

Case Report

Ipsilateral Breast Tumor Recurrence after Previous Lymph Node Transfer for Upper Limb Lymphedema

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Keywords

- Lymphedema
- Triple negative tumor recurrence
- Lymph node transfer

Abstract

Background: Lymphedema is a relatively common secondary effect from breast cancer treatment and could affect the quality of life in breast cancer patients. The management of lymphedema has evolved over the years. Although different surgical techniques are reported, as lymph node transfer from the inguinal area to the axilla and microsurgery, results are variable and controversial. Long term outcomes and complications from the techniques are still awaiting.

Case presentation: We report the case of a patient with a triple negative breast cancer (TNBC) treated with left lumpectomy and axillary lymph node dissection (ALND) who had an ipsilateral breast tumor recurrence (IBTR) ten years after diagnosis. In between, patient developed a lymphedema treated surgically with microvascular anastomosis and a lymph node transfer from the inguinal area.

Conclusions: Due to the multimodal treatment of breast cancer, patients have better survival and in the future it will become more common to have patients with nodes transferred to the axilla for the surgical management of lymphedema who develop ipsilateral tumor recurrences. Management of the axilla of these patients should be individualized balancing the increased risk of lymphedema and the surgical treatment of the ipsilateral recurrence.

ABBREVIATIONS

ALND: Axillary Lymph Node Dissection; ARM: Arm Reverse Mapping; BCS: Breast Conserving Surgery; BMRI: Breast Magnetic Resonance Imaging; CT: Computed Tomography; ER: Estrogen Receptor; FNA: Fine Needle Aspiration; HER2: Human Epidermal Growth Factor Receptor 2; IBTR: Ipsilateral Breast Tumor Recurrence; IDC: Infiltrating Ductal carcinoma; LR: Local Recurrence; MDT: Multidisciplinary Team; PR: Progesterone Receptor, SLNB: Sentiell Lymph Node Biopsy; TNBC: Triple Negative Breast Cancer; US: Ultrasound.

INTRODUCTION

Triple negative breast cancer is a distinct clinical and molecular subtype of breast cancer defined by the lack of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2). Patients who have ER-negative/PR-negative, stage T1a,b, lymph node-negative breast cancer have a higher risk of local recurrence compared with their ER-positive/PR-positive counterparts [1]. The presence of negative ER and PR status elevate the risk of breast cancer-specific mortal-

ity and the risk of relapse in Triple negative Breast Cancer (TNBC) is higher in the first 2-5 years after diagnosis, and late relapses are not common [2,3]. Distant metastases occur within 5 years of diagnosis of TNBC, so do the majority of LRs [4]. Arm lymphedema is a secondary effect of treatment of breast cancer and it is directly related to axillary lymph-node dissection and strongly influenced by the association of external radiotherapy [5,6]. Any axillary surgery increased the risk of lymphedema and incidence varies from 5.6% in patients who undergo sentinel lymph node biopsy (SLNB) to 19.9% in patient who undergo Axillary lymph node dissection (ALND). The relative risk of lymphedema including adjuvant radiotherapy in node regions represents 1.8 [6]. Lymphedema is associated with negative effects for the patients in quality of life, functional and related complications as cellulitis and poor wound healing [7,8]. It can be managed conservative or surgically. Lymphedema conservative management is based on complete descongessive therapy (low-strech bandage, manual lymph grainage, exercises, skin care). But surgical treatments are proposed such as reconstructive techniques (lymphaticovenous or lymphaticovenular anastomosis and lymphaticovenular bypass), liposuction and tissue graft [9]. Multimodal

management of breast cancer has led to an increased survival and we will be facing more patients with lymph node transfer to the axilla who develops an ipsilateral breast tumor recurrence (IBTR). We report the case of a patient diagnosed with left TNBC and treated with lumpectomy and ALND who developed an IBTR 10 years after initial diagnosis. In this patient, late relapse was consistent with the same type of TNBC tumor diagnosed 11 years before. This is an infrequent type of relapse in TNBC.

In the meantime, she underwent a lympho-venous anastomosis and an inguinal lymph node transfer to the left axilla for the treatment of lymphedema developed 6 years after initial surgery.

CASE PRESENTATION

This is a 50 years old woman with a diagnosis in 2004 of left breast cancer. It was an infiltrating Ductal carcinoma (IDC) grade III, T1 N1M0, triple negative breast cancer (TNBC) in the upper inner breast quadrant. She underwent a left breast lumpectomy, SLNB (that did not drained) and ALND in 2004. Pathology report showed an IDC, 18 mm in size, out of axillary lymph nodes, TNBC. She received adjuvant chemotherapy with adrymicine-ciclofosfamide and paclitaxel. Whole breast radiation therapy was also performed.

In 2007, the patient developed a left arm lymphedema that was treated conservatively and in 2013 after no major improvements from the conservative techniques, the patient decided to undergo surgery for the lymphedema. Status of the lymphatic system was assessed by surface scanner nodes (Figure 1). Patient underwent micro vascular venous-lymphatic anastomosis and 2 inguinal lymph node were transferred to the left axilla.

In the follow up after the arm surgery, lymphedema only improved moderately, as reported by the treating physician.

In 2015, three months after clinical follow up, the patient came to the clinic because she felt a lump on the left breast close to the scar from the previous lumpectomy. Physical examination reveals a 1cm mass in upper quadrants of left breast. Mammogram showed Figure (2) an increased density in the upper inner quadrant of the left breast with post surgical changes. Ultrasound (US) (Figure 3) was performed that showed a 10mm round solid nodule adjacent to the previous lumpectomy scar. Breast magnetic resonance imaging (BMRI) (Figure 4) was done to try to assess the size more accurately and it showed a 12x10mm suspicious, irregular lump adjacent to the previous lumpectomy scar with a sub millimeter axillary node with a 2.5 mm cortex on the left axilla. Ultrasound-guided core biopsy of the breast and fine needle aspiration (FNA) of the lymph node was performed. Pathology reported an IDC grade II, TNBC, Ki67 90%. FNA of the axillary node was negative for malignancy with normal lymphocytes. Staging with CT (Computed Tomography) of the thorax and abdomen and a bone scan was performed to rule out metastasis. The patient was presented in the MDT (Multidisciplinary Team) and surgery was recommended as first treatment. Discussion about management of axillary lymph nodes was done and because it was felt that those lymph nodes were the ones transferred and their excision may worsen the lymphedema, a skin sparing mastectomy and immediate breast reconstruction with expanders was performed. Pathologic exam of mastectomy specimen showed a 12mm IDC, TNBC and no ductal carcinoma in



Figure 1 Surface scanner nodes. Active lymphatic channels in the upper left limb.

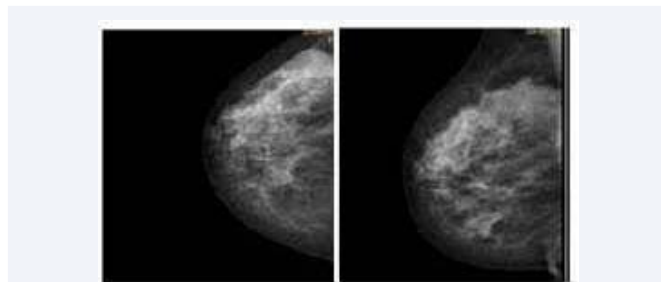


Figure 2 Mammography. Dense breasts heterogeneous type C. Persists focal glandular density on lower quadrant of the right breast, unchanged from previous study. No suspicious micro calcifications are displayed grouped, nodular or signs of malignancy BIRADS 2.



Figure 3 Ultrasound. Round solid nodule morphology and sharp edges 12x10 mm adjacent to scar lumpectomy. There are not pathological axillary lymph nodes BI-RADS 4C.

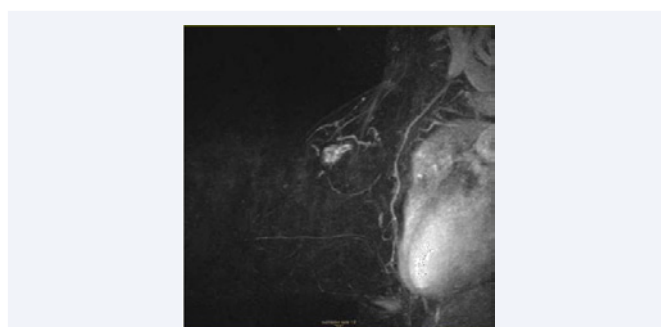


Figure 4 Breast Magnetic Resonance Imaging. Post surgical lumpectomy changes. Tumor recurrence on right breast. Subcentimeter suspicious axillary lymph nodes BIRADS 6.

situ was found. Following surgery, patient underwent adjuvant systemic treatment with myocet-ciclofosfamide and weekly paclitaxel.

A referral to genetic counseling was done, that consider patient's risk of having a hereditary breast and ovarian cancer below the limit to undergo a genetic testing.

DISCUSSION

This case brings up two important issues, first, late relapse in this type of tumor and secondly management of the axilla in patients with lymph nodes transfers for the treatment of lymphedema in breast cancer patients.

TNBC is a clinical and molecular subtype of breast cancer that represents the 12-17% of all breast cancer [10]. Different studies have shown that the risk of relapse in TNBC is higher in the first 2-5 years after diagnosis, and late relapses are more seen in the hormone receptor positive tumors [11]. There has been a controversy on whether TNBC should be managed more radically with surgery, but Studies suggest that the behavior of TNBC is not influenced by the choice of breast conserving surgery (BCS) versus mastectomy, a finding confirmed in three retrospective studies that have directly compared the outcome of mastectomy and BCS in TNBC and found no difference in rates of local recurrence (LR) or survival between procedures [12,13]. It is noteworthy that although rates of LR are increased in TNBC, the 5-year cumulative rate of loco regional recurrence was only 4.2 and 5.4 %, respectively, for patients having BCT and mastectomy in the most recent of these studies [14]. Besides, TNBC have shown to have less frequently nodal metastasis than other subtypes [15]. Because it was a TNBC and the patient was 39 y/o, systemic treatment was administered after the first cancer and whole breast radiation therapy. At that time, genetic counseling was not performed as the indications for it were not so much clear. Patient developed left arm lymphedema 3 years after cancer treatment and was treated conservatively during six years with only minor and temporary improvement. The concern is that the diagnosis of secondary upper limb lymphedema is complicated because of the lack of measurement tool and diagnostic threshold. Some articles demonstrated that bioimpedance spectroscopy has 76-81% of sensibility and 93-96% specificity [16]. There are some surgical treatment of lymphedema, lymph venous anastomosis is the most frequently used with the goal of reducing interstitial volume by improving lymphatic drainage; Boccardo et al., [17] concluded that only 4.05% of 74 patient developed secondary lymphedema after 4-year follow up. Microvascular lymph node grafting is another technique that consists in the transfer of a vascularized lymph node into the affected limb, usually from the inguinal area. This procedure has had some success in improving the severity of lymphedema [18]. Lymph node transfer technique is not out of risk, some complications on donor lymph-node-site territory could appear such as chronic upper lymphedema or pain [19] Furthermore, possible risk of neoplasms in the receiving area have been described by increasing proangiogenic factors, such as angiosarcoma [20]. A micro vascular anastomosis and inguinal lymph node transfer was performed to the patient nine years after breast cancer treatment. Lymphedema improved but did not disappear even after two years. In a systematic review that included 24 studies evaluating outcomes of lymphovenous microsurgery, the majority of patients (90%) reported a subjective improvement in their lymphedema [21]. Other authors have reported complete reduction of their lymphedema [22].

Even though, after two years of lymph node transfer she was still using the compressive sleeve and felt that the arm was less heavy. But objectively, lymphedema was still present. In this case because the patient had an ALND at the time of the first treatment, the two axillary lymph nodes seen were supposed to be the ones that were transferred from the inguinal area. But in case of a patient with SLNB who develops a lymphedema and have an inguinal lymph node transfer to the axilla, it would be more difficult to determine the origin of these axillary lymph nodes. After reviewing the literature, this is the first case reporting an IBTR in a patient who previously had inguinal lymph nodes transferred to the axilla for the treatment of lymphedema caused by an ALND.

We discuss extensively with the patient regarding the management of the axilla. We have reported the use of SLNB in breast cancer recurrence but in this case we thought that doing a SLNB may drain to this lymph nodes and excising them may worsen the lymphedema. And because the US report did not show it was a suspicious node and the FNA was negative we decided only to perform the breast surgery. US guided FNA has been reported to have false negative rate around 9% and the incidence increased in lymph nodes <1.2cm, cortical thickness <3.5mm and <30% involvement [23]. Maybe looking retrospectively another option would be to do a US guided core biopsy of the axillary lymph node. In the last decade, other techniques for reducing lymphedema rates have been reported, as the arm reverse mapping (ARM) [24] but still lymphedema will develop in some patients that may require surgical intervention for it. In conclusion, it is important to be aware of new advances in the surgical treatment for lymphedema and how can these impacts in the management of patients who develop a breast recurrence and the ipsilateral axilla needs to be re-assessed.

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