Breast Cancer Diagnosed during Pregnancy

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Abstract. Cancer is rare during pregnancy, but breast cancer is the second most common cancer in pregnant women. Pregnancy-associated breast cancer (PABC) is defined as breast cancer that occurs during pregnancy or within one year of delivery. Five cases of PABC occurring during the second and third trimester of pregnancy managed at the University Hospital of Vienna during the year 2005/2006 are reported. A review of the available literature is also presented. Five patients were diagnosed with PABC which was detected in completely different weeks of pregnancy. In two women, the diagnosis was made during the second trimester of pregnancy and in three during the third trimester. The treatment depended, among other things, on the gestational age at diagnosis. The patients diagnosed during the second trimester received six courses of neoadjuvant chemotherapy type FEC (5-fluorouracil, epirubicin, cyclophosphamide). Locoregional radiotherapy and surgery were postponed until after delivery. The three patients diagnosed during the third trimester received adequate therapy after delivery. The mean age of the patients at the time of diagnosis was 37 years (range: 33-40 years) and all patients were diagnosed at an advanced stage at presentation. Treatment options seem to be reduced in pregnant women and mainly depend on the patient's condition as well as on the gestational age at presentation. In a multidisciplinary approach, an optimal therapy schedule should be assessed depending on these two conditions.

Breast cancer in pregnancy is rare with an incidence of 1:3,000 to 1:10,000 and is the second most common cancer type after cervical cancer (1, 2). Pregnancy-associated breast cancer (PABC) is defined as breast cancer that occurs during pregnancy or within one year of delivery. Breast cancer diagnosed during pregnancy is often discovered at a late stage but it is not clear whether this pattern relates to diagnostic delay or accelerated growth owing to increased vascularity, hormonal exposure, or suppression of the immune system during pregnancy (3).

The goals of breast cancer treatment, such as local control of the disease and the prevention of systemic metastases, are the same in a pregnant woman as in a non-pregnant woman, but some modifications may be necessary to minimize fetal harm. Breast and chest wall irradiation for example are postponed until after delivery because of the risks of fetal exposure to radiation (4). The need for prompt therapy often presents a clinical dilemma of considerable magnitude as there is always a conflict between optimal maternal therapy and the resultant risks imposed on fetal well-being. As breast cancer diagnosed during pregnancy is more frequently locally advanced at presentation than breast cancer in non-pregnant patients, neoadjuvant or primary systemic chemotherapy may be appropriate during pregnancy (5). Five cases of breast cancer diagnosed during pregnancy and managed at the University Hospital of Vienna between June 2005 and June 2006 are reported. A discussion of the available literature is also presented.

Patients, Methods and Results

The mean age of the patients at the time of diagnosis was 37 years (range: 33-40 years). Breast cancer was detected in completely different weeks of pregnancy. In two women diagnosis was made during the second trimester of pregnancy and in three during the third trimester. The treatment depended, among other things, on the gestational age at the time of diagnosis. Patients diagnosed around the second trimester normally received six courses of neoadjuvant chemotherapy with 5-fluorouracil, epirubicin and cyclophosphamide (FEC) during pregnancy, but locoregional radiotherapy and surgery were usually postponed until after delivery. The patients who were diagnosed during the third trimester received therapy (surgery, chemotherapy, irradiation) after delivery. All five patients presented with an advanced stage at the time of diagnosis.

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Key Words: Pregnancy, breast cancer, risk factors.
diagnosis. The exact histopathology as well as the clinicopathologic parameters of the patients are presented in Tables I and II.

**Patients treated during pregnancy.** The first patient presented with a bilateral breast cancer (T4d, N4a on the right; T3, N4a on the left) at a gestational age of 26 weeks. Both tumors were of low grade. The patient was treated with three courses of neoadjuvant FEC chemotherapy. After cesarean section, she was first treated with three courses of neoadjuvant etoposide (ET) chemotherapy and then had a bilateral mastectomy and lymphonodectomy, followed by adjuvant Taxol and Herceptin chemotherapy and irradiation therapy.

The second patient presented with a left side, low grade breast cancer (T2, N0) at a gestational age of 16 weeks. Six courses of neoadjuvant ET chemotherapy were administered and a lumpectomy with sentinel lymph node dissection (SLND) was performed, where 1 out of 22 lymph nodes was positive. Locoregional radiotherapy and hormonal therapy with Nolvadex were started after surgery.

All patients were alive and free of symptoms and signs at the time of writing.

**Obstetric and neonatal outcome.** All five women had normal single pregnancies with normal fetal development. No congenital malformation, stillbirth or intrauterine growth restrictions were observed in fetuses whose mothers received chemotherapy during pregnancy.

The mode of delivery was mainly cesarean section at 35 to 37 weeks of pregnancy under general anesthesia and tracheal intubation. One patient delivered spontaneously at 38 weeks of gestation.

The APGAR scores (activity, pulse, grimace, appearance, respiration – calculated by the neonatologist 1, 5 and 10 minutes after birth) and cord pH of all infants were in the normal range.

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**Table I. Histopathology and immunohistochemistry of the patients.**

<table>
<thead>
<tr>
<th>Case</th>
<th>Histopathology</th>
<th>Stage</th>
<th>ER</th>
<th>PR</th>
<th>HER2</th>
<th>p53</th>
<th>MIB</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Inflammatory, invasive, lobular</td>
<td>T4b, N4a</td>
<td>neg</td>
<td>pos</td>
<td>pos</td>
<td>neg</td>
<td>50%</td>
</tr>
<tr>
<td>2</td>
<td>Invasive, ductal</td>
<td>T2, N0</td>
<td>neg</td>
<td>neg</td>
<td>neg</td>
<td>pos</td>
<td>80%</td>
</tr>
<tr>
<td>3</td>
<td>Invasive, lobular</td>
<td>T3, N0</td>
<td>pos</td>
<td>pos</td>
<td>neg</td>
<td>neg</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Invasive, ductal</td>
<td>T1c, NOS</td>
<td>neg</td>
<td>neg</td>
<td>neg</td>
<td>pos</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Mucinous</td>
<td>T2, N0</td>
<td>pos</td>
<td>neg</td>
<td>neg</td>
<td>neg</td>
<td></td>
</tr>
</tbody>
</table>

ER: estrogen receptor; PR: progesterone receptor; HER 2: human epidermal growth factor receptor; p53: tumor suppressor; MIB-1: proliferation index; pos: positive; neg: negative.

**Table II. Clinicopathological and obstetric characteristics of the patients with breast cancer.**

<table>
<thead>
<tr>
<th>Case</th>
<th>Maternal age, years</th>
<th>Gestational age at diagnosis, weeks</th>
<th>Therapy during pregnancy</th>
<th>Mode of delivery</th>
<th>Gestational age at delivery</th>
<th>Infant birth weight (g)</th>
<th>APGAR score at 1 minute</th>
<th>APGAR score at 5 minutes</th>
<th>Cord pH &lt; 7.1</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>33</td>
<td>26</td>
<td>yes</td>
<td>C/S spontan.</td>
<td>36</td>
<td>2920</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>40</td>
<td>16</td>
<td>yes</td>
<td>C/S spontan.</td>
<td>38</td>
<td>2940</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>40</td>
<td>22</td>
<td>yes</td>
<td>C/S spontan.</td>
<td>36</td>
<td>2530</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>40</td>
<td>32</td>
<td>no</td>
<td>C/S</td>
<td>35</td>
<td>2380</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>37</td>
<td>34</td>
<td>no</td>
<td>C/S</td>
<td>37</td>
<td>3570</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

spontan.: spontaneous; C/S: cesarean section; APGAR: activity, pulse, grimace, appearance, respiration – calculated by the neonatologist 1, 5 and 10 minutes after birth.

Patients treated only after pregnancy. Case four presented with a left side, T1c, N1a, low grade breast cancer at a gestational age of 32 weeks. A lumpectomy with SLND was performed after delivery and an adjuvant hormonal therapy as well as locoregional radiotherapy was started after surgery.

Case five presented with a left side, T2, N0, low grade breast cancer diagnosed at a gestational age of 34 weeks. Six cycles of neoadjuvant ET chemotherapy were started and lumpectomy and lymph node dissection was performed, where 1 out of 22 lymph nodes was positive. Locoregional radiotherapy and hormonal therapy with Nolvadex were started after surgery.

All patients were alive and free of symptoms and signs at the time of writing.
Discussion

Physiological changes during pregnancy and lactation, due to increased hormone levels, result in an increase in breast volume and firmness. These changes make clinical and radiological detection and evaluation of breast masses difficult (4). It is possible that the increased hormone levels during pregnancy also accelerate the growth of any existing tumors, after transformation from premalignant to malignant breast cells has been triggered (7). PABC has long been regarded as having a poor prognosis, with the earliest reports describing 5-year survival rates of <20%, and the outlook for PABC is less favorable than that for non-pregnant women with breast cancer (8). The poor prognosis was thought to be partly explained by a tendency for pregnant patients to present at a more advanced stage than non-pregnant women, possibly reflecting delay in diagnosis (5, 9). The patients with PABC in this report also presented with advanced stage at the time of diagnosis. Some authors have also proposed that pregnancy itself may be an independent predictor of worse survival (5).

Additionally, the cases in the present report were all at an advanced maternal age at the time of diagnosis, as the mean age of our patients was 37 years.

Chemotherapy has been more widely used in the second and third trimesters, as organogenesis is completed and fetal malformations are therefore unlikely to occur (10). Only one prospective study was found, from the M.D. Anderson Cancer Center, in which 24 women were treated with doxorubicin, cyclophosphamide and 5-fluorouracil for primary or recurrent breast cancer. No detectable congenital anomalies or fetal deaths were observed (11).

Three of our patients received FEC chemotherapy during pregnancy due to early gestational age at the time of diagnosis. Their three infants were healthy and no congenital malformation or intrauterine growth retardations were observed after short term follow-up. Birth weight, APGAR score and cord pH were also in the normal range.

In conclusion, late diagnosis and poor prognosis of PABC is confirmed by our observation in which advanced maternal age at the time of diagnosis was also common. In a multidisciplinary approach, an optimal therapy schedule should be assessed depending on these two conditions.

References


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