Shadow cell differentiation in endometrioid carcinomas of the uterus. Its frequent occurrence and beta-catenin expression

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SUMMARY

Shadow cell differentiation (SCD) is typical for pilomatrixoma and related follicular tumors of the skin. However, it has been described rarely in some extra-cutaneous lesions such as gonadal teratoma, craniopharyngioma, odontogenic cyst, and in rare visceral carcinomas (lung, bladder, gallbladder, uterus, ovary, and colon). In our practice, we have noticed that the occurrence of shadow cells is not very rare in endometrioid carcinoma (EC) of the uterus. For exact determination of SCD in these tumors, we reviewed 59 consecutive cases of uterine EC. The series included curettage and hysteroscopic specimens. We have found SCD in 9 (15.3 %) of the tumors. In these cases, the age of the patients and FIGO grade did not differ significantly from other ECs. Immunohistochemically, all ECs with SCD showed nuclear expression of beta-catenin in areas of SCD, indicating a possible role of the Wnt signaling pathway in tumorigenesis as well as a role of nuclear accumulation of beta-catenin by *trans*-differentiation from glandular toward squamous and shadow cell phenotypes. We have found that the relatively frequent presence of SCD in ECs can assists in the diagnosis of these tumors.

Keywords: beta-catenin – endometrioid carcinoma – shadow cell differentiation – uterus

"Shadow cell" diferenciácia v endometrioidných karcinómoch tela maternice. Jej častý výskyt a pozitivita na beta-katenín

SÚHRN

"Shadow cell" diferenciácia (SCD) je typická pre pilomatrixómy a iné trichogénne kožné tumory. Zriedka bola popísaná v extrakutánnych léziach ako sú gonadálny teratóm, kraniofaryngeóm, odontogénna cysta, niektoré viscerálne karcinómy (pľúc, žlčníka, močového mechúra, hrubého čreva, maternice a vaječníka). V bioptickej praxi sme si všimli, že "shadow" bunky nie sú príliš raritné v endometrioidných karcinómoch dutiny maternice. Pre presnejšie zistenie ich výskytu sme vyšetrili 59 konzekutívnych prípadov endometrioidného karcinómu (hysteroskopické biopsie a kyretáže). SCD sme našli v 9 prípadoch (15,3 %). Vek pacientiek a FIGO grading tumorov sa nelíšili od iných endometrioidných karcinómov. Imunohistochemicky bola u všetkých tumorov so SCD zistená jadrová pozitivita beta-katenínu viazaná na oblasť skvamóznej a "shadow cell" diferenciácie, čo suponuje úlohu mutácie príslušného génu v tumor-genéze (podobne ako u pilomatrixómu) a úlohu nukleárnej akumulácie beta-katenínu v *trans*-diferenciácii od glandulárneho smerom k skvamóznemu a "shadow cell" fenotypu. Vzhľadom k častému výskytu SCD v endometrioidnom karcinóme môže byť jej nález napomocný pri diagnostike tohto tumoru.

Kľúčové slová: beta-katenín – endometrioidný karcinóm – maternica – "shadow cell" differenciácia

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Shadow cells (ghost cells) are a specialized form of keratinized cells. They are typical for pilomatrixoma and other cutaneous lesions with follicular differentiation (1). It was suggested that they represent faulty attempts at differentiation toward hair (1,2). However, the shadow cell differentiation (SCD) was found in non-cutaneous lesions as well, such as gonadal teratomatous tumors (3-7), craniopharyngioma (8), odontogenic cyst (8), and in some visceral carcinomas (9-17). The group of visceral carcinomas, in which SCD was observed, includes carcinomas of the ovary (11,12,15), uterus (9), gallbladder (13), bladder (10,14), colon (9) and lung (16). According to the rarity of reported cases it could seem that SCD in visceral carcinomas represents an unusual finding. However, we noticed in our practice, that SCD is not rare in endometrioid carcinoma (EC) of the uterus. We wanted to ascertain the exact occurrence of this phenomenon, and therefore we searched for SCD in a series of uterine EC. Because cutaneous tumors with SCD are often positive for beta-catenin, indicating a possible role of Wnt signal transduction pathway in their tumorigenesis (18-20), in addition we performed a study of beta-catenin expression in our cases of EC with SCD (to determine whether Wnt signaling pathway may act also in these tumors).

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MATERIALS AND METHODS

Fifty-nine consecutive cases of EC of the uterine corpus were retrieved from routine files of surgical pathology laboratories in Trenčín (Slovak Republic) and Nový Jičín (Czech Republic). The