Acta Oncologica, 2007; 46: 565–566

informa
healthcare

LETTER TO THE EDITOR

Comment on: Incidence, pattern and timing of brain metastases among patients with advanced breast cancer treated with trastuzumab

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To the Editor

We read with interest the article by Yau et al. focusing on incidence, pattern and timing of brain metastases among patients with advanced breast cancer (ABC) treated with trastuzumab [1]. This case series, like several other recent studies [2], reports frequent observation of central nervous system (CNS) recurrence during treatment with trastuzumab.

We would like to stress these findings, reporting here our experience in 14 patients with ABC receiving trastuzumab and chemotherapy, with emphasis on neurological symptoms. Seven of 14 patients (50%) developed brain metastases and underwent a complete neurological evaluation. Table I synthesizes their main characteristics and outcome. Median time from the beginning of the treatment with trastuzumab plus chemotherapy to the diagnosis of brain metastases was 16 months (range 7 – 33). Several neurological symptoms were present, but, interestingly, headache was the most common neurological symptom indicative of CNS involvement at diagnosis (six of seven patients; 85%). At CT scan evaluation of the brain, only one patient had a single metastasis and none of the lesions showed signs of haemorrhage. Six patients received whole brain radiotherapy and one did not receive any treatment due to early death. Median survival was 6 months (range 1 – 11), calculated from the diagnosis of brain metastases.

We agree with Yau and coworkers on the importance of having vigilant surveillance in asymptomatic patients. Physicians should also be aware of the possibility that symptoms related to CNS metastatic involvement can occur in the setting of a good control of neoplastic disease outside the CNS. When this happens, headache can represent an important early symptom. A constant, progressively increasing pain, or a change in the characteristics of

Table I. Clinical characteristics and outcome of seven patients with brain metastases.

Age (years)	Time from trastuzumab start (months)	Neurological symptoms at brain mts. diagnosis	No. of lesions at brain CT scan	Treatment for brain mts. (response)	Survival from brain mts. diagnosis (months)	Status
38	18	headache	4	Radiotherapy (PD)	1	Dead
59	33	impaired walk with fall	1	Radiotherapy (NC)	7	Dead
60	16	headache, impaired walk	5	Radiotherapy (PR)	6	Dead
60	14	headache, cerebral vomiting	8	None (early death)	< 1	Dead
38	24	headache, dysarthria	5	Radiotherapy (PR)	11	Dead
47	8	headache, drowsiness	6	Radiotherapy (PR)	6	Dead
58	7	headache, dizziness, cervical pain	>15	Radiotherapy (PR)	8	Dead

PD = progression disease, NC = no change, PR = partial remission.

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(Received 26 October 2006; accepted 2 November 2006)

ISSN 0284-186X print/ISSN 1651-226X online
DOI: 10.1080/02841860601099258

headache, may be an alert for the physician [3]. CNS remains a sanctuary for the majority of currently available systemic agents. With the more successful and prolonged systemic anti-neoplastic effects achieved in ABC by the presently available drug combinations, the risk of developing CNS metastases might be even higher. This scenario will lead to a consequent more frequent, and possibly earlier, employment of MRI of the brain [4] with the aim of a better clinical surveillance.

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