REAPPEARANCE OF ISOLATED CHEST WALL LOCAL RECURRENCES AFTER RADICAL MASTECTOMY DURING THE FIVE CONSECUTIVE YEAR PERIOD

ZVONIMIR ZORE, DOMAGOJ ELJUGA and MLADEN STANEC

Department of Surgical Oncology, University Hospital for Tumors, University Hospital Center Sestre milosrdnice, Zagreb, Croatia

Summary

Breast cancer is most common cancer in women. After surgical treatment and adjuvant therapy, locoregional recurrences do occur in certain number of patients. Herein we report a breast cancer patient who developed isolated chest wall local recurrence 3 years after mastectomy which was reappearing in next five consecutive years. Multimodal treatment which includes surgical excision and adjuvant chemoradiotherapy can achieve a significant degree of palliation when locoregional recurrences are diagnosed. In our case, inclusion of adjuvant treatment did not provide satisfactory local control of disease therefore repetitive surgical excision was the only modality which offered our patient 7 years of overall survival after first excision of local recurrence.

KEY WORDS: breast cancer, locoregional recurrence, surgery

PRIKAZ SLUČAJA BOLESNICE S POJAVOM LOKALNOG RECIDIVA NA PRSNOM KOŠU PET UZASTOPNIH GODINA NAKON RADIKALNE MASTEKTOMIJE

Sažetak

Rak dojke je najčešći rak u žena. Unatoč kirurškom liječenju i adjuvantnoj terapiji, lokalni recidivi se javljaju u određenom broju pacijenata. Prikazan je slučaj bolesnice s pojavama lokalnog recidiva na prsnom košu u razdoblju od pet uzastopnih godina nakon radikalne mastektomije. Koristeći se multimodalnim tretmanom koji uključuje kirurški zahvat i kemoradioterapiju, načelno se postižu dobri rezultati u liječenju lokoregionalnog recidiva. Unatoč danoj terapiji, uzastopne kirurške ekscizije su se pokazale kao jedini modalitet liječenja koji je bolesnici omogućio sedmogodišnje preživljenje nakon pojave prvog lokalnog recidiva.

KLJUČNE RIJEČI: rak dojke, lokalni povrat bolesti, kirurgija

INTRODUCTION

Locoregional recurrences (LRR) may occur in certain number of patients after primary therapy despite radical surgical treatment of primary breast cancer and adjuvant systemic therapy with irradiation. Most of LRR recurrences occur in the chest wall within 5 years of surgery. LRR are more

frequent among high-risk patients receiving no postmastectomy radiotherapy (1). Here we will report an unusual case of a 65 year old female breast cancer patient treated with radical mastectomy who developed isolated chest wall local recurrence 3 years after mastectomy in the period of five consecutive years.

CASE PRESENTATION

A 65-year-old postmenopausal patient had undergone modified radical mastectomy and axillar lymphadenectomy for stage I left breast cancer in April 2006. Final histopathological examination of the specimen revealed a 2,7 cm invasive ductal carcinoma of the left breast with no metastasis in axillary lymph nodes (T2, N0, M0). Immunohistochemical (IHC) staining of tumor cells showed positive both estrogen (ER) and progesterone (PgR) receptors, weak membrane staining of HER-2 and Ki-67 proliferative index of 1,5 %. The patient received postoperative adjuvant hormone (aromasine) therapy. Until the beginning of 2009, the patient was under regular follow up every six months and there were no signs of any local, locoregional or distant recurrences. In September 2009, a 11mm subcutaneous nodule was found at the center of the left chest wall mastectomy scar. She was referred to te hospital where fine needle aspiration (FNA) was performed. Cytological findings revealed breast cancer metastases. A CT scan of the chest and abdomen was done and no other regional or distant metastases were found. A wide local excision was performed and pathological examination confirmed metastatic adenocarcinoma as it is shown in Table 1. Based on these findings, she was administered the chest wall irradiation (40Gy in 15 fractions) with a 9 MeV electron boost (10 Gy in 5 fractions) to the site of excision. During 2010 another excision was done and final pathological examination confirmed metastatic adenocarcinoma of the skin and metastatic subcutaneous nodule. In 2011 two additional procedures were performed after patient was presented with another suspicious lesions on skin and after 6 months period with another nodule in subcutaneous region in thoracic area. Final pathological examination is shown in Table 1. During 2012 patient presented with another skin metastasis and surgical excision was performed followed with administration of CMF chemotherapy protocol and exemestan was changed to letrosole. During 2013 another excision was performed because patient presented with metastatic nodule in thoracic area. In the period of another two years, there were no signs of any other local or distant metastases.

DISCUSSION

Local recurrence after primary treatment of breast cancer include a diverse group of lesions with various prognosis. Patients with chest wall recurrences and regional nodal involvement after traditional radical surgery can still achieve a significant degree of palliation and even long-term survival with carefully harmonized multimodal treatment (2-4). More than half of patients with chest-wall-only recurrences present with solitary nodules and the remainder have more than one nodule or diffuse chest wall disease. Risk factors for loco-regional failure following mastectomy can be divided into clinical, pathological, and treatment-related categories. Young age (<35 years), nodal status, tumor size (> 3 cm), lymphovascular invasion, multicentricity, the disease free interval (< 2 years) and high histological grade are all risk factors for postmastectomy recurrence (5-7). Other studies suggest that the molecular subtype may also impact local recurrence, with both triple negative estrogen receptor (ER) progester-

Table 1.

PATHOLOGICAL EXAMINATION OF PRIMARY BREAST CANCER AND METASTATIC CANCER

| Year | Final pathological examination | Size of tumor (mm) | ER (%) | PR (%) | Her-2 | Ki-67 (%) |
|------|---|--------------------|-----------|-----------|-------|--------------|
| 2006 | Carcinoma invasivum ductale (T2,N0,M0) | 27x13 | 90 | 60 | neg | 1,5 |
| 2009 | Carcinoma metastaticum cutis | 11x8 | 100 | 50 | neg | 27,1 |
| 2010 | Carcinoma metastaticum cutis Ca metastaticum subcutis | 14x7 20x10 | 100 | 60 | neg | 25 |
| 2011 | Carcinoma metastaticum cutis | 10,15,5 | 100 | 60 | neg | 26,3 |
| 2011 | Carcinoma metastaticum subcutis | 25x15 | 100 | 60 | neg | 25,5 |
| 2012 | Carcinoma metastaticum cutis | 20x10 | 95 | 65 | neg | 52 |
| 2013 | Carcinoma metastaticum | 10x6 | 100 | 100 | neg | 40 |

one receptor (PR) and HER-2-neu negative subtypes associated with a higher rate of local and regional relapse (8-11). There is a high risk (> 50%) of subsequent distant metastases following a clinically isolated chest wall recurrence after initial mastectomy (12-13). Options for treatment of LR following mastectomy include surgery, RT, chemotherapy, hormonal therapy, or a combination of modalities. Patients experiencing LR after mastectomy should undergo a workup for excluding metastatic disease. When possible, surgical excision followed by RT to the involved chest wall and regional lymphatics is the standard treatment approach. Systemic therapy should be considered for most patients following treatment of a clinically isolated chest wall recurrence.

In this case report, we describe a rare case of five consecutive years of local chest wall recurrences of breast carcinoma after mastectomy. Our patient was initially diagnosed with hormone positive and Her-2-negative breast cancer. A reevaluation of the metastatic disease showed identical IHC phenotypes as a primary breast cancer even though some studies found a greater proportion of conversion of ER and PR positivity in primary tumors to negative status in recurrences for women who received hormonal treatment. Hormone receptor heterogeneity within the same tumor mass has been reported. These ER- or PRmetastatic tumors display much aggressive course after loss of hormone receptors compared with those retaining them, which is usually followed with decreased OS (9-10). The discordance between HER-2 status in primary tumors and in metastatic sites occurs less frequently than the discordance between hormonal receptors (8). A detailed analysis of the failures occurring in the patients treated with radiotherapy, with or without surgery, showed that most of the failures were due to inadequate doses of irradiation, the use of fields that were too narrow and primary resistance to radiotherapy (15). Some patients have an early recurrence even though they had a stage I tumor with good prognostic features. These recurrences have been explained by the existence of certain cellular characteristics at the molecular level that make the tumor cells resistant to therapy (16). Following LRR, 5 year overall survival and distant metastasis free survival were 70% and 65% for late chest wall relapse compared to 47% and 42% for early chest wall relapse as showed by Morane et al

(14). Our patient falls in the category of early chest wall relapse and despite received irradiation therapy and adjuvant chemotherapeutic protocol in the period of five years after first local recurrence was discovered, wide surgical local excision provided as good or even better local control than any other treatment modalities with excellent OS of 7 years after first LRR was discovered.

REFERENCES

- Overgaard M. Overview of randomized trials in high risk breast cancer patients treated with adjuvant systemic therapy with or without postmastectomy irradiation. Semin Radiat Oncol. 1999; 9:292–9.
- B. Gerber, M. Freund, T. Reimer. Recurrent breast cancer: treatment strategies for maintaining and prolonging good quality of life. Deutsches Arzteblatt. 2010;107 (6): 85–91.
- 3. Kuo SH, Huang CS, Kuo WH, Cheng AL, Chang KJ, Chia-Hsien Cheng J. Comprehensive locoregional treatment and systemic therapy for postmastectomy isolated locoregional recurrence. Int J Radiat Oncol Biol Phys. 2008;72(5):1456-64.
- 4. Hanrahan EO, Broglio KR, Buzdar AU, Theriault RL, Valero V, Cristofanilli M, et al. Combined-modality treatment for isolated recurrences of breast carcinoma: update on 30 years of experience at the University of Texas M.D. Anderson Cancer Center and assessment of prognostic factors. Cancer. 2005;104(6):1158-71.
- Azrif M, Saladina JJ, Nani ML, Shahrunniza AS, Norlia A, Rohaizak M. Isolated late chest wall recurrence after mastectomy for breast cancer. Med J Malaysia. 2011;66(3):255-6.
- Nielsen HM, Overgaard M, Grau C, Jensen AR, Overgaard J. Loco-regional recurrence after mastectomy in high-risk breast cancer-risk and prognosis. An analysis of patients from the DBCG 82 b&c randomization trials. Radiother Oncol. 2006;79(2):147-55.
- 7. Showalter SL, Grover S, Sharma S, Lin L, Czerniecki BJ. Factors influencing surgical and adjuvant therapy in stage I breast cancer: A SEER 18 Database Analysis. Ann Surg Oncol. 2012; Nov 8. [Epub ahead of print]
- 8. Moran MS, Haffty BG. Local-regional breast cancer recurrence: Prognostic groups based on patterns of failure. The Breast Journal. 2002;8:81-7
- Arihiro K,. Oda M, ,Ogawa K., Tominaga K, Kaneko Y, Shimizu T, et al. Discordant HER2 status between primary breast carcinoma and recurrent/metastatic tumors using fluorescence in situ hybridization on cytological samples. Jpn J Clin Oncol. 2013:43:55-62.
- Lindstrom LS,. Karlsson E, Wilking UM., Johansson U,. Hartman J, Lidbrink EK, et al. Clinically used breast cancer ,markers such as estrogen receptor, progesterone receptor, and human epidermal growth fac-

- tor receptor 2 are unstable throughout tumor progression. JCO 2012; 30:2601-8.
- 11. Lower EE, Glass EL, Bradley DA, Blau R, Heffelfinger S. Impact of metastatic estrogen receptor and progesterone receptor status on survival. Breast Cancer Res Treat. 2005;90:65–70.
- 12. E. Montagna V, Bagnardi N, Rotmensz G, Viale G, Renne G, Cancello A et al Breast cancer subtypes and outcome after local and regional relapse. Ann Oncol. 2012; 23(2):324-31.
- 13. Taghian A, Jeong JH, Mamounas E, Anderson S, Bryant J, Deutsch M, et al.Patterns of locoregional failure in patients with operable breast cancer treated by mastectomy and adjuvant chemotherapy with or without tamoxifen and without radiotherapy: results from five National Surgical Adjuvant Breast and Bowel Project randomized clinical trials. J Clin Oncol. 2004; 22(21): 4247-54.
- 14. Moran MS, Haffty BG. Local-regional breast cancer recurrence: prognostic groups based on patterns of failure. Breast J. 2002;8:81.15.15. Jameel JK, Rao VS, Cawkwell L, Drew PJ. Radioresistance in carcinoma of the breast.Breast. 2004;13(6):452-60.
- 16. Gonzalez-Angulo AM, Morales-Vasquez F, Hortobagyi GN. Overview of resistance to systemic therapy in patients with breast cancer. Exp Med Biol. 2007;608: 1-22.

Corresponding author: Domagoj Eljuga, Department of Surgical Oncology, University Hospital for Tumors, University Hospital Center Sestre milosrdnice, Ilica 197, 10 000 Zagreb, Croatia. e-mail: deljuga@gmail.com