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# A Case of Synchronous Primary of CA Breast and Non-Hodgkins Lymphoma

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**Abstract** **Case Report**

A 66 years old female with diabetes and hypertension was evaluated for a lump in the left breast of six months duration, the lump was gradually increasing in size. On clinical examination it was found that the lump measured 4x4cm and was present in the left upper outer quadrant and was non tender. As a part of metastatic work up a PET CT was done which showed metabolically active lobulated soft tissue density mass lesion with multiple satellite nodules in left breast upper and outer quadrant measuring 3.2x2.1x4.4cms with max SUV 4.4, the lesion maintained fat planes with skin anteriorly and muscles posteriorly. Multiple non FDG avid to mildly FDG avid sub cm to cm size soft tissue density lesion in left breast around the main lesion was noted. Non FDG avid multiple sub cm left axillary lymph nodes were also present. Imageologically Stage II disease. Biopsy from the breast lesion was invasive carcinoma of *nos* type. Patient underwent left sided MRM. The final pathological staging was pT2N1a.Section from one lymph node showed partially effaced lymph node architecture with sheets of medium to large sized atypical lymphoid cells with fine chromatin prominent nucleolus and scant cytoplasm. IHC done showed the tumor cells to be positive for CD20, CD45, CD15, CD30(40%), MUM1, cmyc (30%) and negative for CK, CD3, EBV, ALK, BCL-2CD10, SOX11, Ki67-60%. The final diagnosis was Diffuse Large B Cell Lymphoma, non-germinal center type.

**Keywords:** Synchronous, Dual Primary, Carcinoma, Breast, Hodgkins Lymphoma.



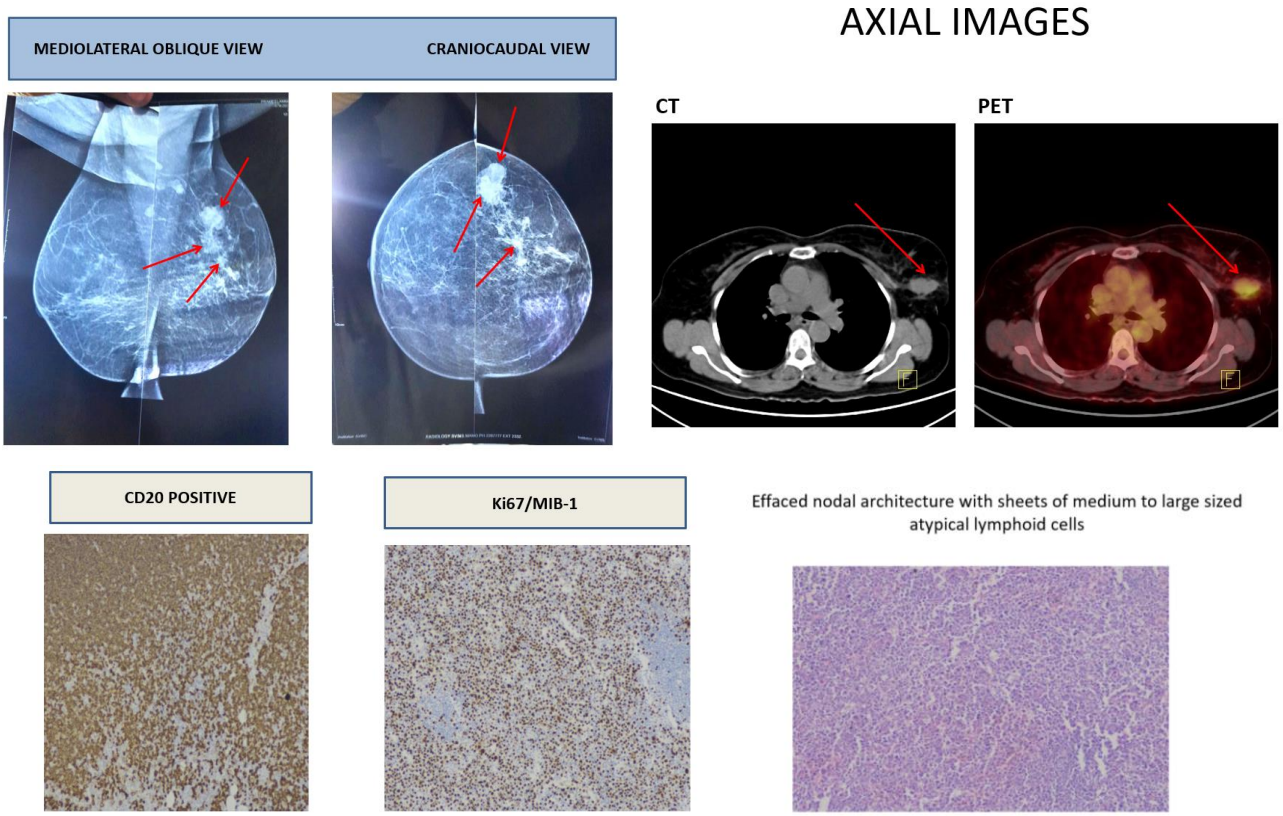
## INTRODUCTION

The incidence of dual primary is increasing due to better diagnostic modalities and increasing longevity of the patient. These tumors can be either synchronous or metachronous. The diagnostic criteria commonly used for diagnosing dual primaries is Warren and Gates criteria. The incidence dual primary varies depends on the index tumor, age of the index tumor, genetic suspectibility. It can also occur due to field cancerization and effects of radiation or chemotherapy that was used to treat the index tumor.Here we present a rare case of carcinoma breast patient who was diagnosed with a synchronous dual malignancy NHL-DLBCL in the lymph node after MRM.

## CASE DESCRIPTION

A 66 years old female with diabetes and hypertension was evaluated for a lump in the left breast of six months duration; the lump was gradually increasing in size. On clinical examination it was found that the lump measured 4x4cm and was present in the left upper outer quadrant and was non-tender. Mammogram done showed--A well-defined circumscribed hypoechoic lesion measuring 2.4cmx2.9cm with micro lobulated margins and posterior acoustic shadowing noted in 2 to 3 °clock

position 2cm from the NAC and evidence of internal vascularity and multiple calcifications was noted within the lesion, BIRADS V lesion in left breast and BIRADS I lesion in right breast. As a part of metastatic work up a PET CT was done which showed metabolically active lobulated soft tissue density mass lesion with multiple satellite nodules in left breast upper and outer quadrant measuring 3.2x2.1x4.4cms with max SUV 4.4, the lesion maintained fat planes with skin anteriorly and muscles posteriorly. Multiple non FDG avid to mildly FDG avid sub cm to cm size soft tissue density lesion in left breast around the main lesion was noted. Non FDG avid multiple sub cm left axillary lymph nodes were also present. Imageologically Stage II disease. Biopsy from the breast lesion was invasive carcinoma of *nos* type. Patient underwent left sided MRM. Post op HPR showed the tumor was measuring 3.5x3x2.8cm in the left outer upper quadrant which was invasive carcinoma of non-special type. Grade of the tumor was 2 stromal tumor infiltrating lymphocytes was <15% lymphovascular invasion was present all margins were negative DCIS was present in <25%, dissected axillary lymph nodes had solid architecture pattern 2 out of the 21 nodes dissected showed macromets. IHC was done on the tumor specimen showed ER/PR positive and HER2neu negative. The final pathological staging was pT2N1a.Section from one lymph node showed partially effaced lymph node architecture with sheets of medium to large sized atypical lymphoid cells with fine chromatin prominent nucleolus and scant cytoplasm. IHC done showed the tumor cells to be positive for CD20, CD45, CD15, CD30 (40%), MUM1, cmyc (30%) and negative for CK, CD3, EBV, ALK, BCL-2CD10, SOX11, Ki67-60%. The final diagnosis was Diffuse Large B Cell Lymphoma, non- germinal center type.




After MRM the patient was taken up for adjuvant chemotherapy for 4 cycles of RCHOP followed by 4 cycles of docetaxel adjuvant radiation of 40Gy in 15# to the chest wall and 30Gy in 15 # to the axilla. And after the completion of adjuvant radiation, she was started on hormonal therapy with T. Letrozole.

## DISCUSSION

The incidence of dual primary is increasing due to better diagnostic modalities and increasing longevity of the patient. These tumors can be either synchronous or metachronous. One of the earliest statistical analyses of double primary malignancies has carried out by Bugher in 1934, who had derived an equation for the probability of death from cancer during a specified period of age with a coincidental second malignancy [5]. Double primary malignancies could be divided into two categories, depending on the interval between tumor diagnoses [6], synchronous and metachronous. In synchronous malignancies second tumors occurs either simultaneously, or within 6 months after the first malignancy whereas in metachronous malignancies secondary tumors develop after 6 months,

or more from the first malignancy. Whether the second lesion is truly a primary or represents metastases is difficult to decide and for this the Warren and Gates criteria (1932) is used which proposed that a diagnosis of multiple primary malignancies requires the following [1]:

(1) Each tumor should present a definite picture of malignancy;
(2) There should be at least 2 cm of normal mucosa between the tumors. If the tumors are in the same location, then they should be separated in time by at least five years.
(3) The possibility that one is a metastasis of the other must be excluded.

A SEER Program database has revealed that the incidence of multiple primaries varies with the site of disease if initial primary is the breast, the percentage of patients expected to develop multiple primaries is 10% and for the lung it is 4% [3]. Meta-analyses show the frequency of second primary tumor as 3–5%, third tumor (TT) as 0.5%, and fourth tumor, that is, quadrant tumor (QT), as 0.3%, in different organ and different histogenesis [4]. In patients with breast cancer the incidence of multiple primaries has been reported in the range of 4.1%-16.4%. The most common cancers accompanying breast carcinoma were ovary, endometrium and lymphomas. Liu *et al.,* reported that the most common tumors accompanying lung cancer were in the aerodigestive tract (in descending order of frequency: larynx, nasopharynx, esophagus, oral cavity, and hypopharynx), followed by colorectal and cervical malignancies [5].

A secondary malignancy could also be defined as a new cancer that has occurred as a result of previous treatment with radiation or chemotherapy. Depending on the schedule of treatment, the most common secondary cancers reported are skin cancer, breast cancer, acute leukemia, colorectal, lung and stomach cancer, the risk of second cancer developing have been 10% at 20 years and 26% at 30 years after the Hodgkin disease treatment, [7] and 3.8 % at 10 years versus 7% at 15 years for patients receiving a doxorubicin-based regimen for breast cancer [8].

Genetic susceptibility and the carcinogenic effects of radiation /chemotherapy have been largely proposed for the development of secondary malignancies. People with a history of malignancy in the family inherit genetic cancer susceptibility as a risk factor. Patients who had been treated, and the survivors of earlier cancers with genetic susceptibility, have an increased risk of multiple primary malignancies. The treatment used for the first malignancy either by chemotherapy or radiation can result in a damage to specific regions of DNA with chromosome rearrangement or loss, responsible for tumorigenesis [9]. The new technologies available could analyze various genetic changes such as punctiform mutations, loss of heterozygosity or genetic instability. Microsatellite instability (MSI) has been noticed that occur more frequently in cases of multiple primary malignancies than in sporadic cancers [10]. The percentage of MSI tumors was similar in patients with synchronous or colorectal metachronous tumors. The mechanisms which trigger microsatellite instability differ in both varieties.

Patients with Head and Neck Squamous Cell Cancer (HNSCC) has a 36% cumulative life time risk of developing second primary malignancy over 20 years [11]. This has been attributed to field carcinogenesis related to exposure to common risk factors like tobacco chewing, smoking and alcohol consumption [11, 13]. Among the head and neck cancer survivors, the cases who have developed lung cancer were 50% (5 of 10 cases). As a part of preventive strategy, the patients particularly with HNSCC should be encouraged to stop use of alcohol and tobacco in any form, adopt healthy diet and exercise regularly. At present there is no evidence to recommend use of chemo preventive agents such as beta carotenoids and antioxidants in the prevention of second primary malignancies [12].

The possibility of multiple primary malignancies existence should always be considered during pretreatment evaluation. Screening procedures are especially useful for the early detection of associated tumors, preferably before clinical manifestations occur [14]. The co-occurrence of carcinoma breast with lymphoma is very rare, the treatment of these types of dual malignancies is challenging, as both malignancies have different biologies and different response and chemotherapy regimens for treatment. The best approach should be to address the biological aggressive malignancy first [15].

When Ax LN metastasis of BC progresses, the lymphatic flow is altered due to the obstruction of the lymph vessels or nodes by the cancer cells, and the lymphatic flow increases to not only other Ax LNs, but also the parasternal LNs [16]. Loss of the original lymphatic flow is considered to reduce the uptake of dye and isotope particles in the SLNs and decrease the identification and positive diagnosis rates of SLNB [17-19]. Therefore, Ax LN dissection should be initially performed in cases with clinical evidence of Ax LN metastasis (N1-2), and the use of SLNB to accurately diagnose Ax LN metastasis should be limited to cases with no clinical evidence of Ax LN metastasis (N0) [20, 21].

An important aspect that has to be noted with this case report is that though there was no uptake of the lymph node on PET CT the lymph node of microscopic and IHC study turned out to be diffuse large b cell lymphoma.

In spite of extensive literature review we could not find a case report or a series with a presentation similar to our case which makes our case unique

With this case report we would like to highlight the importance of careful microscopic examination and IHC study, as both malignancies in our report have their own biological behavior and specific management CD20+ lymphoma require Rituximab and the extensive team work that is required as in any oncology case. The synchronous malignancies if diagnosed at an early stage can be completely cured giving to a better disease-free survival for the patient.

## CONCLUSION

With the timely diagnosis of the coexistent dual malignancy of Ca. breast and NHL-DLBCL in this patient we could give the patient the best possible treatment available, and also we avoid the use of unwanted chemotherapy drugs. So a complete work up of the patient prior to starting of the definitive treatment and a suspicion of the occurrence of a dual malignancy should be kept in patients who present after a long disease free interval of index tumor, when there is spread to regional lymph node from the primary malignancy which will help the patient receive the best possible treatment

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