E10. Breast cancer during pregnancy

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Introduction

It is well known that an early age at the first full-term pregnancy and high parity reduce the risk of breast cancer. Nevertheless, pregnancy and breast cancer do not usually occur at the same time. However, with the increasing age at the first pregnancy in developed countries as well as the decreasing age at the diagnosis of breast cancer, these two conditions are today observed together more frequently. There is also now evidence that an early full-term pregnancy does not decrease the risk of breast cancer in carriers of *BRCA-1* and *BRCA-2* mutations [1]. Instead, each pregnancy increases the risk by 24%.

The prognosis of breast cancer is not negatively influenced by any subsequent pregnancy. Data by Gelber and colleagues show that a pregnancy after breast cancer might even have a positive effect on the outcome [2].

In the following discussion, we will focus on breast cancer diagnosed during pregnancy. All treatment approaches have to focus on the risk of harm to both mother and foetus and therefore require an interdisciplinary approach involving gynaecologists and obstetricians, oncologists, radiotherapists, surgeons, paediatricians, psychologists and medical care personnel.

Breast cancer during pregnancy

Epidemiology

The incidence of cancer during pregnancy is unclear, but is estimated to be approximately one in a thousand pregnancies. This estimate is derived from historical case series. Unfortunately, the current large databases do not collect this information [Surveillance, Epidemiology and End-Results (SEER)]. However, it is very likely that breast cancer is the most common malignant disease during pregnancy.

In Germany, women are (on average) 29.8 years old when they have their first child– with the trend tending towards over 30 years of age. The incidence of breast cancer during pregnancy will therefore definitely rise in the future.

Pathology

The predominant histology during pregnancy is ductal invasive carcinoma, which has been confirmed by several authors [3,4]. Invasive lobular carcinoma has been diagnosed infrequently in pregnant women as well as in young women who are not pregnant [5]. Different studies have demonstrated that most tumours are high-grade [4,6] and lymphovascular invasion is common [7,8]. In a study by Middleton and colleagues from the MD Anderson Cancer Centre, 79% of the patients presented with lymph node-positive disease. This high percentage of lymph node involvement is comparable with the findings from other studies by King and colleagues (62%) and Holleb and Farrow (72%) [9]. Lymph node metastases to the ipsilateral axilla can be a sign of a late diagnosis or aggressive tumour behaviour. In general, young women tend to have lymph node metastases more often at the time of first diagnosis [10]. Moreover, most tumours are hormone-independent, in the series by Middleton and colleagues only 28% of the tumours were oestrogen receptor (ER)-positive and 24% were progesterone receptor (PR)-positive by immunohistochemistry.

Diagnosis

Clinical examination of the breast is mandatory during the first pregnancy check-up. The delay of diagnosis of breast cancer during pregnancy is approximately 8.2 months vs. 1.9 months in women who are not pregnant. If an abnormality is found, diagnostic procedures such as ultrasound and mammography may be used. With adequate shielding, mammography should not harm the foetus. However, the increased density and size of the breast during pregnancy often obscures the radiological signs of malignant lesions. Liberman and colleagues [11] found a sensitivity of only 78%. In a retrospective analysis by Ahn and colleagues [12] of 22 consecutive patients with breast cancer during pregnancy, a sensitivity of 86.7% was found for mammography, but sonography revealed positive findings in all cases (100%). The value of magnetic resonance imaging (MRI) in the diagnosis of breast cancer during pregnancy and the lactation period has not yet been evaluated. A case report by Talele and colleagues [13] of MRI findings in a lactating breast demonstrated an increased gadolinium uptake probably reflecting the physiologically increased vascular permeability.

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Fine needle aspiration, even though it is often recommended, is very difficult to interpret during pregnancy [14]. Therefore, a core-cut biopsy for histological confirmation should be performed. The risk of a subsequent milk fistula is probably overestimated.

Treatment

Treatment of breast cancer during pregnancy should be as close as possible to standardised protocols for patients without concomitant pregnancies.

Every patient needs an individual therapeutic decision, depending on the gestational week at first presentation, the patient's preference and the stage of the disease (International Expert Panel 09/2003).

Surgery can be safely performed during pregnancy. The convention is to wait until the 12th week has been completed because the risk of a spontaneous abortion is highest before the 12th week of gestation. Breast-conserving surgery including axillary lymph node dissection should be applied where possible. Sentinel lymph node biopsy should be avoided. Usually a radioactive drug technique is used for mapping and is therefore not applicable during pregnancy.

However, radiotherapy should be given after delivery. A dose of 50 Gy will be applied to the breast in case of standard radiotherapy. The foetus will receive a minimum of 2 Gy in the first trimester; however, the dose limit for a foetus is approximately 0.05 Gy [15]. It has been shown that radiotherapy can be delayed up to six months after surgery. In the meantime, adjuvant systemic therapy can be given.

Anthracyclines and cyclophosphamide can be safely applied during pregnancy. The MD Anderson Cancer Centre has evaluated a prospective protocol with 5-fluorouracil, epirubicin, cyclophosphamide (FEC) without significant toxicities to infants [16]. The last cycle of the chemotherapy should be given around the 34th week of gestation. Delivery between day 1 and 14 of the chemotherapy cycle should be avoided. Platelet count should be $\geqslant 80 \times 10^9$ cells/l for delivery.

Hormone treatment (if indicated) should be started after delivery and after completion of chemotherapy.

Conclusions

Breast cancer should be treated during pregnancy according to the general guidelines for treatment of breast cancer. However, individual therapeutic options are possible. To know more about breast cancer during pregnancy a prospective registration study has been started by the German Breast Group (GBG) in cooperation with the Breast International Group (BIG) (www.germanbreastgroup.de/pregnancy).

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