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Case Report

Primary Breast Lymphoma: A Rare but Important Differential Diagnosis in Patients with Breast Malignancy

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Abstract

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This report is based upon the case of a young lady who presented with a history of a breast lump, which despite clinically resembling a carcinoma, was subsequently diagnosed to be a primary breast lymphoma (PBL). Though rare in incidence, PBL may masquerade as breast carcinoma. PBL accounts for about 1.7–2.2% of all extranodal non-Hodgkin's lymphoma, and is accountable for up to 0.5% of all breast malignancies. Given that the treatments of breast carcinoma and PBL are markedly different, it is very essential that core-biopsy be preferred in every patient being evaluated for carcinoma of the breast. The diagnosis of diffuse large B cell lymphoma (DLBCL) was confirmed by immunohistochemistry, and the patient has been treated with six-cycles of chemotherapy followed by involved field-radiotherapy to the right breast. After a year's follow-up, the patient remains free of disease.

Keywords

- breast lymphoma
- CHOP
- chemotherapy
- radiotherapy

Introduction

Primary breast lymphoma (PBL) is defined as that malignant lymphoma which primarily arises in the breast in the absence of previously detected lymphoma localizations.[1] The breast is a rare site of lymphoma, with breast lymphomas making up for just 0.4 to 0.7% of all non-Hodgkin's lymphoma (NHL), and only 1.7 to 2.2% of extranodal NHL.[2,3] Diffuse large B cell lymphoma (DLBCL) is the most common variety in both primary and secondary lymphomas of the breast.[3,4] PBL is

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reported to be as common as secondary lymphomatous involvement of the breast, though both forms are rare in absolute terms.[5,6] PBL accounts for up to 0.5% of all breast malignancies.[1] Despite being rare, given that the treatment pathways for breast lymphoma greatly differ from that for breast carcinoma, it is imperative that a timely diagnosis be accurately performed. While surgery followed by chemotherapy, radiotherapy, and hormonal therapy is the standard of care for breast carcinoma, in the case of PBL chemotherapy, anti-CD20 therapy and involved field radiotherapy (IFRT) happens to be the standard of care. The current case highlights the necessity to hold the possibility of PBL as a differential diagnosis among patients clinically suspected to be having breast carcinoma. A brief outline of the investigative work-up and treatment, as well as a discussion regarding the treatment of PBL is provided.

Case Report

A lady aged 25 years presented to a local physician with a 2-month history of having noticed a lump in the right breast. She underwent a fine-needle aspiration cytology and that was reported there as an infiltrating ductal carcinoma. Patient self-referred herself to our institute for a second opinion. On examination, there was a single lump in the right breast in the upper outer quadrant. It measured about 6 cm in maximum dimension, mobile, and was firm to hard in consistency. There were slight features of inflammation notable in the overlying skin, though the mass was non-adherent to the skin. There was no lymphadenopathy in the ipsilateral axilla or the supraclavicular fossa. The opposite breast was normal clinically. There were no findings of organomegaly or lymphadenopathy elsewhere in the body. The patient was without children, and was unmarried. Her familial history was unremarkable for any history of malignancies. Given the young age of the patient, and the lack of any familial/hereditary breast cancer, we felt the need for a reevaluation of the previously established diagnosis.

A core biopsy was obtained from the breast lump. Histophathological examination showed diffuse growth of large lymphoid cells with very frequent mitotic figures. Immunohistochemistry revealed negativity for estrogen receptor, progesterone receptor, and the her2neu receptors. The malignant cells were positive for CD20, LCA, CK-7, bcl-2, MUM-1, and CD79a; while CD 10 was negative. MIB-1 labeling index was more than 80%. On the basis of these findings, a diagnosis of PBL of the DLBCL variety was made. A bone marrow aspiration indicated noninvolvement of the marrow. A whole-body 18-fluorodeoxy-glucose positron emission tomography (FDG-PET) scan revealed the presence of a highly FDG-avid (standardized uptake value maximum: 26) in the right breast and a smaller lesion with a high avidity (standardized uptake value maximum: 17) in the ipsilateral axilla. There was no detection of any other FDG-avid lesion elsewhere in the body. The patient was staged I-E as per the Ann Arbor staging system. Serology for human immunodeficiency virus and Epstein–Barr virus was negative. Serum lactate dehydrogenase (LDH) was within the normal limits, and the erythrocyte sedimentation rate was raised (63 mm/1st hour).

The patient was treated with 6 cycles of chemotherapy with the R-CHOP regimen (rituximab 375 mg/m^2 intravenously on day 1, cyclophosphamide 750 mg/m^2 intravenously on day 1, doxorubicin 50 mg/m^2 on day 1, vincristine 2 mg on day 1, and prednisolone 100 mg/day orally from days 1 to 5) followed by IFRT to right breast delivered via three-dimensional conformal radiotherapy to a dose of 45 Gray delivered in 25 fractions over a span of 5 weeks.

The patient achieved complete remission as per FDG-PET repeated after 3 cycles of chemotherapy. After the completion of a total of six cycles of chemotherapy followed by radiotherapy, the patient remains under regular 2-monthly follow-up and the patient has completed a span of 1.5 years of posttreatment follow-up uneventfully.

Discussion

Though rare, PBL is a clinically important entity since it may clinically masquerade as a breast carcinoma, and misdiagnosis may lead to mistreatment. The breast is a rare site to harbor an extranodal lymphoma, and the incidence of PBL and secondary lymphomatous involvement of the breast are known to be almost equal.[6] Wiseman and Liao in 1972 had described criteria to define a breast lymphoma as a PBL.[7] The criteria include close anatomical association between breast tissue and lymphoma, adequate pathological specimen, no prior diagnosis of extramammary lymphoma, and no evidence of widespread nodal disease other than ipsilateral axillary lymphadenopathy.[7,8] It must be stated that the Wiseman and Liao criteria were formulated in an era when there was no availability of PET scans for clinical use. In this age, the use of FDG-PET scans allows the detection of lymphomatous involvement in any site of the body, and hence provides for a more confident assignment of the diagnosis of PBL. The most common clinical presentation of PBL is described to be that of a painless lump in the upper outer quadrant of the involved breast. Also, it is not uncommon to come across features like nipple retraction, peau'd orange, and erythema that can mimic inflammatory breast cancer. B symptoms are also uncommon.[9] Primary breast DLBCL (PB-DLBCL) is the most common type of PBL. The factors predictive of poor prognosis are stage higher than IE, older age, poor performance status, raised LDH levels, and the size of the primary tumor exceeding 4 to 5 cm. PB-DLBCL is characterized into two types—germinal center B cell like (GCB) and the non-GCB type. The non-GCB type is associated with a poorer prognosis.[10,11] The described patient can be considered as a non-GCB (given the MUM-1 positivity and CD-10 negativity on page 4 of 11 immunohistochemistry). Much of the prognostic information regarding PBL currently is gained from the International Extranodal Lymphoma Study Group (IELSG) data which includes 204 PBL patients. The group observed a poor prognosis of PB-DLBCL in comparison to DLBCL at other locations. The use of anthracycline-based chemotherapy and radiotherapy were found to improve overall survival rates.[8] There is a rather high risk of central nervous system (CNS) relapse in patients with PBL. Some authorities suggest that all patients with PBL should be advised a cerebrospinal fluid analysis.[12] However, data from the IELSG group

indicated a 5% risk of CNS relapse.[8] Thus, the use of prophylactic CNS therapy in a routine manner can neither be supported nor refuted at this point of time. It may, however, be prudent to consider prophylactic CNS therapy among patients with age >60 years, elevated LDH, and poor performance status.[13] Though there are no fixed consensus regarding the optimal approach to the treatment of PBL, the use of chemotherapy as with other lymphomas, and the use of postchemotherapy radiotherapy to the ipsilateral breast and regional lymph nodes is currently the most successful approach. The use of rituximab may be considered for patients with CD-20 positive PBL.[8,11,14–16] The role of surgery is limited in PBL and should ideally be confined for diagnostic purpose (biopsy). Though the mainstay in patients with carcinoma of the breast, radical surgery is found to adversely affect survival in patients with PBL. The IELSG data has revealed that radical mastectomy when performed in patients with PBL, was associated with an increased mortality.[8] There is, however, a likelihood that radical mastectomy could be performed in a patient with PBL due to preoperative misdiagnosis leading to confusion with breast carcinoma. Such patients should always be provided systemic chemotherapy and radiotherapy subsequently.

Authors' Contributions

I.M. conceived and designed the experiment, made critical revisions, and approved the final version. I.M., M.S., V.K., and R.S. analyzed the data and wrote the first draft of the manuscript. I.M., M.S., V.K., and R.S. contributed to the writing of the manuscript. I.M., M.S., V.K., and R.S. agree with the manuscript results and conclusions. I.M., M.S., V. K., and R.S. jointly developed the structure and arguments for the paper. All authors reviewed and approved the final manuscript.

Conflict of Interest

None declared.

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