Clinical Medicine Insights: Oncology

CASE REPORT

Three Cases of Combined Therapy in Primary Breast Lymphoma (PBL) with Successful Outcomes

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Abstract: Primary malignant lymphoma of the breast is a rare tumor, defined as a tumor localized in the breast with or without axillary lymph-node metastases. Such a tumor is mainly found in female patients and located more frequently in the right breast. It is difficult to make primary breast lymphoma (PBL) diagnosis before operation, and PBL diagnosis is mainly based on pathological biopsy and immunohistochemical staining. In this paper, the cases of three patients who had PBL, and who were treated for it at the Institute for Oncology and Radiology of Serbia between 2008 and 2012, are reviewed and discussed. These cases of PBL had no recorded reoccurrence of the disease and were originally treated by surgery, radiotherapy R-CHOP, and/or chemotherapy. While there is no consensus to the question of how to best treat PBL (ie, with chemotherapy, radiotherapy, or combined therapy), it is hoped that this review will offer insight into successful treatment procedures for tumors of this category.

Keywords: breast lymphoma, extranodal non-hodgkin lymphoma, breast cancer

Clinical Medicine Insights: Oncology 2013:7 159–163

doi: 10.4137/CMO.S12044

This article is available from http://www.la-press.com.

Introduction

Primary breast lymphoma (PBL), a rare extra-nodal lymphoma, accounts for approximately 0.04%–0.74% of all malignant breast tumors, and for 0.7% of extra-nodal non-Hodgkin's lymphomas (NHLs).[1] Primary malignant lymphoma of the breast is defined as the tumor localized in the breast with or without axillary lymph node metastases.[2] It is mainly found in female patients and the right breast is more frequently involved. The majority of PBLs are diagnosed by biopsy or postoperative pathological findings.[3] Extra-nodal lymphomas are treated by surgery, radiotherapy, and/or chemotherapy.[4]

Methods chosen for treating PBL through the use of radiation therapy and/or chemotherapy varies in the literature. Currently, the use of combined therapy is considered to be more beneficial for patients with PBL, even in the early stages of their illness.[5]

As to better explore treatment options and methods that result in successful outcomes, the goal of this study is to review three separate but disparate cases of patients with PBL who were treated from 2008 to 2012 and who emerged from the disease without any recorded reoccurrence. Please note: written consent has been obtained from all patients involved to reproduce any pertinent information appearing in this work.

Case 1

A 47-year-old woman was admitted to hospital with a right breast mass. The patient had had no operations or traumas in the breast area.

The physical examination demonstrated symmetric breasts without any evidence of breast skin changes or nipple retraction. A hard, mobile mass approximately 3 cm in diameter was found through ultrasonography localized in the right breast, with no palpable masses in her left breast detected. The mammography demonstrated a condensation of the glandular tissue of 3.5×3 cm in diameter (BI RADS 4), without any suspicious changes or findings in the left breast. The axillary lymph node enlargement was not able to be detected with ultrasonography and mammography examination.

A fine-needle aspiration cytology (FNAC) or core needle biopsy were not carried out as it is not considered standard procedure at the institute where the tumor was diagnosed and treated, and hence not applied to all patients.

The preoperative diagnosis was of a clinical breast carcinoma and surgery intervention was determined to be the best option. As its removal was necessary and since no biopsy was performed, tests on the mass could be subsequently performed. Therein, a partial resection of the central quadrant of the breast was performed.

The subsequent frozen section examination proved to be non-conclusive. The histological analysis showed a Diffuse Large B-Cell Lymphoma (DLBCL; the T-cell rich variant). The immunohistochemical studies showed positive CD 20 and CD 79a results, CD 5: single rare immunoreactivity, CD 3: diffuse immunoreactivity individual. Negative EMA, CD 30, CD 15, bcl, CD 23, and CD 35 results were obtained. A computerized tomography (CT) examination of the thorax and abdomen and a bone marrow examination showed no evidence of the disease's dissemination. Due to these results, the patient was diagnosed as being at clinical stage I.

Subsequent chemotherapy was performed with three cycles of R-CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisolone plus rituximab) and involved field radiotherapy were given. After a total of three cycles of chemotherapy, the physical examination did not reveal any abnormalities.

Since this initial therapy, the patient has currently been followed for 44 months with no evidence of disease recurrence. Subsequent physical examinations have demonstrated no suspicious changes in either breast. Post therapy ultrasonography of the breast, the axillae, and the abdomen was normal.

Case 2

A 65-year-old woman noticed a tumor in her left breast. A physical examination in May of 2008 revealed a tumor in the central quadrant of her left breast of 4×4 cm which infiltrated the subcutis. A CT of the thorax revealed a tumor mass of 6×4 cm in the left breast and the left axillary lymphadenopathy. A biopsy by excision of the tumor of the breast was performed.

A FNAC or core needle biopsy were not carried out, as per standard procedure explained above.

The histopathological and immunohistochemical findings in the tumor mass confirmed the diagnosis of a diffuse large B-cell type: CD20+, CD 79 alpha +, CD 3: diffuse immunoreactivity individual +, bcl 2: single rare immunoreactivity +, CD 43 diffuse immu-

noreactivity +, CD 5−, bcl 6−, CD 23−, cyclin D1−, CD 15−, CD 30−, pan CK−, HMW CK−. The patient was treated with 8 cycles of R-CHOP and involved field radiotherapy was given.

The post therapy physical examination in July of 2009 showed hard scar changes of 1 cm in the left breast. The corresponding ultrasonography of the breast, the axillae, the neck, and abdomen proved to be normal.

As of May 2012, no relapse was observed; both the CT of the thorax and abdomen, and the ultrasonography of the breast and neck was normal.

Case 3

A 78-year-old woman was admitted to the hospital with a right breast mass. The patient had had no operations or recorded trauma in the breast area.

The physical examination demonstrated symmetric breasts without any evidence of breast skin changes or nipple retraction. A hard, mobile mass of 5 × 4 cm in diameter localized in the right breast was found, but no palpable masses in her left breast were observed. The mammography demonstrated a condensation of the glandular tissue of 6.5 × 5 cm in diameter, having no suspicious changes or findings of the left breast (BI RADS 5). The axillary lymph node enlargement was not able to be detected with ultrasonography and mammography examination.

A FNAC or core needle biopsy were not carried out, as per standard procedure explained above.

The patient underwent a partial resection of the joint-upper quadrants of the left breast. The frozen section examination proved to be non-conclusive. The histological analysis showed a NHL. The PCR showed monoclonal population of B lymphocytes. A CT examination of the thorax and the abdomen, as well as a bone marrow examination showed no evidence of the disease's dissemination. The patient was diagnosed as being at clinical stage I.

Only radiotherapy of the right breast and the axilla was carried out.

No symptoms of disease relapse were observed after a follow-up period of 9 months. In addition, no changes in the breast were observed.

Discussion

Malignant lymphoma of the breast, either primary or secondary, has a poorer prognosis than other breast carcinomas.[6] PBL is mainly found in female patients, accounting for 95%–100% of all PBL patients.[7] It is very rare in men and only a few cases have been reported in the literature so far.[8,9] The median ages are recorded as being between 40 and 67 in reports about PBL.[4]

More than 80% of PBL are B-cell lymphomas, mostly CD20+. The most frequent histopathological type is DLBCL which accounts for up to 50% of all PBL, while follicular lymphoma (FL) accounts for 15%, MALT lymphoma accounts for 12.2%, and Burkitt's lymphoma (BL) and Burkitt-like lymphoma account for 10.3%.[10]

Other histological types of PBL include marginal zone lymphoma (MZL), small lymphocytic lymphoma (SLL), and anaplastic large cell lymphoma (ALCL).

DLBCL is the most common histological diagnosis given. These lymphomas have been shown to be of a non-germinal center B-cell phenotype with a high proliferation index and are thought to be associated with poor outcomes.[11]

The most typical clinical characteristic of PBL is an ever increasing mobile mass in the unilateral breast, in which the mass grows rapidly. The typical clinical manifestation of PBL is a painless breast mass in approximately 61% of cases, most frequently located at the outer quadrant of the breast. Other symptoms and signs include the following: local pain (12% of cases), local inflammation (11% of cases), palpable lymph nodes (25% of cases), and incidental mammography finding (12% of cases).

As lymphomas of the breast are uncommon, and the clinical manifestation of which is hard to distinguish from that of breast cancer, they do not usually cast doubt on the diagnosis of breast cancer prior to biopsy. Breast lymphoma tends to be larger in size at diagnosis than breast cancer, but that cannot be regarded as a distinguishable feature. In breast lymphoma, skin retraction, erythema, peau d'orange appearance, and nipple discharge are rarely present.[12–14]

As the symptoms of breast lymphoma are atypical, it is usually misdiagnosed as breast cancer or a benign lesion. It is difficult to make a PBL diagnosis before an operation, and PBL diagnosis is mainly based on pathological biopsy and immunohistochemical staining,[15] in which rapid growth of the mass in the breast should be first and foremost considered to be PBL.[3]

Therefore, it may be important to diagnose breast lymphomas using not only imaging modalities, but cytological (fine-needle aspiration) or histological (core needle biopsy) examinations as well.[16,17] PBL treatment varies widely, and surgical therapy options range from biopsy to modified radical mastectomy. More recently, chemotherapy using various agents has been recognized as the preferred treatment. Radiotherapy may be used as an adjuvant therapy or as a primary local therapy.[18,19] Treatment options may also include immunotherapy or radioimmunotherapy. A very recent study has reported that mastectomy offers no benefit in the treatment of PBL, and treatment that included chemotherapy and/or radiation therapy provides benefits with regard to both survival and recurrence rates.[20]

Miller et al[21] have reported that patients treated with three cycles of a doxorubicin containing regimen such as cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) in addition to radiotherapy had significantly better progression free survival and overall survival than patients treated with CHOP alone. They came to the conclusion that three cycles of CHOP followed by involved-field radiotherapy are superior to eight cycles of CHOP alone for the treatment of localized intermediate- and high-grade NHL. More cases of NHL have been effectively treated by radiotherapy or chemotherapy.[22] Moreover, use of rituximab plus CHOP has been shown to increase survival when compared with CHOP for treatment of diffuse, large B-cell lymphoma in elderly patients.[23]

Conclusion

Awareness of the possibility of a PBL can help in arrive at a correct diagnosis, despite the rarity of the disease. However, it is still difficult to select a proper treatment modality for PBL.

The use of combined therapy is generally considered to be more useful in the treatment of patients with PBL, even in the early stages of their illness. In accordance with general consent to this prescribed regimen of these therapies, the presented cases demonstrate that surgery, when accompanied by radiotherapy with or without chemotherapy using the R-CHOP regimen, can be most effective when faced with problems in the treatment of PBL.

These cases show this use of multiple treatment to be key in securing positive outcomes in which the disease is cured and does not reoccur. This is due to the fact that the patients discussed here have had regular checkups since their initial diagnoses and treatments, but have had no observed sign of recurrence. In this regard, other cases where multiple treatment has been utilized should be explored in further studies to seek similarities and differences in treatment options as to best clarify how multiple treatment can be carried out to the best outcome of the patient.

Author Contributions

Conceived and designed the study: ZI. Performed medical operations: MI, MZ. Pathology: GP. Analyzed the data: II, MZ. Wrote the first draft of the manuscript: ZI. Contributed to the writing of the manuscript: ZI. Agree with manuscript results and conclusions: ZI, MI, MZ, II, GP. Jointly developed the structure and arguments for the paper: ZI, MZ, II, GP. Made critical revisions and approved final version: ZI. All authors reviewed and approved of the final manuscript.

Funding

Author(s) disclose no funding sources.

Competing Interests

Author(s) disclose no potential conflicts of interest.

Disclosures and Ethics

As a requirement of publication the authors have provided signed confirmation of their compliance with ethical and legal obligations including but not limited to compliance with ICMJE authorship and competing interests guidelines, that the article is neither under consideration for publication nor published elsewhere, of their compliance with legal and ethical guidelines concerning human and animal research participants (if applicable), and that permission has been obtained for reproduction of any copyrighted material. This article was subject to blind, independent, expert peer review. The reviewers reported no competing interests.

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