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BRC ASSOCIATED BREAST CANCER: A CASE SERIES AND REVIEW OF LITERATURE

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ABSTRACT Breast cancer is the most common diagnosed cancer in females in developed as well as developing countries including India. There are lot of risk factors associated with development of breast cancer one being genetic mutations. BRCA 1 and BRCA 2 autosomal dominant mutations are most common cause of hereditary breast cancer. It is said that 87% of patients with BRCA mutation are associated with development of breast cancer. The characteristics associated with these cancers are different as compared to sporadic breast cancer. Here we report a series of five cases of BRCA associated breast cancer and review of literature.

KEYWORDS : Breast Cancer, BRCA, Cancer, Genetic mutations

INTRODUCTION

Breast cancer is the most common diagnosed cancer in both developed and developing countries. In India as per Globocan 2020 incidence for breast cancer accounts for 1,78,361 cases(1). There are various risk factors for breast cancer, genetic factor is one of them. Around, 10% are genetic and with 25% being associated with BRCA1 and BRCA2. Hereditary breast ovarian cancer (HBOC) syndrome is autosomal dominant inherited disorder with germline deleterious mutation in BRCA1 or BRCA2(2,3). Mutation in these genes are associated with lifetime risk of 50-85% for developing breast cancer and 13 to 50% for ovarian cancer in women(4). Here we report a series of 5 cases of breast cancer associated with BRCA1 mutation and review of literature.

Case Series

Case 1: A 65 year old female presented with complaints of lump in left breast and biopsy was reported as infiltrating ductal carcinoma (IDC) and immunohistochemistry (IHC) was reported as Triple negative (TN). She had a previous history known case of carcinoma (Ca) ovary for which she was operated and received 6 cycles of taxanes and carboplatin chemotherapy (CT). She underwent modified radical mastectomy (MRM) followed by CT with anthracyclines and taxanes followed by radiation. She was tested for germline BRCA1/2 and was positive for BRCA 1. She is still doing fine and is on follow up.

Case 2 : 50 year old female with a known history of Ca left Breast with MRM done and was reported as IDC Stage 3. She presented with lump in right breast and abdominal distension, computed tomography (CT) scan of chest and abdomen was suggestive of malignant breast mass with bilateral adnexal masses. Biopsy from breast mass was IDC and IHC was TN. She underwent 6 cycles of paclitaxel and carboplatin chemotherapy with significant regression of disease. She underwent Right breast MRM with complete cytoreduction surgery for adnexal masses. Histopathology (HPR) for ovarian mass was reported as serous cystadenocarcinoma. In view of (I/v/o) of such presentation she gBRCA1/2 testing was performed and she was positive for BRCA1. She developed brain metastasis just after surgery and received whole brain radiotherapy (WBRT). She is doing fine 1 year post till now and is on oral maintenance chemotherapy.

Case 3: 35 year old female with no known family history had a lump in right breast and was diagnosed as IDC III and IHC was TN. She underwent breast conservation surgery (BCS) and was reported as IDC III pT3N1M0 and IHC was TN. She underwent adjuvant chemotherapy with Adriamycin cyclophosphamide (AC) followed by taxanes and radiation. She underwent gBRCA1/2 testing i/v/o young age and TN disease and was positive for BRCA1. She is currently doing fine and is on Olaparib maintenance.

Case 4: A 62 year old female with a strong family history of breast cancer, with three first degree relatives diagnosed with breast cancer. She had a previous history of Ca left breast diagnosed 7 years back for which she underwent BCS followed by chemotherapy and radiation. HPR was reported as IDC pT2N0 and IHC was TN. She developed lump in right breast and trucut biopsy was reported as IDC and IHC was TN. Positron emission tomography (PET CT) was suggestive of disease limited to breast and axilla with no evidence of metastasis. She underwent chemotherapy with six cycles of paclitaxel and carboplatin followed by MRM and HPR was IDC pT2N1M0. She was tested for gBRCA1/2 and was positive for BRCA1. Patient is currently maintenance Olaparib and doing fine.

Case 5: 48 year old female presented with lump in right breast since 5 months. She had a previous history of breast cancer at the age of 25 years for which she underwent MRM followed by chemotherapy and radiation. Here recent biopsy was IDC with IHC being TN and was non metastatic. She underwent MRM and HPR was reported as IDC pT2N0. She underwent CT with 6 cycles of paclitaxel and carboplatin. She was gBRCA 1 positive and was counselled for maintenance Olaparib however, due to finances they refused for same. She is currently on follow up.

Table 1: Pathogenic Variant of BRCA1 in Each Case

Serial no	Pathogenic mutation	Variant
1	BRCA1	c.68_69del
2	BRCA1	c.68_69del
3	BRCA1	5566C>T
4	BRCA1	c. 2338C>T
5	BRCA1	c.68_69del

DISCUSSION

Here we report a case series of 5 cases of breast cancer with germline mutation in BRCA1 gene. BRCA 1 and BRCA 2 are the most frequent genetic mutations encountered in breast cancer cases(5). Other than BRCA1 and 2 rest genes encountered are CHEK2, PTEN and P53(6). In a study by Kulkarni et al. the incidence of HBOC was found to be 25.5% with majority being BRCA 1 and BRCA 2 and rest being CHEK2 and TP53 (7). Valarmathi et al. in India reported prevalence of deleterious germline BRCA 1 mutation among breast cancer at 16% which is lower as compared to other studies(8). The most common variant of gBRCA 1 associated in studies is c.68_69del which is reported in two different studies in India(9). In our series three patient had deleterious mutation in c.68_69del gene.

Strong family history is associated with higher chances of germline mutation as evident by our case series. In a study by Singh et al. positive family history significantly increased the possibility of detecting mutation among breast cancer as compared to ovarian cancer(10). There is limitation to our study as it is just a case series, however all the cases are associated with germline mutation in BRCA1 gene and few of

them has strong family history or history of ovarian cancer or history of breast cancer before or at younger age which is supported by past studies.

These study results show that genetic testing is very important irrespective of family history. Also, BRCA positivity has recently been approved as a biomarker to predict sensitivity to platinum drugs as well as PARP inhibitors(11). Thus testing is important not only for prevention or genetic counselling but also for planning further treatment.

CONCLUSION

This current study is a case series with five cases, however it emphasizes the importance of genetic testing and implication associated with it. Hence patient with strong family history or with previous history of breast or ovarian cancer or Triple negative disease at young age should undergo genetic mutation testing.

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