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Original article

Multidisciplinary approach to breast cancer diagnosed during pregnancy: Maternal and neonatal outcomes

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ABSTRACT

Aim: We assessed maternal and neonatal outcome in women diagnosed with breast cancer during pregnancy.
Patients and methods: Retrospective single-centre cohort study of 25 consecutive pregnant women (mean age 36 years) diagnosed and treated for breast cancer between 2000 and 2011. Management was individualized according to type of tumor and time of gestation at diagnosis.
Results: Twelve patients were diagnosed during the second trimester. BI-RADS category <3 mammographic lesions were diagnosed in 7 patients. A suspicious area was detected by ultrasound in 20 of 21 women who underwent ultrasound studies. Nineteen patients had positive hormone receptors and 7 sobreexpressed HER2. One patient was in stage 0, 8 in stage I, 8 in stage II, 3 in stage III and 5 in stage IV. Four patients decided voluntarily to legally terminate their pregnancies, one had a spontaneous miscarriage and in three patients, pregnancy was interrupted at the end of the third trimester before oncological treatment. Eleven patients were treated with chemotherapy during pregnancy after the second trimester using anthracycline-based regimens. In five patients the pregnancy was ended before 34 weeks of gestation. Nine patients had gestation-related complications, including preterm labor, pneumonia, increase in velocity of the middle cerebral artery, oligohydramnios, preeclampsia, extreme prematurity, intrauterine growth restriction, dyspnea, spontaneous miscarriage and chemotherapy-related granulocytopenia. Betamethasone to stimulate fetal lung maturation was used in 6 patients.
Conclusion: Breast cancer women diagnosed during pregnancy presented a high number of complications unrelated to antineoplastic treatment. A multidisciplinary team approach is necessary for satisfactory neonatal results.

Introduction

Breast cancer diagnosed during pregnancy presents a complex set of challenges for the patient and the clinicians, as maternal benefit should be balanced with fetal risk. Cancer diagnosed during pregnancy is a rare occurrence with an estimated frequency of 2.3 cases per 100,000 deliveries.[1] Care for fetal well-being should be added to the algorithm of diagnosis and treatment of breast cancer in the mother. For this reason, assessment of the risk-benefit and a multidisciplinary approach in specialized centers is essential to provide cancer care for the pregnant woman but also to preserve the pregnancy through successful labor and delivery.[2]

The incidence of breast cancer during pregnancy has shown an increasing trend.[1] During the past two decades, the number of women who became pregnant over the age of 35 years rose to more than 35%.[3] Moreover, according to recent data, the overall incidence of breast cancer in our country has shown a decreasing trend except for a steady increase in incidence for women younger than 45 years.[4]

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Two major advances have been a major change in the management of these patients in the XXI century. Firstly, the publication in 1999 of the first clinical data from the M.D. Anderson Cancer Center series confirming the safety of the use of anthracyclines in pregnant breast cancer patients during the second and third trimesters of pregnancy.[5] Secondly, the development of Doppler velocimetry of materno-fetal circulation has proven useful for close monitoring of fetuses with intrauterine growth restriction.[6] However, few studies have assessed the management of patients with breast cancer diagnosed during pregnancy, in particular, in relation to neonatal outcome.[7–10]

We performed a retrospective review of all women with breast cancer diagnosed during pregnancy at our institution. The objective of this study was to assess maternal, antenatal and neonatal outcomes in this population.

Patients and methods

Study design

All consecutive patients diagnosed at our institution of breast cancer during pregnancy between 2000 and 2011 were eligible to participate in a retrospective cohort study. The eligibility criteria for study entry were histological diagnosis of primary or recurrent breast cancer and diagnosis established after publication, in 1999, of a standardized protocol for the management of breast cancer during pregnancy by the group of the University of Texas M.D. Anderson Cancer Center.[5]

The protocol for this single-center study was approved by the Ethics Committee of the Hospital. Because this study was a retrospective descriptive analysis that involved no more than minimal risks for the subjects, the institutional review board granted a waiver of informed consent.

Patients

Data from the breast cancer registry of the Service of Gynecology of Hospital Vall d'Hebron, in Barcelona, Spain, were used to identify study patients. For each case, clinical and radiological variables at the time of diagnosis, treatment received, complications observed, obstetric control studies, fetal monitoring, neonatal outcomes and maternal follow-up are recorded. All patients had been diagnosed and/or treated at our hospital.

Study procedures

Following the diagnosis of breast cancer, laboratory tests, chest X-rays and liver ultrasound examination were performed to determine the extent of the disease. In patients with clinical stages I and IIA, surgical resection was indicated if a conservative approach was feasible; otherwise the possibility to start neoadjuvant chemotherapy was considered. Patients with disseminated disease underwent chemotherapy. In all cases, treatment options were extensively discussed with the patient and her family. Information was provided about the known potential risks and benefits of each modality of treatment. Genetic counseling was offered, with emphasis on the potential effects of chemotherapy on the fetus. The patient was given the option of terminating the pregnancy or continuing it with or without active cancer treatment.

Patients who decided to continue pregnancy and in which primary surgery was indicated, axillary lymph node dissection for axillary staging was performed until 2008. After this time, sentinel node biopsy was performed on a selective basis with preceding ultrasound-guided fine-needle aspiration being undertaken. If the sentinel node was negative or isolated malignant cells were observed,[11] axillary lymph node dissection was not done.

Patients who continued pregnant after the diagnosis of breast cancer and received chemotherapy were followed twice per month by a multidisciplinary team composed by breast-surgery specialists, maternal-fetal specialists and oncologists. One week after each cycle of chemotherapy patient visited the obstetric clinics, where blood pressure and maternal weight were recorded as well as a full obstetric abdominal ultrasound study using 6–4 MHz probes (Siemens Sonoline Antares, Siemens Medical, Germany). Estimated fetal weight, amniotic fluid index and Doppler velocimetry of maternal (uterine arteries) and fetal (umbilical and median cerebral pulsatility index) vessels were evaluated. Intrauterine growth restriction (IUGR) was defined as fetuses with an estimated fetal weight below the 10th percentile and increased impedance on umbilical artery Doppler. Pulsatility index (PI) above the 95th percentile for gestational age according to our population reference values was considered abnormal. The term small for gestational age (SGA) was used for fetuses with an estimated fetal weight below the 10th percentile and normal umbilical artery Doppler.[6] In all cases, estimated fetal birth weight was confirmed as below the 10th percentile after birth. Middle cerebral artery (MCA) peak systolic velocity was also performed for the screening of fetal anemia. Fetal anemia was suspected if V_{max} MCA was above 1.5 MoM for gestational age according to reference values.[12]

Follow-up

Follow-up has been maintained by the database coordinator (O.C.) by reviewing clinical charts and contacting patients by telephone when necessary. For deceased patients, dates and causes of death were obtained from the medical records. Survival was ascertained from the database, which is maintained regularly, with each patient followed up at least once yearly.

Results

Patient characteristics

Between 2000 and 2011, 25 women with breast cancer diagnosed during pregnancy were attended at our institution. The mean age of the patients was 36 years (range 23–48 years). Their baseline characteristics are listed in Table 1. In all patients except one who had a Paget's disease, a lump was detected through breast self-examination. Mammography was performed in 24 patients. Seven patients (29%) were classified into BI-RADS[13] categories 0, 1 or 2, one patient in category 3, four patients in category 4 and eleven patients in category 5. Breast ultrasound examination was performed in 22 patients, with suspicious signs in 21 (95.4%).

In the majority of patients (48%), the diagnosis was made in the second trimester of pregnancy, with a mean gestational age of 21 weeks (range 2–37 weeks). Infiltrating ductal carcinoma was the most common histological type (92%). One case of invasive lobular carcinoma and one case of invasive squamous carcinoma were observed. More than 80% of patients had hormone receptor-positive tumors and one-third overexpressed HER2. Five patients (20%) had metastatic breast cancer (stage IV), with bone metastasis in 2, liver metastasis in 2 and lung metastasis in 1.

Treatment and outcome

Four patients decided to undergo voluntarily interruption of pregnancy (two stage I patients who became pregnant at same time that the cancer was diagnosed, one patient diagnosed at 4 weeks with locally advanced tumor and rapid progression that required