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Breast carcinoma in pregnancy and lactation: A diagnostic and therapeutic dilemma

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ABSTRACT

Objective: To study the clinical presentation, pathological features, receptors type, and reason for the delay of diagnosis of breast carcinoma during pregnancy and lactation.

Patients and methods: This is retrospective study of patients with pregnancy associated breast carcinoma (PABC), treated at our hospital from 2003 to 2009.

Results: Of the 16 patients, 8 (50%) were pregnant and 8 (50%) were lactating with an average age of 30years (range, 21 to 41years). Four (25%) underwent therapeutic abortions, two (12.5%) cesarean section, one (6.25%) patient had spontaneous abortions and one (6.25%) had no follow up. Fifteen (94%) presented with a breast mass, 37.5% with nipple retraction and 31% presented with inflammatory changes in the breast. Symptoms and signs were overlooked by physicians in 8 (50%) of patients, resulting in delay of referral. In 5 (31.25%) the delay was due to patients' fear of cancer and only 3 (18.75%) there was no delay. The majority of cases were ductal 12 (75%). Only one-third presented with early stage, the rest with advanced stage. Half (50%) were Estrogen receptor and Progesterone receptor (ER, PR) negative, while 6 (37.5%) were positive. Human epidermal growth factor receptors type2 (HER2) positivity was found in 3 (18.75%) while 2 (12.5%) were ER negative but PR positive.

Conclusion: Breast masses during pregnancy and lactation is not always benign. It may be overlooked and all appropriate methods should be used to rule out breast carcinoma.

Keywords: Carcinoma, pregnancy, lactation, breast

Running title: Coexistence of breast cancer and gestation

Introduction

Of all newly diagnosed malignant diseases in Saudi women, breast cancer ranked first accounting for 22.4% in 2004, with the Eastern region having the highest age-standardized rate of 22.6 per 100,000 women among all the regions in the Kingdom of Saudi Arabia.¹

Gestational or pregnancy-associated breast cancer (PABC) is defined as breast cancer that is diagnosed during pregnancy or in the first 12 months postpartum with an incidence of approximately 0.03% of pregnancies.²⁻¹⁰

PABC is the most frequent malignancy that is concurrent with pregnancy and lactation.^{3, 5, 11-14} Most patients present with painless masses, 90% of which are detected by self-examination. Early diagnosis of persisting and enlarging masses, nipple or skin retraction, other skin changes, or axillary lymphadenopathy depends on the inclusion of all available and appropriate diagnostic tools to rule out breast carcinoma since the physiological changes induced by pregnancy and lactation may obscure the physical signs of the cancer, and thus may hinder detection of discrete malignant tumors. In this study, the data of patients with PABC who presented to our hospital were analyzed by looking into demographics, clinical presentation, staging, type of receptors, and reasons for any delay of diagnosis.

Patients and methods

The medical records and pathologic materials of 16 patients with PABC who presented and treated at King Fahd Hospital of the University in the Eastern Region of Saudi Arabia between the years of 2003 and 2009 were reviewed. Data collected included

biographic data, symptoms and signs at presentation, age at diagnosis, histopathology type, receptors status, staging of the cancer, reasons for the delay in diagnosis if found, delivery and fetal outcome. In all patients who underwent therapeutic abortions, this was carried out after recommendation by the surgeon, medical oncologist and gynecologist.

Results

The study group consisted of 16 patients with an average age of 30 years (range: 21-41). The majority of patients presented with a breast mass 15 (93.75%) and nipple retraction 6 (37.5%). Almost one third (31%) had skin thickness and signs of inflammatory breast carcinoma as shown in Table1. When patients were asked why they sought medical advice late and not early referral, 8 (50%) mentioned that their primary physician reassured them that the firmness and nodularity of the breast were due to physiologic changes of pregnancy and lactation and no need for further investigation. Five patients (31.25%) mentioned that the primary physicians informed them that they needed further investigation but they declined the advice because of fear of cancer. Only 3 patients (18.75%) carried out the advice of their physicians and attended breast clinic for further investigation.

Twelve patients (75%) were Saudi and 4 (25%) non-Saudi. The breast cancer was diagnosed during pregnancy in 8 (50%) and during lactation in 8 (50%). Eight patients (50%) had normal spontaneous vaginal delivery (NSVD), 4 (25%) had induced abortion, 2 (12.5%) had caesareans section, 1 (6.25%) had spontaneous abortion and 1(6.25%) had no follow up as shown in Table2. The majority of patients 12 (75%) had invasive ductal carcinoma, 2 (12.5%) had

lobular carcinoma and inflammatory breast carcinoma accounted for 2 (12.5%). The stage at presentation was advanced, either stage III or IV in 10 cases (62.5%). ER and PR were negative in 8 cases (50%), both positive in 6 cases (37.5%) and HER2 was positive in 3 cases (18.75%) while 2 (12.5%) were estrogen receptors negative but progesterone receptors positive as shown in Table 3. Concerning fetal outcome, 9 (56.25%) were alive and well, while 6 (37.5%) were unfortunately dead and one patient had no follow up.

Discussion

Pregnant women are at a high risk of presenting with advanced breast carcinoma than non-pregnant women, since small malignant lumps are difficult to detect because of the natural engorgement and tenderness of the breast during pregnancy and lactation. However, the primary presenting symptoms are no different from those of non-PABC patients and the average age at PABC diagnosis is between 30 and 38 years.^{12, 15-16}

The majority of women with breast carcinoma during pregnancy present with a painless mass or thickening of the skin of the breast, 90% of which are detected by self-examination.¹⁷

In our study, 94% of the patients presented with painless breast mass and 37.5% with nipple retraction. Almost one third of the patients had thickening and inflammations of the skin. The average age was 30 years, an age almost similar to what has been reported in the literature^{12, 15-17} and 17 years younger than Saudi non-pregnant patients with breast cancer¹.

There were no differences in the morphological distribution of female breast carcinoma in Saudi Arabia, in the year 2004

and our study. In the cancer incidence report, Saudi Arabia 2004,¹ indicated that 78.7% of breast carcinoma was invasive ductal carcinoma, almost 5% invasive lobular carcinoma and 62.3% were advanced cancer; stage III or IV. In our study, the results were comparable; 75% were invasive ductal carcinoma, 12.5% invasive lobular carcinoma and 67.5% were advanced cancer; stage III or IV. Therefore, we found the advanced stage of PABC at presentation in our study is not different from that noted in the Kingdom, indicating that merely pregnancy and lactation were not the sole reasons for delay of diagnosis.¹

The incidence of inflammatory breast carcinoma probably lies between 1.5 and 4% even though in one series, the incidence was significantly higher in PABC compared with that seen in non-pregnant controls (26% vs. 9%, $p < 0.01$).^{18,19} In our study, inflammatory breast carcinoma accounted for 12.5% of cases.

The prevalence status of positive estrogen and progesterone receptors is usually similar in pregnant and non-pregnant women with breast cancer. A study using binding methods indicated similar receptor positivity between age-matched patients. However, this prevalence is usually lower in pre-menopausal compared to

post-menopausal breast cancer patients, and in PABC patients this trend is even more pronounced.²⁰⁻²³ In general, our study showed similar findings, estrogen and progesterone receptor negativity was 50%, estrogen and progesterone positivity was 37.5% and HER-2 positivity was 18.5%.

Many studies have reported a delay in the diagnosis of breast cancer during pregnancy and pregnant women are at a higher risk of presenting with more advanced disease than non-pregnant women with an average reported

delay of 5 to 15 months from the onset of symptoms.^{12, 17, 24-27}

In this study, there was a significant delay in diagnosis of cancer in women with PABC ranging from 12 to 30 months and almost double than what has been reported above. Primary physician reassurance and overlooking of the diagnosis accounted for a significant proportion of diagnostic delay 50%, while fear of cancer on the part of patients accounted for the rest.

On examination of the breast of a pregnant or lactating patient, the primary physicians may overlook a dominant mass for the normal physiologic alterations of pregnancy and lactation. As the pregnancy progresses; these changes may become more pronounced, potentially obscuring a malignant mass leading to false reassurance to the patients. A low index of suspicion on the part of primary physicians was responsible for eight cases (50%) of delay even though the patients had consulted their physicians more than one occasion. In addition, the reason for the delay was the dependency on fine needle aspiration cytology, as the only measure to exclude breast malignant diseases.

Ultrasound is the preferred initial study for evaluating a palpable breast mass in pregnant or lactating women to determine whether the breast mass is solid or cystic in nature.²⁸ If the ultrasound of the breast shows a solid mass then a diagnosis may be safely accomplished with an ultrasound guided biopsy under local anesthesia and the pathologist should be advised that the patient is pregnant, so that breast carcinoma can be ruled out.^{29,30} In five patients, 31%, the delay was due to the patients fear of cancer and in the other 18.75%, there was no delay.

Our discussions on management of the patients with PABC involved in addition to the patient and her husband, gynecologist,

obstetricians, surgeons, and oncologist. The dilemma and options of therapy were thoroughly discussed. However, we recommended to induction of labor in patients of twenty-eight weeks gestation to term as obstetric advice indicates that the fetus was viable and delivery was safe. During the 2nd trimester of gestation, the recommendation was simple mastectomy and cyclophosphamide and doxorubicin if indicated. In the case of the first twelve weeks, therapeutic abortion was recommended.

One of our patients declined therapy and had no follow-up, eight had normal spontaneous vaginal delivery, while five had therapeutic abortion and two had cesarean section. The fetal outcome depended on the type of delivery, all fetuses with NSVD and one cesarean section were alive and well, but those with therapeutic abortions were unfortunately dead. This work is limited by being a retrospective study and the small number of patients of a single institution.

In conclusion, our data indicate that a high index of suspicion is very important for evaluation of breast lump during pregnancy and lactation. The only way to reassure patients is by using such appropriate diagnostic tools such as ultrasound guided biopsy for any suspicious solid mass to rule out breast carcinoma.

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Table 1: Clinical Presentation

Presenting symptoms of patients	NO.	%
Mass	15	94
Pain	2	12.5
Inflammation	5	31
Ulcer	1	6
Nipple retraction	6	37.5
Discharge	2	12.5
Skin thickness	5	31
Reason of delay		
Physician	8	50
Patients	5	31
No delay	3	19

Table 2: Demographic characteristics

Characteristics	NO.	%
Age of the patients		
range (21 – 41 years)		
Average age (30years)		
Nationality		
Saudi	12	75
Non-Saudi	4	25
Gestational age at diagnosis		
During pregnancy	8	50
Post partum	8	50
Type of delivery		
NSVD	8	50
Induced abortion	4	25
Spontaneous abortion	1	6.25
Caesareans section	2	12.5
No follow-up	1	6.25
Outcome of pregnancy and lactation		
Alive and well	9	56.25
Dead	6	37.5
No follow-up	1	6.25

Table 3: Characteristics of breast cancer during pregnancy and lactation

Characteristics of the cancer	NO.	%
Type of tumour		
Ductal	12	75.0
Lobular	2	12.5
IBC	2	12.5
Stage at presentation		
I	2	12.5
II	3	18.75
III	6	37.5
IV	4	25.0
X	1	6.25
Receptors status (ER, PR, HER2)		
ER, PR receptors negative	8	50
ER, PR receptors positive	6	37.5
HER2+	3	18.75
ER-PR+	2	12.5
Grade		
1	1	6.25
2	10	62.5
3	5	31.25