


# Synchronic presentation of breast ductal carcinoma and follicular lymphoma: a diagnostic challenge

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## ABSTRACT

Synchronic tumors are rare events, even more clinically presenting as a rational metastatic sequence: breast cancer followed by axillary lymph node involvement. In the present case, after mastectomy associated with axillary emptying in a postmenopausal patient, we identified in the pathological report the presence of breast disease: invasive ductal carcinoma. However, differently from what was expected by the clinical examination, axillary lymph node involvement was not due to a disease of mammary origin, but to non-Hodgkin's lymphoma — a new primary. In the world literature, there are few similar reports, and it is still necessary to accumulate similar cases to be able to hypothesize a single causality between these two tumor subtypes or cause-consequence relationship between the two entities.

**KEYWORDS:** Lymphoma; Neoplasms, multiple primary; Breast neoplasms.

## INTRODUCTION

The presentation of synchronous neoplasms is rare<sup>1,2</sup>. In the case of breast cancer, the presence of ipsilateral axillary lymph node enlargement denotes, in clinical terms, lymphatic involvement by the breast disease initially diagnosed. Therefore, the diagnosis of synchronicity of two primary neoplastic diseases, one mammary and the other lymph node, occurs in a post-surgical moment, given the rarity of the condition.

What is known in the literature is the increased incidence of non-Hodgkin's lymphoma in patients treated for malignant breast cancer who underwent radiotherapy<sup>3</sup>, thus a context of metachronous disease.

Some authors, however, have reported cases of primary breast cancer and lymphoma at the initial diagnosis<sup>4</sup>. At the moment, it is not clear whether these cases arise through common underlying mechanisms, causing a parallel trigger, or whether the disease process is totally independent of each other.

Given the rarity of the process and the complete strategic difference in the management of these two distinct entities, there is, of course, a lack of consensus on the ideal treatment strategy<sup>1</sup>.

## CASE REPORT

A 69-year-old female patient was referred to the mastology service due to changes in routine screening mammography, denying having noticed nodulations or other changes in the breasts. She had no previous surgical procedure or previous radiotherapy. The family history was significant, with one sister previously diagnosed with breast neoplasm and another sister with a history of bladder cancer.

Hypothyroidism was being treated as the only comorbidity and continuous use medication. Multiparous, G3P1C2, and menopause at 53 years old, during the initial visit, she denied complaints compatible with symptoms B, with no fever, night sweats, or unintentional weight loss.

On physical examination, a palpable nodule in the left breast was found, at the junction of the upper quadrants, 3.5 × 2.5 cm, and a suspected bulky movable palpable ipsilateral axillary lymph node enlargement; therefore, clinically a T2N1Mx.

The modified screening mammogram showed a 15 mm node in the left breast with well-defined limits. Complementary ultrasound revealed a left breast with multiple simple cysts, the largest was 1.3 cm retroareolar. The right axilla had a 2.5 cm lymph node

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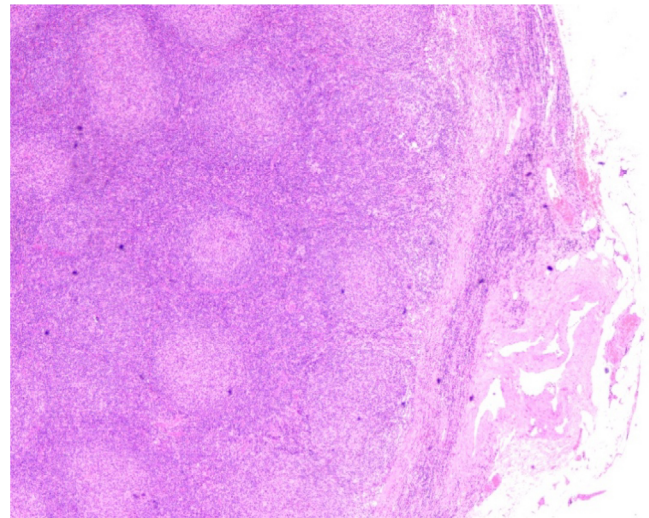
with a reactional aspect, and the left axilla, a palpable mass with atypical lymph nodes grouped in different sizes, the largest measuring 3.9 cm. Some discrepancies between the measurements of the lesion on the clinical examination and the imaging findings are probably related to differences in dates between them and also to the possibility of, at clinical examination, the lesion area being overestimated.

After the first visit to our service, the patient underwent a left breast core biopsy and a fine needle aspiration biopsy (FNAB) of the left axillary lymph nodes. The anatomopathological report showed a well-differentiated invasive breast ductal carcinoma and an associated 1 cm satellite node, with a report of nuclear grade 2 intraductal carcinoma. The immunohistochemical assessment showed a positive response to estrogen receptor and negative response to the progesterone receptor (ER+++ 95%; PR-; HER 2-; Ki67 8%); therefore, a luminal B. The FNAB of the axillary lymph nodes did not show malignancy in the sample, indicating further investigation in the case of a suspected lesion. Tomographic staging of the chest, abdomen, and pelvis did not signal additional secondary involvement, demonstrating only axillary lymph node enlargement measuring up to 2.2 cm.

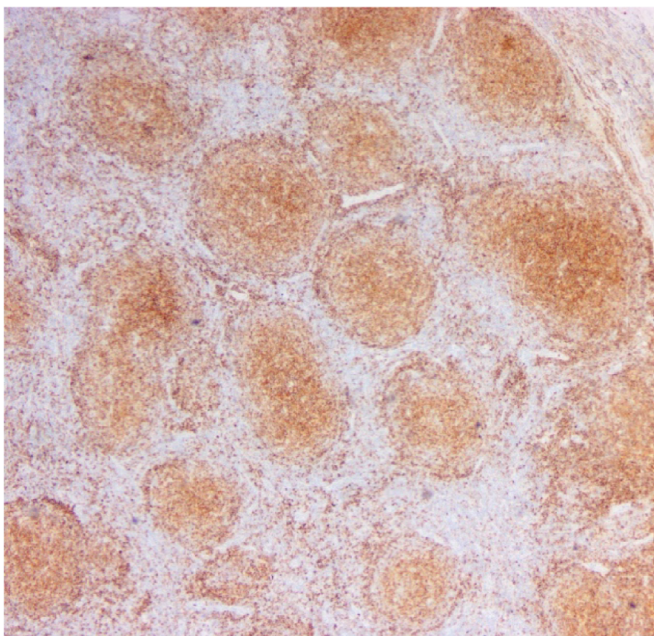
Next, the patient underwent a radical mastectomy and axillary lymphadenectomy with an adjuvant chemotherapy plan, without immediate reconstruction by her own decision. The final anatomopathological report of the surgical specimen revealed a well-differentiated invasive ductal breast carcinoma associated with intraductal carcinoma, with  $2.7 \times 1.9 \times 1.8$  cm and free margins.

As for axillary lymphadenectomy, 45 lymph nodes were removed, all without evidence of involvement by carcinoma, but there was a finding of atypical proliferation strongly suspected for follicular lymphoma, with post-surgical staging pT2pN0 in relation to breast cancer (Figure 1).

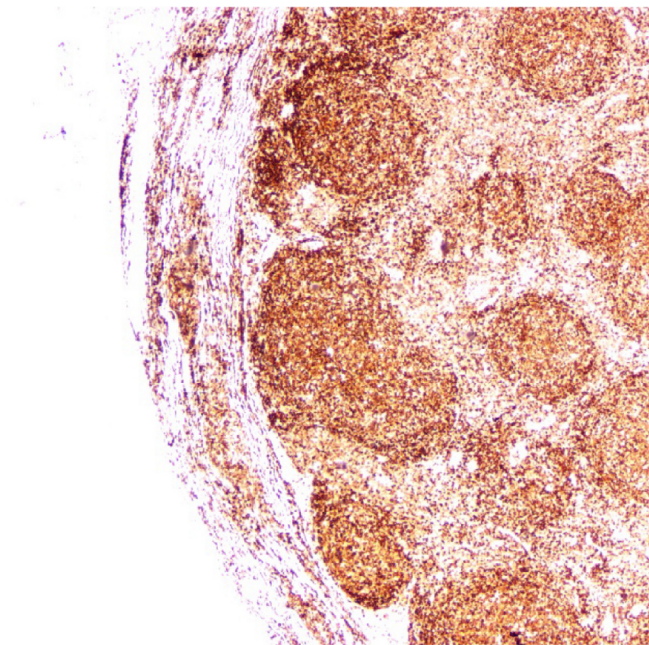
Complementary immunohistochemistry of the surgical specimen showed CD 10 expression (Figure 2) and positive Bcl-6 and Bcl-2 — a condition compatible with grade 1-2 follicular lymphoma (predominantly follicular > 75%).



**Figure 1.** H&E 40 × lymph node cut with cortical and medullary architecture replaced by neoplastic follicles.



**A**



**B**

**Figure 2.** H&E 40 × Cd10 and Bcl2 positive in follicular cells enhancing germinal centers.

The patient is currently undergoing treatment for lymphoma at the hematology service and is being followed up at Hospital São Vicente, in Curitiba, with hormone therapy. She is following follow-up.

## DISCUSSION

The first extramammary site affected by breast cancer is usually the axillary lymphatic chain. Therefore, the rationalization leads us to believe that, in the presence of an axillary lymph node block in a patient with invasive ductal carcinoma of the ipsilateral breast, it is a case of lymph node involvement by carcinoma of mammary origin.

However, in the case described here and in a few similar ones reported in the literature, there is a synchronous involvement of two primary tumors, a carcinoma and a lymphoma.

In 2015, Michalinos et al. reported a similar situation in which a postmenopausal patient also presented intraductal carcinoma and lymphoma, in this case clinically manifested in axillary lymph nodes ipsilateral to the breast lesion and in the inguinal region. In the follow-up, this patient presented a mammographic alteration and histological diagnosis of invasive ductal HER2+ carcinoma, treated with trastuzumab. Furthermore, the authors suggest the hypothesis that the breast tumor may induce an inflammatory lymph node response that evolves to a non-Hodgkin lymphoma<sup>1</sup>.

In 2016, Woo et al. also encountered a case of tumor synchronicity. In their literature review, they presented another 87 similar cases, with diagnoses of synchronic breast-lymphoma disease. In most cases, the presentation was after menopause, and the diagnosis of the second neoplasm was made after beginning the first treatment, as in our case<sup>2</sup>.

All cases reported with this context of neoplasm synchronicity are a real therapeutic challenge, given the great difference in treatment between the two diseases<sup>1,2,5</sup>.

## CONCLUSION

This report allows us to discuss several aspects about the synchronous presentation of the primary breast tumor and lymphoma, among them: the delay in the diagnosis of the secondary neoplasm, the consequent delay in defining the diagnostic strategy, and the prognosis related to the two pathological processes in the synchronous presentation. The literature reviews already carried out show that 88.9% of the case reports failed to diagnose the second neoplasm<sup>1</sup>. Fine needle biopsy and even *core* biopsy of these lymph nodes usually do not guarantee the diagnosis because of the high false-negative rates for these cases, and their findings are often insufficient<sup>4</sup>.

Imaging diagnosis is usually not enlightening in these cases<sup>2</sup>, and, in general, the diagnosis occurs after surgical treatment and the final histological assessment.

## AUTHORS' CONTRIBUTIONS

P.M.: case management, literature review, data collection from medical records, writing, and text review.

M.S.: case management.

A.R.: literature review, data collection from medical records, writing.

M.C.: slide review in pathology and anatomopathological reports, production of case images.

T.C.: anatomopathological analysis and report, immunohistochemical diagnosis, case review.

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