

Eosinophilic dysplasia of the cervix associated with HPV 6 infection – case report and review of the literature

Ondrej Ondič¹, Jana Kašpírková², Radoslav Ferko¹

¹ Šikl's Department of Pathology, Charles University, Medical Faculty Plzeň, Czech Republic
and Biopstická laboratoř s.r.o., Plzeň, Czech Republic

² Department of Genetics, Biopstická laboratoř s.r.o., Plzeň, Czech Republic

SUMMARY

Eosinophilic dysplasia of the cervix is recently described unusual and somewhat obscure dysplastic lesion of squamous epithelium. We present histological features of a lesion in 41 years old woman. It was composed of cells with brightly eosinophilic cytoplasm contoured by a sharp and slightly broader cytoplasmic membrane, lacking maturation, with mild increase in nuclear-cytoplasmic ratio, slight chromatin clumping and uneven mild nuclear clearing. Electronmicroscopic study showed mild crevices of the nuclear membrane in some dysplastic cells. Tissue in situ hybridization study confirmed the presence of HPV 6 in the form of patchy dotted pattern of integrated type. Immunohistochemistry revealed diffuse positive expression of antigen p16, extraordinarily in this case focally sparing basal part of the epithelium. Underestimation of this lesion can be avoided by paying attention to strong eosinophilia of the cytoplasm and sharp cellular contouring of the examined epithelium in routine hematoxylin-eosin staining.

Keywords: Eosinophilic dysplasia – PCR – in situ hybridization – CIN - cervical intraepithelial neoplasia – HPV 6

Eozinofilná dysplázia krčka maternice asociovaná s infekciou HPV 6 – kazuistika a prehľad literatúry

SÚHRN

Eozinofilná dysplázia krčka maternice bola popísaná nedávno ako neobvyklá a trochu nejednoznačná dysplastická lézia dlaždicového epitelu. Popisujeme túto jednotku diagnostikovanú u 41 ročnej ženy. Histologicky pozostáva z buniek s jasne eozinofilnou cytoplazmou, ktoré sú ostro ohraničené výraznou cytoplazmatickou membránou. Epitel je bez vyzrievania, s miernym zvýšením nukleocytoplazmatického pomeru buniek, s miernym zhrudkovatím chromatinu a nerovnomerným miernym prejasňovaním jadier. Elektronová mikroskopia ukazuje mierne zárezy jadrovej membrány v niektorých bunkách. Metóda tkanivovej in situ hybridizácie potvrdzuje prítomnosť HPV 6 ako ložiskovú bodkovitú pozitivitu signálu - integrovaný typ pozitivity. Imunohistochemicky je prítomná difúzna pozitívna expresia antigénu p16, ktorá v tomto prípade neobvykle ložiskovo vynecháva bazálnu vrstvu epitelu. Poddiagnostikovaní tejto lézie sa možno najúčinnejšie vyhnúť, ak si v bežnom farbení hematoxylin-eozín všimneme výraznú eozinofiliu cytoplazmy a ostré bunkové hranice hodnoteného epitelu.

Kľúčové slová: eozinofilná dysplázia – PCR – in situ hybridizácia – CIN – cervikálna intraepiteliálna neoplázia - HPV 6

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The term "eosinophilic dysplasia of the cervix" (ED) was used for the first time by Ma in 2004 (1). It was considered a variant of cervical squamous dysplasia (cervical intraepithelial neoplasia – CIN) presenting itself in „pure“ form or in association with conventional squamous dysplasia (HSIL or LSIL). The analysis of HPV DNA showed the presence of intermediate- and high-risk HPV types in 90 % of analyzed cases (1). Histomorphology (Fig. 1) of the epithelium with eosinophilic dysplasia includes following features: abundant eosinophilic cytoplasm and sharp opaque cell borders; lack of maturation; mild increase in nuclear-cytoplasmic ratio; slight

chromatin clumping; uneven mild nuclear clearing. This morphology is considered to represent intermediate degree of metaplastic differentiation and cytologic atypia. Significant inter-observer variability was apparent by examination of these lesions, with diagnoses ranging from benign reactive changes (10 %) and undetermined atypia to LSIL (CIN I) and HSIL (CIN III) (1). One of the major textbooks of gynecologic pathology - Gynecologic and Obstetric Pathology by Crum (2) - considers this lesion to be a type of immature flat metaplastic LSIL. It comments further on diagnostic difficulty in distinguishing reactive changes from this type of dysplasia presenting spectrum from mild atypia (LSIL) to high-grade dysplasia.

CASE REPORT

41 year old patient underwent conization due to a suspicious colposcopic finding 7 months prior to conization and positive HPV testing using Hybrid capture 2 method (HC2) 6 months before conization. Reviewing patient's history we came across gynecologic screening slides taken 24, 12, 6 and 2 months before conization.

✉ Correspondence address:

Ondrej Ondič, M.D.

Biopstická laboratoř s.r.o.

Mikulášské nám.4, 32600 Plzeň, Czech Republic

tel.: 00420 377 320 667, fax:00420 377 440 539

e-mail: ondic@medima.cz