European Journal of Cancer, Vol. 33, No. 13, pp. 2282–2283, 1997

Printed in Great Britain
0959-8049/97 $17.00+0.00

Letters

PII: S0959-8049(97)00258-X

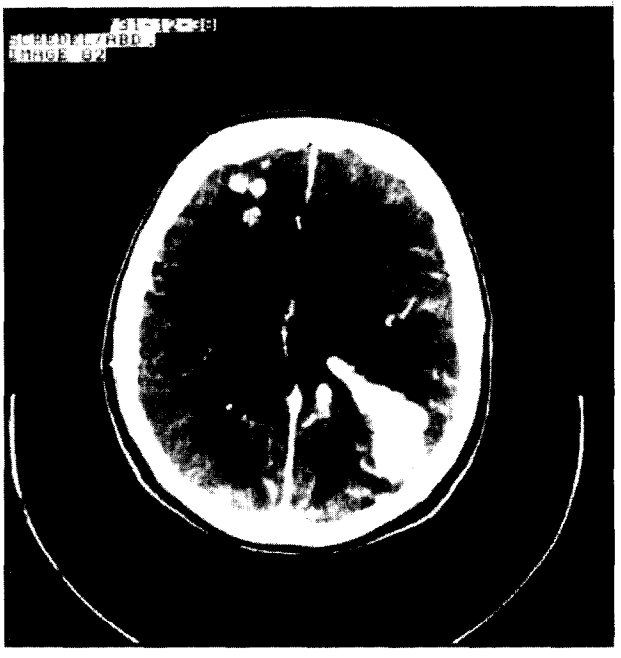
A Case of Brain Metastases from Male Breast Cancer Responding to Tamoxifen

R.E.N. van Rijswijk,[1]
R.J. van Oostenbrugge[2] and
A. Twijnstra[2]

[1]Department of Internal Medicine,
Division of Hematology/Oncology; and
[2]Department of Neurology,
University Hospital of Maastricht,
P. Debyelaan 25, 6202 AZ Maastricht,
The Netherlands

BRAIN METASTASES from breast cancer, especially in the presence of systemic disease, have a poor prognosis. The treatment usually consists of palliative radiotherapy, but incidental responses to hormonal treatment occur [1–4]. We report a male breast cancer patient with brain metastases responding to tamoxifen. In May 1991, at the age of 53 years, the patient underwent a right-sided modified radical mastectomy and axillary lymph node dissection because of a stage $T_1N_0M_0$ oestrogen-receptor positive (ER 100 fmol/mg protein) ductal carcinoma. His previous history was unremarkable and he had never smoked. The family history revealed a sister who had died of liver metastases presumably from colorectal cancer, whereas his father had died of lung cancer. In May 1994, a large-cell adenocarcinoma of the left hilar region and enlarged pretracheal lymph nodes were diagnosed, initially considered to represent a second primary. The lesion was treated with radiotherapy. After pathological revision it was concluded that the lung tumour was most probably metastatic disease, despite an immunohistochemically negative oestrogen receptor, as the bronchial biopsy showed submucosally growing tumour. The small biopsy did not allow for any biochemical assay. In April 1996, the patient experienced slight nausea and vomiting. At physical examination, a cytologically proven adenocarcinoma metastasis was detected in the right neck. Ultrasound of the liver and bone scan did not show other tumour localisations. Tamoxifen 40 mg per day was prescribed, but the patient stopped the medication after 10 days of treatment because of dizziness, nausea and vomiting. In May 1996, nausea and vomiting had worsened, and the patient also complained of visual deterioration.

(a)



(b)

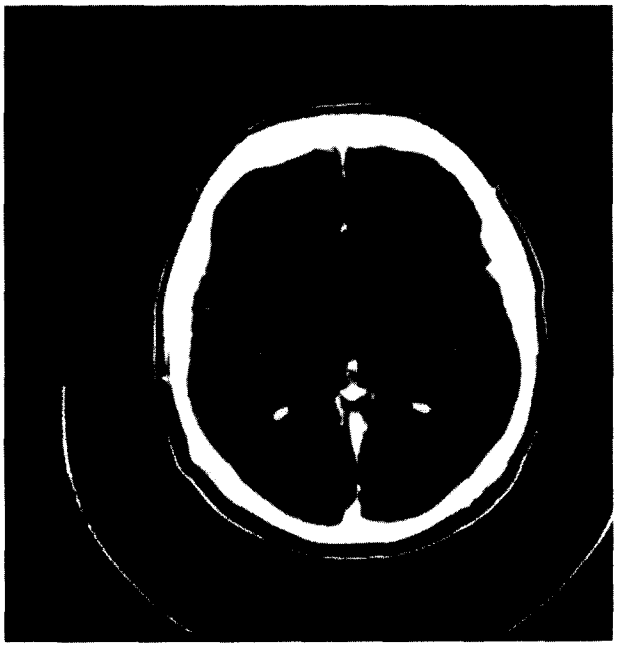


Figure 1. (a) Computer tomography (CT) with contrast of the brain showing multiple supratentorial enhancing lesions with oedema. (b) CT scan 6 months later, showing the complete resolution of the brain metastases with tamoxifen treatment.

Correspondence to R.E.N. van Rijswijk.
Received 28 Apr. 1997; accepted 7 May 1997.

Physical examination revealed cachexia, bradyphrenia, right-sided homonymous hemianopia, a slight motoric aphasia and ptosis of the left eye due to oedema of the eyelid. The mass in the neck was 3 cm in diameter. Computer tomography (CT) of the brain showed multiple cerebral and cerebellar metastases, including a large mass in the left occipital area (Figure 1(a)). Chest X-ray showed no new lesions, but a CT scan of the abdomen showed four suspected peritoneal lesions, while the liver was uninvolved. Treatment consisted of dexamethasone 4 mg four times daily and ranitidine 150 mg twice daily, and tamoxifen was restarted at a dose of 20 mg daily. However, the patient refused radiotherapy to the brain. The treatment resulted in a good symptomatic response until he developed progressive fatigue in July 1996. At that time he was found to have a severe normocytic anaemia (haemoglobin 4.7 mmol/l, prior value in May 8.7 mmol/l), tentatively due to gastrointestinal haemorrhage. Despite the fact that the patient had stopped taking dexamethasone after approximately 10 days, he had no headache, diplopia or other neurological complaints. Six months after the diagnosis of brain metastases, a CT scan of the brain was repeated showing complete resolution of the brain metastases (Figure 1(b)). Also the cervical mass disappeared. The only medication he is currently using consists of tamoxifen 20 mg daily.

Tamoxifen is considered to be the first-line hormonal treatment for male patients with breast cancer [5, 6]. The drug is lipophilic and high concentrations, up to 46-fold higher than the serum concentration, of the parent compound and its main metabolites have been found in brain metastases [7]. Anecdotal reports exist of female breast cancer patients whose brain metastases responded to tamoxifen, but we are unaware of previous reports showing a similar response in male breast cancer patients.

1. Stewart DJ, Dahrouge S. Response of brain metastases from breast cancer to megestrol acetate: a case report. *J Neurooncol* 1995, **24**, 299–301.
2. Salvati M, Cervoni L, Innocenzi G, Bardella L. Prolonged stabilization of multiple and single brain metastases from breast cancer with tamoxifen. Report of three cases. *Tumori* 1993, **79**, 359–362.
3. Pors H, von Eyben FE, Sorensen OS, Larsen M. Longterm remission of multiple brain metastases with tamoxifen. *J Neurooncol* 1991, **10**, 173–177.
4. Hansen SB, Galsgard H, von Eyben FE, Westergaard-Nielsen V, Wolf-Jensen J. Tamoxifen for brain metastases from breast cancer. *Ann Neurol* 1986, **20**, 544.
5. Cutuli B, Lacroze M, Dilhuydy JM, *et al.* Male breast cancer: results of the treatments and prognostic factors in 397 cases. *Eur J Cancer* 1995, **31A**, 1960–1964.
6. Sandler B, Carman C, Perry RR. Cancer of the male breast. *Am Surg* 1994, **60**, 816–820.
7. Lien EA, Wester K, Lønning PE, Solheim E, Ueland PM. Distribution of tamoxifen and metabolites into brain tissue and brain metastases in breast cancer patients. *Br J Cancer* 1991, **63**, 641–645.

European Journal of Cancer, Vol. 33, No. 13, pp. 2283–2284, 1997

Printed in Great Britain
0959-8049/97 $17.00+0.00

PII: S0959-8049(97)00223-2

Co-segregation of *BRCA1* 185delAG Mutation and *BRCA2* 6174delT in One Single Family

R. Gershoni-Baruch,[1,3] E. Dagan,[1] I. Kepten[1] and G. Freid[2]

[1]Department of Medical Genetics; [2]Department of Oncology, Rambam Medical Centre, Technion, Israel Institute of Technology, PO Box 31096, Haifa, Israel; and [3]the Bruce Rappoport Faculty of Medicine, Haifa, Israel

BRCA1 185delAG mutation and *BRCA2* 6174delT mutation constitute the two most frequent mutation alleles predisposing to hereditary breast cancer in the Ashkenazi Jewish population with reported carrier frequencies of 1.09% and 1.52%, respectively [1]. Yet, the calculated contribution of the *BRCA1* 185delAG mutation and the *BRCA2* 6174delT mutation to breast cancer cases diagnosed before the age of 50 years in Ashkenazi Jewish women is approximately 20% and 8%, respectively [2, 3]. *BRCA1* 5382insC is another mutation over-represented in the Ashkenazi Jewish population with a reported carrier frequency of 0.13% [1]. These numbers taken together indicate that the penetrance of *BRCA1* 185delAG mutation is approximately four times that of *BRCA2* 6174delT mutation. The relative risk of developing breast cancer by the age of 42 years is estimated to be 9.3 for 6174delT compared to 31 for 185delAG [4].

Two sisters with breast cancer were referred to us for genetic testing. The younger sister, currently 52 years old, had bilateral breast cancer and underwent right mastectomy at the age of 41 years and left lumpectomy at the age of 50 years. She was found to carry *BRCA1* 185delAG. Her elder sister, currently 56 years old, who at the age of 54 underwent left lumpectomy for breast cancer, tested negative for the 185delAG mutation and was rather considered to have sporadic breast cancer, until further testing showed her to carry the *BRCA2* 6174delT mutation.

Noteworthy is the occurrence of monolateral breast cancer at the age of 54 years in one sister carrying the *BRCA2* 6174delT mutation as opposed to the occurrence of bilateral breast cancer at ages 41 and 50 years, respectively, in the younger sister, carrying the *BRCA1* 185delAG mutation. This case, although single, might serve to underline the observation that the *BRCA2* 6174delT mutation has a lower penetrance compared to *BRCA1* 185delAG. Differences in the cumulative lifetime penetrance for the common Ashkenazi mutations has been noted and it remains to be determined how much of the low penetrance attributed to the *BRCA2* 6174delT mutation is due to a late onset effect.

Correspondence to R. Gershoni-Baruch.
Received 9 Apr. 1997; accepted 21 Apr. 1997.