Primary Follicular Lymphoma of the Breast: A Rare Clinical Entity Diagnosed Using Tissue Flow Cytometry

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Introduction

Primary breast lymphomas are a rare entity and constitute less than 1 % of all the non-Hodgkin's lymphomas, <0.5 % of all breast malignancies and <5 % of extranodal lymphomas [1]. The predominant type of primary breast lymphoma is Diffuse Large B cell Lymphoma (DLBCL), while Follicular Lymphoma (FL) is a still rarer entity. In the study conducted by International Extranodal Lymphoma Study Group (IELSG), on Primary Breast Lymphomas, FL constitute 12.9 % of total 278 cases [1].

A number of markers are used to make a diagnosis of follicular lymphoma on flow cytometry (FCM) as well on immunohistochemistry (IHC). The predominant phenotype used to identify follicular lymphoma is a clonal B cell disorder with the B cells expressing CD5-CD10 + bcl-2 + phenotype [2]. The molecular studies using IgH/bcl-2 translocation is also useful to confirm the diagnosis of follicular lymphoma. The diagnostic difficulty in diagnosing FL is to differentiate it from reactive follicular hyperplasia (RFH). The brighter expression of CD10 and bcl-2 and loss of CD19 expression are the features that support the diagnosis of FL over RFH [2].

Case Report

We hereby report a case of 47 year old female, who went to a physician with the initial complaints of mass in the left

breast. The patient was suggested to undergo ultrasonography (USG) and it showed a hypoechoic mass measuring $11 \times 11 \times 8$ mm. The patient had no history of fever, weight loss, night sweats, headache or cough.

The patient underwent FNAC at an outside facility and was reported possibly as a non-Hodgkin's lymphoma, with an advice to undertake a biopsy. She was referred to our centre and underwent repeat USG along with USG-guided breast biopsy from the lesion. The USG showed findings similar to that was reported earlier. Two cores of biopsy were taken, with one core sent for flow cytometry in saline, while the other was sent to histopathology department in formalin for routine processing.

The tissue was teased to extract the cells and processed routinely for flow Cytometry. In view of the tissue being a core, only limited cell yield was expected and hence only a limited panel was put up. It showed cells present in the lymphoid region on FSC–SSC plot. These cells were gated to exclude the debris and showed most of the cells to have moderate to high CD20 expression. The CD20 + cells were then evaluated for light chain restriction which was seen for lambda light chain. This gave the idea that it is a B cell clonal lymphoproliferative disorder. On further analysis these cells were found to be positive for CD10, CD19 and CD23 (Fig. 1). However, they were negative for CD5. As we did not have bcl-2 on flow Cytometry, the diagnosis of CD5-CD10 + B cell clonal lymphoproliferative disorder, with suspicion of follicular lymphoma was reported.

The biopsy was received next day which showed benign breast ducts with stromal infiltration by sheets of lymphoid cells. These cells had small to intermediate size with high nucleocytoplasmic ratio. The infiltrate showed vaguely nodular pattern. In view of the flow Cytometry findings already available, only a limited panel was put up comprising of CD20, CD3 and bcl-2. The lymphoid cells were

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Fig. 1 Flow Cytometry findings: **a** Gated CD20 population; **b** Lambda restriction; **c** CD19-CD10 positivity; **d** CD23 positivity with CD5 negativity

Fig. 2 Immunohistochemistry: bcl-2 positivity (IHC ×400)

diffusely positive for CD20 and bcl-2 (Fig. 2). Few scattered lymphoid cells in background showed CD3 expression. The definite diagnosis of Follicular Lymphoma was made. The B cell rearrangement for this patient was positive. The full body CT scan of the patient was done which did not reveal any significant lymphadenopathy, thereby labelling the disease as primary follicular lymphoma of the breast.

Discussion

The primary lymphomas of the breast are a rare entity and have been reported rarely. The primary follicular lymphomas of the breasts are still rarer as the most common type is diffuse large B cell lymphoma [1]. The primary follicular lymphoma of breast in India has been reported infrequently. In a retrospective analysis performed by Topalovski et al., they found only 22 cases of breast lymphoma over a period of 31 years, of which only two cases were primary follicular lymphoma [3]. Flow Cytometry of the tissue, or even FNAC material (in the set-ups where FNAC is preferred for breast lesions), is a very robust and dependable tool for the lesions where a lymphomatous pathology is suspected. Many authors have advocated the use of FNAC material for definite diagnosis of lymphomas [4]. The biggest challenge in the diagnosis of follicular lymphoma is the differentiation from follicular hyperplasia. Although clonality is the paramount to differentiate these, but the cases this cannot be done combined approach of CD20 and bcl-2 staining has been advocated [5].

This case is being reported for its rarity and the application of flow Cytometry for the diagnosis of primary follicular lymphoma of the breast. Few authors have also used flow cytometry to even grade the follicular lymphoma, using the forward scatter CD19 dot plot to identify the proportion of centroblasts [6]. We however feel that the grading is left best to histopathology till the time the grading on flow Cytometry is not studied more extensively.

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