

HKSCCP

Clinical pathology conference:

**A case of Adenoid Basal  
Carcinoma of Cervix**

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TKOH/ UCH

# Clinical History

- Madam PPY
- F/ 73
- Para 4+0
- FTNSDx4
- OAH resident

# Clinical History

- 26.6.02
- 1st seen in SOPD for LGSIL
- Menopause at age of 45
- No PMB
- Routine pap smear in Department of Health: LGSIL

# Clinical History

- Past Medical History:
- IHD on TNG and Isordil
- Post RAI hypothyroidism on Thyroxine
- Spinal collapse fracture no OT done
- # Rt tibia with POP 40 yrs ago

# Clinical History

- Vaginal examination: NAD
- 3.10.02
- 1st colposcopy
- Assessment: incomplete
- Atrophic cervix
- No definite lesion seen
- Dx : atrophic changes
- Biopsy not taken
- Plan to FU with smear taking
- Follow on smears (PS/ ECS):
- 1.03: ASC-US
- 7.03: ASC-US

# Clinical History

- Oral Premarin was given
- 2nd Colposcopy on 06.11.03
- Assessment: satisfactory
- Dx: CIN I/ HPV
- Bx at 8 and 10 o'clock
- CIN I, condyloma
- She was counseled for LEEP under LA or observation, she refused operation and requested observation

# Clinical History

- PS/ ECS
- 1.04: LGSIL
- 6.04: HGSIL
  
- She was counseled for LEEP again

# Clinical History

- LEEP under LA was done on 2.9.04
- Histopathology report:
- **Adenoid basal carcinoma** , CIN III, HPV infection. The ectocervical, endocervical margins showed involvement by moderate to severe dysplasia. The endocervical specimen showed focal squamous dysplasia.



# Clinical History

- LAVH+BSO in UCH on 4.11.04
- Findings:
  - uterus was small, cervix was friable with yellow and brown staining, colposcopy was unsatisfactory, no lesion seen in Vagina
- Path:
  - Uterus with a small endometrial polyp, vaginal cuff was unremarkable, the uterine cervix with transformation zone replaced by granulation tissue with inflammation, haemorrhage and haemosiderin deposit consistent with previous surgery
- **no malignancy**, small endometrial polyp
  
- Post-op: on and off pv spotting
- PV: tiny granulation tissue at vault and AgNO3 applied
- Vault smear on 5.1.05: negative

# WHO histological classification of tumours of the uterine cervix

## Epithelial tumours

### Squamous tumours and precursors

Squamous cell carcinoma, not otherwise specified	8070/3	Early invasive adenocarcinoma	8140/3
Keratinizing	8071/3	Adenocarcinoma in situ	8140/2
Non-keratinizing	8072/3	Glandular dysplasia	
Basaloid	8083/3	Benign glandular lesions	
Verrucous	8051/3	Müllerian papilloma	8560/3
Warty	8051/3	Endocervical polyp	8015/3
Papillary	8052/3	Other epithelial tumours	8015/3
Lymphoepithelioma-like	8082/3	Adenosquamous carcinoma	
Squamotransitional	8120/3	Glassy cell carcinoma variant	
Early invasive (microinvasive) squamous cell carcinoma	8076/3	Adenoid cystic carcinoma	8200/3
Squamous intraepithelial neoplasia		Adenoid basal carcinoma	8098/3
Cervical intraepithelial neoplasia (CIN 3)	8077/2	Neuroendocrine tumours	
Squamous cell carcinoma in situ	8070/2	Carcinoid	8240/3
Benign squamous cell lesions		Atypical carcinoid	8249/3
Condyloma acuminatum		Small cell carcinoma	8041/3
Squamous papilloma	8052/0	Large cell neuroendocrine carcinoma	8013/3
Fibroepithelial polyp		Undifferentiated carcinoma	8020/3

### Glandular tumours and precursors

Adenocarcinoma	8140/3
Mucinous adenocarcinoma	8480/3
Endocervical	8482/3
Intestinal	8144/3
Signet-ring cell	8490/3
Minimal deviation	8480/3
Villoglandular	8262/3
Endometrioid adenocarcinoma	8380/3
Clear cell adenocarcinoma	8310/3
Serous adenocarcinoma	8441/3
Mesonephric adenocarcinoma	9110/3

# Adenoid Basal Carcinoma: Definition

- A cervical carcinoma in which rounded, generally well differentiated nests of basaloid cells show focal glands formation or sometimes central squamous differentiation

# ABC:Histopathology

- Characterized by small nests and cords of Small oval cells with a peripheral palisade arrangement
- Grossly the cervix appears normal or shows a mild nodular distortion.

# Microscopically

- Most tumors are located deep to the endocervical glands.
- The overall depth of tumor invasion ranges from 2 to 10mm, with half exceeding 3mm.
- Formed by nest of small, uniformed round or oval cells with scanty cytoplasm and are arranged in cords and nests with focal glandular or squamous differentiation.
- With squamous cells or smaller basal cells located at the periphery of the nests
- Mitotic figures are infrequent

# Microscopically

- The overlying surface is usually minimally involved
- There is frequently associated CIN.
- Almost always beneath and often arising from CIN or small invasive squamous cell carcinomas
- There may be an intraepithelial squamous component, with the tumor budding off the basal layer of the surface epithelium
- The differential diagnosis includes other small cell tumors

# Epidemiology

- ABC is a rare tumor
- Patients are usually more than 50 years old

# Clinical features

Patients are usually asymptomatic and without a clinically abnormality of the cervix

- The tumor is often discovered as an incidental finding
- It is often associated with CIN
- No pure case is known to have metastasized or been considered as cause of death



# Clinical features

- It has been regarded as neoplastic because of its deep infiltrative pattern, occasional extension to the lower uterine segment, and in the occasional case where the tumor grossly was ulcerated and symptomatic
- Based on the available evidence, typical adenoid basal carcinomas behave in a clinically benign fashion.
- Some investigators therefore proposed the term “ **adenoid basal epithelioma**”.

# Histopathology

- The tumor cells stain immunohistochemically for cytokeratin, but not, or only rarely for CEA, EMA and S100 proteins because of relative absence of myoepithelium.
- These tumors also do not stain for collagen IV or laminin, due to the absence of basement membrane-like material.
- Several studies have shown its association with HPV 16 and HPV 33.
  - High risk HPV related tumor?
  - Why the tumor behave in a benign fashion?

# Studies review

- Several studies have emphasized the need to distinguish adenoid basal tumors from adenoid cystic carcinoma or other basaloid tumors of the cervix, such as neuroendocrine carcinoma, carcinosarcoma (MMMT) with basaloid carcinomatous.
- Adenoid cystic carcinomas are associated with a distinctly unfavorable prognosis

# Studies review

- Most reported cases have been associated with benign behavior.
- Of 39 cases reported in 7 studies, only 1 patient died of tumor, but it appears that the tumor in that fatal case had unusual histological features
- “tumor cells grew slender cords that penetrated deeply into a stroma showing striking myxoid change, other unusual histological features, including an anastomosing pattern of cords of tumor with nuclear atypia.
- ? An “Aggressive basaloid carcinoma”?

# Recent study on cervical adenoid basal tumor

- A V Parwani, 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”
- Human Pathology; Jan 2005

# Cervical adenoid basal tumors

- Johns Hopkins Hospital
- Study period 1984-2004
- **Typical low-grade adenoid basal tumors (n=19) were excluded from their study**
- There were 14 potential cases of low grade adenoid basal tumor associated with additional types of invasive carcinoma, 10 retrievable cases were identified.

# Cervical adenoid basal tumors: Results

- In all tumors, the low-grade adenoid basal tumor component merged with areas of invasive carcinoma.
- All those treated by surgery had residual tumor in the cervix.
- Tumor size ranged from 0.4 to 3.3cm in greatest dimension.
- Most cases had negative margins on the hysterectomy specimens.
- There was no evidence of lymph nodes metastases

# Clinicopathologic Features of Cervical Adenoid

Case	Age	Cervico-vaginal smear findings	Diagnostic specimen	Invasive carcinoma type	Intraepithelial lesion	Margin status on excision
1	70	ASCUS, AGUS	LEEP	Adenoid basal/squamous carcinoma	HSIL	Positive
2	71	Abnormal <sup>*</sup> <sub>—</sub>	Cone biopsy	Adenoid basal/squamous carcinoma	HSIL	Positive
3	79	HSIL	Cone biopsy	Adenoid basal/squamous carcinoma and small cell neuroendocrine carcinoma	HSIL	Positive
4	81	Abnormal <sup>*</sup> <sub>—</sub>	Cone biopsy	Squamous carcinoma and adenoid cystic carcinoma	LSIL	Positive
5	61	HSIL	Biopsy	Adenoid basal/squamous carcinoma	HSIL	—
6	65	HSIL	Cone biopsy	Microinvasive squamous carcinoma	HSIL	Positive
7	45	HSIL	Biopsy	Adenoid basal/squamous carcinoma	HSIL	—
8	64	NA	Hysterectomy	Squamous carcinoma	HSIL	—
9	49	HSIL	LEEP	Adenoid basal/squamous carcinoma	HSIL	Positive
10	65	NA	Hysterectomy	Adenoid basal/squamous carcinoma	HSIL	Negative



	Tumor size, cm (maximum dimension / maximum depth)	Treatment	Margin status on hysterectomy	Lymph node status (positive/total)	Follow-up status, months	
1	1.2 / 0.3	Radical hysterectomy, lymphadenectomy	Negative	Negative (0/26)	NED, 27	
2	0.6 / 0.4	Total abdominal hysterectomy, BSO; Radiation therapy	Positive	ND	NED, 72	
3	At least 0.8 / 0.5	Radiation therapy	ND	ND	DOC/NED, 18	
4	2.5 / 1.4	Radical hysterectomy, BSO, lymphadenectomy	Positive, with tumor in parametria	Negative (0/19)	NED, 18	
5	1.0 / 0.8	Total vaginal hysterectomy, RSO	Negative	ND	NED, 29	
6	0.4 / 0.2	Radical hysterectomy, lymphadenectomy	Negative	Negative (0/45)	NED, 78	
7	3.3 / 1.4	Total abdominal hysterectomy, BSO, lymphadenectomy; Radiation therapy	Negative	Negative (0/14)	NED, 84	
8	1.0 / 0.6	Hysterectomy	Negative	ND	NED, 8	
9	1.3 / 1.3	Radical hysterectomy, BSO, lymphadenectomy	Negative	Negative (0/41)	Recent case	
10	1.6 / 0.8	Total vaginal hysterectomy	Negative	ND	Recent case	

# Cervical adenoid basal tumors: Results

- All tumors exhibited diffuse expression of p16 in both the adenoid basal epithelioma and invasive carcinoma components.
- HPV 16 DNA was detected in both the adenoid basal epithelioma and invasive carcinoma components in 9 tumors.

# Cervical adenoid basal tumors: Discussion

- Based on the studies, pure typical adenoid basal tumors (without malignant cytological features and unassociated with other forms of invasive carcinoma) virtually always behave in a benign fashion.
- Some typical adenoid basal tumors can be associated with an unequivocal invasive carcinoma displaying the microscopic features of carcinoma, including increased cytological atypia, mitotic activity with abnormal mitotic figures and deeply infiltrative growth of malignant components

# Cervical adenoid basal tumors: Discussion

- The invasive components can display patterns of differentiation indicating specific subtypes of invasive carcinoma with established malignant behavior.
- Notable cytological atypia and deeply infiltrative growth are pathological features associated with carcinomas rather than benign tumors.

# Cervical adenoid basal tumors: Discussion

- Suggested approach to diagnosing the spectrum of tumors exhibiting adenoid basal differentiation.
- Pure LG adenoid basal tumors lacking appreciable cytological atypia, mitotic activity, and an infiltrative pattern in a desmoplastic stroma, that are confined to an excisional specimen with clearly negative margins can be designated as “**adenoid basal epitheliomas**”.

# Cervical adenoid basal tumors: Discussion

- Tumors composed of both typical LG adenoid basal tumor and an invasive cytologically malignant component exhibiting adenoid basal/squamous, pure squamous, and/ or adenoid cystic differentiation can be diagnosed as invasive carcinomas.
- Those with mixed differentiation can be subclassified according to the patterns of differentiation.

# Cervical adenoid basal tumors: Discussion

- Tumors with features of carcinoma may well behave in a benign fashion after complete excision.
- Thus most adenoid basal tumors can be classified as either epithelioma or carcinoma when the entire lesion is available for evaluation or microscopic features of malignancy are present.

# Cervical adenoid basal tumors: Discussion

- Tumors extending to the margins of an excisional specimen but lacking cytological features of malignancy and the histological features of typical invasive squamous, adenoid basal, or adenoid cystic carcinoma pose some difficulty, in that adequacy of treatment cannot be determined.
- Another excisional specimen or hysterectomy is required to exclude an invasive component and assure adequate treatment.



# Cervical adenoid basal tumors: Discussion

- With in situ hybridization and PCR, Cervical adenoid basal carcinomas, adenoid cystic carcinomas, and small cell carcinomas contain HPV DNA (most often HPV16).
- From this study, both the adenoid basal epithelioma and invasive carcinoma components contain high-risk HPV.

# Cervical adenoid basal tumors: Discussion

- Epitheliomas are neoplastic precursor lesions?
- Immunohistochemical detection of p16 expression is associated with a high-risk HPV infection in CIN and invasive carcinomas
- P16 serve as a surrogate marker of high-risk HPV infection

# Cervical adenoid basal tumors: Discussion

- The finding of various subtypes of high risk HPV-related invasive cervical carcinomas intimately associated with adenoid basal epitheliomas
- Adenoid basal tumors are of putative reserve cell origin
- Potential of these invasive components to undergo divergent differentiation

# Conclusion

- Cervical adenoid basal carcinoma is a rare tumor
- It was frequently associated with CIN or small invasive squamous cell carcinoma
- Pure ABC without malignant component and confined to an excisional specimen with clearly negative margins can be designated as “**adenoid basal epitheliomas**”.
- Tumors with features of carcinoma can be designated as “**adenoid basal carcinoma**”.
- It may well behave in a benign fashion after complete excision.

# Conclusion

- For margins involvement cases, excisional specimen or hysterectomy is required to exclude an invasive component and assure adequate treatment.
- Adenoid basal epithelioma” and “ adenoid basal carcinoma” are both high risk HPV related tumor
- Potential of these invasive components to undergo divergent differentiation should be noted