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Case Presentation
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Aggressive Metastatic Breast Cancer to the Placenta Causing Placental Abruption

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Abstract

Background: The incidence of breast cancer in young women is increasing and will likely affect more pregnancies as women continue to delay childbirth. Metastasis to the placenta is an uncommon finding in pregnant women, and there is only one reported case causing placental abruption, which involved a cancer of unknown primary. Triple-negative breast cancers tend to be more aggressive overall and have a worse prognosis.

Results: A 35-year-old Hispanic woman was diagnosed at 24 weeks gestation with widely metastatic triple-negative breast cancer to the lungs, liver, peritoneum, lymph nodes, and thoracic spine. Chemotherapy was subsequently started with carboplatin and paclitaxel. She was induced at 36 weeks and had a placental abruption despite lacking significant risk factors. Pathology of the placenta revealed intervillous malignant cells consistent with the placental spread of cancer.

Conclusion: Breast cancer in pregnancy can be difficult to manage regarding therapy options and timing of therapy. Chemotherapy after the first trimester is relatively safe to mother and fetus. However, common agents like trastuzumab and tamoxifen are not recommended due to their teratogenic effects. Pregnancy itself does not increase the risk of mortality in breast cancer; however, diagnosis and treatment are delayed, and pregnant women are more commonly diagnosed with advanced stages of cancer compared to their non-pregnant counterparts. Although placental involvement of cancer is rare, it relays a poor prognosis, and any underlies the importance of placental micro examination in all women with known cancer.

Keywords: Metastasis; Chemotherapy; Breast cancer

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Introduction

One in eight women will be diagnosed with breast cancer. Unfortunately, the incidence of breast cancer in young women aged 24 to 35 is rising [1]. Women who are diagnosed with breast cancer at age 40 or less have a higher mortality rate in Hormone-Receptor (HR) positive breast cancer [2]. Recent data suggests that annual screening in women beginning at age 40 has greater mortality reduction than current mammogram screening recommendations [3]. This new screening recommendation has now been endorsed by the American College of Obstetricians and Gynecologists (ACOG), the American College of Radiologists (ACR), the National Consortium of Breast Centers (NCBC), the National Cancer Center Network (NCCN), and the Society of Breast Imaging (SBI). Since the incidence of breast cancer in young women is increasing, and women are delaying childbearing until later in life, it is likely that breast cancer in pregnancy will become more common in the future [4]. We describe a case of a 35-year-old woman who was diagnosed with aggressive, Triple-Negative Breast Cancer (TNBC) at 24 weeks gestation, which metastasized to her placenta, causing placental abruption.

Case Presentation

A 35-year-old G3P2 Hispanic woman at 22 weeks and six days gestation presented to her obstetrician complaining of pain in her left breast and swelling in her axillary region for the past four days. Her physical examination revealed a large, firm and immobile mass of her left breast at the 1 o'clock region with associated lymphadenopathy of her left axilla along with areolar erythema and dimpling. The mass was confirmed by ultrasound, and a core biopsy revealed grade 3 invasive ductal carcinoma. Immunohistochemical evaluation revealed that the tumor was estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2

(HER2) negative. Further analysis revealed a low tumor mutational burden and 0% programmed death-ligand 1 (PD-L1) expression. Additional immunohistochemical information includes positive cytokeratin (CK) 7. A CT scan of her chest revealed a large breast mass with pulmonary and hepatic metastases, pericardial effusion, ascites, peritoneal implants, a T4 lytic bone lesion, as well as hilar, axillary, and mediastinal adenopathy. An endobronchial biopsy and cytology from her ascites fluid revealed malignant cells positive for CK7 and negative for GATA3, thyroid transcription factor-1 (TTF-1), and ER. Shortly after, she began chemotherapy with carboplatin and paclitaxel. After three cycles of chemotherapy, repeat imaging showed a decrease in the size of her metastases. Chemotherapy was then held for her labor induction at 36 weeks and 0 days gestation. Prior to delivery, she began to have significant vaginal bleeding with worsening tachycardia and was diagnosed with placental abruption. She underwent amniotomy, and the infant was successfully delivered via forceps assisted vaginal delivery. Placental pathology revealed retroplacental hemorrhage consistent with abruption, as well as atypical intervillous cell clusters. These cells had a high mitotic rate and did not stain as trophoblastic. The cells stained positive for CK7 and CK20 and were negative for GATA3, TTF-1, and ER. This was consistent with metastatic breast cancer to the placenta. The patient's health declined, and she elected comfort measures. She died shortly afterward.

Discussion

Cancer during pregnancy is not a rare phenomenon and has a reported incidence of approximately 1 in 1,000 women [5]. The most common cancers reported in pregnancy are breast cancer (incidence of 1 in 3,000), followed by cervical cancer, Hodgkin's lymphoma, and melanoma [6,7]. Treatment of breast cancer in pregnancy can be a complicated decision as many common agents are teratogenic, especially older alkylating agents (e.g., procarbazine, busulfan), antimetabolite drugs (e.g., aminopterin, methotrexate), tamoxifen, and trastuzumab [7,8]. The decision of when to initiate chemotherapy should be a mutual decision between the patient and physician after a thorough explanation of the risks and benefits. Teratogenic effects have been noted primarily in the first trimester, while administration of chemotherapy in the 2nd and 3rd trimester has been shown to have minimal fetal effects [7]. While paclitaxel and carboplatin, the agents used in the above case, do not appear to increase fetal malformations, there have been reports of cytotoxic therapy causing growth restriction, death, prematurity, and myelosuppression [9]. The data is limited to small numbers of case reports.

Pregnancy itself does not appear to lead to increased mortality, although there is an average delay of 5 to 7 months in diagnosing breast cancer in pregnant women which leads to more advanced staging and worse outcomes [10,11]. A 2007 case review revealed that 65% to 90% of pregnant women would present in stage II or stage III disease compared to 45% to 66% for non-pregnant women [12].

Metastasis to the placenta is a rare occurrence. A 2003 case series showed 87 cases of placental and/or fetal metastasis between the years of 1866 and 2003 with the most common cancers being melanoma, breast, lung, leukemia, and lymphoma [13]. Fetal metastasis is even more uncommon, with only 15 of the 87 cases involving the fetal transmission and nearly half of those cases secondary to melanoma. Placental metastasis indicates a poor prognosis for the mother, and fetal metastasis has a poor prognostic factor for the fetus [14]. In most cases placental metastasis is limited to the intervillous space; however, there are cases reporting the villous invasion of cancer, placing the fetus at risk for involvement [15]. There has only been one reported case of abruption from placental metastasis, which was from cancer of unknown primary associated with disseminated intravascular coagulation. [16]. In our case, the patient lacked major risk factors for abruption, including smoking, hypertension, pre-eclampsia, alcohol use, cocaine use, trauma, thrombophilia, or previous thromboembolism [17]. Although a slightly increased risk of abruption exists in women over 35 years old, the abnormal cells at the abruption site suggest aggressive cancer as the cause of abruption.

Conclusion

Ultimately, it is predicted that more women will be affected by malignancy in pregnancy. Although rare, there is a risk for metastatic involvement of the placenta that can affect both mother and fetus. Microscopic examination of the placenta is important in all cases of abruption, especially in the setting of women with known or prior cancer. Chemotherapy remains a suitable and relatively safe option in women after the 1st trimester. Breast complaints during pregnancy are common, but they should be thoroughly evaluated as there is a notable delay in diagnosis of breast cancer in pregnant women.

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