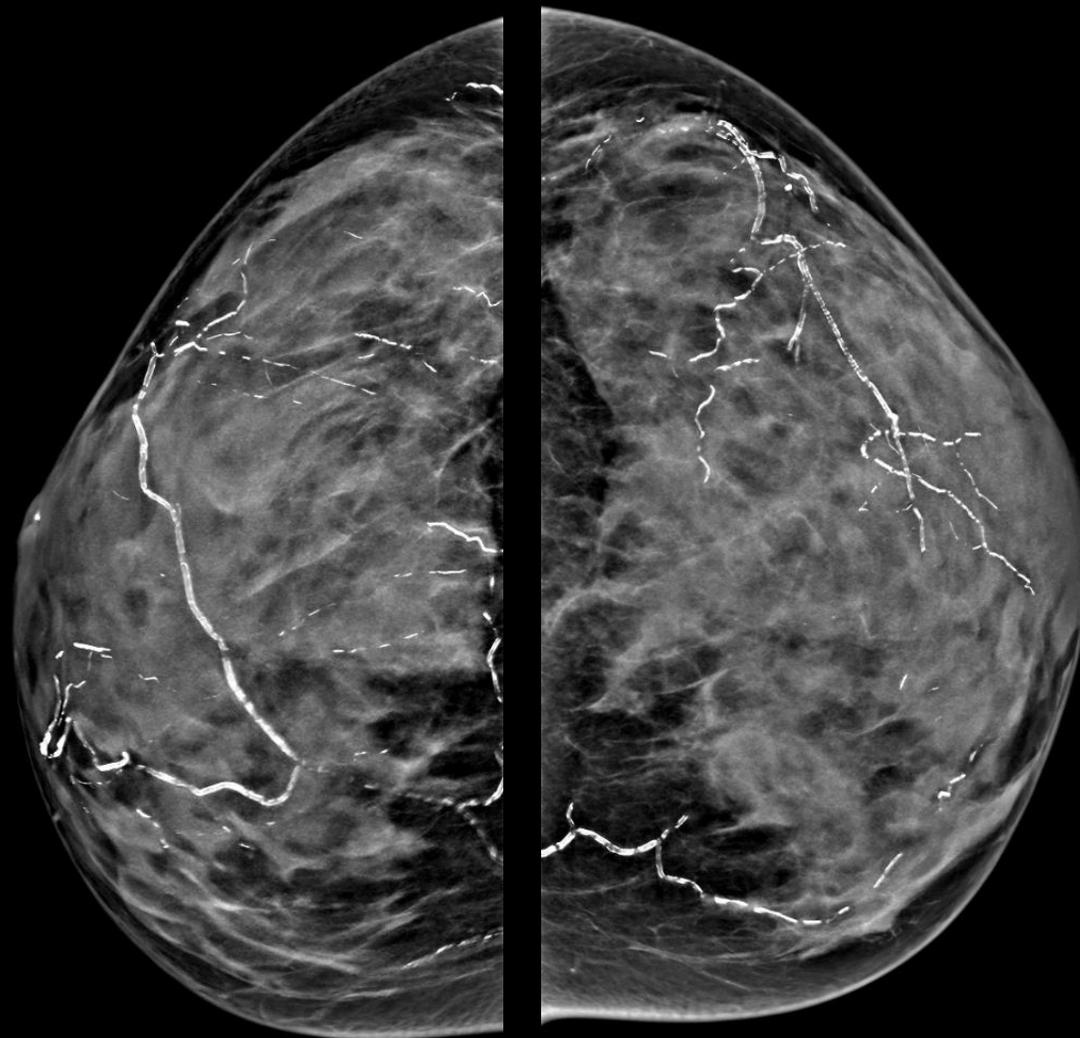


Findings Labeled - MLO Images

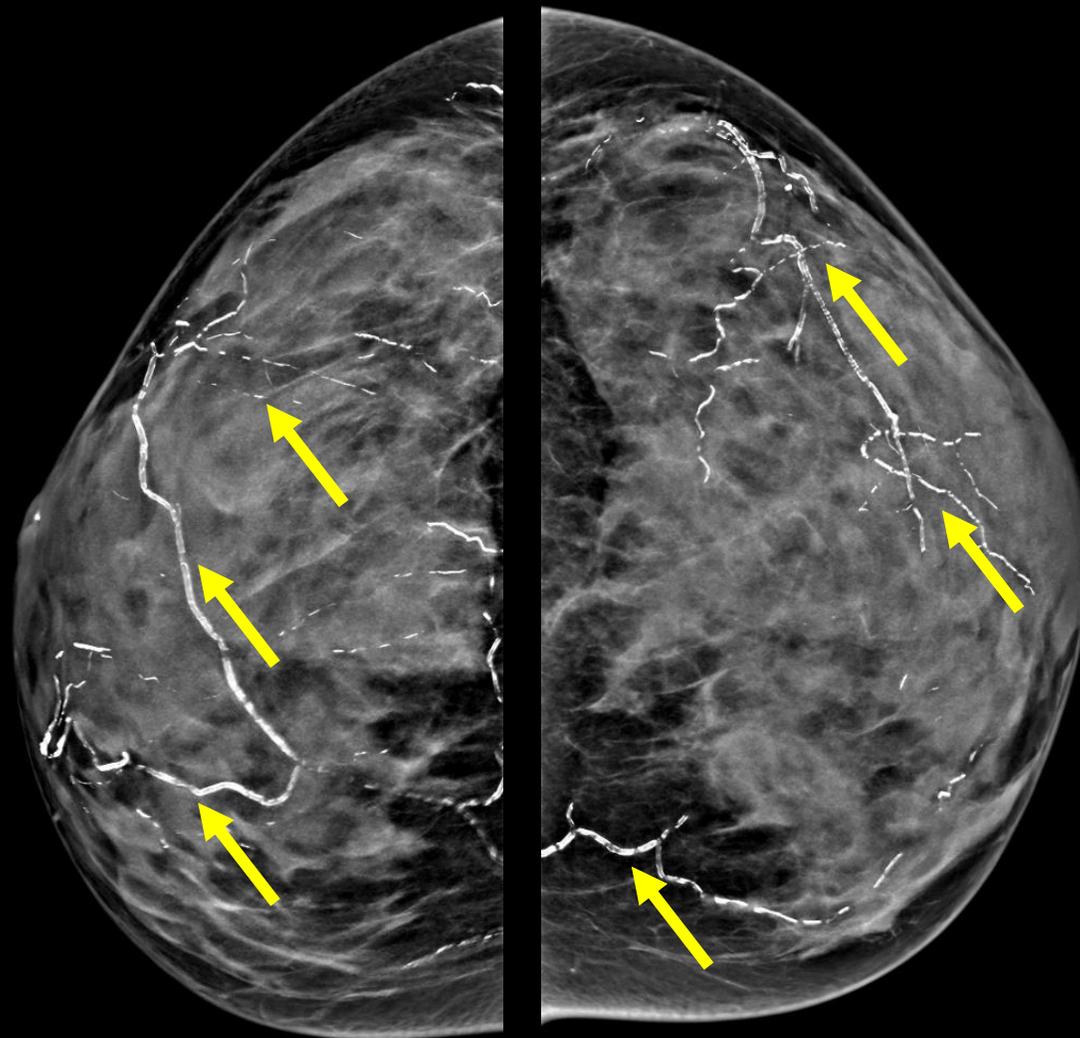


Parallel linear calcifications
identified within a tubular
structure consistent with
vascular calcifications

Findings Unlabeled - CC Images



Findings Labeled - CC Images



Parallel linear calcifications identified within a tubular structure consistent with vascular calcifications

Final Dx:

Vascular Calcifications

BI-RADS 2, Heterogeneously Dense breasts with bilateral vascular calcifications.

No evidence of primary malignancy in the breast.

Case Discussion - Vascular Calcifications

- **Vascular Calcifications** are defined by the BI-RADS atlas as parallel tracks or linear calcifications that are clearly associated with blood vessels.
- Due to calcific deposition in the media of arterioles, known as **Mönckeberg medial calcific sclerosis**.
 - Calcium deposition in the media without narrowing of the lumen
- Presence is considered an independent risk factor for coronary artery disease and is oftentimes seen in older patients.
- Younger patients with extensive vascular calcifications may have associated diabetes mellitus and renal disease, as seen in this patient.
- In young patients with extensive vascular calcifications on mammography, it is important to consider the possibility of calciphylaxis, which is *systemic* medial calcific sclerosis and has features of skin necrosis, which this patient did not have. Calciphylaxis has an extremely poor prognosis.

Teaching Points

- Vascular calcifications on mammography may have many associations, including:
 - Coronary artery disease
 - Diabetes mellitus
 - Chronic kidney disease
- In younger patients, vascular calcifications are unexpected but may be due to:
 - Diabetes mellitus
 - Secondary hyperparathyroidism from severe renal disease
 - Vitamin D + PTH + Ca^{2+} + Phosphorous → increase in calcium phosphate precipitates
 - Calciphylaxis

Case Resolution

- Although PTH was normal, the extensive vascular calcifications on mammography were felt to be due to the patient's known renal dysfunction and hypercalcemia.
- Tacrolimus, an immunosuppressive medication for liver transplant maintenance, dose was lowered to alleviate potential nephrotoxicity while maintaining appropriate immunosuppression.
- Calcium now down-trending to 10.2 mg/dL and GFR is increasing, now 60 mL/min/1.73m².
- The patient was sent for PET/CT to exclude malignancy because of the elevated PTH-RP, and so far no malignant cause of PTH-RP has been identified.
- Additional send-out workup is underway including intact PTH, N Terminal PTH-RP assay which is not affected by renal function, and ACTH/cortisol to evaluate for adrenal disease (which can sometimes elevate calcium).
 - C terminal PTH-RP has been reported to be falsely elevated in patients with renal dysfunction and hypercalcemia, so it is important to obtain N terminal PTH-RP from an outside laboratory if there is no obvious cancer

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