Inflammatory Breast Cancer in a Very Young Genetically Susceptible Woman: Case Presentation in a Tumour Board Session, Discussion and Decision-Making

Sadaf Alipour* a,b, Leila Bayani c, Akram Seifollahi d

a Department of Surgery, Arash Women’s Hospital, Tehran University of Medical Sciences, Tehran, Iran
b Breast Disease Research Center, Tehran University of Medical Sciences, Tehran, Iran
c Department of Radiology, Arash Women’s Hospital, Tehran University of Medical Sciences, Tehran, Iran
d Department of Pathology, Arash Women’s Hospital, Tehran University of Medical Sciences, Tehran, Iran

ABSTRACT

Background: Inflammatory breast cancer is a very aggressive type of breast cancer which invades skin lymphatics. The standard treatment includes neoadjuvant chemotherapy followed by modified radical mastectomy and postsurgical radiation. Preserving the skin or nipple are not considered reasonable due to the involvement of the dermal lymphatics and therefore skin sparing or nipple-sparing mastectomy are not usually carried out for this type of breast cancer.

Case presentation: In this article, we present a case of inflammatory breast cancer in a very young woman who was positive for BRCA2 genes.

Question: The possibility to perform nipple sparing or skin sparing mastectomy and immediate breast reconstruction, and the indication for prophylactic contralateral mastectomy as discussed in the tumor board are presented in this article.

Conclusion: Neither of the more conservative techniques of mastectomy was appropriate for this case. Also, the prognosis of the patient mostly depends on the course of the ipsilateral tumor and prophylactic mastectomy would be wise only if the subsequent course of the disease is favourable.

Introduction

Inflammatory breast cancer (IBC) is a very poor-prognosis type of breast cancer and the 5-year survival is around 40-50%. The incidence is low, comprising between 1 to 5% of all breast cancers in women. By definition, it is an invasive ductal carcinoma that invades and grows in skin lymphatic channels. IBC is considered T4d in TNM ACR classification of breast cancer regardless of tumor size. Therefore, the lowest stage of an IBC would be stage 3, even without lymph node metastases at the time of diagnosis. Its presentation does not follow the classical breast mass, and it commonly appears as an inflammation over the breast; the diagnosis is thus frequently problematic or delayed because even the ultrasound (US) and mammogram may not show typical signs of malignancy, including a mass. Indeed, an important reason for delay in IBC diagnosis is that it can easily be misdiagnosed as a breast infection. The course of IBC is usually aggressive, and it may progress very rapidly over several weeks or months, leading to the diagnosis of a stage 3 or 4 cancer in the interval between two screening mammographies. A clear association has not been proved between BRCA mutations and IBC, but it has been seen that patients with this type of cancer are younger than their non-IBC counterparts among BRCA positive patients.

The standard treatment of IBC includes neoadjuvant chemotherapy, modified radical mastectomy (MRM), and post-surgical radiation. Other treatments include endocrine therapy and...
targeted therapy, which are individualized based on tumor characteristics.\(^1\) Mastectomy is done as standard MRM, because preserving the skin or nipple is not considered reasonable due to the involvement of the dermal lymphatics.\(^4\) Therefore, an important difference in the treatment of localized IBC or not-IBC tumors is that neoadjuvant chemotherapy and post-mastectomy radiotherapy are performed regardless of tumor size and axillary involvement, and that sentinel lymph node dissection and breast conserving surgeries should not be performed for IBC.

The accepted approach to reconstruction after mastectomy for locally advanced breast cancers and IBC is a delayed one,\(^5\) because of the poor prognosis and concerns about possibility of delays in the main treatments, inadequate margin resection while preserving the skin, and probability of higher recurrence with immediate breast reconstruction (IBR).\(^5,6\) However, surgeries other than MRM and even IBR have been studied for cases of IBC.

We present a case of IBC in a very young woman. She was tested for BRCA genes, and the result was positive. Due to the young age of the patient and her request, other types of surgery including nipple-sparing mastectomy (NSM) or skin-sparing mastectomy (SSM) and the possibility of IBR, as well as the indication for prophylactic contralateral mastectomy were discussed on the tumor board. These debates and a concise literature review are presented in this article. The patient has offered her consent for the publication of her case as a manuscript or any scientific presentation provided that her name is not mentioned.

**Case presentation**

A 29-year-old woman attended the breast clinic with a red swollen left breast. She explained that the changes had occurred in the breast since 3 days before, with no pain. She had undergone biannual breast exam and US in the past two years, and the results showed fibrocystic changes with multiple small simple cysts in large, slightly asymmetric breasts. Her family history was positive; as her mother had been diagnosed with a premenopausal, unilateral invasive breast cancer at the age of 48.

In the present breast exam, the left side was markedly enlarged. The nipple was flat, and the skin over the nipple areola complex (NAC) was very thick and dry. The entire breast was erythematous and edematous without significant tenderness. No distinct mass was detected. Round mobile enlarged lymph nodes were palpated in the left axillary fossa.

Considering a faint possibility of mastitis, broad spectrum antibiotics were begun, but a breast US was performed instantly. The US revealed multiple sites of tissue distortions with severe posterior shadowing in the left breast, multiple foci of microcalcifications, skin thickening and multiple suspicious left axillary lymph nodes. The right breast was unremarkable. (Figure 1) The mammogram showed extremely dense breasts (ACR category d) with cutaneous and subcutaneous edema on the left side, but no distinct mass. (Figure 2) US-guided core needle biopsy of breast lesions and axillary adenopathies were performed.

The histologic exam of the biopsy specimens showed invasive ductal carcinoma, and the axillary node was positive for malignancy. Immunohistochemistry was showed positive for estrogen receptors (ER) and progesterone receptors (PR), HER2 was 2+ with a negative FISH assay, and the Ki67 was 35-40%. Therefore, based on breast exam and microscopic assessment, the diagnosis was an ER +, PR +, HER2 –, IBC of the left breast.

A breast MRI with and without intravenous contrast showed severely diffuse enhancement and abnormal enhancement of the nipple, which were interpreted as involvement of the entire breast with malignancy. (Figure 3) A low suspicious (B4) mass
was reported in the right breast, but microscopic assessment of the US-directed biopsy showed a benign lesion.

Metastasis work up was carried by CT scans of the chest, abdomen and pelvis, and whole body bone scan; no distant metastases were seen. Brain MRI was requested by the oncologist due to the headaches of the patient, and it was normal.

The patient was referred for consultations about fertility preservation and genetic assessment. She decided against at first but genetic testing was performed. She asked for markers to be put in the breast lesions before any other treatment in order to undergo breast conserving surgery later, but it was refused because the inflammatory picture hindered breast preservation.

Neoadjuvant chemotherapy was initiated; she received 8 cycles of docetaxel, epirubicin, and cyclophosphamide. She had a good clinical response, and the breast physical and US exam were normal after the 8 cycles.

The result of the genetic test was received while the patient was under chemotherapy, showing that the patient was positive for BRCA2; this was checked in her mother also, with a positive result.

Questions
Left-sided mastectomy was planned for the patient. However, two major questions arose, which were put to debate on the tumor board of the Cancer Institute, Tehran University of Medical Sciences.

1. The patient desired IBR. Considering the tumor type, were NSM or SSM possible for the patient? Could we recommend immediate reconstruction?
2. Given that the patient was very young and genetically high risk, should we advise contralateral prophylactic mastectomy? In other words, would the patient get benefits from contralateral mastectomy considering her risk of metastasis and cancer-related events?

The two questions were discussed on the tumor board while reviewing the history of the patient and going through all paraclinical results.

Despite the complete clinical response of the tumor, the board decided against SSM or NSM, and MRM with delayed reconstruction was recommended. The decision about contralateral prophylactic mastectomy was left to the patient: she could have it done during the left MRM, or at time of reconstruction; the second option was prioritized by the members. The reason for this recommendation is described in the discussion.

Discussion
Skin sparing mastectomy and nipple sparing mastectomy

SSM is normally carried out for cases of early breast cancer only, because it is postulated to be accompanied by a high rate of recurrence in locally advanced disease. However, reviewing 67 cases of SSM and IBR with autologous tissue, of whom 25 were locally advanced cancers, Foster et al. did not find a significant difference regarding cosmetic results and the rate of recurrence.

NSM is appropriate for tumors that are at least 2 cm far from the NAC, but Ryu et al. have shown it to be safe for tumors closer to the NAC. Factors that increase the rate of post-operative complications in NSM and SSM in addition to large ptotic breasts include smoking, obesity, and breast irradiation. In both SSM and NSM, there is a possibility of leaving breast tissue behind nipple areola complex because of the small incisions used, which makes the procedure more challenging technically. This raises concerns about local recurrence. However, Peled et al. showed that SSM did not affect local recurrence in locally advanced breast cancer, and that the major threat in these patients is the distant recurrence of the disease.

The oncologic safety of SSM and NSM in cases that have undergone neoadjuvant chemotherapy is under debate. Studies have recently been carried out to evaluate this issue and found out that locoregional recurrence and recurrence over the nipple were not significantly higher, and that disease-free and overall survival rates were acceptable.

Immediate breast reconstruction

Nowadays, immediate reconstruction after mastectomy is gaining more attention, because it has been shown to be oncologically safe, and novel techniques are leading to better cosmetic results. However, the higher rate of wound infection in IBR has been shown to cause a higher rate of systemic recurrence in a study by Beecher et al., a result which has been contradicted by Mousa et al. IBR can be performed using autologous tissue or a prosthesis. In the latter case, the implant is ideally covered by acellular dermal matrices to improve the results and lessen the complications. A main weakness of this technique is that if radiation is
needed after surgery, the prosthesis may undergo contraction and deformity. The rate of postoperative complications including infection and the need to removal of the implant also increase with irradiation. Under these circumstances, reconstruction is recommended to be performed in the delayed setting. Also, a tissue expander can be used for breast reconstruction cases, respectively, and radiation could increase the post-operative complications and cause deferral of the irradiation. Considering the poor prognosis of the present tumor, a waiting time of 2 years before proceeding to a contralateral mastectomy seemed reasonable in order to observe the patient for local or distant recurrence. In other words, the prognosis of the patient was mostly expected to depend upon the course of the present cancer, and not on a contralateral cancer. These were explained to the patient, and she decided to delay the contralateral procedure.

On the other hand, there were several reasons for prioritizing delayed reconstruction over the immediate technique. The patient was thin with large breasts, so reconstruction would only be possible by an implant. As radiation was part of the treatment plan, prosthesis reconstruction was not a good choice. The tumor was IBC and very diffuse throughout the breast and over the skin before surgery, and radiation afterwards; the chemotherapy and a longer, more complex operation could increase the post-operative complications and cause deferral of the irradiation. Considering the poor prognosis of the present tumor, a waiting time of 2 years before proceeding to a contralateral mastectomy seemed reasonable in order to observe the patient for local or distant recurrence. In other words, the prognosis of the patient was mostly expected to depend upon the course of the present cancer, and not on a contralateral cancer. These were explained to the patient, and she decided to delay the contralateral procedure.

Patient-oriented discussion

Our patient was genetically positive, a case where prophylactic mastectomy is normally recommended. However, the greatest advantage of this procedure is before cancer diagnosis. This patient was not aware of her genetic susceptibility previously. Her tumor was IBC and she had to undergo chemotherapy before surgery, and radiation afterwards; the chemotherapy and a longer, more complex operation could increase the post-operative complications and cause deferral of the irradiation. Considering the poor prognosis of the present tumor, a waiting time of 2 years before proceeding to a contralateral mastectomy seemed reasonable in order to observe the patient for local or distant recurrence. In other words, the prognosis of the patient was mostly expected to depend upon the course of the present cancer, and not on a contralateral cancer. These were explained to the patient, and she decided to delay the contralateral procedure.

As conclusion, because of the inflammatory nature of the breast cancer, neither NSM nor SSM was appropriate for this patient; and MRM was the best approach as in other cases of IBC. IBC is a poor-prognosis type of breast cancer, and its association with BRCA mutations has not been documented. However, our case was positive for the mutation, and despite this genetic susceptibility, immediate contralateral prophylactic mastectomy was not recommended. The rationale was that the prognosis of the IBC is expected mostly to depend on the course of the present disease. The recommendation was to perform the contralateral procedure only after a 2-years interval for observing the patient for local or distant recurrence.
Acknowledgments
I would like to acknowledge the professors, fellows, and residents of the tumor board of the Cancer Institute of Iran, as well as the patients who confidently attend the tumor board, and generously let us share the data on their disease.

Ethical Consideration
The patient has signed informed consent for the presentation of her documents in this article.

Conflicts of interest
There is no conflict of interest to declare.

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