A Rare Case of BRCA2-Associated Breast Cancer in Pregnancy

Abstract:
A 30-year old woman was referred to our department with symptomatic breast cancer at 35 weeks gestation. Genetic testing revealed a pathogenic BRCA2 mutation. Labour was induced at 38 weeks. Mastectomy and axillary clearance were performed with adjuvant chemotherapy, radiation and hormonal therapy. Multidisciplinary involvement is crucial for management of BRCA-associated breast cancer, especially in the context of pregnancy. Bilateral mastectomy may be indicated given the increased risk of ipsilateral and contralateral breast cancers. Tamoxifen may lower contralateral breast cancer risk in those in whom risk-reducing surgery is not performed.

Introduction
Breast cancer is the most commonly diagnosed cancer worldwide and the second leading cause of female cancer deaths. BRCA2 deleterious mutation in the BRCA2 gene has been associated with breast cancer rates of 45%. Pregnancy-associated breast cancer (PABC) is defined as breast cancer occurring during pregnancy, lactation or the first postpartum year. PABC is seen in less than 1/3,000 pregnancies, yet accounts for 10-20% of breast cancers in women under 30. Incidence is increasing as more women delay child-bearing. As the majority of PABCs occur in women less than 40, BRCA mutations are more common in this patient group.

Case Report
A 30-year old woman, at 35 weeks gestation, was referred by her General Practitioner to our breast clinic with a palpable lump in the right breast. Her family history was significant in that her 49-year old mother had recently been diagnosed with breast cancer and been found to carry a pathogenic BRCA2 mutation. Clinical examination revealed a palpable lump in the right breast. Protected mammography demonstrated pleomorphic calcifications spanning 3.8cm. Ultrasoundography revealed a 2.8cm area of hypoechogenity corresponding to the area of clinical and mammographic concern (Figure 1). Core biopsy was performed. Analysis of biopsied tissue revealed grade 2 invasive lobular carcinoma (ILC).

Urgent predictive genetic testing was performed due to patient request and she was found to carry the familial BRCA2 deleterious mutation. Following multidisciplinary case discussion, labour was induced at 38 weeks. Delivery was uncomplicated. Following further case review and counselling, the patient underwent upfront sentinel lymph node biopsy which was negative for metastatic disease. She went on to have a right mastectomy with tissue expander reconstruction and axillary clearance. Histopathological analysis of resected tissue revealed grade 3 ILC extending over 13.4cm. Oestrogen receptor positive, human epidermal growth factor receptor 2 negative (Figure 2). Margins were clear. Four of 36 lymph nodes were positive for metastatic disease. Postpartum, the patient was referred to the Human Assisted Reproduction Ireland unit with a view to oocyte freezing prior to initiation of adjuvant chemotherapy.

Further treatment will include: Ipsilateral mastectomy for management of the known breast cancer and bilateral mastectomy with prophylaxis on the contralateral side, given the increased risk of both ipsilateral and contralateral breast cancers. In this case, given that the patient had a family history of breast cancer, prophylactic mastectomy be delayed. In high risk patients in whom prophylactic surgery is deferred, close surveillance with regular clinical breast examinations, annual mammography and breast MRI scans is recommended. However, the risk of contralateral breast cancer in BRCA carriers with a history of breast cancer. Pregnancy during or after a diagnosis of breast cancer does not adversely affect survival in BRCA mutation carriers. This case highlights the difficulties associated with management of BRCA-associated breast cancer, particularly in the setting of pregnancy. Optimal management necessitates multidisciplinary involvement.

Discussion
Patients with PABC should be managed as non-pregnant patients, with some modifications to protect the foetus.4 In this case, as the patient was 35 weeks pregnant at the time of diagnosis, pregnancy could be expedited and treatment initiated postpartum, without risk of adverse maternal or foetal outcome. This case was further complicated by the discovery of a BRCA2 mutation during treatment. Management options for a BRCA2 mutation carrier during breast cancer include: Ipsilateral mastectomy for management of the known breast cancer and bilateral mastectomy with prophylaxis on the contralateral side, given the increased risk of both ipsilateral and contralateral breast cancers. In this case, given that the patient had a family history of breast cancer, prophylactic mastectomy be delayed. In high risk patients in whom prophylactic surgery is deferred, close surveillance with regular clinical breast examinations, annual mammography and breast MRI scans is recommended. However, the risk of contralateral breast cancer in BRCA carriers with a history of breast cancer. Pregnancy during or after a diagnosis of breast cancer does not adversely affect survival in BRCA mutation carriers. This case highlights the difficulties associated with management of BRCA-associated breast cancer, particularly in the setting of pregnancy. Optimal management necessitates multidisciplinary involvement.

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References