Aim: BM DTC detection is known to be a prognostic factor for distant metastasis and overall survival in early breast cancer. However, distant relapses may occur in patients with no DTC detected at time of primary cancer. In this study, we studied the impact of early breast cancer pathological features (including BM DTC status) on the incidence of CNS metastases.

Methods: In a cohort (1998-2005) of 620 early breast cancer patients in whom BM DTC were detected using an anti-cytokeratin antibody (A45B/B3), 137 had a later metastatic relapse (median follow up 11y). Chi2 test were performed to compare patient with CNS metastasis and patients with other metastases locations. CNS metastasis survivals were estimated using Kaplan-Meier method and compared by log-rank test.

Results: Distant metastases were diagnosed in 137 (22%) patients. In the course of the metastatic disease, 55 of these patients (40%) have been diagnosed with CNS metastases (parenchymal = 30, leptomeningeal = 10, both localizations = 15), as first metastatic or later event. Patients with CNS metastases were mostly less than 50 years old (60% vs 38%, p = 0.01), pN0 (31% vs 10%, p = 0.002), hormonal receptor status negative (54% vs 30%, p = 0.007) and HER2 status positive (50% vs 22%, p = 0.01). Strikingly, although DTC detection was associated with development of distant metastasis in the whole cohort, the occurrence of CNS metastasis was found to be higher in patients who had no DTC detected at primary diagnosis (p = 0.016). From CNS metastasis, median survival was 7.8 months (8.3 months for parenchymal and 2.4 months for leptomeningeal recurrences). For HER2+ patients, the median survival after diagnosis of CNS metastasis was 16.6 months (N = 15) and 4.1 months for Her2- patients (N = 15).

Conclusions: Our study suggests that cancer cells with epithelial differentiation, as detected in the BM, are less prone to CNS dissemination. This study also confirmed previously reported determinants of CNS metastases (age, RH-, HER2+) in the pre-adjuvant trastuzumab era, but also showed that the outcome of HER2+ patients with CNS relapse was longer, probably due to HER2 targeted therapy during metastatic course.

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