ABSTRACT

Introduction: Simultaneous detection of disseminated tumor cells (DTCs) and circulating tumor cells (CTCs) was shown to be associated with an especially poor prognosis and increased incidence of disease-related deaths in non-metastatic breast cancer patients. We analyzed the occurance of DTCs in bone marrow and CTCs in peripheral blood in patients with primary breast cancer, we evaluated the correlation of their presence with other prognostic markers and we investigated the changes in DTCs/CTCs number at different time points during treatment.

Materials and methods: Blood of 50 patients with primary breast cancer were used for immunomagnetic separation and detection of circulating tumor cells using the commercial available system the AdnaTest Breast Cancer™ (AdnaGen GmbH, Langenhagen, Germany). Bone marrow aspirates from 50 patients were analyzed for DTCs by immunocytochemistry using the pancytokeratin antibody conjugated with FITC (Monoclonal Anti-Cytokeratin antibody F3418, Sigma Aldrich, USA).

Results: DTCs were identified in 30% (15/50) and CTCs in 22% (11/50) of patients. We found that DTC positivity could point to a significantly high risk of larger primary tumor size (p- value 0.011) and significantly higher risk of lymph node involvement (p- value 0.002). For CTC positivity, no such relationship was proven. DTCs have shown significantly higher prevalence in ER/PR-negative females and in HER-2-positive cases. CTCs were equally prevalent in patients with the presence and absence of standard prognostic and predictive markers such as ER, PR and HER-2. We found no correlation between CTCs and DTCs findings ($r = -0.097$, $p = 0.504$). We used DTCs/CTCs analysis for therapy monitoring in a small group of 29 patients, who underwent neoadjuvant chemotherapy (NACT). We find out no significant correlation between DTCs/CTCs detection and the primary tumor response to NACT. A pathologic complete response (pCR) was achieved by 31% (9/29) of the patients in our study, however, no association was observed between pCR and the detection of DTCs after NACT.

Conclusion: These results support the use of DTCs/CTCs analysis in early breast cancer to generate clinically useful prognostic information. The study of these cells apart from the impact on refining prognosis, has the exciting potential of individualising treatment for women with breast cancer.

Keywords: breast cancer; disseminated tumor cells; circulating tumor cells; bone marrow aspiration; prognostic/predictive markers; therapy monitoring