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Case report

Hodgkin Lymphoma in Multifocal Unilateral Breast Cancer: Is it Simple Coincidence?

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Abstract

Breast cancer (BC) and malignant lymphoma (ML) each of them are considered as a common primary malignant disease worldwide. Synchronous occurrences of BC and ML are rare. We are presenting a case of a 34 year old patient with breast cancer and Hodgkin lymphoma detected in non-sentinel lymph node biopsy. This represents a rare case of coexistence of dual malignancies. We review the literature and discuss possible etiologies for these synchronous tumors.

Keywords: ***breast cancer, lymphoma, synchronous***

Introduction

Breast cancer (BC) and malignant lymphoma (ML) are both considered as common primary malignant disease worldwide. It is known that patients with Hodgkin's lymphoma (HL) who received radiotherapy for early stages, are at risk of developing breast cancer as a zedoary malignancy, especially in young women. [1,2].

However, the incidence of ML following breast conserving surgery and radiotherapy for BC is rare [3,4].

The presence of breast cancer and lymphoma, as synchronous malignancies is rare [2,5]. The concurrence of both malignancies has a challenge on both the pathologists' diagnosis and treating clinicians as it might lead to staging errors [6]. The suggested contributing factors for the development of these synchronous malignancies are advanced age, genetic predisposition, and immunological impairment related to the primary cancer [7]. We are reporting an interesting case of synchronous breast Invasive ductal carcinoma with incidental Hodgkin lymphoma found in axillary non-sentinel lymph node.

Case Report

A 34 -year- old woman, with no significant medical history presented in May 2019 to Sultan Qaboos University Hospital with a painless lump in left breast of two months duration. There was no family history of breast cancer, ovarian cancer, lymphoma or other malignancies. Clinical examination revealed a mobile and firm left breast lump at 12 o'clock, measuring 4 x 3 cm. The right breast and both axilla were normal. There were no palpable lymph nodes in the neck or inguinal areas. Bilateral mammography and breast ultrasound were done and revealed an irregular heterogeneous mass with indistinct and angulated margins. The Breast Imaging Reporting and Database System score (BI-RADS) was 5 (**Figure1**).

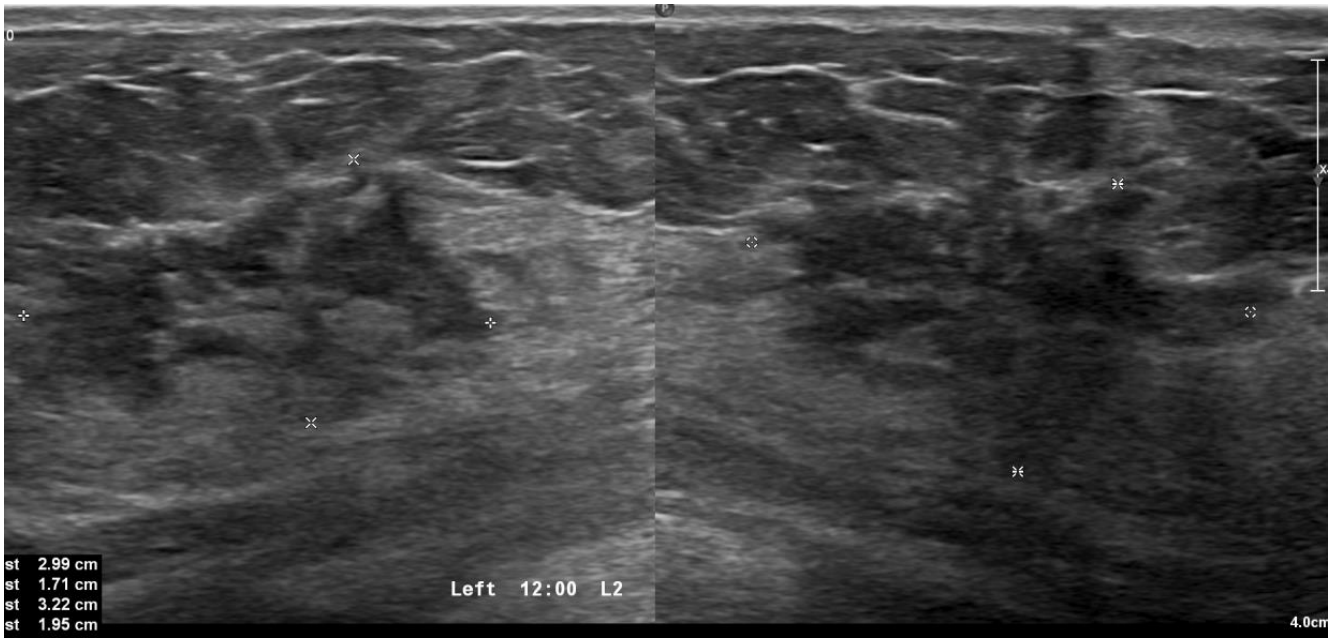

Figure 1: Ultrasound breast showing an irregular heterogeneous mass with indistinct and angulated margins.

The axillary ultrasound showed multiple abnormal lymph nodes seen at level 1 and 2 with thickened cortices that measures 7mm and 6 mm respectively (**Figure 2**). MRI Breast showed a single unilateral mass with abnormal left axillary lymph nodes. True cut biopsy of left breast lump revealed invasive ductal carcinoma, grade II with associated high grade DCIS. The immunohistochemical (IHC) staining was positive for estrogen receptor (ER), progesterone receptor (PR) & human epidermal growth factor receptor2 (HER2) expression. The professional index Ki 67 scored 5-10%. The ultrasound-guided fine needle aspiration (FNA) of the most abnormal left axillary lymph node revealed reactive lymph node. Staging CT chest, abdomen and pelvis and bone scan confirmed a localized disease with no distant metastasis. She was staged clinically as T2N0M0 and underwent left simple mastectomy upon patient preference with sentinel lymph node biopsy (SLNB).

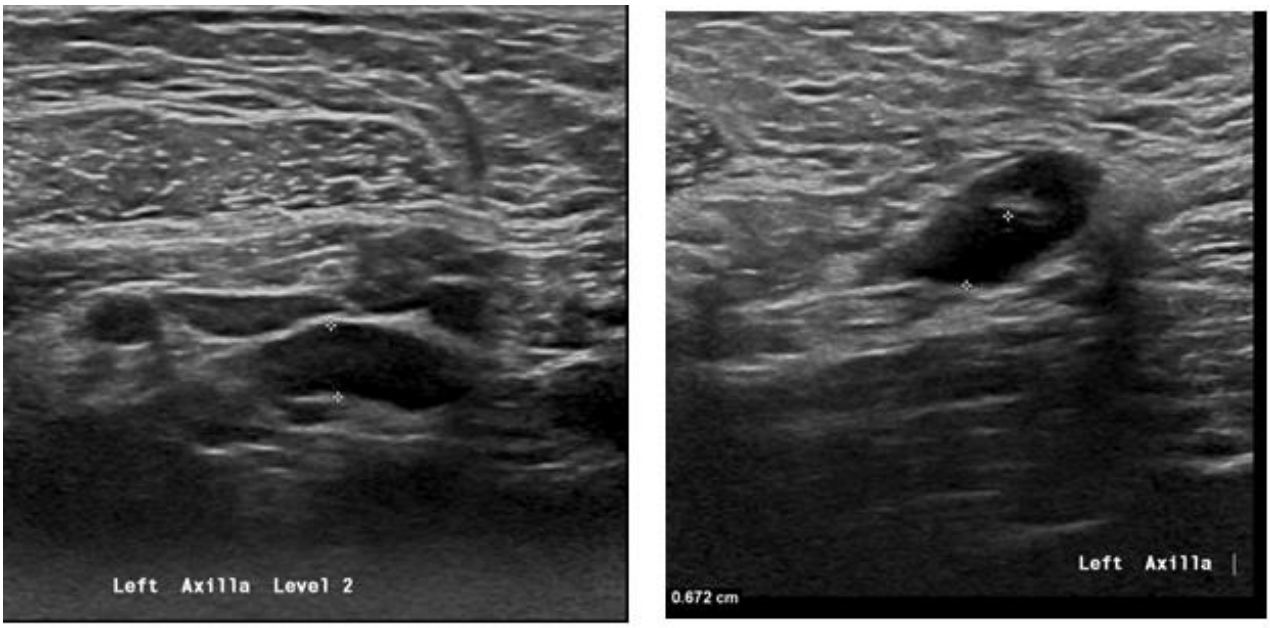

Figure 2: a,b Ultrasound axilla showing two abnormal axillary lymph node. In image a, it is at level 2 and has diffuse cortical thickness. Image 2B, the lymph node is at level I. It is irregular nodular cortical thickening and is very hypoechoic with indistinct medial border

The histopathologic examination (**Figure 3**) demonstrated a multifocal invasive ductal carcinoma classified as grade 3 according to the modified Bloom-Richardson grading system with high grade ductal carcinoma in situ. The whole tumor size was 4.8 cm and all margins were clear. The immunohistochemistry results showed the tumor positive for ER, PR and HER2. A total of three axillary lymph nodes were excised. One lymph node was SLNB and two were non SLNB. The sentinel lymph node was positive for macro-metastasis (2cm) with focal extracapsular extension (**Figure 4**). The non-sentinel lymph nodes were negative for metastatic carcinoma but the largest one showed effaced architecture with atypical cells that are positive for CD20, CD57, PD1 and PAX5. They are negative for CD3, CD15, CD30, and EMA (**Figure 5**), which is consistent with nodular lymphocyte predominant Hodgkin lymphoma. The post-surgical pathological stage was T2 (m) N1.

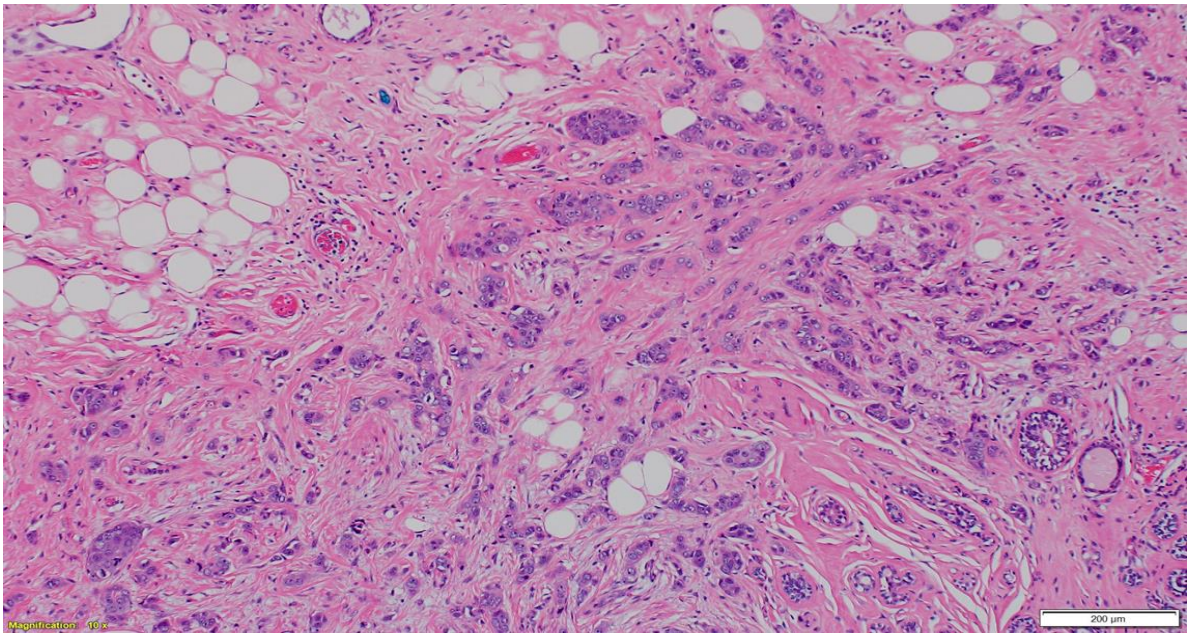

Figure 3: Haematoxylin and eosin (H&E) stain at x100 magnification: Left breast tissue with multifocal invasive ductal carcinoma, grade III. Also High grade DCIS present in the specimens, no lymphovascular invasion. Immunohistochemical (IHC) staining showed that the biopsy specimen was (ER and PR +, Her2 +3 Ki67 10%).

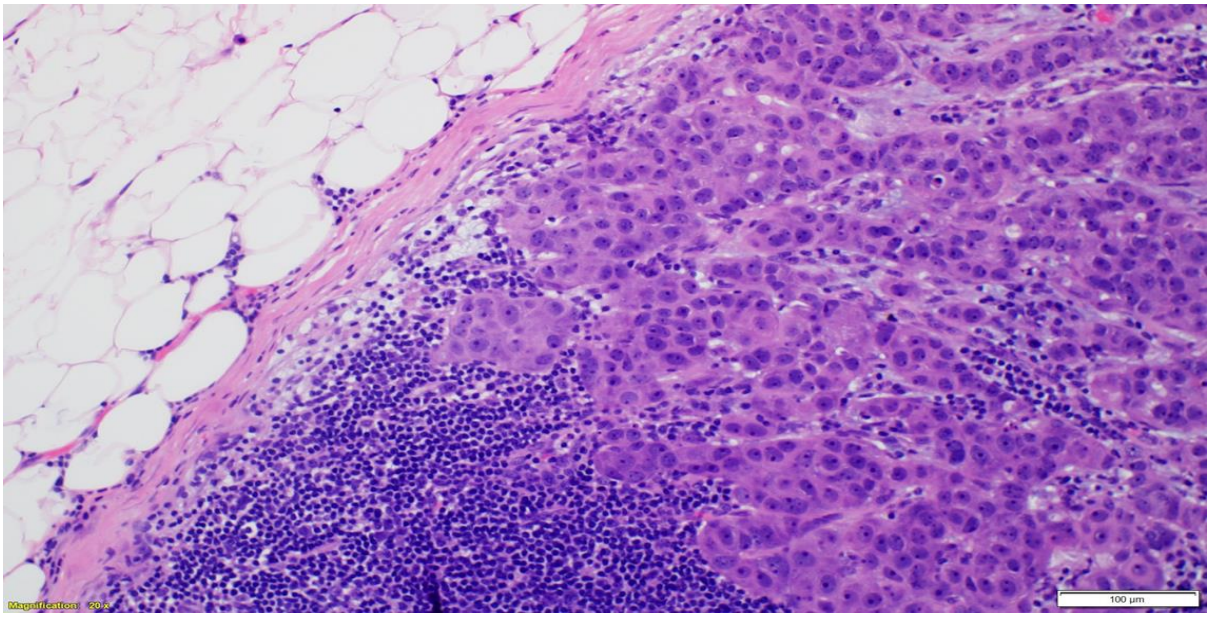

Figure 4: Haematoxylin and eosin (H&E) stain at x200 magnification: Sentinel lymph node with metastatic carcinoma

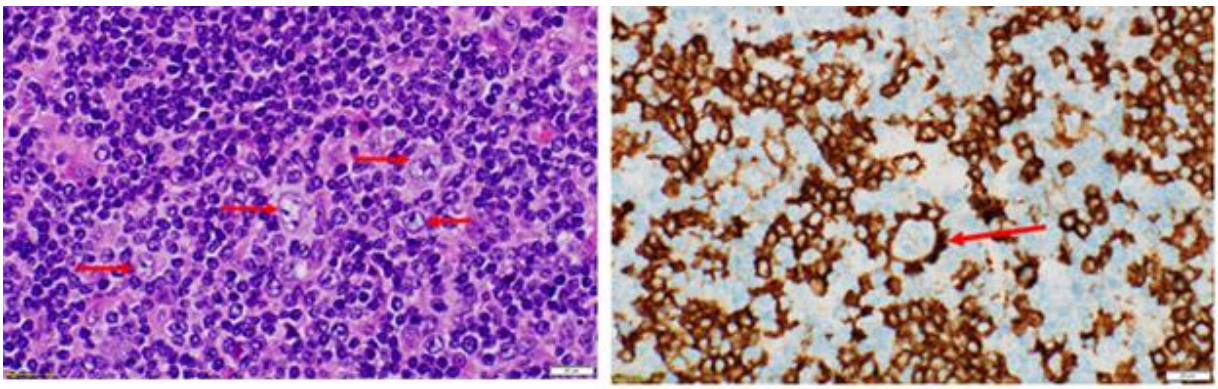

Figure 5(A): Haematoxylin and eosin (H&E) stain at x600 magnification: Nodular lymphocyte predominant Hodgkin lymphoma characterized by large tumor cells with folded and irregularly contoured nucleus, thin nuclear membrane, and small nucleoli (red arrow) in a background of small lymphocytes.

Figure 5 (B):CD20 immunohistochemical stain at x600 magnification: Neoplastic cells are positive for CD20 (red arrow), which also highlights the small B cells in the background.

The case was discussed in the Multidisciplinary tumor board (MDT) and was decided for whole body PET CT to assess the extent of the lymphoma. It showed minimal uptake in the contralateral axilla for which she underwent right axillary lymph node excision biopsy. The histological examination revealed no atypia, in situ or invasive malignancy.

Based on the MDT discussion, the lymphoma is confined to this signal non sentinel lymph node and has indolent pathological features. So she had adjuvant chemotherapy for breast cancer alone. She received (AC-DH) which is regimen of (doxorubicin, cyclophosphamide, paclitaxel and trastuzumab).

Subsequently she underwent adjuvant radiotherapy and was started on tamoxifen (20 mg daily). She completed her target therapy (Trastuzumab & Pertuzumab) and now she is on remission.

Discussion

It is well known that patients with breast cancer who have received adjuvant radiotherapy and chemotherapy are at increased risk of developing non-Hodgkin lymphoma (NHL) [8]. In addition, patients who have been treated with mantle radiotherapy for lymphoma are at higher risk of developing breast cancer but synchronous presentation of both breast carcinoma and axillary lymphoma is exceedingly rare. In the literature, only a few cases were documented [9]. These previously reported cases of breast cancer were synchronizing with different types of lymphoma: like follicular lymphoma and NHL (mainly chronic lymphocytic leukemia) [10,11]. One case reported the existence of locally advanced breast cancer, scleronodular Hodgkin's disease and tuberculosis lymphadenitis simultaneously [12]. Our case is the first report of coexisting breast cancer with Hodgkin axillary lymphoma.

Our patient did not receive previous chemotherapy or radiotherapy, the lymphoma was a true synchronous malignancy, which is not related to treatment of breast carcinoma.

There are many theories which can describe the pathophysiology of this phenomenon [13]. The most likely theory of this condition here is two different pathologies for each malignancy. As our patient did not receive previous chemotherapy or radiotherapy, it is a pure coincidence. Other factors can contribute to synchronous malignancies, including advanced age, impaired immunity produced by the primary tumour, genetic predisposition and exposure to a common inducing agent [14].

Cox et al reported three cases of breast carcinoma with coexistent axillary lymphoma [15]. He explained that if the patient developed lymphoma or lymphoproliferative disease first, then occlusion of lymphatic channels by neoplastic lymphoid cells could be a factor. Other factors might include reduction in tissue necrosis by these neoplastic cells or induction of adhesion of breast carcinoma cells to the endothelial layer of axillary lymph nodes by interleukin (IL) [16].

There is another hypothesis which describes human breast cancer and lymphoma may share mouse mammary tumor virus (MMTV) as a common etiologic agent [17]. Etkind et a. reported MMTV gene sequences detected in two patients with synchronous breast cancer and lymphoma [18]. Preventative measures against this virus such as vaccines, is very crucial if the role of it is proven as a possible cause.

We evaluated the lymphadenopathies using fine needle aspiration (FNA) and core needle biopsy (CNB). However, material retrieved from FNA or CNB are sometimes insufficient for pathological diagnosis of coexistent tumors involving a lymph node. Furthermore, FNA and CNB don't represent the pathological architecture and heterogeneities. Therefore, if the lymph node FNA or CNB are negative for malignancy despite of the clinical and radiological suspicious lymphadenopathy in a patient with breast cancer, excisional lymph node biopsy should be performed for an accurate diagnosis and treatment decision making for which is standard to do SNLB in Breast cancer.

In conclusion; synchronous malignancies have both a diagnostic challenge to the pathologist and a management challenge to the clinician. Multidisciplinary team approach plays a crucial rule in achieving good out.

Ethics approval and consent to participate

Patient identity was hidden, verbal consent was taken from the patient to use her medical data.

List of abbreviations

Breast Imaging Reporting and Database System score (BI-RADS
Breast cancer (BC)
Core needle biopsy (CNB)
Estrogen receptor (ER)
Haematoxylin and eosin (H&E)
Hodgkin's lymphoma (HL
Human epidermal growth factor receptor2 (HER2)
Fine needle aspiration (FNA)
Immunohistochemical (IHC)
Interleukin (IL)
Malignant lymphoma (ML)
Multidisciplinary tumor board (MDT)
Mouse mammary tumor virus (MMTV)
Non-Hodgkin lymphoma (NHL)
Progesterone receptor (PR)
Sentinel lymph node biopsy (SLNB)

Conflicts of Interest

The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper.

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Authors' contributions

Dr. Radhyia performed the histopathological examination of the biopsy samples. Dr. Badryia analyzed and interpreted the patient radiological images, and Dr. Aya and Dr. Suad were a major contributor in writing the manuscript. All authors read and approved the final manuscript.

References

[1] Haberer S, Belin L, Le Scodan R, et al: Locoregional treatment for breast carcinoma after Hodgkin's lymphoma: the breast conservation option. Int J Radiat Oncol Biol Phys 82: e145‑e152, 2012.

[2] Elkin EB, Klem ML, Gonzales AM, et al: Characteristics and outcomes of breast cancer in women with and without a history of radiation for Hodgkin's lymphoma: a multi‑institutional, matched cohort study. J Clin Oncol 29: 2466‑2473, 2011.

[3] Fowble B, Hanlon A, Freedman G, Nicolaou N and Anderson P: Second cancers after conservative surgery and radiation forstages I-II breast cancer: identifying a subset of women atincreased risk. Int J Radiat Oncol Biol Phys 51: 679-690, 2001.

[4] Lee KD, Chen SC, Chan CH, et al: Increased risk for second primary malignancies in women with breast cancer diagnosed at young age: a population-based study in Taiwan. Cancer Epidemiol Biomarkers Prev 17: 2647-2655, 2008.

[5] Cutuli B, Kanoun S, Tunon De Lara C, et al: Breast cancer occurred after Hodgkin's disease: clinico‑pathological features, treatments and outcome: analysis of 214 cases. Crit Rev Oncol Hematol 81: 29‑37, 2012.

[6] Benoit L, Arnould L, Collin F, Fraisse J, Cuisenier J, Chauffert B. Con-current lymphoma and metastatic breast carcinoma in the axillary, con-founding sentinel lymph-node biopsy. Eur J Surg Oncol 2004;30:462-3.

[7] Ambrosiani L, Bellone S, Declich P, et al. Breast carcinoma metastatic toa lymphoma: report of a case with review of literature. Histopathology 1999;34:87e9.

[8] Wiernik PH, Hu X, Ratech H, Fineberg S, Marino P, Schleider MA, et al. Non-Hodgkin's lymphoma in women with breast cancer. Cancer J 2000;6:336-42.

[9] Frey BM, Morant R, Senn HJ, Fisch T, Schid U. Simultaneous occurence of breast carcinoma and malignant lymphoma. Case observations and literature review. Schweiz Med Wochenschr 1994;124(23):1010–6.

[10] Barranger E, Marpeau O, Uzan S and Antoine M: Axillary sentinel node involvement by breast cancer coexisting with B‑cell follicular lymphoma in nonsentinel nodes. Breast J 11: 227‑228, 2005.

[11] Tamaoki M, Nio Y, Tsuboi K, Nio M, Tamaoki M, Maruyama R. A rare case of non‑invasive ductal carcinoma of the breast coexisting with follicular lymphoma: A case report with a review of the literature. Oncology Letters. 2014 Apr 1;7(4):1001-6. DOI: 10.3892/ol.2014.1885

[12] Broughton A, Galant C, Hainaut P. Simultaneous occurrence of metastatic breast cancer, Hodgkin's disease and tuberculous lymphadenitis in homolateral axillary lymph nodes–a case report. Acta Clinica Belgica. 2008 Dec 1;63(6):391-3.

[13] Turhan N, Çetinkaya E, Akkapulu N, Sayek İ. SYNCHRONOUS PRESENTATION OF BREAST CARCINOMA WITH AXILLARY LYMPHOMA; CASE REPORT. Cerrahi Sanatlar Dergisi.;4(2):12-4

[14] Pandey U, Naraynan M, Karnik U, Sinha B. Carcinoma metastasis to unexpected synchronous lymphoproliferative disorder: report of three cases and review of literature. J Clin Pathol 2003;56(12):970-1.

[15] Cox J, Lunt L, Webb L. Synchronous presen-tation of breast carcinoma and lymphoma in the axil-lary nodes. Breast 2005;15(2):246-52.

[16] Mannel DN, Orosz P, Hafner M, Falk W. Mechanisms involved in metastasis enhanced by inflammatory mediators. Circ Shock 1994;44(1):9-3.

[17] Cotterchio M, Nadalin V, Sauer M. Human breast cancer and lymphomas may share a common etiology involving mouse mamary tumour virus (MMTV). Med Hypotheses 2002;59:492-4.

[18] Etkind P, Du J, et al. Mouse mammary tumor virus-loke ENV gene sequences in human breast tumors and in a lymphoma of a breast cancer patient. Clin Cancer Res 2000;6(4):1273-8