Case Report

Bilateral Low-Grade B-Cell Lymphoma of the Breast: A Case Report with Cytological, Histological and Immunohistochemical Studies

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A 45-year-old woman presented with bilateral palpable breast masses, which were clinically suspicious of either mammary carcinomas or phyllodes tumors. Fine needle aspiration (FNA) study suggested low-grade lymphoma. Histological and immunohistochemical studies of an incisional biopsy specimen of the left breast lesion confirmed the diagnosis of low-grade B-cell lymphoma. Computerized tomographic scans of chest and abdomen revealed multiple lymphadenopathy in the mediastinum and intra-abdomen. After receiving chemotherapy, marked reduction in size of both breast masses and the internal lymph nodes was observed. Primary lymphomas of the breast are rare, particularly those with bilateral involvement.

FNA is an inexpensive diagnostic tool for breast lumps that can reliably distinguish carcinoma, sarcoma and lymphoma. Although it is often difficult for the cytological study to differentiate low-grade lymphoma from reactive lymphoid proliferation, FNA results in combination with clinical and radiological studies (triple testing) generally provide guidance for appropriate investigations, and helps avoiding unnecessary major operation.

Keywords: *Breast, Breast neoplasms, Biopsy, Fine-needle, Cytology, Lymphoma*

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Lymphomas of the breast, both primary and secondary, are rare particularly those with bilateral involvement[1]. Primary breast lymphoma only accounts for 0.04-0.5% of primary breast cancer and 2.2% of extra-nodal lymphoma, most of which belongs to the category of diffuse large B cell lymphoma[2-4]. Secondary breast lymphoma could be part of a disseminated disease of either primary or recurrent cases.

Fine needle aspiration (FNA) cytology is a reliable method for investigation of lymphadenopathy[5], and plays a role in the diagnosis of non-Hodgkin's lymphoma (NHL)[6]. However, the usefulness of FNA cytology in the classification of lymphoma remains controversial, particularly in low-grade lesions[7]. Here, the authors report a case of primary breast lymphoma with bilateral involvement. Our case demonstrates that FNA study can provide guidance towards appropriate investigations for definite diagnosis, and helps avoiding unnecessary major operation.

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Case Report

A 45-year-old woman presented with bilateral palpable breast masses, which had gradually increased in size for over 7 months. There was no family history of breast cancer or history of autoimmune disease. On examination, large non-tender masses were noted on both breasts, 5 cm in the right and 5.8 cm in the left. There was no nipple discharge or skin retraction detected. The axillary lymph node was not palpable. Clinical differential diagnosis included mammary carcinoma and phyllodes tumor with bilateral involvement.

FNA, performed on both breast masses, revealed similar findings. The smears were high in

cellularity, and comprised predominately of intermediate-sized lymphoid cells. They were interspersed with a few small mature and large transformed lymphocytes (Fig. 1). A few mitotic figures were noted, with no identifiable tingible body macrophages. Lymphoglandular bodies were found in the background. Low-grade lymphoma of both breasts was suggested on the cytological ground, and this result prompted further investigations, including histological and immunohistochemical studies, computerized tomographic (CT) scans of the chest and abdomen, and bone marrow biopsy for staging.

Incisional biopsy, performed on the left breast lesion, displayed loosely cohesive sheets of small-to-intermediate-sized lymphoid cells, with open chromatin (Fig. 2). The nucleoli were absent or inconspicuous, and the cytoplasm was scant. Lymphoid cells with a moderate amount of cytoplasm, "monocytoid features", were focally noted. There were also a few benign ducts noted among these cells, but no lymphoepithelial lesion was observed. On immunhistochemical study, the atypical lymphoid cells were reactive with CD20 and bcl2 but not with CD45RO. No infiltration of atypical cells among epithelial cells of residual ducts was demonstrated by cytokeratin stain. Together with the histological findings, diagnosis of low-grade B-cell lymphoma was confirmed.

CT chest and abdomen scans demonstrated bilateral breast masses, multiple lymphadenopathy in the mediastinum and intra-abdomen. No bone marrow involvement was noted on biopsy study. Mammographic study was not performed at the time of diagnosis due to limitation of service when prompt treatment was required. Results of other laboratory investigations, including complete blood count, liver function test and blood chemistry, were within normal limits. Low-grade B-cell lymphoma, stage IV (by the Ann Arbor staging system), was finally documented. The patient received cyclophosphamide, vincristine, and prednisolone. After six cycles of treatment, both breast masses were markedly decreased in size (the right and left lesions measured 2.4 cm and 2 cm, respectively), so were the previously enlarged lymph nodes.

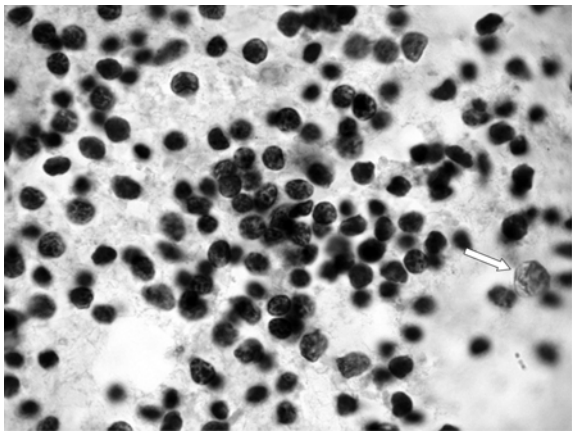

Fig. 1 FNA cytology consists of intermediated-sized lymphoid cells, with a small number of small lymphocytes. A transformed lymphocyte is shown (arrow) (Papanicolaou stain x400)

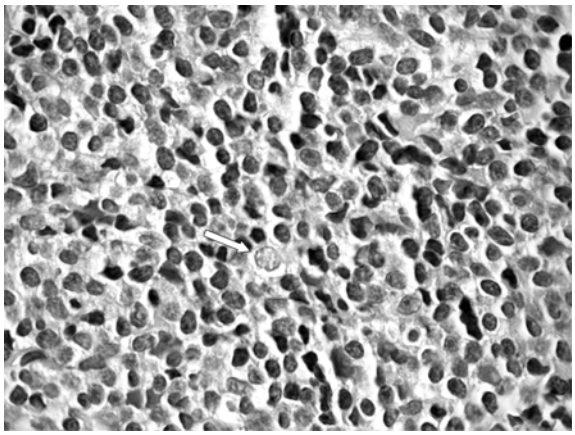

Fig. 2 Histologic section shows loosely cohesive sheets of intermediate-sized lymphoid cells. A transformed lymphocyte is shown (arrow) (H&E stain x400)

Discussion

Breast lymphoma is a rare entity, which occurred mostly in women. For unknown reasons, the right breast is more commonly affected than the left[8]. The age at diagnosis ranges between 22-75 years (mean, 50 years)[1]. Most patients presented with a breast lump, with variable radiological findings; mass with well-defined, partially-defined, or irregular margins could be encountered[1]. Clinical presentations and radiological features of breast lymphoma may, thus, mimic those of mammary carcinoma. Skin retraction, nipple discharge, and calcification on a mammography are, however, especially uncommon to breast lymphoma[1,9].

Although the role of FNA cytology in the diagnosis of lymphoma remains debatable, particularly in low-grade lymphoid neoplasms[7], cytological study can often distinguish between lymphoma and

carcinoma. Nevertheless, since breast lymphoma is very uncommon and constitutes only 0.01% of breast cancer in our institute, it is so heavily outnumbered by mammary carcinoma. Awareness of the hematological malignancy is, hence, crucial for accurate cytological diagnosis because lymphoma is unlikely to be suspected by the clinician, as in our case.

Because of the heterogenous morphologic features, diagnosis of low-grade lymphoma on the cytological specimens is often difficult[10], and this fact has again been highlighted in the presented case in which definite cytological diagnosis of lymphoma could not be made. Flow cytometry study on cytological specimens has been shown to be helpful for diagnosing low-grade lymphoma[11,12], but the technique is not available in the majority of diagnostic laboratories, including ours. Even so, the cytological suggestion of low-grade lymphoma in the presented case was enough to result promptly in tissue biopsy with immunohistochemical study, CT scans of chest and abdomen, and bone marrow biopsy. All of these subsequent tests lead to the definite diagnosis and staging of low-grade B cell lymphoma, without unnecessary major operation to the breast.

Because of the rarity of breast lymphoma, the prognosis and therapeutic management is still uncertain. Intensive treatment is recommended by some studies[13]. Although low-grade lymphoma of the breast tends to remain localized, one study found that the majority of disseminated lymphomas involving the breast were of the low-grade subtype, as in this patient[14].

In conclusion, although rare, malignant lymphoma should always be kept within the differential diagnosis of breast mass. In combination with clinical and radiological findings, known as a triple test, FNA study can still provide guidance for appropriate investigations, and also helps avoiding an unnecessary major operation.

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ลิมโฟมาชนิดเซลล์บีที่มีเกรดต่ำ ของเต้านมทั้งสองข้าง: รายงานผู้ป่วย โดยมีการตรวจวินิจฉัยทั้งทางเซลล์วิทยา, ฮิสโตโลยี และอิมมูโนฮีสโตเคมี

เบญจพร ไชยวรรณ์, นีลยา สุคำวัง, ชรินทร์ ยาอินทร์, ชนพ ช่วงโชติ

ผู้ป่วยหญิงไทยอายุ 45 ปี คลำพบก้อนที่เต้านมทั้งสองข้าง จากการตรวจร่างกายได้รับการวินิจฉัยโรคเบื้องต้นว่าเป็นมะเร็งเต้านมชนิดคาร์ซิโนมา หรือเนื้องอกฟิลโลด ที่เกิดกับเต้านมทั้งสองข้าง ผลการตรวจเซลล์วิทยาด้วยการเจาะดูดด้วยเข็มเล็ก สงสัยลิมโฟมา ผลการตัดชิ้นเนื้อบางส่วนจากก้อนที่เต้านมซ้าย ที่ตรวจทางฮีสโตโลยีร่วมกับการตรวจทางอิมมูนโนฮิสโตเคมี พบเป็นลิมโฟมาชนิดเซลล์บีที่มีเกรดต่ำ จากการตรวจโดยเครื่องเอกซเรย์คอมพิวเตอร์พบมีต่อมน้ำเหลืองโตในช่องท้องและ mediastinum ผู้ป่วยได้รับการรักษาโดยเคมีบำบัด เมื่อได้รับยาครบ 6 ครั้ง พบว่าก้อนที่เต้านมทั้งสองข้าง และต่อมน้ำเหลืองมีขนาดเล็กลงอย่างชัดเจน ลิมโฟมาที่เกิดปฐมภูมิในเต้านมพบได้น้อย โดยเฉพาะที่เกิดกับเต้านมทั้งสองข้าง การตรวจทางเซลล์วิทยาโดยการเจาะดูดด้วยเข็มเล็กมีราคาไม่แพง และยังสามารถช่วยแยกเนื้องอกชนิดต่าง ๆ ของเต้านมได้อย่างแม่นยำ รายงานนี้แสดงถึงประโยชน์ของการตรวจทางเซลล์วิทยาโดยการเจาะดูดด้วยเข็มเล็กในการวินิจฉัยก้อนที่เต้านม เพื่อให้ได้การวินิจฉัยเบื้องต้นซึ่งนำไปสู่การตรวจเพิ่มเติมที่เหมาะสม และหลีกเลี่ยงการผ่าตัดใหญ่ซึ่งไม่จำเป็น เช่นในผู้ป่วยรายนี้