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

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


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


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.
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 (-), Progesterone 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 follicles 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.

**CASE REPORT**

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

<table>
<thead>
<tr>
<th>Author</th>
<th>Age, Sex, Presentation</th>
<th>Pathologic diagnosis of breast lesion</th>
<th>Pathologic diagnosis of axillary lymph nodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ortega P Jr et al. 1951</td>
<td>76, F, breast mass (left)</td>
<td>Breast carcinoma metastasis in ALNs involved with chronic lymphocytic leukemia</td>
<td>All 21 ALNs include only follicular B-cell lymphoma</td>
</tr>
<tr>
<td>Woolam GL et al. 1966</td>
<td>67, F, breast lump (right)</td>
<td>Invasive ductal carcinoma, poorly differentiated</td>
<td>SLN procedure was applied, 3 ALNs included both breast carcinoma metastasis and lymphoma</td>
</tr>
<tr>
<td>Caraway NP et al. 1997</td>
<td>62, F, mass in right breast axillary tail</td>
<td>Invasive ductal carcinoma, Black’s nuclear grade 2 by FNAC</td>
<td>SLN procedure was applied, one SLN included both breast carcinoma metastasis and lymphoma</td>
</tr>
<tr>
<td>Ambrosiani L et al. 1999</td>
<td>67, F, breast lump (right)</td>
<td>Invasive ductal carcinoma, poorly differentiated</td>
<td>SLN procedure was applied, one SLN included both breast carcinoma metastasis and lymphoma</td>
</tr>
<tr>
<td>Barnes R et al. 2005</td>
<td>61, F, NA</td>
<td>Invasive ductal carcinoma, grade 2</td>
<td>SLN procedure was applied, one SLN included both breast carcinoma metastasis and lymphoma</td>
</tr>
<tr>
<td>Pandey U et al. 2003</td>
<td>75, F, breast mass (left)</td>
<td>-</td>
<td>Three ALNs include both breast carcinoma metastasis and lymphoma</td>
</tr>
<tr>
<td>Present 2009</td>
<td>66, F, swelling in left axillary region</td>
<td>Invasive ductal carcinoma, grade 3 and Paget’s disease</td>
<td>The rest of all 20 ALNs include only marginal zone B-cell lymphoma</td>
</tr>
</tbody>
</table>

NA: not available, F: female, FNAC: fine-needle aspiration cytology, SLN: sentinel lymph node, ALNs: axillary lymph nodes.
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 cyclophosphamide (600 mg/m², first day) and doxorubicine (60 mg/m², 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.

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.\textsuperscript{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).\textsuperscript{10} It is controversial whether the SLNB procedure applies in cases with synchronous tumor in their axillary lymph nodes. Benoit et al.\textsuperscript{5} reported a 53-year-old woman with the complaint of a suspicious breast mass. Eleven years earlier she was diagnosed with Waldenström’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.\textsuperscript{3} however, SLNB could be performed successfully 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.\textsuperscript{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


