

# Primary breast lymphoma

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## Summary

**Objectives:** Retrospective evaluation of the clinical behavior, treatment and prognosis in five cases of primary breast lymphoma.

**Methods:** From 1999 to 2003, five patients with primary breast lymphoma were diagnosed in our department.

**Results:** Primary breast lymphoma (PBL) was diagnosed in five patients, whose median age was 63.4 (41-79) years. In four out of five patients, a diagnosis of lymphoma was made after the evaluation of a palpable breast mass measuring 1.5 to 6 cm. All of them were classified as non-Hodgkin's B cell lymphomas and three of five cases were diffuse large cell lymphomas. All patients were submitted to chemotherapy; in only one patient was surgery performed.

**Conclusions:** A relatively high rate of PBL was observed in our department compared with other oncology centers. Beyond its scarce appearance, PBL is very difficult to distinguish from primary breast carcinoma. Histology remains the major diagnostic tool.

**Key words:** Breast lymphoma; Primary lymphoma.

## Introduction

Primary breast lymphoma (PBL) is a rare entity accounting for 0.04 to 1% of all breast cancers [1]. We have been witnessing an increase in incidence of non-Hodgkin's lymphomas (NHL), representing 5% of all new diagnoses of cancer during 2001 [2]. However, only 1.7% of extra-lymphatic NHL are PBL [3].

The criteria of PBL proposed by Wiseman and Liao are: I) adequate specimens; II) close association of breast tissue and lymphomatous infiltrate; III) no evidence of concurrent widespread disease, except positive ipsilateral axillary lymph nodes; IV) no prior diagnosis of lymphoma [4]. Our study was a retrospective analysis over a 5-year period with the aim of understanding the clinical characteristics and the best treatment of this disease.

## Materials and Methods

Patients with a diagnosis of lymphoma of the breast were retrospectively identified and their medical records were reviewed. Five patients were classified as having PBL and met Wiseman's criteria. The data collected included age, clinical diagnosis, mammography results, history of benign breast disease, histology, type of lymphomatous involvement, initial treatment (surgery, radiotherapy, and chemotherapy), recurrence and death.

Staging evaluation of these patients included clinical presentation and physical examination, complete blood count, renal and liver function tests, chest X-ray, bone marrow biopsy and thoraco-abdomino-pelvic computed tomography. Based on this information, the Ann Arbor classification was determined for each patient. Immunophenotypic analysis was performed in the initial biopsy evaluation.

## Results

From 1999 to 2003, five cases of PBL were diagnosed in our department. The median age at diagnosis was 63.4

(41-79) years. Patients were referred from smaller hospitals, primary care institutions and from breast cancer screening organizations.

All patients presented with palpable breast masses; none presented benign breast disorders. All mammograms showed unilateral irregular masses, whose dimensions varied from 1.5 to 6 cm.

The immunophenotyping revealed that all tumors were B-cell type; three of them were diffuse large cell lymphoma (classified as high-grade lymphomas) and two follicular lymphomas (classified as low-grade lymphomas).

Based on the information gathered from the Ann Arbor staging evaluation, of five cases two were staged IE disease, one was staged IIE, one was staged IIIE and one was staged IVP. Classical B signs were absent.

All patients were submitted to chemotherapy as the initial treatment and four attained complete remission. The remaining patient underwent mastectomy after chemotherapy as a result of disease progression.

The chemotherapy regimens consisted of the CHOP (cyclophosphamide, doxorubicin, vincristine and prednisolone) and COP (cyclophosphamide, vincristine and prednisolone) according to histology.

Of the five patients, three (60% of the total) are alive, without evidence of disease. Only one patient relapsed, three months after the diagnosis, corresponding to the one who was submitted to surgery. Two patients died as a consequence of the disease.

## Discussion

This study consisted of a retrospective analysis of five cases of PBL over a 5-year period in our department.

PBL is an uncommon disease and almost all published series include only a small number of patients. The peak age incidence reported differs among authors, between the fifth and the sixth decade [3, 4]; median age of diagnosis in our study was 63.7 years.

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Both non-Hodgkin's and Hodgkin's lymphoma can be diagnosed in the breast, but the latter is less common [5].

Clinical presentation of PBL is similar to that of breast carcinoma. The majority of PBL present as palpable masses that can be detected in mammography; these masses are usually larger than those corresponding to breast carcinoma [4]. Nonetheless, there are no specific mammographic findings that can distinguish lymphoma from carcinoma, as they can vary from irregular nodular masses to just an increase in parenchyma density [3, 4]. Final diagnosis is usually obtained after a biopsy.

Most PBL are B-cell type, with diffuse large cell lymphoma the most common (40 to 70% of cases).

The initial treatment of PBL differs among cancer centers but, at the present time, it is accepted that it depends mainly on the histological grade. For patients with limited-stage low-grade lymphoma (e.g., follicular lymphoma), local conservative surgery with radiotherapy is potentially curative. For patients with intermediate-grade or high grade PBL (e.g., diffuse large cell lymphoma), a course of chemotherapy plus involved field irradiation is the treatment of choice [3, 7].

A recent randomized study, the Southwest Oncology Group (SWOG 8736) study, showed that the optimal treatment for intermediate and high-grade lymphoma is combined chemotherapy and radiotherapy. This trial demonstrated that three cycles of CHOP plus radiotherapy (RT) were more effective than eight cycles of CHOP in patients with nonbulky Stage I or II disease [8].

Another trial, this one conducted by the Eastern Cooperative Oncology Group (ECOG), also compared CHOP-RT versus CHOP, although the population was substantially different. The ECOG trial demonstrated that CHOP for six to eight cycles plus RT (30 or 40 Gy) was more effective than CHOP alone in patients with bulky Stage II (usually mediastinal) disease who achieved complete response to therapy. However, all patients in the study who had a partial response received RT, making it difficult to evaluate its role in this setting [8].

In our department, initial treatment consisted of chemotherapy and performing surgery in tumors non responsive to chemotherapy.

Chemotherapy regimens used in PBL are similar to those used in systemic lymphoma, consisting of COP for follicular lymphoma and CHOP for diffuse large cell lymphoma.

Overall prognosis of PBL depends mainly on the Ann Arbor staging system, with a 5-year survival of 61 to 89% in Stage I disease, 0 to 50% in Stage II disease, and a 3.7-year survival in high-grade PBL [1-7].

## Conclusions

Compared with other reports, our department had a high incidence of primary breast lymphoma (approximately 1 case per year) from 1999 to 2003.

PBL behaves in a similar clinical way as breast carcinoma, making biopsy mandatory.

Imagery reveals breast masses whose clinical behavior can be easily confounded with those of breast carcinoma, except that micro calcifications only appear in breast carcinoma.

Treatment differs from author to author; our report presents a high response with chemotherapy alone considering every stage of disease. Nowadays, it seems logical to perform CNS prophylaxis in PBL with a diffuse large cell histology, as PBL tends to relapse in that location.

Stages of disease and differentiation of grade are major prognostic features.

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