Examination of Pregnancy-Associated Breast Cancer Management in Consideration of Associated Ethical Dilemmas

Amanda Fredericks

Abstract

Pregnancy-associated breast cancer (PABC) is breast cancer that is diagnosed during pregnancy, lactation, or within one year of delivery (Ulery, Carter, McFarlin, & Giuguescu, 2009). While the standard approaches to breast cancer treatment include surgery, chemotherapy and radiation, a concurrent pregnancy poses ethical issues due to the potential teratogenicity (i.e., the capability of producing fetal developmental abnormalities) of treatment options that would benefit the mother. Due to the rarity of the condition, case reports, small retrospective studies and literature reviews about PABC treatment are limited in number within the current literature base, thus making evidence-based treatment recommendations difficult. Contemporary literature suggests that chemotherapy during the first trimester is contraindicated. However, while in-utero exposure to many of the chemotherapeutic agents during the second and third trimesters may increase risk of intrauterine growth retardation and low birth weight, the risk of serious malformation or death of the fetus is not significantly different compared to the risk for the general population of women. PABC treatment requires a strong focus on educating the patient about the risks and benefits of all her options, and providing the appropriate support to make this ethically challenging decision about cancer care and pregnancy. 

Pregnancy-associated breast cancer (PABC) is breast cancer that is diagnosed during pregnancy, lactation, or within one year of delivery (Ulery, Carter, McFarlin, & Giuguescu, 2009). A diagnosis of cancer during pregnancy is very uncommon (Beidler, 2000; Partridge & Schapira, 2005; Pereg, Koren, & Lishner, 2008). Approximately 1 in 3,000 women are diagnosed with breast cancer during pregnancy in the United States (Visco, Meyer, Xi, & Brown, 2009), making PABC rare when compared with the lifetime breast cancer risk of 1 in 8 women among the general population (Goldman & O’Hair, 2009). However, of all pregnancy-associated cancers, breast is one of the most frequently identified primaries (Cardonick, Usmani & Ghaffar, 2009; Payri & Burtens, 2005; Visco et al., 2009). Cancer risk increases with age, and as more women delay childbearing until their 30s or 40s, the incidence of PABC is expected to rise (Goldman & O’Hair, 2009; Pereg et al., 2008). Surgery, chemotherapy and radiation are the standard approaches to breast cancer treatment (Partridge & Schapira, 2005; Visco et al., 2009), however management of PABC with these treatment modalities requires careful consideration of the lives of both mother and fetus.

Dictionary (2002) defines “ethics” as “the science or study of moral values or principles, including ideals of autonomy, beneficence, and justice.” Treatment of PABC poses ethical challenges in upholding these principles in regards to both mother and baby. Chemotherapy is cytotoxic in nature, in that it kills rapidly dividing cells and may result in genetic damage (Partridge & Schapira, 2005; Patni et al., 2007). While the mother may benefit from chemotherapy’s anti-cancer effects, the developing fetus may be at risk for teratogenic (i.e., capable of producing fetal developmental abnormalities) (Mosby’s medical, nursing & allied health dictionary, 2002) effects such as spontaneous abortion, intrauterine growth retardation (IUGR), organ toxicity, premature birth, and low birth weight (Beidler, 2000; Partridge & Schapira, 2005; Visco et al., 2009). Radiation therapy, although an important aspect of maximally effective breast cancer treatment, would expose a fetus to intolerable levels of scatter radiation posing risk of IUGR, congenital malformations, or fetal demise (Beidler, 2000; Goldman & O’Hair, 2009; Partridge & Schapira, 2005; Visco et al., 2009). Even surgical removal of malignant tissue, which is the ultimate goal of breast cancer management, poses potential threats to the health of both mother and baby in the context of PABC. While there is concern about exposing the fetus to anesthesia during surgery, there is also dimin-
ished flexibility in the choice of surgical intervention for the mother, often necessitating the removal of more tissue than if she were not pregnant (Visco et al., 2009). PABC management poses the ethical dilemma of how to prioritize treatment decisions and optimize outcomes for the mother, the baby, or both (Beiderle, 2010).

The existing body of literature about PABC consists mostly of small retrospective studies, case reports, and literature reviews. This is due to small sample sizes, secondary to the rarity of the condition, as well as the lack of feasibility in conducting large prospective studies or randomized clinical trials (Beiderle, 2000; Pereg et al., 2008). This lack of evidence-based knowledge to guide practice forces clinicians to rely on past experience and intuition, making treatment recommendations about this sensitive and ethically charged issue difficult (Partridge & Schapiro, 2005; Ullery et al., 2009; Visco et al., 2009).

Patni et al. (2007) present a dramatic case report that illustrates the significant impacts of “one or baby” decision-making (Beiderle, 2000). The case presented is that of a 40-year-old woman diagnosed at 22-week gestation with metastatic adenocarcinoma of uncertain primary origin (one possibility being the breast). Despite her very poor prognosis, after a long history of infertility she decided to continue her pregnancy without treatment. A caesarean section was planned for 27 weeks gestation, but the baby was delivered at 25 weeks and 3 days due to rapid maternal deterioration, and the mother died 36 hours later. Patni et al. (2007) reviewed her case in the context of Beuchamp and Childress’s “four principles” approach to medical ethics, establishing that respect for autonomy (i.e., ability to make competent decisions based on information provided), beneficence (i.e., promotion of well-being), nonmaleficence (i.e., obligation to avoid harming patients) and justice (i.e., receiving due beneficits or burdens) were upheld in the patient-directed management of her pregnancy and cancer care. This case demonstrates the life-or-death nature of this issue, and that the choices on how to manage pregnancy and cancer care, weighing risks and benefits for both herself and her unborn child, are ultimately up to the patient.

The rarity of PABC poses issues in establishing standardized approaches in its management, thus Cardonick et al. (2009) pooled information regarding diagnosis and treatment of PABC in 128 women nationwide using the Cancer and Pregnancy Registry. Of these patients, 117 were alive at the time of publication, 6 had spontaneous miscarriage, and 99 received chemotheraphy during their second or third trimester. Mean birth weight of the babies exposed to chemotherapy in-utero was significantly lower than those who were not. Of the neonates exposed to chemotherapy, 13 experienced complications at birth or during the newborn period, including sepsis and anemia, gastrointestinal reflex, difficulty feeding, hyperbilirubinemia, transient tachycardia and respiratory distress syndrome.

Using the Cancer and Pregnancy Registry, Cardonick et al. (2009) followed the neonates born to PABC patients for an average of 12.9 months. Mean height and weight of these children were in the 40th and 50th percentile, respectively, but a few experienced long-term issues such as gastrointestinal reflex, eczema, sinusitis, mild sleep delay, mild hearing loss, recurrent otitis media, reactive airway disease, selective IgG deficiency (no treatment required) and corneal abrasion. This other papers acknowledge the need for more stringent long-term follow up of children born to women treated for PABC during pregnancy to gather more information about the long-term effects of in-utero maternal chemotherapy (Visco et al., 2009). Exposure (Cardonick et al., 2009; Logue, 2009). Cardonick et al. (2009) conclude that if the risk to the mother outweighs the benefits of delayed treatment, and termination of pregnancy is not an acceptable option to the patient, chemotherapy may be considered during pregnancy without significantly increasing the risk of malformations above that of the general population.

Pereg et al. (2008) performed a literature review about the diagnosis and treatment of cancer in pregnancy using MEDLINE and Cochrane Controlled Trials Register databases. They reported information about PABC prognosis, tumor characteristics, barriers to standard cancer care, and treatment considerations to reduce risk to mother and baby. The first barrier to effective PABC treatment is delayed diagnosis by an average of five to seven months, because symptoms consistent with breast cancer, including lumps, discharge, swelling and tenderness, are often attributed to the normal breast changes experienced during pregnancy (Partridge & Schapiro, 2005; Pereg et al., 2008; Ullery et al., 2009; Visco et al., 2009). PABC diagnosis may also be delayed due to the high incidence of false negative mammography results in PABC patients, which also translates to a greater risk of metastases and poorer patient outcomes (Ullery et al., 2009). PABC patients exhibit poor histological and prognostic features, with a majority of tumors having estrogen and progesterone receptors (ER, PR) negativity and human epidermal growth factor receptor 2 (HER2) positivity. Young women, pregnant or not, generally present with aggressive disease, and PABC patients are often diagnosed with more advanced disease and are at greater risk for metastases (Pereg et al., 2008).

Pereg et al. (2008) explain that most chemotheraphy agents are able to cross the placenta and reach the fetus. Exposure to these cytotoxic agents during the first trimester, at the height of fetal organogenesis, may increase the risk of miscarriage, fetal death and major malformation. Chemotherapy exposure during the second and third trimesters, however, is not as associated with teratogenic effects, but increases the risk of IUGR and low birth weight. Certain drugs must be avoided during pregnancy, such as Herceptin (used to treat HER2+ cancer) which is associated with anhydramnios, and Methotrexate which has anti-folate activity and is associated with fetal malformation (Visco et al., 2009). Tamoxifen, which is widely used in the treatment of ER+ breast cancers, is a category D drug and is also contraindicated during pregnancy due to its potentially teratogenic effects and associated gynecologic toxicities (Ullery et al., 2009). Labor and delivery pose risk for infection and hemorrhage, which is increased in the context of chemotherapy-induced myelosuppression, so chemotherapy should be suspended at least 3-4 weeks prior to expected or scheduled delivery. Finally, Pereg and colleagues address the ethical controversy surrounding self-murdering that while the mother may derive life-saving benefits from chemotheraphy, the baby could be at risk for malformation or death.

The current approaches to management of PABC include delay of treatment until after normal delivery, protein delivery of the baby, treatment during pregnancy, or termination of the pregnancy (Beiderle, 2000; Cardonick et al., 2009; Logue, 2009; Partridge & Schapiro, 2005). Since radiation therapy is contraindicated during pregnancy, the favored surgical approach to PABC is usually modified radical mastectomy with axillary dissection, with chemotherapy to be administered either before or after surgery if appropriate (Halaska et al., 2009; Partridge & Schapiro, 2005). While some choose to delay receiving potentially teratogenic treatment until after the baby is born, chemotherapy cannot safely be delayed for long periods (Cardonick et al., 2009; Patni et al., 2007). Delaying PABC treatment by just three to six months can raise risk of metastases by 5-10% (Logue, 2009). Thus the ethical dilemma lies in the “maternal-fetal conflict” (Pereg et al., 2008), and the goal of management is to decide how to optimize outcomes for both mother and baby (Pereg et al., 2007). PABC care requires a multidisciplinary care team, including oncology, obstetrics, neonatology, and nursing, and an individually tailored approach depending on the stage of cancer, gestational age of the fetus, and personal and familial preferences of the patient (Pereg et al., 2009; Cardonick et al., 2009; Halaska et al., 2009; Logue, 2009; Partridge & Schapiro, 2005; Patni et al., 2007).

Given the complexity of PABC and the potential for associated psychological distress, nursing roles in education, toxicity management and psychosocial support are particularly important. Nursing care for the PABC patient requires a focus on patient and family education about treatment options, identification of knowledge deficiencies, and referral for support services while the patient and family are making difficult decisions (Goldman & O'Hair, 2009; Logue, 2009). Even prior to a PABC diagnosis, a cancer patient is at risk for PABC and should perform a baseline breast exam at the first prenatal visit. Nurses should educate their patients about the hormone effects of breast cancer, including the risk of breast cancer for women who use hormone therapy. It is possible that the risk of PABC may be lower for women who use estrogen replacement therapy to manage their menopause, as PABC most commonly presents as a painless lump palpated by the patient or clinician (Ullery et al., 2009). During treatment, symptoms that occur during pregnancy and chemotherapy separately, such as nausea and vomiting, may be more severe, thus oral hydration and food intake must be encour...
aged and assessment for dehydration is vital. Hematology and chemistry labs should be monitored regularly, and ultrasound imaging of the fetus may be indicated prior to each cycle of chemotherapy (Logue, 2009).

The lack of evidence-based practice guidelines for this rare patient population poses barriers to providing clinically and ethically sound recommendations. Clinical priorities will vary across disciplines; however, it is not the role of clinicians to impose their opinions during the decision-making process. Instead, the goal is to provide the patient and her family with the information and tools to make choices that support their own on their values and beliefs.

References


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Deadline for Fall 2010 issue: October 31, 2010

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