

Incidence and predictors of cerebral metastases among newly diagnosed breast cancer patients with & without HER-2 neu overexpression

Eman Foad; Eman T. El-Sheikh; Dalia Abdelghany

Department of Clinical Oncology and Nuclear Medicine, Ain Shams University Hospitals, Cairo, Egypt

PAJO, December 2012, 5(2): 16-23

Abstract

Background: CNS metastases contribute to significant morbidity and mortality in patients with advanced cancers. As systemic therapies for cancer continue to improve, it is likely that CNS metastases will become increasingly prevalent and control of extra-cranial disease may no longer be the limiting factor determining the outcome in breast cancer patients with synchronous metastases. Our purpose was to analyze the risk of brain metastasis in patients with human epidermal growth factor receptor 2 (HER-2) positive breast cancer patients in comparison with HER-2 negative patients.

Patients and Methods: To determine the incidence of brain metastases in HER-2-overexpressing patients, data was retrospectively collected and analyzed from the medical records of previously treated 280 HER-2 positive and 760 HER-2 negative patients identified between August 2005 and December 2010 at Ain Shams University, Department of Clinical Oncology and Nuclear Medicine.

Results: Between August 2005 and December 2010, 1040 patients with breast cancer were retrospectively analyzed and included. No adjuvant Herceptin was given. Patients were divided into 2 groups according to HER-2 status: Group A including 760 HER-2 negative patients and group B included 280 HER-2 positive patients. Both groups were matched demographically. After a median follow-up period of 44 months; Brain metastases (BM) were identified in 11.4% (32 patients) with HER-2 overexpressing breast cancer compared with only 3% (23 patients) in the HER-2 negative patients (hazard ratio, 5.09; 95% CI, 2.9 to 12.34; $p=0.006$). Comparisons of overall survival (OS), and disease-free survival (DFS) between group A and group B patients all favored group A. At 5-years the OS rates were 80% and 52% for groups A and B respectively ($p=0.001$), while DFS rates were 71% and 48% in groups A and B respectively ($p=0.001$). HER-2 positive patients had a 5-year brain metastasis-free survival of 86.6% versus 90% for HER-2-negative patients ($p=0.001$). HER-2-overexpression, hormone receptor negativity, tumor size larger than 2 cm, lymph node positive disease and lung metastases were predictors of brain metastases in univariate analysis. Multivariate analysis confirmed these prognostic factors to be significantly associated with increased risk of brain metastasis.

Conclusion: We have shown that patients with newly diagnosed breast cancer and HER-2 – overexpressing tumors are at increased risk for brain metastases. Because more than two thirds of brain metastases occur after the development of systemic disease, these findings prompt consideration of brain prophylaxis strategies with HER-2 inhibiting small molecules able to cross the blood brain barrier and/or serial radiologic screening to detect asymptomatic brain metastases.