Adenoid cystic carcinoma of the vagina
A case report
Lan-Zhi Zhang, MDab, Li-Yan Huang, MDab, An-Liang Huang, MDab, Jin-Xing Liu, MDab, Fan Yang, MDab,*

Abstract
Rationale: Squamous carcinoma is the most common malignancy of vagina. Adenoid cystic carcinoma (ACC) in the vagina is very rare.

Patient concerns: In the present study, we present a 45-year-old woman with a palpable swelling in the vagina. The patient reported body paresthesia, chest congestion, expiratory dyspnea, and itching in the thigh root.

Diagnosis: The ultrasound results revealed inhomogeneous echoes of the muscular layer in the middle and distal area of the vagina, and probed a slightly richer blood flow signal. Then biopsy was performed. On microscopic examination, it was observed that tumor cells were arranged in a tubular or cribriform pattern, and exhibited a consistent size, small nuclei, and nuclear fission. The myoepithelium was lined around the glandular cavity, but the myoepithelium was tumorous. Immunohistochemistry was performed for further verification. Vimentin was positive in mesenchyme and CK-P was positive in epithelial cells. P63 and calponin were spotted, which were focal positive around the glandular cavity. Finally, the patient was diagnosed as ACC.

Interventions: At last, the patient chose chemoradiotherapy, not surgical excision.

Outcomes: The patient is alive and well 13 months after the initial diagnosis.

Lessons: ACC in the vagina is extremely rare. To our knowledge, this report is the first case of ACC arising from the vagina in English-language literature. Extensive surgical section of the tumour and chemoradiotherapy are recommended for therapy. Because of rarity, the prognosis of ACC in vagina is not known.

Abbreviation: ACC = adenoid cystic carcinoma.

Keywords: adenoid cystic carcinoma, biopsy, clinical treatment, clinicopathologic diagnosis, vagina

1. Introduction
Adenoid cystic carcinoma (ACC) has been described in many organs, such as the trachea, mammary glands, uterine cervix and, sinuses.[1–4] Indeed, it is an epithelial tumor that usually originates in the salivary glands, submandibular glands, and minor salivary glands.[1–3] This tumor is malignant, has low local recurrence, and rarely leads to distant metastasis,[1,4] but is strictly location-dependent. Typically, it consists of small basaloid cells with a solid cribriform pattern or epithelial cells with a tubular growth pattern in histology.[5] The occurrence of ACC is fairly scarce in the vagina, and it has not been reported in literature. The present report intends to share 1 case of ACC that occurred in the vagina.

2. Case presentation
The present study was conducted in accordance with the declaration of Helsinki and with approval from the Ethics Committee of our Hospital. A written informed consent was obtained from the patient.

A 45-year-old woman complained of a palpable swelling in the vagina while taking bath 2 months ago. She reported body paresthesia, chest congestion, expiratory dyspnea, and itching in the thigh root. The outpatient examination revealed a 2 to 3 cm nodule from the vaginal orifice, which was fixed with the pubis. The nodule was approximately 2 × 3 cm in size. Biopsy by local hospital provided a description, but there was no definitive diagnosis. Therefore, the patient visited West China Second Hospital (Chengdu, Sichuan) for consultation in August 2017. An ultrasound was first performed on the patient. The results revealed inhomogeneous echoes of the muscular layer in the middle and distal area of the vagina, and a slightly richer blood flow signal (RI = 0.64, Fig. 1) was probed at the same site (Fig. 1). This result could provide guidance for consideration of a malignant tumor. However, the clinical tumor marker detection results were all within the normal range. Positron Emission Tomography-Computed Tomography (PET-CT) indicated a local malignant tumor in the left behind the pubic bone and left vagina. In addition, osteolytic lesions were found in the 10th thoracic vertebra, which was considered as bone metastasis (Fig. 2).

Pathological consultation revealed that tumor cells were arranged in a tubular or cribriform pattern, and exhibited a consistent size, small nuclei, and nuclear fission. The myoepithelium was lined around the glandular cavity. These histological features suggested a diagnosis of ACC. Immunohistochemistry...
was performed for further evidence. It was found that vimentin was positive in mesenchyme cells and CK-P was positive in epithelial cells. Furthermore, AR, CgA, Syn, CD56, S-100, calretinin, and BerEP4 were all negative, hinting that it was exactly an epithelial tumor. It is noteworthy that P63 and calponin were spotted. These were focal positive around the glandular cavity, which verified the existence of the myoepithelium. Indeed, Ki-67 was detected and positive in approximately 20% of the tumor cell nuclei. Based on the pathological report, the patient was advised by clinical doctors to receive chemo-radiotherapy (Fig. 3). The patient is alive and well 13 months after the initial diagnosis.

3. Discussion

Theodor Billroth was the first to describe ACC as cylindromas in his histological studies in 1856. The incidence of ACC is not very high, in general.[10] These are usually observed in the salivary gland. The average age of onset was 57.4 years old, and approximately 60% of patients are women.[11] ACC makes up approximately 6% of all salivary gland tumors. In addition, these make up 15% to 30% of submandibular gland tumors, 30% of minor salivary gland tumors, and 2 to 15% of parotid gland tumors.[12]

Furthermore, this has been reported in many organs in recent years. For instance, lacrimal sac tumors are rare but was reported in 1 case of ACC. The case was a 41-year-old woman with late diagnosis, who underwent ophthalmological examination and multidisciplinary treatment, and was finally confirmed as primary ACC.[13] The ACC also occurred in the female reproductive system. For instance, a 23-year-old woman was diagnosed ACC in left ovary, the tumor had the typical cribriform pattern of ACC, lacked any component of surface epithelial carcinoma, and showed myoepithelial differentiation. And there is a higher incidence in vulva of ACC according to the literature. In another example, ACC of the buccal mucosa has also been reported. Among intraoral ACC, the buccal mucosa was among the rarest sites.[14] In the present case, ACC of the vagina is also very rare. Literatures were searched, but a similar case report could not be found.

In the early stage of ACC, the most common symptom is painless mass, in which few experience this with pain. The level of

Figure 1. Ultrasonographic image showing inhomogenous echoes in the vagina (A, B).

Figure 2. PET-CT scans of the lesion in the vagina (A: PET, B: CT) and the osteolytic lesions in the 10th thoracic vertebra (C: PET, D: CT). PET-CT, Positron Emission Tomography-Computed Tomography.
pain and the process of illness are not the same in different situations. However, tumor cells always spread along the nerve. For instance, it can cause facial nerve paralysis when it occurs in the parotid gland. Correspondently, the major complaint of the patient in the present study was paresthesia of the left body. This symptom was an important tip for consideration of ACC. ACC commonly metastasizes to the lung, bone, and viscera, even with adequate locoregional control, and the imaging tests of the present patient revealed that distant metastasis to bone had already occurred. The preoperative diagnosis is very hard for clinicians, in general, and most cases are dependent on biopsy. Despite its microscopic features, the gross type of ACC should also be given attention, such as painless nodules, indurated, firm, immobile and small telangiectatic vessels.

The treatment aspect of this tumor was chiefly surgery or/and coupled with radiotherapy. Since the tumor in the present case had distant metastasis, the patient was advised to receive chemoradiotherapy before surgery. However, the ACC was unresponsive to chemotherapy, although palliative chemotherapy might have been used in symptomatic patients. Hence, local mass resection is the main radical cure for ACC. Furthermore, adjuvant radiotherapy appears to be a useful way to improve locoregional control and disease-free survival. However, extensive excision was not performed in this case of ACC considering the actual condition of the patient.

Basic studies on ACC have not received much attention at present. This has only been mentioned in one literature, in which the Notch signaling pathway, including NOTCH1 and NOTCH2, mutated functionally in ACC, while TP53, KRAS, and BRAF, as common cancer genes, were unexpectedly identified without mutations. Furthermore, ACC is often driven by the MYB-NFIB fusion gene, resulting in the overexpression of the
proto-oncogene MYB. This may provide as a new marker for clinical diagnosis and treatment.

Author contributions
Conceptualization: Lan-Zhi Zhang and Fan Yang.
Data curation: Lan-Zhi Zhang, Li-Yan Huang, An-Liang Huang, and Jin-Xing Liu.
Formal analysis: Lan-Zhi Zhang, Li-Yan Huang, An-Liang Huang, and Jin-Xing Liu.
Investigation: Lan-Zhi Zhang, Li-Yan Huang, An-Liang Huang, and Jin-Xing Liu.
Methodology: Lan-Zhi Zhang and Fan Yang.
Project administration: Fan Yang.
Resources: Li-Yan Huang, An-Liang Huang, and Jin-Xing Liu.
Software: Li-Yan Huang, An-Liang Huang, and Jin-Xing Liu.
Supervision: Fan Yang.
Writing – original draft: Lan-Zhi Zhang.
Writing – review & editing: Li-Yan Huang, An-Liang Huang, Jin-Xing Liu, and Fan Yang.

References
[1] Cavanzo FJ, Taylor HB. Adenoid cystic carcinoma of the breast. An analysis of 21 cases. Cancer 1969;24:740-5.
[2] Cleveland RH, Nice CM Jr, Ziskind J. Primary adenoid cystic carcinoma (cylindroma) of the trachea. Radiology 1977;122:597-600.
[3] Prempee T, Villasanta U, Tang CK. Management of adenoid cystic carcinoma of the uterine cervix (cylindroma): report of six cases and reappraisal of all cases reported in the medical literature. Cancer 1980;46:1631-5.
[4] Lawrence JB, Mazur MT. Adenoid cystic carcinoma: a comparative pathologic study of salivary gland, breast, lung, and cervix. Hum Pathol 1982;13:916-24.
[5] Laurie SA, Ho AL, Fury MG, et al. Systemic therapy in the management of metastatic or locally recurrent adenoid cystic carcinoma of the salivary glands: a systematic review. Lancet Oncol 2011;12:815-24.
[6] Chaudhry AP, Leifer C, Catler LS, et al. Histogenesis of adenoid cystic carcinoma of the salivary glands. Light and electronmicroscopic study. Cancer 1986;58:72-82.
[7] Ghabach B, Anderson WF, Curtis RE, et al. Adenoid cystic carcinoma of the breast in the United States (1977 to 2006): a population-based cohort study. Breast Cancer Res 2010;12:R54.
[8] Bhosale SJ, Kshirsagar AV, Panji RR, et al. Adenoid cystic carcinoma of female breast: a case report. Int J Surg Case Rep 2013;4:480-2.
[9] Canyilmaz E, Uslu GH, Memiş Y, et al. Adenoid cystic carcinoma of the breast: a case report and literature review. Oncol Lett 2014;7:1599-601.
[10] Spero RH, Huvos AG, Strong EW. Adenoid cystic carcinoma of salivary origin. A clinicopathologic study of 242 cases. Am J Surg 1974;128:512-20.
[11] Ellington CL, Goodman M, Kono SA, et al. Adenoid cystic carcinoma of the head and neck: Incidence and survival trends based on 1973-2007 Surveillance, Epidemiology, and End Results data. Cancer 2012;118:4444-51.
[12] Gondivkar SM, Gadball AR, Chole R, et al. Adenoid cystic carcinoma: a rare clinical entity and literature review. Oral Oncol 2011;47:231-6.
[13] Ramos A, Pozo CD, Chinchurreta A, et al. Adenoid cystic carcinoma of the lacrimal sac: case report. Arq Bras Oftalmol 2016;79:333-5.
[14] Garg V, Roy S, Khanna KS, et al. Adenoid cystic carcinoma of buccal mucosa: a rare case report. Indian J Otolaryngol Head Neck Surg 2016;68:370-3.
[15] Coupland A, Sewpaul A, Darne A, et al. Adenoid cystic carcinoma of the submandibular gland, locoregional recurrence, and a solitary liver metastasis more than 30 years since primary diagnosis. Case Rep Surg 2014;2014:381823.
[16] Harish K, Mangala Gouri SR. Adenoid cystic carcinoma of the parotid metastasizing to liver: case report. BMC Cancer 2004;4:41.
[17] Nascimento AG, Amaral AL, Prado LA, et al. Adenoid cystic carcinoma of salivary glands. A study of 61 cases with clinicopathologic correlation. Cancer 1986;57:312-9.
[18] Sant DW, Tao W, Field MG, et al. Whole exome sequencing of lacrimal gland adenoid cystic carcinoma. Invest Ophthalmol Vis Sci 2017;58: BIO240-6.
[19] Persson M, Andrén Y, Mark J, et al. Recurrent fusion of MYB and NFIB transcription factor genes in carcinomas of the breast and head and neck. Proc Natl Acad Sci U S A 2009;106:18740-4. Persson et al Proc Natl Acad Sci USA 2009.
[20] Witterskog D1 , Lopez-Garcia MA, Lambros MB, et al. Adenoid cystic carcinomas constitute a genomically distinct subgroup of triple-negative and basal-like breast cancers. J Pathol 2012;226:84-96.