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Case Report

Nipple Skin Sparing Mastectomy and Immediate Reconstruction with implant using Acellular Dermal Matrix (ADM)in a Patient with TP53 mutation - First Experience in Bangladesh

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Abstract:

A 28-year-old lady presented with 3.5 cm lump in her right breast and normal axilla. Histopathologically the lump revealed as invasive duct cell cancer (IDC), Grade II with ER negative, PR positive and HER2 equivocal. On genetic testing, BRCA1 & BRCA2were found negative but p53 was positive with pathogenic variant. She received neoadjuvant chemotherapy while waiting for genetic testing. As she had TP53 mutation and considered high risk for developing contralateral breast cancer, bilateral mastectomy and immediate reconstruction with implant using acellular dermal matrix was performed on 9th of March,2020 at our Breast Unit during 2nd live surgery & workshop on oncoplastic breast surgery, organized by Breast Care Unit and Research Centre, Department of Surgery, Anwer Khan Modern Medical college.

This is the first reported case of a breast cancer patient with TP53 mutation who has undergone nipple skin sparing mastectomy with immediate implant/ADM reconstruction and creates a milestone in the history of modern breast cancer management in Bangladesh.

Keywords: Acellular Dermal Matrix, Nipple Skin Sparing Mastectomy. Immediate Breast Reconstruction. TP53 mutation.

Introduction

Breast cancer is a highly complex, heterogeneous and multifactorial disease and is the leading cause of cancer-related mortality in women worldwide. Family history and genetic mutations are important risk factors for breast cancer. About 5% to 10% of breast cancers are thought to be hereditary. Triple negative breast cancer(TNBC) has a high risk of TP53 mutation (80% in TNBC versus 33% in Other BC)[1]. This has a poor prognosis due to its aggressive clinical behavior and lack of response to hormonal or HER2 receptor-targeted therapy. Mutations in the BRCA1 and BRCA2 genes are the most common genetic mutation in a patient of breast cancer with strong family history. Germline mutations in TP53 are rarer than BRCA1/BRCA2 mutations. Approximately 5-8% of women presenting with breast cancer less than 30 years of age have a germline TP53 gene mutation[2]. The TP53 gene is a crucial tumour suppressor gene which has been called 'the guardian of the genome'. The cellular tumour antigen p53 protein acts as a checkpoint control following DNA damage. It either activates downstream genes to repair the damage or initiates apoptosis.

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Nipple-skin sparing mastectomy (NSSM) followed by immediate breast reconstruction (IBR) with autogenous tissue and/or silicone implants have been proven as effective treatment options for selective breast cancer patients. Standard NSSM removes the entire breast tissue with preservation of the NAC(nipple areolar complex)which is deemed oncologically safe. This also improves the cosmetic outcome of the reconstructed breast[3].

Nipple-sparing mastectomy allows for preservation of the entire nipple-areola complex using various incision patterns. Choice of incision is inframammary fold incision, lateral radial incision, vertical radial incision,wise pattern incisionand periareolarincision etc[4].

Acellular dermal matrices (ADMs)(Fig-1) are biotechnologically human, bovine or porcine derived tissues that have become a cornerstone of implant-based breast reconstruction over the last 2 decades. Tissue processing removes the cellular antigens capable of producing an immunologic response while maintaining the structural matrix that encourages angiogenesis and tissue regeneration. Despite the increasing availability of breast conserving surgery, removal of the breast is performed in up to 40% to 50% of breast cancer patients. Their use in both dual-plane and pre-pectoral approaches have provided greater soft tissue coverage and implant support with good cosmetic outcome and low rate of complication.The ADM-assisted surgical techniques that have advanced the field and broadened implant-based reconstructive options[5]. ADM reconstruction with implants can be done through two approaches-sub-pectoral and pre-pectoral[6].

Case Summary

A 28 year old lady, came with a lump in her right breast associated with mastalgia but no nipple discharge. She has strong family history of breast cancer; as her mother was diagnosed with breast cancer at the age of 40 years. She is a mother of 2 children; age of her last child is 2 years. She has a C cup breast, suspicious 4cm mass at right upper outer quadrant with another vague mass close to nipple areolar complex (NAC). Left breast and both axillae werenormal. No nipple discharge was noted.

Spiculated lesion with partial nipple retraction was seen in right- retro-areolar area (BIRADS- IV) in mammogram. Ultra-sonogram of both breasts showed a hypoechoic focal lesion 3.5 cm in right breast and a right axillary node with slightly increased cortical thickening. Left breast and axilla were normal. Core biopsy from right breast lump showed IDC, grade II with ER negative, PR positive and HER2 equivocal. USG guided FNAC from right axillary node revealed reactive changes only. Staging CT chest, abdomen and pelvis were normal. Results of genetics testing were negative for BRCA1 & BRCA2 but p53 was positive with pathogenic variant.

She received neoadjuvant chemotherapy because she was young with a 3.5 cm cancer which was ER negative and Her2 equivocal. Her2 status could not be reassessed with Fluorescence in situ hybridization due to financial constraint. Neoadjuvant chemo-therapy showed good response and she then underwent surgery. As she had TP53 mutation, thorough counseling was undertaken prior to making the surgical decision. Due to high risk of contralateral breast cancer, decision was taken in favour of bilateral mastectomy and immediate reconstruction with axillary SNB on cancer side. Having considered various options, bilateral nipple skin sparing mastectomy with implant reconstruction using acellular dermal matrix was planned.

Surgical Technique

Nipple skin sparing mastectomy and SNB in right breast for carcinoma with frozen section of under surface of nipple and left sided risk-reducing nipple skin sparing mastectomy and immediate breast reconstruction with ADM and implant has been done on 9th of March, 2020. Skin was marked. (Fig-2). Patent V blue dye injected deep to right subareolar region (Fig-3). About seven cm incision was made at UOQ of both breasts (Fig-4). On right side through same incision, axilla was accessed and two blue nodes were identified and sent for frozen section. Nipple sparing mastectomy was carried out identically by dissecting through subcutaneous plane down to chest wall. Specimen weighed around 450 grams on each side (Fig-5). Specimen was sent for histology with orientation. Tissue from undersurface of right NAC was sent for frozen section with orientation. Both the nodes were found reactive and margin of the right under surface of nipple was free from cancer, therefore, no need to excise nipple areola complex. Wound was washed thoroughly with saline and povidone iodine solution. New drapes and gloves were taken. ADM was prepared in room

temperature with saline solution, soaked adequately and 425 gm round implant was warped with ADM (Fig-6) and edges apposed with 3/0 poli-glecaprone sutures. Implants were impregnated with gentamicin solution prior wrapping. Suction drain placed in both mastectomy cavities. Implant/ADM was placed in the cavity (Fig-7) pre-pectorally, and edges of ADM secured to chest wall with interrupted 3/o polyglactin sutures (Fig-8). Three layer closure of wound was done with polyglactin, skin using 4/0 poliglecaprone subcuticular suture (Fig-9). Skin glue applied on top followed by brown tape. A well fitted supporting bra placed immediately after operation (Fig-10). Patient was under antibiotic cover few more days while drain in situ. Drain tube was removed two weeks after surgery. Post-operative outcome was uneventful. She recovered with excellent cosmetic outcome, with minimal comorbidities (e,g. Pain, shoulder joint movement restriction).

Fig.-1: *Acellular Dermal Matrix*

Fig.-2: *Pre-operative Skin marking*

Fig.-3: *Patent V Blue dye for SNB*

Fig.-4: *Incision at upper outer quadrant*

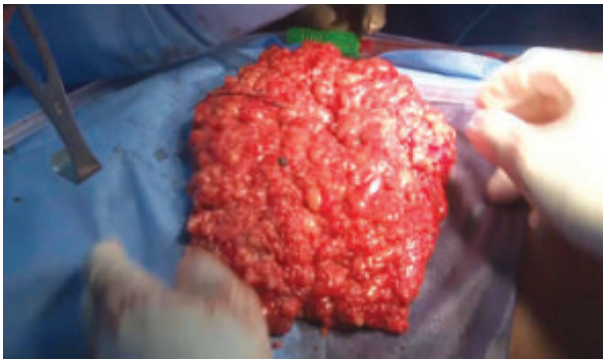

Fig.-5: *Mastectomy specimen weight 450gram*

Fig.-6: *Implant Wrapped with Acellular Dermal Matrix*

Fig.-7: *Acellular Dermal Matrix with Implant introduction into breast*

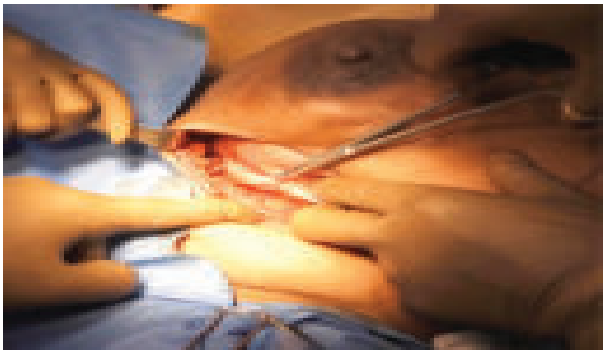

Fig.-8: *Implant wrapped with ADM and edges suture to chest wall*

Fig.-9: *Post-operative*

Fig.-10: *Post-operative support bra.*

Final histopathology report revealed Grade 2 IDC, pT2 (3.5 cm) on right mastectomy specimen, nonspecific reactive change was noted in right axillary sentinel node; right intra mammary lymph node was positive. ER was negative and HER-2++. Benign breast disease was found in left mastectomy specimen. The patient was scheduled as six monthly follow up for one year then annually for 5years.

Discussion

Women who carry germline pathogenic mutations in the TP53 gene have a very high risk of breast cancer of up to 85% by age 60 years[7]. Most of these breast cancers are early onset with a median age at diagnosis is 34years [8]. The syndrome was first observed in 1969 by Li and Fraumeni who described four families of having a very high lifetime risk of malignancy and the commonest cancers are soft tissue sarcomas and breast cancer in women. The TP53 gene is located on chromosome 17p13.1 and encodes the cellular tumour antigen p53. The gene has 11 exons and is 20 kb in genomic length. The majority of pathogenic variants are missense variants. 95% of mutations can be detected by sequence analysis of all exons[9].Only approximately 1% of mutations are deletions or duplications involving the coding region, exon 1 or the promoter. Mastectomy is recommended over lumpectomy in TP53 mutation carriers who have breast cancer so that adjuvant breast radiotherapy can be avoided. Due to high risk of contralateral breast cancer development, risk reducing surgery is recommended[2].

Acellular dermal matrices (ADM) are used across surgical subspecialties for various reasons. In last twenty years, an increase in demand for breast reconstruction is noted. Out of this, significant rise in immediate breast reconstruction (IBR) has been practiced[5]. IBR performed at the time of mastectomy has the advantage of preserving the skin envelope intact, creating a natural looking breast with reduced scarring in comparison with a delayed reconstruction. The removal of cellular components from the connective tissue leaves the water-insoluble matrix, commonly known as the acellular matrix / scaffold / graft. An acellular tissue matrix can be prepared from any organ or tissue based upon the purpose of the research or intended clinical application, including tissues from the digestive system, urinary system, and the dermis of skin[10]. ADM has been used in soft

tissue reconstruction since 1995[11]. These allografts have also been used in prosthesis-based breast reconstruction since 2003[12]. In breast reconstruction, ADM is used mainly for lower pole coverage and the shaping of a new breast. It helps to controlling the position of the implant in the inframammary fold, also mimics the normal ptotic character of soft tissues in the lower pole of the reconstructed breast. This type of implant is more resistant to extrusion, less visible and less palpable. ADM can also minimize periprosthetic fibrosis, less inflammatory response associated with prosthetic devices. Guidelines for care and treatment of breast cancer patients states that women should be informed about the option of breast reconstruction at the time of cancer surgery which facilitate informed decision-making[13].

Pre-pectoral breast reconstruction has gained popularity in recent times as it avoids the surgical morbidity associated with chest wall muscle dissection; eliminating animation deformity and replacing the new breast implant in its normal anatomical plane where the breast tissue was removed[14].

Indication for pre pectoral breast reconstruction are (i)immediate breast reconstruction (ii)Immediate delayed breast reconstruction following neoadjuvant therapy (iii)Delayed breast reconstruction, (iv) Risk-reducing surgery, (v)Breast revision surgery for: a. Animation, b. Capsular contracture, c. Breast deformity, d. Muscular problems associated with submuscular implant reconstruction.

Patient selection criteria is very simple. Pre-pectoral implant reconstruction generally can be considered in anyone who would normally be considered suitable for an implant breast reconstruction.

Patients with a reasonable subcutaneous layer over the breast tissue and options for fat grafting, non- or ex-smokers, well-perfused mastectomy skin flaps, no history of neoadjuvant radiotherapy, patients with an active lifestyle, particularly athletes who require extensive use of their pectoralis muscle, patients who prefer or require preserved shoulder functionality, breasts with grade 1 or 2 ptosis and an estimated weight of less than 500 g, breasts with grade 3 ptosis and anticipated weight more than 500 g can be offered this technique with a dermal sling[6].

Michigan Breast Reconstruction outcome study shows that women who underwent mastectomy without reconstruction reported a loss of perceived femininity, depression, anxiety, and interpersonal, marital, and sexual dysfunction[15]. IBR proved to be oncological safe[16]. Al-Ghazal reported improved overall satisfaction, body image, self-esteem, attractiveness of feeling, and decreased anxiety and depression in IBR patients compared with delayed-reconstruction patients[17].

This 28 year old lady, mother of two who was found to have TP53 mutation with right sided breast cancer, has become the first patient in the history of modern breast cancer management of Bangladesh who has undergone nipple, skin sparing mastectomy with immediate implant/ADM reconstruction. She has made excellent recovery, with minimal comorbidities. Postoperative cosmetic outcome was excellent and patient was very pleased with it. She would be referred to oncologist to continue adjuvant treatment.

The purpose of sharing this experience is to reiterate the fact that high tech reconstructive procedures for breast cancer are perfectly feasible in Bangladesh and should be an option to be discussed during counselling with breast cancer patients or patients with BRCA1 &BRCA2, P53 mutation.

Conclusion

This is the first reported case of bilateral nipple skin sparing mastectomy for breast cancer with TP53 mutation who has gone through immediate reconstruction with acellular dermal matrix (ADM), pre-pectoral approach, never used before in Bangladesh. This is now available in Bangladesh with affordable cost comparing to western world. Breast cancer patients of Bangladesh deserves better as immediate reconstruction has significant positive psychological impact due to better body image and confidence and better quality of life. Immediate breast reconstruction is psychologically beneficial by restoring a female body image.

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