Pregnancy-associated breast cancer: Mother’s survival or fetal life?
A Case Series and Review of the Literature.

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Abstract

Breast cancer is the most common cancer diagnosed during pregnancy and has a complex line of management. Delayed first birth is itself a risk factor for breast cancer, hence the incidence is increasing due to trend of women delaying child bearing to later age. Breast cancer can be safely diagnosed, staged, and treated during pregnancy with good outcomes for both mother and fetus. However, some modification needs to be considered according to gestational age and stage of the breast cancer itself. We reported 5 case series of pregnancy-associated breast cancer (PABC) that were managed in our facility.
Introduction

Pregnancy-associated breast cancer (PABC) is uncommon and diagnosed during pregnancy or within 1 year after delivery. It occurs in approximately 1 of every 3000 pregnancies (1). Management needs to consider life of mother as well as the fetus and involvement of other related specialty is crucial. This clinical condition needs to be managed in a centre with medical oncologists, obstetricians, surgeons, and paediatricians because the line of management is very delicate to the mother, as well as the fetus. Survival of mother who has PABC is no difference comparing with non-pregnant patients. This finding reported by Javaid Iqbal et al in their retrospective cohort study. 5-year overall survival was 87.5% for women with no pregnancy, 82.1% for women with pregnancy-associated breast cancer, and 96.7% for women who had pregnancy 6 months or more after diagnosis of breast cancer. The difference in survival between pregnancy groups was not statistically significant (2).

Case A

A 33 years old lady was diagnosed with left breast cancer and noted to be pregnant at 7 weeks. Clinical staging at that time was T3N1. CT staging showed multiple liver metastasis. After termination of pregnancy (TOP) she was started on neoadjuvant chemotherapy with 4 cycles of Adriamycin and cyclophosphamide. After completed chemotherapy, left mastectomy and
Axillary clearance was done. Histopathological examination showed invasive breast cancer, no special type, with pathological staging of ypT2N1a. Her ER/PR status was negative, as well as her HER-2 status. After one month post operation, she developed local recurrent and lung metastasis, hence was started on second line chemotherapy with carboplatin and gemzar.

Case B

A 23 years old primigravida who was diagnosed with right breast cancer a year before she gets pregnant, but defaulted after surgical option was offered to her. Her initial staging was T2N1M0. She was referred back to us by primary care doctor at 15 weeks of gestation and her clinical staging at that time was T3N1. Right mastectomy and axillary clearance was performed at 19 weeks of gestation. Histopathological examination showed invasive carcinoma, no special type with 35% of DCIS component. Pathological staging was pT3N3a with ER negative, PR positive and Her-2 negative. Subsequently she was started on adjuvant chemotherapy with FEC regime. After third cycle of FEC, she had PPROM secondary to UTI at 32 weeks of gestation and delivered a healthy baby prematurely. Another 3 cycles of FEC was resumed after delivery followed by 15 fraction of chest radiotherapy. She is doing well after 2 years completed the treatment without any local recurrent or distant metastasis.
Case C

34 years old pregnant lady who was diagnosed with left breast cancer with clinical staging of T1N0 at 19 weeks of gestation. Wide local excision and axillary clearance was done at 21 weeks of gestation, followed by normal delivery at 38 weeks of gestation. Histopathological examinations showed invasive breast cancer, no special type with ER/PR positive and Her-2 negative. Adjunct therapy post breast conserving surgery was completed. CT surveillance after treatment completion showed showed bone, pleura and liver metastasis, hence given second line chemotherapy.

Case D

38 years old diabetic grandmultipara who was diagnosed with left breast cancer during her 21 weeks of pregnancy. Staging at that time was T3N1M0. She was given 3 cycles of neoadjuvant chemotherapy followed by left mastectomy and axillary clearance. Histopathological examination showed invasive carcinoma with no special type. The ER/PR status was positive and Her-2 negative. At term, she was in labor with macrosomic baby, hence proceeded with EMLSCS & BTL. After delivery, she was given 3 cycles of adjuvant chemotherapy and 12 fractions of radiotherapy. CT thorax, abdomen and pelvis after chemotherapy and radiotherapy completion shows suspicious bone metastasis.
Case E

This 35 years old patient was diagnosed to have left breast cancer during her pregnancy at 23 weeks 4 days. Staging of breast cancer at time of diagnosis was T4N1M0. She has family history of breast cancer. Her paternal aunty was diagnosed with breast cancer at the age of 30 years old. Neoadjuvant chemotherapy were given and then followed by left mastectomy and axillary clearance with left chest wall reconstruction pedicle transverse rectus abdominis myocutaneous (TRAM) flap. Histopathological examination showed invasive ductal carcinoma with negative ER/PR and Her-2 status. Subsequently her chemotherapy was resumed after delivery. However, CT surveillance 2 months post operation showed local recurrence and progressive disease with contralateral breast, liver and bone metastasis. Unfortunately she succumb to death after developed complications from the metastasis.
<table>
<thead>
<tr>
<th>Patients</th>
<th>Age (years)</th>
<th>Parity</th>
<th>Clinical staging at diagnosis</th>
<th>Receptor status</th>
<th>Systemic /surgery</th>
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<tbody>
<tr>
<td>A</td>
<td>33</td>
<td>G3P3 (1 set of twin)</td>
<td>T3N1M0</td>
<td>ER: Negative PR: Negative Her-2: Negative</td>
<td>Systemic</td>
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<tr>
<td>B</td>
<td>23</td>
<td>G1P0</td>
<td>T3N1M0</td>
<td>ER: Negative PR: Positive Her-2: Negative</td>
<td>Surgery</td>
</tr>
<tr>
<td>C</td>
<td>34</td>
<td>G3P2</td>
<td>T2N0M0</td>
<td>ER: Positive PR: Positive Her-2: Negative</td>
<td>Systemic</td>
</tr>
<tr>
<td>D</td>
<td>38</td>
<td>G5P4</td>
<td>T3N1M0</td>
<td>ER: Positive PR: Positive Her-2: Negative</td>
<td>Systemic</td>
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<tr>
<td>E</td>
<td>35</td>
<td>G3P2</td>
<td>T4aN1M0</td>
<td>ER: Negative PR: Negative Her-2: Negative</td>
<td>Systemic</td>
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DISCUSSION

MULTIMODALITY OF TREATMENTS

Breast cancer is optimally treated with multimodality therapy, which may include surgical resection, radiation therapy, and systemic chemotherapy. A similar treatment strategy can be used for breast cancer during pregnancy. However, the timing and type of surgery for breast cancer in pregnancy is a challenging decision. Many studies fail to show a survival benefit with termination of the pregnancy (3). It means that management during first trimester of pregnancy may not necessarily involve termination of pregnancy (TOP) and it is a personal choice to be made on case-to-case basis. However, we need to consider the patient’s further treatment for her breast cancer during the first trimester. Like in our case series, Case A was diagnosed at 7 weeks of gestation and after discussion, patient agreed for termination of pregnancy (TOP), followed by mastectomy and axillary clearance (MAC). Operation may be deferred until 12th weeks of gestation in view of risk of spontaneous abortion during the first trimester, however it will delay the treatment for her. The main reasons to advocate therapeutic abortions are the following: (a) pregnant women requiring systemic treatment during the first trimester of pregnancy, (b) pregnant women with very aggressive primary breast cancer and (c) pregnant women with advanced disease and dismal prognosis (4).
Option of breast conserving surgery (BCS) in first trimester need to be considered wisely in view of the need of adjunct therapy with radiotherapy after operation. Radiation therapy is contraindicated in pregnancy due to its teratogenic effects (5)(4). Radiotherapy can have adverse effects to the fetus such as intrauterine growth restriction, congenital malformations, mental retardation and carcinogenesis. As a general guideline, BCS can be safely administered during third trimester of pregnancy, because radiotherapy can be given after delivery without delay (6). One of our case series, case C underwent BCS at 19 weeks of gestation. We performed left wide local excision and axillary dissection followed by adjuvant chemotherapy before and after delivery then subsequently radiotherapy to the chest wall. Being given chemotherapy during pregnancy at second trimester, she delivered a healthy baby at term.

The use of chemotherapy after first trimester is acceptable as mentioned in multiple guidelines and papers (1)(4)(5)(7)(8). Majority of patients in our case series (case B, C, D and E) received chemotherapy as neoadjuvant treatment during their pregnancy after first trimester. All their babies were delivered safely without any abnormalities. Anthracycline-based regimens are the most widely studied in pregnancy (9). Use of FAC once every 3 weeks as evaluated by Karin et al in a prospective study. They concluded that use of FAC chemotherapy during the second and third trimesters is safe without significant short-term complications (10).
Conclusion

Managing pregnancy-associated breast cancer (PABC) is complex and challenging, involving multiple subspecialties to ensure mothers survival and fetal well-being. Surgery is not contraindicated during pregnancy and options available is similar to non-pregnant patients. Chemotherapy that was used to be completely contraindicated during pregnancy is shown safe to be given during second and third trimester of gestation. Continuous assessment of mother’s progress and fetal well-being is vital throughout the treatment.

REFERENCES


5. Zagouri F, Dimitrakakis C, Marinopoulos S, Tsigginou A DM. Cancer in pregnancy: disentangling treatment modalities. ESMO open. 2016;(May 1;1(3)).


