# Brief Report of a Special Case Excellent response to letrozole in brain metastases from breast cancer

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# Summary

Breast cancer with multiple parenchymal brain metastases carries an extremely poor outcome. Cranial radiotherapy improves survival by only a few months and the role of systemic therapy is marginal and largely unexplored. We report a patient with recurrent carcinoma of breast presenting with multiple bilateral cervical nodes and brain metastases manifesting as a right hemiparesis and facial nerve palsy, who was treated with palliative whole brain irradiation and letrozole. At the follow up at 20 months, neurological function had fully recovered, and both cerebral and extracerebral lesions had completely resolved, with calcification of the cerebral lesions. This report suggests that letrozole has beneficial effects both in extracranial and intracranial disease in hormone responsive metastatic breast cancer.

*Keywords:* Breast cancer; brain metastases; letrozole; radiotherapy.

#### Introduction

Brain metastases are seen in 10–30% of patients with metastatic breast cancer. Cranial radiotherapy is the standard treatment. The role of chemotherapy is evolving, with the availability of newer agents such as temozolomide, which cross the blood brain barrier (BBB), while that of hormone therapy is largely unclear. We report a patient with breast cancer, with brain and cervical nodal metastases developing after a long disease-free period, and a dramatic and sustained response with whole brain irradiation (WBRT) and letrozole.

#### **Clinical details**

A 51 year old postmenopausal female presented with severe headache and vomiting for 2 months, and rightsided weakness for 1 month. She gave no history of seizures or visual impairment. She had been treated 10 years earlier for hormone receptor-positive invasive ductal carcinoma of the right breast  $(T_3N_1M_0)$ , with radical mastectomy, anthracycline-based chemotherapy, and 5 years of tamoxifen. Examination revealed poor performance status, muffled speech, right facial nerve palsy, right hemiparesis and unstable gait, multiple right cervical lymph nodes each 1-2 cm in size and a left supraclavicular node positive for malignancy. No local or contralateral breast recurrence was evident. The CT brain suggested multiple brain metastases (Fig. 1a and b). Other systemic workup was normal. She received medical decompression with steroids and diuretics, and palliative WBRT (20 Gray in 5 fractions). One month later, she showed marginal neurological improvement. Letrozole (2.5 mg daily) was started after she refused chemotherapy. Twenty months later, her neurological deficits and lymphadenopathy had disappeared. The CT head showed calcification of cerebral lesions. Perilesional edema had resolved (Fig. 1c). Locoregional and systemic workup returned normal. Maintenance letrozole monotherapy was continued.

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Fig. 1. (a) Transverse and (b) Coronal views of CT brain (contrast enhanced) showing well defined rounded lesions with thick peripheral nodular enhancement, central necrosis and perifocal oedema scattered in both cerebral hemispheres in a patient with breast cancer. (c) CT head of the same patient with contrast showing several small calcified metastases scattered bilaterally and complete resolution of the perilesional oedema following cranial irradiation and letrozole therapy

## Discussion

CNS-metastatic breast cancer has a median survival of 2-8 months with WBRT. Intensified local treatment (resection or radiosurgery) may increase survival time. BBB disruption due to metastases or radiotherapy may increase the intracerebral concentration of methotrexate, fluorouracil, cisplatin and temozolomide [5]. Receptorpositive disease has a favorable outcome but the role of hormone therapy is unknown. Tamoxifen and metabolites have a 46-fold higher concentration in brain metastases and brain tissue than in serum [1]. Isolated reports have shown near-complete responses with tamoxifen and magestrol acetate [4, 6]. Tamoxifen failures unfit for chemotherapy have limited options. Data on CNS activity of aromatase inhibitors is lacking. Letrozole monotherapy has produced calcification of cerebral lesions and resolution of scalp metastases, and responses in leptomeningeal metastases in conjunction with chemotherapy, with progression-free survival of 17-20 months [2, 3]. Similar observation in the present report strengthens the case for use of aromatase inhibitors. Calcification of cerebral metastatic lesions is uncommon and has been observed earlier by Madhup et al., suggesting that such a mechanism of healing may be unique to letrozole [2].

This report presents several key observations. Hormonereceptor positivity and long recurrence-free interval were favourable features while several others including poor performance status, multiple parenchymal brain lesions, extracranial disease, and poor response to steroids and radiotherapy suggest an aggressive disease. The excellent response to letrozole suggests that it is a viable option even in intracranial disease, and the mechanism of action and quantum of benefit needs prospective evaluation in clinical trials.

## References

- Lien EA, Wester K, Lonning PE, Solheim E, Ueland PM (1991) Distribution of tamoxifen and metabolites into brain tissue and brain metastases in breast cancer patients. Br J Cancer 63: 641–645
- Madhup R, Kirti S, Bhatt ML, Srivastava PK, Srivastava M, Kumar S (2006) Letrozole for brain and scalp metastases from breast cancer – a case report. Breast 15: 440–442
- Ozdogan M, Samur M, Bozcuk HS, Sagtas E, Yildiz M, Artac M, Savas B (2003) Durable remission of leptomeningeal metastasis of breast cancer with letrozole: a case report and implications of biomarkers on treatment selection. Jpn J Clin Oncol 33: 229–231
- Pors H, von Eyben FE, Sorensen OS, Larsen M (1991) Long term remission of multiple brain metastases with tamoxifen. J Neurooncol 10: 173–177
- Rosner D, Nemoto T, Lane WW (1986) Chemotherapy induces regression of brain metastases in breast carcinoma. Cancer 58: 832–839
- Stewart DJ, Dahrouge S (1995) Response of brain metastases from breast cancer to megestrol acetate: a case report. J Neurooncol 24: 299–301

## Comment

The clinical problem in this paper has been very much in the hands of oncologists at this late phase of illness and is actually well suited for a case study. The patient had multiple brain metastases, with very short life prognoses and was confused with hemipareses. She was given corticoids and 5 WBRT shots, improves, goes home with letrozole and comes back after almost two years practically cured with small changes in CT.

The cure is amazing, but there were positive prognostic signs, metastases came late, it was ER+, there are 10-15% of patients with WBRT treatment only who may live for 2–3 years [1]. The molecular background has not been discussed or investigated, but of course who would have done it then. The question remains: should it be published so people could learn from lost and forgotten cases and keep their eyes and ears open.

This cannot be an example for everyone how to treat very ill, almost lost patients with this disease. It is an economic but as well an ethical quality of life question, in Western Europe and not less in India. The authors say nicely, that more research is needed, but I hope that this research has started already. The authors should check in a more controlled and prospective way some 8–12 of their own patients and go back to their patients treated at the time of aromatase inhibitors for breast tumour brain metastases to confirm the value of this early finding.

## Reference

 LeScodan R, Massard C, Mouret Fourme E *et al* (2007) Brain metastases from breast carcinoma; validation of the RTOG RPA classification and proposition of a new psognostic scale. Int J Radiat Oncol Biol Phys 69(3): 839–845

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