

Fine Needle Aspiration Cytology of Bilateral Non-Hodgkin's Lymphoma of the Breast with Leukemic Phase in a Pre-pubertal Girl

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Abstract

Non-Hodgkin's lymphoma (NHL) of the breast is very rare and is mostly seen in young puerperal women bilaterally or unilaterally and in older women with distinctly different clinicopathologic presentation. Bilateral NHL is rarely seen in very young non-puerperal patients and such an entity with bone marrow involvement along with a leukaemic phase in young patients has not been reported in literature. We report this case of a 13 year old girl who presented with bilateral breast lumps and malaise with blasts in peripheral blood smear. Fine needle aspiration cytology of breast helped in the diagnosis of NHL with leukaemic phase thereby preventing further unnecessary work-up. Examination of the bone marrow was adopted to stage the patient and initiate prompt treatment without delay.

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Key Words: Non-Hodgkin's lymphoma, fine needle aspiration cytology.

Introduction

Non-Hodgkin's lymphoma (NHL) of the breast is an extremely uncommon occurrence accounting for between 0.04% and 1.1% of all malignant tumours of the breast and 1.7 – 2.2% of extra-nodal lymphoma.¹⁻⁶ A review of the literature on this topic revealed around 350 well-documented cases of primary NHL with two distinct clinicopathologic presentations, one "bilateral diffuse" Burkitt's lymphoma group that affects young puerperal women with a history of recent pregnancy or childbirth disseminating rapidly to involve the central nervous system, ovaries, gastrointestinal tract or endocrine organs but not the lymph nodes. The second group accounting for 80% of the cases in the literature is seen among older women with unilateral breast involvement mimicking primary breast carcinoma and a variable clinical course depending on histologic grade and stage is generally a NHL of the B cell type. Recent studies have indicated that majority of the cases in the latter group may belong to lymphomas arising from the mucosa-associated lymphoid tissues

(MALT's).² We report fine needle aspiration cytology (FNA) of an unusual case presentation of bilateral NHL in leukaemic phase in a 13 year old pre-pubertal girl clinically mimicking juvenile fibroadenomas in which FNA cytology of the breast helped in determining the diagnosis and also FNA cytology of the bone marrow helped with the staging of the disease. To the best of our knowledge this case is unique in its clinicopathologic presentation and also emphasizes the role of FNA cytology as a simple, reliable, cost-effective test for accurate diagnosis and also for staging of malignant neoplasms.

Case Report

A 13-year-old girl presented in May 2000 with bilateral breast lumps, approximately 5x5x3.5 cm in size which had gradually increased in size from a month prior to presentation in G.K.N.M. Hospital, Coimbatore. There was no prior trauma to the breast, pain or discharge from the nipples. She was also complaining of malaise of 15 days duration. She was pale and exhibited generalized lymphadenopathy with hepato-splenomegaly. The breast lumps were firm in consistency and fixed to the chest wall. Rest of the systemic examination was normal. Her chest radiograph showed mediastinal widening. There was mild hepatomegaly with normal echo texture on ultrasonography. Fine needle aspiration cytology

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of both breast lumps using a 23 gauge needle was done and the smears were air dried and stained with May-Grünwald-Giemsa stain (Fig. 1). The smears were very cellular and showed a monomorphic population of a mixture of cleaved and non-cleaved lymphoid cells with very high N/C ratio, reticular chromatin and multiple nucleoli resembling lymphoblasts. Diagnosis of non-Hodgkin's lymphoblastic lymphoma, cleaved and non-cleaved type was made. Patient's hematological examination revealed hemoglobin of 8.7g%, total white blood count of 38,700-cells/mm³ with a differential of 60% lymphoblasts. Peripheral smear showed lymphocytosis with leukaemoid reaction. Biochemical investigations showed blood urea of 16mg%, serum creatinine was 1.2mg%, serum uric acid of 8.7mg%, serum bilirubin of 0.7mg%, serum alkaline phosphatase was 405 IU, SGPT was 32 and serum LDH was 228u /l. Bone marrow smears showed more than 90% lymphoblasts similar in morphology to those seen in the breast fine needle aspiration (Fig. 2). The complete work-up confirmed the diagnosis of Non-Hodgkin's lymphoma in leukaemic phase. The patient was started on steroids, vincristine and L-asparaginase. The patient responded well initially to treatment with the total resolution of breast lumps and remission of leukaemoid reaction. In April 2001, she developed relapse along with central nervous system (CNS) symptoms and the subsequent cerebrospinal fluid showed lymphoma involvement of the CNS. She was treated further with high dose cytosine arabinoside (ARA-C) and intrathecal chemotherapy and is doing well 4 years since her initial diagnosis.

Discussion

Primary lymphoma of the breast is considered one of the rare sites for extra nodal malignant lymphomas comprising 2.2% of extra nodal malignant lymphomas and an overall incidence of 0.04% to 0.53% of all malignant diseases of the breast.⁴

Clinicopathologic features: Jeon et al⁴ in their review of this phenomenon of 152 patients with primary lymphoma of the breast in Japan found a broad age distribution and yet a bimodal peak

incidence, with a discrete younger population with frequent bilateral involvement and an older population with unilateral breast involvement. In their study, unilateral involvement of primary breast lymphoma seen among older women constituted 75% of their cases where there was a greater predilection for the right breast. This has also been reported by Wiseman et al⁶ earlier in the literature. In the Japanese study, bilateral involvement with lymphoma occurred synchronously in 26 of 37 patients where in the other 11 patients with asynchronous involvement, there was a time lag of two weeks to 84 months.⁴ Patients who were younger than 45 years (13 patients) with massive bilateral breast enlargement had a rapidly fatal clinical course. In the series of 16 cases of primary lymphoma of the breast reported by Wiseman and Liao⁶, the age of the patients ranged from 22-57 years and only two cases were bilateral with ages of 33 and 39 respectively. Anuradha et al¹ described the criteria shared by most of the primary lymphomas of the breast i.e., 1) usually right sided, 2) mostly in females, and 3) of B-cell type. Singh et al⁵ reported fine needle aspiration cytology of lymphoproliferative disease of the breast in 12 cases with ages ranging from 12 to 60 years. They had only two patients with bilateral lymphoproliferative disease with ages 12 and 40 respectively. Both patients had secondary involvement of the breasts with leukemia and lymphoma respectively. Borrow et al² reported primary lymphoma of the breast in 9 patients with age distribution of 51 to 76. They had two cases with bilateral breast involvement where the patients' ages were 73 and 51.

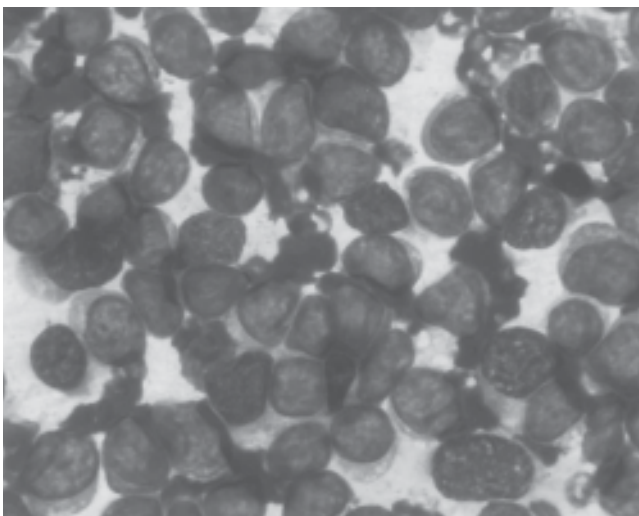


Fig. 1 : FNAC of the breast showing single large cleaved and non-cleaved lymphocytes with high nucleo-cytoplasmic ratio, reticular chromatin and prominent nucleoli consistent with a diagnosis of non-Hodgkin's lymphoma of the breast (MGG, x 400).

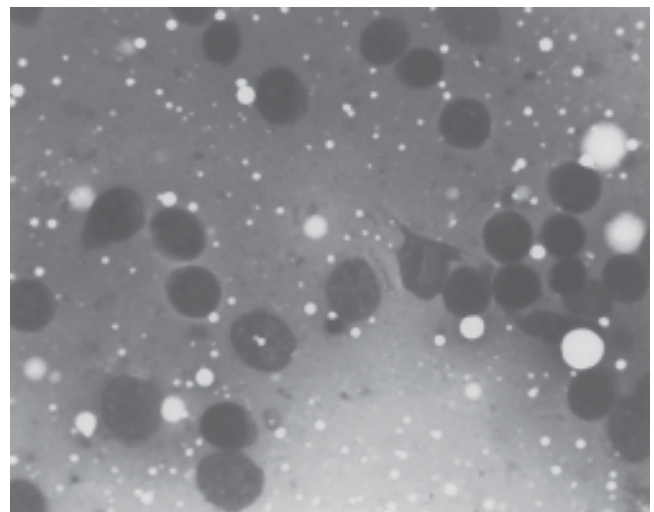


Fig. 2 : FNAC of the bone marrow showing atypical, large cleaved and non-cleaved lymphocytes with high nucleo-cytoplasmic ratio, reticular chromatin and prominent nucleoli resembling those in Fig. 1 (MGG, x 400).

In the present case, the patient presented with bilateral non-Hodgkin's lymphoma synchronously with lumps in both breasts, with bone marrow involvement and with a leukaemic phase initially. After treatment, she had a CNS relapse after a year but is doing well post treatment.

Histologic and immunophenotype: In Wiseman's series, 9 out of 16 cases were diagnosed as histiocytic lymphoma, five were diagnosed as poorly differentiated and two were well-differentiated lymphoma.⁶ Immunophenotyping was not done in any of these cases. Borrow et al² reported that 7 out of their 9 cases were high-grade B-cell polymorphic diffuse type of lymphomas; one was a true histiocytic lymphoma while one other was reported as low-grade B-cell follicular centroblastic/centrocytic lymphoma. In the series of seven primary breast lymphoma cases reported by Jeon et al,⁴ five patients had diffuse large cleaved and non-cleaved cell lymphoma and two patients had diffuse mixed small and large cell lymphomas. All the seven patients were immunophenotyped as B-cell reactive with LCA, L26, MB1, and LN1. Singh et al⁵ reported that five cases among the twelve in their series were diagnosed as B cell lymphomas and in four other cases immunophenotyping was not done, one had Hodgkin's disease, one had acute myelogenous leukemia involving both breasts and in one other case a definitive diagnosis of non-Hodgkin's lymphoma was not rendered but given as a differential diagnosis along with anaplastic carcinoma. Elavathil et al³ reported an unusual case of primary intermediate grade diffuse large cell lymphoma (follicular center cell) of the breast with a predominant population of multilobulated cells that typed as B cell type with intracytoplasmic expression of IgM in the tumour cells and a positive reaction of the tumour cells with LN-1 and a negative staining with MT1. Hugh et al⁷ in their study of 20 cases of PNHL of the breast found 84% of their cases occurred in older women and were classified as MALT (Mucosa Associated Lymphoid

Tumours). This occurrence of lymphomas of MALT is not unexpected since breast like stomach, salivary gland or thyroid where similar lymphomas of MALT are reported contains a large epithelial component without naturally occurring lymphoid tissue but are acquired either as part of aging process or due to autoimmune disease. Hugh et al⁷ reported that in two of their cases estrogen and progesterone receptor assays were strongly positive. But this seems to be a rare occurrence rather than a regular feature in the literature. The current case under discussion was reported as large cell lymphoblastic lymphoma with cleaved and non-cleaved cells. Unfortunately, immunophenotyping was not done in the present case.

In summary, the present case serves as a reminder to consider primary lymphoma of the breast even in young pubertal girls when presenting with breast masses and also emphasizes the role of fine needle aspiration cytology in diagnosis and staging of lymphoma for prompt and accurate diagnosis.

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