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

Abstract

Diagnosis of synchronous primary cancers in one patient is a relatively rare event, although breast cancer and endometrial cancer are two common female malignancies. We report on a rare case of synchronous breast cancer, endometrial cancer and small lymphocytic lymphoma in a Libyan female patient. A 49 year old female patient presented with right breast mass for 6 months. An ultrasound scan showed irregular suspicious mass in right breast and axillary lymph node enlargement. Wide local excision was done outside Misurata Cancer Center, histopathology report showed invasive ductal carcinoma of the breast (G2) with positive resection line, then this patient admitted to Surgery department, Misurata Cancer Center. CT scan chest, abdomen and pelvis no distal metastasis seen, according to Multidisciplinary Team decision, patient underwent right mastectomy and axillary clearance. Histopathology and immunohistochemical report showed residual invasive ductal carcinoma, which was positive for the estrogen receptor and the progesterone receptor, free resection margins and small lymphocytic lymphoma (SLL) involving the axillary lymph nodes, confirmed with immunohistochemical staining positive for CD20,CD5,CD23 and BCL-2 while negative for CD3 and Cyclin D1. Second malignancies are known to be associates with SCLL, some observers reported that an increased risk of second cancers in patient with SCLL. We represent a rare combination of synchronous primary SCLL with breast cancer and endometrial cancer in a woman.

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] Since then, numerous reports of MPMNs have been published. Despite its increasing rates, MPMs remain rare. Occurrence ranges between 0.7% and 11.7%.[2]

MPMN is defined as ″'two or more primary cancers located at different sites or at the same site, if histological characteristics are different″.[3] Classified multiple primary cancers observed at the same time or within six months as synchronous multiple primary cancers, and cancers developing with more than six months as an interval as metachronous multiple primary cancers.[4]

A concurrent presentation of multiple primary neoplasms is a rare occurrence. [5] They present a therapeutic challenge to the physician and should be treated by a

multidisciplinary team with a patient-oriented approach.[6]

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

Case presentation

A 49 year old female, Libyan patient presented with right breast mass for 6 months. An ultrasound scan showed irregular suspicious mass in right breast and axillary lymph node enlargement. Wide local excision was done outside Misurata Cancer Center, histopathology report showed invasive ductal carcinoma of the breast with positive resection line,

Then this patient was transferred and admitted to Surgery department, Misurata Cancer Center. Pathology review was done revealed invasive ductal carcinoma (G2) (Fig; 1).

CT scan chest, abdomen and pelvis no distal metastasis seen. According to Multidisciplinary Team decision, patient underwent right mastectomy and axillary clearance.

Histopathology and immunohistochemical report showed residual invasive ductal carcinoma, which was positive for the estrogen receptor (ER) and the progesterone receptor (PR) 80%, HER-2 status were negative, free resection margins and surprisingly small lymphocytic lymphoma (SLL) (Fig. 2) involving 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 they are negative for CD3 and Cyclin D1. The proliferation index Ki67 is positive in 15% of tumor cells.

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. Then total abdominal hysterectomy, bilateral salpingoopharectomy, omentum and bilateral iliac LNs biopsied was revealing high differentiated endometrial carcinoma (Fig; 3), chronic nonspecific cervicitis and fibrocystic change.

Patient now good general condition, was started adjuvant treatment, on regular follow up.

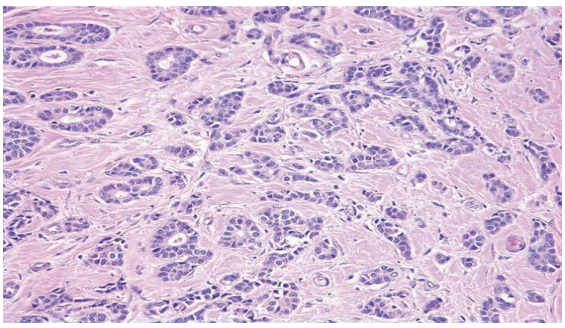

Fig 1: Invasive ductal carcinoma (H&E) (X40)

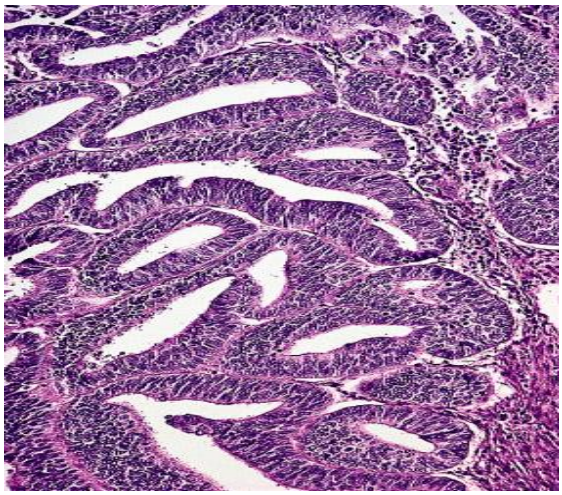

Fig 2 : Endometrioid carcinoma of the endometrium(X (H&E)

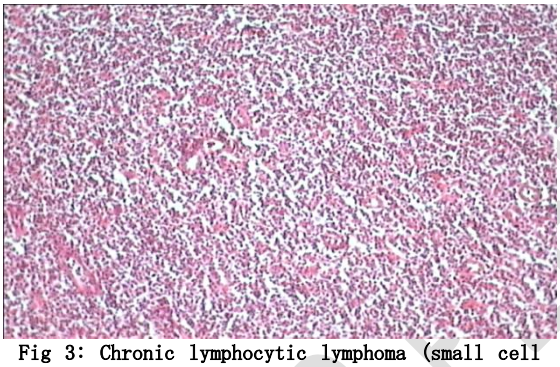

Fig 3: Chronic lymphocytic lymphoma (small cell lymphoma). (H&E) (X40).

Discussion

MPMs 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] The diagnosis of synchronous primary cancers in one patient is a relatively rare event.[10]

The possibility of synchronous breast cancer and endometrial cancer in one person is extremely low and might be only a coincidence, as reported in one study the diagnosis of endometrial cancer within one year after the diagnosis of primary breast cancer is less than 0.05%.

The coexistence of breast and endometrial cancer reflects the fact that there are many environmental and hormonal risk factors that may predispose the patient to both breast cancer and endometrial cancer, such as genetics, hormonal, environmental and obesity.[11,12]

There are many other factors increasing risk of endometrial cancer, such as age (i.e. more common in older patients), postmenstrual period,[13,14] nulliparous, and a positive history of irregular menstrual cycle.[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 through the nuclear protein EBNA-3C interacting with the human metastatic suppressor protein Nm23-H1 reversing its ability to stop breast and lymphoma cell migration.[16] It was reported that CX3CR1, a non-B cell adhesion molecule, may be expressed on mantle cell lymphoma and aid in lymphoma dissemination in breast carcinoma patients.[17] A study also showed that inactivation of a single gene within the BRCA pathway can increase the risk of

developing small Cell lymphoma.[18] Based upon above-mentioned evidence, the synchronous occurrence of both breast carcinoma and small cell lymphoma may beyond simple secondary cancer theory and actually related to a common etiology.

The study of MPMs may provide useful information not only for clinical purposes, but it can also provide clues for the etiology and the management of cancer. They can generally be categorized into three major groups depending on the main etiologic factor. The first group includes treatment related neoplasms, the second includes syndromic cases, and the third includes neoplasms that may share common etiologic factors, such as genetic predisposition or same environmental factors.[19] Additionally, two or more cancers can also be a result of pure chance.[20].

Research needs to be done to further explore the correlative pathogenesis between those two cancers. In particular, we emphasize the importance of a comprehensive review of systems and a more attentive physical examination of patients for improved detection of these synchronous malignancies.

References

1. Ghosh S, Rao PB, Sarkar S, Kotne S, Turlapati SP, Mishra A. A rare case of a synchronous anaplastic carcinoma thyroid with ductal carcinoma breast. Case Rep Oncol Med. 2014;2014:468159.
2. Coleman MP. Multiple primary malignant neoplasms in England and Wales, 1971-1981. Yale J Biol Med 1986;59:517-31.
3. Working Group R. International rules for multiple primary cancers (ICD-0 third edition). Eur J Cancer Prev. 2005;14(4):307-8.
4. Soo-Kyung Noh, Ji Yeong Yoon, Ui Nam Ryoo, Chel Hun Choi, Chang Ohk Sung, Tae Joong Kim, Duk-Soo Bae, Byoung-Gie Kim. A case report of quadruple cancer in a single patient including the breast, rectum, ovary, and endometrium, J Gynecol Oncol Vol. 19, No. 4:265-269, December 2008 DOI:10.3802/jgo.2008.19.4.265
5. Dutta Roy S, Stafford JA, Scally J, Selvachandran SN. A rare case of breast carcinoma coexisting with axillary mantle cell lymphoma. *World J Surg Oncol* 2003;1:27
6. Wallace D, Arul D, Chitale S. Synchronous tumours of the breast and bladder. J Surg Case Rep. 2014;2014(7).
7. Aydiner A, Karadeniz A, Uygun K, et al. Multiple primary neoplasms at a single institution: differences between synchronous and metachronous neoplasms. Am J Clin Oncol 2000;23:364-70.
8. Derwinger K, Gustavsson B. A study of aspects on gender and prognosis in synchronous colorectal cancer. Clin Med Insights Oncol 2011;5:259-64.
9. Travis LB, Hill D, Dores GM, et al.: Cumulative absolute breast cancer risk for young women treated for Hodgkin lymphoma. J Natl Cancer Inst. 2005; 97(19): 1428-37

10. Chang-Ching Yeh, Peng-Hui Wang, Chiung-Ru Lai, Min-Shyen Yen, Kuan-Chong Chao. Synchronous breast invasive ductal carcinoma and endometrial endometrioid adenocarcinoma: Case report, The journal of Obstetrics and Gynaecology Research, 20011

11. Mellemkjaer L, Friis S, Olsen JH, et al. : Risk of second cancer among women with breast cancer. *Int J Cancer.* 2006; 118(9): 2285-92. 10.1002/ijc.21651

12. Amir E, Freedman OC, Seruga B, et al. : Assessing women at high risk of breast cancer: a review of risk assessment models. *J Natl Cancer Inst.* 2010;102(10):680-91. 10.1093/jnci/djq088

13. Saadat M, Truong PT, Kader HA, et al. : Outcomes in patients with primary breast cancer and a subsequent diagnosis of endometrial cancer : comparison of cohorts treated with and without tamoxifen. *Cancer.* 2007;110(1):31-7. 10.1002/cncr.22734

14. Burke TW, Fowler WC, Jr, Morrow CP: Clinical aspects of risk in women with endometrial carcinoma. *J Cell Biochem Suppl.* 1995;59(S23):131-6. 10.1002/jcb.240590917

15. Soliman PT, Oh JC, Schmeler KM, et al. : Risk factors for young premenopausal women with endometrial cancer. *Obstet Gynecol.* 2005;105(3):575-80. 10.1097/01. AOG.0000154151.14516.f7

16. Subramaniam C, Cotter MA, Robertson ES: Epstein-Barr virus nuclear protein EBNA-3C interacts with the human metastatic suppressor Nm 23-H1: A molecular link to cancer metastasis. Nature Medicine 200, 7:350-355.

17. Andréasson U, Ek S, Merz H, Rosenquist R, Andersen N, Jerkeman M, Dictor M. B cell lymphomas express CX3CR1 a non-B cell lineage adhesion molecule. Cancer Lett. 2008; 259: 138-145.

18. Friedenson B. The BRCA1/2 pathway prevents hematologic cancers in addition to breast and ovarian cancers. BMC Cancer. 2007; 7: 152.

19. Takalkar U, Asegaonkar BN, Kodlikeri P, et al. An elderly woman with triple primary metachronous malignancy: A case report and review of literature. Int J Surg Case Rep 2013;4:593-6.

20. Wood ME, Vogel V, Ng A, et al. Second malignant neoplasms: Assessment and strategies for risk reduction. J Clin Oncol 2012;30:3734-45.