

TCT for Atypical Glandular Epithelium in 1 Case and Clinical Analysis

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Abstract: *Objective:* Cervical adenocarcinoma (ECA) screening has low sensitivity and is prone to missed diagnoses. By analyzing a case of atypical glandular epithelium on TCT, this study aims to improve the clinical diagnosis and treatment of such diseases. *Methods:* The clinical examination findings, laboratory tests, and diagnostic process of a case with atypical glandular epithelium on TCT were analyzed. *Results:* The patient was diagnosed with cervical adenocarcinoma. Preoperative symptoms and imaging studies suggested the possibility of adenocarcinoma, and postoperative pathology confirmed the diagnosis of cervical adenocarcinoma (ECA). *Conclusion:* Through the analysis of this case, we aim to improve the clinical diagnosis and treatment of this condition.

Keywords: TCT; Adenocarcinoma of the uterine cervix (ECA); Clinical analysis

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1. Introduction

Endocervical adenocarcinoma (ECA) is a malignant tumor that occurs in the glandular epithelium of the uterine cervix. In recent years, with the popularization of cervical cancer screening technology, the incidence of squamous cell carcinoma (SCC) of the cervix has been decreasing, while the relative incidence of ECA has increased, and its prognosis is worse than that of the same period of time of SCC. The challenges of screening for ECA include: difficulty in sampling the cervical adeno-epithelial neoplasia (AIS) foci, low sensitivity of cytology, poor morphologic features in colposcopy, and about 20% to 40% of the cases are not typical, which makes it difficult to identify ECA. typical, and negative high-risk human papillomavirus (HR-HPV) testing in about 20% to 40% of ECA cases. Studies have shown that cervical cytology combined with HR-HPV testing significantly improves the sensitivity of AIS/ECA detection. However, pathologists and colposcopists are generally relatively inexperienced in the diagnosis of cervical adenoepitheliopathy. For this reason, this article reports a case of cervical liquid-based

cytology (TCT) suggestive of atypical adenoepithelial cells, aiming to improve clinicians' knowledge of this disease.

2. Case information

2.1. General information

The patient, female, 54 years old, was admitted to the hospital with the main cause of “contact bleeding for half a year, and cervical lesions were found on examination for 13 days.” She was admitted to the hospital. The patient is a late menopausal woman, reported contact bleeding half a year ago, the amount of small, bright red, and then consulted the local hospital, the internal examination did not see any obvious abnormalities, and only carried out the symptomatic treatment of hemostasis. more than a month ago, contact bleeding again, the amount of small, and then again in the local hospital, cervical cancer screening: HPV16 (+), HPV58 (+), and then in our hospital for TCT: specimens sent to the examination of the glandular epithelium, atypical glandular epithelium, please take into account the clinical advice, and recommend that the cervical lesions should be found. The patient was asked to combine the clinical examination with the clinical examination and further examination was recommended. She underwent colposcopy on March 2024 in the hospital. Pathology report (1074379): (cervical canal) scattered heterogeneous glands were seen in the sent specimen, immunohistochemical staining supported HPV-associated adenocarcinoma, and no exact mesenchymal stroma was seen, please combine with the clinic. Past history: cesarean section 28 years ago and hysteroscopic polypectomy in 2020.

2.2. Gynecological examination

There was no obvious abnormality in vulvar development, vaginal patency, disappearance of mucosal folds, small amount of bloody vaginal discharge, bright red in color, no odor, thickening and hardening of the cervix, anterior uterine position, atrophy, and poor mobility, no obvious shortening of the main ligaments and sacral ligaments was palpated bilaterally, and no obvious abnormality was palpated in the adnexal area bilaterally.

2.3. Gynecological ultrasound

The uterus was anteriorly positioned, atrophied, and had the usual morphology; the uterine cavity line was clearly displayed. The endometrium was 0.2 cm thick, and the echogenicity of the myometrium was less than homogeneous. The length of the cervix was 2.7cm, and the cervix was visible as a nuchal sac. There was no obvious mass in both adnexa, and CDFI: No abnormal blood flow signal was seen; CDFI: No abnormal blood flow signal was found.

2.4. Pelvic nuclear magnetic resonance imaging

The uterus was in anterior tilt and flexion position; the cervical region was characterized by a long T1-slightly long T2 signal shadow with a size of about 11mm × 10mm × 13mm, involving the cervical stroma; the DWI showed a high signal shadow, the ADC showed a low signal shadow, and the enhancement of the lesion showed a mild enhancement. There was no abnormality in the parafatty interstitial space. Multiple rounded long T2 signal shadows were seen in the cervical region. There was no enhancement on the enhancement scan. No obvious abnormal signal was seen in the bladder and rectum. No lymph nodes with a short diameter greater than 10 mm were seen adjacent to bilateral iliac vessels, and fluid signal shadows were seen in the pelvis. There was no

obvious abnormal signal in the pelvic bone. The soft tissue of the pelvic wall shows no obvious abnormal signal.

She was admitted to the hospital and underwent wide hysterectomy + bilateral adnexectomy + pelvic lymphatic drainage. Postoperative pathology: cervix: HPV-associated adenocarcinoma, SlivaC type, lymphocyte and plasma cell infiltration in the interstitium, infiltration of the superficial cervical layer (inner 1/3 of the layer), no choroidal invasion, no carcinoma in bilateral paracervical tissues and vaginal dissection, atrophic endometrium, no carcinoma in bilateral adnexa, no carcinoma metastasis in the left pelvic lymph node (0/13) and the right pelvic lymph node (0/8), pTNM staging. pT1b1NOMx.

3. Discussion

3.1. Cytologic sensitivity of ECA is low

ECA can occur anywhere within the cervical canal, a characteristic that makes it difficult for the sampling brush to ensure that all potential lesions are reached. In addition, the cells in the cervical glandular crypts are often hidden in the deeper layers of the cervical canal, so it is not easy to reach the glandular cells on the surface of the cervix. In addition, the focal and segmental nature of ECA makes sampling more difficult. Even with adequate sampling by clinicians, the diagnosis of adenopathy by pathologists is challenging ^[1]. In summary, for ECA, the detection rate of TCT positivity is low, and most of them are detected as ASCUS and ASCH. In view of this, relying solely on cytological methods to screen for cervical adenocarcinoma is not as effective as it should be, and combined screening with HPV testing technology and cytological testing can maximize the sensitivity of screening ^[2].

3.2. Clinical symptoms of ECA are atypical

Symptoms of cervical adenocarcinoma are usually inconspicuous and lack specificity. Some patients may experience contact bleeding, such as after sexual intercourse or gynecologic examination. In addition, patients may experience leukorrhea or increased vaginal discharge. However, cervical adenocarcinoma can be difficult to detect in the precancerous stage due to the high false-negative rate of cervical adenocarcinoma on cytologic screening ^[3].

3.3. Characteristics of the case

Combining the above factors, the patient presented with symptoms six months ago, but the local hospital did not conduct relevant cervical cancer screening and only performed internal examination, which was unable to identify adenocarcinoma in situ, adenocarcinoma and atypical hyperplasia. Therefore, how to detect and diagnose adenocarcinoma early in perimenopausal women is particularly important.

3.4. HPV and adenocarcinoma

Persistent infection with high-risk human papillomavirus (HPV) has been recognized as an essential cause of cervical cancer, and the application of HPV testing has gradually expanded, initially as a triage test to assist in the determination of ASC-US (atypical squamous cells of uncertain significance), and then to the development of combined cytology and HPV screening, to the point where experts are now suggesting that HPV testing can be used as a stand-alone screening tool. HPV testing is favored for its high sensitivity and good reproducibility ^[1]. However, it is worth noting that not all cervical adenocarcinomas (ECAs) are associated with HPV infection and there are cases of false-negative HPV tests, which shows the limitations of HR-HPV testing (high-risk HPV testing) ^[4, 5].

The majority of cervical cancers are squamous carcinomas and a small proportion are adenocarcinomas,

with a low detection rate of adenocarcinomas; however, with the spread of standardized screening and treatment tools for cervical cancer and cervical lesions, as well as the active promotion of human papillomavirus (HPV) vaccination and the implementation of vaccination programs, the proportion of squamous cell carcinomas in the composition of cervical malignant tumors has been showing a downward trend, and on the contrary, there is a rising trend of the detection of adenopathy of the uterine cervix ^[2, 6].

3.5. Classification of adenocarcinoma

Cervical adenocarcinoma is regarded as a heterogeneous group of tumors, which differ significantly from squamous cell carcinoma of the cervix in terms of their histology, epidemiological features, prognostic factors, and treatment outcomes ^[4]. For this reason, the 2020 World Health Organization (WHO) guidelines refer to the International Cervical Adenocarcinoma Criteria and Classification (IECC), which was first proposed in 2018, and classify cervical adenocarcinoma into two main categories, HPV-associated and HPV-independent, based on its association with human papillomavirus (HPV) ^[7, 8]. Professor Silva of the Department of Pathology at the Anderson Cancer Center in the United States of America first proposed the Silva classification of cervical adenocarcinoma in 2013, which replaces depth of infiltration (DOI) of the tumor with infiltrative modality and divides cervical adenocarcinomas into three types, A, B, and C, according to the presence or absence of destructive mesenchymal infiltration and the extent of its infiltration ^[9, 10]. Numerous studies have demonstrated the greater validity of the Silva classification in risk assessment of patients with human papillomavirus-associated (HPVA). In particular, type A tumors are less likely to have lymphovascular invasion (LVI) and lymph node metastasis, are usually in the early stages of the disease, and are free of recurrence compared to type B and C tumors. In contrast, type C tumors have a higher risk of recurrence and a poorer prognosis ^[11, 12].

3.6. Treatment of adenocarcinoma

Among the therapeutic strategies for cervical adenocarcinoma, the prognosis for patients with Silva type A is more optimistic, with a longer tumor-free survival and a relatively low risk of lymph node metastasis and recurrence. Therefore, for Silva A patients with negative margins after cervical conization, conservative treatment can be considered to avoid hysterectomy and lymph node dissection.

For Silva type B patients, treatment options usually include cold knife conization, loop electrosurgery (LEEP), or hysterectomy with concomitant sentinel lymph node sampling. If the margins are negative but the sentinel lymph nodes are positive or the pathologic type is reassessed as Pattern C, radical hysterectomy with lymphatic dissection and postoperative adjuvant therapy, such as radiation and chemotherapy are considered on a case-by-case basis ^[13].

In contrast, patients with Silva type C have a poorer prognosis, with a significantly increased risk of recurrence and metastasis. Therefore, this type of patient usually needs to undergo extensive hysterectomy and lymph node dissection, combined with a combination of treatments such as radiotherapy, chemotherapy, and immunotherapy, if necessary ^[14, 15].

Currently, NCCN guidelines recommend radical surgery with lymph node dissection as the standard treatment option for most patients with cervical adenocarcinoma. However, these surgical operations are accompanied by a significant risk of complications, including early complications such as dysuria, urinary tract infection, bleeding, pain, fever, and nerve damage, as well as late complications such as lymphedema, lymphocysts, urinary incontinence, and venous thrombosis. In addition, young patients may face loss of fertility as a result ^[14].

The NCCN guidelines for radiotherapy in locally advanced cervical cancer recommend concurrent radiotherapy with platinum-containing chemotherapy (cisplatin alone [preferred] or cisplatin/fluorouracil) as the treatment of choice for stage IB3, II, III, and IVA disease. These studies have shown that the use of simultaneous radiochemotherapy reduces the risk of death by 30% to 50% compared to radiotherapy alone^[16].

Various cervical cancer screening methods aim to prevent cervical cancer. From the previous cervical cytology to the current combined screening and the application of HPV alone as primary screening, the effectiveness of new screening techniques in preventing cervical cancer has become a hot and controversial topic of current research.

3.7. Experience sharing

Although the detection rate of AGC (atypical glandular cells) is relatively low, its specificity is high^[3, 17]. Therefore, high priority should be given to it once it is detected, and when the cervical cytology result is AGC and positive for HPV16/18, a thorough colposcopic evaluation, biopsy, and cervical sampling should be carried out^[3, 18]. According to cervical cancer screening guidelines, all women under 65 years of age should be screened. If a patient has no history of cervical cancer screening, it may lead to the development of cancer when symptoms appear and then examined. Therefore, for the female patients in the hospital, especially perimenopausal women, it is imperative that they undergo comprehensive screening once contact bleeding or irregular bleeding occurs, to avoid missed diagnosis^[4]. The US ASCCP guidelines recommend that for young women under 25 years of age, the preferred strategy is observation follow-up, but treatment is equally recognized as a viable option. For patients on observational follow-up, treatment should be considered if colposcopy results are unsatisfactory during follow-up, or if the diagnosis of CIN3 is confirmed by histologic examination, or if CIN2 or CIN2/3 persists for up to 24 months^[19].

Implementing a combined screening strategy based on HPV testing technology and cytologic examination is important to avoid underdiagnosis and facilitate clinical diagnosis and treatment. At the same time, increasing the acceptance of screening by the population will be a key measure to reduce the burden of cervical adenocarcinoma, which will strongly promote the implementation of the “Healthy China” strategy and positively respond to the initiative of the World Health Organization (WHO) to eliminate cervical cancer globally, thus accelerating the process of cervical cancer elimination in China^[20].

4. Conclusion

The diagnosis of endocervical adenocarcinoma (ECA) is fraught with many challenges, including the difficulty in sampling the lesion, the low sensitivity of cytological examination, the lack of typical morphological features under colposcopy, and the fact that some cases are HR-HPV negative. To improve the detection rate of ECA, it is recommended to implement a dual screening strategy combining cervical cytology and HR-HPV testing. Clinicians should enhance their understanding of the clinical features of this disease to effectively reduce the risk of missed and misdiagnosis.

Disclosure statement

The authors declare no conflict of interest.

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