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28566 – PRIMARY BREAST LYMPHOMA ASSOCIATED WITH INVASIVE BREAST CARCINOMA: A CASE REPORT

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Introduction: This case report describes a 54-year-old patient who developed invasive breast carcinoma in her left breast without further specifications, of the luminal B molecular subtype, concurrently with a primary breast lymphoma (diffuse large B-cell lymphoma with the germinal center B-cell subtype), which was definitively diagnosed only after surgical intervention. Synchronous occurrence of breast cancer and non-Hodgkin lymphoma (NHL) is an uncommon situation, with only 38 cases reported in the literature. It is extremely rare for both tumors to present as a collision tumor within the same breast. A collision tumor refers to the coexistence of two histologically distinct tumors occurring at the same site. The mechanisms underlying this collision are highly complex, and it remains unclear whether the pathophysiological association between them can be attributed to being induced by the same causal factor. Breast lymphoma is an uncommon hematological neoplasm originating in the breast lymphoid tissue. Its prevalence is low, ranging from 0.04%–0.7%. It is classified into primary breast lymphoma (PBL), when it occurs in the breast without concomitant widespread disease, and secondary breast lymphoma (SBL), when there is metastatic involvement of the breast. The average age of onset for PBL varies from 60 to 65 years; it does not have a specific manifestation but usually presents as a unilateral, painless, palpable mass. Most PBLs are high-grade B-cell lymphomas, with diffuse large B-cell lymphoma (DLBCL) being the most common subtype, as well as the one with the worst prognosis and highest recurrence rate. After diagnosis, treatment of breast lymphoma is based on a combination of surgery, radiotherapy, chemotherapy, and immunotherapy. It is believed that the development of breast lymphoma associated with invasive breast carcinoma could be induced by the same virus or by hormonal alterations, primarily estrogen. Another hypothesis is that breast cancer could act as a stimulating factor for lymphoma, just as the reduced immune function caused by lymphoma may promote the development of carcinoma. The association between non-Hodgkin lymphoma and breast carcinoma is extremely rare, and currently, there is no clear treatment pattern or detailed information regarding its prognosis. **Methodology:** In January 2022, a 54-year-old single female patient, a native and resident of São Paulo/SP, sought medical attention due to the appearance of a palpable nodule in the left breast for more than a year, accompanied by intermittent bleeding from the lesion that began a month prior. She had a diagnosis of systemic arterial hypertension and was being treated with two antihypertensive medications. The patient was nulliparous, her menarche occurred at age 12, she experienced menopause at age 46 (without hormone replacement therapy), and she denied having used combined oral contraceptives. She had a family history of esophageal cancer in her brother, who was a smoker and alcohol consumer. On physical examination of the breasts, inspection revealed an ulcerated lesion in the healing process involving the entire left breast, primarily in the lateral quadrants, without active bleeding. Palpation showed that the lesion measured approximately 15x12 cm, was hardened, and had limited mobility. In the left axillary region, a fibroelastic lymph node measuring 1.5 cm was palpated. During the first consultation, the patient brought an external breast ultrasound from December 2021, which described an infiltrative architectural distortion affecting nearly all quadrants, diffusely heterogeneous with poorly defined hypoechoic areas, involving the skin and subcutaneous tissue, especially in the lateral quadrants; presence of atypical axillary lymphadenopathies measuring up to 15x11 mm. Bilateral mammography at our institution revealed a 50 mm retroareolar nodule in the left breast, with irregular margins and poorly defined borders (Breast Imaging Reporting and Data System — BI-RADS 4); Our breast ultrasound showed a large, solid lesion in the left breast that was difficult to measure, while the right breast appeared normal. Additionally, CT scans of the chest, abdomen, and pelvis, as well as a bone scintigraphy, were performed to exclude other primary neoplastic sites; all examinations showed no abnormalities. The patient underwent an incisional biopsy of the left breast in the surgical center, and the histopathological report indicated atypical lymphocytic infiltration of mixed B and T cells, suggestive of reactive lymphoid hyperplasia. A core biopsy guided by ultrasound of the left breast nodule was

also performed. The histopathological and immunohistochemical analysis of the biopsied tissue revealed mammary tissue with foci of moderate lymphocytic inflammatory infiltrate in a perivascular, periductal, and interstitial distribution, fibrosis, hyalinization of the stroma, and focal pseudoangiomatous hyperplasia of the stroma. The tissue was estrogen receptor positive in the ducts, p63 positive in myoepithelial cells, and AE1/AE3 positive in the ducts. Following the review of supplementary tests and clinical examination, a decision was made to proceed with initial surgical treatment. The patient underwent a mastectomy with left axillary approach, based on intraoperative frozen section results, and closure was achieved using a latissimus dorsi flap (performed in collaboration with the plastic surgery team). Histopathological analysis of the surgical specimens revealed areas of invasive breast carcinoma without further specification (20%), histological grade II, nuclear grade 3, multifocal (with three foci, the largest measuring 17x15 mm), no ductal carcinoma in situ (DCIS) detected, with extensive lymphovascular invasion present, associated with an extensive large cell lymphoma (80%) measuring approximately 20 cm, involving and ulcerating the skin and infiltrating muscle. Surgical margins were negative for invasive carcinoma; however, the deep margin coincided with the lymphoma. Immunohistochemical analysis of the invasive breast carcinoma showed high expression of estrogen (ER) and progesterone (PR) receptors (95%), a Ki-67 proliferation index of 80%, and HER2 was negative (score 0). The expression of AE1/AE3 cytokeratins confirmed the epithelial histogenesis of this neoplasm. The expression of GATA3 and estrogen receptor (ER) indicates the breast as the primary site of this carcinoma. Negativity for P63 confirms the absence of myoepithelial cells surrounding the tumor, thereby corroborating the diagnosis of invasive carcinoma. The expression of E-cadherin and β-catenin confirms that it is an invasive carcinoma of unspecified type (CI SOE or CINE). Meanwhile, the lymphoma component shows negativity for cytokeratins and positivity for CD20, confirming a B-cell immunophenotype lymphoma. Positivity for BCL6, along with negativity for MUM1, supports the diagnosis of a large B-cell lymphoma with an immunophenotype indicative of the germinal center B-cell (GCB) molecular subtype. Thus, the findings indicate a multifocal luminal B invasive carcinoma associated with extensive large B-cell lymphoma with an immunophenotype pointing to the GCB subtype. Pathological staging (pTNM, AJCC 8th edition): mpT1c pN1a pMx. Following surgery, the patient was referred to oncology and hematology for adjuvant treatment planning. She was indicated to receive six cycles of R-CHOP (rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate, and prednisone) along with adjuvant radiotherapy to the left thoracic wall at a dose of 40.05 Gy in 15 sessions. The patient is currently under regular follow-up, on endocrine therapy with anastrozole since May 2023, with good treatment tolerance and remains asymptomatic to date. **Conclusion:** The association between NHL and breast cancer is extremely rare. The mechanisms that lead to this tumor collision are highly complex and not yet fully understood, particularly regarding the main causal factors. Clinical diagnosis remains challenging, given the small number of reported cases to date.