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Brain metastases from breast cancer during pregnancy

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Abstract

Background: Brain metastasis during pregnancy is a rare occurrence. In particular, there have only been three prior cases regarding breast cancer metastasis. We report a patient with breast cancer metastasis to the brain during pregnancy and review the literature.

Case Description: The patient was a 35-year-old female with a history of breast cancer (estrogen receptor/progesterone receptor negative, human epidermal growth factor receptor 2/neu positive, status post-neoadjuvant docetaxel/carboplatin/trastuzumab/pertuzumab therapy, status post-bilateral mastectomies), and prior right frontal brain metastases (status post-resection, capecitabine/lapatinib/temozolomide therapy, and cyberknife treatment). Patient was found to be pregnant at 9 weeks' gestation while on chemotherapy; the patient elected to continue with the pregnancy and chemotherapy was discontinued. At 14 weeks' gestation, she returned with recurrent right frontal disease. She was taken for a craniotomy at 16 weeks' gestation, which confirmed metastases. Six weeks later, patient returned with worsening headaches and fatigue, with more recurrent right frontal disease. She was started on decadron and chemotherapy (5-fluorouracil, adriamycin, and cyclophosphamide). Serial magnetic resonance imaging (MRI) demonstrated enlarging right frontal lesions. She underwent a craniotomy at 27 weeks' gestation, and chemotherapy was discontinued promptly. Starting at 30 weeks' gestation, she received whole brain radiation for 2 weeks. Subsequently, she delivered a baby girl via cesarean section at 32 weeks' gestation. At 6 weeks follow-up, an MRI brain demonstrated no new intracranial disease, with stable postoperative findings.

Conclusion: There is a lack of guidelines and clinical consensus on medical and surgical treatment for breast cancer metastases in pregnant patients. Treatment usually varies based upon underlying tumor burden, location, gestational age of the fetus, and patient's preference and symptomatology.

Key Words: Brain metastases, brain surgery, breast cancer

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BACKGROUND

Brain metastasis during pregnancy is a rare occurrence. In particular, there have only been three prior cases regarding breast cancer metastasis. Not surprisingly, pregnancy complicates the management of brain metastases. We report a patient with breast cancer metastasis to the brain during pregnancy and review the literature.

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CASE PRESENTATION

The patient was a 35-year-old female who had a history of breast cancer (invasive ductal carcinoma of the left breast, estrogen receptor (ER)/progesterone (PR) negative, human epidermal growth factor receptor 2 (HER2)/neu positive, status post-neoadjuvant docetaxel/carboplatin/trastuzumab/pertuzumab therapy (TCH-P therapy), status post-bilateral mastectomies and left axillary lymph node dissection), with a prior right frontal brain metastases (status post-gross total resection, capecitabine/lapatinib/temozolomide therapy (TTX therapy), and cyberknife treatment). Patient was found pregnant at 9 weeks' gestation; despite potential complications with the fetus during TTX therapy, patient elected to continue with the pregnancy; TTX therapy was discontinued. At 14 weeks' gestation, she returned with headaches. Imaging showed recurrent right frontal dural-based lesion with significant surrounding vasogenic edema [Figure 1]. Magnetic resonance imaging (MRI) of the spine was negative. She was taken for a craniotomy at 16 weeks' gestation, which again confirmed metastatic adenocarcinoma.

Six weeks later, patient returned with worsening headaches and fatigue. CT head showed recurring disease in the right frontal lobe [Figure 2a]. She was started on decadron and chemotherapy (5-fluorouracil, adriamycin, and cyclophosphamide). Serial MRI demonstrated enlarging right frontal lesions [Figure 2b and c]. She underwent a craniotomy at 27 weeks' gestation, and chemotherapy was discontinued promptly. Starting at 30 weeks' gestation, she received whole brain radiation (10 fractions, each at 3000 cGy) for 2 weeks. Subsequently, she delivered a baby girl via cesarean section at 32 weeks' gestation; at the same time, patient had an elective bilateral tubal ligation. Overall, her pregnancy was complicated by intrauterine growth restriction, with estimated gestation weight at 6th percentile. She was getting weekly biophysical profiles/umbilical arterial Doppler which had been reassuring; in addition, she had a normal fetal echocardiogram at 20 weeks' gestation. At 6 weeks follow-up, an MRI brain demonstrated no new intracranial disease, with stable postoperative findings [Figure 3].

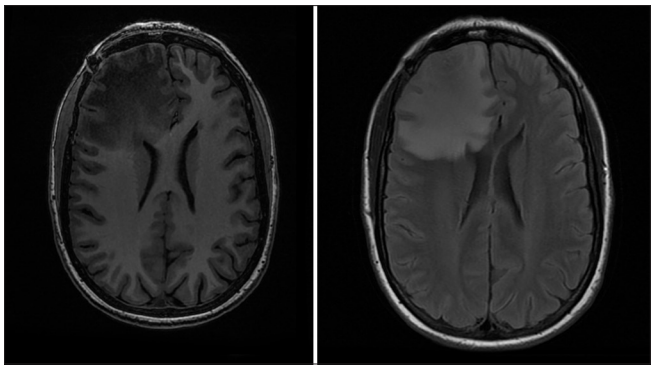

Figure 1: Axial magnetic resonance T1 (left) and fluid-attenuated inversion recovery demonstrates right frontal dural-based lesion

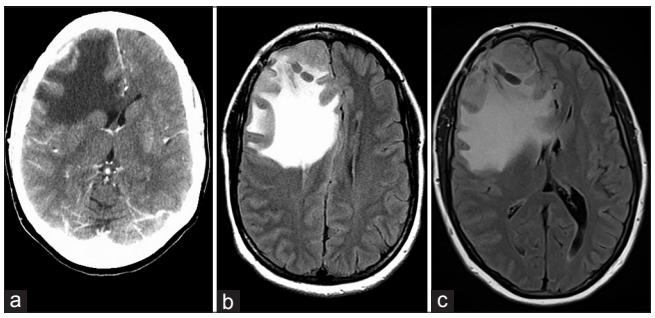

Figure 2: Axial computed tomography of the head (a), and serial fluid-attenuated inversion recovery (b, c) demonstrate progressive growth of recurrent right frontal lesion, with midline shift

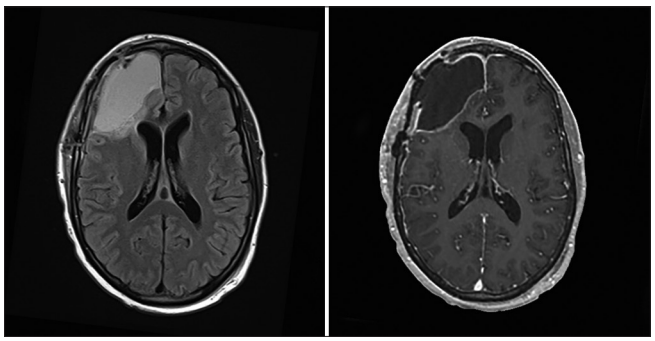

Figure 3: Axial magnetic resonance fluid-attenuated inversion recovery (left) and T1 with contrast demonstrate no residual or recurrent disease

DISCUSSION

The literature is limited regarding intracranial neoplasms during pregnancy. The estimated incidence is 15 per 100,000.[5,7] Common lesions include primary tumors, typically gliomas, pituitary adenoma, and meningiomas.[5,12,15] Brain metastasis during pregnancy is rather rare, where choriocarcinoma is the most common pathology.[5,13] Overall, the management of intracranial neoplasms can be challenging. Patients may opt for less aggressive treatment or to postpone treatment in order to decrease risk to the fetus while others may opt to terminate the pregnancy and proceed with full therapy. Future fertility may also be compromised, which remains an important consideration. Management needs to be tailored for each patient with interdisciplinary cooperation.

Breast cancer is the most common malignancy during pregnancy.[2] Of the reported cases, up to 3.8% exhibit metastatic disease.[5] Brain metastasis during pregnancy, however, has been rare and has only been reported in three other instances.[5,8,10] These are summarized in Table 1. Mandrawa *et al.*[8] reported the case of a 25-year-old female who underwent craniotomies

Table 1: Review of literature

Literature	Year	Age	Gestation age at diagnosis of brain disease	Breast cancer	Brain metastases location	Treatment during pregnancy for brain lesions	Ongoing breast cancer treatment during pregnancy	Pregnancy Outcome	Last follow-up
Gupta *et al*.[2]	2014	24	22	ER/PR negative, Her2/Neu positive, BRCA1 mutation	left thalamic, left parietal	decadron, whole brain XRT	trastuzumab, paclitaxel	C section at 38 weeks	Baby doing well at 6 months; mother passed 23 months after diagnosis
Mandrawa *et al*.[7]	2011	25	23	ER/PR negative, Her2/Neu positive	left frontal, right frontal-parietal, posterior fossa	stereotatic craniotomies at 23 weeks gestation and 25 weeks gestation	trastuzumab	Forceps assisted delivery at 37 weeks	Baby doing well at 28 months; mother with progressive liver and lung metastases, along with recurrent brain metastases
Okuda *et al*.[8]	2016	35	18	ER/PR negative, Her2/Neu negative	left temporal	craniotomy	n/a	Termination of pregnancy at 21 weeks due to worsening brain metastases	No long-term follow up presented
Our case	2016	36	28	ER/PR negative, Her2/Neu positive	right frontal	craniotomy x 2, decadron, whole brain radiation (10 fractions, each at 3000 cGy)	TTX therapy (stopped after pregnancy discovered), FAC therapy	Scheduled cesarean section at 32 weeks	Patient and baby doing well at 6 weeks follow-up

at 23 weeks' gestation and 25 weeks' gestation for brain metastases; patient took ongoing trastuzumab; forceps-assisted delivery occurred at 37 weeks' gestation; baby continued to do well up to 28 months follow-up. Gupta *et al*.[5] presented the case of a 24-year-old female, diagnosed with intracranial metastases at 22 weeks' gestation, who received whole brain radiation and dexamethasone; patient underwent a cesarean section at 38 weeks; baby continued to do well at 6 months follow-up. Okuda *et al*.[10] noted a 35-year-old female who underwent a craniotomy for a metastases at 18 weeks' gestation, however, symptoms worsened, necessitating a termination of pregnancy at 21 weeks' gestation, followed by aggressive whole brain radiation and adjuvant chemotherapy.

Chemotherapy for the treatment of breast cancer during pregnancy appears to be well-tolerated by the fetus; a large series reported 104 cases where chemotherapy was given starting at a mean gestational age of 20.4 weeks; the malformation rate of exposed neonates was not significantly different than the general population.[2] Radiation to the brain may be feasible during pregnancy, if adjusted accordingly. Mazonakis *et al*.[9] demonstrated that, for an isocentric dose of 65 Gy, the radiation dose to the fetus does not exceed 100 mGy, a limit where risks toward the fetus are effectively marginalized.[14] According to a meta-analysis by Cohen-Kerem *et al*.,[4] non-obstetric surgery during pregnancy does not heighten the risk of birth defects, even during the first trimester. On the other hand, scant data exists regarding craniotomies for tumor resection.[3,6] The American College of Obstetrics and Gynecology endorses fetal ultrasound and Doppler before and after the procedure and states that known anesthesia has not been linked to teratogenic effects at any gestational age.[1] Overall, pregnancy-associated breast cancer is more advanced and aggressive at diagnosis than breast cancer during non-pregnancy; on the other hand, patients who become pregnant after breast cancer do not appear to have worse outcomes than patients who do not become pregnant.[11]

Our patient is the fourth case of breast cancer metastases to the brain. She was able to undergo two craniotomies, at 16 weeks' gestation and at 27 week's gestation, without surgical complications. Her baby was delivered at 32 weeks' gestation; though the patient exhibited low gestational weight, the patient exhibited no malformation.

CONCLUSION

There is a lack of guidelines and clinical consensus on medical and surgical treatment for breast cancer metastases in pregnant patients. Treatment usually varies based upon underlying tumor burden, location, gestational age of the fetus, and patient's preference and symptomatology. In this patient, our treatment rationale was based upon prolonging the gestational age and attempted gross total-resection of the metastases.

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Conflicts of interest
There are no conflicts of interest.

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