Primary lymphoma of breast - a rare case report
KAMALESHWARI K KESAVAN
Department of Pathology,
THANJAVUR MEDICAL COLLEGE

Abstract:
Malignant lymphoma of breast is rare, which may either be primary or secondary. We report a rare case of primary breast lymphoma in a 55 year old female, who presented with mass in the right breast. A fine needle aspiration (FNA) was done and a differential diagnosis of lymphoma poorly differentiated carcinoma neuroendocrine carcinoma was given. A histopathological study and further immunohistochemical analysis with a panel of markers confirmed the diagnosis of non-Hodgkin's lymphoma of breast of diffuse large B cell type.

Keyword:
Primary breast lymphoma, immunohistochemistry, poor prognosis

Introduction:
Breast lymphomas, both primary as well as secondary are rare to occur. The presentation of lymphoma of breast is the same as that of the commonly occurring breast carcinoma. A thorough examination and detailed history of the patient is required for the differentiation between a primary and secondary lymphoma.

Women of postmenopausal age are commonly affected. A small proportion of breast lymphomas occur in pregnant and lactating women. Lymphomas of breast have a poor prognosis and nearly half of the patients have a relapse. Breast lymphomas can mimic a poorly differentiated carcinoma and must be confirmed by an immunohistochemical analysis, since the treatment strategies differ in both the conditions.

Case History:
A 55 year old female was referred from surgery outpatient department for FNA with complaints of painless lump in right breast for 2 months duration, which was increasing in size rapidly. On examination a firm, nodular, painless immobile swelling measuring 4x3 cm in right breast was noted. She had no other complaints. On general examination she had no lymphadenopathy except for tiny node in ipsilateral axillary region. Her past history revealed no significant details.
pertaining to lymphoma.

**FNAC REPORT:**
Aspirated smear studied showed a cellular smear composed of monotonous population of neoplastic cells in diffuse sheets and dispersed manner. Individual cells are small round blue cells with hyperchromatic nuclei and a scant cytoplasm. (Figure: 1)

![Figure 1: FNAC – Monotonous population of small round cells with hyperchromatic nuclei and scant cytoplasm-H&E, 40X](image1)

A differential diagnosis of poorly differentiated carcinoma / lymphoma / neuroendocrine carcinoma was given and advised to proceed with biopsy for evaluation.

**SURGERY:**
Only after 3 months the patient turned up for the surgery, and a modified radical mastectomy was performed and the specimen sent to our department for histopathological examination.

**GROSS EXAMINATION:**
Received a modified radical mastectomy specimen measuring 28x14x7 cm, with skin ellipse measuring 17x12x0.5 cm. External surface: Nipple and areola eroded with an ulcerative lesion measuring 10x8 cm, few nodules made out on the skin surface (Figure: 2) Cut surface: Revealed a circumscribed homogenous grey white firm growth measuring 15x10x6 cm involving the skin and base grossly, and separated from medial and lateral margins by 1 cm. (Figure: 3)

![Figure 2: Gross - External surface: Mastectomy specimen with ulcerated skin ellipse and few nodules made out on the surface.](image2)

![Figure 3: Cut surface: Showing a circumscribed homogenous grey white firm growth almost occupying the entire breast involving the skin and base grossly.](image3)

Cut surface of axillary pad of fat measuring 5x5x4 cm revealed 4 nodes, largest measuring 2x1cm, smallest measuring 0.5cm diameter and the other two nodes each measuring 1cm diameter.
MICROSCOPIC EXAMINATION:
Hematoxylin and eosin stained sections from the tumour showed a malignant neoplasm composed of tumour cells arranged in diffuse sheets (Figure:4). The individual cells were larger (2-3 times the size of a normal lymphocyte) resembling immunoblasts and centroblasts. (Figure: 5)

Figure 4: Neoplastic proliferation of tumor cells in diffuse sheets-H&E, 10X

Figure 5: Individual tumor cells about 2 times larger than small lymphocyte, resembling centroblasts, with scant cytoplasm-H&E, 40X.

IMMUNOHISTOCHEMISTRY:
Imuno histochemistry was performed in our Department of Pathology. 4µm thin paraffin embedded sections from the representative block of this case were taken. The Super SensitiveTM

Section from the interface of tumour and margin of breast revealed normal breast tissue adjacent to the tumour (Figure:6).
Polymer-HRP detection system using a non-biotin polymeric technology where the secondary antibody conjugated to Poly-HRP reagent is bound to the primary antibody and visualized by the DAB (Diaminobenzidine) chromogen. A panel of markers were used including, CD20, CD3, cytokeratin and synaptophysin to diagnose the exact diagnosis and to rule out the other possible differential diagnosis made.

**CD 20** (B cell marker) – **positive** (Figure: 7)  
**CD 3** (T cell marker) - **focal positive** (Figure: 8) - immunologic response to the neoplastic B cells.

**DISCUSSION:**
Primary lymphoma of breast accounts for about 0.04 – 0.5 percent of all breast malignancies and accounts to about less than 0.5 percent of non-Hodgkin’s lymphomas, 1.7

**Figure 7:** Immunohistochemistry – CD 20: tumor cells showing strong diffuse cytoplasmic positivity - 40X

**Figure 8:** Immunohistochemistry – CD 3: tumor cells showing focal cytoplasmic positivity - 40X

**Cytokeratin** (epithelial marker) – **negative** (Figure: 9)  
**Synaptophysin** (neuroendocrine marker) – **negative** (Figure: 10)

**Figure 9:** Immunohistochemistry – cytokeratin - negativity of tumor cells - 40X

IHC confirms the diagnosis of lymphoma of B cell origin, focal positivity of CD3, T cell marker shows the immunologic response to the neoplastic B cells.
-2.2% of all extranodal non-Hodgkin’s lymphoma (11). According to the International Extranodal Lymphoma study group, the incidence of non-Hodgkin’s lymphoma of breast is rising (4). More than half of the lymphoid malignancies arising in the breast are primary (6,8). There are no morphological differences between a primary and secondary lymphoma of breast. According to the WHO, Wiseman and Liao have proposed a criteria for a diagnosis of primary breast lymphoma (1)

Criteria for diagnosis:
1. Adequate histological sample available
2. Presence of breast tissue in or adjacent to the lymphoma
3. No concurrent nodal disease except for ipsilateral axillary nodes
4. No previous history of lymphoma in any other organ or tissue

Our case has fulfilled all the 4 criteria for primary breast lymphoma. It occurs as rapidly growing masses affecting women of postmenopausal age (55-65 years), mostly unilateral, bilaterality seen in 11 – 15 % (1). For unknown reasons right breast is commonly involved (1). The origin for lymphoid tissue in breast is probably from the mucosa associated lymphoid tissue (1,3,5) or the lymphatic tissue within the breast adjacent to the ducts and lobules or the intra-mammary lymph nodes (1). Some studies, have shown an association of autoimmune thyroiditis with primary breast lymphoma (4). More than 80 percent of lymphomas of breast are of B cell type, most of which are pan B marker CD-20, CD79a, Bcl2 positive (2,6,9,11). The differential diagnosis are poorly differentiated carcinoma and neuroendocrine carcinoma, which can be ruled out by an immunohistochemical study. Ulcerative lesions are common with T cell non-Hodgkin’s lymphoma, but in our case, it is confirmed to be a B cell type that has ulcerated. This case is submitted also because of this rare type of presentation.

Lymphomas of breast are associated with a poor outcome (1,9,10). Clinical picture is often similar to corresponding lymphoma of nodes. Relapse is common in nearly half of the patients. Common sites involved are contralateral breast, other nodes and CNS (9). Involvement of CNS has a grave prognosis. Diffuse large B cell lymphoma is the most common type of lymphoma (2,3,5), followed by follicular (15%), MALT lymphoma (12%) and burkitt’s lymphoma (11) which is commonly bilateral and frequently seen in pregnant and lactating women (1,2,6). Other types seen are anaplastic, marginal zone etc (7,9). Anaplastic large cell lymphoma is found to be associated with breast implants. Many recent studies recommend treatment strategy of surgery along with CHOP regimen (7). Some studies debate the role of surgery, suggesting only axillary dissection. Regarding treatment, chemo/radiotherapy is of choice (4). A high dose chemotherapy and peripheral blood stem cell transplant (10) decreases the incidence of relapse. In CNS relapse- involved field radiotherapy is found to be effective (5,11).

CONCLUSION:
A histopathological analysis and immunohistochemical study that can be done even with biopsy samples to diagnose lymphoma of breast, so that, treatment can be initiated to the patient at an appropriate time.
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