Case Report

Rare case of multiple primary malignant neoplasms

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Abstract

Multiple Primary Malignant Neoplasms (MPMNs) are rarely reported and are defined as the diagnosis of ≥2 independent, primary malignancies of different histologies/ origins in a single individual. In this study, we report a patient with Male Breast Cancer (MBC) and coexisting Small Lymphocytic Lymphoma (SLL) and Chronic Lymphocytic Leukemia (CLL). A 65-year-old male with complaints of a lump in his left breast since 2 years. CT scan findings were a non-homogeneous mass in the left breast along with bilateral axillary lymphadenopathy. Modified radical mastectomy was done. Microscopic examination showed the features of infiltrating duct carcinoma NOS: Modified Nottingham Bloom Richardson's Grade II in breast specimen. A peripheral smear of the patient showed features of chronic lymphocytic leukemia (absolute lymphocyte count was 16400 cells/mm^3). IHC of breast tumor showed ER/PR positivity with H scores of 350 and 240 respectively and HER-2/Neu protein expression was negative with a score of (1+). Lymph nodes were immunoreactive for CD 19, CD 23 and CD 5. Cells were non-reactive for Cyclin D1a and CD3. This is probably the first case of MBC with SLL and CLL. The diagnosis is consistent with synchronous MPMNs, which are increasingly reported nowadays.

Key words

Multiple primary malignant neoplasms, MPMNs, Case report, Male breast cancer, Small lymphocytic lymphoma, Chronic lymphocytic leukemia.

Introduction

Multiple Primary Malignant Neoplasms (MPMNs) are rarely reported and are defined as the diagnosis of ≥2 independent, primary malignancies of different histologies/ origins in a single individual. The prevalence of Multiple Primary Malignant Neoplasms varies from 0.73% to 11.70% of all patients diagnosed with carcinomas in western countries. In this study, we report a patient with Male Breast Cancer (MBC) and coexisting Small Lymphocytic Lymphoma (SLL) and Chronic Lymphocytic Leukemia (CLL).

Case report

A 65-year-old male with complaints of a lump in his left breast since 2 years. CT scan findings were a non-homogeneous mass in the left breast along with bilateral axillary lymphadenopathy. A lumpectomy was performed and diagnosed as infiltrating duct carcinoma breast. Modified radical mastectomy was done. On gross examination, the subareolar cavity was surrounded by a whitish solid area of 2 cm without skin involvement. Total of 26 lymph nodes were retrieved. Lymph nodes were whitish and fleshy.

Sections were stained with H&E and Immunohistochemistry (IHC) was performed. Microscopic examination showed the features of infiltrating duct carcinoma NOS: Modified Nottingham Bloom Richardson's Grade II in breast specimen. All lymph nodes showed the complete effacement of lymph nodes by small lymphocytes having slightly irregular round nuclei. The chromatin was condensed and the cytoplasm was scanty.

None of the lymph nodes showed any metastatic deposits. A peripheral smear of the patient showed features of chronic lymphocytic leukemia (absolute lymphocyte count was 16400 cells/mm^3) (**Figure – 2**).

IHC of breast tumor showed ER/PR positivity with H scores of 350 and 240 respectively and HER-2/Neu protein expression was negative with a score of (1+). Lymph nodes were immunoreactive for CD 19, CD 23 and CD 5. Cells were non-reactive for Cyclin D1 a and CD3 (**Figure – 1**).

Final diagnosis

IDC breast Stage II B with Small lymphocytic lymphoma and chronic lymphocytic leukemia.

Figure – 1: a) Invasive ductal carcinoma, NOS Breast (40X), b) Immunostaining for ER+ (H Score 350) c) Immunostaining for PR+ (H Score 250) d) Immunostaining for HER-2 Negative.

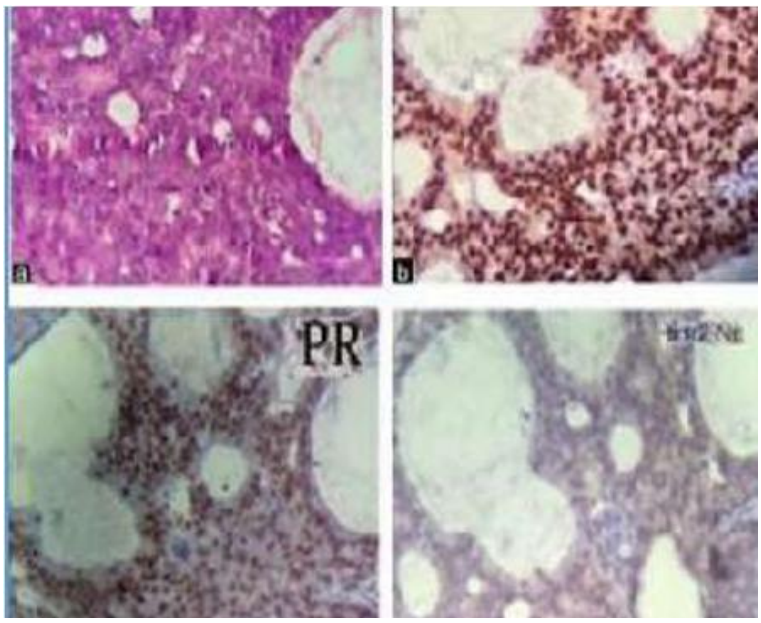
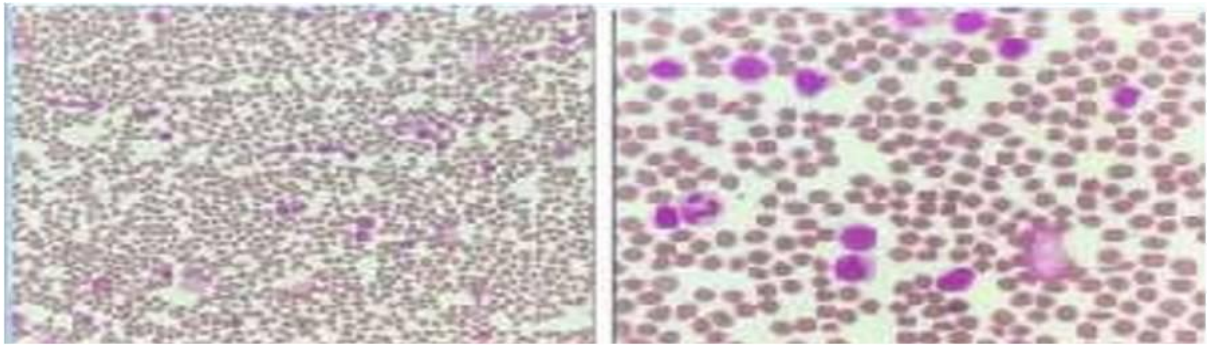


Figure – 2: Peripheral smear showing mature lymphocytes and smudge cells (ALC = 16400 cells/ mm^3).



Discussion

Multiple Primary Malignant Neoplasms (MPMNs) are rarely reported and are defined as the diagnosis of ≥2 independent, primary malignancies of different histologies/ origins in a single individual. The prevalence of MPMNs varies from 0.73% to 11.70% of all patients diagnosed with carcinomas in western countries [1]. In this study, we report a patient with Male Breast Cancer (MBC) and coexisting Small Lymphocytic Lymphoma (SLL) and Chronic Lymphocytic Leukemia (CLL).

Clinically, most breast carcinomas present in elderly men as breast masses with or without associated nipple abnormalities [2]. Similarly, grossly, microscopically and immunohistochemically, carcinomas of the male breast are like those seen in females. Incidental lymphomas are discovered in a small percentage of patients who undergo radical lymph node dissection for the staging of various carcinomas. The most common type of lymphoma found in these patients is CLL/ SLL [3].

The diagnosis of multiple primary malignancies in this study was made according to the criteria developed by Warren and Gates [1]. Depending on the time of diagnosis, the dual malignancies can be synchronous or metachronous. This case showed a combination of MBC and SLL and CLL, two completely different cancer types diagnosed at the same time and therefore met the criteria for simultaneous MPMNs.

The pathogenesis behind the increased tendency to develop multiple tumors (Synchronous or Metachronous) in some subjects probably may be either due to an individual predisposition or by the action of carcinogenic factors acting on different organs at different times [4].

The frequency of MBC is 1% in Western nations, and 0.5% in some Asian countries [5]. Risk factors for the development of male as well as female breast cancer are similar and include increasing age, first-degree relatives having carcinoma breast, exogenous oestrogen therapy and ionising radiations. Other factors are obesity, infertility and pre-existing proliferative benign breast disease. From 3% to 5% of cases are associated with Klinefelter syndrome and decreased testicular functions. The typical age at diagnosis is between 60 and 70 years [6].

The difference between CLL and SLL is only in the degree of lymphocytosis in the peripheral smear. In most of the affected patients, absolute lymphocyte count > 5000 cells/mm^3; criteria for the diagnosis of CLL. In the Western world, CLL is the most common leukemia in adults with 60 years as the median age of the diagnosis. Slight male preponderance is noted with a ratio of 2:1. SLL accounts for only 4% of NHLs. Chromosomal translocations are also less common in CLL/SLL as compared to other lymphoid malignancies.

The deletions of 13q14.3, 11q and 17p and trisomy 12q is the most common genetic abnormality. CLL/SLL have distinctive

immunophenotyping. The cells are strongly immunoreactive for pan B-Cell markers CD19 and CD20, and for CD23 and CD5 also.

In the absence of any therapy, the simultaneous presence of both malignancies is rare. These findings suggest that there must be some link between CLL and breast cancer [7]. The simultaneous presence of breast cancer and leukemia has been reported in BRCA2 germline mutation-carrying families [8, 9]. In SLL/CLL cases, literature data is available regarding the tumor suppressor locus at 13q12-13 at the BRCA2 gene. This provides a possible link between these two malignant neoplasms through chromosome 13 [4].

Our case of MPMN may be also associated with some underlying genetic abnormality. However, we cannot conclude that MBC and SLL/CLL in our case occurred simultaneously or consecutively in our case. Therefore, pathologists, radiologists and clinicians have to be aware about different combinations, patterns and clinical presentation of multiple malignant tumors.

Conclusion

This is probably the first case of MBC with SLL and CLL. The diagnosis is consistent with synchronous MPMNs, which are increasingly reported nowadays. Careful vigilance is therefore really necessary for early diagnosis of such MPMNs. The underlying mechanisms are unknown. Further studies are required to define the risk factors and any underlying genetic and chromosomal anomalies, which will help in the targeted therapies as well as prevention of MPMNs.

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