Breast Cancer Arising from a Suspected Fibroadenoma during Pregnancy: A Case Report and Review of Literature

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Abstract

Introduction: Fibroadenomas are the most common benign neoplastic lesion of the breast. These hormone-sensitive tumors can grow rapidly under the influence of pregnancy hormones. Although rare, malignant transformation of these lesions has been reported. The risk of the standard treatment regimen on the fetus makes the PABC (Pregnancy-Associated Breast Cancer) a challenging task for clinicians. Overall treatment is based on guidelines for the general population with some variations to decrease the risk of fetal damage as much as possible.

Case report: A 37-year-old Indian female, G6 P4 A1 presented to OBG during pregnancy should be investigated carefully [8]. Pregnancy-related diagnosis and proper management may lead to the transformation of a cancer) and presents a challenging clinical situation in diagnosis and treatment [7]. Hormonal and physiological changes within the breast tissue may impede the accurate interpretation and analysis of clinical examinations of the breasts. Since even a short delay in the timely diagnosis and proper management may lead to the transformation of a benign fibroadenoma into a breast cancer, any breast mass discovered during pregnancy should be investigated carefully [8]. Pregnancy-associated breast cancer treatment is always a clinical challenge due to the worrisome risk of the standard treatment regimen on the fetus in on hand and danger of suboptimal treatment to the mother in another hand [9]. When PABC is diagnosed, surgery is always the mainstay treatment and based on clinical circumstances either a mastectomy or breast-conserving surgery may be considered. Other treatment modalities like radiotherapy and chemotherapy though less favorable, may be used when indicated and after thorough evaluation and assessment [10].

Case Report

A 37-year-old Indian female, G6 P4 A1 presented to OBG department with a palpable mass in her right breast in the first month of pregnancy. The patient was a known case of uncontrolled diabetes mellitus for six years and asthma for 12 years and currently on insulin and β2 agonist. She had a history of laparotomy six years ago for an unknown abdominal cyst and a salpingectomy of the right fallopian tube four years ago. There was no family history of breast cancer. She experienced menarche at the age of 12 with regular periods since then, she got married at the age of 18, and her first pregnancy was at the age of 19; she had four live birth, and all of the babies were breastfed for at least one year. There was no history of oral contraceptive use. Ultrasonography at the time of admission found a 2.4 cm × 2 cm mass and the soft tissue nodules along the upper outer quadrant of right breast. A preliminary diagnosis of fibroadenoma with cystic changes was made, but despite the strict advice of obstetrician, patient refused to do FNAC (Fine Needle Aspiration Cytology) and further evaluation at the time. The course of pregnancy was uneventful until week 39 of gestation when the patient presented with severe vaginal bleeding as well as a noticeably large mass in her right breast, labor was induced upon diagnosis of intrauterine fetal death, and the patient was referred to the surgery department for further evaluation of her breast mass. According to the patient, the mass has been progressively increasing in size during pregnancy and has been painful in last two months. There was not any history of systemic symptoms. On physical evaluation,
patient's BMI was 25, and vital signs were within normal limits. On local examination of the right breast, there was an immobile, hard huge mass measuring about 16 cm with a lobular surface occupying whole right breast. There was no skin change, ulceration, nipple discharge or axillary lymph node enlargement. Ultrasonography at this time revealed a well-defined lobulated soft tissue mass with multiple cystic areas and internal vascularity; measuring 15.8 cm × 12.7 cm × 5.8 cm, located on the outer half of the right breast which compressed rest of the breast tissue. There was another similar lesion at breast tail measuring 9.7 cm × 5.8 cm. Marked subcutaneous edema underlying the lesion was also noted. The surgeon proposed a tru-cut needle biopsy as the next proper diagnostic procedure, but the patient refused and decided to undergo excisional biopsy under general anesthesia. In the operation theater, whole mass was excised in toto and sent for histopathological evaluation. Figure 1 Microscopic HPE reported the presence of Grade 3 invasive ductal carcinoma with Indefinite lymphatic infiltration. Figure 2. The patient refused any further assessment and treatment and decided to continue the treatment in her home country.

Discussion

During pregnancy, a woman’s breasts undergo several physiological changes. These are hyperplastic changes which occur due to elevated levels of estrogen and progesterone. In particular, under the influence of estrogen, ductal proliferation accelerates which in turn causes a significant growth of vasculature accompanied by increased blood flow and infiltration of mononuclear cells. These changes are believed to provide the proper milieu for neoplastic lesions during pregnancy [10,11]. Fibroadenoma is the most commonly detected neoplastic lesion during pregnancy. It can be a preexisting lesion which increases in size under the effect of pregnancy hormones or may appear de novo; in rare cases, especially in giant fibroadenomas infarction inside the lesion may occur [12]. These benign tumors of the breast, commonly found in young women between the ages of 15 and 35 years, generally present as multiple painless, firm and mobile nodules which can be managed conservatively [2,3]. While fibroadenomas are usually small but rapid growth has been observed in 0.5% to 2% of cases [2,4,13]. Although fibroadenomas are not considered premalignant, rarely breast cancer may arise within these lesions. Occasional cases of malignancy arising from fibroadenomas have been reported in women between the ages of 41 and 44 years [5,14,15]. In the literature, the incidence of malignancy arose from fibroadenoma ranges from 0.02% to 0.1% [16]. The exact frequency of this transformation is nearly impossible to determine as some larger carcinomas may replace a fibroadenoma in the course of malignant growth [15]. However, when such transformation occurs, carcinomas in situ is the most commonly found lesion with the incidence of 70% to 95%; invasive carcinoma which occurs less frequently is reported to be present in 5% to 30% of cases [4,5,16,17]. Although extremely rare, sarcomas such as angiosarcoma, osteosarcoma have also been reported to arise within fibroadenomas [18,19]. There is not much data about the malignant transformation of fibroadenoma during pregnancy, researchers have not been able to propose the exact molecular mechanism which initiates and propagates the progression of malignancy within fibroadenoma, but the rapid growth of fibroadenoma under the effect of pregnancy hormones may play an important role [20,21]. Although comparative studies in determining the natural history of fibroadenomas seem to be equivocal, Kuijper et al. in a clonality study showed that given the right condition fibroadenomas could progress in both epithelial (cancer) and stromal direction (phyllodes tumor) [22]. Higher incidence of CIS (Carcinoma in situ) found in transforming fibroadenoma highlights the importance of appropriate evaluation of such condition because, by early diagnosis and proper management, breast CIS is highly manageable with an excellent prognosis [23]. Breast cancer is the most common malignancy occurring during pregnancy. It may complicate 1 in 3000 pregnancies [1,2,7,24,25]. The tendency of women in delaying the pregnancy is expected to increase the incidence of this problem in future [24,25]. The diagnosis of breast cancer in pregnant women follows the same principles as in non-pregnant cases. It is based on an assessment of clinical examination, imaging, and biopsy. Any breast mass during pregnancy should be viewed as a potential malignancy, and systematic investigation must be done if the mass persists for more than two weeks. There are considerable challenges in the diagnosis and management of breast cancer during pregnancy. Physiological changes in the breast tissue and the risk of radiation exposure to the fetus may hold back the necessary clinical evaluation [7]. Another challenge in
the management of breast cancer during pregnancy arise from the fact that pregnancy associated immunological and hormonal changes may augment the growth of cancerous cells more intensely; hence even a short delay of just 1-2 months in the start of therapy may change the outcome greatly [25,26]. Despite the importance of precise timing, the delay in the diagnosis of pregnancy-associated breast cancer has been reported to be common and is believed to be the cause of presentation of the patients in the more advanced stages of the disease and consequently with a poorer prognosis. These delays do not happen only because of the difficulty in the interpretation of clinical investigations, but sometimes also the unwillingness of the physician to do a biopsy during pregnancy plays a role [27]. Similar to the general population, genetic predisposition may increase the risk of breast cancer in pregnant women as well, it is postulated that in women with a mutation in BRCA2, the protective effect of multiparity on breast cancer has been lost [9,28-30]. Family history as a strong risk factor may increase the possibility of breast cancer in young women by at least two-fold. However, studies fail to show any significant increase in the cancer risk among pregnant women with the family history of breast cancer when compared to women without a family history [31,32]. Similar to the general population the most commonly found subtype of breast cancer during pregnancy is infiltrating ductal carcinoma. However, breast cancers during pregnancy tend to be poorly differentiated high-grade lesions at the time of diagnosis. Additionally, inflammatory breast cancer has been reported to be more frequently seen in pregnant women although the literature is not consistent about it [33-36]. Although well-being of the fetus is a factor in the management of pregnancy-associated breast cancer, it is important to understand that overall treatment is based on guidelines for the general population with some changes to decrease the risk of fetal damage as much as possible. Since any delay in initiation of the treatment may have grave consequences, the clinicians must approach these cases with high vigilance and curative intent [7]. The decision to continue the pregnancy is made based on clinical evaluation and staging of the disease in coordination with patient preference; when such a decision is made, mastectomy remains the treatment of choice. Harmful effects of radiotherapy on fetus make it inadvisable during the first and second trimesters, so breast conserving surgery (a lumpectomy and a partial mastectomy plus radiation therapy) may be considered only in the third trimester [37]. Sentinel node biopsy also utilizes the radiation as part of the procedure so axillary lymph node dissection should be used for surgical staging [25,38]. Teratogenic effects of chemotherapeutic agents are believed to be limited to the period of organogenesis, so the use of this treatment modality is relatively safe after the first trimester [39]. Although hormonal therapy is a promising adjuvant therapy in non-pregnant receptor positive patients, its use during pregnancy is not recommended [25,40]. Despite the previous belief, clinical studies demonstrate that termination of pregnancy would not improve the survival. Hence it is not advised anymore, but if breast cancer is diagnosed in the early stage of gestation, cessation of pregnancy may become a more viable choice considering the risks associated with a delay in standard treatment [39]. In general, the five-year survival rate in PABC is similar to the non-pregnant population; however, two primary risk factors which may affect the survival rate of PABC are a history of recent pregnancy and delay in treatment for 3 to 6 months [41-44].

Conclusion

Breast cancer arising within fibroadenoma during pregnancy is extremely rare but presents unique challenges in evaluation and management. An enlarging breast mass during pregnancy should never be neglected, and thorough investigation including biopsy is strongly advised to establish a definitive diagnosis. It is vital to have a multidisciplinary approach toward diagnosed PABC in which well-being of both mother and fetus is considered carefully. Higher incidence of CIS found in transforming fibroadenoma necessitates the judicious evaluation of such condition because, by early diagnosis and proper management, breast CIS is highly manageable with an excellent prognosis.

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Ethics Approval

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