Adenoid Basal Epithelioma of the Uterine Cervix in 21-Year-Old Patient. Report of a Case with Histologic and Immunohistochemical Study

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Summary

A case of adenoid basal epithelioma (ABE) of the uterine cervix in 21-year-old woman is reported. The patient's age appears to be lowest among cases of ABE reported to date. The tumor showed typical histologic features of ABE and was associated with CIN3. In addition, rare tumor cells had surface cilia-appearing structures suggesting tubal differentiation. Immunohistochemically, the tumor was reactive for p63, CD10, ER, PR, p16 and bcl-2, and negative for CEA. Thus, the immunophenotype also suggests possible partial tuboendometrioid differentiation in the glandular component of the lesion. It further indicates, along with finding of associated CIN, a role of oncogenic HPV in pathogenesis of ABE.

Key words: **adenoid basal epithelioma – CIN – CD10 – tuboendometrioid differentiation – uterine cervix**

Súhrn

Adenoidne bazaloidný epitelióm cervixu u 21-ročnej pacientky. Popis prípadu s histologickým a imunohistochemickým nálezom

Popisujeme prípad adenoidne bazaloidného epiteliómu (ABE) cervixu u 21-ročnej pacientky. ABE sa vyskytuje typicky v postmenopauze a v našom prípade ide o doposiaľ najmladšiu pacientku s týmto tumorom. Tumor bol asociovaný s CIN3. Histologický obraz bol typický, navyše boli u ojedinelých glandulárnych buniek zreteľné štruktúry podobné cíliam tubálneho typu. Imunohistochemicky bola zreteľná pozitivita p63, CD10, estrogénových a progesterónových receptorov, p16 a bcl-2. CEA bol negatívny. Imunohistochemický nález svedčí spolu s morfológiou pre tuboendometrioidnú diferenciáciu v tumore pochádzajúcom z rezervných buniek. Nález koilocytických zmien a expresia p16 potvrdzujú predpokladanú úlohu vírusu HPV v onkogenéze tohto tumoru.

Kľúčové slová: **adenoidne bazaloidný karcinóm – CIN – CD10 – tuboendometrioidná diferenciácia – krček maternice**

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Introduction

So-called adenoid basal epithelioma (ABE) of the cervix [originally termed adenoid basal carcinoma] is rare tumor with excellent prognosis after its complete surgical removal (1-9, 17, 22, 25). The tumor occurs typically in postmenopausal patients and is associated almost constantly with cervical intraepithelial neoplasia (CIN) or invasive squamous carcinoma**.** The origin of the lesion is still obscure. We present a case of ABE occurring in 21-year-old woman who is to the best of our knowledge the youngest patient with ABE reported to date. Immunohistochemically, the tumor showed hitherto undescribed expression of CD10, and it was also reactive for p16, ER, PR and bcl-2. This immunophenotype indicates a role of oncogenic HPV in pathogenesis as well as a possible partial tuboendometrioid differentiation in the glandular component of the tumor.

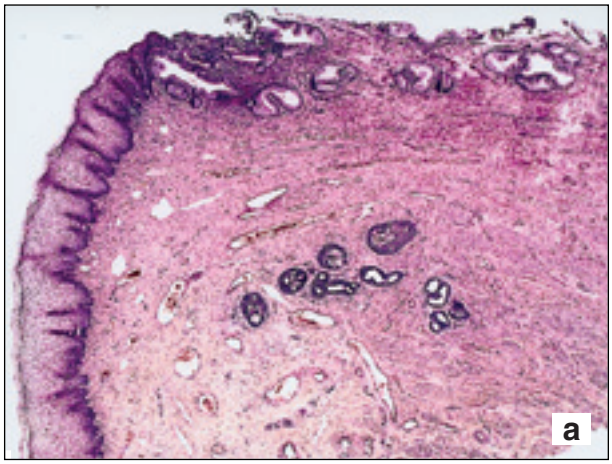
Materials and Method

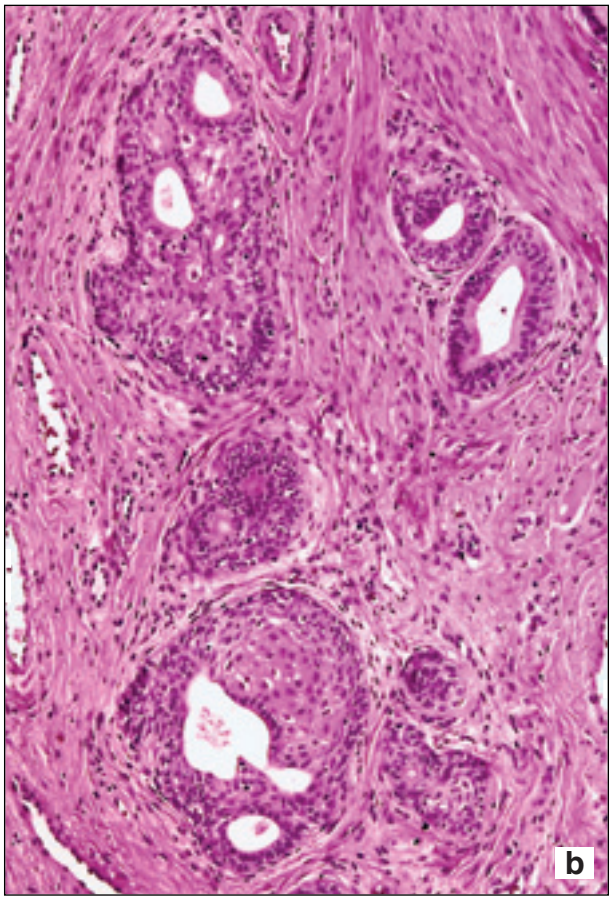
The formalin fixed cone biopsy specimen was routinely processed in 12 tissue blocks, and the

sections were stained with hematoxylin and eosin, mucicarmine, PAS, PAS with diastase and alcian blue at pH 2.5. For immunohistochemistry, the sections were stained with antibodies against vimentin (clone V9), bcl-2 (clone 124), carcinoembryonic antigen (polyclonal), androgen receptor (clone AR441) (all from DAKO, Glostrup, Denmark), CD10 (56C6, Lab Vision/Neomarkers, Fremont, CA, USA), cytokeratins AE1/AE3 (Boehringer, Manheim, Germany) and CAM5.2 (Becton Dickinson, Erembogeden-Alst, Belgium), estrogen receptor (ER1D5, Marseille, France), progesterone receptor (1A6, Marseille, France) using the avidin-biotin peroxidase complex technique. Appropriate controls were used.

Case Report

Previously healthy 21-year-old woman, gravida 0, para 0, was admitted for recent clinical and cytological finding of LSIL, and the conization was performed. The patient was well and without recurrence one month after the surgical treatment. The cone specimen measured 15x15x10mm and did not show any grossly visible tumor mass. **Histologically**, the sections from one of 12 tissue blocks contained ABE measuring 3x2mm. The tumor was located in the stroma in 2mm distance from normal cervical squamous epithelium, and no connection between the tumor and the overlying epithelium was found (fig. 1A). The lesion was composed of small nests of basaloid cells with peripheral palisading and with focal formation of glandular lumina (fig. 1B). The glan-





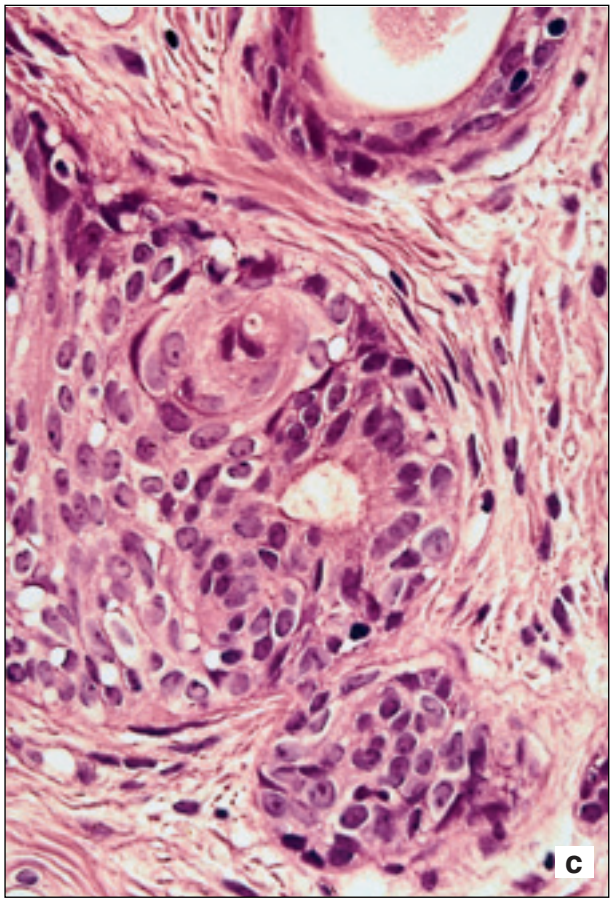
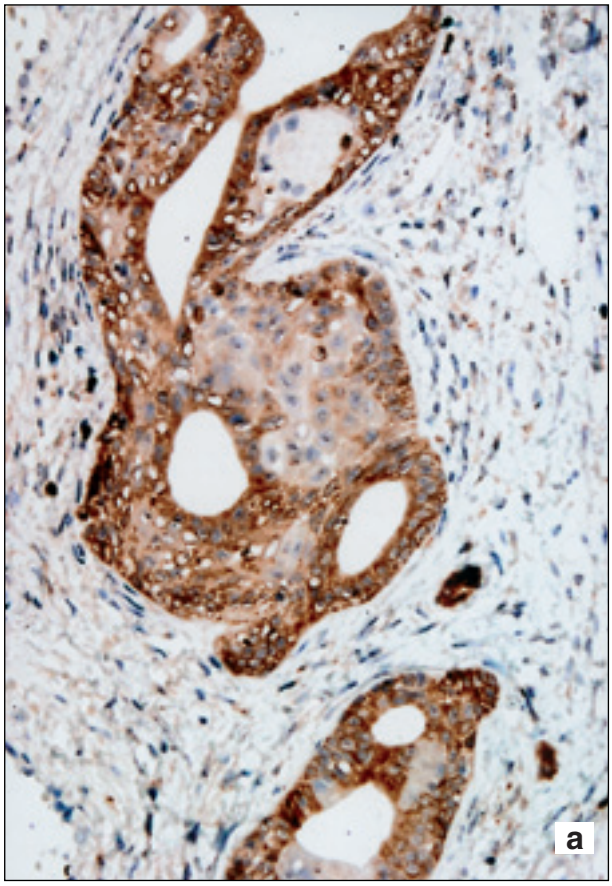


Fig. 1. Histological findings. A, low-power view shows ABE without connection with cervical epithelium. B, the islands of ABE contain basal cells that differentiate toward both squamous and glandular direction. C, at high-power, the basaloid cell morphology and some cilia-like structure on the luminal cell membrane of the glandular cells (in the center of the photomicrograph) are seen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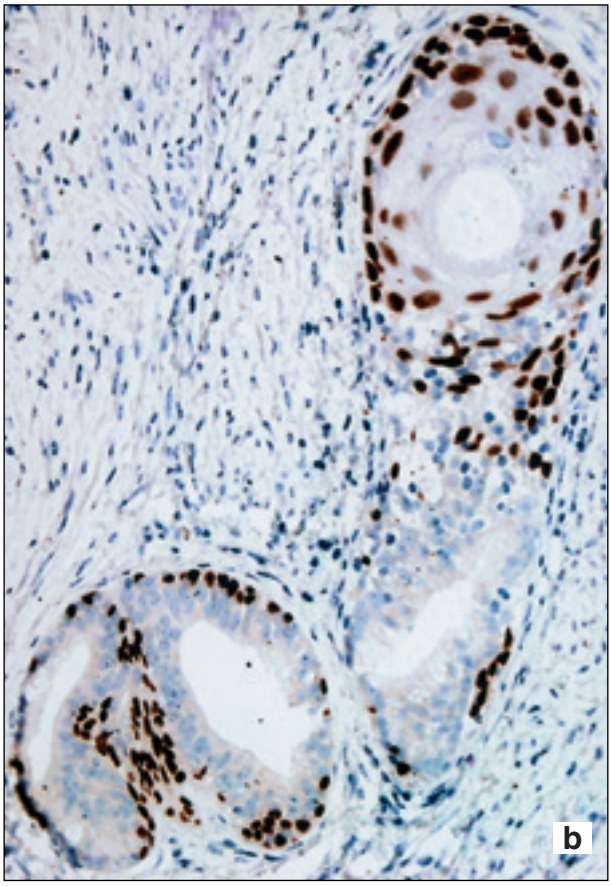
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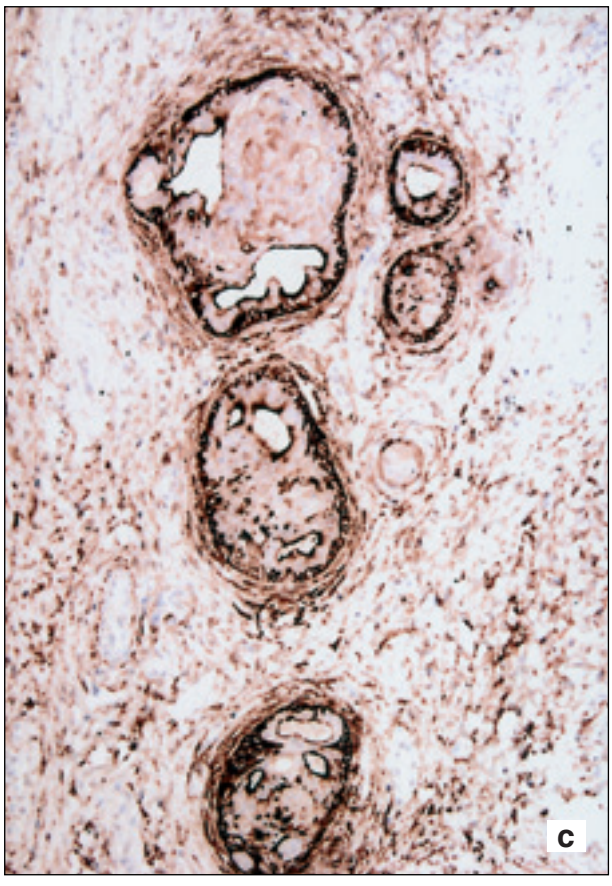
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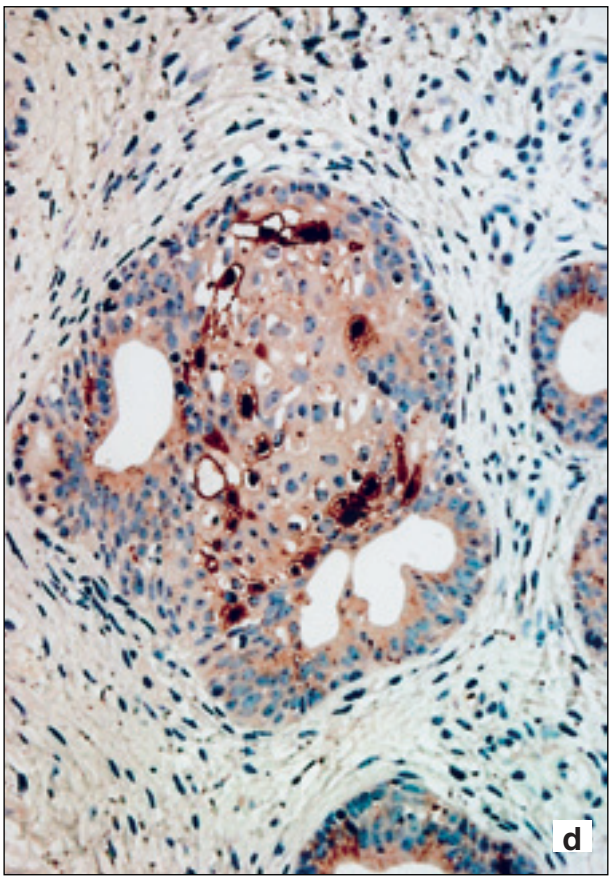
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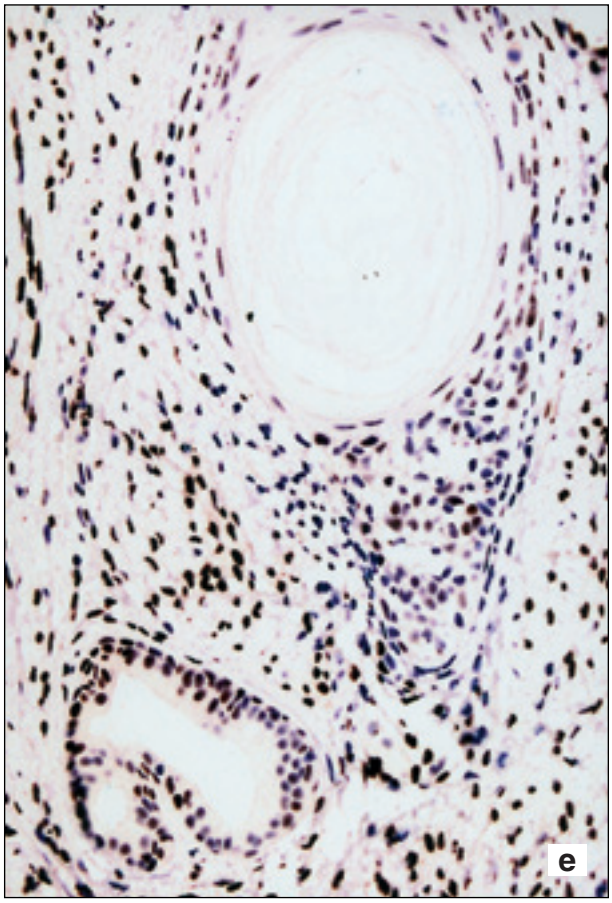

Fig. 2. Immunohistochemical findings. A, bcl-2 is positive in basaloid and glandular cells. B, p63 is positive in basaloid cells. C, CD10 immunoreactivity is seen in both basaloid and glandular cells. Numerous stromal cells of the cervix are positive as well. D, p16 reactivity is limited to the squamous cells. E, progesterone receptor positive nuclei in both stromal and neoplastic cells are shown

dular epithelium was cuboidal to cylindrical. On the luminal surface of rare glandular cells some structures had appearance of partly developed ciliation (fig. 1C). Several cell nests showed central squamous cell differentiation with rare koilocytic features. Nuclear atypia of the lesion was low and mitotic figures were very rare. Desmoplastic stromal reaction was not present. Mucin stains (PAS-D and alcian blue) were slightly positive in glandular content and in cytoplasm of some glandular cells. In addition to ABE, the cone specimen contained conventional CIN with grade ranging from CIN1 to CIN3. **Immunohistochemically**, the cells of ABE were positive for cytokeratins and bcl-2 (fig. 2A), and negative for vimentin. p63 [a marker for reserve cell phenotype] was strongly reactive in basal cells and in numerous squamous cells, and was negative in a majority of glandular cells (fig. 2B). CD10 was strongly positive in basaloid cells and in luminal part of the cells of the adenoid component (fig. 2C). p16 positivity was found in numerous squamous cells (fig. 2D). Carcinoembryonic antigen (CEA) reactivity was slight and limited to luminal surface of the glandular cells. Estrogen receptor (ER) and progesterone receptor (PR) were positive in approximately one third of tumor cells, with accentuation of the positivity to the glandular and basaloid cells (fig. 2E).

Discussion

ABE of the uterine cervix was described in 1966 by Baggish and Woodruff (1) under the name “adenoid basal carcinoma”, and subsequently additional cases were added to the literature (2-9, 17, 22, 25). ABE is typically an indolent lesion found in postmenopausal patients. Some authors observed a strong predominance of patients of non-white race in their series (5, 6) whereas other studies did not confirm it (4, 8). In most cases, ABE is not apparent grossly and represents incidental microscopic finding. The tumor is almost constantly associated with CIN or/and with conventional invasive squamous cell carcinoma (2, 4). All of the published cases of typical ABE had benign course after the complete removal of the tumor, and for that reason Brainard and Hart (2) proposed to label the lesion as “epithelioma” rather than as “carcinoma”.

From clinical point of view, the present tumor was typical except for the young age of the patient [21 years]. The mean age in two larger series of ABE was 71 and 65 years, respectively (2, 17). To the best of our knowledge, the youngest patient reported to date was 30-year-old one in the series of Brainard and Hart (2). Thus, the age of our patient is lowest among the reported cases of ABE.

Histologically, ABE is composed typically of small nests of basaloid cells with focal glandular and squamous differentiation, and it usually lacks desmoplastic stromal response. Nuclear atypia is low and mitotic figures are infrequent. The overall appearance of the lesion suggests usually benign to low-grade lesion. In our case the histological features were similar to those reported previously (1–9, 17, 22, 25) except for cilia-like structures found on luminal surface of some cells. The ciliated cells in female genital tract tumors are typical for tuboendometrioid differentiation (20, 23), and thus their finding may indicate this type of differentiation in the present tumor. The origin of ABE is unknown, although two theories have been proposed. One theory suggests that ABE is related to basal and adnexal skin tumors and is derived from ectodermal elements misplaced in the cervix (22). The second theory is that ABE arises from pluripotential reserve cells (5, 6, 21), and that high-risk HPV probably play role in evolution of ABE [like it does in

evolution of associated conventional CIN or invasive carcinoma]. The strong expression of ER and PR, as seen in our case, is frequent in mullerian derived epithelium whereas it is not observed in cutaneous epithelia, with exception of apocrine glands (18). As the morphology of ABE does not show any similarity with apocrine lesions, our finding of ER and PR positivity favors the later theory. The present tumor was immunohistochemically reactive for p16. Expression of p16 is strongly associated with the presence of oncogenic HPV genome in the tumor cells (10, 19), and therefore this finding along with the observation of associated CIN supports the theory of important role of HPV in the pathogenesis of ABE (5, 8). Immunohistochemical expression of CD10 in ABE was hitherto not examined to our knowledge. CD10 was originally regarded in genital glandular lesions as a marker for mesonephric differentiation (16), but subsequent published findings showed that CD10 could be positive also in endometrioid [i.e., mullerian derived] carcinomas (15, 26). Normal cervical glands are CD10 negative except for rare luminal surface positivity (15). Alike, conventional cervical adenocarcinomas are CD10 negative or they show only luminal surface positivity, and this contrasts with strong CD10 reactivity seen in the present tumor. The negativity for CEA found in our case is unusual for endocervical-type adenocarcinoma as well (11, 14). Thus, CD10 positivity in the present case probably does not reflect endocervical type differentiation, but it should indicate either mesonephric or endometrioid (tuboendometrioid) line of differentiation. Mesonephric cells express often androgen receptor and are negative for ER and PR (21) whereas tuboendometrioid epithelium expresses sex steroid receptors almost constantly (23). The present lesion was reactive for ER and PR and negative for AR, favoring the tuboendometrioid phenotype that was favored already by the morphological finding of cilia-like structures. Considering our morphological and immunohistochemical results in sum, we hypothesize that the finding of cilia-like structures and koilocytic change, along with synchronous immunoreactivity for p16, p63, CD10, ER and PR, indicate partial endometrioid or tuboendometrioid differentiation in ABE that is HPV induced neoplasm arising probably from cervical reserve cells. However, the definite conclusion about origin and line of differentiation based on study of one case is of course not possible. Studies of additional ABEs are needed to determine the frequency of mentioned findings, as well as to interpret them from histogenetic point of view more exactly.

In conclusion, we reported further case of ABE of the uterine cervix. The age 21 years of our patient is the lowest one reported in the literature till now. Histological features were similar to the cases described previously, except for cilia-like structures found on the luminal surface of some cells. In our immunohistochemical study, we described in ABE for the first time the positivity for CD10, ER, and PR. These findings suggest a partial tuboendometrioid differentiation of the tumor. Additional studies are needed for knowledge of the frequency of these findings as well as for better understanding of the histogenesis of ABE.

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INFORMACE

Ve dnech 3.–8. září 2005 se v Paříži konal 20. kongres European Society of Pathology, v jehož rámci celkem zaznělo 264 přednášek a bylo vystaveno 998 posterů. Jako nejlepší byl vyhlášen poster

Mrhalová, M., Plzák, J., Betka, J., Kodet, R.: Head and neck squamous cell carcinomas (HNSCC): epidermal growth factor receptor (EGFR) protein expression and EGFR gene copy numbers.

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Prof. Pierre Bedossa, President of the 20th European Congress of Pathology při předání ceny za nejlepší posterové sdělení na kongresu RNDr. M. Mrhalové, Ph.D.