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Case Report

Secondary breast lymphoma: A case report[☆]

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ABSTRACT

Lymphoma is the most frequent hematologic malignancy that involves the breast. It represents less than 1% of all breast cancer. The most common subtype is the secondary B-cell lymphoma. Clinically, lymphomas are divided into primary and secondary breast lymphoma. We presented a case of 49-year-old female, who has diagnosed of Non-Hodgkin's Lymphoma, finalizing the treatment 2 months ago. Currently, she came for a check-up due to a palpable lump in the right breast. Mammography shows a dense, oval, and circumscribed mass. Ultrasound revealed a 3.6 cm oval, hypoechoic, lobulated mass with internal vascularity at color Doppler. Axillary nodes show cortical thickening of 7 mm, cortical blood flood, and absence of fatty hilum. The histopathology report corresponds to infiltration of the right breast and bilateral axillary nodes by Non-Hodgkin Lymphoma. This case corresponds with lymphoma recurrence manifested in breast. The diagnosis of lymphoma is an imaging challenge that simulates benign and malignant pathologies.

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Introduction

Lymphoma is the malignant hematologic tumor most frequently involving the breast with an incidence of 0.04%–0.7%. According to the WHO, there are 5 subtypes of breast lymphoma; diffuse B-cell lymphoma, Burkitt lymphoma, anaplastic large cell lymphoma associated with breast implants,

mucosa-associated lymphoid tissue, and follicular lymphoma. Breast lymphoma is clinically divided into primary and secondary, being diffuse B-cell lymphoma the most common. In the literature there are more reported cases of secondary than primary lymphoma. The average age of presentation of secondary lymphoma is between 60 and 65 years [1–5].

Hypothetically, these tumors could be originated from 3 possible lymphoid tissues that exists in small quantities in the

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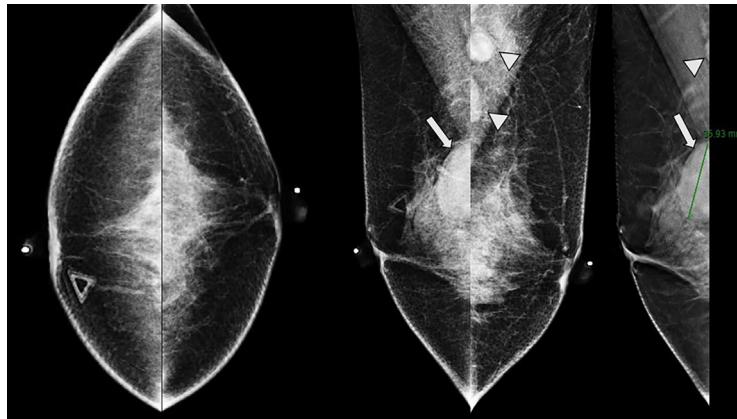


Fig. 1 – (A) Craniocaudal projection. Breast tissue is heterogeneously dense (category “C” of American College of Radiology, 2013). **(B) Mediolateral oblique projection.** In the right breast, at the posterior third of upper quadrants, exists an oval, circumscribed and dense mass (arrow) and is not associated with microcalcifications. The lump corresponds to the palpable area, indicated by a triangular marker. Additionally, left axillary lymph nodes are seen dense, with loss of morphology and hilum (head of arrows). **(C) By tomosynthesis, the borders of the mass are defined precisely, corroborating circumscribed margins of 3.6cm (arrow).** In this image, we can observe the presence of right axillary lymph node (head arrow).

breast: one is associated with the mucosa, another covers the ducts, and lobes or can be originated from the intramammary nodes [1–3].

Clinically, it is observed as a palpable, painless mass (61%), located in the upper external quadrant of the breast and 13%–40% of cases have palpable lymph nodes.

Lymphoma breasts have nonspecific imaging characteristics therefore the diagnosis represents a challenge which may result in delayed treatment.

Case report

A 49-year-old female patient with positive family history of breast cancer is diagnosed with Non-Hodgkin Lymphoma in 2019, treated until 2 months prior a palpable lump in right breast. She was afebrile and denied cough and weight loss. Further evaluation with mammogram and ultrasound was recommended.

By mammography, the tissue breast is the heterogeneously dense (category “C” of the American College of Radiology, 2013). In the right breast exists a dense, oval, and circumscribed mass, seen only in the Mediolateral oblique projection, is localized in the posterior third of upper quadrants. No microcalcifications are associated. The lump corresponds to the palpable area, marked with a triangular marker. Additionally, dense and round lymph nodes are seen in the left axillary (Fig. 1). By tomosynthesis, the margins of the mass are defined precisely and also a right axillary node is visible (Fig. 2).

Ultrasound revealed a 3.6 cm oval, hypoechoic, lobulated mass, located at 1:00 o'clock position, 3 cm from the nipple of the right breast. On color Doppler, internal vascularity is identified. This mass corresponds with the findings described in the mammography and tomosynthesis (Fig. 3).

In the ultrasound images, right axillary lymph nodes are observed round, with hypoechoic cortical thickening of 7 mm



Fig. 2 – Digital breast tomosynthesis in mediolateral oblique projection.

A right axillary lymph node is seen, only in this projection (arrow). Nodes of left axillary are dense, round and with loss of hilum (head arrow).

and nonhilar blood flow. Gray-scale ultrasound in transverse axis shows left axillary lymph nodes containing eccentric displaced hilum, round, and oval morphology and 8 mm thickened and hypoechoic cortex (Fig. 4).

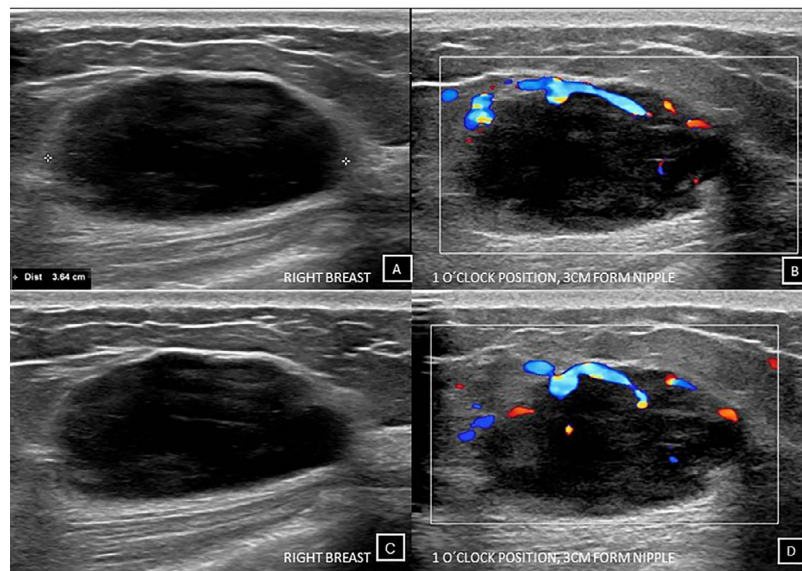


Fig. 3 – (A and C) Gray-scale ultrasound shows a 3.6 cm oval, hypoechoic, lobulated mass, localized at 1 o'clock position, 3 cm from the nipple of the right breast. (B and D) Color Doppler demonstrates internal vascularity of the tumor. This mass corresponds with the findings described in the mammography.

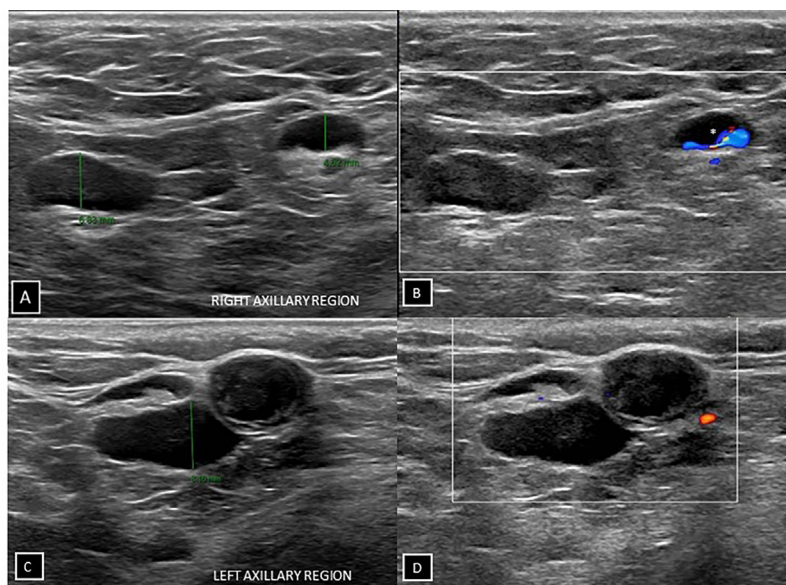


Fig 4 – Gray-scale and color Doppler ultrasound. (A and B) Right axillary lymph nodes are observed round, with hypoechoic cortical thickening of 7 mm and (* asterisk) shows nonhilar blood flow. (C and D) Left axillary lymph nodes contain eccentric displaced hilum, round, or oval morphology and 8 mm thickened and hypoechoic cortex.

Mass and axillary lymph nodes were suspicious (BI-RADS 4B) and subsequently an ultrasound-guided core biopsy was indicated. A percutaneous biopsy of the mass and bilateral axillary nodes was performed under ultrasound guidance, using 12-Gauge needle. Six cores were obtained and were sent in formalin for pathology analysis (Fig. 5). The histopathology report corresponds to infiltration of the right breast and bilat-

eral axillary nodes by Non-Hodgkin Lymphoma. Hematoxylin and eosin stain slides revealed transition between breast tissue and lymphoid neoplasia, and also immunohistochemical demonstration of CD20 confirms subtype B-cell lymphoma (Fig. 6).

This case report corresponds to a secondary breast lymphoma in a patient with recurrence of non-Hodgkin Lym-

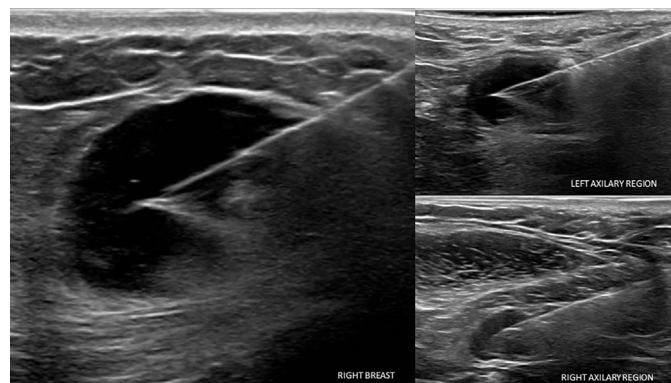


Fig. 5 – Images of ultrasound-guided biopsy of the mass localized in the right breast and lymph nodes of right and left axillary region.

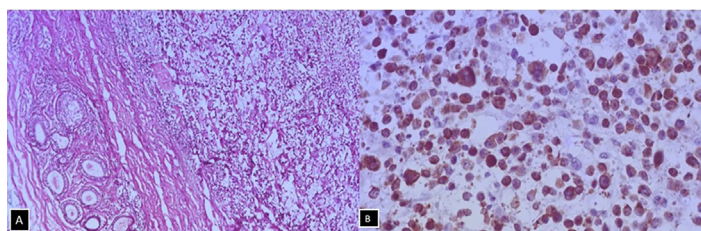


Fig. 6 – Hematoxylin and eosin stain slides revealed transition between breast tissue and lymphoid neoplasia and also immunohistochemical demonstration of CD20 confirms subtype B-cell lymphoma.

phoma. The patient was referred to the Hematology service. The patient was initial evaluated with anteroposterior chest radiography. Apparently widened mediastinum is seen, measuring 7 cm. In the right breast is evident a radiopaque and round mass (Fig. 7). There are no pulmonary findings. Further, FDG-PET/CT and treatment plan will follow up her hematologic appointment.

Discussion

Lymphoma is a hematologic malignancy that frequently involves the breast. Lymphoma appears as a primary tumor or as an extranodal manifestation of a secondary disease [4,7,13,17].

Lymphomas represent 0.04%-0.7% of malignant breast lesions. Secondary lymphoma corresponds to 17% of breast metastases and is more common than primary lymphoma [2,4,10–14].

The pathophysiology is still unclear, it is probably derived from lymphoid tissue associated with the mucosa, from lymphoid tissue adjacent to the ducts and lobes or from intramammary lymph nodes. These lymphoid tissues are barely absent in the breast [10].

The main differential diagnosis of secondary lymphomas is the primary tumor. The criteria to establish the diagnosis of primary lymphoma consist of; 1) the clinical location of presentation is the breast, 2) a previous history of lymphoma or

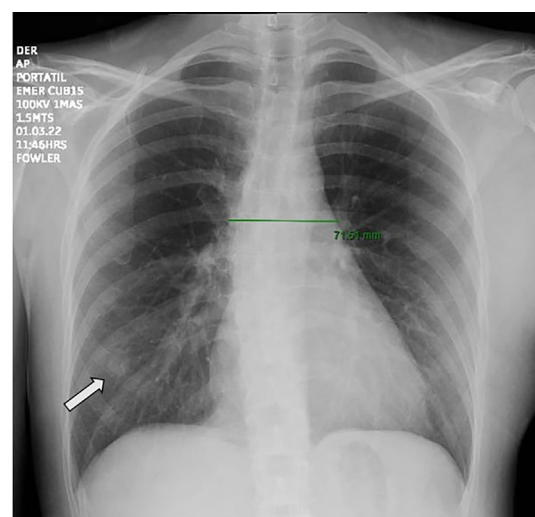


Fig. 7 – Anteroposterior chest radiography. Apparently widened mediastinum is seen, measuring 7 cm. In the right breast, there is a radiopaque and round mass (arrow). There are no pulmonary findings.

indication of widespread disease are absent at diagnosis, 3) the lymphomatous lesion is closely related to breast tissue in a specimen sufficient for pathological analysis, 4) ipsilat-

eral axillary and supraclavicular nodes may be affected [2,6,8–10,12,16,18].

In secondary lymphoma, there is evidence of lymph node disease or involvement of 1 or more organs, 6 months prior to the diagnosis of the breast tumor. Non-Hodgkin lymphoma with B-cell histological characteristics is the most common. It is related to multifocal, multicentric, and bilateral involvement. It may manifest as metastatic disease or recurrent disease. The age of presentation is 60–65 years [2–5,7,12,15].

Clinically, lymphoma appears a palpable and painless mass (61%), located in the upper external quadrant, 13%–40% of the cases lymph nodes are palpable. Other associated findings are nipple retraction, telorrea, and local inflammatory signs such as diffuse thickening, erythema, and edema of skin (11%). B symptoms (fever, sweat, weight loss) rarely occur in primary lymphoma, they are common in secondary tumors [2,3].

The role of diagnostic imaging in lymphoma evaluation is fundamental. Mammography, ultrasound, and magnetic resonance image (MRI) help to characterize the disease, inform locoregional extension, guide biopsies, and facilitate follow-up evaluations. Lymphoma breasts have nonspecific imaging features therefore the diagnosis represents a challenge which may result in delayed treatment [3].

Mammography shows a hyperdense, rapidly growing mass, unique (75%) or multiple in the case of secondary lymphoma, with an oval or round morphology (50%), circumscribed or indistinct margins (69%). Other manifestations are global asymmetries (20%), architectural distortion (9%–19%), and skin thickening (8%). Abnormal axillary nodes may be seen ipsilaterally in primary lymphoma and bilaterally in secondary lymphoma. Microcalcifications and mass with spiculated margins have not been reported in the literature in this type of tumors [2–4,7,9,10,13–15,17,18].

Ultrasound reveals an oval or round mass, with circumscribed or indistinct margins, hypoechoic or mixed echogenicity, usually associated with posterior acoustic reinforcement, peripheral echogenic halo, and hypervascularity. Abnormal axillary nodes are also seen. In cases with skin involvement, small superficial nodules, and skin thickening are identified due to lymphatic blockage of the tumor, resulting in retrograde edema [2–4,7,9,10,13–17].

MRI evaluates the presence and extent of multicentric and multifocal lesions, as well as the invasion to the chest wall. This method is used to evaluate the response to treatment and detect recurrence. The findings visualized are an oval or round enhanced mass, hypo, or isointense in T1-sequence with some hyperintense areas on T2-sequence. The enhancement is variable, it can be homogeneous or heterogeneous with kinetic curve type 2 or 3. MRI can demonstrate the presence of axillary lymph nodes and abnormal nodes in other regions [2,3,10,13–15,17].

Lymphoma requires confirmation by immunohistochemistry to determine the subtype. Most B-cell lymphomas express B-cell antigens such as CD20. The Ki-67 proliferation rate helps distinguish between low-grade lymphoma (10%–20% for follicular lymphoma) and high-grade lymphoma (>40% for diffuse large B-cell lymphoma, DLBCL) [2].

The 5-year survival rate is 50%–60% for primary breast lymphomas and 25.2% in the case of secondary lymphomas that

represent patients with advanced disease. The recurrence rate is 15% [5,10,11].

Treatment consists of chemotherapy and radiation. Surgical resection is not indicated [2,12].

The diagnosis of the present case is secondary breast lymphoma, the frequency in our Institution is 0.15% (from 2006 to October 2023), which coincides with what is reported in the literature. The patient in our case is 49 years-old, an unusual age of presentation according to case reports of females up to 60 years-old. This patient's breast tumor manifested 2 months after finishing systemic treatment for Non-Hodgkin Lymphoma, which corresponds to a case of recurrence disease manifested in the breast. By imaging, the tumor was observed with the most frequent characteristics of lymphoma described in different publications, in which is described as an oval, microlobulated, hypoechoic mass with increased vascularity and posterior acoustic enhanced. The important thing for the radiologist to keep in mind is that enlarged lymph nodes demonstrate breast lymphomas and are commonly the first finding or are associated with circumscribed mass of breast and imaging studies are the only methods for diagnosis.

Conclusion

Breast lymphoma is a diagnostic challenge and radiological images can simulate benign and malignant pathologies. Therefore, clinical history, imaging studies, and biopsy are required to establish the diagnosis. In a patient with a history of lymphoma who presents with an oval or round breast mass, its margins are circumscribed and no microcalcifications associated, the diagnosis of lymphoma has to be considered also with abnormal axillary nodes. The follow-up is done by *diagnostic imaging* as with any other oncological disease - local staging and restaging by US/Mammography/MRI and full body exams by CT/PET-CT. Clinical laboratory tests should accompany this to determine biochemical progression. A multidisciplinary consensus should do the treatment.

Patient consent

Written informed consent was obtained for publication of this case report.

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