PRIMARY NON-HODGKIN LYMPHOMA OF THE BREAST - A CASE REPORT AND REVIEW OF LITERATURE

Ashish Singhal¹, Rahat Hadi², Namrata P. Awasthi³, Kiran Malhotra⁴, Charu Mahajan⁵

¹Associate Professor, Department of Surgical Oncology, Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow.

²Associate Professor, Department of Radiation Oncology, Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow.

³Associate Professor, Department of Pathology, Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow.

⁴Associate Professor, Department of Pathology, Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow.

⁵Senior Resident, Department of Surgical Oncology, Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow.

ABSTRACT

BACKGROUND

Primary breast lymphoma (PBL) is a rare but well-defined subtype of non-Hodgkin lymphoma (NHL) representing 0.5% of all malignant breast tumours, 1% of NHL and 2% of extra-nodal lymphomas.¹ However, primary NHL (PNHL) is the most frequent hematopoietic tumour of the breast with diffuse large B-cell lymphoma (DLBCL) as the most common histological type.² Clinical picture and imaging mimics carcinoma breast and diagnosis is usually established on biopsy. Chemotherapy and radiotherapy is the mainstay of treatment. The role of surgery is limited to biopsy to establish the correct histological diagnosis.

KEYWORDS

Lymphoma, Chemotherapy, Radiotherapy Surgery.

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BACKGROUND

Primary breast lymphoma (PBL) is an uncommon disease with poor clinical outcome. PBL is used to define malignant lymphomas primarily occurring in the breast in the absence of previously detected lymphoma localisations. Wiseman and Liao are credited with defining the clinical criteria for PBL.³ The majority of PBL are diffuse large B-cell lymphomas (DLBCL), but other less frequent subtypes including mucosal-associated lymphoid tissue lymphoma, follicular lymphoma, Burkitt lymphoma and T-cell lymphoma.⁴ It appears that the prognosis of PB-DLBCL is generally comparable with that of nodal DLBCL and that standard treatment should consist of immunochemotherapy with an anthracycline-based regimen and include consolidation with radiotherapy especially in stage I_E patients.⁴

CASE REPORT

The patient is a 65-year-old female, known diabetic and hypertensive, who presented to our outpatient department with a complaint of painless bilateral breast lumps since 3 months. There is no history of nipple discharge, weight loss, fever, night sweats or history suggestive of metastatic disease. Clinical examination revealed a 4 x 3 cm lump in the right breast central quadrant and 2 x 2 cm lump present in the left breast with restricted mobility. There were no palpable axillary or cervical lymph nodes. General and systemic examination was normal. Routine haematological and biochemistry were normal. Bilateral mammogram shows

spiculated marginated heterogenous lesion with adjacent breast parenchymal invasion and architectural distortion in right breast with areas of nodularity at least two in left (opposite breast) (Fig. 1 & 2). Fine needle aspiration cytology (FNAC) was done from both the lumps which were suggestive of haematolymphoid neoplasm with possible diagnosis of non-Hodgkin lymphoma. Core biopsy was done from both lumps which show fibro-adipose tissue infiltrated by sheets of atypical lymphoid cells with medium to large, oval to round hyperchromatic nuclei with prominent nucleoli and scant cytoplasm with frequent mitosis. Immunohistochemistry was done which is consistent with the diagnosis of diffuse large B cell non-Hodgkin lymphoma of the breast (LCA+, CD20+, CD3-, PAN CK-, Ki67 60%) (Fig 3). Bone marrow biopsy was normal. Positron emission tomography (PET CT) did not reveal any other sites of disease. Patient was administered 6 cycles of R-CHOP (Rituximab 375 mg/m², Cyclophosphamide 750 mg/m², Doxorubicin 50 mg/m², Oncovin 1.4 mg/m², with dose of prednisolone modified to 80 mg because of her diabetes) following which her lesion resolved completely. Thereafter, she was administered external beam radiotherapy 50 Gray to both breasts. Patient has completed 9 months and is being followed with PET CT which did not reveal any areas of increased activity (Fig. 3).

Figure 1. Right Mammogram showing Irregular Lobulated Lesion in the Central Quadrant

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Corresponding Author:

Dr. Ashish Singhal,

Department of Surgical Oncology,

Dr. RMLIMS, Vibhuti Khand,

Gomti Nagar, Lucknow-226010

Uttar Pradesh.

E-mail: ashishpgi@yahoo.co.in

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Figure 2. Left Mammogram showing Ill-defined Hyperdense Areas of Nodularity

Figure 3. A: Shows Tumour composed of Large Round Cells Disposed in Sheets, Haematoxylin & Eosin 100X; B: IHC for CD20 showing Diffuse Positivity in Tumour Cells; IHC for CD3 (C), Cytokeratin (D) showing Negative Staining in Tumour Cells; Ki67 IHC showing a Proliferation Index of 60%.

DISCUSSION

Breast lymphoma is classified as primary or secondary (SBL). The term PBL is used when the breast is the principal and the only site of lymphoma. In 1972, Wiseman and Liao³ first defined PBL using four criteria: (i) mammary tissue and lymphoma must be in close anatomic proximity, (ii) no preceding diagnosis of extra-mammary lymphoma, (iii) no evidence of disseminated disease other than ipsilateral axillary lymphadenopathy, and (iv) adequate quality of the histopathological specimen. The usual clinical feature of a

breast lymphoma is a rapidly expanding, painless mass with a slight predilection for the right breast, but the explanation for this remains unclear.⁵ Bilateral PBL accounts for 6 to 13 % of all PBL and is still controversial with regard to stage and prognosis.⁶ For the sake of uniformity, and in view of a possible worse prognosis of bilateral PBL, these rare cases may well be classified as stage IV disease, whereas others have defined them as stage I_E or II.⁷

As in other nodal forms of DLBCL, an anthracycline-based regimen is the mainstay of treatment, with CHOP being the most frequent regimen used for 4-6 cycles. Most PBL studies report favourably on the administration of systemic chemotherapy even for apparently localised disease.⁸

Radiotherapy appears to have a positive impact on the outcome of PB-DLBCL, especially in patients without axillary node involvement (stage I_E). The data on the role of irradiation for DLBCL in the rituximab era are still immature, but in light of results of the clinical trials and observations on PBL, we feel it should still be recommended as an adjuvant to systemic immunochemotherapy for localised disease.⁹

Surgery should be used for diagnosis only and must be minimally invasive as extensive surgery carries a high morbidity rate without any proven advantage over lumpectomy alone. Axillary dissection has no role in the treatment of PB-DLBCL. Surgery should not be regarded as a therapeutic modality, and if it has been performed due to the misdiagnosis of breast carcinoma, subsequent systemic therapy should always be given.⁴

The role of central nervous system (CNS) prophylaxis in DLBCL of the breast is controversial. There have been no prospective trials of CNS prophylaxis in this population. Case series have reported a high incidence of CNS recurrence, estimated at 12 to 27%. Nevertheless, given this high incidence of CNS recurrence, central nervous system (CNS) prophylaxis should be considered.¹⁰

CONCLUSION

Primary and secondary lymphomas of the breast, though rare, should be considered in the differential diagnosis of breast malignancies. Flow cytometry and or biopsy is required to achieve the diagnosis. The rare possibility of occurrence of these tumours with high index of suspicion may prevent one from doing unnecessary mutilating surgery for a disease which can be cured by chemotherapy and radiotherapy.

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