Original Article

Frequency and Characteristics of Breast lymphomas presenting to a tertiary care hospital, Pakistan

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Abstract

Objective: To assess the relative frequency of (primary and secondary) mammary lymphomas presenting to a tertiary care hospital, Pakistan and its categorization according to WHO classification of lymphoid neoplasms.

Methods: All NHLs (nodal and extra nodal) diagnosed in the section of histopathology during 1992-2004 were retrieved and reviewed. All patients (n=30) diagnosed with lymphomatous involvement of the breast were selected. Distinction between primary and secondary breast lymphomas was not made owing to lack of availability of clinical information.

Results: A total of 5637 breast malignancies were diagnosed in our department during the study period of 10 years and the total number of NHLs (Nodal and extra Nodal) was 2632. Thirty (n=30) patients accounting for 1.13% were diagnosed to have lymphomatous involvement of the breast. The Female to Male ratio was13.5:1; age range was 12-92 years with a median age of 43 years (Mean age 46.5 years and Standard deviation of age was 16.88 years). The sites of the lesions were the right breast in 11 cases (37.93%), left breast in 9 cases (31.03%) and both breasts in 2 cases (6.89%), while the location of 8 masses (27.58%) was unknown. Immunohistochemical studies were negative for cytokeratins (MNF and Cam 5.2) in all cases. All cases of DLBCL expressed B cell lineage antigens and were positive for LCA and Pan B (CD20 and 79a).

Conclusion: We concluded that breast lymphomas represent 1.13% of all NHL and 0.5% of all breast malignancies in this study. The most frequent morphologic type was diffuse large B-cell lymphoma. As patients with primary breast lymphoma have a better prognosis than those with carcinoma of the breast or patients with extranodal lymphomas, a multidisciplinary approach including surgery, radiotherapy, and chemotherapy when needed would result in a more favourable outcome (JPMA 56:441;2006).

Introduction

Non-Hodgkins lymphomas of the breast are rare, accounting for 1.7% to 2.2% of extra nodal and 0.38% to 0.7% of all NHLs in various series.[1] One of the series from Japan has shown an incidence of 0.3% of all extra nodal NHL.[2] This difference in frequency may be explained in part by the absence of large scale studies of breast NHL in Japan. Breast NHL accounts for about 0.12 to 0.15% of all breast malignancies in most reports, but as high as 1.1% in others.[3] Until recent past, approximately 300 cases have been reported in the literature.[1] Although secondary breast lymphomas are rare, they represent the largest group of metastatic tumors of the breast.[1,4] The most common cancers to metastasize to the breast are, in declining order of frequency, malignant melanoma, lymphoma, lung cancer, ovarian carcinoma, soft tissue sarcoma, and gastrointestinal and genitourinary tumors.[5] A relationship between primary breast lymphoma and lymphomas of mucosa associated lymphoid tissue (MALT) has been suggested.[3]

The objective of this study was to assess the relative frequency of (primary and secondary) breast lymphomas and its categorization according to WHO classification of lymphoid neoplasms.

Material and Methods

All NHLs (nodal and extra nodal) diagnosed in the section of histopathology during 1992-2004 were retrieved by using Systemized nomenclature of medicine (SNOMED) coding system. Code for lymphoma is M-9590/3.6 All the cases were reviewed. All patients (n=30) diagnosed with lymphomatous involvement of the breast were selected. These cases represented both lesions i.e. either primarily involving the breast (Primary breast lymphomas) or the expression of generalized disease extending into the breast (Secondary breast lymphomas). Distinction between primary and secondary breast lymphomas was not made owing to lack of availability of clinical information. All specimens were fixed in 10% buffered formalin, routinely processed under standardized conditions for paraffin embedding, sectioned and stained with Harry's Haematoxylin and Eosin using standard procedures. Immunohistochemistry panel included CD45 (LCA), B cell markers: CD20 and CD79a ,T-cell markers CD45RO (UCHL1) and CD3.An additional panel of CD30 (Ki-1), CD 15 (GAA), Ki 67(MIB 1), ALK protein, Epithelial membrane antigen (EMA), CK MNF & Cam 5.2, HMB45, S-100 and Vimentin was also used. PAP and later envision

system (Dako, Denmark) was used for immunostaning. Descriptive analysis was done for all variables of interest using SPSS software 10.0.

Results

Total number of breast malignancies diagnosed in this department was 5637 during the study period of 10 years and the total number of NHLs (Nodal and extra Nodal) was 2632. Thirty (n=30) patients accounting for 1.13% were diagnosed to have lymphomatous involvement of the breast. Of these 28 (96.5%) cases were seen in females and 2 (6.89%) were seen in males. The F: M ratio was13.5:1. Age range was 12-92 years with a median age of 43 years (Mean age 46.5 years, SD $\pm$ 16.88 years).

Lymph node involvement was noted in 5 patients. The breast tumours generally were soft and fleshy in consistency and their sizes ranged from 2.5 - 13.5 cm. There were 19 cases (65.5%) of diffuse large B- cell Non-Hodgkins lymphoma (DLBCL), 6 cases (20.68%) of Non-Hodgkins lymphoma; not otherwise specified (NHL; NOS), 1 case (3.44%) each of Burkitt's lymphoma, peripheral T cell Lymphoma (PTCL), Small lymphocytic lymphoma (SLL), multiple myeloma (MM) and Mycosis fungoides (MF) which was involving the skin of nipple and areola.

The sites of the lesions were the right breast in 11 cases (37.93%), left breast in 9 cases (31.03%) and both breasts in 2 cases (6.89%), while the location of 8 masses (27.58%) was unknown. The specimen received included 6 (20.68%) mastectomy specimens, 8 (27.58%) excision biopsy specimens and 11 (37.93%) incision biopsy specimens. In 5 (17.24%) cases blocks were received. Immunohistochemical studies were negative for cytokeratins (MNF & Cam 5.2) in all cases. All cases of DLBCL expressed B cell lineage antigens and were positive for LCA and Pan B (CD20 & 79a). The only case of multiple myeloma was a known case of this disease with secondary mammary involvement. Two bilateral cases were diagnosed to have DLBCL and Burkitt's lymphoma respectively.

Discussion

Breast involvement by non-Hodgkins lymphoma is rare. Our study has also shown a frequency of 0.5% among all breast malignancies, an incidence well in accordance with other studies. Ferguson[7] suggested that primary breast lymphomas are rare because the breast contains less lymphoid tissue than other organs such as lungs and intestines, where primary lymphomas are more common. The breast has been considered as a potential site for so called mucosa associated lymphoid tissue (MALT), and lymphoma arising thereof could be expected.[8,9] Differences between primary and secondary lymphoma have been reported. Criteria for diagnosis of primary lymphoma of the breast included confinement to one or both breasts, with or without ipsilateral lymph node involvement, but no further evidence of disease else where in the body; the lack of previous extra mammary lymphoma; and the presence of normal breast tissue around a focus of lymphoma. Among patients with malignant breast neoplasms, patients with primary breast lymphoma reportedly represent 0.04% to 0.53% of all primary malignant tumors of breast.[9] Primary lymphomas of the breast have also been recently reported to be of lower grade than secondary breast lymphomas. Due to lack of availability of relevant clinical data this distinction was not made in our study.

In our series, as in several others, breast lymphoma appeared to be a disease of the middle and old age with more than half of the patients from fifth and sixth decade. Only case of Burkitt's lymphoma was seen in a young 28 year old female who had bilateral breast involvement. Non endemic Burkitt's lymphoma accounts for 2% to 10% of non-Hodgkins lymphoma and only 3% have breast involvement at presentation.[10]

Our data lacks any information about the systemic involvement in this case. Literature suggests that Burkitt or Burkitt-like lymphoma are more common among the young population, as seen in our study, and are typically more aggressive.[9] Mammograpy has limited role in the evaluation of breast lymphomas as compared to that of the other breast malignancies. Breast lymphoma diagnosis almost always requires excisional biopsy or needle aspiration biopsy.[11]

A lymphocytic mastopathy characterized by a lymphocytic infiltrate within the breast epithelium has been described, but its relevance as a precursor lesion of mucosa-associated lymphoid tissue (MALT)-type lymphoma of the breast is uncertain.[12]

Immunophenotypyic analyses of mammary lymphomas show a preponderance of B cell lineage tumours as also seen in our series. Diffuse large B- cell Non-Hodgkins lymphoma (DLBCL) was the most common type of NHL in the breast (65.5%), this frequency is again comparable to the study done in Japan which showed a frequency of 60-70%.[2,8]

Previous evaluations have suggested that cystic mastitis is involved in the genesis of mammary lymphoma. Rooney et al have described the association of primary breast lymphomas with pre-existing lymphocytic lobulitis.[13] This progression illustrates the relationship between extranodal lymphomas and underlying autoimmune disease and the location of lymphomas to related sites.[14]

Our study showed that lymphomatous involvement was predominantly seen in the right breast, Shouten and associates[15] have also reported that the right breast was

more susceptible to NHL than the left.[15] Involvement of both breasts was seen in two cases, which is comparable to the study conducted by Aozasa K et al (6%)[2], however this rate is lower than that reported from Western countries (13%).[15]

Anaplastic large cell lymphoma (ALCL) is an unusual variant with apparently aggressive features. Abdullah et al have reported such a case with a very favourable long-term outcome in a 15-year-old girl who had a 5-cm ulcerating lump in her left breast of five months duration[16] whereas our series showed no ALCL.

Lihara et al described spontaneous regression of diffuse large B cell lymphoma of the breast which has originally metastasized from the brain. Presences of CD 8 positive small lymphocytes are suggestive of aiding the spontaneous regression.[17]

Illes et al reported a case of bilateral primary malignant lymphoma of the breast presenting during pregnancy in a 24-year-old woman which on autopsy and histological examination turned out to be Burkitt-type lymphoma in the breast, ovary, brain, liver, kidney, adrenal gland, pancreas, stomach, bone marrow and myocardium.[18]

We concluded that breast lymphomas represent 1.13% of all NHL and 0.5% of all breast malignancies in this study. The most frequent morphologic type was diffuse large B-cell lymphoma. The frequency and morphologic findings are comparable with the Western published data.

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