Adenoid Basal Carcinoma of the Uterine Cervix

Yi-Duen Huang, Wu-Chou Lin, Lian-Shung Yeh, Guan-Chin Tseng[1], Wei-Chun Chang

Department of Obstetrics and Gynecology, [1]Department of Pathology,

China Medical University Hospital, Taichung Taiwan.

Adenoid basal carcinoma of the uterine cervix is a very uncommon neoplasm; in fact, only 65 cases have been reported in the English literature. Previous reports have indicated that this tumor is usually diagnosed during follow-up of abnormal Papanicolaou smear in asymptomatic postmenopausal women; the prognosis is usually favorable. We report two asymptomatic menopausal women who had abnormal cervical smear screening results; adenoid basal carcinoma of the uterine cervix was diagnosed in one of the women after conization of the cervix and in the other woman at follow-up after hysterectomy. **(Mid Taiwan J Med 2007;12:51-7)**

Key words

adenoid basal carcinoma, adenoid cystic carcinoma, cervical carcinoma

INTRODUCTION

Adenoid basal carcinoma (ABC) of the uterine cervix was first recognized as a distinct clinicopathologic entity by Baggish and Woodruff in 1966 [1]. ABC and adenoid cystic carcinoma (ACC), first reported by McGee et al in 1965, were both presumed to be derived from the reserve cell layer of the cervical epithelium because they had very similar histological morphology. Moreover, mucin and immuno-histochemical analysis led Grayson et al. to suggest that ABC may be the precursor of ACC. Distinction between these two neoplasms is of clinical significance because ABC usually has a more favorable prognosis and less local recurrence or distant metastasis than ACC. We report two cases of ABC of the cervix discovered incidentally in patients with high-grade squamous intraepithelial neoplasia (HSIL) of the uterine cervix. The clinical and histological features are described and the relevant literature is reviewed.

Received : 16 June 2006. Revised : 19 July 2006.
Accepted : 6 November 2006.

Address reprint requests to : Wei-Chun Chang, Department of Obstetrics and Gynecology, China Medical University Hospital, 2 Yuh-Der Road, Taichung 404, Taiwan.

CASE REPORT

Case 1

A 69-year-old woman with a history of Parkinsonism and stroke was found to have an abnormal Papanicolaou (Pap) smear during routine screening. She had been menopausal for 20 years and did not have any gynecologic symptoms. Cervical biopsy revealed carcinoma in situ; she was therefore referred to our outpatient department. The colposcopic exam showed a retracted transformation zone in the cervical cannel. Conization and endocervical curettage (ECC) of the cervix was performed. Surgical pathology showed ABC composed of small nests of basaloid cells with focal glandular differentiation. The tumor had invaded the underlying stroma (invasive lesion up to 13 mm in width and 4 mm in depth). Cervical intraepithelial neoplasia 3 (CIN 3, HSIL) with glandular involvement was also noted. The ABC involved the inner margin but not the basal

margin. No definite lymphovascular permeation or perineural invasion was seen. Cervical ABC stage Ib1 was diagnosed and the patient underwent postoperative radiotherapy. There was no evidence of disease at 11-month follow-up.

Case 2

A 75-year-old woman was found to have an abnormal cervical smear during routine screening. Her last menstrual period was at the age of 44 years and she had no gynecologic symptoms. Colposcopy revealed an atrophic cervix and a retracted transformation zone, but no definite acetowhite lesion except for patches of punctation-like change at the 6 to 9 o'clock positions. Cervical biopsy and ECC specimens revealed CIN 1 and CIN2 separately. The specimens taken by loop electric excision procedure (LEEP) of the cervix revealed CIN 3 with glandular involvement and section margin involvement. Hysterectomy was performed 3 months later because the follow-up smear had revealed atypical squamous cells, and the presence of high-grade squamous intraepithelial lesion could not be excluded. Surgical pathology of the removed uterus confirmed ABC extending into more than 80% of the cervical wall, (about 9 mm in depth, close to the parametrium) and upwards to the endocervix; perivascular invasion and desmoplastic reaction were also noted. The tumor cells were arranged in nests and cords, with central cystic change and squamoid differentiation; peripheral nuclear palisading was also seen. There was little mitotic activity, and no definite perineural invasion (Figure). After operation, the patient underwent six courses of concurrent chemoradiation therapy with cisplatine (50 mg/M^2). No recurrence was noted at 26-month follow-up.

DISCUSSION

ABC of the uterine cervix is a rare primary neoplasm, accounting for less than 1% of all cervical adenocarcinoma. Only 67 cases have been reported since it was first described in 1966. The clinical characteristics and treatment modalities are summarized in Tables 1 and 2. Clinically, ABC occurs almost always in postmenopausal women (mean age, 65 yr). As in our two patients, ABC is usually diagnosed after an abnormal Pap smear result and patients are usually asymptomatic (47/67; 70%). Grossly, most of the cervix appears normal (56/67; 84%) and usually no gross mass is present. An associated squamous neoplasm was identified in 93% of reported patients (62/67); most consisted of either high-grade squamous intraepithelial neoplasia or carcinoma in situ (55/67; 82%). One of the patients also had an adenocarcinoma in situ [1]. Invasive squamous carcinoma was reported in 11 patients; microinvasive squamous cell carcinoma was reported in 3 patients [2-4]. Generally, the clinical outcome is favorable;

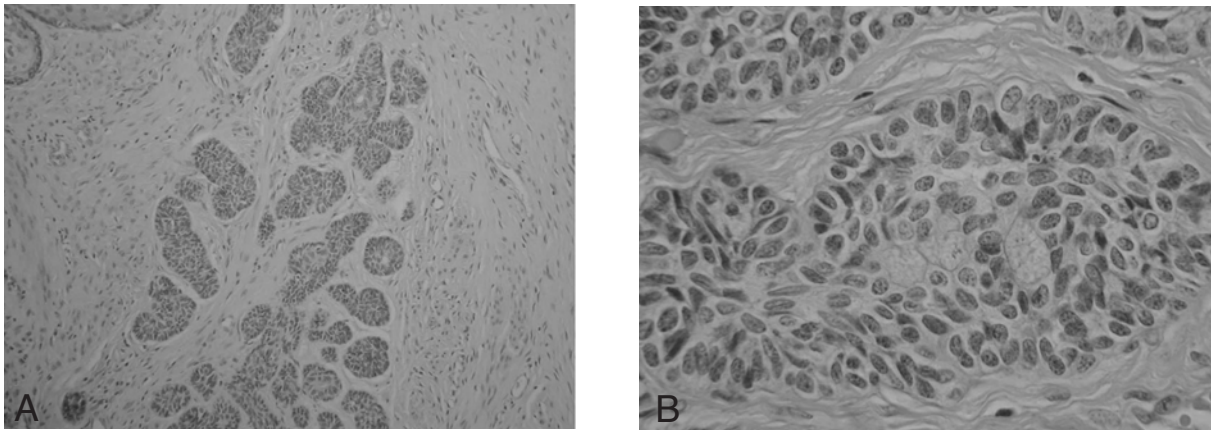

Figure. Adenoid basal carcinoma. A: Multiple small nests without stromal reaction comprising bland basaloid epithelial cells with peripheral palisading cells (H & E, 40×). B: Tumor cell nests are composed of small basaloid cells with scant cytoplasm and hyperchromatic nuclei. Note the peripheral palisading of tumor cells, squamous differentiation and microcyst formation (false lumen) in the center. Very little mitotic activity and central necrosis are visible (H & E, 400×).

Table 1. Literature summary of reported cases of cervical adenoid basal carcinoma

Year	Authors	No. of patients	Mean age (yr)	Signs and symptoms (No./type)	Gross cervical lesion (No./type)	Associated cervical squamous lesion (No./type)	Therapy (No./type)	Lymph node metastasis	Follow-up (No./status)
1966	Baggish & Woodruff[1]	3	55	1/Vaginal atrophy 1/Uterine prolapse 1/Asymptomatic	None	3/CIS	3/ATH or VTH	N/A	3/ANED; 5,7,13 yr
1971	Baggish & Woodruff[5]	2	75	1/Lower abdominal pressure 1/PMB	None	1/CIS 1/HSIL	1/ATH 1/Died before therapy	N/A	1/postoperative death* 1/ANED;6 mo
1972	Shilkin[11]	1	78	1/PMB	1/cervical mass	1/CIS	1/VTH, RT	N/A	1/DNED; 16 mo
1980	Daroca & Dhurandhar[6]	3	58	1/Vaginal bleeding 1/PMB 1/Asymptomatic	1/None 2/Cervical erosion	1/Invasive carcinoma 1 / CIS 1 / None	2/ATH, pelvic LN 1/ATH	None (42 nodes)	2/ANED; 1, 7.8 yr 1/DNED; 3 mo
1985	VanDinh & Woodruff[7]	4	56	4/Asymptomatic	3/None 1/Slight ulcer	3/HSIL/CIS 1/None	4/ATH or VTH	N/A	4/ANED; 2,3,9,12 yr
1988	Ferry & Scully[2]	14	64	11/Asymptomatic 2/PMB 1/Uterine prolapse	11/None 2/Induration 1/Not available 12/HSIL/CIS	12/HSIL/CIS 1/Microinvasive carcinoma 1/Unknown	9/ATH or excision of cervix 2/ATH, excision of cervix, RT 2/Not available 1/Cone	N/A	11/ANED; 2-10 yr, mean 5 yr 1/DNED; 2 yr 1/DOD; 3 mo† 1/ANED; immediately postoperatively
1994	Samartunga[8]	1	63	1/PMB	1/mucosal abnormality	1/CIS	1/ATH	N/A	1/ANED; 1.5 yr
1995	Peterson & Neumann[17]	1	64	1/Asymptomatic	1/None	1/HSIL	1/cone	N/A	N/A
1997	Senzaki[9]	1	69	1/PMB	1/None	1/CIS	1/ATH, BSO, LN	None (18)	1/ANED; 6 mo
1998	Brainard & Hart[3]	12	71	8/Asymptomatic 2/Dysuria 1/PMB 1/Not available	11/None 1/Focal hemorrhage	10/HSIL/CIS 1/Microinvasive carcinoma 1/None	3/ATH; 3/RAH, LN 3/Cone 1/BSO, LN, RT 1/ATH, RT; 1/ATH, LN	None (104 nodes)	9/ANED; 4-82 mo, mean 30 mo 3/DNED; 24 mo, 63 mo, 87 mo
1999	Grayson[15]	9	66	2/Vaginal bleeding 7/Asymptomatic	2/Cervical erosion 7/None	6/HSIL 2/LSIL	9/N/A	9/N/A	9/N/A
2002	Takeshima[12]	1	84	1/Lower abdominal mass	1/None	1/HSIL/CIN3	1/ATH, BSO, CT, RT	1/N/A	1/DNED; 2 mo
2004	Khoury[18]	1	79	1/Asymptomatic	1/None	1/HSIL	1/RAH	1/N/A	1/N/A
2005	Parwani[4]	10	65	8/Asymptomatic 2/Uterine prolapse	10/None	7/HSIL/SCC 1/HSIL/SCC/ small cell ca. 1/HSIL/micro-invasive ca. 1/LSIL/SCC	4/RAH, LN 2/VTH ; 1/ATH 1/Cone, RT 1/ATH, BSO, RT 1/ATH, BSO, LN, RT	None (145)	7/ANED, 8-84 mo, mean 45 mo 1/DNED; 18 mo 2/ANED; immediately postoperatively
2005	Teramoto[10]	2	64	2/Asymptomatic	2/None	1/CIN3 1/SCC	1/Cone 1/RAH, LN	1/N/A 1/None	2/ANED; 9 yr, 18 mo
2006	Current series	2	72	2/Asymptomatic	2/None	2/HSIL/CIN3	1/Cone, RT 1/ATH, BSO, CCRT	2/N/A	2/ANED; 8, 27 mo

ANED = alive no evidence of disease; ATH = abdominal total hysterectomy; BSO = bilateral salpingooophorectomy; CIN = cervical intraepithelial neoplasia; CIS = carcinoma is situ; CT = chemotherapy; CCRT = concurrent chemoradiation therapy; DNED = dead no evidence of disease; DOD = dead of disease; HSIL = high-grade squamous intraepithelial lesion; LN = lymph node dissection; LSIL = low-grade squamous intraepithelial lesion; N/A = not applicable; PMB = postmenopausal bleeding; RAH = radical abdominal hysterectomy; RT = radiation therapy; SCC = squamous cell carcinoma; VTH = vaginal total hysterectomy. *Died of complications of uterine perforation at D&C for evaluation of postmenopausal bleeding. †Aggressive adenoid basal carcinoma.

distant metastasis has only been reported in one patient [2]. Our 2 patients were both menopausal and ABC was diagnosed after initial abnormal cervical smear. ABC was associated with CIN lesion in both women.

Follow-up information of the 67 patients revealed that 46 (71%) were alive without evidence of recurrent or metastatic disease after follow-up intervals ranging from 4 months to 13 years (mean, 4.3 years), regardless of the type of

Table 2. Clinical characteristics of 67 patients with adenoid basal carcinoma of the uterine cervix

Characteristic		n (%)
Symptom	Asymptomatic	47 (70.1)
	Genital bleeding	11 (16.4)
	Cervical prolapse	4 (6.0)
	Abdominal mass	1 (1.5)
	Lower abdominal pressure	1 (1.5)
	Dysuria	2 (3.0)
	Not available	1 (1.5)
Gross appearance	Normal	56 (83.5)
	Erosion	4 (6.0)
	Indurations	2 (3.0)
	Slight ulcer	1 (1.5)
	Cervical mass	1 (1.5)
	Mucosal abnormality	1 (1.5)
	Focal hemorrhage	1 (1.5)
	Not available	1 (1.5)
Associated lesion multiple items	CIN	58 (86.6)
	LSIL	3 (4.5)
	HSIL	55 (82.1)
	Carcinoma	4 (6.0)
	None	3 (4.5)
	Unknown	1 (1.5)
Prognosis	Alive	46 (68.7)
	Dead, no evidence of disease	8 (11.9)
	Died of other cause	1 (1.5)
	Died of tumor	1 (1.5)
	Not available	11 (16.4)

CIN = cervical intraepithelial neoplasia; LSIL = low-grade squamous intraepithelial lesion; HSIL = high-grade squamous intraepithelial lesion.

therapy used [1,3,4,5-10]. Eight patients (12%) died without evidence of recurrence of cervical tumor from 2 months to 7.3 years after diagnosis [2-4,6,11,12]. Five patients were treated with conization only [2,3,13]. Most patients underwent some form of hysterectomy, often with bilateral salpingo-oophorectomy and lymph node dissection. None of the patients who underwent lymph node dissections had evidence of lymph node metastases [3,6,9,14]. One patient with a component of small cell carcinoma died of other causes, without evidence of disease on imaging studies 18 months after diagnosis [14]. Only one patient with ABC of the cervix was reported to have had lung metastasis; she died of lung cancer within 3 months of diagnosis [2]. Ferry and Scully reported that the patient had an aggressive ABC characterized by slender cords which had penetrated deeply into the stroma; the cells showed striking myxoid change with nuclear atypia [2]. However, Brainard and Hart reported that it should be excluded from the documented cases of ABC of the cervix [3].

Histologically, ABC is composed of small, oval, and uniform cells that lack nuclear atypia and resemble basal cell carcinoma of the skin. The cells are arranged in nests and cords; they are characterized by a high N/C ratio and peripheral nuclear palisading. Squamous differentiation in the center of the tumor nests with microcystic change is sometimes present. ABC may be confused with ACC since they both have similar histologic morphology and are both associated with cervical intraepithelial neoplasms. However, it is necessary to differentiate ABC from ACC of the cervix because the latter is associated with a distinctly unfavorable prognosis. ACC usually has larger and less uniform cells, causes more necrosis, and shows more mitotic activity than ABC. Intraluminal hyalinization in the stroma is another characteristic of ACC. ABC is much less aggressive, has less lymphatic invasion and rarely

metastasizes. It appears that pure, typical ABC lacks many of the features of a malignant neoplasm and virtually always behaves in a benign fashion, even when present deep within the cervical stroma. Immunohistochemical and mucin stains are usually not useful in distinguishing between ABC and ACC. Staining of type IV collagen and laminin in the extracellular basement membrane is characteristic of ACC; however, relying on type IV collagen and laminin immunohistochemistry to differentiate between ABC and ACC is still debatable [15].

Recent studies have implicated infection by high-risk human papilloma virus (HPV) types as well as abnormalities in p53 as causes of cervical ABC [13,14]. In addition to the well-documented histologic and biologic differences between the two types of cancer, Grayson et al. have proposed that there may be a histogenetic relationship between ABC and ACC of the uterine cervix [14-16]. Both tumors have certain similarities, including 1) the striking propensity to occur in black postmenopausal women, 2) the capacity for divergent differentiation, and 3) a proven association with integrated high-risk HPV types. In addition, there have been cases of tumors where classic ABC is seen merging with ACC, exhibiting areas of transition between the two components [2,15]. They propose that ABC may be a precursor lesion of ACC if left undetected [15].

Since the prognosis of ABC is favorable, radical surgery is adequate. ABC behaves in a benign fashion even after conization of the cervix with and without postoperative radiation therapy [2-4]. However, if the tumor is associated with adenocarcinoma or squamous cell carcinoma, treatment will depend on the stage of these carcinomas [7]. The two patients presented in this report had cervical ABC, stage Ib, and received adequate treatment. The prognosis for both of them is good.

REFERENCES

1. Baggish MS, Woodruff JD. Adenoid-basal carcinoma of the cervix. *Obstet Gynecol* 1966;28:213-8.
2. Ferry JA, Scully RE. "Adenoid cystic" carcinoma and adenoid basal carcinoma of the uterine cervix. A study of 28 cases. *Am J Surg Pathol* 1988;12:134-44.
3. Brainard JA, Hart WR. Adenoid basal epitheliomas of the uterine cervix: A reevaluation of distinctive cervical basaloid lesions currently classified as adenoid basal carcinoma and adenoid basal hyperplasia. *Am J Surg Pathol* 1998;22:965-75.
4. Parwani AV, Smith Sehdev AE, Kurman RJ, et al. Cervical adenoid basal tumors comprised of adenoid basal epithelioma associated with various types of invasive carcinoma: clinicopathologic features, human papillomavirus DNA detection, and P16 expression. *Hum Pathol* 2005;36:82-90.
5. Baggish MS, Woodruff JD. Adenoid basal lesions of the cervix. *Obstet Gynecol* 1971;37:807-19.
6. Daroca PJ, Dhurandhar HN. Basaloid carcinoma of uterine cervix. *Am J Surg Pathol* 1980;4:235-9.
7. VanDinh T, Woodruff JD. Adenoid cystic and adenoid basal carcinomas of the cervix. *Obstet Gynecol* 1985; 65:705-9.
8. Samaratunga H, Beresford A, Davison A. Squamous cell carcinoma in-situ involving mesonephric remnants: a potential diagnostic pitfall. *Am J Surg Pathol* 1994;18:1265-9.
9. Senzaki H, Osaki T, Uemura Y, et al. Adenoid basal carcinoma of the uterine cervix:immunohistochemical study and literature review. *Jpn J Clin Oncol* 1997;27: 437-41.
10. Teramoto N, Nishimura R, Saeki T, et al. Adenoid basal carcinoma of the uterine cervix: report of two cases with reference to adenosquamous carcinoma. *Pathol Int* 2005;55:445-52.
11. Shilkin KB. Adenoid basal carcinoma of the cervix uteri. *J Clin Pathol* 1972;13:301-5.
12. Takeshima Y, Amatya VJ, Nakayori F, et al. Co-existent carcinoma and adenoid basal carcinoma of the uterine cervix and correlation with human papillomavirus infection. *Int J Gynecol Pathol* 2002; 21:186-90.
13. Jones MW, Kounelis S, Papadaki H, et al. The origin and molecular characterization of adenoid basal carcinoma of the uterine cervix. *Int J Gynecol Pathol* 1997;16:301-6.
14. Grayson W, Taylor LF, Cooper K. Adenoid basal carcinoma of the uterine cervix: detection of integrated papillomavirus in a rare tumor of putative "reserve cell" origin. *Int J Gynecol Pathol* 1997;16:307-12.

15. Grayson W, Taylor LF, Cooper K. Adenoid cystic and adenoid basal carcinoma of the uterine cervix: comparative morphologic, mucin, and immunohistochemical profile of two rare neoplasms of putative "reserve cell" origin. *Am J Surg Pathol* 1999; 23:448-58.
16. Grayson W, Taylor LF, Cooper K. Detection of integrated high risk human papillomavirus in adenoid cystic carcinoma of the uterine cervix. *J clin Pathol* 1996;49:1-5
17. Peterson LS, Neumann AA. Cytologic features of adenoid basal carcinoma of the uterine cervix. A case report. *Acta cytol* 1995;39:563-8.
18. Khoury T, Lele S, Tan D. Pathologic quiz case: an asymptomatic 79-year-old woman with an abnormal Papanicolaou test. Adenoid basal carcinoma of the cervix. *Arch Pathol Lab Med* 2004;128:485-6.

子宮頸腺樣基底癌

黃意惇 林武周 葉聯舜 曾冠欽[1] 張維君

中國醫藥大學附設醫院 婦產部 病理部[1]

子宮頸腺樣基底癌相當少見。我們搜尋本院近七年來的子宮頸癌病理資料庫，發現僅有兩例個案，整理過去英文文獻的個案報告也僅有65例，其發生率小於子宮頸癌的百分之一。此二個案皆爲停經後的婦女，因例行性的子宮頸抹片檢查發現子宮頸上皮內贅生瘤而來本院求診，進一步的子宮頸圓錐狀切除或全子宮切除後的病理檢查發現合併有腺樣基底癌存在。回顧過去文獻指出，子宮頸腺樣基底癌通常發生在停經後無症狀的婦女，因子宮頸抹片異常而被發現，這一類的子宮頸癌必須和子宮頸腺樣囊狀癌小心區別，子宮頸腺樣囊狀癌通常易於轉移且預後較差，子宮頸腺樣基底癌則有較好的預後。（中台灣醫誌 **2007;12:51-7**）

關鍵詞

腺樣基底癌，腺樣囊狀癌，子宮頸癌

聯絡作者：張維君

地　　址：404台中市北區育德路2號

中國醫藥大學附設醫院　婦產部

收文日期：2006年6月16日　　修改日期：2006年7月19日

接受日期：2006年11月6日