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Case Report

Primary Non-Hodgkin Lymphoma of Breast in Young Female-A Rare Entity

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Abstract: Primary lymphoma of the breast is an uncommon malignant breast tumour which is rarely distinguished from other more common forms of breast cancer due to its low occurrence. As the management of Non-Hodgkins lymphoma of breast differs from adenocarcinoma of breast, here the mainstay of treatment is systemic chemotherapy. Thus, reaching an accurate diagnosis is crucial. A young woman presented with breast lump and on fine needle aspiration cytology a diagnosis of granulomatous inflammation was made. Subsequent biopsy revealed Non-Hodgkins lymphoma of breast.
Keywords: Breast, Malignancy, Non-Hodgkin lymphoma.

Introduction

Breast lymphoma is a rare malignancy accounting for only 0.5% of malignant breast neoplasms and less than 2% of extra nodal Non-Hodgkin's lymphoma. It is an extra nodal lymphoma originating from the breast with or without axillary lymph node metastases and was originally described by Wiseman and Liao in 1972.[1] The lack of lymphoid tissue in the breast is probably to blame for this low prevalence.[2] Patients range in age from 60 to 65 years old on average.[3] Almost solely women are affected by the condition. 11% of all breast lymphomas showed bilateral breast involvement. This unusual occurrence is more common during pregnancy or after childbirth implying the importance of hormonal influence on tumour growth.[4]

A painless lump is the most common clinical manifestation which is most often present in the external superior quadrant.[5] Localised discomfort; inflammation and lymphadenopathy are some other symptoms. Skin retraction, erythema, peau d'orange and nipple alterations however are comparatively uncommon.[6] Non-Hodgkins lymphoma of the breast and the more prevalent adenocarcinoma of the breast are typically not recognized before surgery or biopsy.[7] A fast growing mass, the absence of nipple discharge or nipple retraction, multiple or bilateral lesions, violet-coloured skin and when present axillary nodes that have a softer consistency than expected are some clinical characteristics that could indicate the presence of lymphoma.[8]

Mammography findings are nonspecific. Oval-shaped, high-density masses are the characteristics of majority of lesions. The masses that ultrasound examination reveal are often single, bounded, microlobulated and oval. The mass typically has a hypoechoic echo pattern. There are no calcified or spiculated edges on any lumps.[9] Mucosa-associated lymphoid tissue (MALT) is likely to be the source of breast lymphoid cells.[10] Additionally, lymphomas can develop from intramammary lymph nodes or the lymphatic tissue that surrounds ducts and lobules of the breast.[11]

B cell lymphomas are primarily CD20 positive making up more than 80% of these lymphomas of the breast. The most common histopathologic types are diffuse large B cell lymphoma which makes up to 50% of all cases, follicular lymphoma which accounts for 15% of cases, MALT lymphoma which accounts for 12.2% of cases, Burkitt's lymphoma and Burkitt-like lymphoma makes up 10% of the cases.[12] Since diffuse large B-cell lymphoma (DLBCL) is the most typical histological diagnosis. A non-germinal centre B cell phenotype with a high proliferation index has been identified in these lymphomas.[13] When compared to other extra nodal lymphomas, lymphoma of the breast is an aggressive and rapidly developing cancer that has a poor prognosis.[14] Although the prognosis is currently estimated using the Ann Arbor clinical stage and International Prognostic Index (IPI) score, it is still challenging to do so precisely due to the wide range of histological subtypes, the complexity of the contributing factors and due to the low occurrence. Case studies and retrospective analyses of research with small sample sizes are the primary sources of its present understanding.[15]

Breast lymphoma subtyping and definitive diagnosis require immunohistochemical (IHC) confirmation on smears, cell blocks or tissue slices. The subtype is identified using morphological, IHC and genetic characteristics. A core biopsy can be used for the same. The majority of breast lymphomas are B cell types, which express B cell antigens such as CD20 and exhibit monotypic light chain restriction.

The Ki67 proliferation rate aids in differentiating between low grade lymphomas (10%–20% for follicular lymphomas) and high grade lymphomas (>40% for DLBCL) is an important pathologic parameter which needs to be taken care of. The IHC marker Ki67 antigen indicates a higher rate of proliferation. It is preferentially expressed during all active phases of the cell cycle but is not present in dormant cells, degrades quickly in the non-proliferative state and does not express itself during DNA repair activities.[16]

The role of fine-needle aspiration cytology (FNAC) for the diagnosis of various lymphoproliferative disorders has been questioned because it has been considered very tough to differentiate reactive lymphoid lesions from neoplastic ones by means of cytomorphology only. Recently due to the increasing use of immunophenotypying, FNAC might achieve accurate diagnosis in more than 90% of Non-Hodgkins lymphoma especially when the morphological assessment is supported by immunophenotypical analysis. Equally good results have been reported on the diagnostic accuracy of FNAC in extra nodal lymphomas.[17] In this paper, we report a case of breast lymphoma in a young female in her third decade of life.

Case Report

A 24 year old female presented with the complains of a painless, mobile mass in the upper inner quadrant in the right breast. FNAC was performed twice and Giemsa and Papanicolaou stained slides were examined which showed numerous lympho-histiocytic clusters in a background of lymphoid cells in various stages of maturation. No ductal cells were seen. Cytological diagnosis of granulomatous inflammation was given **(Figure 1, 2, 3).**

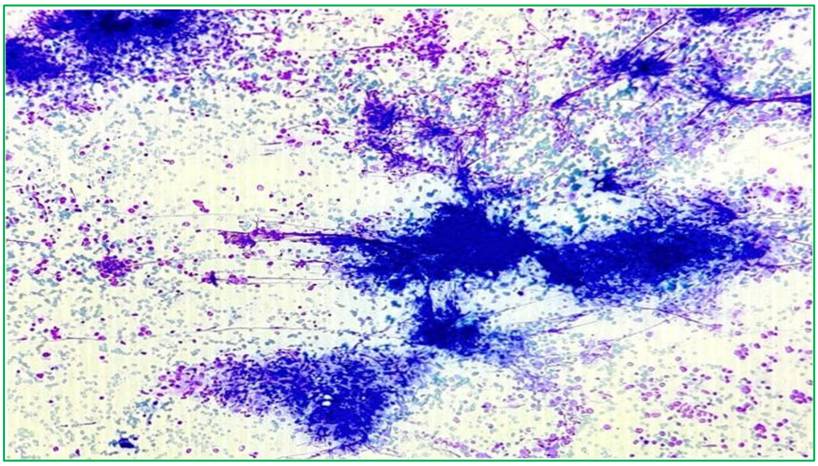

Figure 1. Giemsa stained cytosmears show presence of lymphohistiocytic clusters assuming epithelioid morphology along with scattered lymphocytes in various stages of maturation. (100X magnification).

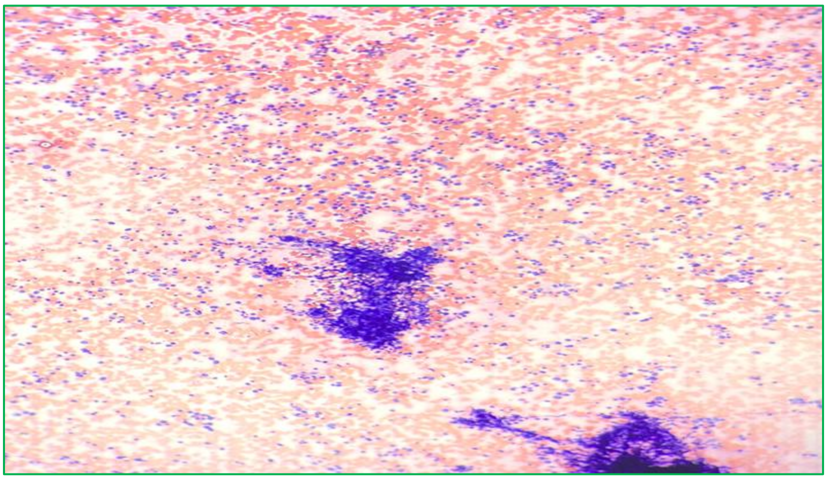

Figure 2. Giemsa stained cytosmears (100X magnification) show presence of tangled lymphohistiocytic clusters along with scattered lymphocytes in the background.

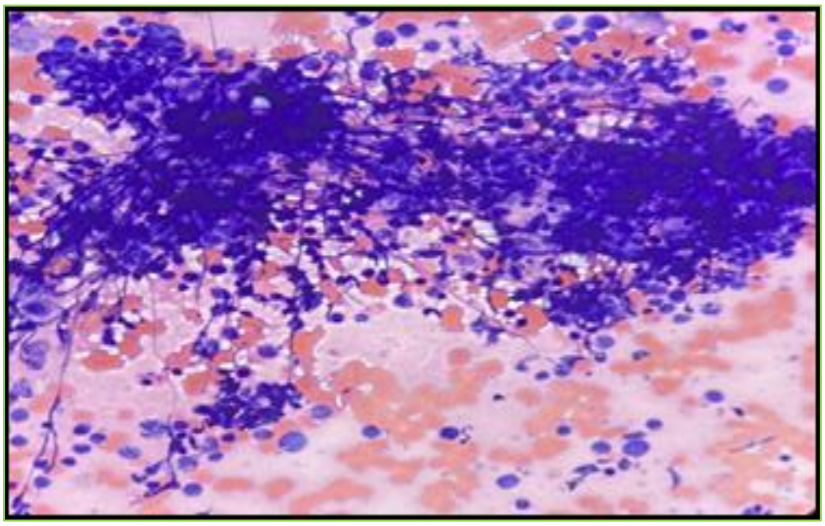

Figure 3. Giemsa stained cytosmears (400X magnification) show presence of tangled lymphohistiocytic clusters along with scattered lymphocytes in the background.

Following which tissue biopsy of same was done. Three grey brown to yellow soft tissue masses were received measuring 9.5 x 3.5 x 3cm, 5.8 x 3.5 x 2cm and 3.2 x 1.5 x 0.5cm. On cut section all three masses were grey white in appearance.

Microscopic examination of the tissue sections revealed tumor cells arranged in sheets, small clusters and groups. The cells were large with irregular nuclear contour, vesicular chromatin and prominent nucleoli along with areas of sclerosis. The periphery of the lesion showed large number of giant cells with granulomatous inflammation **(Figure 4, 5, 6).**

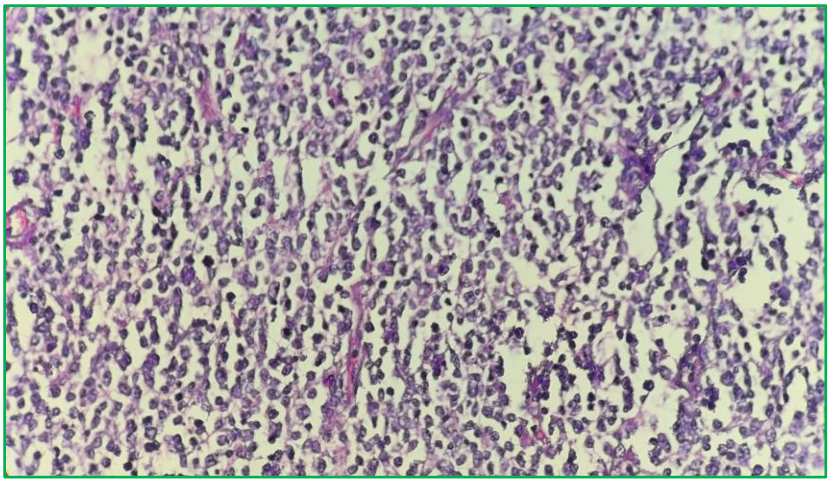

Figure 4. H & E stained slide (100X magnification) shows tumor cells arranged in sheets, small clusters and groups. The cells were large with irregular nuclear contour, vesicular chromatin and prominent nucleoli.

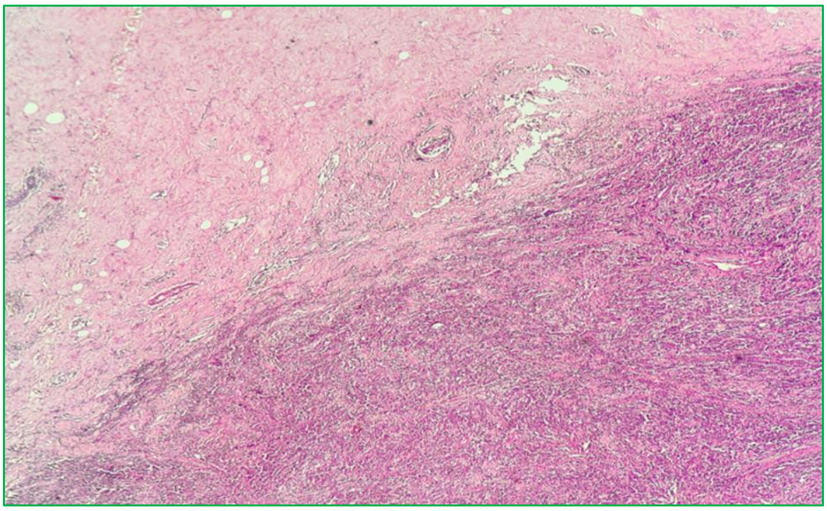

Figure 5. H& E stained slide (100X magnification) shows areas of sclerosis and with granulomatous inflammation.

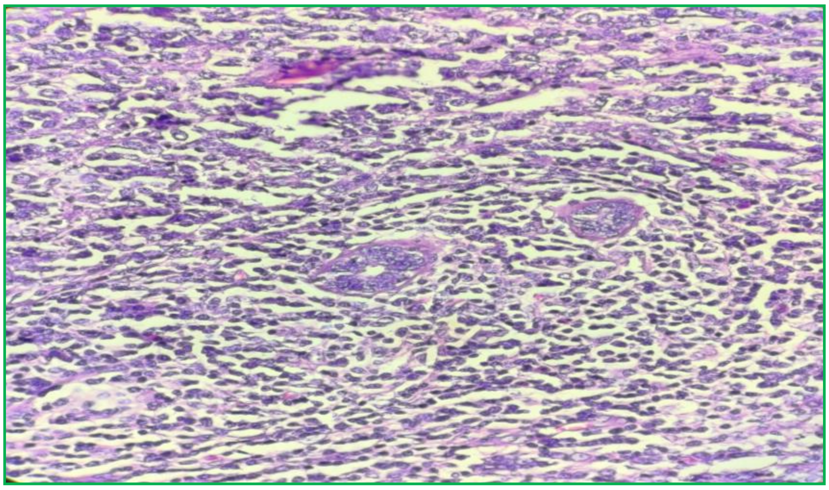

Figure 6. H& E stained slide (400X magnification) shows giant cells.

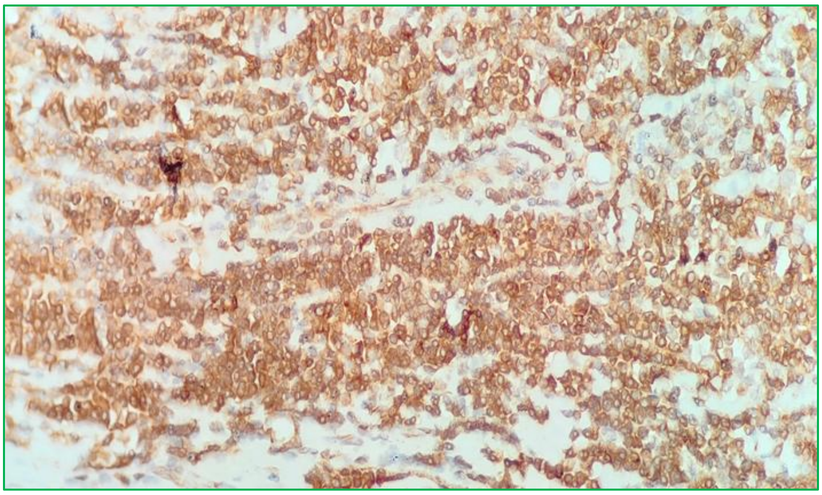

Figure 7. (100X magnification) Positivity of tumor cells for LCA.

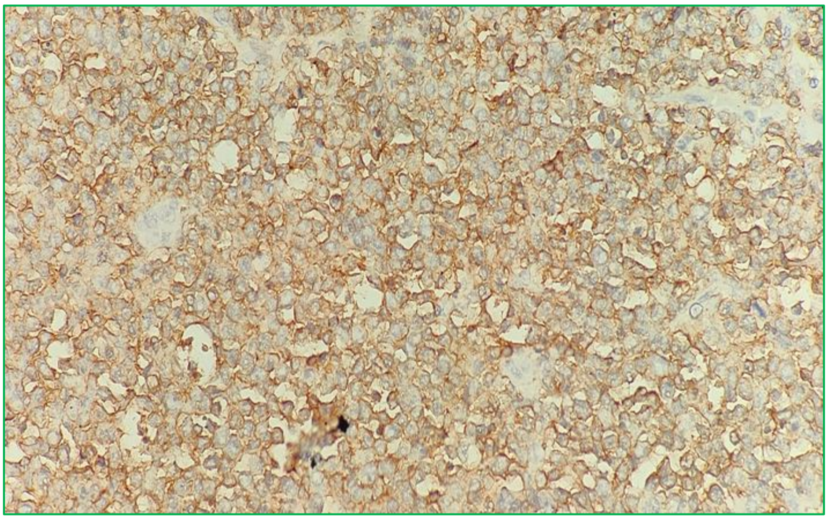

Figure 8. (100X magnification) Positivity of tumor cells for CD 99.

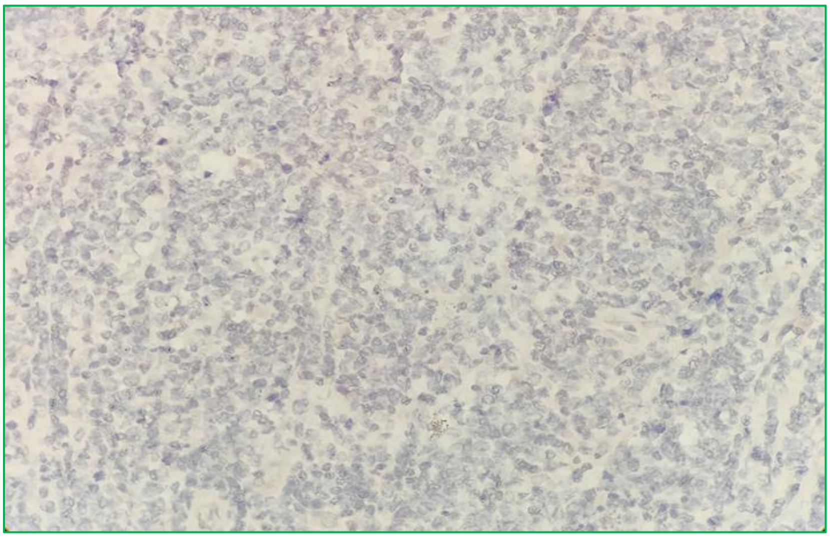

Figure 9. (100X magnification) Negativity of tumor cells for cytokeratin.

Immunohistochemically, the tumor cells showed positivity with leukocyte common antigen (LCA) and CD20. No staining occurred with cytokeratin **(Figure 7, 8, 9).**

With these histologic and immunohistochemical findings, the case was reported as lympho-proliferative disorder possibly Non-Hodgkins lymphoma.

Discussion

About 500 primary breast lymphoma cases are included in the currently available published sources, most of which are case reports and a handful of which are case series. Along with primary breast lymphoma, nodal lymphoma invasion into the breast instances were also documented.[18]

There are two distinct clinicopathological types known.[19] Case evaluations have showed a bimodal age distribution with a unilateral type that resembles the conventional age distribution of breast cancer and a bilateral, diffuse form that affects young females who are pregnant or lactating.[20] Our patient is an exception as she is in the third decade that is reproductive age group but presents with a unilateral lump in the right breast.

The most common site for a primary extra nodal lymphoma is the gastrointestinal tract- stomach and ileocoecal region are commonest, but any extra nodal location may be a primary site. Since secondary breast involvement is frequently difficult to rule out, many reported instances of breast lymphoma may not have been truly primary, on the basis of the Revised European American Classification of Lymphoid Neoplasms (REAL).

According to Wiseman and Liao, the case must meet the following requirements in order to be accepted as primary breast lymphoma: (a) technically adequate tissue (b) close interaction between lymphoma infiltration and breast tissue; (c) absence of evidence of widespread disease at the time of diagnosis (d) absence of a prior diagnosis of a non-breast lymphoma. These requirements were met, hence the present case was approved as primary breast lymphoma.[18]

Breast lymphomas are relatively uncommon and a large spectrum of histological types have been reported. Most of these are of the B cell type. A very few cases of T cell phenotype have been reported so far.[7] Malignant lymphoma is rarely considered in the preoperative evaluation of patients with breast tumors because of its low incidence. Also, in the reference with the available literature there are no specific clinical or radiological findings that lead the clinician to suspicion of lymphoma.[1] When compared to other malignant breast tumours, mammography is less useful in the diagnosis of breast lymphomas. Excisional biopsy or needle aspiration biopsy are almost always necessary for breast lymphoma diagnosis.[21]

Also, as breast lymphoma usually presents as a palpable mass simulating a carcinoma or a fibroadenoma clinically. Thus FNAC of the lump is the first step in the diagnostic approach.[22,23,24] Cytology offers a fast and appropriate confirmation of the nature of the lesion, reducing the waiting time and allows for the appropriate planning of the therapeutic strategy. Therefore cytology offers the possibility of a diagnosis and can set the indication for the need of biopsy to define the immunophenotype of the lymphoma.[23]

As in our case on FNAC a diagnosis of granulomatous inflammation was made and only after biopsy the final diagnosis of Non-Hodgkins lymphoma was made with help of IHC.

Conclusion

In conclusion, although primary Non-Hodgkins lymphoma of breast is extremely rare in comparison with primary breast carcinoma, it should be considered in the differential diagnosis of breast lump. In order to avoid any delay in the diagnostic process and to ensure accurate subtyping, the specimen should be properly obtained and sent for flowcytometry, histopathologic and cytogenetic assessments then only final diagnosis can be made with certainty.

Declarations

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Conflict of interest: None Declared
Ethical approval: Not Required

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