Synchronous Invasive breast carcinoma, Endometrial cancer and Small lymphocytic lymphoma in a 49 year-old female Libyan patient. Case report and Literature review

Abstract

Although breast cancer and endometrial cancer are two frequent female cancers, finding synchronous primary cancers in the same patient is a comparatively uncommon occurrence. We present the case of a Libyan woman who developed synchronous breast cancer, endometrial cancer, and small lymphocytic lymphoma. For the previous six months, a 49-year-old female patient had a right breast mass. An ultrasound scan revealed an uneven doubtful growth in the right breast as well as swollen of the axillary lymph nodes. After a wide local excision, histopathology revealed that the patient had invasive ductal carcinoma of the breast with a positive resection margin, and he was admitted to the Surgery Department. No distal metastasis was seen on a computed tomography (CT) scan of the chest, abdomen, or pelvis, so the patient had a right mastectomy and axillary clearance. Residual invasive ductal carcinoma was found on histopathology and immunohistochemistry with positivity for the estrogen receptor and the progesterone receptor. Small lymphocytic lymphoma (SLL) affected the axillary lymph nodes, affirmed by immunohistochemical staining positive for CD20, CD5, CD23 and BCL-2 while negative for CD3 and Cyclin D1. Resection margins were free. Second cancers are characterized by being linked to SCL, and some researchers have described that the risk of second cancers is elevated in SCL patients. We represent a combined case of synchronous primary SCL with breast cancer and endometrial cancer in a woman which is a rare occurrence.

Key words:

Multiple primary malignancies, Synchronous malignancies, Breast carcinoma, Endometrial adenocarcinoma

Introduction

The first report of Multiple Primary Malignant Neoplasms (MPMN) was published by Billroth in 1889 (1, 2). Since then, numerous reports of MPMN have been published. In spite of their increasing prevalence, MPMN are still uncommon. The frequency of occurrence varies between 0.7 and 11.7 percent (3).

MPMN is defined as ″‘two or more primary cancers located at different sites or at the same site, if histological characteristics are different″ (4). Multiple primary cancers that developed at the same time or within six months were classified as synchronous multiple primary cancers, while cancers that developed over six months were classified as metachronous multiple primary cancers (5).

Multiple primary neoplasms pose a therapeutic challenge to the physician and

should be handled by a diverse specialists with a patient-oriented approach (6).

We presented a rare instance of synchronous breast cancer, small lymphocytic lymphoma and endometrial adenocarcinoma with a literature review.

Case presentation

A 49-year-old Libyan woman reported to us at Misrata Cancer Center with a 6-month-old right breast growth. A right breast ultrasound revealed an uneven doubtful corpus and axillary lymph node swollen. Past medical history of the patient showed that she has received surgical treatment using a wide local excision approach and its histopathology analysis revealed presence of invasive ductal carcinoma of the breast with a positive resection margin. Subsequently, the patient was transferred and admitted to Surgery department. Pathology review was done revealed invasive ductal carcinoma where the cancer cells are growing at a speed of and look less like normal cells (G2) (Fig. 1).

No distal metastasis was found on a CT scan of the chest, abdomen, or pelvis. The patient had a right mastectomy and axillary clearance based on the Multidisciplinary Team's recommendation at Misrata Cancer Center.

Histopathology and immunohistochemistry revealed remaining invasive ductal carcinoma that was positive for the estrogen receptor (ER) and the progesterone receptor (PR) in 80% of cases, but negative for the HER-2 protein. surprisingly small lymphocytic lymphoma (SLL) (Fig. 2) affecting the axillary lymph nodes without any evidence of breast cancer, confirmed with immunohistochemistry study was showed that the neoplastic lymphoid cells are positive for CD20, CD5, CD23 and BCL-2 while CD3 and Cyclin D1were negative. The proliferation index Ki67 is positive in 15% of cancer cells. Free resection lines has been found. Bone marrow biopsy was done revealed Lymphoid cell infiltration of bone marrow, the peripheral blood film revealed lymphocytosis with normochromic anaemia.

Then patient started adjuvant therapy for both invasive breast cancer and lymphoma. After two months during the follow-up, patient complained from heavy menses which since long time ago but ignored by the patient. Gynecology consultation was done and abdominal ultrasound was requested and revealed significant thickening of uterine endometrium, then Pap smear was done revealed Pap-IV adenocarcinoma. A Pap smear, also known as a Pap test, is a cervical cancer screening test. It was named after Dr. Georgios Papanikolaou, who pioneered its use in detecting early signs of cervical cancer. Then total abdominal hysterectomy, bilateral salpingoopharectomy, omentum and bilateral iliac lymph nodes biopsied was revealing well differentiated endometrial carcinoma (Fig. 3), chronic nonspecific cervicitis and fibrocystic change.

Patient now in good general condition, started adjuvant treatment with chemotherapy with regular follow up.

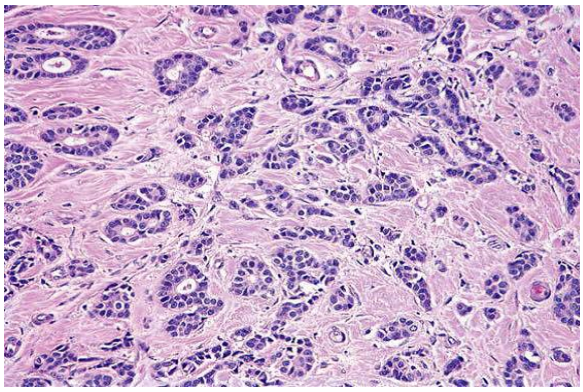

Fig 1: Invasive ductal carcinoma (H&E) (X40)

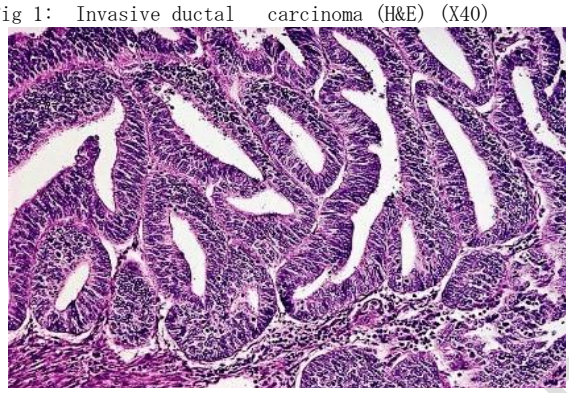

Fig 2: Endometrioid carcinoma of the endometrium (H&E) (X40)

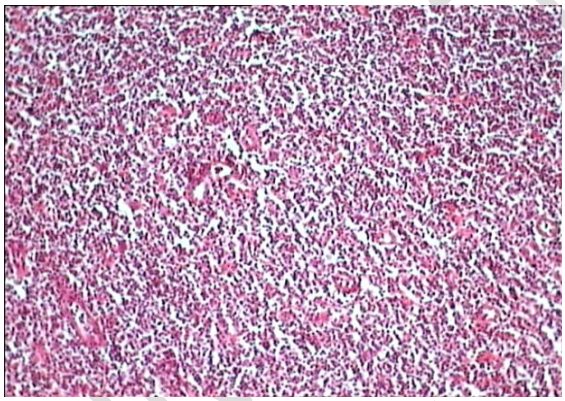

Fig 3: Chronic lymphocytic lymphoma (small cell lymphoma). (H&E) (X40).

Discussion

MPMN have three criteria that must be present: (I) each tumor must be distinct from each other; (II) each tumor must present definite features of malignancy; and (III) the possibility that the one is a metastasis of another must be ruled out. Which are divided into two large categories according to the time of diagnosis of each tumor. If the tumors are diagnosed simultaneously or within a six month interval, they are called synchronous. If the interval is longer, the tumors are called metachronous (7, 8).

The risk to develop a new primary cancer in cancer survivors is 20% higher than in the general population (9). It is a rare occurrence to find synchronous primary cancers in the same patient (10).

The chance of having synchronous breast cancer and endometrial cancer in the same person is extremely low, and it could simply be a coincidence; according to one study, the risk of developing endometrial cancer within a year of having primary breast cancer is less than 0.05 percent. Breast and endometrial cancer often coexist because many environmental and hormonal risk factors including genetics, hormonal, environmental, and obesity, can prompt a patient to these two malignancies (11, 12).

Many other factors, such as age (which is more common in older patients), postmenstrual period, nulliparous status, and a positive history of irregular menstrual cycles, all increase the risk of endometrial cancer (13-15). Our case had some of these risk factors, such as nulliparous and irregular heavy menstrual cycle.

We also performed a literature search to estimate possible links between the pathogenesis of breast cancer and small cell lymphoma. Subramaniam et al reported that the oncogenic Epstein-Barr virus may be responsible for spread of both invasive breast carcinoma and lymphomas via the nuclear protein Epstein-Barr virus nuclear antigen 3C (EBNA-3C) acting together with the human metastatic suppressor protein Nm23-H1 reversing its ability to stop breast and lymphoma cell migration(16). It

has been mentioned that Chemokine Receptor 1(CX3CR1), a non-B cell adhesion molecule, may be expressed on mantle cell lymphoma and help in lymphoma spreading in breast carcinoma patients (17). A study also showed that inactivation of a single gene within the breast cancer gene (BRCA) pathway can increase the risk of developing small Cell lymphoma (18). Accordingly, the occurrence of breast carcinoma and small cell lymphoma at the same time may be linked with a frequent cause, rather than a simple secondary cancer theory.

MPMN research may be valuable not only for clinical intentions, but also for etiology and cancer management. Based on the main etiologic factor, they can be divided into three major groups. Treatment-related neoplasms fall into the first category, syndromic cases fall into the second, and neoplasms that share common etiologic factors including genetic predisposition or exposure to the same environmental factors fall into the third(19). Furthermore, the occurrence of two or more cancers can be due to mere coincidence (20).

Conclusion

For enhanced diagnosis of these synchronous malignancies, we highlight the significance of a thorough review of systems as well as paying closer attention toward physical patients' examination.

A better understand about the pathogenesis of those two cancers require More exploration.

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