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Case Study

Breast conservation surgery and radiation for a patient with synchronous primary breast cancers and BRCA1/BRCA2 positivity: is mastectomy required?

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Abstract

The role of breast conservation in patients expressing BRCA1 and BRCA2 genetic mutations is controversial. A patient who was found to have bilateral synchronous breast cancers and expressed a BRCA genetic mutation was recently evaluated. The patient had a strong desire for breast preservation. This case and a review of the pertinent literature are presented to discuss the role of breast conservation and radiation in patients with BRCA1 or BRCA2 genetic mutations.

Keywords

BRCA1; BRCA2; Radiation; Mastectomy; Breast Conservation

INTRODUCTION

The management of patients with BRCA1 and BRCA2 genetic anomalies is a complex and rapidly evolving cancer strategy with respect to both local and systemic therapy. Numerous reports compare the clinical and pathological features of BRCA-associated cancers and sporadic cancers. Local therapy has traditionally involved ipsilateral therapeutic mastectomy and contralateral prophylactic mastectomy.[1,2] The physical and emotional body self image distress associated with mastectomy has been well described.[3,4] Most women prefer breast conservation over mastectomy when presented an equivalent outcome of both.[3,4]

Newer research data question the role of mastectomy in this cohort of patients.

For patients who undergo breast-conserving therapy with radiation therapy, the overall survival is equivalent comparing the general population of patients with patients with known BRCA1 or BRCA2 lesions.[5] There is no difference in acute normal tissue reactions however; there is increased risk of contralateral breast tumours.[6,7] Pierce *et al.* evaluated the outcomes of BRCA1 and BRCA2 mutation carriers with breast cancer treated with breast conservation therapy compared with matched sporadic controls with less than a 5% prior probability of having a detectable mutation in either gene.[7]

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The risk of ipsilateral breast tumour recurrence (IBTR) at 10 years was similar in BRCA1 and BRCA2 carriers treated with breast conservation surgery who undergo oophorectomy compared with the sporadic controls. Turner *et al.* have shown that many patients who develop IBTR and whose genetic status was originally unknown are BRCA positive in retrospect.[8] Therefore, it appears that a significant proportion of mutation carriers may have silently participated in breast conservation studies and are included in the currently accepted local control statistics.

CASE HISTORY

A 54 year old G2P2 post-menopausal woman presented with a palpable breast right breast mass 2 years prior to seeking a medical opinion. The primary care physician identified a 1.5 cm lesion of the upper outer quadrant of the right breast. She was then referred for diagnostic mammography which demonstrated a BIRADS (Breast Imaging-Reporting and Data System) Category 5 spiculated lesion in the upper outer quadrant of the right breast measuring 1.9 cm in greatest dimension and corresponding to the area of palpable mass. Additionally a non-palpable spiculated lesion measuring 0.9 cm in greatest dimension was also identified in the upper outer quadrant of the contralateral breast. An magnetic resonance imaging (MRI) was performed which confirmed both suspicious lesions including their size and their solitary bilateral nature. Core biopsies were performed, both of which revealed invasive ductal cancers. A metastatic workup included a computed tomography (CT) scan of the thorax abdomen and pelvis co-registered with a positron emission tomography (PET) scan which demonstrated only mass lesions corresponding with standard uptake value elevation coincident with the mammographically identified breast lesions. Routine complete blood count and differential as well as a complete metabolic panel were normal. Bone scan revealed only degenerative changes. Past medical history was remarkable for well-controlled hypertension and non-insulin dependent diabetes mellitus. Menarche occurred at age 12 and menopause was 5 years prior to diagnosis. The patient had no history of exogenous hormone usage. Family history revealed two sisters with early stage breast cancer diagnosed at age 58 and 61. Because of these risk factors, BRCA testing was performed which demonstrated BRCA1 positivity. BRCA2 was negative. The patient strongly desired breast conservation.

DISCUSSION

MRI and the changing role of imaging

Warner *et al.* have reported on a surveillance study of 236 Canadian women which demonstrated 95% sensitivity in the detection of breast cancers in BRCA1 and BRCA2 carriers when bilateral breast screening MRI complimented screening mammography, ultrasound and clinical self breast exam.[9] All patients with suspicious lesions on any of the three imaging modalities went on to core biopsy. MRI or Mammogram biopsy criteria was a BIRADS 4 or 5 score. Twenty-two breast cancers were detected (16 invasive) when screening patients over a 3-year period. Fourteen percent of women had benign biopsies, although the rate of benign biopsy dropped significantly in 2 and 3 years after MRI stability was established (9.6 and 7.1% respectively). The addition of MRI scanning to the current routine standards of mammography and (when clinically indicated) ultrasound is at least as effective in carriers as in the normal non-mutated population for the detection of occult lesions.

Increased tumour cell radiation sensitivity in BRCA mutation carriers

The high rate of local control with breast-conserving therapy in patients whose tumour is homozygous for a BRCA mutation compared to non-mutated patients may be explained by increased radiosensitivity caused by a defect in DNA repair. Many authors have speculated about hypersensitivity of mutation carrier tumour cells to radiation[10,11] and experimental models have demonstrated such.[12,13] Thus, this high rate of local control in patients whose

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tumour is homozygous for these specific mutations suggests that breast-conserving treatment may be appropriate for patients with BRCA1 and BRCA2 mutations.

The role of breast conservation

In their analysis of 655 patients, Pierce *et al.*[5] found that addition of adjuvant chemotherapy abrogated the nearly five-fold increase in IBTR in patients treated with breast conservation surgery and radiotherapy. Patients who did not receive chemotherapy had 15 and 20 year local recurrences of 43.7 and 53.2% compared to 10.7% for the same time intervals in those patients receiving adjuvant chemotherapy. The adjuvant chemotherapy IBTR rate did not significantly differ from the mastectomy patients. Interestingly, 70% of IBTR were either ''elsewhere'' failures occurring outside of the original tumour region different histology, or both suggesting that these recurrences are really new primary tumours.

Additionally, Kirova *et al.* have compared a cohort of 131 high genetic risk patients (family history of breast and/or ovarian cancers; 20.6% incidence of mutation of BRCA1 or 2) to a cohort of 261 non-mutated control patients. All patients in both cohorts were treated with breast conservation therapy consisting of primary surgery followed by whole breast irradiation. With a median follow up time of 13.4 years, there was no difference in IBTR in mutation carriers; however the contralateral risk was double (40.7% for carriers versus 20% for non-carriers).[6]

Heemskerk-Gerritsen *et al.* reviewed 390 patient records of patients who were BRCA1 positive. Two hundred and fifty two patients in this cohort were treated with breast conservation therapy, while 138 patients received mastectomy. At a median 7.4 year follow up, the breast cancer specific survival rates did not significantly differ between the two groups despite the fact that more women in the mastectomy group also underwent risk-reducing salpingo-oophorectomy than the conservatively treated group (74% versus 46%; $p < 0.001$). The authors concluded that risk-reducing mastectomy did not improve survival.[14] These findings suggest that mastectomy, whether therapeutic or prophylactic, may have no impact on survival in patients who express BRCA mutations.

After careful counselling that this was a controversial therapy and obtaining informed consent, the patient decided upon breast preservation and recently completed her systemic chemotherapy prior to her planned post operative radiotherapy.

CONCLUSION

The local therapy of BRCA1 and BRCA2 positive patients has traditionally been bilateral mastectomy, both therapeutic and prophylactic. Newer data and the improved utility of MRI scanning have questioned the traditional need for such treatment. Consideration should be given for breast preservation in those women who desire it, especially in those patients receiving adjuvant chemotherapy. Appropriate informed consent must be utilised. Women choosing this approach must be willing to undergo more careful breast cancer surveillance with MRI including a lower threshold for stereotactic biopsy of questionable lesions.

Conflict of interest

The authors declared no conflict of interest.

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