Malign Melanoma on the Irradiation Field After Adjuvant Treatment of Breast Cancer: A Case Report

Aziz KARAOĞLU*, Yunus SARAL, Emin T. ELKIRAN*, Bilge AYGEN***, Erkan TOPKAN****, Bengü ÇOBANOĞLU*****, Nilufer GÜLER******

* Fırat Üniversitesi Tıp Fakültesi, Tıbbi Onkoloji Bilim Dalı,
** Fırat Üniversitesi Tıp Fakültesi, Dermatoloji Anabilim Dalı,
*** Fırat Üniversitesi Tıp Fakültesi, İç Hastalıkları Anabilim Dalı,
**** Harput Devlet Hastanesi, Radyasyon Onkolojisi Kliniği,
***** Fırat Üniversitesi Tıp Fakültesi, Patoloji Anabilim Dalı, ELAZIĞ
****** Hacettepe Üniversitesi Onkoloji Enstitüsü, Medikal Onkoloji Bölümü, ANKARA

ABSTRACT

Patients with breast cancer have a chance of long-term survival. All subsets of breast cancer patients are therefore at risk of developing second malignancies. Melanomas are among to the infrequent nonepithelial second neoplasm. We report an developed malign melanoma which was appeared in the irradiation area after 11 months of adjuvant treatment.

Key Words: Breast cancer, Irradiation, Malign melanoma

ÖZET

Meme Kanserinin Adjuvant Tedavisi Sonrasında Radyasyon Alanı İçinde Gelişen Malign Melanom: Olgu Sunumu

Meme kanserli hastalar uzun dönem sağkalım şansına sahiptir ve bu nedenle meme kanserli tüm alt gruplarda ikincil kanserler gelişme riski vardır. Meme kanserli hastalarda gelişen non-epitelyal ikincil kanserler arasında malign melanoma da bulunur. Bu olgu sunumunda adjuvan tedaviden 11 ay sonra radyasyon alanı içinde gelişen bir malign melanoma olgusu bildirilmektedir.

Anahtar Kelimeler: Meme Kanseri, Radyoterapi, Malign melanom

INTRODUCTION

Breast cancer is the most frequent malign tumor among women in developed countries. Patients with breast cancer who undergo proper treatment have a chance of long-term survival. All subsets of breast cancer patients are therefore at risk of developing second malignancies. There are some possible causes of these malignancies such as underlying genetic and environmental factors that predisposed the patient to the breast cancer and side effects of adjuvant therapies of breast cancer [1]. In the breast cancer survivors % 10-50 greater risk of developing a second cancer risk compared to the general population have been reported [2-4].

Several previously population-and hospital based-studies have shown that the most common second cancers following breast cancers, excluded the second primary breast cancers, are lung cancers, colorectal cancers, ovarian cancers, uterine cancers, malign melanoma and non-melanomatous skin cancers, and soft tissue cancers [2-8]. Rubino et al and Galper et al reported that second cancers following breast cancers are associated with radiotherapy in the initial therapy for breast cancer [4,7]. The cancer risk induced by ionizing radiation has been extensively studied and there is an abundance of data about radiation-induced cancers in the human [9]. Radiation has been describe as a "two-edged sword" because while it is an important modality for treatment of cancer, and it has side effect for the cause of second primary cancers [10]. In the radiation fields the most frequently occurred neoplasm are carcinomas, and the occurrence of malign melanomas are extremely rare. We describe here a case of malign melanoma that appeared in the irradiation area after 11 months adjuvant treatment for breast carcinoma.

CASE REPORT

A 43-year-old, woman who was initially diagnosed as having invasive ductal carcinoma of the left breast in October 2001. She has treated with a modified radical mastectomy and level II axillary lymph node dissection. Post-operative pathologic examination revealed Stage IIB (T2N1M0) invasive ductal carcinoma (Figure 1). Estrogen receptor and progesteron receptor were positive, and c-erb B2 was negative. Adjuvant FAC (5-Fluorouracil, Adriamycin, Cyclophosphamide) combination chemotherapy regimen was applied after operation. After 3 cycles FAC regimen, the patient underwent post-operative adjuvant irradiation therapy with telecobalt; conventionally fractionated to 25 sessions. She was treated with radiation therapy to the supraclavicular fossa and axilla receiving the 200 cGy/daily, total 5.000 cGy. She was also received 200 cGy/daily, total 5.000 cGy to her chest wall. After radiotherapy, she received 3 cycles of FAC chemotherapy again. The patient was well tolerated this radiotherapy and chemotherapy. After completion of chemotherapy and radiotherapy, adjuvant tamoxifen 20 mg/day per oral was started and the patient was followed-up with 3 months intervals.

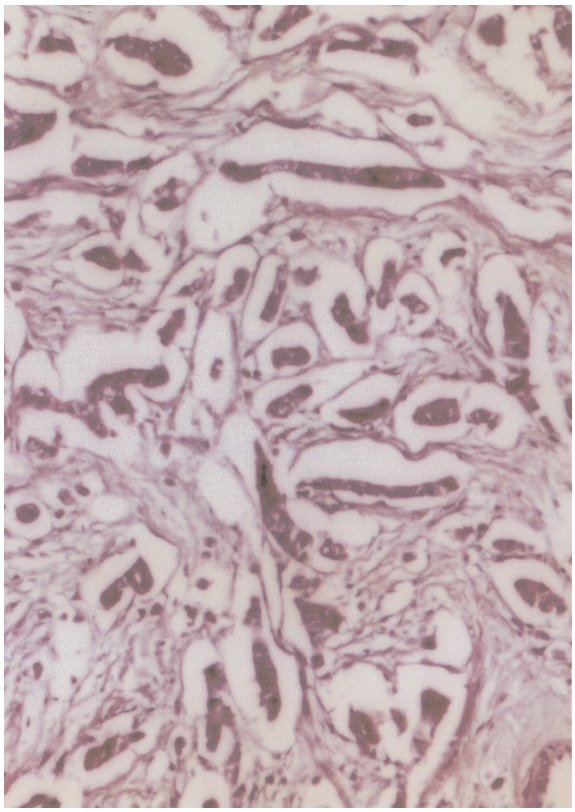
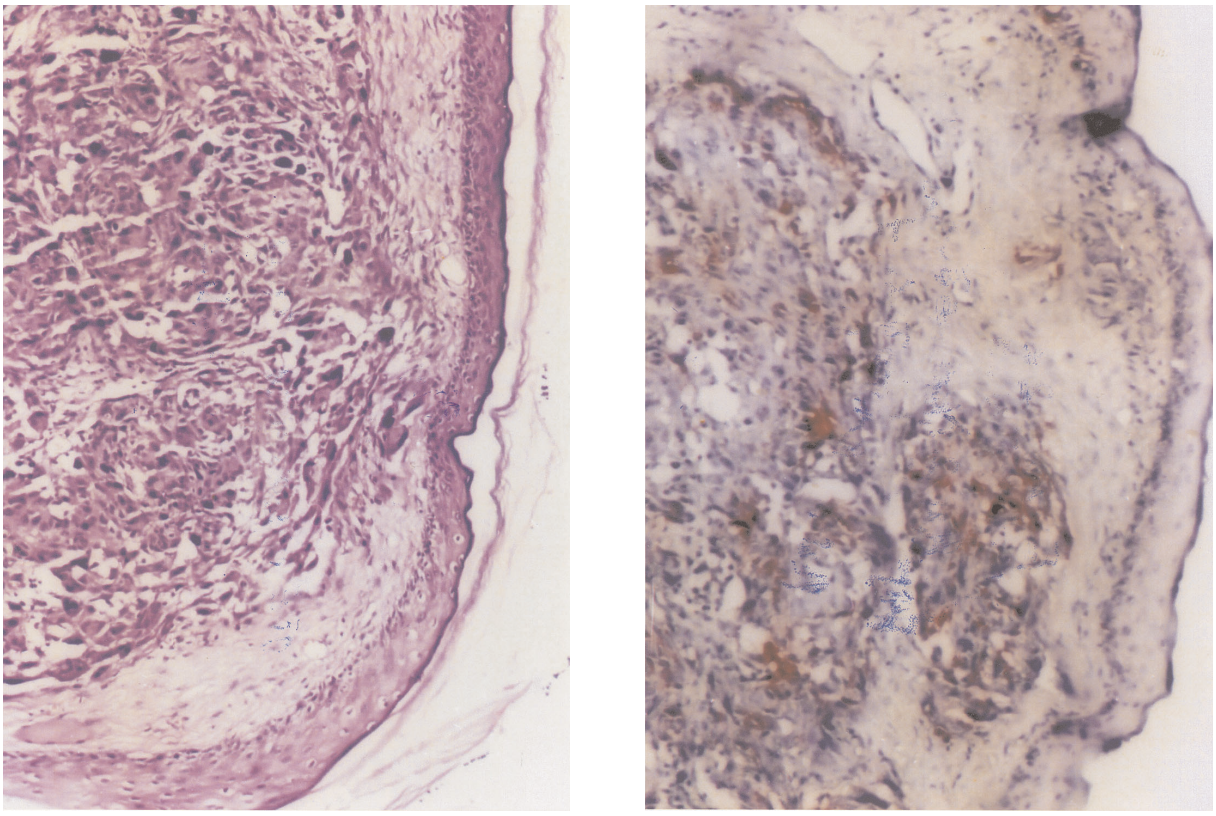


Figure 1. Photomicrograph shows invasive ductal carcinoma from modified radical mastectomy specimen. (hematoxylin-eosin stain; magnification x 400)



A B

Figure 2. Photomicrograph shows cutaneous malignant melanoma in the irradiation area. (A) Hemotoxylin-eosin stain, (B). Positive immunostaining of tumor cells with HMB45

The patient who has fair-skinned and has not sun-habbit hausewife, presented with a pigmented cutaneous lesion on the anterior chest wall after 9 months from the radiotherapy. The pinkish-brown colored lesion size was 0.5 x 0.5 cm in diameter and located on the midclavicular line and was 3 cm below the operation scar. The lesion was within irradition field on the chest wall. The lesion was resected with excisional biopsy. Pathologic evaluation revealed to diagnose nodular type malign melanoma and the Clark's level was III. Tumor thickness was measured 1.57 mm for Breslow. Tumor tends to be symmetrical at scanning magnification. There was no adjacent nontumorigenic radial growth phase component. The cells of the tumor exhibited severe uniform cytological atypia. The uniformly atypical nuclei of the cells that constitute the tumor nodule had irregular nuclear membranes, hyperchromatic chromatin and prominent nucleoli. In this tumor, there was contiguous growth of uniformly atypical melanocytes in the dermis. Mitotic figures were present. Tumor cells included considerable melanin. Immunohistochemical staining for HMB45 was positive in tumor cells (Figure 2 A and Figure 2 B).

DISCUSSION

Breast cancer patients treated with a number of cohort studies have pointed out an increased incidence of second malignancies following breast cancer occur second primary breast cancer, lung, skin cancers, ovarian cancers, soft-tissue cancers, uterine cancers, and kidney cancers [2-8]. In the second malignancies after breast cancer therapy, risk of malign melanoma is not frequent. An excess risk of malign melanoma was reported by Harvey and Brinton in a cohort study that including 41.109

women with diagnosed breast cancer [6]. They calculated relative risk for malign melanoma in association with breast cancer is 1.5. Previously published two studies reported also a Standardised Incidence Ratio (SIR) for malign melanoma following breast cancer ranged between 1.41 (95 % confidence intervals (CI) 0.91-2.09) and 2.7 (C95 % CI 1.4-4.8) [4,7]. In addition, an increased risk of second malignancies in women was reported Rubino et al in a study of second cancers developing after initial treatment, including a cohort 4416 patients initially treated. Interestingly, in their cohort study a higher risk for second cancer was found among women who had received radiotherapy as initial treatment.

We report here a malign melanoma case as second malignancy following adjuvant radiotherapy and chemotherapy for breast cancer. In our case, lesion was detected on trunk within irradiation field. Generally, malign melanoma lesions locate primarily on the extremities (lower leg and arms) in female [10]. But in our case we detected melanoma lesions on the trunk within irradiation field. So this localization suggests that radiotherapy can play a role in development of the malign melanoma following breast cancer. Rubino et al reported that the SIR of melanoma was higher in the group of treated with radiotherapy (SIR: 3.6 (95 % CI 1.6-7.0) than no treated radiotherapy and chemotherapy group (SIR: 1.0 (95 % CI 0.1-4.4) (10). But they did not found statistical difference between these two groups.

In our case, it is interesting that malign melanoma arose in the irradiation field after only 9 months from radiotherapy. In a classic paper Cahan et al. pointed out that identified criteria to reasonably ascertain whether or no a secondary neoplasm was radiation-induced: [1] The localization of the second malignancy had to occur within the confines of the radiotherapy field, [2] An interim time must have elapsed between the radiotherapy and the development of the second malignancy, which they define as a minimum of 5 years, [3] Second neoplasm is of a different histology than the primary lesion (11). And thus rule out recurrence of the primary neoplasm. In our case, interim time between radiotherapy and development of the malign melanoma is only 9 months. So, in our case we can not claim clearly, a causal association radiotherapy and melanoma. Besides radiotherapy, other factors also responsible for developing malign melanoma after breast cancer such as: 1) Common etiologic factors (ie genetic, hormonal or environmental) that predisposed the patient to breast cancer. 2) Carcinogenic effects of chemotherapy, 3) Immunsupressive effects of radiotherapy and/or chemotherapy.

Oncologists and dermatologists should be aware of possibility of cutaneous located malignant neoplasm in irradiated patients. And in the follow up visits physician should perform a careful examination of the skin especially on the irradiation fields for diagnose of second neoplasm at earlier stages.

REFERENCES

1. Fox MS. On the diagnosis and treatment of breast cancer. JAMA 241: 489-494, 1979.
2. Volk N, Pompe-Kirn V. Second primary cancers breast cancer patients Slovenia. Canc Caus Control 8: 764-770, 1997.
3. Doherty MA, Rodger A, Langlands AO, Kerr GR. Multiple primary tumours in patient treat with radiotherapy for breast cancer. Radiother Oncol 26:125-131, 1993.
4. Rubino C, Vatherie FD, Diallo I, et al. Increased risk of second cancers following breast cancer: Role of the initial treatment. Breast Cancer Res Treat 61: 183-195, 2000.
5. Rosen PR, Groshen S, Saigo PE, et al. A long term follow up study of survival in stage I (T1 N0 M0) and stage II (T1N1 M0) breast carcinoma. J Clin Oncol 7: 355-366, 1989.
6. Harvey EB, Brinton LA. Second cancer following cancer of the breast in Connecticut, 1935-82. Natl Cancer Inst Monograph 68: 99-102, 1985.
7. Galper S, Gelman R, Recht A, et al. Second non-breast malignancies after conservative surgery and radiation therapy for early-stage breast cancer. Int J Radiat Oncol Biol Phys 52: 406-414, 2002.
8. Levi F, Te VC, Randimbison L, La Vecchia C. Cancer risk in women with previous breast cancer. Ann Oncol 14: 71-73, 2003.
9. Boice JD. Cancer following medical irradition. Cancer 47: 1081-1090, 1981.

10. Mackie RM. Current epidemiology of malignant melanoma and clinical implications. Proceedings of 3rd European Society Pigment Cell Research, Amsterdam 8-11th Sept, 1991: p74.
11. Cahan WG, Woodard HQ, Higinbatham NL. Sarcoma arising in irradiated bone: report of eleven cases. Cancer 1: 3, 1948.

Correspondence:
Dr. Aziz KARAOGLU
Fırat Üniversitesi Tıp Fakültesi
Tıbbi Onkoloji Bilim Dalı
23100 ELAZIĞ

Tel: (0.424) 233 35 55 / 1663
Fax: (0.424) 238 80 96
E-mail: azizk6@yahoo.com