

# Primary diffuse large B-cell lymphoma of the breast

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## SUMMARY

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**Primary breast lymphoma is rare location of this disease. Diffuse large B-cell lymphoma is the most common histological subtype. We presented two cases of primary diffuse large B-cell lymphoma of the breast and reviewed a literature about this topic.**

**Key words:** Breast Neoplasms; Lymphoma, B-Cell

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## INTRODUCTION

Breast lymphomas present 0.5% of all breast tumors and 0.7% of all non-Hodgkin lymphomas (NHL) (1). Wiseman and Liao (2) proposed the criteria for defining a primary breast lymphoma (PBL) and those criteria include adequate pathological specimen, anatomic association with breast tissue, and lymphomatous infiltrate with no other lymphoma focus at the time of diagnosis except for the presence of compromised ipsilateral axillary lymph nodes and absence of previous extramammary lymphoma. Since those criteria were established in 1972, modern authors include the definition of PBL cases in which breast is the first or major site of presentation, even if staging procedures show the involvement of distant sites or bone marrow (3). PBL accounts about 2% of all extranodal lymphoma (4) and most of the cases are B-cell lymphoma, diffuse large B-cell type (5-7). In this paper, we presented two cases of primary diffuse large B-cell lymphoma of the breast.

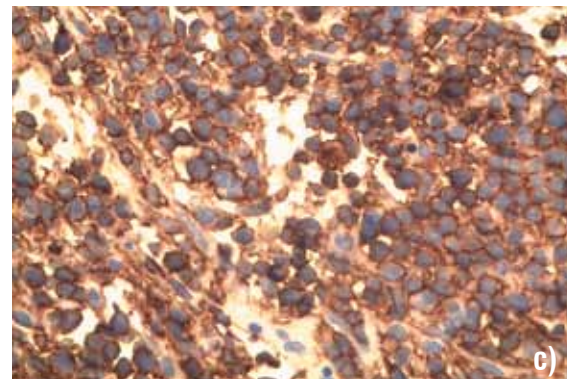
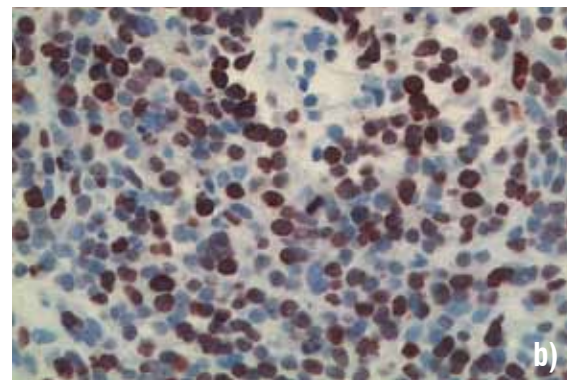
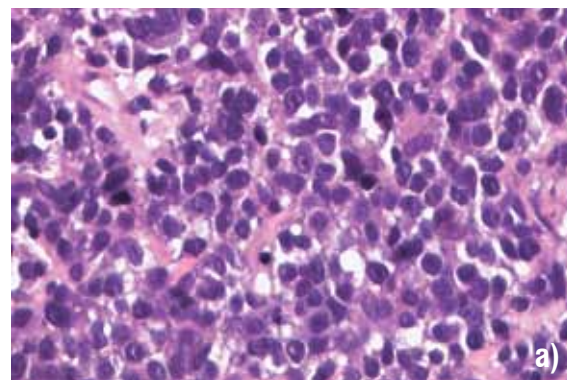
## CASE REPORTS

### Case #1

A 53-years old woman came to our institution with infiltrated left breast, ulceration within areola, and conglomerate of lymph nodes in ipsilateral axilla. She had severe pain, decreased mobility of left hand, and night sweats. Her father died from neck cancer and mother and brother had cardiovascular diseases. Probably the onset of a disease with first changes in her left breast had occurred six months before she came to our clinic. Three months later, she noticed enlarged lymph nodes in axilla. Core biopsy was performed in our institution and preliminary histopathology findings, without immunohistochemistry analysis, suggested it was a case of breast cancer. Immunohistochemical findings were LCA+, CD20+, CD79alpha+, CD3-/+, CD5-/+, CD45RO-/+, and the final diagnosis was diffuse large B-cell lymphoma (DLBCL) (Figure 1).

Chest CT showed massive tumor of the left breast 9,5x10cm, with areola infiltration and necrotic center. Lateral of this tumor were two smaller lymph nodes. Big conglomerate of lymph nodes was found in left axilla, 5 x 2.5cm, a conglomerate in mediastinum, and pleural effusion with atelectasis (Figure 2). Abdominal CT showed spleen infiltration. Bone marrow was without lymphoma cells so patient was in stage IIIB according to Ann Arbor classification. Complete blood count detected anemia, hemoglobin 88g/l and leucopenia 2.8g/l. LDH was 1.5 times above upper limit and other results of biochemistry analysis were normal. We decided to start therapy with rituximab (R) + CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisolone) and symptomatic therapy with analgesics and fluids. During six cycles of immunochemotherapy patient had grade 2 of leucopenia and no other adverse event. After six cycles, CT scan showed reduction of tumor mass in breast to 4 x 4.5 cm and complete disappearance of axillary and mediastinal lymphadenomegaly, and disappearance of spleen infiltration. Ultrasound examination of breast showed the presence of 3.5 cm large lesion. LDH and CA 15-3 markers were normal.

We continued treatment with two more R-CHOP cycles, which were followed by a control CT. The obtained CT results were similar to those obtained after 6 cycles of therapy. At that time, we did not have PET-CT so we did a rebiopsy. Histopathological finding was fibrosis without signs of malignancy. The patient is now in good condition and still is in complete remission after 2 years of follow up.



**Figure 1. Histopathology with immunohistochemistry; Patient # 1 (a – HE 40x, b – Ki67 65-70%, c – CD20+)**

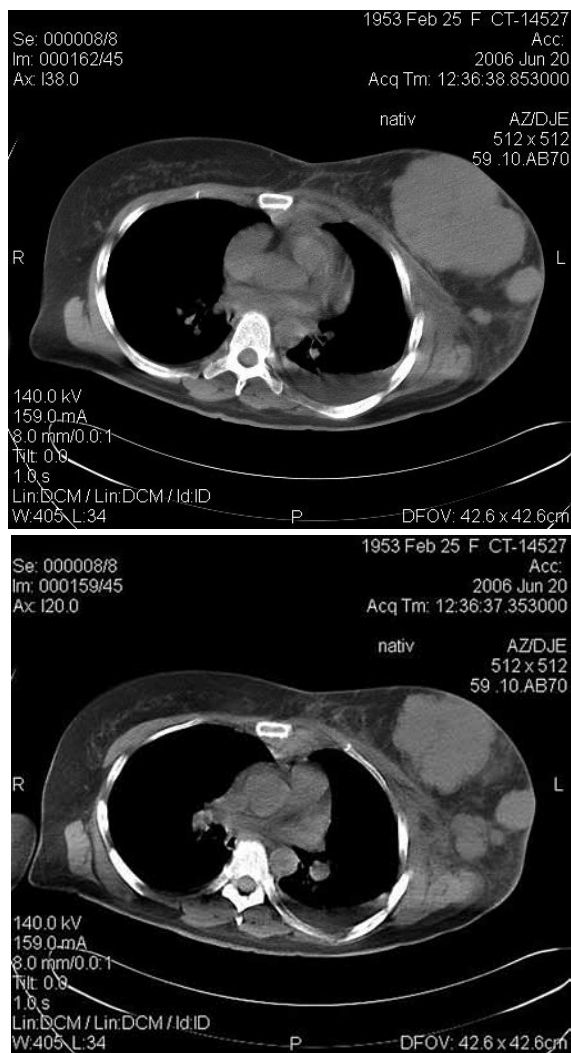


Figure 2. Chest CT; Patient # 1

### Case #2

A 74-year-old woman has noticed a few nodes in her left breast. She went to see her doctor who referred her to a surgeon. Extempore histopathological analysis showed malignant cells and complete mastectomy and axilla evacuation was preformed. Final histopathological finding was diffuse large B-cell lymphoma. Immunohistochemistry results were CD20+, CD79alpha+, CD5+, CD3+, bcl-2+, CD30-, CD23-, CD43-, CD15-, Ki67 about 70%. Based on those findings the patient was referred our institution. The patient complained of weight loss (over 10 kg in less than 6 months), night sweats, and back pain. She had a medical history of hypertension for 15 years. She has never smoked nor has she abused alcohol. There were no hereditary diseases among the member of her family. Complete blood count results detected pancytopenia: hemoglobin 86 g/l, white blood cells 3.3 g/l, and platelets 141 x 109. LDH result was normal; patient had low albumin and high beta-2-microglobuline. Chest and abdominal CT did not show any signs of lymphoma, and only dilatative cardiomyopathy was found. We started R-CVP (rituximab, cyclophosphamide, vincristine, prednisolone) immunochemotherapy protocol. Patient received six cycles with only depression occurring as adverse event. She is in a complete remission for a year.

### DISCUSSION

Primary breast lymphoma is rare localization of this disease. Only 0.7% of all and 2% of extranodal NHL are localized in breast. In our institution for a past three years, we treated five patients for breast involving lymphoma (8). Two of those cases were primary and three were secondary lymphoma of the breast. As in most series (4-7), in our institution DLBCL was most common subtype. Fifteen retrospective and just one prospective study were published about breast lymphoma (4,9). Most of those papers include all subtypes of lymphoma and only retrospective International extranodal lymphoma study group (IELSG) study, assigned DLBCL (4). In that study, 204 patients with primary DLBCL of breast were included. Median age was 64 years and 5% of patients had bilateral disease. Median overall survival was 8 and median progression free survival was 5.5 years. They observed poorer prognosis, comparing to other early stage DLBCL on other localizations, in patients with breast DLBCL, but only in anthracycline naïve patients. Patients who received anthracycline containing regimen and radiotherapy had similar outcome as patients with DLBCL on other localizations. Our two patients received only chemotherapy - eight and six cycles, respectively. Our patient #1 received doxorubicin-containing regimen and patient #2 did not. The reasons for excluding doxorubicin were old age, cardiac disease, and absence of lymphoma after complete surgery. Another conclusion of that study is that international prognostic index (IPI) score (10) is significant prognostic factor for overall, progression free, and cause specific survival (4). Some of the studies show relatively often relapse in central nervous system (CNS) 5% to 29% (5, 6, 7), but IELSG study shows relatively low incidence under 5% (4). In 5 of our breast lymphoma patients, we did not have any CNS relapses (8). Mastectomy does not improve outcome in breast lymphoma and should be avoided (4-7). Our patient #2 had mastectomy and axilla evacuation in another institution, because she was treated as a breast cancer without a core biopsy. We gave to that patient "adjuvant" immunochemotherapy because of poor prognosis of patients without any further treatment after surgery (4,5). Rituximab is golden standard in DLBCL (11,12). Although primary breast lymphoma was poorly represented in rituximab-containing trials in DLBCL, there is not much experience with this agent in breast DLBCL. We include rituximab in therapy of both patients because of good experience with that agent in other types of lymphoma. In conclusion, we consider that recommendation given by IELSG should be accepted for the treatment of primary breast DLBCL. Those criteria recommend limited surgery/biopsy, followed by three or more cycles of anthracycline-containing chemotherapy + radiotherapy to the ipsilateral breast and possibly regional nodes. CNS prophylaxis should not be indicated routinely. Patients with bilateral disease appear to be in poor prognosis group and intensification of chemotherapy should be considered (9). Use of rituximab in this setting remains investigational, but we use and recommend usage of this agent due to very good results both in nodal and extranodal DLBCL.

### Conflict of interest

We declare no conflicts of interest.

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### Errata

In the article titled *Metastatic renal hemangiopericytoma: A rare case report*, A. Bilici et al. (*Arch Oncol*, Vol. 17, No. 1-2, p. 32-5) a reference No. 47: *Brescia A, Pinto F, Gardi M, Maria Vecchio F, Bassi PF. Renal hemangiopericytoma: case report and review of the literature. Urology. 2008;71(4):755. e9-12.*, was omitted by technical oversight. We apologize to the authors and the readers of *Archive of Oncology*.

Editorial Office