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Jacobs Journal of Clinical Case Reports

Case Report

Breast Lymphoma. Report of 2 Cases and Review of Literature

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Received: 07-28-2015

Accepted: 08-20-2015

Published: 09-03-2015

Abstract

Breast lymphoma is an uncommon lymphoma and rare type of breast cancer. Primary breast lymphoma represents 1% of all extranodal lymphomas and close to 0.7% of all lymphomas. Primary breast lymphoma can present as an aggressive disease with aggressive histology and mimics breast carcinoma in age distribution. It is usually unilateral. In pregnant and lactating females, primary breast lymphoma is typically bilateral. DLBCL is the most frequent histopathological subtype. Staging relies on physical exam, CT scan, or better FDG PET scan. Treatment follows guidelines and recommendations of lymphoma therapy. Chemotherapy using anthracycline based regimen is the preferred treatment. Radiotherapy may be used as part of the adjuvant regimen, or as single modality primary therapy for local only disease. CNS prophylaxis is indicated in aggressive histologies and higher stages. We present herein 2 cases of breast lymphoma. The first case in the peripartum and may have appeared during pregnancy and the second in a postmenopausal woman.

Introduction

Breast lymphoma is an uncommon lymphoma and rare type of breast cancer. It accounts for about 0.1% of all breast malignancies and 1 to 2 percent of all extranodal lymphomas [1]. Primary breast lymphoma represents 1 % of all extranodal lymphomas and close to 0.7% of all lymphomas. Secondary involvement of the breast by systemic lymphoma is the commonest metastatic disease to the breast, its reported incidence is similar to the primary Breast NHL. This is typically, but not exclusively, a disease of older women, with a median age in the Western societies of 62 to 64 years, 60% of the affected women older than 60 years [2].

While PBL is a cancer of the elderly women, and the majority of patients are diagnosed between age 60 and 65 years, cases diagnosed between ages 16 and 77 years are reported in the English literature.

Diagnostic criteria of primary breast lymphomas, or secondary breast lymphoma (metastatic to the breast) are not clearly defined, both entities not being recognized as such by the WHO classification. In our review we describe the most commonly used criteria in the medical literature in this regard. These are outlined below in the discussion.

We present herein 2 cases of Diffuse Large B Cell Lymphoma diagnosed in the same group practice. The first case in a young lady, diagnosed shortly after delivery and may have appeared during her pregnancy, the second was diagnosed in a post menopausal lady.

Case Presentation

Case 1

A 32-year-old lady, presented with a 2 months history of worsening abdominal discomfort, epigastric and back pain with intermittent episodes of diarrhea, immediately after giving birth to her second child. An abdominal ultrasound revealed large matted retroperitoneal lymphadenopathies with a diameter of 10 cm. A contrast enhanced CT scan of the neck chest abdomen and pelvis revealed only a bulky retroperitoneal conglomerate of 9x7 x5 cm.

A CT guided biopsy was performed and pathology reported Large B Cell Non Hodgkin Lymphoma with positive LCA, CD20, CD79a and BCL2. The index of proliferation was high with a Ki-67 is of 50%. She had no B symptoms.

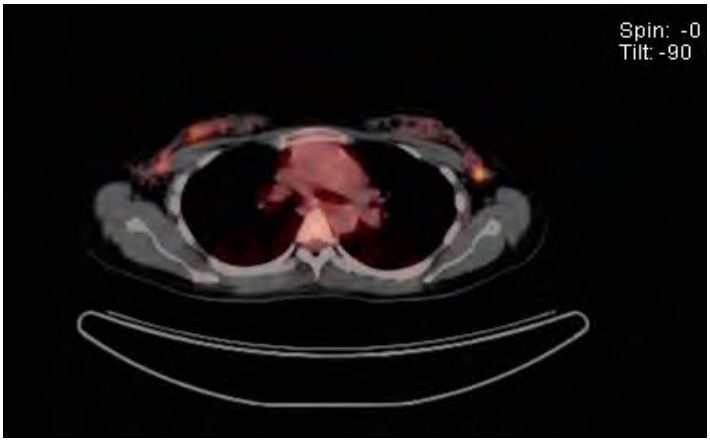

Figure 1. PET CT Scan of Case 1.

Note the bilateral FDG avid lesions in the glands.

An FDG PET CT scan was obtained for staging and revealed multiple hepatic lesions and multiple bilateral FDG Avid breast lesions (Figure 1 and 2); biopsies were taken from both breast lesions and were positive for lymphoma (Figure 3). Bone marrow biopsy was negative for lymphoma involvement, final stage was IV AE. Baseline echocardiogram showed an LVEF > 60%.

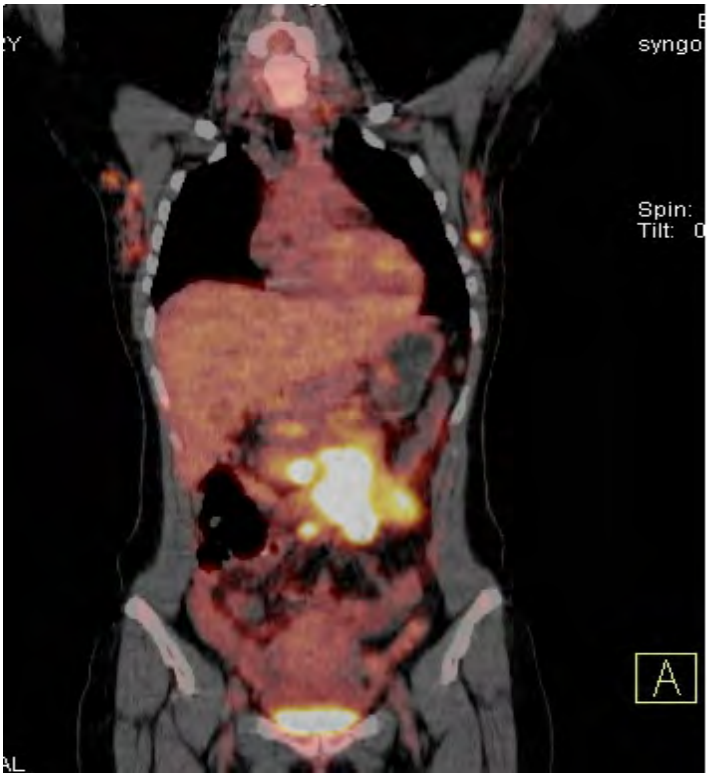

Figure 2. Coronal image from the PET CT Scan of Case 1.

Note the bilateral FDG avid lesions in the breasts, and the retroperitoneal FDG avid and enlarged lymph nodes.

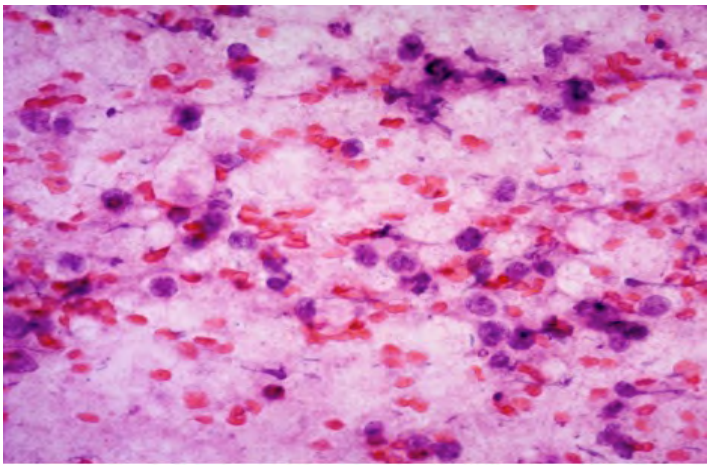

Figure 3. From the FNA of breast lesions of patient in case 1.

Breast smear x400: neoplastic lymphoid cells are seen in the smears.

While the systemic involvement and non Burkitt histology made of the diagnosis of primary breast lymphoma an assumption. The younger age of the patient, bilateral breast involvement, peri-partum presentation and possible occurrence during pregnancy, favored primary breast lymphoma as the most likely diagnosis, nevertheless treatment being the same, once staging completed, it was initiated.

She was started on birth control pills, and offered R-CHOP based combination with intrathecal methotrexate for prophylaxis with the first 4 treatments.

We documented complete remission by FDG PET criteria and CT scan criteria following 3 cycles and the patient received a total of 6 cycles. She remained in complete remission at her most recent follow up 3 1/2 years after therapy.

Case 2

A 64-year-old lady presented following left breast lumpectomy for a homogeneous well circumscribed lesion seen on screening mammography (Figure 4). Pathology examination reported diffuse large B cell lymphoma, immunostains revealed that the tumor cells expressed CD20, and BCL2 while negative for (CD5, CD10 and CD3) (Figure 5). Staging comprised PET scan reporting only minimal activity in the surgical cavity at the initial site. A bone marrow biopsy and a lumbar puncture, both bone marrow and cerebrospinal fluid were uninvolved.

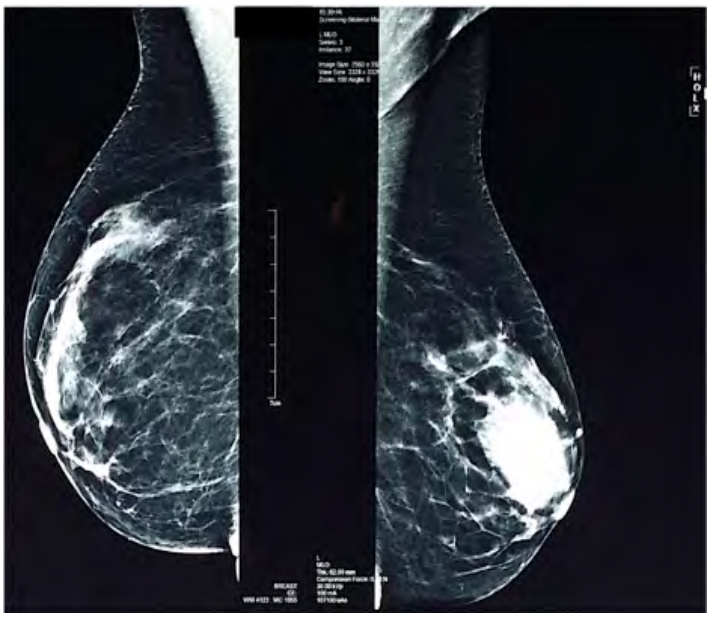

Figure 4. Mammography of patient in case 2.

Note the oval shaped, well-circumscribed hyperdense mass seen on the left.

She received 6 cycles of R-CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisolone plus rituximab) with intrathecal methotrexate with the 4 first cycles, and involved field radiotherapy. She attained a complete remission following two cycles only and remains today in remission more than 2 years after completion of treatment.

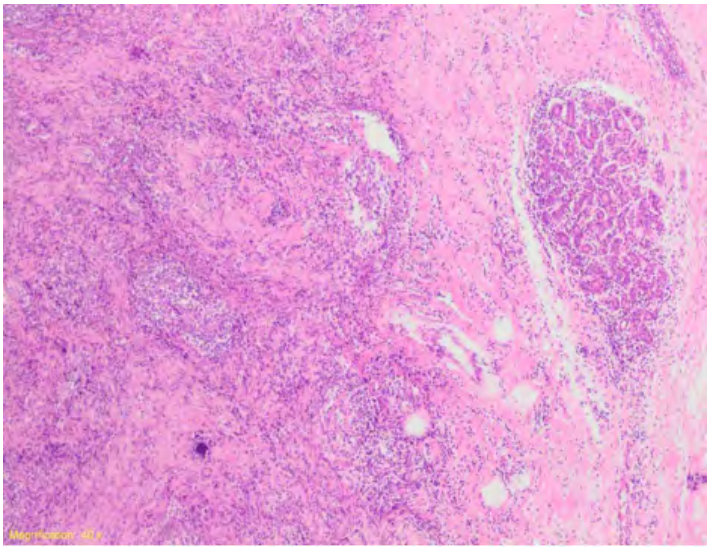

Figure 5. Pathology of Case 2.

HE 40x. Shows the infiltrate of neoplastic lymphoid cells with adjacent normal breast tissue.

Discussion

Breast Lymphomas are divided in two groups, primary breast lymphomas and secondary disease to the breast. In 1972, Wiseman and Liao defined primary breast lymphomas as lymphomas that were found primarily in the breasts, they had to have close association to mammary tissue, and they should not show any signs of systemic or extra-mammary lymphoma, except simultaneous ipsi-lateral axillary node involvement. In contrast, lymphomas which rather than that involved the breasts after the disease had progressed or relapsed were considered secondary breast lymphomas [4]. Primary breast lymphoma can present as an aggressive disease with aggressive histology and mimics breast carcinoma in age distribution. It is usually unilateral but can be bilateral in 4-13% of the cases at the time of diagnosis [5]. The unilateral type affects the right breast more than the left and is mainly represented by B-cell Non Hodgkin Lymphoma CD20+, usually diffuse large B cell lymphoma [6]. In pregnant and lactating females, primary breast lymphoma is typically bilateral and is further characterized by widespread dissemination with prominent ovarian and central nervous system involvement, and characteristic histological findings identical to those of Burkitt lymphoma have been reported in African women [7]. It has a very poor prognosis [8]. The definition of PBL unfortunately cannot comprise more advanced

cases of breast lymphomas that may have spread beyond the axilla, or stage II and above. These would therefore be considered as secondary breast lymphoma. Breast Lymphoma has also been reported in men, systemic "B" symptoms (ie, fever, weight loss, night sweats) are uncommon [1].

Radiographically, it is shown as non specific circumscribed masses that lack calcification or retraction on mamography [9]. A large biopsy is needed for histological diagnosis. A fine needle aspiration may lead to the diagnosis but may not be sufficient for classification [3]. On pathology, the most frequent histopathological type is DLBCL accounts for 60-85% of all PBL, while follicular lymphoma, MALT lymphoma, Burkitt's lymphoma and Burkitt-like lymphoma account for the rest [5].

Staging relies on physical exam, CT scan, or better FDG PET CT scan, bone marrow biopsy, and if indicated CSF cytology. Note that it is important to check the contralateral breast as well. The value of magnetic resonance (MR) imaging for the evaluation of breast lymphomas is not yet firmly established, but strong and rapid enhancement of breast lymphomas has been observed on T1-weighted MR images with IV contrast [10,11]. The literature is heterogeneous in terms of staging since primary breast lymphomas are not recognized as a distinct entity in the World Health Organization (WHO) classification [12]. Primary Breast Lymphoma is by definition an extranodal lymphoma, stage IE disease being limited to breast involvement only, and higher stages defined according to the Ann Arbor staging system with minor modifications. However, some experts include lesions that have extended beyond the breast at the time of diagnosis if the breast is the first or major site of presentation, even with involvement of distal nodal sites and/or bone marrow involvement [13].

Treatment of PBL varies widely, and surgical therapy options range from biopsy to modified radical mastectomy. Currently, chemotherapy using various agents is recognized as the preferred treatment [14,15]. S. Ariad et Al. studied and reviewed the treatment of 16 patients with breast lymphoma over 10 years; they found that the initial local control of the breast tumor, whether of the primary or the secondary type, was achieved with chemotherapy alone, irrespective of the chemotherapeutic regimen employed. Only 2 patients were classified as having a partial response but those had evidence of persistent disease at other sites. Local breast disease recurred in 5 patients [16]. Treatment with chemotherapy in stage II patients (node positive) showed benefit in both survival and recurrence rates. Treatment that includes radiation therapy in stage I patients (node negative) shows benefits in both survival and recurrence rates. Mastectomy offers no benefit in the treatment of primary breast lymphoma [17]. Extra-nodal lymphomas are treated by surgery, radiotherapy, and/or chemotherapy [18]. More specifically, the International Extranodal Lymphoma Study (IELSG) demonstrated that diffuse large B cell lymphoma (DLBCL) of the breast treated with combination of limited surgery, anthracycline-containing chemotherapy, and involved field radiotherapy, had the best outcome [19]. Studies with anthracycline based regimen alone or with IFRT report more than 61% of overall survival at 5 years [20], this shows the importance of anthracycline in treating DLBCL PBL. Rituximab use was still controversial until recently, and may not be associated with a survival advantage [21]. More studies on rituximab in this setting are needed. Finally, when treating extranodal lymphomas one should be aware of higher incidence of leptomeningeal dissemination and offer prophylactic intrathecal treatment as indicated, in this particular subtype where the incidence of CNS relapse seemed higher [14].

Survival rate is dictated by the extent of the disease, histological tumor grade and the type of lymphoma [17]. Breast lymphoma, whether it's primary or secondary, has a poorer prognosis than other breast carcinomas [22]. The reported overall survival rate (61%) and the disease free survival rate (46%) are similar to nodal lymphoma of corresponding histology and stages [23]. The median overall survival (OS) is 8 years, and median progression-free survival 5.5 years [19].The five-year and 10-year overall survivals were 57% and 15%, respectively. Bcl-2 positive and Bcl-6 negative patients were associated with worse prognosis [24].

Conclusion

Breast lymphoma is a rare disease but should be on the list of differential diagnoses when imaging studies report benign appearing breast disease. Diagnosis is made by anatomic pathology and immuno-histo-chemistry stains. Combination anthracycline based chemotherapy followed by radiotherapy yields better outcomes. Rituximab added to CHOP is finding its way into the chemotherapy regimen. Mastectomy is not recommended. One should remember it is a primarily extranodal disease, hence CNS prophylaxis is indicated in aggressive histologies and higher stages.

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