Synchronous Axillary Lymph Node Involvement by Breast Cancer and Nodal Marginal Zone Lymphoma: A Case Report and Review of the Literature

Meme Kanseri ve Nodal Marjinal Zon Lenfomaya Bağlı Eş Zamanlı Aksiller Lenf Nodu Tutulumu: Olgu Sunumu ve Literatürün Gözden Geçirilmesi

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ABSTRACT We report an unusual condition, "tumor in tumor", in a 66-year-old woman who presented with a swelling in her left axillary region for a period of one month. Metastasis of invasive ductal carcinoma of the breast was shown in axillary lymph nodes which were involved by nodal marginal zone B-cell lymphoma. Since sentinel lymph node biopsy has been performed increasingly in cases without palpable axillary lymph nodes, the probability of synchronous malignancies, especially lymphomas, should be kept in mind since identifying coincident tumors is important for proper treatment. The differential diagnosis of low grade non-Hodgkin lymphomas from non-neoplastic reactive lymphoid proliferations may be really challenging. Therefore systematic clinical examination as well as detailed histological and immunohistochemical evaluation is mandatory.

Key Words: Lymph nodes; lymphoma; carcinoma, ductal, breast

ÖZET Sol aksiller bölgede bir aydır devam eden şişlik nedeniyle başvuran 66 yaşındaki bir bayan hastada nadir görülen bir durum olan "tümör içinde tümör" olgusu bildiriyoruz. Nodal marginal zon B-hücreli lenfoma tutulumu gösteren aksiller lenf düğümlerinde memenin invaziv duktal karsinomu metastazı saptandı. Palpe edilebilir aksiler lenf düğümü olmayan meme tümörlerinde giderek artan sıklıkta sentinel lenf düğümü biyopsisi yapıldığından, senkronöz malignitelerle karşılaşma olasılığı akılda tutulmalıdır. Çünkü rastlantısal birliktelik gösteren tümörlerin saptanması uygun tedavi seçimi için önem taşır. Düşük dereceli non-Hodgkin lenfomalar ile non-neoplastik reaktif lenfoid proliferasyonların ayırıcı tanısı bazen çok zor olabilir. Bu nedenle detaylı histolojik ve immunhistokimyasal inceleme yanı sıra sistemik klinik muayene zorunludur.

Anahtar Kelimeler: Lenf nodları; lenfoma; karsinoma, duktal, meme

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In cases without a previous history of radiotherapy and/or chemotherapy, it is rare to find the involvement of ipsilateral axillary lymph nodes in conjunction with breast carcinoma metastasis and synchronous lymphomatous proliferation (tumor in tumor). Table 1 summarizes the cases reported in the literature.[1-4]

Here, we present a case with simultaneous presentation of invasive ductal carcinoma metastasis and nodal marginal zone B-cell lymphoma involvement in the same axillary lymph nodes.

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TABLE 1: Clinicopathologic features of cases with synchronous involvement of invasive breast carcinoma and lymphoma in the same axillary lymph nodes (tumor in tumor).

Author	Age, Sex, Presentation	Pathologic diagnosis of breast lesion	Pathologic diagnosis of axillary lymph nodes
Ortega P Jr et al. 1951	NA	Breast carcinoma	Breast carcinoma metastasis in ALNs involved with chronic lymphocytic leukemia
Woolam GL et al. 1966	NA	Breast carcinoma	Breast carcinoma metastasis in ALNs involved with small lymphocytic lymphoma
Caraway NP et al. 1997	62, F, mass in right breast axillary tail	Invasive ductal carcinoma, Black's nuclear grade 2 by FNAC	Metastatic invasive ductal carsinoma and small lymphocytic lymphoma in ALNs (by FNAC)
Ambrosiani L et al. 1999	67, F, breast lump (right)	Invasive ductal carcinoma, poorly differentiated	Diffuse centroblastic-centrocytic non-Hodgkin's lymphoma in all ALNs Six ALNs include breast carcinoma metastasis
Barrenger E et al. 2005	61, F, NA	Invasive ductal carsinoma, grade 2	SLN prosedure was applied, one SLN included both breast carcinoma metastasis and lymphoma All 21 ALNs include only follicular B-cell lymphoma
Pandey U et al. 2003	75, F, breast mass (left)	-	Three ALNs include both breast carcinoma metastasis and lymphoma The rest of all ALNs include small lymphocytic lymphoma (chronic lymphocytic leukemia, B-cell)
Present 2009	66, F, swelling in left axillary region	Invasive ductal carcinoma with a predominant ductal carcinoma in situ component, grade 3 and Paget's disease	2 ALNs include both breast carcinoma metastasis and lymphoma The rest of all 20 ALNs include only marginal zone B-cell lymphoma

NA: not available, F: female, FNAC: fine-needle aspiration cytology, SLN: sentinel lymph node, ALNs: axillary lymph nodes.

CASE REPORT

A 66-year-old woman admitted to a public hospital with the complaint of swelling in her left axillary region lasting for a month. The biopsy of the left axillary lymph node was reported as metastatic carcinoma, suggesting primarily an invasive ductal carcinoma metastasis of the breast. The patient then was consulted by staff at the University Hospital. In her physical examination, bilateral cervical and axillary multiple lymphadenopathies were present, however, there were no palpable masses in breasts. Radiological evaluation revealed a suspicious mass with microcalcifications in the upper external quadrant of the left breast. Excisional biopsy was thereafter applied. The biopsy showed an invasive ductal carcinoma (0.5 cm in diameter, histological grade: 3, nuclear grade: 3) with a predominant intraductal carcinoma component. Immunostaining revealed the following: Estrogen (-), Progesteron 60% (++), p53 10% (+), Ki-67 20% (+) and c-erb-B2 score 3 (+). The patient underwent modified radical mastectomy and axillary lymph node dissection. Mastectomy material showed additional *in situ* ductal carcinoma foci, fibrocystic changes and pagetoid involvement of the nipple. Interestingly, the normal nodal architecture of all dissected 22 lymph nodes were effaced by uniform small lymphoid cells with regular nuclear contours and scant cytoplasm. Two out of 22 lymph nodes also included invasive ductal carcinoma metastasis without extracapsular invasion (Figure 1). The diffuse pattern of lymphoid cells without any intervening lymphoid follicules and focal capsular involvement of these lymphocytes in some nodes suggested low grade non-Hodgkin lymphoma rather than benign reactive diffuse lymphoid hyperplasia. Immunohistochemical analysis was performed in order to make the differential diagnosis among low grade non-Hodgkin lymphomas such as small cell lymphoma, nodal marginal zone lymphoma, lymphoplasmacytic lymphoma and mantle cell lymphoma. These lymphoid cells were CD20 and bcl-2 positive, whereas they were CD3, CD5, CD10, CD23 and cyclin-D1 negative. Immunophenotype of these lymphoid cells was consistent with nodal marginal zone B-cell lymphoma

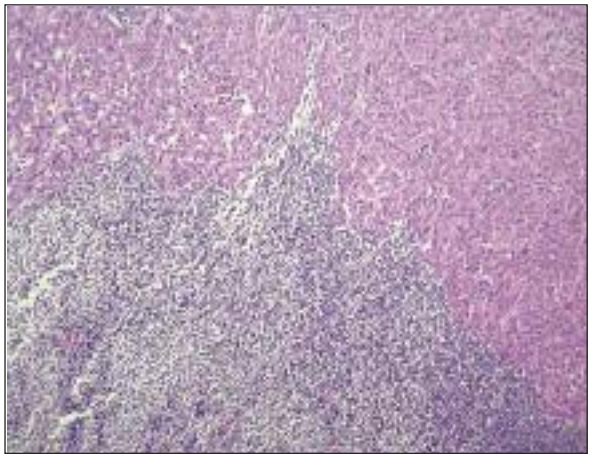

FIGURE 1: Invasive ductal carcinoma and nodal marginal zone lymphoma in the same axillary lymph node (H&E, x200).

(Figure 2). Therefore, the patient was referred to the Department of Hematology. Physical examination revealed other lymphadenopathies in the left posterior cervical, right anterior cervical and right axillary regions. She had no symptoms of lymphoma (night sweats, fever, weight loss) and no hepatosplenomegaly.

Thorax computed tomography (CT) revealed multiple lymphadenopathies in bilateral axillary regions (greatest dimension 25 mm on the left and 21 mm on the right) and in left hilar region. Furthermore, sequel adenopathies were seen in the subcarinal region, a paranchimal nodule and linear atelectasis were seen in the left lung and an air cyst was present in the right lung. No abnormalities were found in abdominal CT and bone scintigraphy. Routine blood tests, erythrocyte sedimentation rate, renal and liver function tests and LDH were in normal ranges. Ejection fraction of the patient was 65% and no abnormality was found on cardiologic examination. Antracyclin-based chemotherapy was therefore planned [cyclophophamide (750 mg/m^2, second day), doxorubicine (50 mg/m^2, second day), vincristine (1.4 mg/m^2, second day), prednisone (40 mg/m^2, second day) and rituximab (375 mg/m^2, first day)], which was convenient for both tumor types. After the first cycle of initial chemotherapy, side effects such as grade 3-4 nausea-vomiting, grade 3-4 mucositis, grade 2 diarrhea and grade 2 hematological toxicity (Hemoglobin: 9.0 gr/dl) appeared and thereafter the patient refused this chemotherapy regimen. Treatment modality was then changed to cyclophophamide (600 mg/m^2, first day) and doxorubicine (60 mg/m^2, first day). Thorax and abdominal CT were normal after three cycles with the same regimen. Anastrazole 1mg p.o. was started progesteron hormone receptors were positive. The patient has been followed-up for since one year after the initial diagnosis. There were no recurrences of either invasive ductal carcinoma or lymphoma. Informed consent was obtained from the patient for publication.

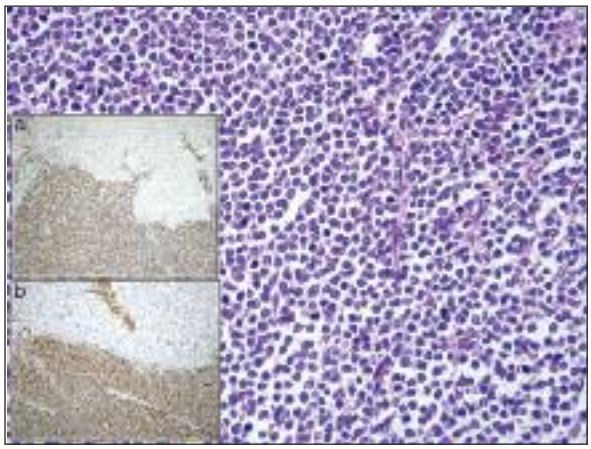

FIGURE 2: Marginal zone lymphoma, details of tumor cell morphology (H&E, x400, **a)** bcl-2, x100, **b)** CD 20, x200).

CONCLUSION

Only few cases have been reported with breast carcinoma occurring simultaneously (tumors diagnosed within a 6-month period) with lymphoma in the axillary lymph nodes. These tumors show two different distributions in the ipsilateral axillary lymph nodes; 1- Both breast carcinoma metastasis and lymphoma involvement were present either in the same or in the different nodes.[1-7] 2- Axillary lymph nodes were involved with lymphoma proliferation without breast carcinoma metastasis. In this condition, lymphomatous infiltration was identified unexpectedly in patients who underwent sentinel lymph node procedure or axillary dissection after the diagnosis of breast carcinoma in their biopsy materials.[5,8,9] Therefore, careful examination of axillary lymph nodes is important for exact diagnosis and staging of the tumors.

Caraway et al.[2] reported a case with synchronous malignancies initially diagnosed by fine-needle aspiration cytology (FNAC). The diagnosis was then supported with immunohistochemistry and flow cytometry. A 62-year-old woman presented with a mass in her left abdomen, weight loss and a right breast mass. Physical examinations and radiological evaluations revealed a mass in the axillary tail of her right breast with local erythema and skin ulceration as well as right axillary lymphadenopathies. FNAC of the axillary lymph node showed hypercellularity composed of both lymphoid and epithelial cell populations. The epithelial cell groups had large cytoplasm with irregular nuclear membranes and prominent nucleoli. The lymphoid cells showed a uniform population of small, round cells with coarsely clumped chromatin and inconspicuous nucleoli.

Sentinel lymph node biopsy (SLNB) is a technique performed increasingly in cases without palpable axillary lymph nodes (clinically node negative).[10] It is controversial whether the SLNB procedure applies in cases with synchronous tumor in their axillary lymph nodes. Benoit et al.[5] reported a 53-year-old woman with the complaint of a suspicious breast mass. Eleven years earlier she was diagnosed with Waldenstrom's macroglobulinemia. SLNB was performed and two sentinel lymph nodes were identified. Both had lymphoproliferative infiltration alone without any carcinoma metastasis, therefore, the axillary dissection was completed. Interestingly, a carcinoma metastasis with extracapsular spread was found in one out of nine non-sentinel lymph nodes. Authors mention that false negativity of SLNB procedure may arise from concurrent infiltration by lymphoma and this may cause inappropriate staging of breast carcinoma. In the case of Barrenger et al.[3] however, SLNB could be performed succesfully and the involvement of both tumors were revealed. A 61-year-old woman presented a palpable breast tumor (8 mm) in the left upper external quadrant and clinically negative axillary lymph nodes. She underwent lumpectomy with SLNB and two sentinel lymph nodes were found in the ipsilateral axilla. Metastatic carcinoma (2 mm) was found in one of two sentinel lymph nodes and then axillary lymph node dissection was completed. All 21 non-sentinel lymph nodes showed lymphoma infiltration (follicular B-cell lymphoma) but no evidence of breast cancer metastasis.[3]

To the best of our knowledge, six concomitant breast carcinoma metastasis and lymphoma infiltration cases have been reported in the same ipsilateral axillary lymph node. Five of these six cases had low grade B-cell non-Hodgkin Lymphoma (follicular lymphoma, small lymphocytic lymphoma, Waldenström type lymphoma and extranodal marginal zone lymphoma) and one had high grade B-cell non-Hodgkin Lymphoma (diffuse large cell lymphoma).

Consequently, it is important to identify coincident tumors for proper treatment. The possibility of simultaneous breast carcinoma and lymphomatous involvement should be taken into consideration in the presence of bulky axillary lymph nodes (unilateral or bilateral) and/or cervical/supraclavicular lymphadenopathies with a relatively small size breast mass by clinic/radiologic examinations. Careful histopathological examination as well as immunohistochemical staining is important for the correct diagnosis.

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REFERENCES

1. Ambrosiani L, Bellone S, Declich P, Tavani E, Pavia GF. Breast carcinoma metastatic to a lymphoma: report of a case with review of literature. Histopathology 1999;34(1):87-9.
2. Caraway NP, Wojcik EM, Saboorian HM, Katz RL. Concomitant lymphoma and metastatic carcinoma in a lymph node: diagnosis by fine-needle aspiration biopsy in two cases. Diagn Cytopathol 1997;17(4):287-91.
3. Barranger E, Marpeau O, Uzan S, Antoine M. Axillary sentinel node involvement by breast cancer coexisting with B-cell follicular lymphoma in nonsentinel nodes. Breast J 2005;11(3):227-8.
4. Pandey U, Naraynan M, Karnik U, Sinha B. Carcinoma metastasis to unexpected synchronous lymphoproliferative disorder: report of three cases and review of literature. J Clin Pathol 2003;56(12):970-1.
5. Benoit L, Arnould L, Collin F, Fraisse J, Cuisenier J, Chauffert B. Concurrent lymphoma and metastatic breast carcinoma in the axillary, confounding sentinel lymph-node biopsy. Eur J Surg Oncol 2004;30(4):462-3.
6. Susnik B, Jordi Rowe J, Redlich PN, Chitambar C, Chang CC, Kampalath B. A unique collision tumor in breast: invasive ductal carcinoma and mucosa-associated lymphoid tissue lymphoma. Arch Pathol Lab Med 2004;128(1):99-101.
7. Broughton A, Galant C, Hainaut P. Simultaneous occurrence of metastatic breast cancer, Hodgkin's disease and tuberculous lymphadenitis in homolateral axillary lymph nodes--a case report. Acta Clin Belg 2008;63(6):391-3.
8. Cox J, Lunt L, Webb L. Synchronous presentation of breast carcinoma and lymphoma in the axillary nodes. Breast 2006;15(2): 246-52.
9. Dutta Roy S, Stafford JA, Scally J, Selvachandran SN. A rare case of breast carcinoma co-existing with axillary mantle cell lymphoma. World J Surg Oncol 2003;1(1):27.
10. Özmen V. [Sentinel lymph node biopsy]. Turkiye Klinikleri J Surgery 2002;7(2): 78-90.