Complete Response of Brain Metastases Originating in Breast Cancer to Capecitabine Therapy

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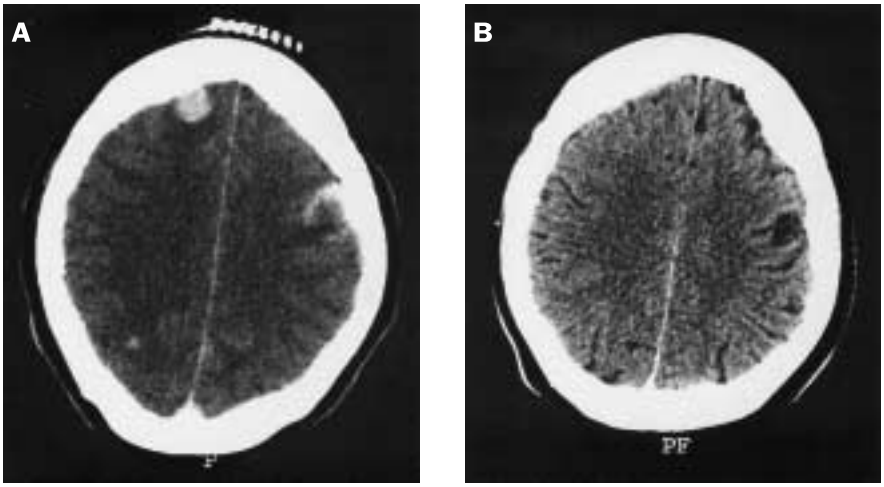
Brain metastatses are often pre-terminal events in patients with solid cancers; median survival is only a few months. We report the case of a heavily pretreated breast cancer patient who developed brain metastases along with ascites due to profound liver involvement. Symptoms rapidly resolved upon initiation of capecitabine therapy. Imaging studies showed complete resolution of the brain metastases.

Patient Description

A 53 year old peri-menopausal woman diagnosed 3.5 years earlier with receptor-positive Her2-negative cT4N1M1 breast cancer (bone and pulmonary metastases) received systemic therapy with the CAF combination (cyclophosphamide, doxorubicin, 5-fluorouracil) followed by tamoxifen. Upon the development of liver metastases she received sequential therapy with paclitaxel, vinorelbine and anastrozole. In July 2001, the patient complained of headache and was found to have minimal disturbances in gait and speech.

Computerized tomography of the brain with intravenous contract material revealed multiple cerebral and cerebellar lesions surrounded by edema and measuring up to 2.2 cm [Figure A]; hydrocephalus of lateral and third ventricles was noted. Abdominal CT scan showed progression of multiple known liver metastases. Steroids were given along with whole-brain irradiation to 3,000 cGy in daily fractionation of 300 cGy. A follow-up brain CT scan with intravenous contract material performed 6 weeks after completion of irradiation showed stable brain lesions (response less than 30%, defined according to the RECIST criteria by measuring five target lesions). Clinically, the patient was free of neurologic complaints.



[A] CT scan of the brain, showing two of several measurable lesions: one in the left frontal lobe, the other in the right frontoparietal lobe. The lesions are surrounded by edema. The findings are consistent with brain metastases.
[B] CT of the brain after cycle 10 of capecitabine, showing complete resolution of brain metastases.

Her performance status, however, deteriorated to 3 (World Health Organization criteria) and she developed new ascites, prominent pedal edema, and marked elevation of liver function tests. Oral capecitabine was started at 2,000 mg/m^2/day on days 1 to 14 on 21 day cycles together with diuretics. A repeat clinical evaluation after three cycles of therapy showed that the patient's performance status was 0; she lost 10 kg in weight and there was complete resolution of ascites and pedal edema and near normalization of liver function tests. A brain CT scan with intravenous contract material after cycle 10 of therapy showed complete resolution of cerebral and cerebellar metastases [Figure B]. Liver scans demonstrated small areas of persistent abnormality, which could represent metastases or scarring; the ascites completely resolved. After continuation therapy for 30 cycles she is now free of cancer symptoms and complains only of drug-related grade 1-2 hand foot syndrome.

Comment

Brain metastases are found in 20–30% of patients with metastatic breast cancer at the time of death. With steroids and irradiation the median survival time is 6–7 months in those with good performance status and controlled systemic disease, but only 2–3 months in others [1]. Most

chemotherapeutic agents used to treat breast cancer do not penetrate the blood-brain barrier. Nonetheless, responses in 38–61% of brain metastases and a median survival time of 8–12 months were reported in previously untreated breast cancer patients receiving cyclophosphamide, 5-fluorouracil, prednisone, doxorubicin, methotrexate, vincristine, cisplatin and etoposide in various combinations, possibly due to disturbances in the BBB by the metastatic process [2]. Anecdotally, hormonal agents such as tamoxifen and megestrol acetate have also elicited response [3]. In heavily pretreated patients, topotecan, an agent thought to penetrate the BBB, is associated with a 37% response of brain metastases and median survival time of 6.25 months [4]. Wang et al. [5] reported brain metastases originating in cancer of the breast and responding to capecitabine.

Maximal radiation effect is usually observed 4–6 weeks after irradiation completion. The late (10 months) complete disappearance of brain lesions together with normalization of liver enzymes, complete resolution of ascites and pedal edema, normalization of liver enzymes and change in performance status from 3 to 0 suggest that all these events are likely capecitabine-related. Capecitabine is a fluoropyrimidine carbamate with antineoplastic activity. It is an orally administered systemic prodrug of 5'-deoxy-5-fluorouridine that is converted to 5-fluorouracil. This drug has been approved by the U.S. Food and Drug Administration for the treatment of metastatic breast and colorectal cancer. In the era of modern oncology, more heavily pretreated patients might present with brain metastases at late stages of their disease. Capecitabine produces systemic responses in 20% of breast cancer patients in whom anthracyclines and taxanes failed, and it is relatively well tolerated.

The original phase II studies in breast cancer patients excluded women with brain metastases. Our report, as well as the one by Wang et al. [5], suggests that capecitabine might prove to be a convenient and beneficial option for some patients with brain metastases.

BBB = blood-brain barrier

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