Discussion

Pregnancy associated breast cancer (PABC) is diagnosed during or after recent pregnancy. It is the most common cancer diagnosed during pregnancy and the postpartum period and is the leading cause of cancer death in women age 15-29 years in the United States (1). PABC occurs in 1 in 3000 to 1 in 10,000 deliveries (2). Despite the recent trend towards reduction in total incidence of breast cancer, the annual incidence in the under 40 age group is not decreasing. Over 246,000 women were diagnosed with breast cancer in 2016 and 11.7% of these were in women between 20 and 44 (3). Interestingly, this age group reflects the dominant child-bearing population.

Women who have their first term pregnancy after 30 years of age have two to three times higher risk of developing breast carcinoma compared to those who have their first pregnancy before 20 years of age (2). As mammographic screenings are generally only done in women ≥40 years, PABC is often detected during clinical examination. However, 70-80% of masses detected during pregnancy are benign (2). It is important to note that examination of the axilla is also necessary, as PABC is more likely to be diagnosed at an advance stage.

Overall, these tend to be larger tumors with high histologic grade and an increased risk of positive lymph nodes and worse survival (4). These are usually negative for estrogen receptor, progesterone receptor and HER2 (2, 4), as was in our case. Given these aggressive pathologic features, it is not surprising that PABC is associated with a poor prognosis, with an increased risk of distant recurrence and death from breast cancer within 5 years (4).

The adverse features of PABC appear to be time dependent, decreasing as the time between last pregnancy and BC diagnosis increases. A recent study performed at our institution, categorized parous women on the basis of the interval between pregnancy and BC diagnosis (0-2, >2-5, >5-10 and >10-15 years) and found that women with a 0-2 year interval were the only group who were more likely than control women to have grade 3 tumors, positive lymph nodes and triple negative tumors (4).

Pregnancy is thought to confer a dual effect on breast cancer, with both a short term increased risk of breast cancer followed by long term protection (1). Pregnancy may stimulate the growth of cells that have undergone the early stages of malignant transformation but in the long term induces the differentiation of normal mammary stem cells that have the potential for neoplastic change (1). It has also been proposed that, in some women, the mammary microenvironment might become tumor promoting after pregnancy as the mammary gland is remodeled to its pre-pregnant state. This pro-inflammatory state is thought to support tumor cell dissemination and may account for the poor prognosis of PABC (1, 5). A number of recent studies have shown that the genomic signatures of PABCs are significantly different that those of age and stage matched non-PABC controls and that complex interactions of the local immune system and the tumor cells in the tumor microenvironment of these carcinomas may influence tumor progression and overall prognosis (6-9).

PABC can be surgically excised with either mastectomy or lumpectomy. If the latter is performed, subsequent breast irradiation can be delayed until after delivery (2). With regards to chemotherapy, the timing of administration greatly impacts the risk of fetal malformation and spontaneous abortion (2). Various chemotherapeutic regimens including FAC (5-fluorouracil, doxorubicin and cyclophosphamide), CMF (cyclophosphamide/methotrexate/5-fluorouracil), and taxane-based regimens have been used (2). The role of immune based therapies against these aggressive tumors that affect young women is currently under investigation.
References:


