CASE REPORT

Triple-negative breast cancer with brain metastasis in a pregnant woman

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SUMMARY

A woman aged 35 years was diagnosed with triple-negative breast cancer in October 2012. During the investigation, it was discovered that she was pregnant, the patient decided to have an abortion. She was submitted to a radical modified mastectomy and adjuvant chemotherapy followed by adjuvant breast radiotherapy of the left breast. 2 months after the adjuvant treatment, she began to have headaches and dizziness. The cranial MRI (head MRI) showed brain metastasis. She was then treated with whole brain radiotherapy, stereotactic radiosurgery and concomitant temozolomide which resulted in complete response. 1.5 year later, she was able to get pregnant and gave birth to a baby without complications. The previous imaging reassessment performed in September 2016 shows no evidence of recurrent breast cancer.

BACKGROUND

Breast cancer during pregnancy is very rare and diagnosed in about 1 pregnant woman out of 3000.¹

Breast cancer is also one of the most common malignancies that cause central nervous system (CNS) metastasis.² The 10-year incidence of CNS involvement in early-stage breast cancer is 5.2%;³ and 10–15% of the patients with metastatic breast cancer (MBC) develop CNS metastasis.⁴ However, considering previous autopsy series, the real incidence of CNS metastases in MBC patients is probably higher and detected in ~30% of the patients.^{5 6}

The prognosis of patients with breast cancer who develop brain metastases is influenced by several factors. Tumour subtypes have been related with the prognosis and the overall survival of such patients.⁷ Considering all of the molecular subtypes, the triple-negative breast cancer (TNBC) is the one with the worst prognosis and is associated with an overall survival of 3–4 months.^{8 9}

CASE PRESENTATION

A woman aged 35 years with no personal or oncological history noted a lump in the left breast in August 2012. For this reason, an eco-mammogram was performed which showed a nodule of 25×12×34 mm in the superior-outer quadrant of the left breast.

In October 2012, she underwent a core needle biopsy that showed aspects compatible with invasive ductal carcinoma, receptors of oestrogens and progesterone negative, *Cerb-B2*–2 +, *FISH*– and *Ki-67* of 100% (TNBC).

Remaining imaging studies were carried out and showed no metastatic disease.

At that time, it was discovered that she was 12 weeks pregnant. The treatment options were explained to the patient, but by a personal choice, she decided to abort.

A radical modified mastectomy was performed in November 2012. Anatomopathology showed an invasive ductal carcinoma. Of the 20 axillary nodes, 19 were with metastasis, pT3 pN3a M0, corresponding to a stage IIIC.

She underwent adjuvant chemotherapy from November 2012 to March 2013 with docetaxel, adriamycin and cyclophosphamide for six cycles followed by adjuvant breast radiotherapy until May 2013.

In July 2013, she began to have headaches and dizziness during 5 days.

For this reason, a head MRI was performed which showed the presence of brain lesions in the right temporal and cortico-subcortical junction, in the region of the internal capsule, the left caudate nucleus and the right cortico-subcortical frontal and parasagittal area (figures 1 and 2).

Chest–abdomen–pelvis tomography at that time showed no evidence of metastatic disease.

Figure 1 Head MRI performed in July 2013 showing brain metastasis in the right temporal and cortical–subcortical junction.

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Figure 2 Head MRI performed in July 2013 showing brain metastasis in the left caudate nucleus.

Between July and August 2013 was treated with whole brain radiotherapy (WBRT) and stereotactic radiosurgery (SRS) with concomitant temozolomide.

The head MRI performed in November 2013 showed an almost total regression of the metastatic lesions with only residual areas of about 1 mm in the right temporal cortex and in the left internal capsule.

The genetic studies showed no mutations in the BRCA 1 or 2 genes.

Subsequent follow-up imaging studies were without detectable lesions or evidence of disease recurrence.

In February 2015, she started having bone pain at the right ileopubic level. Imaging studies showed changes compatibles with aseptic necrosis of the head of the right femur (figure 3). Bone scintigraphy showed no metastatic lesions.

During the investigation, it was detected and later confirmed that she was 19 weeks pregnant having chosen not to end it. She was evaluated in orthopaedics and managed with conservative treatment.

She gave birth to a baby at 37 weeks without complications.

A total right hip prosthesis was placed in December 2015 (figure 4).

OUTCOME AND FOLLOW-UP

The patient completed WBRT, SRS and chemotherapy more than 3 years ago.

She has been on regular oncological follow-up and the previous imaging reassessment of September 2016 continues to show no evidence of recurrent breast cancer.

DISCUSSION

Breast cancer in pregnancy increases as more women became pregnant at a later age. The management of a pregnant woman with breast cancer is challenging and involves the collaboration of a multidisciplinary team. In this case, the patient did not know that she was pregnant until the time of the diagnosis of the malignancy and opted to end the pregnancy.

Figure 3 Pelvic X-ray performed in February 2015 with changes compatibles with aseptic necrosis of the head of the right femur.

Figure 4 Pelvic X-ray performed in December 2015 showing the total right hip prosthesis.

TNBC is defined by the lack of receptors of oestrogen, progesterone and HER2. It is a molecular subtype that has a bad prognosis, early CNS metastasis and a short survival.^{10 11}

In most studies, the use of WBRT extended the survival to 3–5 months.^{12 13}

SRS is a method that delivers a high-dose fraction of ionising radiation to a small and defined target volume.^{14 15} It can be performed in any brain location¹⁶ and used to treat multiple brain lesions.^{17 18}

An overall survival improvement of 1.6 months was observed in the subgroup of patients with a single brain metastasis who received WBRT and SRS.¹⁹

Patients with brain metastases from TNBC lacks targeted therapies and chemotherapy is the only systemic option.

Temozolomide is an orally administered alkylating agent with the ability to cross the blood–brain barrier.²⁰ The efficacy of temozolomide in monotherapy is modest, but the studies combining temozolomide with WBRT reported more favourable response rates and a median overall survival of 4.1–12 months.²¹

The highest objective response rate in trials that combined temozolomide with radiotherapy was achieved in patients with brain metastases from advanced lung and breast cancer.²²

In this case, after WBRT, SRS and concomitant temozolomide, the patient had a complete response and remains free of disease after more than 3 years.

Given the lack of effective treatment options for patients with breast cancer and brain metastases, this currently represents a field with a lot of room for improvement and in which more effective therapies are needed.²³

Learning points

- Think about the possibility that a woman with cancer in fertile age could be pregnant.
- In oncological patients with neurological symptoms, brain metastasis must be excluded.
- Always consider bone metastasis in patients with bone pain.

Contributors TT identified and managed the case. MI, RD and FT managed the case. All authors contributed in the writing of the paper and approved the final manuscript.

Competing interests None declared.

Patient consent Obtained.

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