

PRIMARY BILATERAL BREAST LYMPHOMA: A REVIEW OF LITERATURE AND REPORT OF FOUR CASES FROM A SINGLE CENTRE

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Abstract

Primary breast lymphoma is a rare entity and carries poor prognosis, bilateral breast lymphoma is even rarer and carries worst prognosis. Bilateral breast lymphoma is a rare disease and lacks treatment. Out of the 2766 cases of non-Hodgkin's lymphoma registered at our institute from 1994 to 2013, 31 cases of breast lymphoma were found, of which four cases had bilateral involvement. In this review, we describe clinical presentation, histopathological subtypes, treatment administered and outcome of those four cases retrospectively. All patients were female with a median age of 31 years (range 24–64 years). Three patients were diagnosed with diffuse large B-cell lymphoma and mucosa-associated lymphoid tissue lymphoma detected in one patient. Chemotherapy remained the main treatment modality and surgery (excision biopsy) was reserved for diagnostic purpose only, none of the patients received radiation therapy.

Key words: Breast lymphoma, histopathological subtypes, palliation

Introduction

Primary breast lymphoma (PBL) is a rare form of breast malignancy and accounting 0.4–0.5% of all breast cancers and 1.7–2.2% of extranodal non-Hodgkin's lymphoma (NHL).^[1] PBLs are classified as disease confined to the breast only in the absence of previously existing lymphoma.^[2] According to Wiseman and Liao criteria, PBL is defined by the presence of following features: (1) Breast should be the primary site, (2) there should be no evidence of the distant organ involvement, (3) tissue sample should be adequate and (4) there should be a close association between breast tissue and lymphoma.^[3] According to this definition, lymphoma confined to the breast alone will be classified as PBL. However, some researchers would also category PBL when bone marrow is involved in addition to lymphoma in the breast.^[4] Bilateral breast lymphoma accounts for about 11% of lymphoma involving the breast, whereas a study of 204 primary diffuse large B-cell lymphoma (DLBCL) patients by Ryan *et al.* showed bilateral breast involvement by lymphoma in only 5% of cases.^[5,6] Cancer registry

at Shaukat Khanum Memorial Cancer Hospital and Research Centre (SKMCH and RC), Lahore, recorded 12,866 cases of breast cancer between December 1994 and December 2013. Amongst those patients, four cases of PBL were identified whose details are given in this case report.

Materials and Methods

Data on four PBL patients treated at SKMCH and RC were collected by review of their case notes using hospital electronic medical records in a retrospective manner. Following patient variables searched: Patients' demographics such as age and gender, presenting clinical symptoms such as B-symptoms and pathological characteristics such as histopathology and immunohistochemistry of breast biopsy as well as bone marrow infiltration and its response to chemotherapy if positive at baseline, details of treatment and measurement of outcome. A formal ethical approval was obtained from the institutional review board.

Case Series

Baseline patient characteristics are shown in Table 1. All patients were female, median age at the time of diagnosis

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was 31 years (range 24–64 years). All patients underwent breast ultrasound, mammogram, bone marrow biopsy and whole-body computed tomography for staging of lymphoma at presentation. Diagnosis was made on review of the blocks as all four patients had undergone lumpectomy at peripheral hospitals before being referred to our institute for further. Ann Arbor system was used for staging of lymphoma according to which bilateral cases were classified as Stage IVE due to poor prognosis and according to Wiseman and Liao criteria.^[3]

At presentation, one patient has multiple bilateral skin nodules and two were diagnosed with pregnancy/lactation-associated breast lumps. Two of our patients had B symptoms and another two had bone marrow involvement at baseline. Histopathological diagnosis of DLBCL was made in three patients and one case had morphology consistent with mucosa-associated lymphoid tissue (MALT) lymphoma. Immunohistochemistry consistent with the given diagnosis was the positivity of CD 20, CD 30 and Ki 67 in three cases; however, immunohistochemistry was unknown for a single patient. There was no distant organ involvement at the time of presentation in all four cases.

The main stay of treatment was R-CHOP chemotherapy (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone). Surgery was limited for diagnostic purpose only, none of our patients received radiation

therapy to breast. Response to the treatment was assessed by bone marrow biopsy after chemotherapy and PET scan. One patient died during the chemotherapy and the second patient had complete response, while rest of the two patients had progressive disease after chemotherapy, none of the patient received extensive surgery or radiation therapy, survival period ranges from 1 to 13 months; three patients died and two were lymphoma specific deaths [Table 2].

Discussion

PBL is a rare entity, it represents 0.04–0.5% of all breast malignancies.^[6] Breast lymphomas are staged according to Ann Arbor staging system, although staging of bilateral PBL is still controversial, Ryan *et al.* classified bilateral PBL in Stage IVE,^[5] this was the largest study of PB-DLBCL; they reviewed retrospectively 204 patients, whereas other studies include in Stage IE and IIE.^[7,8] We included bilateral involvement in Stage IVE as they had poor prognosis. Bilateral PBLs have some association with pregnancy as mentioned in some studies.^[9] It is difficult to differentiate radiologically between breast lymphoma, fibroadenoma and breast cancer.^[1,10]

The most common subtype is DLBCL accounts for about 50% of all BCLs, other rare types include MALT lymphoma, Burkitt lymphoma, anaplastic and follicular, small lymphocytic.^[11] Aggressive form of PBL is known

Table 1: Demographics

Case	Age	Diagnosis	B symptoms	Pre-treatment bone marrow	Post-treatment bone marrow	Risks
1	27	DLBCL	No	Positive	Negative	Pregnancy associated
2	35	DLBCL	No	Negative	Negative	Multiple skin lesions
3	64	MALT lymphoma	Yes	Positive	Positive	None
4	24	DLBCL	Yes	Negative	Negative	Lactation associated

MALT: Mucosa-associated lymphoid tissue, DLBCL: Diffuse large B-cell lymphoma

Table 2: Treatment and outcome

Case	Chemotherapy	Radiotherapy	Response	Local relapse	Distant relapse	Outcome
1	R-CHOP X 6	No	PR	No	No	Dead
2	R-CHOP X 6	No	CR	No	No	Dead
3	R-CHOP X 5	No	Progressive	No	No	Dead
4	R-CHOP X 4, RICE X 5	No	Progressive	No	No	Alive

to have association with younger age group; three of our patients were young.^[12]

Another largest study by Jeanneret-Sozzi *et al.* included a review of 84 cases of PBL from 20 institutions, they concluded that PBL has better prognosis if managed by combined chemotherapy and radiotherapy.^[13] MALT lymphoma breast is an extremely rare entity amongst the NHL, and bilateral involvement is even rarer, we found only single patient with bilateral MALT lymphoma.^[14]

Chemotherapy stays the main treatment modality for breast lymphomas; R-CHOP is the preferred regime, as it increases 5-year survival. Aviv *et al.* recommended addition of Rituximab to chemotherapy may reduce central nervous system relapse and may be given intrathecal injections,^[2,15] whereas other studies describe it as ineffective.^[16] Radiotherapy can be combined with chemotherapy, but the role of surgery is limited only to diagnosis and palliation of symptoms in progressive disease. Jennings *et al.* observed high mortality rate in patients undergoing mastectomy and axillary dissection; therefore, they concluded that there is no role of axillary lymph nodal dissection and extensive surgery for breast lymphoma.^[17,18]

Conclusion

Bilateral breast lymphoma is very rare, but aggressive disease with poor prognosis usually present at younger age group, aggressive treatment with chemotherapy should be considered and surgery should be reserved for diagnosis and palliation.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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