

CONCOMITANT PRESENCE OF BREAST CANCER AND CHRONIC LYMPHOCYTIC LEUKEMIA

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MEME KANSERİ VE KRONİK LENFOSİTİK LÖSEMİNİN BİRLİKTELİĞİ: OLGU SUNUMU

ÖZET

Maligniteler aynı anda veya birbirini takiben aynı hastada görülebilir. Biz bu çalışmada kronik lösemi ile aynı anda olan meme kanseri nedeniyle modifiye radikal mastektomi yapılan bayan hastayı sunduk. Histopatolojik incelemede tipik meme kanseri bulguları yanında hem memede hem de aksiller spesmen- de atipik lenfoid proliferasyon ve mikroskopik lenfositik infiltrasyon odakları saptandı. Periferik kandan alınan lenfositler ve kemik iliği CD5 ve CD20 ile boyandı. Kronik lenfositik lösemi (KLL) tanısı doğrulandı. KLL, meme kanseri ile senkron malignite olarak teşhis edildi. Meme kanserinin özellikle KLL gibi diğer maligniteler ile birlikte olabileceği akılda tutulmalıdır. İkinci maligniteler, KLL hastalarında immün defekt sebebiyle daha fazla görülebilir.

Anahtar sözcükler: meme kanseri, kronik lenfositik lösemi, senkron maligniteler.

ABSTRACT

Certain malignancies may occur concomitantly or consecutively. We present a female patient with breast carcinoma who had chronic leukemia concurrently with breast cancer. She underwent a modified radical mastectomy. The histopathologic examination of both mastectomy and axillary specimen revealed diffuse, atypical lymphoid proliferation and microscopic foci of lymphocytic infiltrations beside the typical breast carcinoma findings. Lymphocytes taken from peripheral blood and bone marrow aspirates were stained with CD5 and CD20. The diagnosis of chronic lymphocytic leukemia (CLL) was confirmed. CLL was diagnosed as a synchronous malignancy together with breast carcinoma. It should be kept in mind that breast carcinoma may occur concomitantly with other malignancies especially CLL. Second malignancies occur with an increased frequency in patients with CLL, mainly because of the immune defects associated with this disease.

Keywords: breast cancer, chronic lymphocytic leukemia, synchronous malignancy.

Introduction

Chronic lymphocytic leukemia (CLL) is defined as a clonal expansion of neoplastic B lymphocytes, in the blood, bone marrow, lymph nodes, and spleen. The Majority of the CLL patients have somatic deletions of the chromosome 13q12.3 locus encompassing BRCA2 (1). An increased incidence of other malignant neoplasms has been reported in patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL). Additionally, it was found that the risk of all cancers increased two-fold in patients with CLL when compared to an age- and sex-matched control population (2). In another study of 2,028 patients, it was observed that 324 (16%) had a history of other cancers and 227 (11.2%) developed other malignancies during the follow-up period. Of those cancers 9% were breast cancer. From a different point of view, the risk of a second cancer was found 2.2 times higher than the expected risk (3).

Breast cancer is the most common cancer in women. The BRCA1 gene, located on chromosome 17q21, and the BRCA2 gene, located on chromosome 13q12-13, are both tumor suppressor genes. Subjects with germ line mutations of BRCA1 and BRCA2 genes are known to have a very high risk of developing breast and ovarian cancer (4).

Chemotherapy, hormone therapy, and radiotherapy have been shown to be very effective in reducing cancer recurrence and death in women with breast cancer (5). The development of secondary malignancies after the treatment of breast cancer has been well studied (6, 7, 8). Although potential associations between leukemia risk and various adjuvant treatment regimens have been evaluated in many patients with breast carcinoma, existence of both tumors in the same patient at the time of diagnosis without previous treatment has rarely been described. Additionally, concomitant malignancies with untreated breast carcinoma were reported rarely (9, 10, 11). Although there were a few studies describing the association of breast cancer with chronic lymphocytic leukemia (CLL), the concurrence of both malignancies are intriguing (12, 13). Here, we present a patient who underwent surgery for breast carcinoma and later was found to have CLL concomitantly.

Case report

a 41 year old premenopausal woman underwent an excisional biopsy due to a lump in her right breast. The pathologic results determined a diagnosis of invasive ductal carcinoma, the patient was referred to our hospital. The physical examination revealed a 4 cm incisional scar

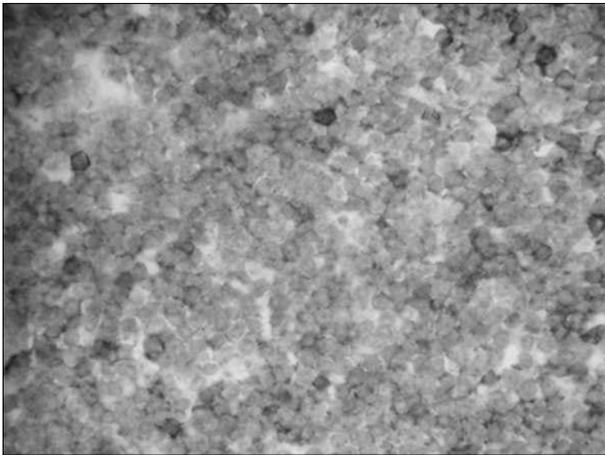


Figure 1. Cells stained for CD20 in the lymph node.

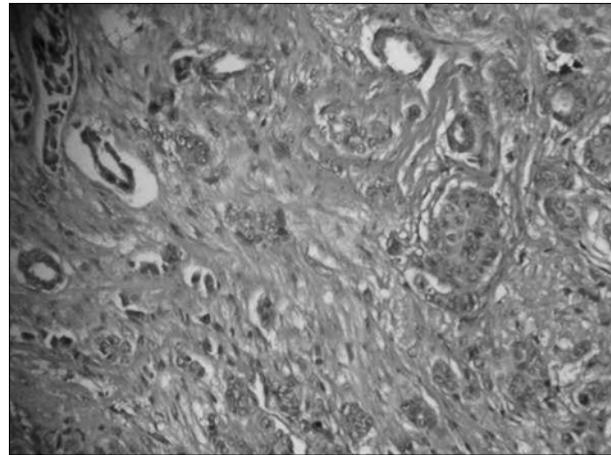


Figure 2. Histopathological examination with H&E of breast mass showing breast cancer

in the upper outer quadrant of the right breast and an axillary lymphadenopathy. The other breast had no pathology in physical examination. At the time of presentation her hemoglobin, white blood cell count and lymphocytic count were 10.4 g/dl, 17.200, % 62 respectively. CA 15-3 level was 24.55 U/ml. The excised tumor measured 2 cm in diameter. Because there was no information about the resection margins, the patient was treated with modified radical mastectomy. Pathologic examination showed that both mastectomy and axillary lymph nodes contained microscopic foci of lymphocytic infiltrations. Neither the mastectomy material nor the lymph nodes had ductal carcinoma. However, the lymph nodes were stained strongly with CD20 (Figure 1). All lymph nodes had diffuse infiltration with small atypical lymphoid cells and there were also small foci of infiltrations in the breast parenchyma. Both infiltrations revealed strong immunostaining with CD 20 antibody. The pathologic examination of excised breast tissue confirmed the prior diagnosis of invasive ductal carcinoma (Figure 2). Both the blood smear and bone marrow aspirates demonstrated the predominance of lymphocytes which were shown to be strongly CD5+ by using flow cytometric analysis with a CD5-specific monoclonal antibody. Estrogen and progesterone receptors in the tumor were positive.

Discussion

A woman's chance of developing breast cancer in her lifetime is 1/8. Identification of factors responsible for increasing an individual's chance of acquiring breast cancer is important in daily clinical practice for clinicians. In a study by Tsimberidou AM et al., in patients with CLL/SLL, independent factors predicting development of other cancers were reported to be: older age, male sex, and elevated levels of β 2-microglobulin, lactate dehydrogenase, and creatinine. Furthermore, the risk of developing second cancers in patients with CLL/SLL was found higher than the risk reported by others. Some exceptions like bladder and all gastrointestinal cancers with a lower frequency were also reported. They also noted that the number of hematologic malignancies, melanoma, and female breast cancers was higher than expected in their patients with CLL/SLL (3). Our patient has no cancer other than breast cancer and CLL.

CLL, a disease of adults, is a type of leukemia and malignancy of white blood cells. Most patients are asymptomatic and the diagnosis is usually achieved by a routine complete blood test and cell count demonstrating a high leucocyte count. Swollen lymph nodes, spleen, liver, and eventually anemia, infections are involved in advanced CLL. Cellular expressions of CD5, CD19, CD20, and CD23 are shown in CLL. B-cell form presents in almost all cases, and patients with CLL are more likely to develop secondary malignancies (14). Our patient was referred to us with the diagnosis of breast cancer following an excisional biopsy of her breast with no apparent symptoms of CLL. CLL was diagnosed in this case, just after the pathological examination of mastectomy tissue and lymph node specimens following surgery. This showed microscopic foci of lymphocytic infiltrations. Lymph nodes were stained strongly with CD20. Retrospective evaluation of our patient revealed laboratory findings of leucocytosis, especially predominance of lymphocytes which might be suggestive of CLL.

Concurrent malignant tumors, defined as the occurrence of two tumors within a six month period in the same patient, is rare. In an autopsy study, of 68 patients with multiple malignancies in 1870 cancer deaths, only 15 (0.8%) of the total had multiple synchronous primaries. The association of breast cancer with another primary tumor was the lowest although it was the second most frequent tumor in this study (15). While the presence of both tumors may be simply due to chance; other factors like genetic predisposition, immunological disturbance, and common environmental influences may play a role. Concomitant malignancies with untreated breast carcinoma were reported rarely. The concomitant occurrence of two malignancies is a well-known and intriguing subject for the geneticist because of the suggestion of a possible linkage between two diseases through the same chromosome (16). Fruscalzo et al described the case of a BRCA2 mutation carrier Caucasian female, who developed (6), primary malignancies in 30 months: ductal breast cancer, chronic lymphatic leukemia, ovarian papillary serous carcinoma, and endocervical adenocarcinoma (16). Patients with CLL are at increased risk of developing second malignant neoplasms, one of which is breast cancer. In one recent study, it was reported that CLL associated scirrhous carcinoma of the breast occurred in

a 55-year-old woman with Sweet's syndrome (acute febrile neutrophilic dermatosis) (12). Another study reported a woman who had been diagnosed with CLL 5 years ago, presented with invasive ductal carcinoma with axillary lymph node metastasis. Immunohistochemical staining for CD5 using a monoclonal antibody showed that there was extensive infiltration of axillary lymph nodes and tumor stroma with CD5 positive B lymphocytes. Widespread CD5 positivity was also seen in primary and metastatic breast carcinoma cells. Cheung et al (17) presented a case with both invasive ductal carcinoma and CLL in the breast. In our case, both infiltrations of breast and axillary lymph nodes revealed strong immunostaining with CD 20 antibody. The blood smear and bone marrow aspirates demonstrated the predominance of lymphocytes that were shown to be strongly CD5 positive by using flow cytometric analysis with a CD5-specific monoclonal antibody.

While simultaneous presentation of both diseases in the absence of therapy is rare, the findings suggest a possible link between CLL and breast cancer. Any allelic loss on chromosome 13 could not be

detected in this particular patient (11). However, breast cancer and leukemia have been previously reported in families with BRCA2 germ line mutation, (18, 19). Literature data regarding tumor suppressor locus at 13q12-13 at the BRCA2 gene in CLL and deleted regions on chromosome 13q containing BRCA2 or RB genes in sporadic breast cancer provide a possible link between these two diseases through chromosome 13. Concomitant diagnosis of two malignancies in our case may be also associated with an underlying genetic pathology. However, we can not conclude whether two particular diseases occurred simultaneously or consecutively in our case.

As a conclusion, concomitant presence of breast cancer and CLL suggests that there may be a possible link between these two malignancies, either through chromosome 13 or an unidentified specific chromosomal abnormality which requires further investigations. Increased lymphocyte counts in breast cancer patients should alert surgeons to further investigate for concomitant leukemia since associated malignancies occur with an increased frequency in patients with CLL due to immune defects.

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