Issues Surrounding Adjuvant Chemotherapy for Breast Cancer During Pregnancy

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Case Study

Mrs. P is a 28-year-old African American woman who detected a nodule during breast self-examination. A mammogram was performed, and the radiologist interpreted the mass to be a cluster calcification. Mrs. P was instructed to return for follow-up in six months. Approximately two months later, she noted a slight increase in the size of the nodule (which measured 2.8 cm) and was sent to have a biopsy, which revealed an invasive ductal carcinoma that was poorly differentiated at stage IIIB. During the two-month interval after the initial mammogram, she became pregnant. At the time of diagnosis, it was determined she was seven weeks pregnant. A modified radical mastectomy and immediate reconstruction was performed when she was 10 weeks pregnant.

Chemotherapy was delayed until the thirteenth week of pregnancy (second trimester) based on an extensive literature search to evaluate the risks of chemotherapy during pregnancy. Mrs. P received four courses of doxorubicin (60 mg/m²) and cyclophosphamide (600 mg/m²). Docetaxel (100 mg/m²) was delayed until after the delivery because of potential teratogenicity.

The nurses who cared for Mrs. P were very anxious regarding treatment with chemotherapy and the impact of the treatment on both Mrs. P and her unborn child. The patient’s care was complicated further by the fact that Mrs. P’s husband was working in a different state (more than 1,000 miles away). Her parents accompanied her to the consultations with the oncologist and to subsequent treatments.

Although multidisciplinary planning is a regular component of patient care, this patient required some additional effort. The nurses devoted two conferences to issues and concerns regarding the treatment of Mrs. P and to anticipate potential problems. These discussions resulted in a focused approach to her care and ultimately helped to decrease some of the anxiety among the nursing staff. The primary areas of concern centered on the safety of the drugs administered during pregnancy, informed consent, psychosocial concerns, fertility, and genetic susceptibility for Mrs. P’s offspring. Mrs. P delivered a healthy baby girl (5 lbs., 11 oz.) by cesarean section because of a breech presentation four weeks prior to the calculated due date.

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Commentaries

Safety of Cytotoxins, Antiemetics, and Epoetin Alfa Administered During Pregnancy

In the years following the thalidomide disaster in the early 1960s (Lenz, 1962), concerns regarding the safety of medications administered to pregnant women have increased. These concerns become magnified when the drug therapy in question involves antineoplastics. Antineoplastics are a class of compounds containing agents known to be carcinogenic, mutagenic, and teratogenic (Yodaiken & Bennett, 1986). These toxicities are a result of the effects on DNA, genetic information, and chromosomes. The gestational age of the fetus or pregnancy trimester when the chemotherapeutic drugs are administered also affect the toxicity level (Weibe & Sipila, 1994). Based on a review of the available literature, a consensus exists among clinicians that administration of medications (including antineoplastics) during the first trimester of pregnancy places the fetus at higher risk for development of fetal anomalies.

The antineoplastics selected for this patient included doxorubicin and cyclophosphamide. The cytotoxic mechanism of action of doxorubicin involves intercalation between DNA base pairs and interference with nucleic acid synthesis. Doxorubicin also has been shown to produce protein-linked DNA double-strand breaks and prevent DNA transcription (Powis, 1987). Cyclophosphamide functions as an alkylating agent to cross-link DNA strands, thus preventing cell division. Single-strand breaks in DNA also occur following exposure to activated cyclophosphamide (Crook, Souhami, & McLean, 1986). Doxorubicin and cyclophosphamide are a well-established regimen for treating women with breast cancer (Fisher et al., 1990). The dose of doxorubicin administered to Mrs. P was 60 mg/m² (94 mg), given as IV bolus injection every three weeks for four doses. The dose of cyclophosphamide administered was 600 mg/m² (942 mg), given as an IV infusion, mixed in 100 ml 0.9% sodium chloride for injection, USP and infused over one hour every three weeks for four doses.

Doxorubicin has been shown to be carcinogenic in animals; however, in humans, it only has been reported to be a “possible carcinogen” (International Agency for Research on Cancer, World Health Organization, 1990). Doxorubicin also has been reported to be a mutagen and a teratogen, as well as toxic to chromosomes. Placental transfer of doxorubicin (or its metabolites) has been documented in several studies; however, a great deal of variability exists among reports. Several published reports are available on doxorubicin administration during all three trimesters, with varying outcomes that range from fetal death to normal, healthy newborns (Briggs, Freeman, & Yaffe, 1994). Administration of doxorubicin during the second and third trimesters does not appear to lead to an increased risk of fetal abnormalities in the offspring (Berry et al., 1999).

Cyclophosphamide is known human carcinogen, mutagen, teratogen, and toxin to