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Adenoid Basal Carcinoma of the Cervix with Squamous Differentiation: A Case Report and Literature Review

Jianhua Hao[1], Yafei Zhao[2], Jinmei Li[3], Bingjuan Zhou[3], Jirui Sun[3], Qiushuang Ma[3]*

[1]Department of Pathology, Hebei Yixian Hospital, Baoding 074200, Hebei Province, China

[2]Department of Orthopedics, Baoding No. 1 Hospital of TCM, Baoding 071000, Hebei Province, China

[3]Department of Pathology, Baoding No. 1 Central Hospital, Hebei Provincial Key Laboratory of Molecular Pathology and Early Diagnosis of Tumors, Baoding 071000, Hebei Province, China

***Corresponding author:** Qiushuang Ma, 578854375@qq.com

Abstract: Adenoid basal carcinoma (ABC) of the cervix is a rare and low-incidence low-grade cervical cancer. In our practice, we encountered a case of cervical ABC with squamous differentiation and high-grade squamous intraepithelial lesion (HSIL) with gland involvement in the peripheral cervix. Reviewing relevant literature and analyzing its clinical manifestations, pathological morphology, and immunohistochemical characteristics would help deepen the understanding of this malignant tumor, so as to make a comprehensive diagnosis with differential diagnosis and prevent misdiagnosis.

Keywords: Adenoid basal carcinoma of cervix; Squamous differentiation; Immunohistochemistry

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1. Case study

A 64-year-old lady was admitted to a local hospital in view of postmenopausal bleeding. Internal examination revealed no abnormalities in the uterus and its appendages, including tenderness (negative), cervical atrophy, mild erosion, friability, and bleeding. Pelvic ultrasound showed postmenopausal uterus, with normal size and shape, the lining of the uterus showed strong linear echo, and the muscle layer showed uniform echo, with no obvious space-occupying lesions or abnormal echoes in the appendages. Cervical HPV showed high-risk P16 positive, ThinPrep cytologic test (TCT) showed high-grade intraepithelial lesions (HSIL) with severe inflammation. Cervical biopsy showed high-grade intraepithelial neoplasia (CIN III) at points 3, 6, 9, and 12 of the cervix. Total hysterectomy + bilateral salpingo-oophorectomy + pelvic lymph node dissection was performed.

Pathological examination

(1) Gross examination

The excised uterus was 6 cm × 3.5 cm × 2.5 cm. The length of the cervical canal was about 1.5 cm with an outer diameter of 1.8 cm. No obvious mass was seen under the naked eye. The endometrial thickness was about 0.1 cm; the muscle wall thickness was about 1.5 cm; the size of the left ovary was 2.8 cm x

1.8 cm x 0.4 cm; the cut surface was solid, gray, and white; and the quality of the section was of medium quality. The right oviduct was about 5.8 cm long and 0.3 cm in diameter.

(2) Microscopic findings

Adenoid basal cell carcinoma of the cervix with squamous differentiation, and high-grade intraepithelial neoplasia (HSIL) with gland involvement in the peripheral cervix. In the underlying fibrous stroma, small nests of infiltrating tumor cell clusters were seen, some of which were solid, while some were glandular structures; some glands showed squamous cell metaplasia (**Figure 1**). Tumor cells with small cell body, little cytoplasm, round or oval hyperchromatic nuclei, inconspicuous nucleoli, and rare mitotic figures (**Figure 2**) were observed, along with surrounding HSIL areas (**Figure 3**).

(3) Immunohistochemistry

Carcinoembryonic antigen (CEA, scaled +), Ki-67 (+ 40%), cytokeratin (CK)7 (scaled +), P63 (+), P40 (+), cluster of differentiation (CD)117 (-), and P16 (+) (**Figure 4**–**10**).

Pathological diagnosis: adenoid basal cell carcinoma of the cervix with squamous differentiation, and high-grade intraepithelial neoplasia (HSIL) with gland involvement in the surrounding cervix.

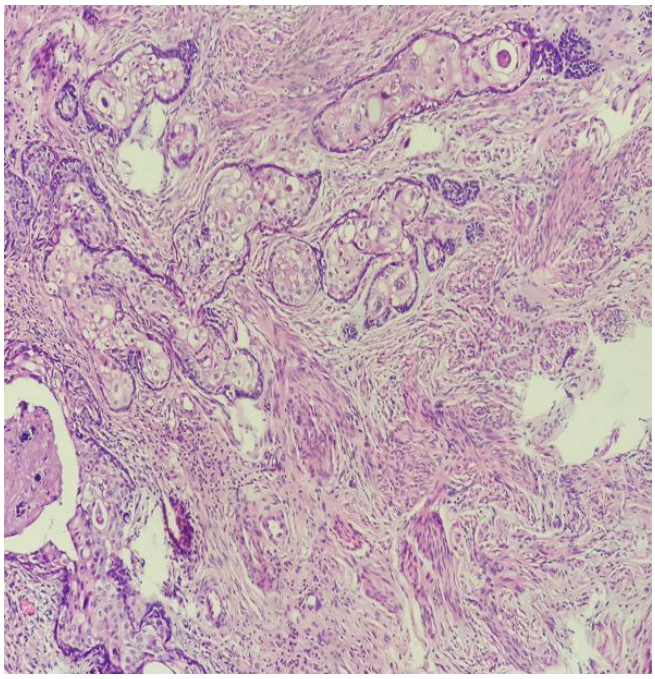

Figure 1. Part of the tumor cell mass having gland-like structures, with squamous metaplasia seen in some glands

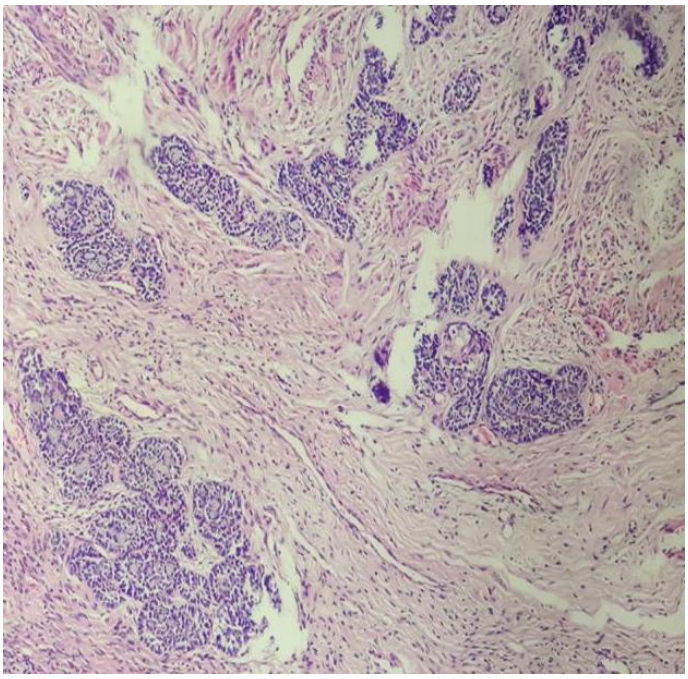

Figure 2. Tumor cells with small cell body, little cytoplasm, round or oval hyperchromatic nuclei, inconspicuous nucleoli, and rare mitotic figures

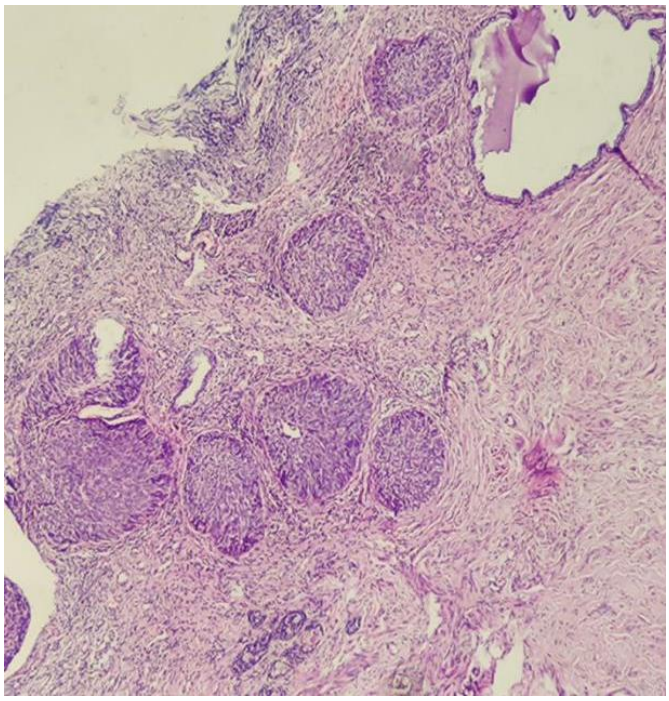

Figure 3. Visible surrounding HSIL area

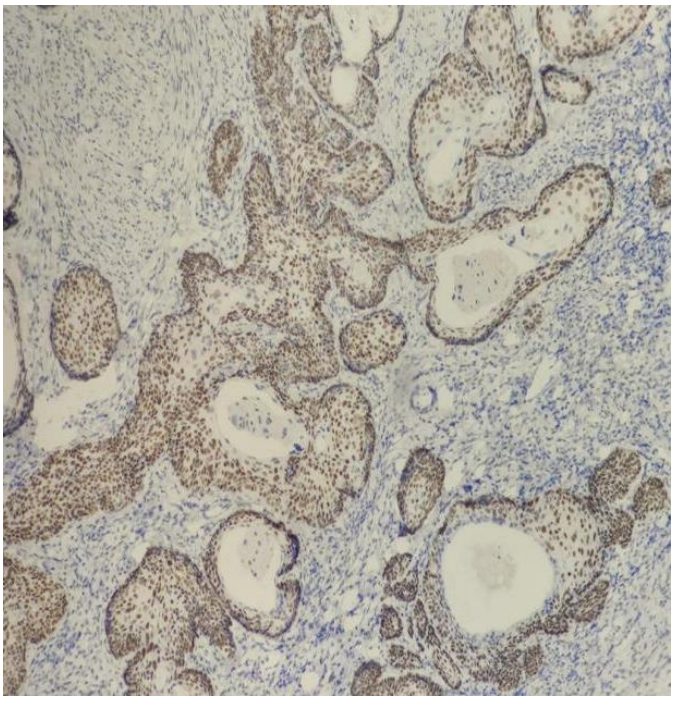

Figure 4. P63 positive ×100 on immunohistochemistry

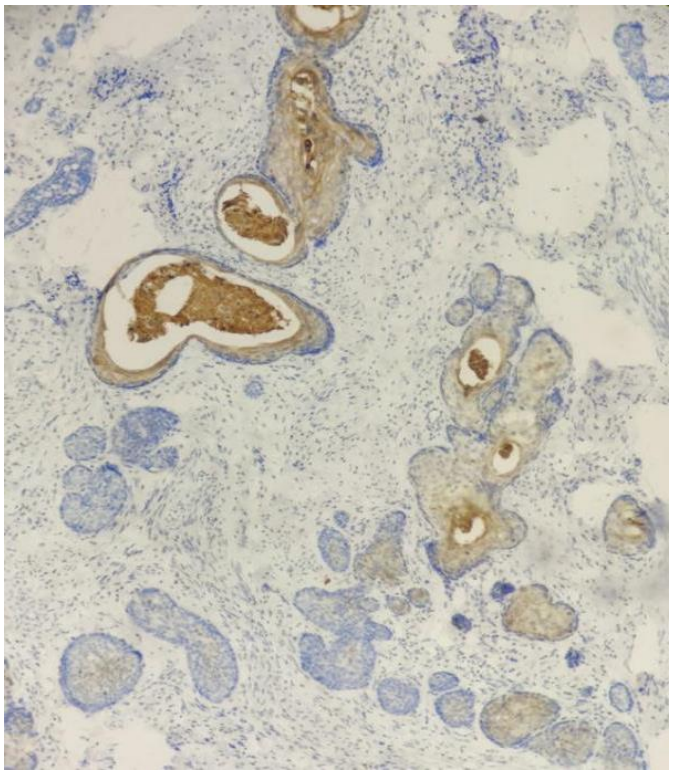

Figure 5. CEA sporadic positive ×100on immunohistochemistry

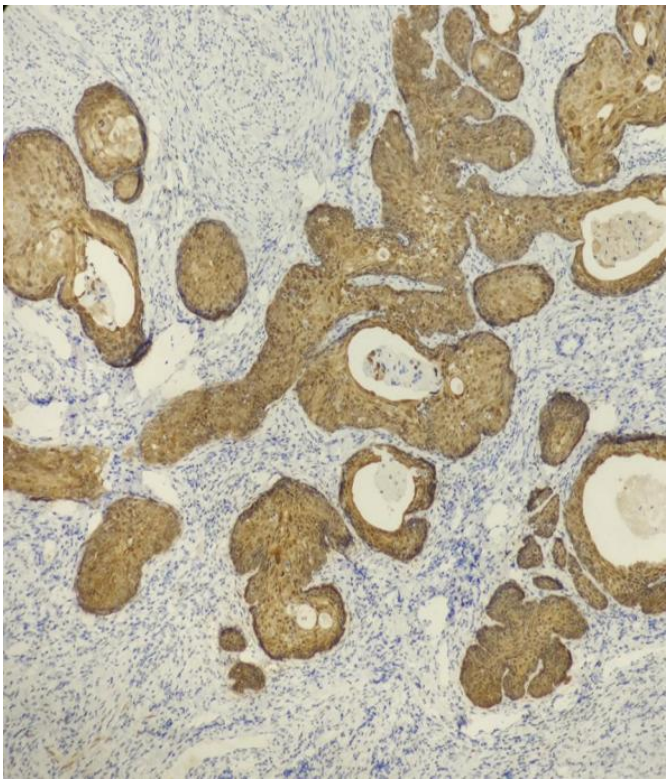

Figure 6. P16 positive ×100 on immunohistochemistry

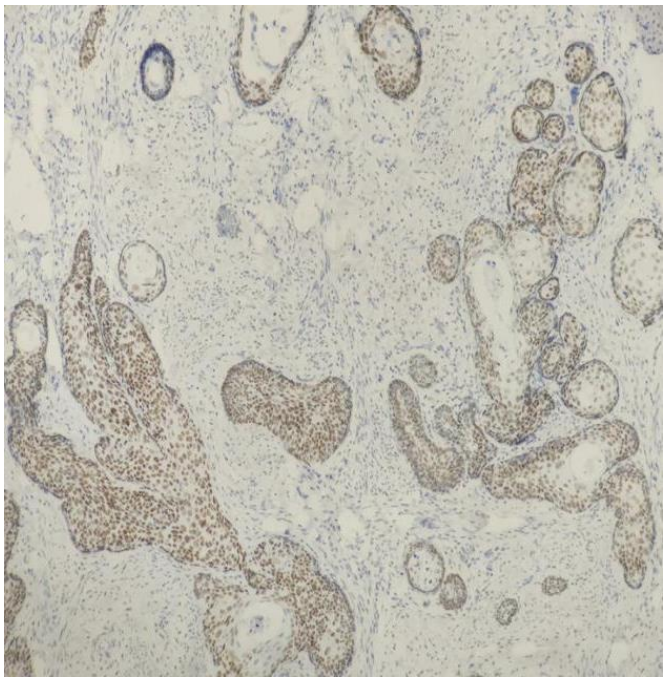

Figure 7. P40 positive ×100 on immunohistochemistry

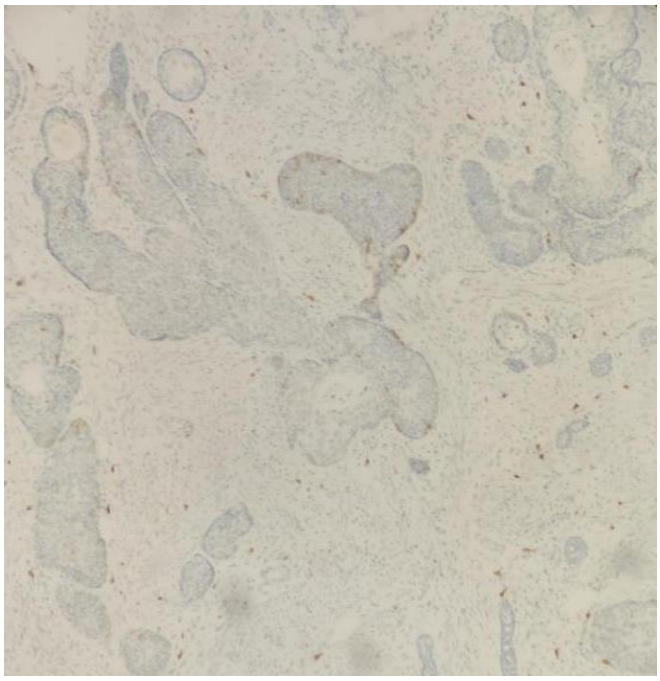

Figure 8. CD117 negative ×100 on immunohistochemistry

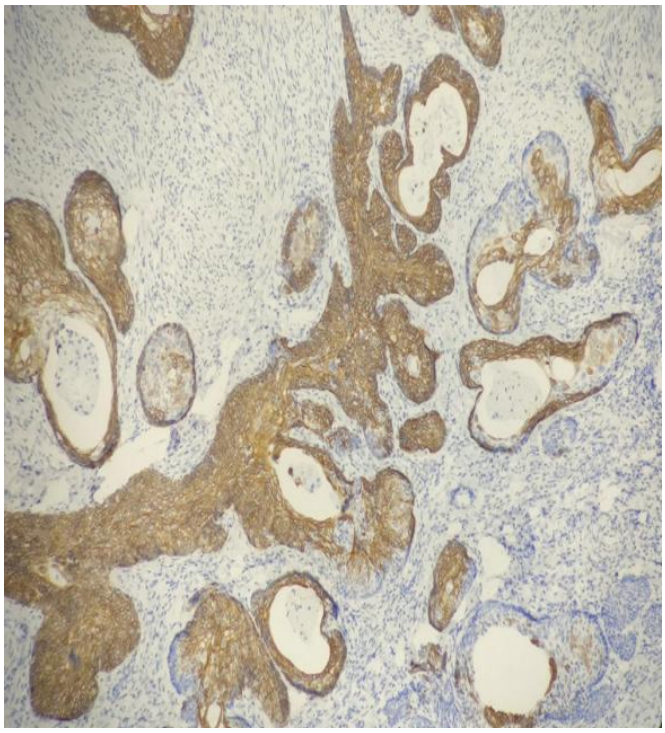

Figure 9. CK7 sporadic positive ×100 on immunohistochemistry

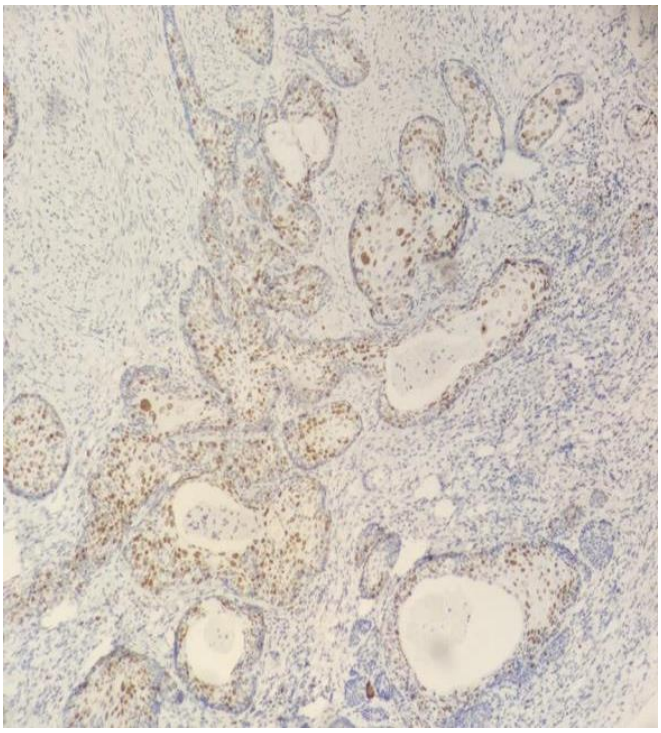

Figure 10. Ki67 (40% positive) ×100 on immunohistochemistry

2. Discussion and literature review

Cervical adenoid basal carcinoma (ABC) is a rare cancer with a low incidence. This disease was first reported by Baggish [1] in 1966. In 1985, van Dinh and Woodruff [2] proposed ABC as an independent tumor. Although the biological behavior of ABC is mostly inert, it often shows invasive growth [3]. This cancer commonly occurs in postmenopausal women. With the deepening of research, it has been found that its incidence is gradually increasing in young women [4]. The majority of patients with ABC have no specific

clinical manifestations. Some patients present with postmenopausal vaginal bleeding, while others with lower abdominal pain. In the majority of these cases, no obvious mass is observed in the cervix, and there are no specific abnormalities seen in gynecological examination. Some patients visit the doctors because of high-risk HPV infection and/or abnormal cytology screening [5]. In this case, the patient was referred for postmenopausal bleeding, and high-risk HPV infection and abnormal cytology were found upon examination.

With regard to its microscopic features, ABC is often arranged in small nests or cords, and the cell body of the cancer cells is small and round- or spindle-shaped, similar to basal cells, with little cytoplasm, round and oval nuclei, inconspicuous nucleoli, and partial nucleoli. The cells are transparent, and the peripheral cells are arranged in a palisade-like manner; the cells are densely arranged, mostly in a solid mass, with a cavity in the center, similar to a gland-like structure, which can form a cavity or cribriform structure, and occasionally squamous epithelial differentiation [6]. In this case, there was squamous differentiation. ABC alone is rare; in most cases, high-grade squamous intraepithelial lesions co-exist with ABC, with some cases having malignant tumors, such as squamous cell carcinoma, small cell carcinoma, and adenoid cystic carcinoma.

Immunohistochemistry shows that ABC is often positive for BCL-2, CK5/6, and P63, negative for CK7, and strongly positive for P16. According to literature, P16-positive patients are often accompanied by HPV16 infection [7]. In this case, the patient was high-risk P16-positive. On the other hand, P53 is often weakly positive in ABC, but there are a few cases that show strongly positive P53. The immunophenotype of this case is generally consistent with that reported in literature.

In terms of differential diagnosis, cervical ABC needs to be differentiated from several diseases.

(1) Basaloid squamous cell carcinoma

Basaloid squamous cell carcinoma is a special subtype of squamous cell carcinoma, with very few primary cervical cases [8]. Under the microscope, it is mainly observed as solid nests or islands; additionally, comedo-like necrotic material can be seen in the center of the cancer nests, with the interstitium showing obvious fibrous connective tissue reaction; cell atypia and mitotic figures are evident, with the peripheral cells of the cancer nest arranged in a palisade [9]. ABC has adenoid-like structures, with cavities and a cribriform arrangement, small and uniform cells, with little atypia, rare mitotic figures, and rarely seen desmoplastic connective tissue.

(2) Adenoid cystic carcinoma

Adenoid cystic carcinoma is more common in salivary glands and has a high degree of malignancy [10]. It rarely occurs in the cervix. Two types of tumor cells can be seen under the microscope: glandular epithelial cells and variant myoepithelial cells. The glandular epithelial cells are arranged in adenoids, and variant myoepithelial cells are distributed around them. Pale eosinophilic secretions can be seen in the gland cavity. Some cells are solid and have cribriform arrangement but some may be in tubular arrangement [11]. In terms of immunohistochemistry, glandular epithelial cells express CD117, whereas variant myoepithelial cells express P63 and S-100; adenoid cystic carcinoma is characterized by t(6;9)(q22-23;p23-24) gene translocation, resulting in *MYB-NFIB* fusion gene, expressed as MYB protein overexpression [12]. Cervical ABC differs from adenoid cystic carcinoma in terms of the tumor cells, immunohistochemistry, and molecular detection.

(3) Neuroendocrine tumors (NTCs)

NTCs are relatively rare, accounting for about 5% of all cervical malignancies [13]. They have certain characteristics, including strong invasiveness, easy recurrence, and easy metastasis. They are similar to small cell carcinoma of the lung and have poor prognosis [14]. Studies have shown that NTCs are related to HPV infection [15], especially HPV18 [16]. Although carcinoid syndrome and Cushing's syndrome are occasionally seen [15], some studies have reported that cervical NTCs may originate from the reserve

cells under the cervical columnar epithelium [17], mainly manifested as insular, trabecular, organoid, or diffuse flaky distribution, accompanied by necrosis, apoptosis, and a large number of mitotic figures (> 20/10 HPF); small cells with few cytoplasm, hyperchromatic nucleoli, inconspicuous nucleoli, and large cells often with organoid differentiation; as well as medium or large tumor cells, with vacuolar nuclei and large nucleoli. Immunohistochemical expressions of neuroendocrine markers CgA, SSTR-2, Syn, and CD56 are absent in ABC.

The pathological morphology of this case shows typical features of ABC with squamous epithelial differentiation. In this context, attention should be paid to the possibility of well-differentiated squamous cell carcinoma since this patient also has high-grade intraepithelial lesion (HSIL). However, well-differentiated squamous cell carcinoma usually forms papillary or nest-like structures, the cancer cells are arranged in a tiled pattern, keratinized beads and single cell keratinization can be seen, and necrosis can also be seen in the center of the cancer nest, which is not seen in this case.

Simple ABC develops slowly and has good prognosis as lymph node metastasis and invasive growth are usually rare. Therefore, for patients with ABC alone or combined with CIN, the treatment should be determined according to the age of the patient. For women in childbearing age and those who still wish to be pregnant, cervical conization should be performed. For postmenopausal women, total hysterectomy with follow-ups should be considered. Other than that, ABC is known to be associated with other malignant tumors; thus, the treatment and prognosis also depend on the histological type and clinical stage of the associated tumors.

Disclosure statement

The authors declare no conflict of interest.

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