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Taiwanese Journal of Obstetrics & Gynecology 52 (2013) 407–410

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Case Report

Coexistent squamous cell carcinoma and adenoid basal carcinoma in the uterine cervix and infection with human papillomavirus (HPV 31)☆

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Accepted 30 April 2012

Abstract

Objective: Adenoid basal carcinoma (ABC) is an uncommon neoplasm of the uterine cervix. ABC can be accompanied by carcinoma *in situ* or invasive carcinoma. Most cases are discovered accidentally during radical hysterectomy. ABC is associated with a high risk of human papillomavirus infection (HPV), most often HPV 16 infection.
Case report: We present a rare case of an 86-year-old Taiwanese married woman who suffered from bloody vaginal discharge and occasional lower abdominal pain and received cervical biopsy. The pathological report revealed squamous cell carcinoma (SCC) of the uterine cervix. After radical hysterectomy, bilateral salpingo-oophorectomy, and bilateral pelvic and para-aortic lymph node dissection, the final pathological report revealed SCC coexisting with ABC, and both of the components were infected by HPV 31. After receiving radiotherapy, she maintained outpatient department follow-up.
Conclusion: A literature review revealed that this was a rare case of combined ABC–SCC associated with HPV 31 infection. In this case, the ABC component did not affect the tumor stage because it was confined to the cervix. However, we must avoid overestimating the clinical stage because the ABC component is thought to be a benign lesion.

Keywords: adenoid basal carcinoma; human papillomavirus 31; squamous cell carcinoma

Introduction

Adenoid basal carcinoma (ABC) of the uterine cervix is a rare neoplasm usually occurring in postmenopausal woman. ABC combined with other carcinomas *in situ* or invasive carcinomas has been previously reported [1–6]. The coexistence of squamous cell carcinoma (SCC) with ABC is very rare, and is usually associated with human papillomavirus (HPV) 16 and HPV 33 infection. Our case is believed to be the first of combined ABC–SCC associated with HPV 31 infection. In our case, both the SCC and ABC components were positive for HPV 31 infection. HPV DNA was detected in both components by polymerase chain reaction (PCR).

Case report

We report the case of an 86-year-old Taiwanese married woman, who had never received a Papanicolaou smear and

☆ No funding was received for this work from any organization.
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1028-4559/$ - see front matter
http://dx.doi.org/10.1016/j.tjog.2012.04.040

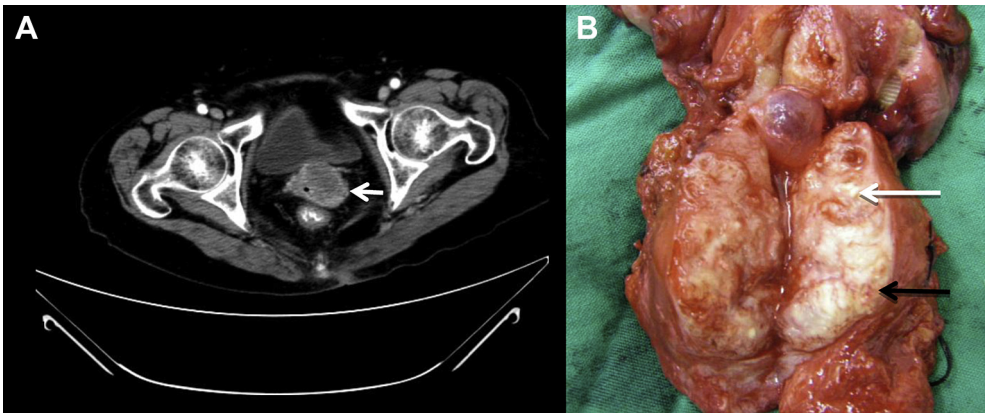


Fig. 1. (A) Computed tomography showed one ill-defined and poorly enhanced lesion measuring 4.2 cm × 3.6 cm × 2.6 cm situated in the uterine cervix (white arrow). (B) Gross appearance of the tumor, squamous cell carcinoma (black arrow), and adenoid basal carcinoma (white arrow).

had a past history of hypertension with regular follow-up. She suffered from bloody vaginal discharge and occasional lower abdominal pain in the past 2–3 months prior to when she visited our gynecologist. After a physical examination, cervical erosion was found, and cervical biopsy was performed. The pathology report revealed SCC of a large cell, nonkeratinizing type. Abdominal computer tomography showed an ill-defined, poorly enhanced lesion measuring 4.2 cm × 3.6 cm × 2.6 cm (Fig. 1A). Serum levels of tumor markers including SCC and carcinoembryonic antigen were <1 ng/mL. Initially, the International Federation of Gynecology and Obstetrics (FIGO) stage IB, American Joint Cancer Committee (AJCC) staging: cT1bN0M0, stage IB was diagnosed by a clinician, and the patient underwent radical hysterectomy (Fig. 1B), bilateral salpingo-oophorectomy, and bilateral pelvic and para-aortic lymph node dissection.

Microscopically, the tumor had two components (Fig, 2A): (1) a nonkeratinizing large cell type of SCC characterized by nested tumor cells with pleomorphic nuclei and frequent mitotic figures, and an absence of keratin pearl formation, with stromal invasion; and (2) an ABC characterized by small, uniform basaloid cells arranged in small nests or glandular patterns. The tumor cells were smaller with fewer pleomorphic nuclei and infrequent mitotic figures. Therefore, the final pathological diagnosis was SCC, large cell, nonkeratinizing type coexistent with ABC. Both components were immunoreactive for P16 (Fig. 2B). A biopsy of both the SCC and ABC components was positive for HPV DNA using PCR (Fig. 3). The DNA of the SCC and ABC components was directly sequenced, and a search of the sequences using the National Center for Biotechnology Information (NCBI) Basic Local Alignment Search Tool (BLAST) for similarity to HPV [7], and it revealed a HPV 31 infection in the SCC and ABC components (Fig. 4). Finally, according to the pathological T stage, excluding the size of ABC, the pathological AJCC stage of our case was pT1b2N0MX, stage IB2.

Discussion

ABC was first described in 1966 [8]. It is a rare tumor, usually asymptomatic clinically, and usually discovered accidentally during hysterectomy and after an abnormal Papanicolaou smear. Most patients are postmenopausal, except for one case of a 20-year-old woman [9]. Adenoid cystic carcinoma and ABC have some common features and the latter may be distinguished from adenoid cystic carcinoma by its aggressive behavior. However, immunohistochemical stains for epithelial membrane antigen, collagen IV, and laminin can

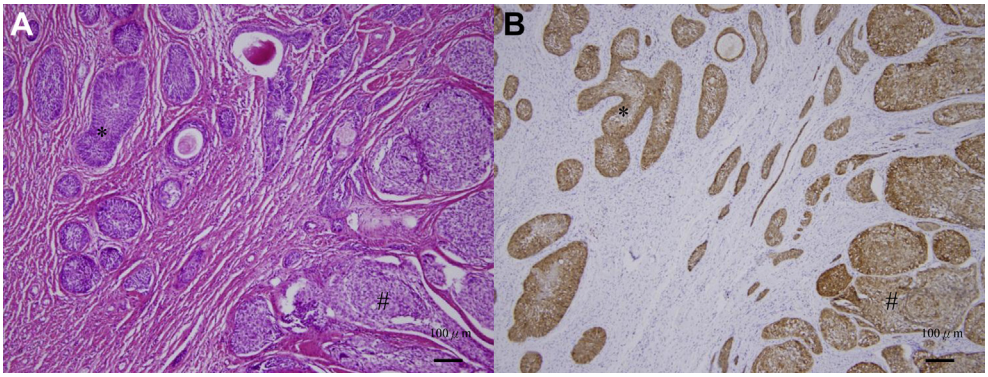
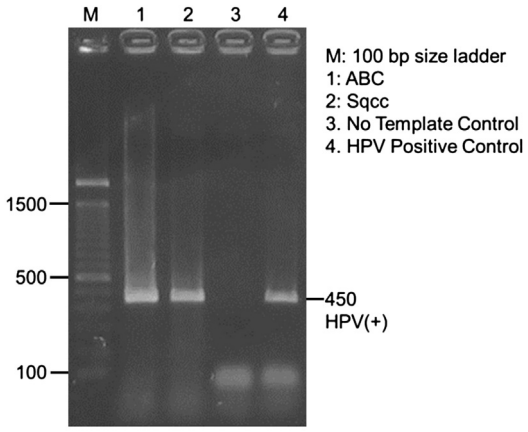


Fig. 2. (A) Section of hematoxylin and eosin stained (10× objective lens) showed squamous cell carcinoma, large cell, nonkeratinizing type (#) characterized by nested tumor cells with stromal invasion, and adenoid basal carcinoma (*) characterized by solid and glandular tumor cells beneath the component of squamous cell carcinoma (B). The two components were immunoreactive for P16 (10× objective lens).



PCR = polymerase chain reaction.

Fig. 3. We punched the squamous cell carcinoma and adenoid basal carcinoma components individually for PCR analysis. We chose the primer (MY11: 5′-GCM CAG GGW CTA TAA YAA TGG-3′ and MY09: 5′-CGT CCM ARR GGA WAC TGA TC-3′, M = A or C, R = A or G, W = A or T, Y = C or T), and performed the PCR analysis. The PCR showed human-papillomavirus-positive signals in both components (450 bp).

help to distinguish ABC from adenoid cystic carcinoma [6,10]. Microscopically, ABC is composed of small, round, uniform basaloid cells in small nests or cord growth patterns. Some pathologists think ABC should be redesignated adenoid basal epithelioma because of its benign nature [11]. Therefore, in the AJCC staging of the invasive carcinoma in the present case, taking into account the size of the ABC, would have led to overstaging.

Most of the carcinomas that coexist with ABC are *in situ* lesions [4,8]. Few cases of SCC accompanied by ABC have been reported.

According to the literature review, immunohistochemical staining is less sensitive than PCR analysis for high-risk HPV detection [12,13]. We looked for the presence of HPV infection in the SCC and ABC by immunohistochemical staining for P16 and detection of HPV DNA by PCR analysis, respectively. The results showed that both components were immunoreactive for P16, and the PCR analysis revealed that both the SCC and ABC components were infected with HPV 31. Our results support the findings of linking infection with

Accession	Description	Max score	Total score	Query coverage	E value	Max ident	Links
gi|333048|J04353.1	Human papillomavirus type 31 (HPV-31) complete genome	742	742	99%	0.0	98%	

Alignments

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>gi|333048|gb|J04353.1|PPH31A  Human papillomavirus type 31 (HPV-31) complete
Length=7912

 Score =  742 bits (822),  Expect = 0.0
 Identities = 426/434 (98%), Gaps = 2/434 (0%)
 Strand=Plus/Plus

Query  2     CAGGGACTATACAATGGTATTTGTTGGGGCAATCAGTTATTTGTTACTGTGGTAGATACC  61
             |||||||    | ||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  6503  CAGGGACACAATAATGGTATTTGTTGGGGCAATCAGTTATTTGTTACTGTGGTAGATACC  656

Query  62    ACACGTAGTACCAATATGTCTGTTTGTGCTGCAAT-GCAAACAGTGATACTACATTTAAA  120
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Sbjct  6563  ACACGTAGTACCAATATGTCTGTTTGTGCTGCAATTGCAAACAGTGATACTACATTTAAA  662

Query  121   AGTAGTAATTTTAAAGAGTATTTAAGACATGGTGAGGAATTTGATTTACAATTTATATTT  180
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Sbjct  6623  AGTAGTAATTTTAAAGAGTATTTAAGACATGGTGAGGAATTTGATTTACAATTTATATTT  668

Query  181   CAGTTATGCAAAATAACATTATCTGCAGACATAATGACATATATTCACAGTATGAATCCT  240
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Sbjct  6683  CAGTTATGCAAAATAACATTATCTGCAGACATAATGACATATATTCACAGTATGAATCCT  674

Query  241   GCTATTTTGGAAGATTGGAATTTTGGATTGACCACACCTCCCTCAGGTTCTTTGGAGGAT  300
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Sbjct  6743  GCTATTTTGGAAGATTGGAATTTTGGATTGACCACACCTCCCTCAGGTTCTTTGGAGGAT  680

Query  301   ACCTATAGGTTTGTAACCTCACAGGCCATTACATGTCAAAAAACTGCCCCCCAAAAGCCC  360
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Sbjct  6803  ACCTATAGGTTTGTCACCTCACAGGCCATTACATGTCAAAAAACTGCCCCCCAAAAGCCC  686

Query  361   AAGGAAGATCCATTTAAAGATTATGTATTTTGGGAGGTTAA-TTAAAMGAAAAGTTTTCT  419
             |||||||||||||||||||||||||||||||||||||||| ||||| ||||||||||||
Sbjct  6863  AAGGAAGATCCATTTAAAGATTATGTATTTTGGGAGGTTAATTTAAAAGAAAAGTTTTCT  692

Query  420   GCAGATTTAGATCA  433
             ||||||||||||||
Sbjct  6923  GCAGATTTAGATCA  6936
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Fig. 4. Gel of the SCC and ABC components were sent for direct sequencing. DNA sequences from the SCC and ABC components matched the sequence of human papillomavirus 31 (98%). ABC = adenoid basal carcinoma; SCC = squamous cell carcinoma.

HPV to invasive carcinoma and ABC, and our case is believed to be the first to show HPV 31 infection [3,14,15].

In conclusion, coexistent SCC and ABC in the uterine cervix are rare, and this is believed to be the first case with infection with HPV 31. Although coexistent SCC and ABC are noted, only the SCC component should be estimated for clinical staging. In our case, the ABC component did not affect the staging because the tumor was confined to the cervix. However, we must keep in mind that we might overestimate the clinical stage, resulting in overtreatment.

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