Prevalence and clinicopathological factors of brain metastasis in EGFR mutant NSCLC

RattanawadeeTeocharoen MD, KomkritRuangritchankul MD, PiyadaSitthideatphaiboon MD

Background: Despite advances in systemic therapy and improvements in survival for advanced epidermal growth factor receptor (EGFR) mutant non-small cell lung cancer (NSCLC), brain metastasis (BM) remains a major problem and poor outcome. This study aimed to determine factors predicting BM in EGFR mutant NSCLC patients.

Methods: We retrospectively analyzed the medical records of patients diagnosed with recurrent or metastatic NSCLC who were enrolled in the King Chulalongkorn Memorial Hospital (KCMH) during January 2013 to December 2017. Formalin-fixed paraffin embedded tissues were analyzed for vimentin/E-cadherin expression using immunohistochemistry (IHC). The clinicopathologic factors and treatment outcomes were analyzed in correlation with BM status (with Chi-square or Fisher exact test). Univariate and multivariate analysis assessed factors associated with the development of brain metastases and analyzed by odds ratios (OR). Survival data was analyzed using the Kaplan-Meier method and was compared between groups by the log-rank test. Hazard ratios (HR) and corresponding 95% confidence intervals (95% CI) were calculated. The p value less than 0.05 was considered as statistically significant.

Results: A total of 948 patients were included, from which 449 patients had been tested for EGFR mutation and mutated-EGFRs were found in 304 (67.7%) patients. Of these, 73 patients (24%) experienced BM at diagnosis and 76 patients (25%) developed BM in the course of their disease. EGFR-mutant patients were more likely to develop BM in the course of disease than EGFR-wild type patients (25% vs 17.8% respectively, p=0.020). Heterogeneity in factors determined BM were identified. In multivariate analysis, patients who had BM at diagnosis were associated with aged <60 years (OR 2.81, 95% CI 1.51 to 5.24, p=0.001) and ≥3 metastatic sites (OR 3.00, 95% CI 1.57 to 5.74, p=0.001) whereas only age <60 years (OR 2.63, 95% CI 1.47 to 4.69, p=0.001) was associated with subsequent BM compared to patients without BM. Moreover, high vimentin expression also predicted overall BM development in EGFR-mutant patients (67.4% vs. 32.6%, respectively, OR 2.88, 95% CI 1.35 to 6.16; p= 0.006) and conferred worse survival. Median overall survival was 20.00 months (95% CI, 14.51 to 25.50) in high vimentin expression and 30.91 months (95% CI, 20.98 to 40.84) in low vimentin expression, respectively (HR, 1.56; p=0.040).

Conclusions: The Incidence of BM in EGFR-mutant NSCLC was 49%. Younger patients with EGFR mutation who had high disease burden were more likely to development of BM. Vimentin served as biomarker predicting BM and poor prognostic factor in EGFR-mutant patients. Our findings may have important implications for treatment and follow-up strategies in these high-risk patients. Vimentin may be a prognostic biomarker and therapeutic target for brain metastasis in patients with EGFR mutant NSCLC.