Case Report Open Access

Archives Of Breast Cancer

DOI: 10.19187/abc.20174270-74

Synchronous Invasive Lobular Carcinoma of Breast With Hodgkin Lymphoma: A Case Report

Massoome Najafi[a], Afsaneh Alikhassi[b], Sanaz Zand[c], Shahram Movafaghi[d], Gholamreza Toogeh*[e,f]

[a] *Division of Surgical Oncology, Department of General Surgery, Cancer Institute, Tehran University of Medical Sciences, Tehran, Iran*
[b] *Department of Radiology, Cancer Institute, Tehran University of Medical Sciences, Tehran, Iran*
[c] *Kaviani Breast Disease Institute (KBDI), Tehran, Iran*
[d] *Department of Pathology, Laleh Hospital, Tehran, Iran*
[e] *Thrombosis Hemostasis Research Center, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran*
[f] *Department of Internal Medicine, Hematology and Medical Oncology Ward, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran*

ARTICLE INFO

Received:
08 May 2017
Revised:
13 May 2017
Accepted:
16 May 2017

Keywords:
Breast cancer, synchronous tumor, hodgkin lymphoma

ABSTRACT

Background: Multiple Primary Malignant Neoplasms (MPMN) is a well-known entity. Most of these tumors are metachronous. The treatment of Hodgkin lymphoma increases the risk of developing second malignancies including breast cancer. However, the synchronous occurrence of breast cancer and Hodgkin lymphoma is rare.

Case presentation: We presented a case of a 31-year-old woman with simultaneous diagnosis of lobular carcinoma of the breast and Hodgkin lymphoma. The patient underwent modified radical mastectomy followed by hormone therapy as adjuvant treatment of breast cancer and simultaneous chemotherapy for Hodgkin lymphoma.

Conclusions: To the best of our knowledge, this is the first report of coexistence of breast cancer and Hodgkin lymphoma. Synchronous cancers present therapeutic challenges to the clinicians, and the treatment planning should be discussed in a multidisciplinary team.

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. MPMNs constitute 0.4% to 21% of all cancers [2] and the incidence is increasing.[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] MPMNs are considered synchronous, if the second primary tumor is diagnosed within 6 months of the first tumor diagnosis. If the time interval between diagnoses of the tumors is more than 6 months, the tumors are considered metachronous.[2] Synchronous primary tumors are rare.[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 concurrent breast cancer and Hodgkin lymphoma.

Address for correspondence:
Gholamreza Toogeh, M. D.
Thrombosis and Hemostasis Research Center, Imam Khomeini Hospital Complex, Keshavarz Blvd., Tehran, Iran
Tel: 0912 134 6329
Email: gh_toogeh@yahoo.com

Case presentation

A 31-year-old woman was referred to the oncology clinic with the diagnosis of Hodgkin lymphoma. She was visited by her family physician a year earlier with night fever, chills, weight loss, and retrosternal pain. She was treated with antibiotics without any improvement. Gradually, a swelling developed over her sternum, and a biopsy of the lesion showed granuloma. Since she lived in an

endemic area for tuberculosis, the treatment of tuberculosis with Isoniazid, Rifampin, Ethambutol and Pyrazinamide was started for her and it was continued for 6 months. The size of sternal swelling decreased, but she noticed the development of new swellings in her lower neck and axillary areas. The biopsy of the right supraclavicular lymph nodes was performed and the pathology result showed Hodgkin lymphoma, nodular sclerosis with mixed cellularity nodule type.

While referring the patient to the oncology clinic, physical examination revealed bilateral supraclavicular and axillary lymphadenopathy, and 2 masses in the right breast at 12 and 7 o'clock measured 4 and 2 cm, respectively. No other organomegaly was detected. She had no significant medical or surgery history. She mentioned a family history of breast cancer in her 3 cousins. Her menarche was at 15 years of age and her first child birth was when she was twenty-one.

Considering her family history of breast cancer and no report of breast involvement in Hodgkin lymphoma, the possibility of a second primary malignancy was probable. The result of mammography showed 2 suspicious masses and skin thickening in the right breast (figure 1). Breast ultrasonography was performed and the result revealed 6 highly suspicious masses in the right breast. The masses ranged from 6 to 34 mm.

The result of MRI of the breast revealed 2 adherent large irregular shape enhancing masses in the right breast with multiple smaller masses around them in favor of multi-centric breast cancer (figure 2 and 3). In addition, there were multiple enlarged pathologic appearing lymphadenopathies in both axillae (figure 4). An irregular shape chest wall mass in medial deep part of the right side of chest wall was detected with the involvement of ribs and pleura and extension to the mediastinum (figure 5).

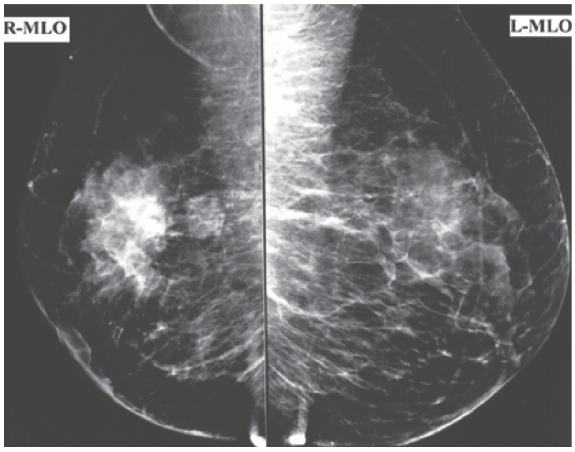

Figure 1. MLO mammography showing a large lobulated irregular shape mass with ill-defined border in the right breast upper part and another mass posterior to the main mass. Mild skin thickening of the central part of the right breast is also noted.

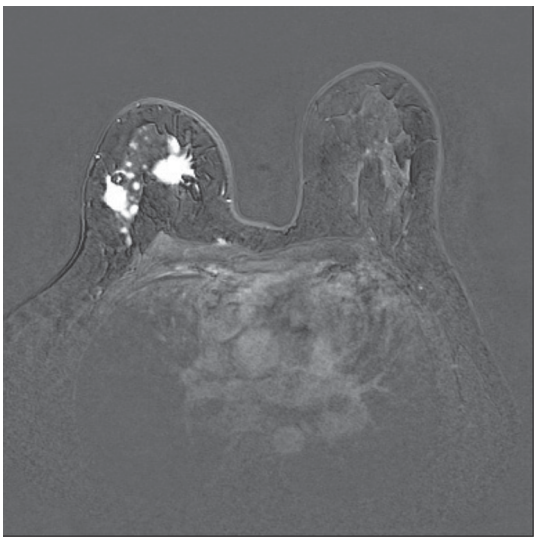

Figure 2. Breast MRI, T1 with contrast subtraction axial image, showing multiple irregular shaped enhancing masses in central and outer part of right breast

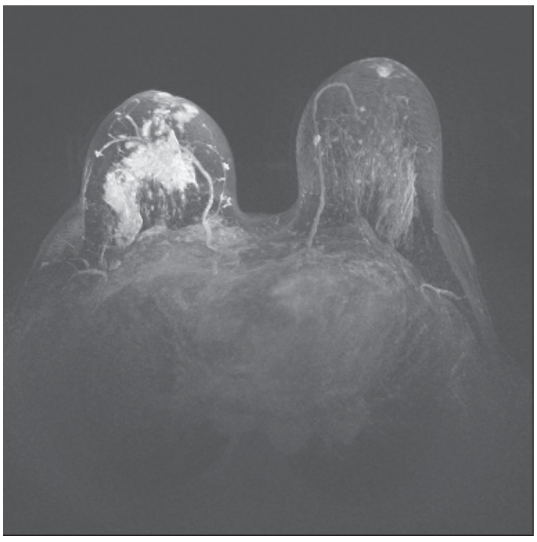

Figure 3. Breast MRI, T1 with contrast and subtraction in MIP axial image, showing 2 adherent large irregular shaped enhancing masses in the right breast with multiple smaller masses around them in favor of multi-centric breast cancer

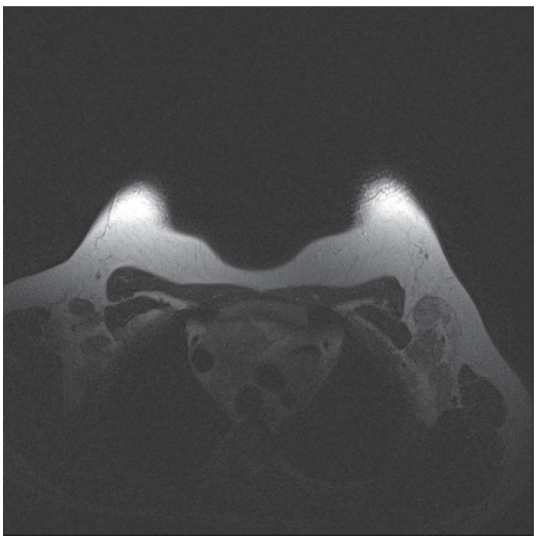

Figure 4. Breast MRI, axial T1 image, Multiple enlarged pathologic appearing lymphadenopathies are seen in both axillae

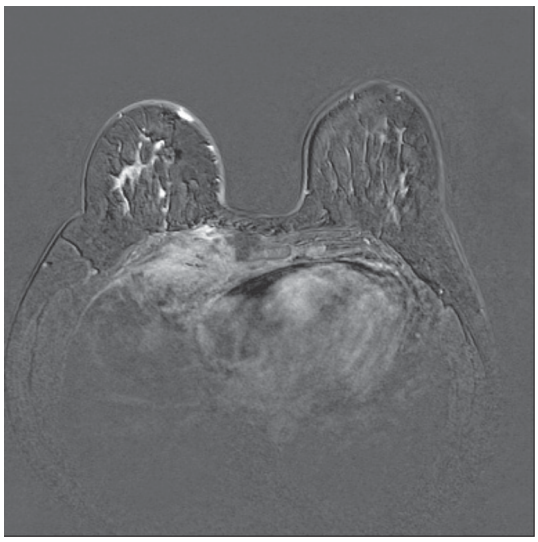

Figure 5. Breast MRI, T1 with IV contrast and subtracted axial image, showing irregular shape chest wall mass in medial deep part of right side of chest wall with involvement of ribs and pleura and extension to the mediastinum

The biopsy of the masses of the right breast was performed and the pathology was multi-centric invasive lobular carcinoma. Estrogen and progesterone receptors were positive, HER-2 neu was negative, and Ki-67 was 15%. The FNA of left axillary lymph nodes was consistent with Hodgkin lymphoma, and there was no involvement with lobular carcinoma.

Blood work showed mild microcytic anemia, high platelet count, elevated ESR, and mildly elevated bilirubin. Liver function tests and LDH were within normal range. Bone marrow biopsy did not show involvement with Hodgkin lymphoma. Computed tomography scan of neck and thorax revealed numerous bilateral supraclavicular, infraclavicular, axillary, and mediastinal lymph nodes. Abdominal and pelvic CT scans were normal.

The patient was diagnosed with synchronous stage II Hodgkin lymphoma and locally advanced breast cancer. The management of each malignancy was discussed in the multidisciplinary oncology conference of the hospital. The multidisciplinary team agreed on the surgical treatment of breast cancer followed by simultaneous adjuvant treatment with tamoxifen for breast cancer and chemotherapy for Hodgkin lymphoma.

The patient underwent right modified radical mastectomy and axillary lymph node dissection. A small area of pectoralis major muscle, involved with one of the masses, was resected. The pathology report revealed multi-centric invasive mixed lobular and ductal carcinoma, histologic and nuclear grade II with angiolymphatic and perineural invasion. The smallest tumor was 7 mm and the largest one was 5 cm in diameter. All margins were free from tumor. Seven out of 8 axillary lymph nodes were involved with metastatic tumor. The microscopic examination of lymph nodes revealed lymph node tissue with the presence of sheets and nests of epithelial neoplastic cells. In some foci, there was diffuse obliteration of nodal architecture without capsular thickening or broad bands of parenchymal fibrosis. In addition, numerous classical Reed- Sternberg cells were present in a background of small lymphocytes, eosinophils, histiocytes, plasma cells, and occasional neutrophils (figure 6).

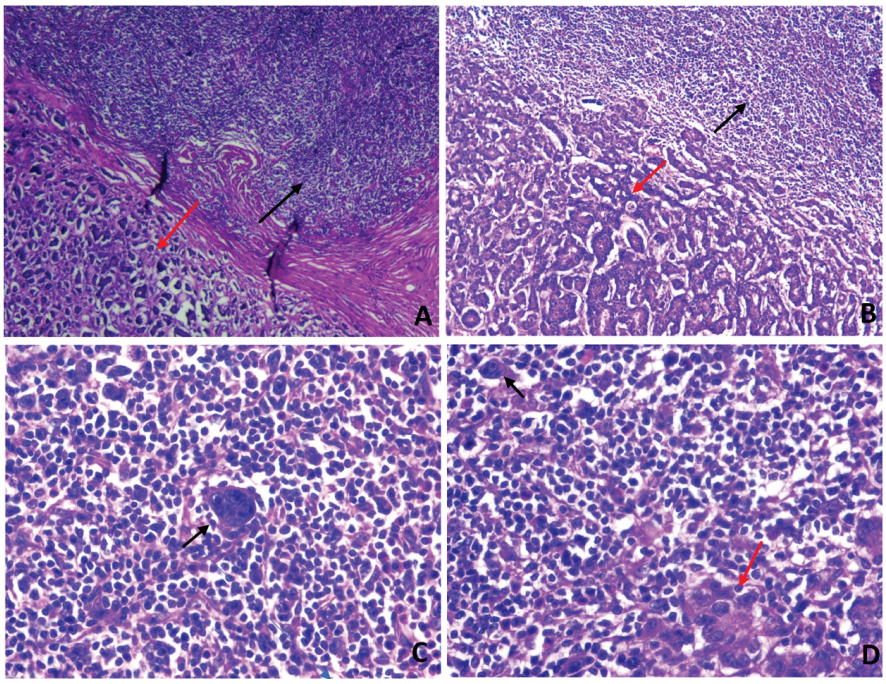

Figure 6. Histological analysis of the lymph node involved by Hodgkin lymphoma and breast carcinoma (magnification: A =x 40, B =x 100, C&D =x 400) A & B) Black arrow: Nodular Hodgkin lymphoma, red arrow: Invasive Ductal Carcinoma. C) Black arrow: Reed-Sternberg cell. D) Black arrow: Reed-Sternberg cell, red arrow: Invasive Ductal Carcinoma

Following the surgery, she received 12 cycles of chemotherapy for Hodgkin lymphoma with Adriamycin, Bleomycin, Vinblastine, and Dacarbazine (ABVD) regimen. Concurrently, she received Tamoxifen and Diphereline as adjuvant therapy for breast cancer. A CT scan, after 8 cycles of chemotherapy, showed no evidence of disease in the neck, axillae, and mediastinum. A PET- CT scan, 3 months after the completion of chemotherapy, showed no metabolically active lesion throughout the body, indicating complete metabolic response to the treatment. She received adjuvant radiotherapy for breast cancer.

Discussion

After the first report of MPMN by Billroth, Warren, and Gates collected 1259 cases from the literature and described the criteria for the diagnosis of MPMNs.[7] The criteria of Warren and Gates required: 1) the histologic confirmation of the malignant nature of each tumor, 2) the existence of tumors in geographically separate sites and 3) the lack of possibility of metastasis from another neoplasms. These criteria have been updated by an international working group in 2004.[4]

MPMNs are, likewise, categorized as synchronous or metachronous. Tumors diagnosed at the same time or within 6 months of the first tumor are considered synchronous and tumors diagnosed at more than a 6-month interval are considered metachronous. Metachronous MPMNs are more common than synchronous neoplasms[8,9] with a ratio of 2 to 2.7:1.[2,6] The present percentage of MPMNs is increasing [3,10,11] and this increase might be attributed to more successful treatment of the primary tumors.[12]

There are several explanations for the occurrence of MPMNs. One theory is increased survival of patients with cancer due to more effective therapies.[13] The cancer survivors have a 20% increase in their risk of new primary cancer development.[14] Another explanation is the effect of the therapies for the first cancer. Curtis reported Alkylating agents as a risk factor for developing acute non-lymphocytic leukemia and preleukemia following breast cancer treatment.[15] Patients treated with radiation therapy are predisposed to the development of a second cancer. One example is the development of breast cancer following radiation therapy for Hodgkin lymphoma[16-19] and contralateral breast cancer in patients who received radiotherapy for breast cancer.[20]

Furthermore, it has been suggested that during fetal life, cells with a predisposition to malignant transformation migrate to multiple organs. Later, exposure to environmental carcinogens could induce multiple primary neoplasms.[21, 22] In other cases of MPMNs, inherited mutations are responsible for multiple malignancies. The examples of these mutations are BRCA1 and 2, P53, PTEN, etc.

There are multiple reports of breast cancer occurring after radiation therapy for Hodgkin lymphoma.[16, 17, 19, 23-25] There are also reports of breast involvement by hematologic malignancies, but breast involvement by Hodgkin lymphoma has not been reported.[26] There has been numerous reports of synchronous occurrence of breast cancer and other malignancies, including bladder,[5] thyroid,[27] pancreas,[28] renal cell carcinoma,[29] thymoma,[30] lung, and melanoma,[8] etc. To the best of our knowledge, this is the first report of synchronous occurrence of breast cancer and Hodgkin lymphoma. The treatment of synchronous cancers presents a therapeutic challenge to both clinicians and patients. The treatment of these patients needs to be planned by a multidisciplinary team. Clinicians need to be aware of the chance of multiple primary cancers to prevent delayed diagnosis of the second cancer.

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. Liu Z, Liu C, Guo W, Li S, Bai O. Clinical analysis of 152 cases of multiple primary malignant tumors in 15,398 patients with malignant tumors. PLoS One. 2015;10(5):e0125754.
3. Lopez ML, Lana A, Diaz S, Folgueras MV, Sanchez L, Comendador MA, *et al.* Multiple primary cancer: an increasing health problem. Strategies for prevention in cancer survivors. Eur J Cancer Care (Engl). 2009;18(6):598-605.
4. Working Group R. International rules for multiple primary cancers (ICD-0 third edition). Eur J Cancer Prev. 2005;14(4):307-8.
5. Wallace D, Arul D, Chitale S. Synchronous tumours of the breast and bladder. J Surg Case Rep. 2014;2014(7): rju066.
6. Testori A, Cioffi U, De Simone M, Bini F, Vaghi A, Lemos AA, *et al.* Multiple primary synchronous malignant tumors. BMC Res Notes. 2015;8:730.
7. Warren S. Multiple primary malignant tumors, a survey of the literature and statistical study. Am J cancer. 1932;16:1358-414.
8. Kurul S, Akgun Z, Saglam EK, Basaran M, Yucel S, Tuzlali S. Successful treatment of triple primary tumor. Int J Surg Case Rep. 2013;4(11):1013-6.
9. Sakellakis M, Peroukides S, Iconomou G, Boumpoucheropoulos S, Kalofonos H. Multiple primary malignancies: a report of two cases. Chin J Cancer Res. 2014;26(2):215-8.
10. Dong C, Hemminki K. Second primary neoplasms in 633,964 cancer patients in Sweden, 1958-1996. Int J Cancer. 2001;93(2):155-61.

11. Filali K, Hedelin G, Schaffer P, Esteve J, Arveux P, Bouchardy C, *et al.* Multiple primary cancers and estimation of the incidence rates and trends. Eur J Cancer. 1996;32A(4):683-90.
12. Hemminki K, Aaltonen L, Li X. Subsequent primary malignancies after endometrial carcinoma and ovarian carcinoma. Cancer. 2003;97(10):2432-9.
13. Yancik R, Ries LA. Aging and cancer in America. Demographic and epidemiologic perspectives. Hematol Oncol Clin North Am. 2000;14(1):17-23.
14. Luciani A, Balducci L. Multiple primary malignancies. Semin Oncol. 2004;31(2):264-73.
15. Curtis RE, Boice JD, Jr., Moloney WC, Ries LG, Flannery JT. Leukemia following chemotherapy for breast cancer. Cancer Res. 1990;50(9):2741-6.
16. van Leeuwen FE, Klokman WJ, Hagenbeek A, Noyon R, van den Belt-Dusebout AW, van Kerkhoff EH, *et al.* Second cancer risk following Hodgkin's disease: a 20-year follow-up study. J Clin Oncol. 1994;12(2):312-25.
17. Hilal T, Rudy DW. Radiation-induced breast cancer: the question of early breast cancer screening in Hodgkin's lymphoma survivors. Oxf Med Case Reports. 2016;2016(2):17-8.
18. Howell SJ, Searle C, Goode V, Gardener T, Linton K, Cowan RA, *et al.* The UK national breast cancer screening programme for survivors of Hodgkin lymphoma detects breast cancer at an early stage. Br J Cancer. 2009;101(4):582-8.
19. Sanna G, Lorizzo K, Rotmensz N, Bagnardi V, Cinieri S, Colleoni M, *et al.* Breast cancer in Hodgkin's disease and non-Hodgkin's lymphoma survivors. Ann Oncol. 2007;18(2):288-92.
20. Murakami R, Hiyama T, Hanai A, Fujimoto I. Second primary cancers following female breast cancer in Osaka, Japan--a population-based cohort study. Jpn J Clin Oncol. 1987;17(4):293-302.
21. Schwartz LH,Ozsahin M, Zhang GN, Touboul E, De Vataire F, Andolenko P, *et al.* Synchronous and metachronous head and neck carcinomas.Cancer. 1994;74(7):1933-8.
22. Bedi GC, Westra WH, Gabrielson E, Koch W, Sidransky D. Multiple head and neck tumors: evidence for a common clonal origin. Cancer Res. 1996;56(11):2484-7.
23. Allen SD, Wallis MG, Cooke R, Swerdlow AJ. Radiologic features of breast cancer after mantle radiation therapy for Hodgkin disease: a study of 230 cases. Radiology. 2014;272(1):73-8.
24. Horst KC, Hancock SL, Ognibene G, Chen C, Advani RH, Rosenberg SA, *et al.* Histologic subtypes of breast cancer following radiotherapy for Hodgkin lymphoma. Ann Oncol. 2014;25(4):848-51.
25. Tieu MT, Cigsar C, Ahmed S, Ng A, Diller L, Millar BA, *et al.* Breast cancer detection among young survivors of pediatric Hodgkin lymphoma with screening magnetic resonance imaging. Cancer. 2014;120(16):2507-13.
26. Cox J, Lunt L, McLean L. Haematological cancers in the breast and axilla: a drop in an ocean of breast malignancy. Breast. 2005;14(1):51-6.
27. Zhong J, Lei J, Jiang K, Li Z, Gong R, Zhu J. Synchronous papillary thyroid carcinoma and breast ductal carcinoma: A rare case report and literature review. Medicine (Baltimore). 2017;96(7):e6114.
28. Castro M, Vierkoetter K, Prager D, Montgomery S, Sedgwick K. Synchronous Onset of Breast and Pancreatic Cancers: Results of Germline and Somatic Genetic Analysis. Case Rep Oncol. 2016;9(2):387-94.
29. Arjunan R, Kumar D, Kumar KV, Premlatha CS. Breast Cancer with Synchronous Renal Cell Carcinoma: A Rare Presentation. J Clin Diagn Res. 2016;10(10):XD03-XD05.
30. Athanasiou E, Michalopoulou-Manoloutsiou E, Bobos M, Hatzibougias DI, Zarogoulidis P, Katsikogiannis N, *et al.* Coincidence of thymoma and breast cancer and in a 56-year-old female patient. Ann Transl Med. 2016;4(22):446.