

4th World Congress on

BREAST CANCER

May 08-10, 2017 Singapore

Expression of D2-40 in benign and malignant breast lesions and study the correlation between lymphovascular density and other prognostic factors of breast cancer

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Background: D2-40 is a mouse monoclonal antibody specific for human podoplanin and has been used in identifying lymphovascular invasion (LVI) of tumors also its expression has been used as a marker for myoepithelial cells (MEC) of breast. Lymphangiogenesis, assessed as lymphovascular density (LVD), is the initial step of generalized tumor lymphovascular invasion (LVI). It also involves VEGF-C as the most important protein family. Lymphangiogenesis among breast cancer cases correlates with several clinicopathological factors are important to determine prognosis and treatment strategies, but results have been controversial and require clarification.

Aim: The aim of this work is to explore the expression of D2-40 as a marker for myoepithelial cells (MECs) of the breast lesions, to investigate the clinicopathological significance of VEGF-C, D2-40 expression and lymphovascular density (LVD) in breast cancer patients.

Methods: Sections from 88 paraffin-embedded archival specimens of breast lesions were selected to include benign breast lesions as fibrocystic changes of the breast and ductal hyperplasia (15 cases) and invasive breast cancer (73 cases). Immunohistochemistry (IHC) for D2-40, calponin and VEGF-C were performed and IHC staining results and the associations of intratumoral and peritumoral LVD were correlated with clinicopathological features and prognosis were assessed.

Results: D2-40 highlighted the MECs of benign breast lesions beside its identified lymphatic vessels and LVI in breast carcinomas. VEGF-C expression was significantly higher in invasive breast cancer than benign breast lesions ($p < 0.01$). VEGF-C ($p < 0.001$) expression was significantly associated with peritumoral LVD, but not intratumoral LVD. VEGF-C expression, peritumoral LVD and LVI were significantly associated with lymph node metastasis ($p = 0.025$, $p = 0.006$ and $p = 0.017$, respectively). Moreover, peritumoral LVD was an independent risk factor for axillary lymph node metastasis, disease-free survival in multivariate analysis.

Conclusions: Our results show that D2-40 is a reliable marker highlights MECs in benign breast lesions beside it is a useful tool for identification of LVI in breast carcinomas which is reflecting a potential for lymphatic metastatic spread and possible poor prognosis. Our study also demonstrated that high expression of VEGF-C in invasive breast carcinoma may induce lymphangiogenesis in the peritumoral area. Peritumoral LVD appeared to be a potential independent prognostic factor in breast cancer patients.

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