Primary Diffuse Large B-Cell Lymphoma of Breast: A Rare Form of Gestational Breast Cancer

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Abstract

Primary diffuse large B cell lymphoma of the breast is an uncommon form of gestational breast cancer and its presentation during pregnancy is challenging.

In our case report, a patient presented with a right breast lump during the first trimester of her pregnancy. Biopsy was taken from right breast mass, which was diffuse large b cell lymphoma (DLBCL) double expressive type. She underwent termination of pregnancy and received 6 cycles of multiagent intense chemotherapy along with central nervous system prophylaxis followed by consolidation involved site radiotherapy (ISRT) to breast and axilla after achieving a complete response.

Studies suggest no improvement in the outcome of gestational breast cancer with the termination of pregnancy. However, the presentation of primary DLBCL during pregnancy is extremely rare and the decision regarding pregnancy termination is weighted upon a case by case basis. The paucity of data makes our case report a valuable source for the management of DLBCL breast in pregnancy.

Keywords: *Gestational breast cancer, radiotherapy, lymphoma, double expressor, pregnancy.*

INTRODUCTION

Primary diffuse large B cell lymphoma of the breast is rare and accounts for less than 1% of all extra non-Hodgkin's lymphomas (NHLs). Although DLBCL breast is the most common nodal subtype of NHL but constitutes 0.4 % of all breast malignancies and is typically seen to affect older women [1]. Diagnosis and staging workup of breast cancer is more difficult for pregnancy-associated breast cancer due to the physiologic changes in the breast during pregnancy and preference to limit the impact on the fetus [2]. Currently, there are no prospective data regarding diagnosis, management, and outcome of primary DLBCL breast cancer during pregnancy is available and most of the clinical evidence is derived from limited case series and case reports regarding breast cancer in pregnancy. Importantly, all patients diagnosed with primary DLBCL breast cancer required adequate immunophenotyping and Positron Emission Tomography - Computed Tomography (PET/CT) scans for initial staging and risk stratification, followed by multiagent chemotherapy, radiotherapy, and central nervous system (CNS) prophylaxis accordingly. Improvement in the outcome of gestational breast cancer with early termination of pregnancy is not proven but women with a more aggressive disease like DLBCL breast may be likely to get benefit from early termination of pregnancy in an attempt to improve the outcome.

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CASE REPORT

A 32 years old lady, gravida 3 with no known comorbidity, 11 weeks pregnant, presented in the oncology clinic with complaints of a painless lump in her right breast for the last 3 months. The lump had increased in size during pregnancy however, there was no discharge or change in skin color overlying breast lesion, no history of weight loss, fever, or night sweats. The patient denied any significant medical history. Her past surgical history includes previous 3 cesarean sections. She had no substantial family history. Her systemic examination was unremarkable except for the Pfannenstiel scar. However, on breast examination, there was swelling in her right breast. On palpation of swelling, the mass was hard in consistency, approximately 4x4cm in size and there was no bleeding or discharge from the nipple. The axillary lymph nodes were not palpable and the examination of the contralateral breast was unremarkable.

On investigating, her ultrasound breast showed two cystic masses; one at 11 o clock and the other at 1 o clock along with benign-looking axillary lymphadenopathy in the right axilla. The maximum size of the lesion was 4.4x3cm. Trucut biopsy specimen consisting of medium-sized lymphoid cells positive for LCA, CD20(Pan B) with Mib-1 (Ki-67) index almost 100%. Further, IHC showed BCL-2 diffuse positive and C-Myc positivity, which confirmed the diagnosis as large B-cell Non-Hodgkin Lymphoma, double expressive (C-Myc and BCL-2 positive) (**Figs. 1&2**).

This case was discussed in the multidisciplinary tumor board in the presence of medical oncologists,

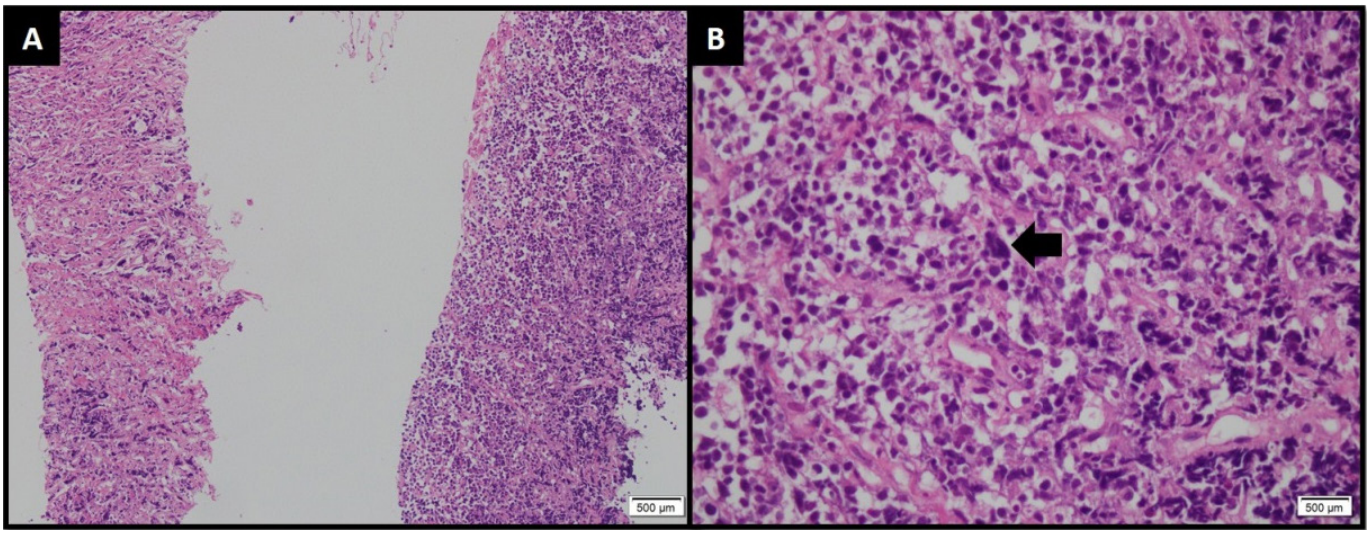

Fig. (1): **(A)** Linear cores of a lymphoid neoplasm arranged in sheets (H&E stain; 40x magnification) **(B)** The neoplastic cells are intermediate to large size and show moderate to markedly pleomorphic, hyperchromatic nuclei (arrow) (H&E stain, 400x).

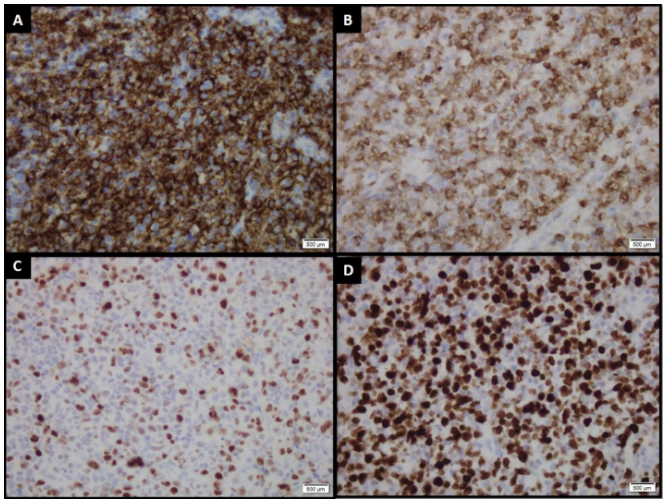

Fig. (2): Neoplastic cells demonstrating positive expression for **(A)** CD20, **(B)** Bcl-2, **(C)** c-Myc IHC stains, and **(D)** Ki-67 (Mib-1) proliferative index is markedly raised.

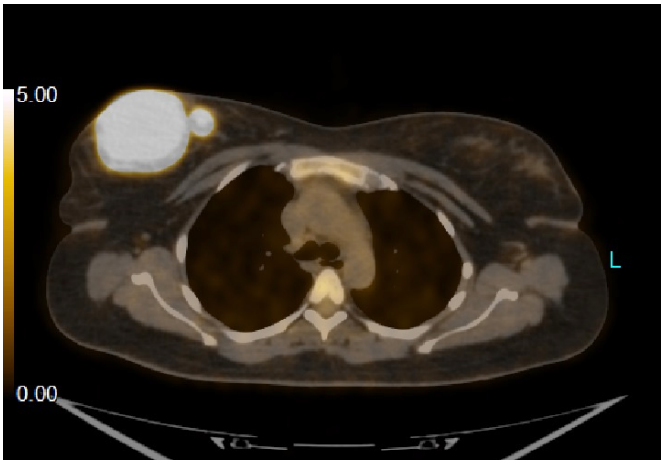

Fig. (3): PET/CT scan showing FDG avidity in Right breast lesion.

obstetricians, radiation oncologists, radiologists, pediatricians, and hematology oncologists. She was recommended to terminate pregnancy for completion of staging workup and treatment of her recently diagnosed double-expressive lymphoma. Whole-body PET CT was performed to complete the staging workup, which revealed hypermetabolic multiple soft tissue lesions involving the right breast, the largest lesion in the outer quadrant with maximum SUV 45.6 (**Fig. 3**).

Another positive finding was hypermetabolic right supraclavicular and axillary node with SUV 26.8 and 17.8 respectively. Bone trephine and lumbar puncture were negative and it was staged as IIE disease. Pregnancy-induced physiologic changes in the breast (*e.g.* engorgement and hypertrophy) interpret finding more difficult on physical examination and mammography and obtaining pathology with pertinent immunohistochemical staining helps in final diagnosis and risk stratification accordingly. The patient received 6 cycles of dose-adjusted chemotherapy R-EPOCH (Rituximab-Etoposide, Prednisone, Vincristine, Cyclophosphamide, Doxorubicin) along with intrathecal methotrexate (IT MTX) due to double expresser lymphoma. Follow-up PETCT showed a complete metabolic response. She was offered Involved Site Radiation Therapy (ISRT) and clinical target volume includes whole right breast and involved nodes. Radiation therapy was planned with Three Dimensional Conformal Radiotherapy (3DCRT) technique. The radiation dose of 30 Gy in 15 fractions @ 2Gy per fraction was delivered with curative intent as consolidation radiotherapy after chemotherapy. The follow-up PET/CT scan after 3 months of radiotherapy showed a complete metabolic response and the patient has completed 2 years of regular follow-up, doing well in Clinical Hematology & Oncology.

DISCUSSION AND CONCLUSION

Diffuse large B cell double expressive lymphoma is a rare presentation of gestational breast cancer and represents only between 0.38 and 0.7% of all NHL. Diffuse large B cell lymphoma (DLBCL) is an aggressive but potentially

curable tumor whose optimal management remains undefined [3-5]. In most studies regarding DLBCL management, the multimodality approach has been used with a combination of chemotherapy and radiation. Although our patient was diagnosed with primary breast lymphoma (PBL) at a young age, the peak age for PBL is usually the sixth decade [4]. Gestational DLBCL breast is complex and requires a multidisciplinary approach as the presentation is quite similar to breast carcinoma.

The role of mastectomy in the management of primary breast lymphomas is not favorable. In a retrospective international study comprising of case reports of 204 patients of DLBCL, published during the last three decades, there was no benefit from mastectomy and mastectomy does not appear to improve survival or risk of recurrence [5]. Studies suggest improved outcomes with more aggressive chemotherapy regimen R-EPOCH in patients with double expressor lymphoma and consolidation with radiation therapy is associated with improved locoregional control of patients with early-stage DLBCL, who have achieved complete remission following at least four cycles of chemotherapy [6]. In the study by Aviles *et al.* combined therapy with chemotherapy and radiation results in complete response in one-third of patients with primary breast lymphoma but risk stratification of lymphoma was not discussed [7]. Retrospective studies have also shown high central nervous system relapse rates resulting in poor overall survival, and adding methotrexate is recommended in patients with DLBCL as CNS prophylaxis [8]. The largest cohort study discussed maternal and neonatal outcomes of seven patients with gestational breast cancer between 1986 to 2019 in which all patients diagnosed during the first trimester, offered the option of termination as administration of chemotherapy and radiation at any stage in pregnancy was associated with an increased risk of intrauterine death, fetal growth restriction (FGR) and higher incidence of neonatal and obstetric complications [9]. Methotrexate is also a mainstay of treatment and is a known teratogen and abortifacient. Some series suggest decreased survival in pregnant women with breast cancer who electively terminate their pregnancies compared with those who continue the pregnancy but there is a lack of subgroup analysis including high-risk pathology. Concerning aggressiveness of lymphoma, gestational age, and side effects of treatment, the patient was offered termination of her pregnancy in our case report.

Treatment that included radiation therapy in the early stage of DLBCL showed benefits in survival and recurrence rates [10]. In the present study, the patient received the R-EPOCH regimen due to the presence of double hit expresser lymphoma. Our patient achieved a complete response after chemotherapy. Therefore, consolidation radiotherapy was delivered to the whole breast and involved nodes. One report indicates that the consolidation radiotherapy for PBL node-positive should include whole breast and involved node radiotherapy.

In the present case report, our patient was diagnosed with DLBCL double expressor on IHC but FISH or karyotype testing for the detection of gene rearrangements was not done due to the unaffordability of the patient. The case was diagnosed during the first trimester of her pregnancy, and treatment approaches are more difficult in the earlier stages of pregnancy. Therefore, factors such as aggressiveness and stage of gestational breast cancer pathology, gestational age, and toxicity associated with desired treatment influence the termination of a pregnancy decision to improve disease outcome. Further long-term follow-up reporting of this patient will help find the outcome.

CONSENT FOR PUBLICATION

The patient's consent was obtained to publish this Case report.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Declared none.

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