CASE REPORT

Adenoid basal carcinoma-like tumor combined with invasive squamous cell carcinoma foci of uterine cervix – a case report of 55-year-old woman with literature review

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Abstract

Background: Adenoid basal carcinoma (ABC) of uterine cervix is an extraordinary example of carcinoma with both basal and glandular cell types. Here we present such a case of ABC combined with invasive squamous cell carcinoma (SCC) of 55-year-old woman. Methods: The tumor was stained with Hematoxylin–Eosin (HE), Mucicarmine, PAS/Alcian Blue, CK AE1/AE3, CK7, CD117, and Ki67. Results: The whitish-grey 1 cm in-depth infiltration of endocervix was composed of infiltrative coalescing areas of CK AE1/AE3 positive carcinoma with peripheral palisading of basal cell type with spaces lined by Mucicarmine- and Alcian Blue-positive benign looking, glandular epithelium. There were also foci of apparently malignant squamous epithelium with evident dyskeratosis. Thus, a lesion was diagnosed of adenoid basal carcinoma combined with invasive squamous cell carcinoma foci of uterine cervix. The tumor was further CD117 negative what favored diagnosis of ABC over adenoid cystic carcinoma (ACC). There were rare mitoses on HE slides but 60% of all tumor cells were positive for Ki67 that would partially contradict reported benign nature of ABC lesion. Moreover, tumor was CK7-positive and this finding was controversial and according to one report favored diagnosis of ABC-like adenosquamous carcinoma (ACC). Due to CK7 positivity and high index of Ki67, the neoplasm was re-classified as adenoid basal carcinoma-like tumor. Conclusions: It seems reasonable to treat the patient in the same manner as in case of pure simple invasive squamous cell carcinoma because much more aggressive, minor component of invasive SCC was found within ABC in our case.

Keywords: adenoid basal carcinoma/epithelioma/tumor, basal cell type differentiation, glandular component, squamous cell metaplasia, squamous cell carcinoma.

Introduction

Adenoid basal carcinoma/epithelioma (ABC) is a rare tumor. Pure ABC is characterized by indolent course and excellent prognosis [1]. However, a few cases of ABC were described in females in their early twenties [2, 3]. Hart has already given an excellent review on histochemical, immunohistochemical, and molecular profiles of adenoid basal carcinoma with regard to its biology and clinical course [4]. Young and Clement classified adenoid basal carcinoma to the group of rare cervical tumors with glandular component, which also includes adenosquamous carcinoma adenoid cystic carcinoma and adenocarcinoma admixed with a neuroendocrine tumor [5]. Although the most common cervical cancer types squamous-cell carcinoma and adenocarcinoma arise from different precursor lesions such as cervical intraepithelial neoplasia (CIN) and adenocarcinoma in situ (AIS), they share a common etiology, which is infection with high-risk types of HPV that drive tumorigenesis and progression of these lesions [1, 6]. ABC occurs mostly among post-menopausal women. Carcinogenesis of both squamous cell carcinoma and endocervical adenocarcinoma is mediated by persistent human papillomavirus (HPV) infection [6].

In this context, it should be stressed that adenoid basal carcinomas are also HPV positive [1, 6]. In one study, so-called rare cervical cancers (adenosquamous, papillary, villoglandular, anaplastic, transitional, spindle, adenoid basal, colloid, neuroendocrine, and glassy cell carcinomas) showed presence of HPV 16 type up to 66% of cases [6]. Interestingly, there were rare HPV types (52, 84, 26, 35, and 58), that were detected only in these rare cervical cancers. In another one study of quite uniform group of 10 ABC, that were accompanied by predominantly high grade squamous intraepithelial lesions, all of them were p16-positive, while HPV 16 DNA was discovered in nine tumors by in situ hybridization, and HPV 33 was found with appliance of polymerase chain reaction in one tumor [7].

As adenoid basal carcinoma contains both basal cells and benign-looking glandular cells its diagnosis remains a potential pitfall in cervicovaginal cytology [8]. However, because of the fact that ABC is usually associated with squamous intraepithelial lesions (SIL), it can be easily diagnosed and therefore any potential coexistent ABC appears difficult to be missed [8]. Thus, in later procedures like cervical biopsy or endocervical curettage eventual presence of ABC can be detected. Besides SIL lesions,
adenoid basal carcinomas are very seldom described to grow together with squamous, adenoid cystic, and small cell neuroendocrine carcinomas as well [7].

**Patient, Methods and Results**

A female patient was subjected to classic, probative excision of uterine cervix. In the past history, the patient was two time pregnant and gave natural birth to two healthy children (the last one at the age of 30 years). She occasionally drank alcohol and smoked cigarettes only socially. No drug abuse was noted in her medical history. She applied oral contraception afterwards until to her mid forties. Her mother was diagnosed with a few uterine leiomyomas. Besides that, no relevant facts in medical history of the patient and her family were noted. On the base of obtained tissue samples, cervical intraepithelial neoplasia 2 (CIN2) was diagnosed in the described case with indication of some tissue thermal destruction and some crushing of the material during excisional procedure. In the background, infiltrates of small basaloid-like cells were present. However, they were partially assumed to be of chronic inflammatory nature due to mentioned, artifactual change of material. Some glands of endocervical type were cystically dilated. Dysplastic foci involved endocervical glands but without apparent invasion of cervical stroma (not shown). Next, a patient underwent the loop electrosurgical excision procedure (LEEP) of uterine cervix. On the ground of obtained material preinvasive squamous cell cancer was diagnosed with a note that invasion could not be excluded.

In consequence of such a diagnosis, 55-year-old woman underwent total hysterectomy with bilateral salpingo-oophorectomy. The removed uterus measured 10×5×3.5 cm. Ectocervix was wrinkled with some scaring. In endocervix there was a 2 cm long 1 cm in-depth whitish-grey infiltration (microscopically confirmed to be cancer invasion) that produced hardening of endocervical wall, which did not reach resection margins (minimal lateral circumferential resection margin: 0.2 cm). We did not found either blood/lymphatic vascular invasion or uterus extension. Endometrium was smooth without visible macroscopic changes. There was also a 3 cm in-diameter mural tumor of leiomyoma outlook with whorled appearance on cutting surfaces. Additionally local lymphadenectomy was preformed.

Besides standard Hematoxylin–Eosin (HE) technique the tumor was stained with Mucicarmine, PAS/Alcian Blue and labeled with pan-cytokeratin (CK) AE1/AE3, CD117, CK7 and Ki67.

The tumor was composed of infiltrative coalescing foci with occasional peripheral palisading of basal type cells that resembled basal cell carcinoma of cutaneous counterpart (Figure 1, A and B). In between there were scattered some minute foci of squamous differentiation – some of them were consistent with apparently malignant squamous epithelium with evident dyskeratosis consistent with diagnosis of invasive well-differentiated, keratinizing, squamous cell carcinoma G1 (Figure 1, C and D).

![Adenoid basal carcinoma-like tumor with foci of squamous cell carcinoma. HE staining. (A) Adenoid basal carcinoma: basal cell type areas with glandular spaces, ×100. (B) Adenoid basal carcinoma: basal cell type areas with glandular differentiation, ×200. (C) Foci of well-differentiated squamous cell carcinoma G1, ×200. (D) Well-differentiated squamous cell carcinoma G1 with evident dyskeratosis, ×400.](image-url)
In the basal cell type, foci there were glandular spaces, which were lined by Mucicarmine- and Alcian Blue-positive glandular columnar to cuboidal epithelium. Precisely, both Mucicarmine and Alcian Blue were positive in lumens of glandular spaces and luminal smooth border of benign-looking glandular cells with basally oriented nuclei (Figure 2, A and B). Basal and squamous cell component was strongly positive for pan-cytokeratin (CK) AE1/AE3 in invasive cancer islands (Figure 2C). Thus, a lesion was diagnosed of adenoid basal carcinoma combined with CIN3 and invasive squamous cell carcinoma foci of uterine cervix pT1b1 (FIGO IB1) according to 7th edition of pTNM Classification. The tumor was further CD117 negative what favored diagnosis of ABC over adenoid cystic carcinoma (ACC) (Figure 3A). There were rare mitoses on HE slides but 60% of all tumor cells were positive for Ki67 that would partially contradict reported benign nature of ABC lesion (Figure 3B). Moreover, tumor was CK7 positive and this finding was found to be controversial and according to one report inconsistent in differential diagnosis with ABC-like adenosquamous carcinoma (ACC) [11]. Due to CK7 positivity (Figure 3C) and high index of Ki67, the neoplasm was re-classified as adenoid basal carcinoma-like tumor.

Endometrium was inactive and undergoing partial atrophy. Mural tumor was recognized to be leiomyoma with hyalinization. An acute purulent salpingitis was found in left oviduct, while in both ovaries there were no pathological changes and only presence of corpora albicantia were reported. In removed regional lymph nodes, there was only reactive chronic lymphonodulitis without metastases.
Differential diagnosis of doubtful cases, which are suspected to be ABC, includes various entities in which, immunohistochemistry can be helpful. In our case, only pan-cytokeratin (CK) AE1/AE3 staining was additionally preformed to confirm epithelial nature of some small basaloïd cell foci, particularly those that were a bit artifically crushed. With appliance of this marker, we simply wanted to be completely sure about true extent of cancer infiltration whenever there was slight doubt of epithelial nature of small basaloïd cells.

Most of cancer foci were composed of solid areas of relatively small neoplastic cells and only a few of them contained small cyst-like dilated spaces with were lined by taller cells of glandular benign appearance. To confirm glandular nature of these spaces, histochemical stains (Mucicarmine and PAS/Alcian Blue) were applied. They highlighted glandular component of the epithelial lining in cystically dilated spaces with evident positivity.

As there was a mixture of solid basaloïd cancer texture and glandular component in our case, adenoid cystic carcinoma (ACC) was considered in differential diagnosis. In spite of the fact that the diagnosis seemed to be straightforward on HE slides, we employed CD117 (c-kit) staining in our procedure. CD117 negativity was enough to exclude any suspicion of mixed adenoid basaloïd component of the epithelial lining in HE-stained microscopic slides in our case [9]. This marker is expressed by adenoid cystic carcinoma of uterine cervix, but adenoid basaloïd carcinomas remains negative [9]. It is worth mentioning that in further differential diagnosis from adenoid cystic carcinoma, the other important features are that adenoid basaloïd carcinoma is immunoreactive for EMA and negative for collagen IV and laminin [2]. Precisely, EMA was co-expressed both in ACC and ABC, while ACC was also positive for collagen IV and laminin in opposition to adenoid cystic carcinoma (ACC) [10]. Nevertheless, we concluded that morphology and CD117 negativity was enough for our evaluation.

Another similar tumor, an ABC-like adenosquamous cell carcinoma (ASC) is composed of nests basaloïd cells mimicking ABC, but with some features indicating more aggressive potential [11]. Indeed, in our case solid fields of relatively small basaloïd neoplastic cells should be differentiated with basaloïd squamous cells component. Nevertheless, glandular component constituted exclusively the lining of small cyst-like dilated spaces. In HE slides, any signs of malignancy were not found. Namely, taller cells of glandular benign appearance had uniform bland and basally oriented nuclei and smooth luminal border – as depicted in Figure 1. CK7 stain was performed in our case as it was once reported that cytokeratin 7 was expressed in all of six examined ABC-like lesions of ASC on the contrary to two negative ABCs [11]. Consequently, CK7 was about to emerge as marker for differential diagnosis, whenever HE-based histopathology was not enough for a firm diagnosis [11]. Unfortunately, in our case gland-like component was without any morphological features of malignancy the tumor looked more like basaloïd cell carcinoma of cutaneous type with peripheral palisading than adenosquamous cancer. Taking this into account, morphology of our case was not consistent with adenosquamous cell cancer outlook, where both of components are truly malignant so that they usually consist of closely intermingled adenoacanthoma and squamous cell carcinoma areas. Moreover, CK7 seems to be controversial as marker of differential diagnosis between ABC and ABC-like ASC because CK7 was found positive in adenoid basaloïd carcinoma in a few reports [10, 12]. Precisely, tumor cells including the peripheral palisading cells were positive for keratin 7 in ABC [12].

There was no necrosis, only few mitotic figures and there was benign looking glandular lining of intratumoral small spaces in HE-stained samples of the tumor so a quoted in one report [11] aggressive potential was not found in our case except for frankly malignant areas of squamous cell carcinoma foci and infiltrative nature of islands of basaloïd cells. However, MIB index was as high as 60% Ki67-positive ones of all neoplastic cells. Such our result was similar to finding of Senszaki et al. [12], who revealed that another one immunohistochemical marker of proliferation PCNA was positively expressed in the majority of tumor cell nuclei in adenoid basaloïd carcinoma but simultaneously mitoses were rare in HE-stained slides [12]. Moreover, Viriyapak et al. reported Ki67 labeling at the level of 40% in squamous cell carcinoma component in comparison to 25% of such immunoreactivity in adenoid basaloïd carcinoma component [13].

ABC, which occurred together with CIN3, was also reported to express p63, CD10, ER, PR, p16 and bcl-2, while being negative for CEA [3]. ABC should also be distinguished from ABC-like lesion of adenosquamous cell carcinoma (ASC) of the cervix [11]. In our case, adenoid basal carcinoma was characterized by endophytic growth, while Kuroda et al. described the same entity in the cervical polyp [14]. In spite of the fact, that ABC is reported not to induce any desmoplasia, Kuroda et al. revealed a smaller number of CD34-positive and CD31-negative stromal cells, namely fibroblasts, in the central intratumoral stroma in comparison with cervical stroma outside tumor. Such a decrease may be a sign of early stromal reaction to cancer infiltration [14]. In opposition to CD31 and CD34 positive cells, myofibroblasts expressing alpha-smooth muscle actin were not found in interstitium of tumor centre [14].
Ki67 index was used in differential diagnosis of our entity from endocervical benign lesions that can be composed of basal cells. Until now, some lesions of basal cell type, which are related to adenoid basal carcinoma, counterpart have been defined [15]. Adenoid basal hyperplasia (ABH) is a benign entity of a similar texture as adenoid basal carcinoma, but it substantially differs from the later by the absence of deep invasion into the cervical stroma [15]. The high percentage of Ki67 positive tumor cells that were revealed in our case, further confirmed malignant nature of our entity. Our results corresponded with statement of Kerdraon et al. that squamous metaplasia and increase in mitotic index are quite frequent in adenoid basal carcinoma, while they are very rare in adenoid basal hyperplasia [15]. He reported a few cases of this lesion that were composed of small nests of cells and spread less than 1 mm from the basement membrane [15]. He also proposed origin of adenoid basal hyperplasia from cervical reserve cells, because the lesions were adjacent to the squamocolumnar junction, and looked like they grew from the line of neighboring subcolumnar reserve cells [15]. Furthermore, the immunoprofile of keratin 5/6, keratin 14, keratin 7 and p63 was performed in adenoid basal hyperplasia to confirm reserve cell origin. However, no human papillomavirus was detected in situ hybridization. Consequently, it was consistent with negative immunohistochemistry for p16 to further exclude a common counterpart have been defined [15]. Adenoid basal hyperplasia (ABH) can be defined through different clinical and histological criteria [15]. For now, it cannot be excluded that ABH lesion is a name of carcinoma for a non-metastasizing, clinically benign lesion, so Russell and Fadare recommended a name Adenoid Basal Epithelium (ABE) or Adenoid Basal Tumor for this entity [16]. Nevertheless, features that favor malignancy are high PCNA index in ABC reported by Senzaki et al. [12] and high Ki67 MIB index and infiltrative nature in our case, which demonstrated at least ABC-like morphology.

Conclusions

In spite of the fact that ABC is assumed as not metastasizing and therefore regarded to be clinically benign, it coexists with SCC in the presented case. Certainly, high Ki67 index and infiltrative nature are features of malignancy in our case. Regarding clinical significance of our pathological findings, it seems reasonable to treat the patient in the same manner as in case of pure simple invasive squamous cell carcinoma whenever, we find much more aggressive, minor component of invasive SCC within ABC. Thus, a pathologist should be alert in any case of diagnosis of adenoid basal carcinoma and ABC-like tumors and extensively look for any SCC foci, which would dramatically change prognosis of patient.

References


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Received: April 20, 2014

Accepted: October 14, 2014