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Carcinoma Breast in Pregnancy

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1. Case Report

- A 28 year old woman p1l1A0 complaints of pain and lump in left breast for the past 5 months .Patent feeds her child. No history of discharge, ulceraton, eversion of nipple. No lump in the Axilla. No history any contraceptive pills.
- Fnac: Shows Infltative Ductal Carcinoma Grade 3.

2. Introduction

- Cancer is diagnosed in one in every 1000–2000 pregnancies, with 2500–5000 new cases in Europe each year.
- Approximately 0.2% to 2.6% of all breast cancers occur during pregnancy.

Pregnancy-associated breast cancer (PABC)

Definition

PABC is defined as breast malignancies diagnosed/occurring during gestation or till one year postpartum

PABC is often diagnosed at an advanced stage and its prognosis is inferior compared to non-PABC

1 in incidence per 3, 000 to 10, 000 pregnancy, 3 other studies report from 2.3 to 40 per 100 000 deliveries.

The incidence is lower (0.7% in India) 5 in developing countries as the age of the mother at delivery is younger.

Incidence of PABC has been increasing as evident from large registry study that included four million deliveries over five decades. Overall incidence.

Reasons for increased incidence of PABC

Delaying of childbearing to a later age, increasing incidence of cancer with age, increasing number of premenopausal women diagnosed with breast cancer, Lack of detection and increasing awareness.

Breast Changes in Pregnancy

- Pregnancy induces both proliferation and differentiation of the mammary epithelium.
- Both lobular and alveolar growth occurs.
- Weight and blood supply
- Differentiation of the alveoli into mature milk-producing cells requires the stimulus of cortisol, insulin, and prolactin. Cellular microenvironment leading to breast tumor progression.

Causes of breast lump in pregnancy

1. Hormonal
2. Reprod Focal lobular hyperplasia
3. Abscess
4. Early menarche
5. Late menopause
6. Parity
7. Breasteeding Galactocoele
8. Late age at first pregnancy
9. Use of oral contraceptive
10. Hhormone replacement therapy
11. Lactatng adenoma
12. BRCA1 and BRCA2 mutatons

Histopathology

Ductal carcinoma 79%
Lobular carcinoma 10%
Tubular/cribriform carcinoma 6%
Mucinous carcinoma 2%
Medullary carcinoma 2%
Papillary carcinoma 1%
Clinical presentation

- A lump in or near the breast or in the underarm area • A change in the size or shape of the breast
- A dimple or puckering in the skin of the breast • A nipple turned inward into the breast
- Fluid, other than breast milk, from the nipple, especially if it's bloody
- Scaly, red, or swollen skin on the breast, nipple, or areola
- Dimples in the breast that look like the skin of an orange, called peau d'orange Associated with pregnancy
- May undergo H/P changes due to hormonal stimulation.

Differential Diagnosis

1. Fibroadenoma
2. Lipoma Bloody nipple discharge
- Cytology is always warranted
- Not a contraindication
3. Papilloma
4. Fibrocystic disease to breast-feeding
5. Lactating adenoma

Peculiar to breast feeding.

1. Hormonal pain.
2. Galactocele
3. Mastitis
4. Breast abscess (Wall should be biopsed)

Differential Diagnosis

1. Physiological
2. Infection
3. Duct papiloma
4. Carcinoma

Effect of Pregnancy on Breast Cancer

- Increased AFP and hCG are protective
- PABC are more likely to be advanced/ metastatic (due to increased blood/ lymphatic supply)
- Microscopic lymph node involvement more likely in pregnancy (60%)
- Stage I- 30%, Stage II- 30%, Stage III & IV- 40%
- Higher incidence of Inflammatory Cancers • 80% lesions are ER/PR negative
- Interruption of pregnancy does not alter the prognosis

Causes of delayed diagnosis

- Imaging diagnosis is difficult due to pregnancy-induced breast changes, such as engorgement
- Self-examination is difficult and is not performed frequently
- Young women are not potential candidates for screening test
- Patents reluctant to biopsy during pregnancy

Diagnosis delayed metastasis by by one month increases axillary lymph node approximately 0.9% to 1.8%4

Diagnosis

- Ultrasound
- For evaluation of palpable breast mass during pregnancy
  - Distinguishes solid from cystic masses
- No radiation exposure to the fetus
- Also used in ultrasound guided biopsy
- Mammography
- With abdominal shield can be done in all trimesters
- Increase water content in the breast may decrease sensitivity- 70%

Malignant masses have a more speculated appearance

Diagnosis

- BIOPSY
- About 90%
- Gold standard in diagnosis- sensitivity of 95%

Staging studies

- Should be tailored to minimize fetal exposure to radiations

Pulmonary metastasis should be checked

- Chest radiographs with abdominal shielding Liver metastases
- Liver Ultrasound

Bony metastasis

- Skeletal survey via MRI or a modified bone scan

Central nervous system symptoms

- MRI of the brain

Factors affecting treatment plan and prognosis

1. Gestatonal age at diagnosis of cancer
2. Staging of tumor
3. Biology of tumor
4. Type of breast cancer
5. Age of the fetus
6. Hormonal receptor status
7. Involvement of lymph nodes
8. Whether there are signs or symptoms
9. Patent's general health

Treatment options

- Surgery
- Chemo therapy
- Targeted therapy
- Radiation therapy
- Hormonal therapy

Treatment

Protocol of treatment should be as close as possible to non-pregnant.
Multidisciplinary approach is essential
First line of treatment is surgery- mastectomy/conservative surgery
Selection criteria for breast conservative surgery Single lesion clinically and on mammography
Tumour not larger than 3cm
Tumours more than 2cm away from nipple/areola Lesion of lower histological grade
No nodal involvement

Treatment

CONSERVATIVE surgery include; wide local excision and Quadrantectomy.
MASTECTOMY can either be – MRM or TM
INDICATIONS FOR MASTECTOMY

Large tumor size.
Central tumor beneath the areola or involving nipple.
Multi focal disease.
Local recurrence.

- Treatment of choice for non-metastatic disease
- Peri-operative hazards- position, anaesthesia, risk of preterm labour
- Modified radical mastectomy (MRM) with axillary clearance- done in most cases
- Breast Conserving Surgery (BCT) Lumpectomy/ Quadranectomy +Axillary Clearance

Needs adjuvant RT after delivery (<8 weeks) Only for localized Tx diagnosed in 3rd trimester

- Sentinel LN biopsy

Tc99sulphur colloid- NOT detrimental (fetal exposure 0.5 cGy)

- Surgical resection is the mainstay of treatment for early breast cancer diagnosed during pregnancy1, 2
- Modified radical mastectomy is standard of care in 1st and 2nd trimester of pregnancy3
- Breast-conserving surgery (lumpectomy with lymph node dissection) should be preferred in the 2nd and 3rd trimester1, 2
- Surgery can be performed in all trimesters with minimal risk for the foetus (particularly after the 12th week of gestation) 1st and 2nd Trimester Mastectomy
- 3rd Trimester <2cm Lumpectomy >2cm Mastectomy

Radiotherapy

- Not recommended during pregnancy owing to its teratogenic effects on the fetus
- In patients diagnosed in late 1st and 2nd trimester of pregnancy, consider delaying radiotherapy to the postpartum period 1
- However, evidence from literature suggests that a conservative estimate of the lifetime risk of radiation induced by fetal exposure to 0.01 Gy is about 1 in 1700 cases2
- So based on theoretical assumptions and few experiences, it may be assumed that radiotherapy is relatively safe only during the 1st and 2nd trimester of pregnancy1, 3
- Hormone therapy
- Most PABC are hormone receptor negative.
- Tamoxifen is contraindicated in pregnancy due to its – affects on growing embryonic tissues,

– Associated with miscarriage – preterm labor
– Genital tract anomalies
– Congenital disorders like Goldenhar syndrome, ambiguous genitalia, Pierre Robin sequence

• If indicated, hormonal therapy can be started after delivery and after completion of chemotherapy

- Targeted therapy
- Trastuzumab- not recommended

– High incidence of oligohydramnios and abnormal implantaton1

• Lapatnib- not recommended

– Evidence of massive trans-placental transfer 2, 3, 4

• Bevacizumab- not recommended

– Unclear mode of acton 2, 3, 4

• Rituximab- not recommended

– Transient neonatal lymphopenia24

• Imatnib- not recommended

– Associated with low birth weight and premature delivery 4

• Erlotnib- not recommended

– Due to lack of data, not advised during gestaton4

Termination of pregnancy

- No survival benefit with termination of the pregnancy
- Evidence also suggests improved survival for patents who continued their pregnancies compared to those who terminated
- However there exists bias of lower risk patents continuing versus those with more active disease choosing to terminate
- Therapeutic abortion may be preferred in – women with advanced-stage disease

– Patents insisting on breast conservation therapy,
– Whom a significant delay of this treatment would jeopardize maternal health

Overview

- Malignancies in pregnancy- Focus on PABC
- Diagnosis of PABC
- Available treatment options
- Chemotherapy in PABC
- Chemotherapeutc agents used in cancer during pregnancy
- Concerns with Chemotherapy treatment in PABC
- Management of PABC: evidence from NCCN guidelines
- Post partum care
- Need for Indian-specific registry for PABC

Chemotherapy

- Delaying chemotherapy until after delivery may be reasonable in some cases
- Most multi-drug protocols may be administered without increased risk for severe malformations

- Contraindicated due to possible damage to organogenesis
- The estimated risk of fetal malformations is up to 17%
- Certain chemotherapy regimens can be relatively safely administered

The risk of congenital malformations drops from 10-20% in first trimester to 1.3% in the third trimester of pregnancy.

Treatment

Supportive should be given as

Ondansetron
Granulocyte colony-stimulating factor
Methylprednisolone
Hydrocortisone
Psychological support
Foetal Surveillance
USS for anatomic evaluation.
Growth scan every 4 weeks and Doppler USS if concern for growth.
Antepartum foetal testing at 32 weeks or sooner if growth restriction noted.
Delivery at close to term as possible.
Not an indication for caesarean section.
Concerns with Chemotherapy
Maternal efects
Altered drug clearance
Delayed elimination of agents such as methotrexate
Difficult to predict the appropriate dose
Increase maternal and fetal toxicity
Fetal effects
Nucleic acid synthesis, microtubule function, cell division rate
Potential to cross the placenta
Spontaneous abortions, fetal death, and major congenital malformations
Eyes, ears, teeth-palate, genitalia, hematopoietc system, and CNS remain vulnerable.
Infants exposed to chemotherapy in utero had a lower birth weight.
To determine whether treatment for breast cancer during pregnancy is safe for both mother and child.

447 Patents with a primary diagnosis of early breast cancer during pregnancy
48% women received chemotherapy during pregnancy with a median of four cycles

•178 received an anthracycline

15 received cyclophosphamide, methotrexate, and fuorouracil
14 received a taxane.

Primary endpoint was fetal health for up to 4 weeks after delivery

NCCN treatment guidelines

NCCN Clinical Practice Guidelines in Oncology. Breast Cancer. Version 2.2012.Depends on

Clinical algorithm for Management of PABC
Breast lump in pregnancy
Breast imaging; Core Biopsy; Staging investigations (with precauitons)
< 12 weeks of gestation > 12 weeks of gestation
Avoid Chemotherapy

Consider mastectomy since radiation may be delayed until after delivery

Termination of pregnancy can be consider in very poor ECOG PS and/or very poor prognosis patents to be discussed with patent Operable

Mastectomy or BCS SNB or Axillary sampling or clearance
Adjuvant chemotherapy
Locally advanced
Neo-adjuvant chemotherapy
Delivery at 35-37 weeks of gestation
Measures to attain fetal maturity
Radiation therapy and/or Targeted Therapy
Lactation

- As a rule, women on cancer chemotherapy after delivery should not be breastfeeding as neither short-term nor long-term safety has been established
- Mother can discontinue, or temporarily interrupt, breast-feeding if the risk is perceived to be high
- Cancer chemotherapy schedules may allow breastfeeding women to store their own milk for near-future use
- Women on chemotherapy should perceive the importance of breastfeeding and the risks associated with it differently from women taking non-cancer related medications
- Given the nature of the maternal diseases in question, risk-benefit assessment of breastfeeding during maternal chemotherapy needs to be carefully individualized

Future Pregnancy

- ER/PR +ve breast Ca may be theoretically aggravated by future pregnancy (no evidence)
- Most of the recurrence- within 2-3 years
- Better to plan next pregnancy after 2-3 years of completion of therapy
- Chemo may cause POF
- No adverse effect on future obst outcome
- Survival is even BETTER! than those who don't conceive
- Breast feeding possible even from the affected breast after BCT & RT

Take home messages

PABC needs multi-disciplinary management.
Standard chemotherapeutc drugs can be used safely, especially in the 2nd or 3rd trimesters.
Targeted therapy and hormonal therapy should be deferred until after delivery.
Investigations involving ionizing radiation should be avoided unless absolutely necessary.
Radiation therapy is best deferred until after delivery

References

[1] Bajpai J et al. Pregnancy and Breast Cancer in Oncology Gold Standard. Chapter 18 2014; 327