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Case Report

A rare case of primary breast lymphoma presenting as calcifications on screening mammography ☆

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ABSTRACT

Extranodal marginal zone lymphoma (EMZL) is a low-grade subtype of B-cell non-Hodgkin lymphoma that can affect any mucosal tissue, most commonly the GI tract. Primary involvement of the breast, known as primary breast lymphoma (PBL), is a very rare manifestation. We report an unusual case of a 65-year-old woman with primary breast EMZL presenting as calcifications discovered during screening mammography. This represents an exceedingly atypical appearance of primary breast lymphoma that is rarely described in the literature.

Introduction

Extranodal marginal zone lymphoma (EMZL), also known as mucosa-associated lymphoid tissue lymphoma (MALT), is a subtype of B cell non-Hodgkin lymphoma that can affect any mucosa. EMZL represents approximately 7-8% of all non-Hodgkin lymphomas, with the most common site involving the stomach [1]. Primary involvement of the breast, known as primary breast lymphoma (PBL), is a very rare manifestation of lymphoma representing less than 1% of all breast cancers [2,3]. While characteristic imaging features of primary breast lymphoma are non-specific, the literature describes associated calcifications as extremely rare [4–6]. We report an unusual case of an asymptomatic 65-year-old woman with primary breast EMZL presenting as calcifications discovered during screening mammography. The uncommon disease in combination with an exceedingly atypical appearance highlights the challenges of diagnosing this rare entity in an asymptomatic patient.

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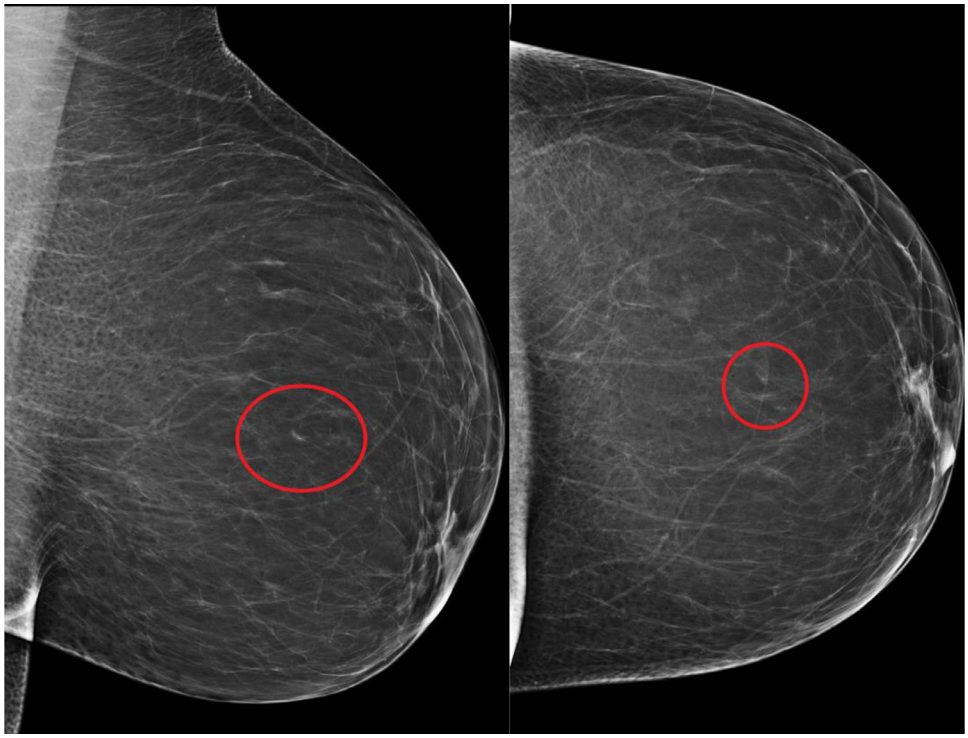

Fig. 1 – Left breast medial lateral oblique (left) and craniocaudal (right) images demonstrate new calcifications in the left breast at middle depth. *The breast density is almost entirely fatty.*

Case presentation

An asymptomatic 65-year-old women without significant past medical history or known family history of breast cancer presented to our institution for screening mammography, which showed new isolated calcifications in the left central breast (Fig. 1). The patient returned for diagnostic mammography with magnification views which demonstrated grouped coarse heterogeneous calcifications measuring 3 mm (Fig. 2). The findings were classified as BI-RADS 4, and stereotactic biopsy (Fig. 3) was subsequently performed, which was successful in sampling the calcifications (Fig. 4).

Histopathological examination revealed lymphoid tissue showing foci of amorphous material with associated calcifications on multiple core biopsies. On additional pathologic testing, the lymphoid tissue showed changes consistent with kappa restricted mature B-cell neoplasm. Findings were consistent with cutaneous marginal zone lymphoma with plasmacytic differentiation.

The patient was referred to medical hematology/oncology for further workup. Initial labs including CBC were unremarkable. Peripheral blood flow cytometry was negative for lymphoma and leukemia. PET/CT demonstrated no evidence of hypermetabolic breast lesion or metastatic disease (Fig. 5). The patient's final diagnosis was stage IE marginal zone lymphoma involving the breast. Given the absence of clinical symptoms and the patient's negative PET/CT, systemic therapy and local radiation therapy were both deferred. The patient will undergo active surveillance with close follow-up with her hematologist/oncologist.

Discussion

Primary breast lymphoma (PBL) is a rare disease that represents approximately 1% of all non-Hodgkin lymphomas (NHL) and less than 1% of all breast malignancies [2,3,7]. The large majority of primary breast lymphomas (56%-84%) are represented by the diffuse large B-cell subtype, with the remainder due to the more indolent marginal zone lymphoma (9-28%) and follicular lymphoma (10%-19%) [8]. MZL is categorized into 3 subtypes according to the WHO classification of lymphoid neoplasms: nodal MZL, splenic MZL, and extranodal MZL (EMZL), which is also referred to as MALT lymphoma [9]. The most common sites of involvement for EMZL include the gastrointestinal tract (50%), ocular adnexa (5%-10%), and salivary glands, while disease of the breast accounts for only approximately 3% of EMZL [1]. Primary EMZL of the breast is very rare. In a large multicenter retrospective study, Martinelli et al. [10] only reported 24 cases of breast EMZL out of a total of 278 patients with primary breast lymphoma between the years 1980 and 2003. Similarly, Iyer et al. [11] identified only 13 patients with breast EMZL out of 654 with MZL (comprising 2% of their total MZL cases) between 1995 and 2021 at a single center.

The diagnostic criteria for PBL includes the breast tissue as the primary site of disease with absence of disseminated disease beyond the ipsilateral axillary lymph nodes, as well as no previous lymphoma diagnosis [12,13]. The low prevalence of PBL is likely related to the paucity of mucosa-associated lymphoid tissue in the breast. The exact etiology of breast lymphoma is not known, but it is thought to derive from the pres-

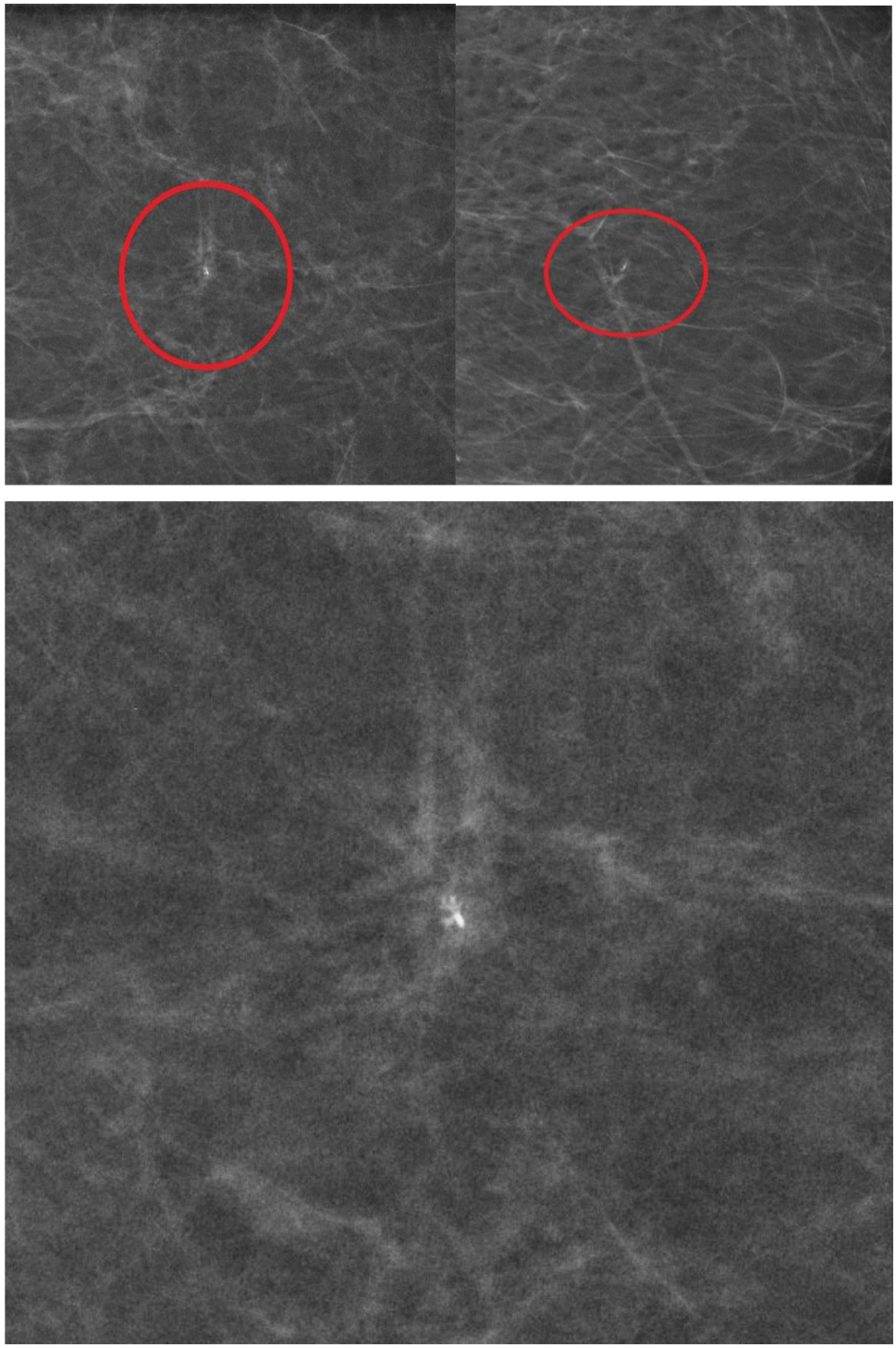

Fig. 2 – Magnification craniocaudal (left) and medial-lateral (right) and cropped magnified images show grouped coarse heterogeneous calcifications in the central breast. *Calcifications measure 3 mm.*

ence of intramammary lymph nodes or lymphoid tissue adjacent to breast ducts and lobes [4,14,15].

Most commonly, PBL presents in women aged 60-65 years [4]. Disease has been documented in men but is comparatively rare. The most common presentation includes a painless palpable lump. Additional symptoms and signs include pain and adenopathy, while in 10% of cases the patient is asymptomatic [4,12].

Imaging features of PBL are nonspecific and overlap with those of breast carcinomas. The most common mammographic presentation, described in upwards of 70%-80% of cases, is a noncalcified, iso-to-hyperdense, circumscribed oval

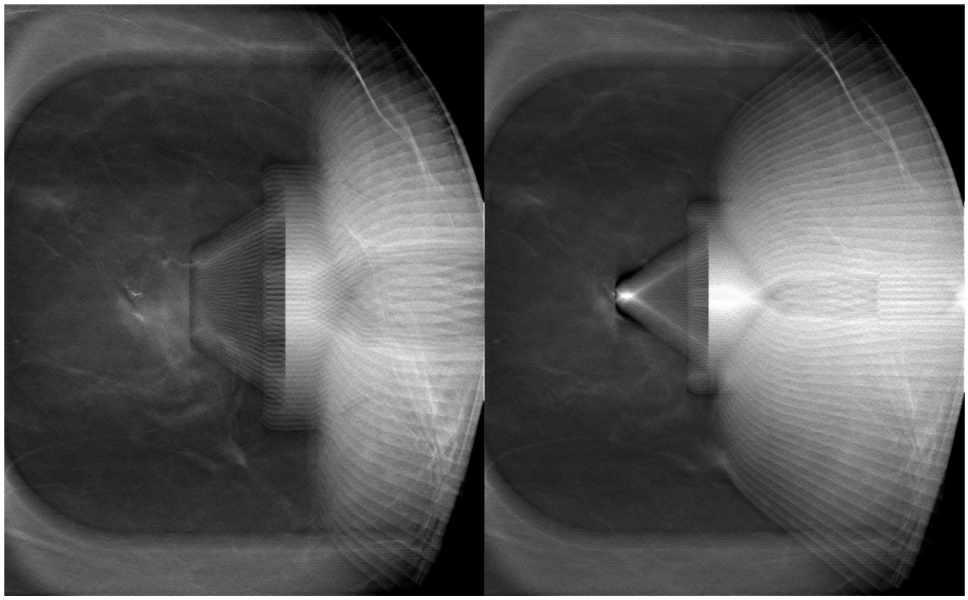

Fig. 3 – Craniocaudal prefire (left) and postfire (right) images obtained during tomosynthesis-guided left breast biopsy demonstrate satisfactory targeting of calcifications. *On the postfire image, the calcifications are immediately adjacent to the biopsy needle trough.*

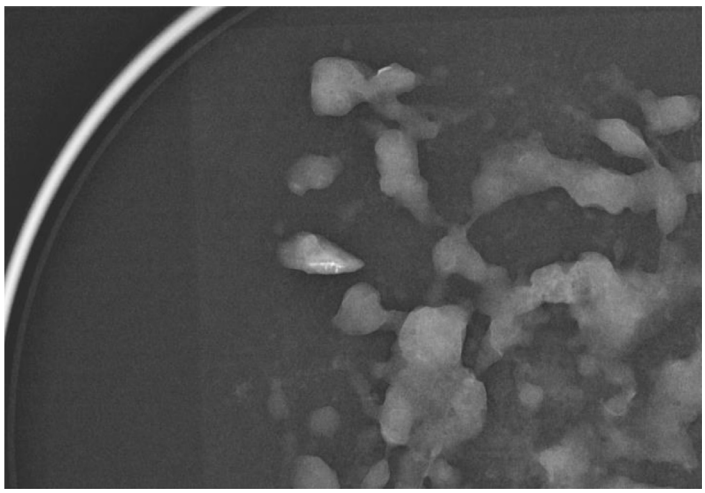

Fig. 4 – Specimen radiograph from left breast tomosynthesis-guided biopsy shows the targeted calcifications in one core specimen.

mass [2,4,12]. Axillary lymphadenopathy, skin thickening, and edema represent the majority of the remaining mammographically detected PBL. Other typically suspicious imaging findings such as asymmetries and architectural distortion are infrequent. The presence of calcifications is exceedingly rare and has been reported as a characteristic feature of breast cancer that is distinctively absent in lymphoma [5–7,11].

The staging of PBL is based on the Luganos modification of the Ann Arbor staging system. Disease limited to only the breast is defined as stage IE, and disease involving the breast and ipsilateral axillary lymph nodes is defined as stage IIE [16].

Given the rarity of primary breast lymphoma and the lack of large, multicenter studies to guide treatment decision, the optimal treatment of many of the PBL subtypes, including EMZL, is not definitively established. The current treatment of PBL largely depends on the lymphoma subtype and stage of disease, and usually involves radiation therapy, chemotherapy, or a combination thereof. Importantly, the role of surgery has diminished as it has not been shown to lead to better outcomes than less invasive interventions, and surgery is now mostly used in rare instances for diagnostic purposes [7,16]. In an article reviewing data from 465 patients reported in 92 publications, Jennings et al. concluded that mastectomy offers no benefit in disease-free survival or prevention of recurrence [17]. Similarly, the multicentric retrospective study by Martinelli et al. [10] found a higher

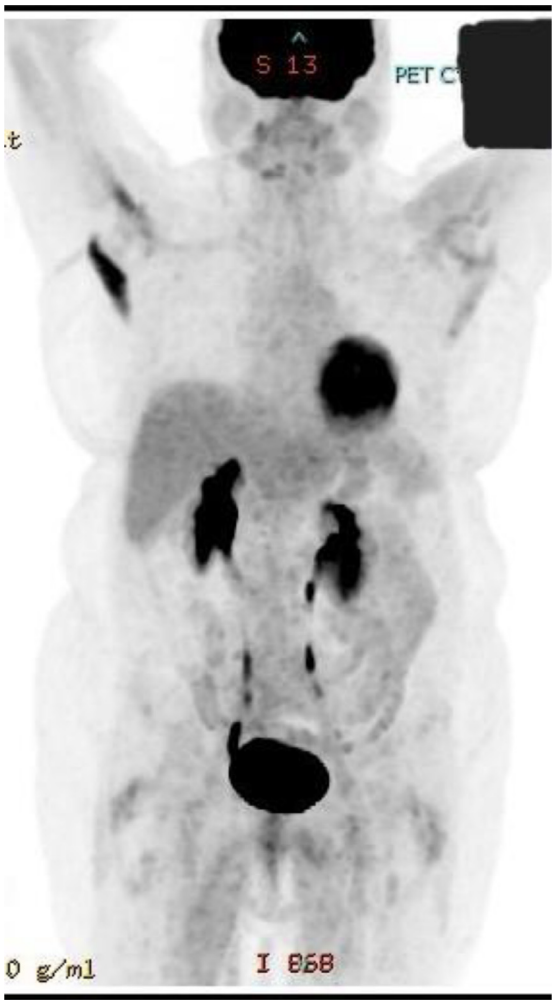

Fig. 5 – PET/CT 3D MIP image demonstrates no pathologic hypermetabolic activity. *Normal metabolic activity is noted most prominently in the brain, heart, and urinary collecting system.*

rate of relapse in patients who were treated with surgery only.

Treatment for aggressive or higher-stage disease may include the most common chemotherapy regimen utilizing cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) with the possible inclusion of rituximab (R-CHOP), as well as radiation therapy, which can be used to decrease the risk of local recurrence. There is increased evidence supporting watchful waiting and routine surveillance in early, low-stage, or indolent disease. In a recent retrospective study of 370 patients with early-stage primary breast marginal zone lymphoma, Liu et al. [18] found that conventional oncological treatments of chemotherapy, radiation, and surgery all failed to demonstrate increased survival benefits, with chemotherapy associated with higher mortality. Their study suggests that observation may be the optimal management approach for early-stage primary breast EMZL. As there are no precise management guidelines, treatment often varies among institutional centers, with treatment plans often personalized to the patient's age, subtype of lymphoma, and stage of disease [10,19]. Large multicenter studies are needed to help establish optimal treatment for this rare disease.

Conclusion

Primary breast lymphoma is a rare disease, with extranodal marginal zone lymphoma representing one of its exceedingly rare and indolent subtypes. Most patients diagnosed with PBL present with a painless breast mass and imaging findings are nonspecific. Our case highlights the unusual presentation of primary breast EMZL as new calcifications detected on screening mammography.

Patient consent

Informed consent for publication of this case was obtained from the patient.

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