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Case report

Treatment of metastatic breast cancer during pregnancy: We need to talk!

Hatem A. Azim Jr., Fedro A. Peccatori*

Department of Medicine, Division of Haematology Oncology, European Institute of Oncology, Via Ripamonti 435, 20141 Milan, Italy

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Abstract

Metastatic breast cancer during pregnancy is a challenging situation. The literature yield in this topic is poor given the rarity of the disease. Management strategies should be discussed in a multidisciplinary manner and each case have to be counselled separately and informed about the pros and cons of different treatment options. Here, we report a case of metastatic breast cancer initially diagnosed during pregnancy. We discuss the clinical course and dilemmas governing the management decisions.
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Keywords: Breast cancer; Pregnancy; Chemotherapy; Counselling

Introduction

Approximately 1/3000–1/10000 term pregnancies are complicated by breast cancer.[1] It is usually diagnosed at more advanced stages compared to non-pregnant women, and tumours tend to be highly proliferative, poorly differentiated and with low endocrine responsiveness.[2] Nonetheless, most of the cases described in literature are localized to the breast.[3–5] The maternal prognosis, limited treatment options, possible influence of metastatic tumour on pregnancy outcome and uncertainties about the late effect of maternal chemotherapy on the newborn should all be taken into consideration. In such situations, evidences from literature are scanty, so each case should be discussed individually. A multidisciplinary approach could provide therapeutic options to be discussed with the patient.

Case report

A 36-year-old woman presented with a painless left breast lump. She did not have a family history of breast cancer and her past medical history was unremarkable. She reported an 8-weeks delay in menstrual cycle and a positive urine pregnancy test. Clinical examination was unremarkable except for a 3 cm left breast mass. Breast ultrasound showed an irregular 35 × 30 mm nodule, and pathology revealed a grade 2 invasive ductal carcinoma with elevated Ki-67, oestrogen receptor (80%), progesterone receptor (1%) and Her-2-neu +1. Abdominal ultrasound showed a regular 15-weeks pregnancy, but also multiple hepatic focal lesions, largest measuring 68 × 46 × 56 mm. A liver biopsy was consistent with metastatic breast carcinoma. Laboratory workup was unremarkable apart from elevated CA15.3 (1.3folds). Chest X-ray was normal, while bone scan was not performed.

The case was discussed at a multidisciplinary meeting, including an oncologist, a surgeon, an obstetrician and a neonatologist and different treatment options were illustrated to the patient and her family. They included pregnancy termination, no active treatment until delivery and chemotherapy during pregnancy. Several aspects were discussed with the patient and her family including whether pregnancy termination would affect prognosis or not. It was made clear that metastatic breast cancer is not a curable disease, with unpredictable response to treatment and limited survival. She was then informed about the possibility that disease progression in the liver could hamper the normal foetal development and the risks of premature delivery. Chemotherapy toxicities for the mother and the foetus were also discussed, and the patient was informed about

* Corresponding author. Tel.: +39 02 574 89538; fax: +39 02 943 79241.
E-mail addresses: hatemazim@cairocure.com (H.A. Azim Jr.), fedro.peccatori@ieo.it (F.A. Peccatori).

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the ongoing chemotherapy protocols for pregnant women at the European Institute of Oncology (IEO). After 1 week, the patient decided to start chemotherapy and preserve her pregnancy. Treatment was started at 17 weeks of gestation consisting of weekly Epirubicin (35 mg/m^2), with metoclopramide premedication. After 10 consecutive weeks, liver ultrasound demonstrated a partial response. Chemotherapy was continued up to 29 weeks with unremarkable foetal conditions, and caesarean section was carried out at 34 weeks of gestation. A healthy 2200 g girl was delivered, Apgar score at 1 and 5 min was 9 and 10, respectively, and heart and skull ultrasound appeared normal. The baby was placed in the intensive care unit for 2 days and was sent home after 22 days in a normal condition. Chemotherapy was resumed 2 weeks afterwards with Fluorouracil, 500 mg/m^2, Epirubicin 90 mg/m^2, Cyclophosphamide 500 mg/m^2 for six cycles. Reassessment one month later showed complete disappearance of the hepatic lesions, normal bone scan and no evidence of palpable disease in the breast. The patient was then placed on Triptorelin 3.75 mcg q 4 weeks and Tamoxifen 20 mg/daily. She maintained a complete remission for six months then hepatic progression became apparent in 12/2007. At the time of reporting this case, the patient's daughter is 1 year old with normal physical and behavioural development. Repeated cardiac ultrasound have not demonstrated any apparent abnormality.

Discussion

Metastatic breast cancer during pregnancy is a rare event. Among the two largest case-series reported in literature, only two cases were initially metastatic, yet they were not separately analysed.[3,4] Otherwise, no other case reports addressed this subject. Related case reports of metastatic disease during pregnancy either described cases with recurrent disease[6–9] or cases who were initially metastatic but did not receive and/or respond to chemotherapy.[10,11]

The first question of our patient was about pregnancy termination and the influence of abortion on prognosis, particularly in the face of an already diffuse disease. Literature on this issue is scanty. In 1943, it was suggested that pregnancy should always be terminated in the presence of a breast neoplasm,[12] but more recent data have demonstrated that pregnancy termination does not improve prognosis.[13–15]

The second question concerned prognosis. Even if prognosis of breast cancer during pregnancy is usually severe, most studies that addressed this issue suggested a similar prognosis compared to non-pregnant controls with the same stage and biological tumour characteristics.[2]

The third question was about the effect of chemotherapy on the tumour and on the foetus. Several chemotherapeutic agents including anthracyclines,[3,4] taxanes[7,8] and vinorelbine[9] had been used during pregnancy. They all appear safe during the second and third trimesters, even if the number of treated patients remains low.

In the two series previously mentioned,[3,4] no maternal mortality was reported during pregnancy or in the postpartum period. No stillbirths, miscarriages or perinatal deaths occurred with the exception of one spontaneous abortion.[4] Four congenital anomalies were also described (Down syndrome, club foot, bilateral ureteral reflux and abdominal haemangioma). Even if long term follow up of newborns whose mothers received chemotherapy during pregnancy is scanty, preliminary data do not demonstrate an increased risk of leukaemia, infertility or cardiac events in this population.[16] At the IEO, weekly Epirubicin for high risk, locally advanced and metastatic breast cancer has been implemented since 2002. Preliminary results showed good clinical activity without significant foetal adverse events.[17] The weekly regimen allows lower Epirubicin peak blood concentration with lower maternal myelotoxicity and possibly lower placental transfer of the drug. This concurs in a more favourable safety profile with less maternal and foetal cardiotoxicity and facilitates maintenance of the correct dosing schedule and completion of the administration cycles.[18]

In conclusion, this case report reinforces the notion that pregnancy associated cancer, including metastatic breast cancer, should be managed by a multidisciplinary team and that patients and their family need a thorough counselling to reach an informed decision.[19]

Conflict of interest

None declared.

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