Breast Cancer RESEARCH

LETTER

Association between the spread of circulating tumor cells and breast cancer subtypes

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See related research by Fehm *et al.*, http://breast-cancer-research.com/content/11/4/R59

We read with great interest the recent publication by Fehm and coworkers [1] about the association between the spread of circulating tumor cells (CTCs) and breast cancer subtypes. The authors observed that the highest CTC positivity rate was obtained in triple-negative patients followed by those with estrogen receptor (ER)-positive and/or progesterone receptor (PR)-positive tumors, while no CTCs could be detected in the human epidermal growth factor receptor 2 (HER2)-positive subtype group. However, another study [2] showed contradictory results, indicating that HER2 was the only primary tumor characteristic that correlated with the presence of CTCs, while ER and PR status were not association with their presence.

To clarify the correlation between CTCs and breast cancer subtypes, a total of 156 operable breast cancer patients admitted to our hospital were enrolled. This study was approved by the regional ethics committee. Written informed consent was obtained from all participating patients. Mononuclear cell enrichment and CTC detection were done as previously described [3]. The expression of ER, PR and HER2 in primary tumors was routinely detected.

Results showed that the overall positive rate of CTCs in operable breast cancer patients was 32.1% (50 out of 156). There existed significant differences in the positive rate of CTCs between patients at different pTNM stages (P = 0.0219) and between those with different immunohistochemical subtypes (P = 0.0003). Further analysis revealed that the positive rate of CTCs in the HER2-positive and triple-negative subtypes was significantly higher than that of the luminal subtype (P = 0.0034 and 0.0003, respectively). In subgroup analysis by pTNM stage, significant differences in the positive rate of CTCs between patients with different breast cancer subtypes were identified at stages I (P = 0.0207), II (P = 0.0478) and III (P = 0.0324) (Table 1), further supporting that the presence of CTCs was associated with the HER2-positive and triple-negative subtypes.

Table 1. Correlation of CTCs and immunohistochemical subtypes of breast cancer in subgroup analysis by pTNM stage

	Luminal subtype		HER2-positive subtype		Triple-negative subtype		
pTNM stage	CTC-positive cases	Total cases	CTC-positive cases	Total cases	CTC-positive cases	Total cases	P^a
I	2	23	1	6	4	10	0.0207[b]
II	7	38	5	10	8	18	0.0478
III	8	28	6	9	9	14	0.0324

[a]Pearson's χ^2 test. [b]Fisher's exact test. CTC, circulating tumor cell.

In the present study, the presence of CTCs was more frequently found in patients with HER2-positive and triple-negative subtypes than the luminal subtype, which might be ascribed to primary tumors of the former two subtypes being more aggressive histologically and having increased potential to be invasive, to migrate and to metastasize. In addition, recent research has suggested that the epithelial-mesenchymal transition plays a critical role in cancer progression, which could endow cancer cells with aggressive and stem cell-like properties, and promote the dissemination of CTCs from the primary site to the circulation [4]. Most importantly, it has been shown that CTCs could express epithelial-mesenchymal transition and/or cancer stem cell markers, which would support the hypothesis derived from the clinical data that CTCs are closely associated with distant metastasis in breast cancer patients [5]. Therefore, all these observations further support the need to clarify the correlation of primary tumor characteristics and CTCs in breast cancer patients.

In conclusion, our study suggests that the spread of CTCs was correlated with the HER2-positive and triple-negative subtypes in breast cancer patients. Identifying

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patients at higher risk of harboring CTCs would be helpful for the purpose of establishing the clinical values of CTCs as well as better evaluating the prognosis of breast cancer patients.

Abbreviations

CTC = circulating tumor cell; ER = estrogen receptor; HER = human epidermal growth factor receptor; PR = progesterone receptor.

Competing interests

The authors declare that they have no competing interests.

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