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CASE REPORT

HEART CARE TEAM/MULTIDISCIPLINARY TEAM LIVE: CARDIO-OBSTETRICS 2023

Chemotherapy in Pregnancy

Assessing the Safety of Adriamycin Administration in Pregnancy Complicated by Breast Cancer

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ABSTRACT

Pregnancy-associated breast cancer is challenging to treat. Treatment with chemotherapeutic agents such as anthracyclines poses a risk of cardiotoxicity, despite being considered safe after the second trimester of pregnancy. Management requires multidisciplinary comanagement with cardio-obstetrics, cardiology-oncology, maternal-fetal medicine, and oncology. (J Am Coll Cardiol Case Rep 2023;28:102141) © 2023 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

CASE PRESENTATION

A 39-year-old gravida 4 para 3 female presented at 8 weeks gestation with a twin pregnancy complaining of a right breast mass with on/off bloody nipple discharge for about 1 year. Past medical history was significant for obesity (body mass index: 45.4 kg/m^2) and medically controlled essential hypertension. She had no family history of breast or ovarian cancer. She has no history of substance abuse, is a nonsmoker, and consumes alcohol occasionally. Biopsy of breast mass confirmed weakly estrogen receptor 5% progesterone receptor 13% human epidermal growth factor receptor-2 negative, node+, stage IIb pregnancy-associated breast cancer (PABC). She was offered termination of pregnancy in lieu of her high-risk pregnancy, but she declined. She underwent a right radical mastectomy with axillary lymph node dissection at 11 weeks gestation.

LEARNING OBJECTIVE

- To decrease cardiovascular morbidity in pregnant patients undergoing cardiotoxic chemotherapy by regular surveillance and a multidisciplinary team approach.

Due to high-risk features in the PABC, the oncology team planned adjuvant chemotherapy at 15 weeks of gestation with 4 cycles of adriamycin and cyclophosphamide (AC) based chemotherapy at every 3-week intervals. A baseline echocardiogram revealed a new diagnosis of cardiomyopathy with a left ventricular (LV) ejection fraction (EF) of 45%-50% and a severely dilated LV (Figure 1A). She was in NYHA functional class I-II symptoms at the presentation to the cardio-oncology clinic. She had no family history

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ABBREVIATIONS AND ACRONYMS

AC = adriamycin and cyclophosphamide

APGAR = Appearance, Pulse, Grimace, Activity, and Respiration

CT = computed tomography

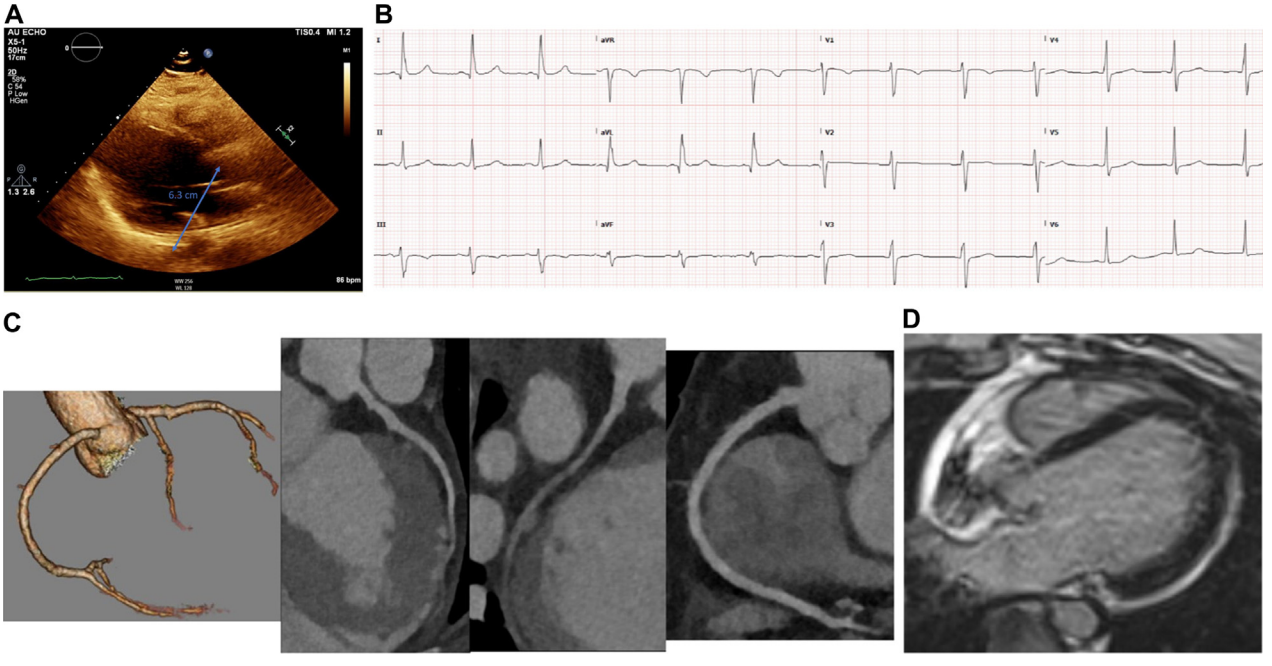
EF = ejection fraction

LV = left ventricle

PABC = pregnancy-associated breast cancer

of cardiomyopathy. After a work-up with complete blood count, complete metabolic panel, thyroid studies, iron studies, electrocardiogram (Figure 1B), and limited genetic testing, the only remaining differential was idiopathic cardiomyopathy. The patient has NYHA functional class I-II symptoms and LVEF of 45%-50% indicated an overall stable cardiac condition. After careful deliberations involving the patient, oncology team, and cardio-oncology team, carvedilol 12.5 mg twice daily was initiated before beginning AC to offer cardioprotection. After each AC cycle, the cardio-obstetrics and cardio-oncology team measured maternal echocardiogram, brain natriuretic peptide, and troponin for surveillance. She tolerated 4 AC cycles with no change in LVEF from baseline and no symptoms of heart failure. Her pregnancy care was managed by Maternal and Fetal medicine with serial fetal ultrasounds, all of which were normal. A shared decision of an early delivery at 32 weeks was made, driven by the need to expedite due to the high-risk nature of PABC and potential implications of delayed treatment. Maternal and fetal medicine specialists collaborated closely to ensure the optimal timing of delivery that balanced the health of both mother and twin fetuses. Per the patient's request and to not increase the afterload during vaginal delivery per recommendations of cardio-obstetrics, Cesarean section was chosen as mode of delivery. She delivered healthy male and female infants with no complications (male: APGAR 5 and 7; female: APGAR 8 and 7). Due to in-utero adriamycin exposure, a pediatric echocardiogram was performed on both infants, which showed no cardiotoxicity. Postpartum LVEF decreased to 40%-45%, necessitating an increase in carvedilol dosing to 25 mg twice daily as well as the addition of sacubitril/valsartan 24/26 mg twice daily and spironolactone 25 mg daily. Chest pain complaint after delivery prompted evaluation with computed tomography (CT)-based angiogram (Figure 1C), ruling out epicardial coronary artery disease or spontaneous coronary artery dissection. There was no evidence of delayed enhancement to suggest fibrosis or infarction on cardiac magnetic resonance imaging (Figure 1D). There was no evidence of LV hypertrophy to suggest hypertensive heart disease. Considering the possibility of microvascular disease,

FIGURE 1 Patient With PABC



(A) Echocardiogram (quality - average - contrast not used due to pregnancy) of a patient with PABC planning anthracycline-based treatment; (B) electrocardiogram of the same patient at the cardio-oncology clinic visit; (C) curved planar reconstructions of all 3 coronaries and 3-dimensional reconstruction of the coronary tree of the same patient obtained using a computed tomographic angiogram after pregnancy; (D) cardiac magnetic resonance single-shot steady-state free precession image of late gadolinium enhancement - 3-chamber view. PABC = pregnancy-associated breast cancer.

isosorbide mononitrate 30 mg daily and aspirin 81 mg daily were initiated with a favorable response to chest pain. Postpartum staging scans, including bone scan, CT abdomen, and chest, revealed no metastasis, and she started 11 cycles of paclitaxel weekly to complete 12 paclitaxel cycles before starting endocrine treatment for 5-10 years. She was closely followed up postpartum by the cardio-obstetrics and cardio-oncology team.

QUESTION 1: IS DIAGNOSIS OF PABC ASSOCIATED WITH POOR OUTCOMES?

Answer 1: No, a diagnosis of PABC does not impact prognosis if standard treatment is provided. PABC frequently presents with a more aggressive histopathologic profile than the age-matched cohort.[1] Consequently, it is crucial to not avoid delay in treatment until after delivery, as such delays have been associated with poor outcomes.[2] The focus of managing PABC lies in balancing effective treatment of the mother without any delay while ensuring the safety and well-being of the developing fetus.

QUESTION 2: WHAT ARE THE TREATMENT OPTIONS IN PABC?

Answer 2: Surgery is considered the safest treatment option at any stage of pregnancy, whereas chemotherapeutic agents like adriamycin are safe during second and third trimesters.[3-5] Although drugs like adriamycin are associated with an increased risk of cardiomyopathy, they are essential components of chemotherapy regimens for breast cancer. Patients with PABC on adriamycin therapy require regular monitoring and evaluation by a collaborative team of cardio-obstetrics and cardio-oncology specialists.

QUESTION 3: IS ADRIAMYCIN SAFE FOR TREATMENT IN PABC?

Answer 3: There is a paucity of available data about the survival outcomes of patients with PABC limiting our understanding of this condition. A meta-analysis by Hartman et al[6] comprising 13 studies and 900 cases of PABC found a 47% increased risk of all-cause death and a 13% increased risk of cancer relapse or disease progression compared with nonpregnant patients. Pregnancy is high risk in patients with LVEF <45% and is contraindicated in LVEF <30% as indicated by CARPEG II (Cardiac Disease in Pregnancy Study) and modified world health organization (mWHO) scores scores.[7,8] Notably, in this case, her low LVEF (40%) increased her risk of decompensation, thus necessitating appropriate aggressive interventions. This approach ensured a thorough evaluation, mitigated potential risks, and potentially improved maternal-fetal outcomes. It is imperative to expand the body of research evidence to develop policies and programs that cater to the specific needs of pregnant patients with breast cancer undergoing chemotherapy.

QUESTION 4: HOW CAN WE IMPROVE MATERNAL AND FETAL OUTCOMES IN PABC?

Answer 4: Over the past 2 decades, there has been a concerning and consistent increase in maternal mortality rates in the United States. Cardiovascular disease is the leading cause of these maternal deaths, predominantly stemming from cardiomyopathy.[8] PABC is a challenging diagnosis for patients and physicians; therefore, a comprehensive and collaborative approach involving obstetricians, maternal-fetal medicine, cardio-obstetrics, oncology, cardio-oncology, and pediatrics is needed to address the unique needs and challenges associated with PABC treatment. The decision to continue the pregnancy should be based on carefully discussing cancer prognosis, treatment, and future fertility with the patient and her partner and the multidisciplinary team.[9]

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