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Metastatic breast cancer during pregnancy: a case report



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ABSTRACT

Introduction: Breast cancer is the most prevalent malignancy among women and a notable comorbidity during pregnancy. Pregnancy-associated breast cancer (PABC) presents unique challenges due to physiological breast changes that complicate early diagnosis. This case report aimed to present a 31-year-old female with a diagnosis of bilateral breast tumors, pleural effusion, and multiple thoracic soft tissue tumors during her second pregnancy, highlighting the complexities and treatment considerations involved.

Case presentation: A 31-year-old female patient, referred to Prof. Dr. I. G.N.G Ngoerah General Hospital, Denpasar, was in her second pregnancy at 20–21 weeks of gestation. She presented with bilateral breast lumps, worsening pain, and shortness of breath. Her obstetric history included a previous cesarean delivery and two abortions. Clinical examination revealed pleural effusion and multiple nodules suggestive of metastases. Biopsies confirmed tubular adenoma in the right breast and invasive breast carcinoma in the left breast. Ultrasound and chest x-ray findings indicated metastases to the liver and lungs. The patient was diagnosed with G4P1021 at 20 weeks of gestation with pregnancy-associated bilateral breast cancer and metastases.

Conclusion: PABC diagnosis and treatment are fraught with challenges due to the need to balance maternal and fetal health. Delays in diagnosis, limited antenatal care, and the aggressive nature of PABC contribute to poor outcomes. This case underscores the necessity of early detection, prompt multidisciplinary intervention, and tailored treatment strategies to improve PABC patients' prognoses.

Keywords: breast cancer, PABC, pregnancy.

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INTRODUCTION

Breast cancer is the most common malignancy in women and one of the comorbidities in pregnant women. Although cases are rare, the incidence is increasing worldwide, including in Indonesia, where more than 80% of non-pregnant women are diagnosed with late-stage breast cancer.¹ Delays in diagnosis often occur in pregnant women because physiological changes in the breast during pregnancy make it challenging to identify tumor masses. Some studies show that the prognosis for breast cancer in pregnant women is similar to that in non-pregnant women. Still, some studies show that breast cancer in pregnant women tends to be more aggressive, with a higher stage, larger tumor size, and is more often hormone

receptor-negative. Gestational breast cancer, or pregnancy-associated breast cancer (PABC), is breast cancer diagnosed during pregnancy or up to one year after giving birth.² PABC requires special treatment because of the aggressiveness of the tumor and gestational age, and has a different disease course compared to breast cancer outside of pregnancy or postpartum. The incidence of PABC has increased over the past few decades. This trend can be explained by increased detection and awareness, but delaying childbearing until old age is most often cited as the reason for increasing PABC rates.^{3,4}

Diagnosis of breast cancer is often delayed in pregnant or breastfeeding women due to physiological changes in the breast that complicate clinical examination,

ultrasound, and fine needle aspiration biopsy (FNAB). As a result, many patients with PABC present in poor condition with advanced cancer.⁵ Handling PABC requires special attention because it must take into account the health of the mother and fetus. Termination of pregnancy is not an option in the treatment of PABC because research shows no significant benefit. Breast changes during pregnancy and lactation also make it difficult for patients to recognize abnormalities, so they often present late with a poor prognosis. Some literature shows that the prognosis of PABC is not different from that of non-PABC breast cancer but is more determined by the cancer stage and histopathological characteristics.⁶ Diagnosis of cancer during pregnancy adds complexity to management. Still,



Figure 1. Clinical appearance of the mammae and abdomen.



Figure 2. Thorax X-ray examination.



Figure 3. The condition of baby at birth with severe asphyxia.

current data suggest that pregnant cancer patients can receive optimal treatment through a multidisciplinary approach involving oncologists, surgical oncologists, radiologists, and fetomaternal surgeons. Through active patient involvement, decisions must be made in the best interests of the mother and fetus. The goal of therapy is to maximize cancer cure, so correct diagnosis is essential for patient management and prognosis.⁷ Therefore, this case report aimed to discuss a case of PABC to become an informative reference in managing similar cases.

CASE PRESENTATION

A 31-year-old female patient was presented by a surgical colleague at Prof. Dr. I. G.N.G Ngoerah General Hospital, Denpasar, with a reference letter from a private hospital, with a diagnosis of tumor mammae dextra and sinistra, massive pleural effusion sinistra, multiple soft tissue tumors of the thoracic region, second pregnancy with a gestational age of 20-21 weeks. From the anamnesis, the patient complained that there were lumps in both breasts for 2 weeks. Pain in the right and left breasts has been felt for two weeks and has gotten worse since two days. Complaints in the field of obstetrics, such as abdominal pain and vaginal bleeding, were denied, and good fetal movement was felt since September 2021. The patient only had antenatal care (ANC) examinations twice, where an interpretation of labor was obtained on March 25th, 2022. From the obstetric history, it was known that this pregnancy was the fourth pregnancy; the patient had previously given birth by abdominal (cesarean section) in 2017 due to dystocia. Then, there was a history of two abortions, namely in 2020 and 2021. From the results of the anamnesis, it was also known that the patient did not take any other medicines during pregnancy apart from vitamins and did not smoke or drink alcohol. From the vital sign examination, blood pressure was found to be 110/70 mmHg, pulse rate 98 times/minute, respiratory rate 26 times/minute,

with oxygen saturation 96-97% using a 6 lpm oxygen face mask.

Based on the obstetric examination, it was discovered from the anamnesis that the patient was referred by a surgical oncologist with a left-right breast mammary tumor and massive pleural effusion in the left lung. The patient complained of a lump initially felt in the left breast on July 3rd, 2021. Then the lump was felt to enlarge, and a lump appeared in the right breast and in the armpit, accompanied by pain since July 14th, 2021. On November 3rd, 2021, an FNAB was carried out at Bhayangkara Hospital, Jakarta. If a lump in the breast results in an epithelial neoplasm, it is suspicious of malignancy. On November 6th, 2021, the patient complained of shortness of breath and came to Prof. Dr. I. G.N.G Ngoerah General Hospital. A 750 ml pleural fluid puncture was performed. The patient denied complaints of abdominal pain and vaginal spotting. This pregnancy is the fourth pregnancy, with a previous history of birth by cesarean section in 2017 and a history of two miscarriages, namely in 2020 and 2021. The first day of the last menstruation was June 18th, 2021, with an estimated delivery date of March 25th, 2022. On physical examination, blood pressure was within normal limits. Respiratory rate 24 times/minute with oxygen saturation 97% with oxygen support from 3 nasal cannulas. The height of the uterine fundus is central; the fetal heart rate is found to be 154 times/minute.

Ultrasound examination revealed a single live fetus with an estimated fetal weight of 363 grams. Chest x-ray examination revealed pleural effusion in the right and left lungs, accompanied by lytic lesions on the right rib 1 and rib 4, suspicious for metastatic bone disease.

Laboratory examination showed a hemoglobin level of 9.00 g/dL. On November 8th, 2021, the surgical oncology team performed biopsies on the right and left breast. Right breast biopsy results showed tubular adenoma, while left breast biopsy showed a special type of invasive breast carcinoma, grade 2. Ultrasound examination of the breast found a solid nodule with well-defined borders in the upper-outer quadrant of the right breast, according to BIRADS 3 (possibly benign); heterogeneous solid nodule with lobulated edges in the mid-superior to retro nipple quadrant of the right breast, according to BIRADS 4 (suspected of malignancy); heterogeneous solid nodule with micro-lobulated edges in the upper-outer quadrant of the left breast, as per BIRADS 4 (suspected of malignancy); heterogeneous solid nodule with micro-lobulated edges in the upper-mid quadrant of the left breast, according to BIRADS 4 (suspected of malignancy); and multiple malignant glandular masses in the left axillary tail and left parasternal. Ultrasound examination of the liver revealed hepatomegaly with multiple nodules in both the right and left lobes, suggesting metastases. The final diagnosis was G4P1021 at 20 weeks of gestation, with PABC (right and left) and metastases to the liver and lungs.

The patients were treated by multidisciplinary disciplines such as surgical oncology, a fetal/maternal consultant obstetrician, an internal medicine fellow, and the clinical nutrition department. A team meeting was held to approve the administration of chemotherapy drugs to the patient. The chemotherapy regimen that will be used is cyclophosphamide, adriamycin, and fluorouracil, including FDA category D. These drugs can be given if it is really necessary. The risks that can occur are stunted fetal growth, preterm labor, and fetal death. Four days after administering chemotherapy drugs, the patient complained of abdominal pain and wanted to strain. On December 2nd, 2021,

at 01.00 local time, the patient gave birth spontaneously vaginally, a female baby weighing 630 grams, had severe asphyxia, was given neonatal resuscitation, and was treated in the NICU. The next day, the baby's condition worsened, resuscitation was carried out, and he was finally declared dead. Seven days after vaginal delivery, the patient's condition worsened, and after failed cardiopulmonary resuscitation, the patient was declared dead due to multiple organ failure.

DISCUSSION

The patient is a 30-year-old woman with a bad obstetric history, namely miscarriage in her second and third pregnancies. The age at the time of the first pregnancy was 26 years (in 2017); she was born via c-section because she experienced dystocia during delivery. Several studies report that a woman's age is a significant risk factor for PABC.⁸ Several studies also suggest a 4.3% reduction in lifetime breast cancer risk for every 12 months of breastfeeding, and breastfeeding for >55 months is less likely to experience breast cancer compared with parous women without breastfeeding.⁹ A prolonged period of lactation, which would drive all cells to terminal differentiation, might kill these oncogene-expressing cells by the involutational environment, freeing the breast of these protumorigenic cells. In contrast, little or no breastfeeding may increase the survival of these oncogene-expressing cells in an inflammatory microenvironment.¹⁰ However, it is regrettable that in this case, information regarding the patient's breastfeeding of her first child is not known, so comparisons cannot be made with existing journals.

The patient was said to have experienced her first menstruation at the age of 13 years. Early menarche, often associated with a delay in first pregnancy, is another known risk factor for breast cancer. Based on a study conducted by the collaborative group on hormonal factors in breast cancer, a comprehensive analysis involving 118,964 women with invasive breast cancer from 117 epidemiological studies found that the risk of breast cancer increases by 5% for each year younger at menarche. Additionally, the risk increases by approximately 3% for each year older at

menopause. Premenopausal women aged 45-54 have a 43% higher risk of breast cancer compared to postmenopausal women of the same age. These associations are less pronounced in postmenopausal women with higher body fat. The effects of menarche and menopause are more potent for lobular tumors and estrogen receptor-positive breast cancer. This study highlights the significant role of endogenous ovarian hormones in the development of breast cancer, particularly for estrogen receptor-positive and lobular tumors.¹¹

A family history of PABC greatly influences its incidence. However, in this case, the patient admitted having no family history of the disease. Based on the history, the patient complained of pain in the right and left breast around two weeks before being admitted to the hospital, and it worsened around two days before admission. Pain is also felt in the body and throughout the bones. New lumps were felt in the right and left breast, armpit, left lateral and posterior thorax, and lumbar. A view of women with PABC shows erythema and inflammation, or inflammatory carcinoma, mimicking the presentation of mastitis or abscess. Other symptoms include bleeding from the nipple and an unspecified nipple. Discharge, nipple retraction, palpable supraclavicular lymph nodes or other palpable lymph nodes, skin metastases, Paget's disease, and distant metastases.¹²

In this case, the patient underwent several supporting examinations, including FNAB, mammary ultrasound, and thorax X-ray. The FNAB result indicated an epithelial neoplasm highly suspicious for malignancy. This aligns with research showing that most PABC cases are diagnosed at an advanced stage.¹³ The patient is suspected of having metastases, indicated by symptoms such as shortness of breath, lung metastases, and pain in various body parts. Bone metastases are also suspected. Ideally, bone metastases should be examined with a CT scan. However, multiple journals and PABC management guidelines advise against CT scans for pregnant women due to the high radiation risk and potential impact on the fetus.¹⁴ Instead, chest x-rays and liver ultrasounds are recommended for evaluating metastasis in PABC. Tumor

markers like CA15-3, CEA, and CA125 are not used for early breast cancer diagnosis, can be misleading during pregnancy, and are not recommended.¹⁵

Ultrasound examination revealed multiple nodules in the right and left lobes of the liver and the paraaortic region, suggesting metastases. The thorax x-ray showed consolidation and pleural effusion, also suspected to be due to metastases. The patient was diagnosed with stage IV PABC. Most evidence indicates that pregnancy does not worsen the disease but can mask it, allowing metastasis to progress. Increased vigilance by doctors is essential during pregnancy examination.¹⁶

Previous studies have shown that women with PABC diagnosed at a later stage have poorer survival rates.¹⁷ In this case, the patient is managed based on symptoms and given chemotherapy. Symptom-based therapy includes hydration with 0.9% NaCl, oxygen administration for shortness of breath, and a WSD to remove pleural effusion fluid. After evaluating the patient's condition, the oncology department decided to administer chemotherapy with cyclophosphamide and doxorubicin.

Pregnancy is not an absolute contraindication for systemic chemotherapy in breast cancer patients. Treatment should be based on the stage and biology of the cancer. The primary concern is the gestational period due to chemotherapy's potential effects on fetal development.¹⁸ During organogenesis, the risk of congenital malformations and fetal loss is high. While chemotherapy is generally safe and well-tolerated during the second and third trimesters, a multidisciplinary approach is essential, including close fetal monitoring and maternal blood pressure control. Chemotherapy has been linked to an increased risk of preterm birth, intrauterine growth restriction, and hypertensive disorders of pregnancy.¹⁹

Chemotherapy should not be administered after 34 weeks of gestation due to the risk of spontaneous delivery during the hematological nadir period. While there is no consensus on specific chemotherapy regimens, AC (doxorubicin, cyclophosphamide) or EC (epirubicin,

cyclophosphamide) regimens are commonly considered the first treatment options.¹⁹ In this patient, the chemotherapy regimen used was cyclophosphamide, adriamycin, and fluorouracil, all categorized as FDA category D drugs, which can be administered if necessary. Potential risks include stunted fetal growth, preterm labor, and fetal death. Four days after receiving chemotherapy, the patient experienced abdominal pain and a strong urge to push, leading to preterm labor. The baby, a female weighing 630 grams, was delivered vaginally with severe asphyxia. Pediatric colleagues performed neonatal resuscitation, and the baby was treated in the intensive care unit. Unfortunately, the baby's condition worsened the following day, and despite further resuscitation efforts, the baby was declared dead. Seven days after vaginal delivery, the patient's condition worsened, and after failed cardiopulmonary resuscitation, the patient was declared dead due to multi-organ failure. Patients with PABC, if found at an early stage, usually have a better prognosis. There are primary factors that influence the prognosis of patients with PABC, namely the time of diagnosis at an advanced stage, as well as the delay in making the diagnosis.¹⁷

The limitations of this case include a late diagnosis of breast cancer and metastases, which likely impacted treatment options and outcomes. Early detection might have allowed for a different management strategy and improved prognosis. The patient had only two antenatal care (ANC) visits before referral, limiting monitoring and early detection of pregnancy and cancer-related complications. Additionally, the delay in seeking medical evaluation for breast lumps contributed to the advanced stage of cancer at the time of treatment. The use of FDA category D chemotherapy drugs posed significant risks to fetal development, including stunted growth, preterm labor, and fetal death, which were realized in this case. Despite a multidisciplinary approach, challenges in coordination among surgical oncology, obstetrics, internal medicine, and nutrition may have affected treatment effectiveness. The adverse fetal outcome, including preterm birth and

severe asphyxia, underscores the risks of chemotherapy during pregnancy. Finally, the rapid deterioration of the patient's condition following chemotherapy and delivery highlights the need for closer monitoring and potentially more proactive interventions.

CONCLUSION

PABC is diagnosed during pregnancy or within 12 months after giving birth. A woman's age significantly increases the risk, with a 5.3% rise each year after age 25 during the first pregnancy. Early menarche and family history are additional risk factors. Most PABC masses are painless, with only 8% causing pain and 4% showing erythema and swelling similar to mastitis or abscess. Chest x-rays and liver ultrasounds are recommended for evaluating PABC metastases. Pregnancy is not an absolute contraindication for systemic chemotherapy. PABC is the most common malignancy in pregnant women, requiring careful monitoring, especially in those over 30. Detecting breast abnormalities is challenging during pregnancy and breastfeeding, often leading to late and more aggressive presentations. Ultrasound is the preferred method for breast examination during pregnancy. Delays in seeking medical help contribute to PABC's poor prognosis.

DISCLOSURE

Conflict of Interest

The authors assert that no conflicts of interest are associated with this case report's publication.

Patient's informed consent

The patient's family and the department head in charge have given a written informed consent to utilize and disseminate the case of this patient.

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All authors have been involved in preparing this case report.

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