EXPRESSION OF GALECTIN-3, CYTOKERATIN 19, NEURAL CELL ADHESION MOLECULE AND E-CADHERIN IN CERTAIN VARIANTS OF PAPILLARY THYROID CARCINOMA

Laco J.[1], Ryška A.[1], Čáp J.[2], Čelakovský P.[3]

[1]The Fingerland Department of Pathology, [2]Second Department of Internal Medicine, and [3]Department of Otorhinolaryngology, Charles University Faculty of Medicine and Faculty Hospital in Hradec Králové

Summary

The immunohistochemical expression of galectin-3 (Gal3), cytokeratin 19 (CK19), neural cell adhesion molecule (NCAM), and E-cadherin (Ecad) was evaluated to assess their use in diagnostics of papillary thyroid carcinoma (PTC). A total of 84 PTCs - 36 classical variants (cPTCs), 26 follicular variants (fPTCs), and 22 papillary microcarcinomas (mPTCs) were studied. Expression of Gal3 was found in 36/36 (100%) cPTCs, 24/26 (92%) fPTCs, and 19/22 (86%) mPTCs. CK19 expression was detected in 34/36 (94%) cPTCs, 17/26 (65%) fPTCs, and 13/22 (59%) mPTCs. Expression of NCAM was seen in 5/36 (14%) cPTCs, 7/26 (27%) fPTCs, and 9/22 (41%) mPTCs. Ecad expression was found in 23/36 (64%) cPTCs, 17/26 (65%) fPTCs, and 18/22 (82%) mPTCs. A significant difference in CK19 expression was observed between cPTC and both fPTC and mPTC ($p < 0.001$). Furthermore, extrathyroid tumor spread significantly correlated with both level of CK19 expression and loss of Ecad expression ($p = 0.001$, $p = 0.04$). Our findings suggest that Gal3 and CK19 are useful markers for PTC, although decreased CK19 expression in mPTC and fPTC must be considered. Furthermore, CK19 and Ecad may play a role in extrathyroid tumor spread.

Key words: papillary thyroid carcinoma – galectin-3 – cytokeratin 19 – neural cell adhesion molecule – E-cadherin

Souhrn

Exprese galektinu-3, cytokeratinu 19, neural cell adhesion molecule a E-cadherinu ve variantách papilárního karcinomu štítné žlázy

Cílem studie bylo pomocí nepřímé imunohistochemie zjistit expresi galektinu-3 (Gal3), cytokeratinu 19 (CK19), neural cell adhesion molecule (NCAM) a E-cadherinu (Ecad) ve variantách papilárního karcinomu štítné žlázy (PTC) s ohledem na možné využití těchto markerů v bioptické diagnostice. Soubor tvořilo 84 případů – 36 klasických variant PTC (cPTC), 26 folikulárních variant PTC (fPTC) a 22 papilárních mikrokarcinomů (mPTC). Gal3 byl exprimován ve 36/36 (100 %) cPTC, ve 24/26 (92 %) fPTC a v 19/22 (86 %) mPTC. Exprese CK19 byla zastižena ve 34/36 (94 %) cPTC, v 17/26 (65 %) fPTC a ve 13/22 (59 %) mPTC. Exprese NCAM byla prokázána v 5/36 (14 %) cPTC, v 7/26 (27 %) fPTC a v 9/22 (41 %) mPTC. Ecad byl exprimován ve 23/36 (64 %) cPTC, v 17/26 (65 %) fPTC a v 18/22 (82 %) mPTC. V expresi CK19 byl zjištěn signifikantní rozdíl mezi cPTC versus fPTC a mPTC ($p < 0,001$). Dále byla prokázána signifikantní korelace mezi expresí CK19 a ztrátou exprese Ecad ve vztahu k šíření nádoru mimo štítnou žlázu ($p = 0,001$, $p = 0,04$). Detekci exprese Gal3 a CK19 lze tedy doporučit jako pomocné kritérium v diagnostice PTC, nicméně je třeba upozornit na nižší expresi CK19 ve fPTC a v mPTC. K detailnímu posouzení úlohy CK19 a Ecad při šíření PTC mimo štítnou žlázu je třeba dalších studií.

Klíčová slova: štítná žláza – papilární karcinom – galektin-3 – cytokeratin 19 – neural cell adhesion molecule – E-cadherin

Čes.-slov. Patol., 44, 2008, No. 4, p. 103–107

Papillary thyroid carcinoma (PTC) is the most frequent endocrine malignancy with worldwide increasing incidence (9). In the last WHO classification (2004), at least fifteen variants of PTC differing not only by their microscopical appearance but also by their biological behaviour and prognosis are recognized (9). The classical variant of PTC (cPTC) is characterized by overall papillary architecture of the tumor; on the contrary, the follicular variant of PTC (fPTC) displays a follicular growth pattern making sometimes the differentiation from follicular adenoma/carcinoma a challenge. The papillary microcarcinoma (mPTC) is defined as an incidentally found PTC measuring 1 cm, irrespective of its growth pattern; its differential diagnosis includes mainly a fibrous scar with entrapped normal follicles - a condition known as fibrosing thyroiditis (26).

Galectin-3 (Gal3), a member of a family of ß-galactoside binding lectins, has been proved to be implicated in various biological processes, incl. regulation of cell growth, cell-cell and cell-matrix interactions, as well as apoptosis and neoplastic transformation and metastatic spread (17). The alterations in Gal3 expression in various malignant tumors, e.g. gastrointestinal carcinomas (29), breast carcinoma (6), and prostatic carcinoma (32), have been observed. Most previous studies focused on Gal3 expression in thyroid gland tumors have reported Gal3 presence in malignant tumors, whereas it was absent in benign lesions as well as in normal gland tissue (2, 3, 5, 7, 10, 14, 19, 24) .

Cytokeratin 19 (CK19) is expressed in various types of normal epithelial cells as well as in wide range of malignant epithelial tumors, e.g. gastrointestinal carcinomas, breast carcinoma etc. (21). In thyroid gland, CK19 is reported to be expressed namely in PTC, thus making its detection useful in differential diagnosis between fPTC versus follicular adenoma (FA) and/or follicular carcinoma (FC) and between PTC versus papillary hyperplasia in goiters (3, 13, 16, 20, 24, 25).

Neural cell adhesion molecule (NCAM), a transmembrane glycoprotein, plays an important role in cell-cell interactions (8). There are only few studies focused on NCAM expression