Section: Miscellaneous

Case Report

PRIMARY BREAST LYMPHOMA: A RARE CASE REPORT

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Abstract

Primary lymphoma of breast is commonly characterized as lymphoma localized to one or both of the breasts and/or the regional lymph nodes in the absence of a previous history of lymphoma. Primary breast lymphoma represents less than 0.5% of all malignant breast neoplasms and roughly 2% of all extranodal lymphomas. The most prevalent histology form is diffuse large B-cell lymphoma, however imaging results are nonspecific. The prognosis and course of treatment vary depending on the type of lymphoma. The authors describe a patient who had treatment for a breast lump that turned out to be primary breast lymphoma in a tertiary care hospital.

INTRODUCTION

Primary breast lymphoma (PBL) can be defined as lymphoma confined to one or both breasts and/or regional lymph nodes, in the absence of a prior history of lymphoma. PBLs are uncommon and accounts for 0.04-0.5% of the total malignant breast tumors. They represent <1% of non-Hodgkin's lymphoma patients and 1.7–2.2% of extra nodal lymphoma patients.[1,2]

PBL patients are generally middle aged or elderly women and in 11% of cases, it is bilateral. Although any type of lymphoma can occur, majority of PBLs are B cell in origin among which the most prevalent subtype is Diffuse Large B cell lymphoma(40–73% of cases) followed by Follicular lymphomas which constitute 15% of PBL, Mucosal associated Lymphoid Tissue (MALT) lymphomas is seen in 12.2%, and Burkitt and Burkitt-like lymphomas makes up 16.3% of PBL.[3] Marginal zone lymphoma, small lymphocytic lymphoma (SLL), and breast implant associated anaplastic large cell lymphoma are also among the other kinds of PBL described. Although the pathophysiology of it is yet understood, it is believed to originate from intra-mammary lymph nodes, or lymphoid tissue that is close to breast ducts and lobes.[4]

Diagnosis of breast lesions depends on clinical, imaging and pathological correlation. In PBL, the imaging findings are inconclusive with majority of lesions on mammography corresponds to hyperdense (91%) as well as oval (71%) masses. On ultrasonography they generally present as solitary (75%), circumscribed (50%), microlobulated (38%), and oval (50%) lesions. They often have a hypoechoic status (87%); calcifications or speculated margins are uncommon.[5]

Here the authors describe a patient with Chronic Lymphocytic Leukemia(CLL) / SLL in the breast.

CASE REPORT

A 65 year old woman presented with lump in left breast for 10 months which was rapidly progressing in size. On examination of left breast, a hard mass of size 20x20 cm was felt, occupying all quadrants. Mass was hard in consistency, fixed and not mobile without skin involvement. Dilated veins were present. Axillary nodes were not palpable.

Patient was a known diabetic for the past 5 years and was on regular treatment. No other comorbidities noted. Patient attained menarche at 14 years of age and menopause at 40 years of age. Multipara (P2L2), last childbirth was 38 years back. No relevant family history. Laboratory investigations (Complete Blood Count) were within normal limits.

Bilateral sonomammogram showed a large fairly well-defined hypoechoic mass lesion distorting the mammary zone of left breast parenchyma measuring 20.7x13.7x16.4cms having increased vascularity noted in Doppler signals – likely neoplastic etiology.

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Non-Enhanced Computed tomography (NECT) chest showed a large soft tissue density area involving all four quadrants of left breast with lobulated appearance with extension and infiltration. No evidence of bony erosion. Likely mitotic etiology lesion and was suggested for histopathology correlation. [Figure 1,2]

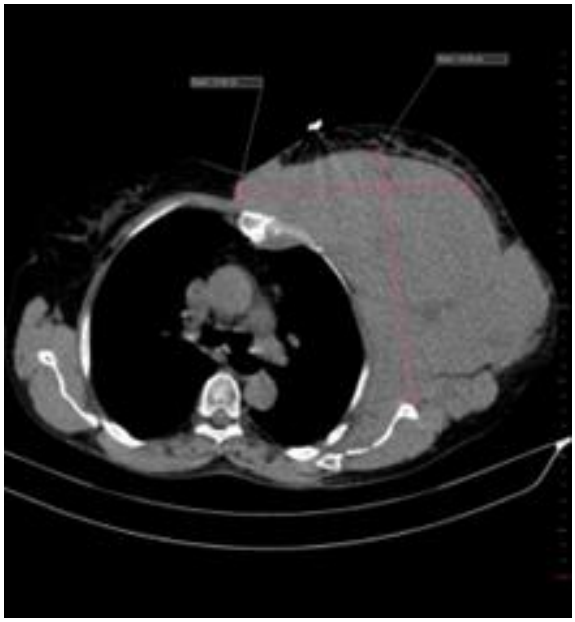

Figure 1: NECT – sagittal view

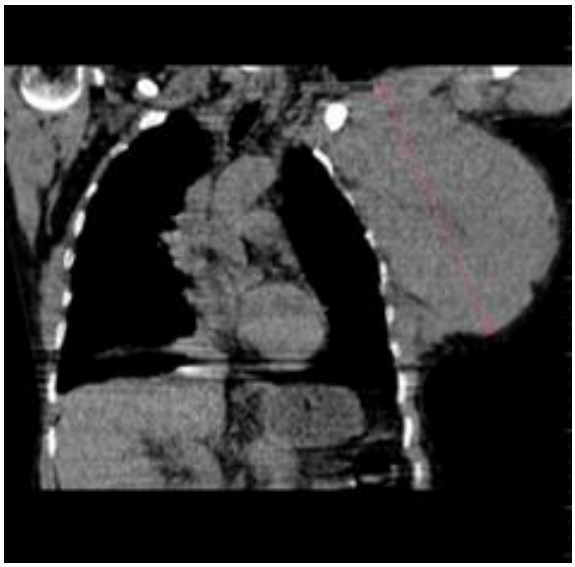

Figure 2: NECT chest - Axial view

Magnetic Resonance Imaging (MRI) of chest showed homogenous signal intensity space occupying lesion involving left anterior chest wall and axilla displaying T2/STIR hyperintense signal intensity with diffusion restriction. Lesion involve left pectoralis muscles. Axillary lymph nodes appeared normal. Features favored neoplastic etiology, suspicious of Lymphoma.

Positron Emission Tomography (PET) scan showed metabolically active primary left breast malignancy suggested biopsy correlation and left supraclavicular, right upper paratracheal & left deep pectoral lymph nodes showed metabolically active lymph nodal involvement.

Tru-cut biopsy was done from breast lump. Preliminary histopathological diagnosis was Lymphoproliferative neoplasm, (Fig:3,4) with the immunohistochemistry showing positive reactions for CD 20, CD 5, CD 23 and BCL2. Ki67 was positive in 20–25% of the tumor cells. The final diagnosis was CLL/SLL.

The patient received 5 cycles of chemotherapy with Inj. Rituximab 375mg/m^2 and Inj. Bendamustine100mg - D1D2. She tolerated her treatment very well. The patient was under regular follow up. Now the patient has complete resolution of the tumour clinically.

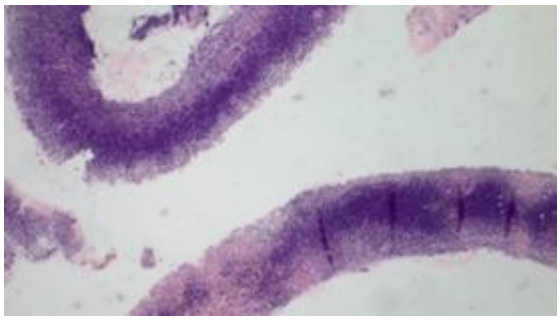

Figure 3: Core biopsy showing diffuse sheets of tumor cells. (H&E 10x)

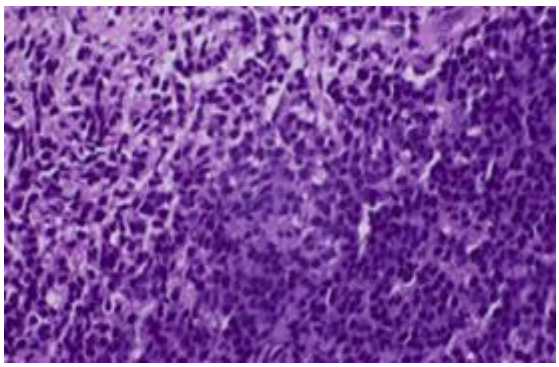

Figure 4: Diffuse sheets of small round cells with hyperchromatic nucleus and scanty cytoplasm (H&E 40x)

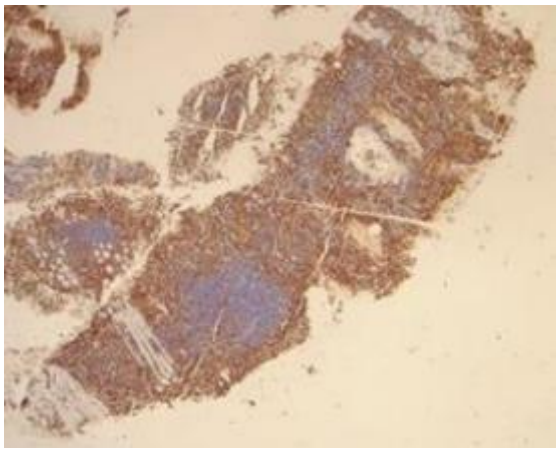

Figure 5: Positive BCL2 immunoreaction with score 3+ (IHC 10x)

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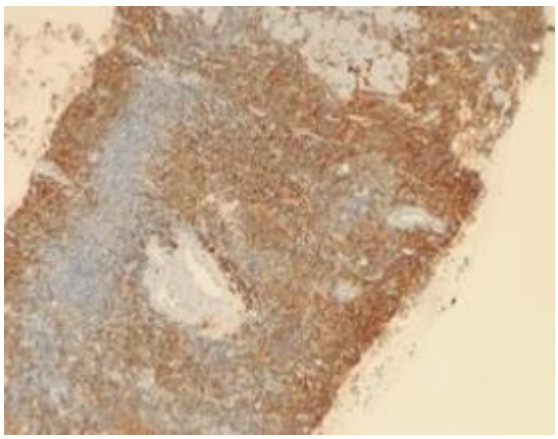

Figure 6: Positive CD20 immunoreaction with score 3+ (IHC 10x)

Figure 7: Positive CD23 immunoreaction with score 3+ (IHC 10x)

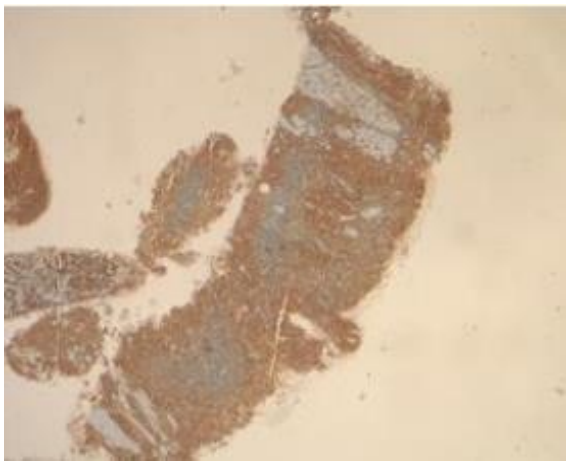

Figure 8: Positive CD5 immunoreaction with score 3+ (IHC 10x)

DISCUSSION

Wiseman and Liao initially described PBL of the breast in 1972. The diagnosis was based on the following conjectures: no prior diagnosis of lymphoma; the breast as the site of primary presentation; breast tissue closely associated with lymphomatous infiltration; and absence of disseminated disease beyond the ipsilateral axillary lymph nodes. Because PBLs of the breast have a very low incidence or sometimes appear with concomitant breast cancer, they can be readily mistaken on imaging as an invasive carcinoma.[6]

Chronic lymphocytic leukaemia/small lymphocytic lymphoma (CLL/SLL) is a B-cell lymphoma comprising of small mature B-cells that are functionally incompetent. Although, CLL and SLL represent the same disease and share similar properties, the diagnosis of SLL is usually preferred for those cases which have lymphocytosis > 5000/microL and have nodal, splenic or extramedullary involvement.[7] A diagnosis of SLL requires organ enlargement and infiltration by the neoplastic B cells. In the current case, the lesion showed up as a breast mass with infiltration by neoplastic B cells and had no circulationg leukemic cells, hence meeting the criteria for SLL.[8,9]

Although a definite etiology of CLL/SLL in breast remains unclear, it has been documented that mutation of the ATM gene (11q22–q23, involved in ataxia-telangiectasia) are linked to lymphoid neoplasia and breast cancer, which could be one cause of development of CLL in the breast. However, the most frequently mutated genes seen in CLL/SLL at the time of initial treatment include NOTCH1 (10-15%), ATM (10-15%), SF3B1 (10%), TP53 (5-10%), and BIRC3 (5%). Both lymphomas and breast tumors may share a viral etiology, such as Epstein-Barr virus and mouse mammary tumor virus. However, the role of these viruses play in the development of breast cancer is not clearly elucidated.[10]

Susnik et al,[11] hypothesized that, similar to the impact of Helicobacter pylori infection on the pathogenesis of MALT lymphoma observed in the stomach, antigenic stimuli from breast cancer may have triggered lymphomagenesis of a nearby MALT tumor. A comparable mechanism for CLL and breast cancer may be conceivable in such an instance. Furthermore, there is experimental data indicating that leukemic tumorigenesis may be facilitated by antigenic activation of B-CLL.

Both the imaging features and the clinical presentation are identical to those of breast cancer. A palpable mass, with or without local pain, is the most common sign among a variety of clinical presentations. It is most commonly found in the upper outer quadrant of the breast. In as many as 25% of cases, it could also be linked to palpable axillary lymphadenopathy.[12] Other less common signs include nipple or skin retraction, erythema, nipple discharge, ulceration or peau d'orange. PBL patients hardly ever experience the typical B symptoms that are evaluated in lymphomas, such as weight loss, fever and night sweats.[13]

While mammography has demonstrated a high degree of sensitivity in the detection of breast cancer, imaging alone is not sufficient to diagnose breast lymphoma. The lesion in this particular case was a large oval or spherical mass, as is typical of most cases of breast lymphoma. Asymmetry, skin thickness, and lymphedema detected on

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mammography are other less frequent radiological abnormalities.[14]

Flow cytometry (in hematological and solid specimens) and IHC are used as auxiliary tools in diagnosing CLL/SLL. Using flow cytometry, the neoplastic cells show light chain restriction (dim expression) and are positive for monotypic surface IgMdim+, IgD (IgG+ in ~10% cases), CD19, CD5, CD23(CLL/SLL is characterized by co-expression of CD5 and CD23), CD43, CD20dim+ and negative for CD10, CD79b, CD25.[15] On IHC they express pan-B-cell markers (CD19, CD20, CD79a, and PAX5), CD5, and CD23, and are negative for CD10 and other Germ cell markers. In the present case IHC showed positive reaction for CD 20, CD 5, CD 23 and BCL2. Treatment in the front-line scenario typically involves rituximab-based chemotherapy. The sole purpose of surgery is to obtain tissue for diagnosis; there is no benefit to survival from mastectomy. As of right now, primary breast SLL management and treatment lack current standard guidelines. Since mastectomy does not appear to improve survival or lower the chance of recurrence, it is not a recommended treatment for any breast lymphoma. Furthermore, there is no additional therapeutic advantage from axillary dissection.[16,17]

Primary breast lymphoma is thought to be similar to other lymphomas of the same histological type, despite the fact that it was once assumed to have a dismal prognosis. There is equal use of the International Prognostic Index and the Ann Arbor stage method. Stage I and II have a five-year survival rate of 89% and 50%, respectively, depending on the case series. Age is regarded as an independent predictor of long-term survival in several reports.[18]

CONCLUSION

This unusual example demonstrates that, even in the absence of clinical CLL, pure SLL should be considered in the differential diagnosis for a painless breast tumor. Additionally, these individuals react clinically as well as radiologically to systemic anti-lymphoma therapy, and they rarely require surgical resection and dissection of the axillary lymph nodes.

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