Primary Breast Lymphoma
30 Years of Experience With Diagnosis and Treatment at a Single Medical Center

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In our retrospective study covering the past 30 years at a tertiary cancer care institution, we review 30 patients with primary breast lymphoma (stage I or II) and analyze the different treatment modalities. All 30 patients had unilateral disease, and the median age was 67.5 years. Two patients refused treatment and, hence, were excluded from our study. Of the 28 remaining patients, 11 (39%) were treated with a single treatment modality, and 17 (61%) underwent different combinations of surgery, radiation therapy, and chemotherapy. Seventeen patients underwent a surgical resection as the primary modality or as part of a multimodality therapy. Seven patients (25%) experienced a local or distal recurrence of the disease. Of these 7 patients, 6 underwent surgery as the primary treatment or as part of a combined treatment modality, and 1 underwent radiation therapy only. Eighteen patients (64%) died during the follow-up period ranging from 6 to 230 months, but only 5 of these 18 patients (28% [18% of all patients]) died of disease-specific causes. Of the 2 patients who were only treated with chemotherapy, 1 had primary breast lymphoma that never went into remission. In our study, surgery as the primary modality therapy or as part of a multimodality therapy for primary breast lymphoma is associated with a higher rate of treatment failure, whereas a combination of chemotherapy and local radiation therapy provides the best results. However, because our sample size is small, for such a rare neoplasm, definitive treatment recommendations are difficult to determine.

Results

Of the 30 patients with stage I or II primary breast lymphoma, 1 (3%) was a man, and 29 (97%) were women. The median age was 67.5 years (range, 35-95 years). At presentation, 21 patients (70%) had stage I primary breast lymphoma, and 7 patients (23%) had stage II primary breast lymphoma. Fourteen patients (47%) had malignant, large B-cell lymphoma, and the rest (16 patients [53%]) had variable pathology (namely, marginal zone lymphoma, follicular cell lymphoma, poorly differentiated nodular lymphocytic lymphoma, and Hodgkin lymphoma). Two patients refused treatment for personal reasons and were excluded from our study. Eligible patients underwent different modalities of treatment, as shown in our Table.

Methods

After obtaining approval from our institutional review board, we retrospectively reviewed data from the cancer registry database at our institution of patients who received a diagnosis of stage I or II primary breast lymphoma; these patients were all seen and managed at our facility between 1981 and 2011. A total of 30 patients were identified. Data on the patient’s sex, age at the time of diagnosis, stage of cancer, modality of treatment used (surgery, chemotherapy, radiotherapy, or different combinations thereof), survival rate, follow-up time, recurrence rate, and cause of death were collected. Because this is a retrospective study covering a long period of time, few cases had information for analysis that was deficient in any way.

Primary breast lymphoma, a rare malignant neoplasm, was described for the first time in 1959 by Dobrotina et al.1,2 It represents 1% to 2% of all non-Hodgkin lymphomas and less than 0.5% of all malignant neoplasms of the breast.2-5 There are very few cases reported in the literature, mostly in retrospective analyses of small series of patients. Breast lymphomas are mostly of the B-cell lineage, and the most common subtype is diffuse, large cell lymphoma. The clinical and radiological presentations of the disease are very similar to those of breast cancer. Multiple treatment strategies involving surgery, radiation, and chemotherapy (alone or in various combinations and sequences) have been reported. Owing to the rarity of the disease and to the wide variation reported in the literature with regard to its histopathology, staging, and clinical characteristics, it is difficult to draw definite conclusions regarding prognostic factors and treatment.2 In a retrospective study covering the past 30 years at our tertiary cancer care institution, we review 30 patients with primary breast lymphoma (stage I or II) and analyze the different treatment modalities, comparing the results of treatment with those found in the available literature.
Of the remaining 28 patients, 11 (39%) were treated with a single modality as first-line therapy, which included surgery (4 patients [14%]), radiation (6 patients [21%]), and chemotherapy (1 patient [4%]).

Overall, of the 28 patients, 16 (57%) underwent radiotherapy (alone or in combination with another modality), 17 (61%) underwent a surgical intervention (alone or in combination with another modality), and 15 (54%) underwent chemotherapy (alone or in combination with another modality). Of the 17 patients who underwent a surgical intervention, 14 (82%) underwent a lumpectomy, and the other 3 (18%) underwent a simple mastectomy. An anthracycline-based regimen was used for 12 of the 15 patients (80%) who received chemotherapy. The radiation therapy dose ranged from 3000 to 4500 cGy, and the field ranged from localized breast irradiation to extended irradiation fields, including the axilla, the chest wall, or supraclavicular regions, depending on the disease. The follow-up period ranged from 6 to 225 months. Twenty-one patients (75%) showed sustained remission of symptoms with primary therapy, whereas 7 patients (25%) experienced recurrence or progression of disease during follow-up. Three patients (11%) experienced local recurrence, and all of these patients underwent a combination of segmental mastectomy and chemotherapy without radiation. No patient having had either a mastectomy or radiotherapy experienced a local recurrence. Distal recurrence was seen in 4 patients (14%), of whom 3 had undergone surgery (2 also underwent adjuvant chemotherapy and radiotherapy) and 1 had undergone only radiation therapy as primary therapy. Eighteen patients (64%) died during follow-up. Five patients (18%) died of disease-specific causes (3 experienced local recurrence, and 2 experienced distal recurrence). Secondary malignant neoplasms developed in 3 patients (11%) and included endometrial cancer (1 patient), glioblastoma (1 patient), and lung cancer (1 patient). Of these 3 patients, 1 developed these secondary malignant neoplasms 4 years after treatment, and the other 2 developed them more than 10 years after treatment.

### Discussion

The lifetime risk of developing non-Hodgkin lymphoma for a woman is approximately 1.8%, and primary breast lymphoma accounts for 2% of all extranodal non-Hodgkin lymphomas.3-8 It represents 0.5% of all malignant neoplasms of the breast and presents clinically as breast cancer.7,8 It generally presents as a solitary mass on the breast in women in the fifth and sixth decades of life, but it sometimes can present bilaterally.9 Wiseman and Liao10 outlined the criteria for the diagnosis of primary breast lymphoma, which are (1) having an adequate specimen for the diagnosis, (2) having mammary tissues and lymphomatous infiltrates in close proximity to each other, (3) showing no evidence of concurrent widespread disease, and (4) having had no prior diagnosis of extramammary lymphoma.4 There are very few cases reported in literature, and almost all of them are reported in retrospective series with variable results. Therefore, the optimal modality of treatment has not yet been defined. Earlier studies suggested that radiotherapy was the treatment of choice.6 However, other studies11-14 suggest that a combination of therapies using different modalities will produce optimal results. Wong et al,9 in their retrospective analysis from the Mayo Clinic, reported that all their patients underwent surgical resections that varied from a mastectomy to a local excision. In their study, 9 of 15 patients received local radiation therapy, whereas 10 patients were treated with chemotherapy. They reported a 5-year overall survival rate of 70% and a relapse-free survival rate of 42%, whereas they reported a local control rate of 75% and a distal control rate of 51%. Wong et al9 recommended that the modality chosen should depend on the histologic type of lymphoma and that systemic therapy should be reserved for high-grade disease.

Avilès et al15 reported a prospective study in which none of the patients had undergone a surgical excision of a tumor and in which all the patients were treated with a combination of chemotherapy and radiation therapy. According to these authors,11 no prognostic factors can define treatment, and therefore they recommend a combination of chemotherapy and radiation therapy for all patients with primary breast lymphoma. In another large retrospective study reported by the International Extranodal Lymphoma Study Group,12 the authors recommend that, in future studies, a combination of limited surgery/biopsy, followed by 3 cycles or more of anthracycline-containing chemotherapy and radiation therapy to the ipsilateral breast and regional nodes, should be standard therapy. In their analysis,16 a mastectomy afforded no advantage over a limited resection. Patients presenting with bilateral disease appear to be a poor prognosis group, and intensification of chemotherapy should be considered.13
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Conclusions

Primary breast lymphoma is a rare subset of extranodal lymphoma that behaves differently from nodal lymphoma, and the optimal treatment modality is still in question. In our study, radiotherapy decreased the incidence of local recurrence. We also realized that a mastectomy seemed to provide better local control. Our study suggests that combination therapy (i.e., using various modalities) produces the most favorable results and that there is a definite role for surgical excision and local radiation for better local control.

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REFERENCES


