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

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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 post-surgical 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.[1] 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.[2] 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.[1] 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.[3]

The standard treatment of IBC includes neoadjuvant chemotherapy, modified radical mastectomy (MRM), and post-surgical radiation. Other treatments include endocrine therapy and

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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

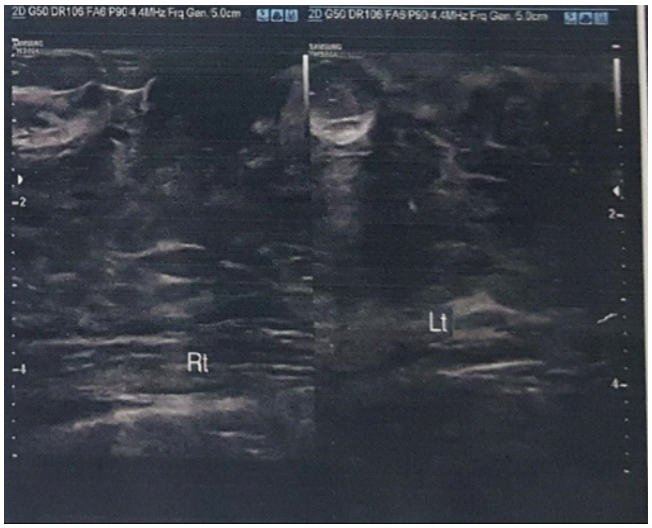

Figure 1. Ultrasound shows multiple sites of tissue distortion in the left breast.

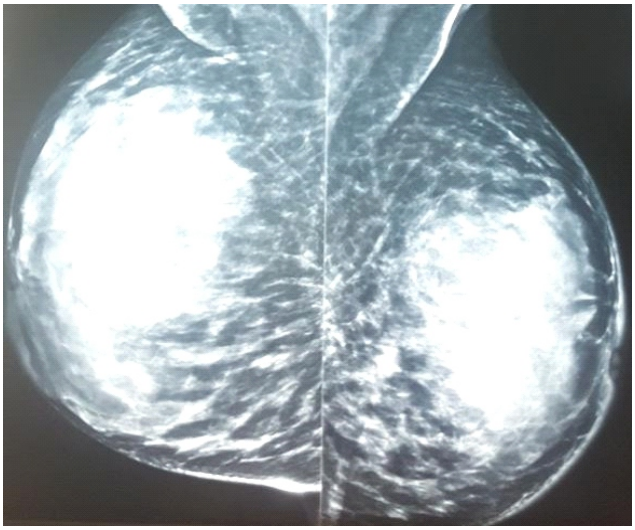

Figure 2. Mammography shows extremely dense breasts with cutaneous and subcutaneous edema in the left side.

was reported in the right breast, but microscopic assessment of the US-directed biopsy showed a benign lesion.

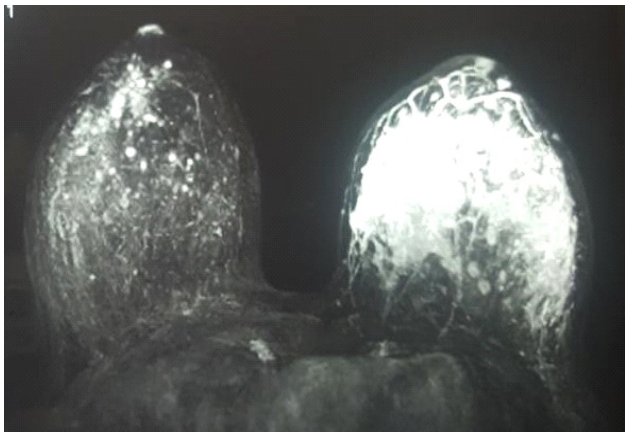

Figure 3. MRI shows severely diffuse enhancement of the left breast and abnormal enhancement of the nipple.

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.[7] 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.[8]

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.[9] 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.[10] 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.[11]

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.[9]

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 .12 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.,[13] a result which has been contradicted by Mousa et al.[14] 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.[15] A main weakness of this technique is that if radiation is

needed after surgery, the prosthesis may undergo contraction and deformity.[16] The rate of postoperative complications including infection and the need to removal of the implant also increase with irradiation.[17,18] Under these circumstances, reconstruction is recommended to be performed in the delayed setting. Also, a tissue expander can be placed and inflated, and get deflated at the time of irradiation.[19]

Interestingly, dissection of the axillary lymph nodes and the number of dissected nodes have been shown to be directly associated with the rate of post-operative complications when IBR is performed using tissue expanders.[20]

One of the major drawbacks of IBR is the delay it may cause in the completion of adjuvant therapies. Henry et al. conducted a study on 76 cases of mastectomy to assess this probability, and showed that adjuvant treatments had been deferred for around 90 days in the 44 breast cancer patients who had undergone IBR compared to the 32 who did not.[21]

Newman et al. assessed IBR in locally advanced breast cancer and showed that completion of IBR did not affect recurrence, although the adjuvant treatments were delayed because of the additional procedure.[22] They recommended against the use of implants and emphasized that autologous reconstruction should be performed in these patients.

Wang et al. assessed the rate of IBR in patients with non-metastatic T4 breast cancer, and detected a low (10%) albeit increasing rate (from around 4% to 18% between 1998 and 2015) of IBR.[23] They did not find any association between IBR or prophylactic contralateral mastectomy and survival. They concluded that IBR could be an oncologically safe procedure in IBC.[23] Patel et al. investigated the effect of IBR on mortality rate among 1472 cases of IBC who had undergone mastectomy.[5] IBR had been performed for 44 patients; these were mostly younger, showed less comorbidities, and had a higher income. Their results did not show any association between IBR and mortality. Nakhlis et al. assessed 240 cases of non-metastatic IBC, of whom 13 and 27 had undergone IBR and delayed breast reconstruction (DBR), respectively.[4] The rate of recurrence, whether locoregional or distant, was more than 92% in the IBR group and 37% in the DBR cases, but the sample size of the IBR patients was too small to be judged for significance. Simpson et al. studied 60 patients with IBC for consequences of breast reconstruction.[6] Here, the reconstructive procedure had not been performed in most of the patients (39 cases), bur 16 had undergone IBR, and DBR had been performed for 5 others. The rate of local complications was much higher in the IBR group (37.5% vs 2.6% and 0% in DBR and no reconstruction cases, respectively), and radiation had begun later. However, the rate of recurrence and mortality did not differ among the groups. Chen et al. reviewed 3374 non-metastatic IBC cases between 1998 and 2013, and found out that the rate of autologous or implant-based breast reconstruction and contralateral prophylactic mastectomy was increasing over the years for these patients.[24] They detected no significant effect of breast reconstruction on the patients' survival. Their data did not show the rate of IBR and DBR, but the authors argued that IBR should be safe in IBC from the point of view of oncologic concerns.

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 surgery 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 chemotherapy, with the proliferation index being high. These considerations, along with the fact that NSM and SSM are not yet totally approved techniques for IBC, lead to a decision against these procedures.

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.

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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.

References

1. Irakleidis F, Tan PH. Inflammatory Breast Cancer; Diagnostic and Therapeutic Challenges. Therapy. 2019; 2:126.
2. Fouad TM, Barrera AMG, Reuben JM, Lucci A, Woodward WA, Stauder MC, et al. Inflammatory breast cancer: a proposed conceptual shift in the UICC–AJCC TNM staging system. The Lancet Oncology. 2017; 18:e228-e32.
3. Gutierrez Barrera AM, Fouad TM, Song J, Webster R, Elsayegh N, Wood AL, et al. BRCA mutations in women with inflammatory breast cancer. Cancer. 2018; 124:466-74.
4. Nakhlis F, Regan MM, Chun YS, Dominici LS, Caterson S, Bellon JR, et al. Patterns of breast reconstruction in patients diagnosed with inflammatory breast cancer: The Dana-Farber Cancer Institute's Inflammatory Breast Cancer Program experience. The Breast Journal. 2020; 26:384-90.
5. Patel SA, Ng M, Nardello SM, Ruth K, Bleicher RJ. Immediate breast reconstruction for women having inflammatory breast cancer in the United States. Cancer medicine. 2018; 7:2887-902.
6. Simpson AB, McCray D, Wengler C, Crowe JP, Djohan R, Tendulkar R, et al. Immediate reconstruction in inflammatory breast cancer: challenging current care. Annals of surgical oncology. 2016; 23:642-8.
7. Medina-Franco H, Vasconez LO, Fix RJ, Heslin MJ, Beenken SW, Bland KI, et al. Factors associated with local recurrence after skin-sparing mastectomy and immediate breast reconstruction for invasive breast cancer. Annals of surgery. 2002; 235:814.
8. Foster RD, Esserman LJ, Anthony JP, Eun-sil SH, Do H. Skin-sparing mastectomy and immediate breast reconstruction: a prospective cohort study for the treatment of advanced stages of breast carcinoma. Annals of Surgical Oncology. 2002; 9:462-6.
9. Ryu JM, Nam SJ, Kim SW, Lee SK, Bae SY, Yi HW, et al. Feasibility of nipple-sparing mastectomy with immediate breast reconstruction in breast cancer patients with tumor-nipple distance less than 2.0 cm. World journal of surgery. 2016; 40:2028-35.
10. Galimberti V, Vicini E, Corso G, Morigi C, Fontana S, Sacchini V, et al. Nipple-sparing and skin-sparing mastectomy: review of aims, oncological safety and contraindications. The Breast. 2017; 34:S82-S4.
11. Peled AW, Wang F, Foster RD, Alvarado M, Ewing CA, Sbitany H, et al. Expanding the indications for total skin-sparing mastectomy: is it safe for patients with locally advanced disease? Annals of surgical oncology. 2016; 23:87-91.
12. Malata C, McIntosh S, Purushotham A. Immediate breast reconstruction after mastectomy for cancer. British journal of surgery. 2000; 87:1455-72.
13. Beecher S, O'Leary D, McLaughlin R, Sweeney K, Kerin M. Influence of complications following immediate breast reconstruction on breast cancer recurrence rates. British Journal of Surgery. 2016; 103:391-8.
14. Mousa M, Barnea Y, Arad U, Inbal A, Klausner J, Menes T. Association between postoperative complications after immediate alloplastic breast reconstruction and oncologic outcome. Clinical breast cancer. 2018; 18:e699-e702.
15. Bertozzi N, Pesce M, Santi P, Raposio E. One-stage immediate breast reconstruction: a concise review. BioMed research international. 2017; 2017.
16. Vandeweyer E, Deraemaecker R. Radiation therapy after immediate breast reconstruction with implants. Plastic and reconstructive surgery. 2000; 106:56-8; discussion 9-60.
17. Jagsi R, Jiang J, Momoh AO, Alderman A, Giordano SH, Buchholz TA, et al. Complications after mastectomy and immediate breast reconstruction for breast cancer: a claims-based analysis. Annals of surgery. 2016; 263:219.
18. Pu Y, Mao T-C, Zhang Y-M, Wang S-l, Fan D-L. The role of postmastectomy radiation therapy in patients with immediate prosthetic breast reconstruction: A meta-analysis. Medicine. 2018; 97.
19. Kronowitz SJ, Hunt KK, Kuerer HM, Babiera G, McNeese MD, Buchholz TA, et al. Delayed-immediate breast reconstruction. Plastic and reconstructive surgery. 2004; 113:1617-28.
20. Verma R, Klein G, Dagum A, Khan S, Bui DT. The Effect of Axillary Lymph Node Sampling during Mastectomy on Immediate Alloplastic Breast Reconstruction Complications. Plastic and Reconstructive Surgery Global Open. 2019; 7.
21. Henry L, Morris L, Downs R, Schwarz R. The impact of immediate breast reconstruction after mastectomy on time to first adjuvant treatment in women with breast cancer in a community setting. The American Journal of Surgery. 2017; 213:534-8.

22. Newman LA, Kuerer HM, Hunt KK, Ames FC, Ross MI, Theriault R, et al. Feasibility of immediate breast reconstruction for locally advanced breast cancer. Annals of surgical oncology. 1999; 6:671-5.
23. Wang M, Chen H, Wu K, Ding A, Zhang P, Zhang M. Post-mastectomy immediate breast reconstruction is oncologically safe in well-selected T4 locally advanced breast cancer: a large population-based study and matched case–control analysis. Breast cancer research and treatment. 2019; 176:337-47.
24. Chen H, Wu K, Wang M, Wang F, Zhang M, Zhang P. A standard mastectomy should not be the only recommended breast surgical treatment for non-metastatic inflammatory breast cancer: A large population-based study in the Surveillance, Epidemiology, and End Results database 18. The Breast. 2017; 35:48-54.