CASE 4

• Female 31
• LLETZ for borderline nuclear abnormalities

Ectopic Prostatic Tissue in Cervix

• AJSP 2006;30;209-215
• Usually incidental microscopic finding
• Usually in ectocervical stroma
• ? Developmental anomaly, ? metaplasia
• Positive with PSA and PrAP

TUBULOSQUAMOUS POLYP OF VAGINA (AJSP 2007;31;1013-1019)

• Vaginal polyp
• Usually postmenopausal
• Most in upper vagina
• Constant histology
• Prior reports of Brenner tumour of vagina (same lesion)
**UNIFYING THEORY**

AIJGP 2011;30;605-612

A vaginal tubulosquamous polyp and ectopic prostatic tissue in cervix are same lesion

A probably derived from paraurethral Skene’s glands (female equivalent of prostatic glands in male)

A occasionally also see in vulva

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**VULVAL EXAMPLES**

**SKENE’S GLAND ADENOCARCINOMA**

A extremely rare

A derived from periurethral Skene’s glands

A positive with prostatic markers

A PART OF SPECTRUM OF SKENE’S GLAND LESIONS IN LOWER FEMALE GENITAL TRACT

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**CASE 5**

A 40

A VIN III (classic, usual, HPV-related) on biopsies on 3 separate occasions

A large area of excoriation

A underwent multiple punch biopsies prior to anterior vulvectomy to try to rule out invasion
IMMUNOHISTOCHEMISTRY
- p16 - diffuse nuclear and cytoplasmic staining
- CK7, EMA, CAM5.2, CEA, GATA3 diffusely positive
- p63 - residual keratinocytes positive

OTHER ANCILLARY INVESTIGATIONS
- Mucin stains positive
- HPV negative

DIAGNOSIS
- Florid Paget’s disease with confluent epidermal involvement, epidermal hyperplastic changes, effacement of residual keratinocytes and involvement of skin appendages mimicking VIN
2 CASES OF THIS PHENOMENON

- International Journal of Gynecological Pathology 2013; 32; 221-227
- Both in patients with long histories (2 and 8 years)
- May be reflection of long standing disease with confluence of Paget’s cells and associated epidermal hyperplastic changes

p16 in Paget’s Disease

- Not previously investigated
- Positive in most cases- variable intensity, pattern and distribution (International Journal of Gynecological Pathology 2013; 32; 221-227)

EXTRAMAMMARY PAGET’S DISEASE

- Vulva is most common site
- Most cases relatively easy to diagnose
- May be difficult diagnosis if Paget’s cells few in number
- Opposite scenario- large confluent sheets with associated epidermal hyperplastic changes resulting in diagnostic problems
USEFUL MARKERS OF PAGET’S
- CK7
- EMA
- CAM5.2
- CEA
- GCDFP15
- androgen receptor
- HER2-neu
- GATA3
- ER/PR usually negative

EPIDERMAL “HYPERPLASTIC” CHANGES IN PAGET’S
- Described by Brainard and Hart (American Journal of Surgical Pathology 2000;24;543-552)
- Hyperplastic changes may mask Paget’s cells if few in number
- 3 patterns: hyperplasia, NOS
  - papillomatous
  - fibroepithelioma-like
VARIANT OF VIN MIMICKING PAGET’S

A classic VIN with mucinous differentiation (AJSP 2009; 33; 945-949)- 2 cases, both HPV 16 positive

**p16**
SUMMARY OF IMMUNOHISTOCHEMISTRY
- Mucinous cells positive with CK7, CEA, EMA, CAM5.2 (these markers also positive in Paget’s disease)
- Squamous cells positive with p63
- p16 diffusely positive
- CK20, GCDFP15, ER, S100 negative
- MIB1 - areas of classic VIN high proliferation index; mucinous cells virtually negative

MOLECULAR STUDIES
- HPV 16 demonstrated (linear array genotyping)

HISTOGENESIS
- Probably metaplastic phenomenon in premalignant squamous lesion
- Looks like SMILE in cervix (may arise from reserve cells)
CASE 6

F30
LLETZ for abnormal glandular cells

STRATIFIED MUCIN PRODUCING INTRAEPITHELIAL LESION (SMILE)

- relatively common
- form of high grade reserve cell dysplasia (some consider as from of adenosquamous carcinoma in situ)
- WHO 2014 considers as form of AIS
- Morphological features of both CIN and AIS/ CGIN
- variable morphology: mucin rich to mucin poor
- often associated with CIN and CGIN but may occasionally occur in pure form
- may involve surface or glands
SMILE

PMID 25039487. HISTOPATHOLOGY 2015;66;658-663

69 cases over 6 year period (0.6% of all cervical specimens)
Coexisted with high grade CIN in 93%; CGIN/ AIS in 42%; invasive carcinoma in 10%
Best regarded as form of high grade reserve cell dysplasia
Management as for CGIN/ AIS (state on pathology report)

DIFFERENTIAL DIAGNOSIS OF SMILE

- CIN undermining glandular epithelium
- CIN involving immature metaplastic squamous epithelium
- Immature squamous metaplasia
- Pregnancy oedema
- Desquamated endocervical cells

CIN INVOLVING/UNDERMINING GLANDS

IMMATURE SQUAMOUS METAPLASIA MIMICKING SMILE

PREGNANCY OEDEMA
Desquamated Endocervical Cells

INVASIVE STRATIFIED MUCIN PRODUCING CARCINOMA
AJSP. PMID 26523540
May be associated with SMILE
Invasive counterpart of SMILE

CASE 7
F40
Biopsy of 3cm vaginal mass
IMMUNOHISTOCHEMISTRY

- CK20, CEA, CDX2 diffusely positive
- CK7, PAX8, ER, CA125 negative
- p16 focally positive

FURTHER INVESTIGATIONS

- Colonoscopy negative
- Radiology - no tumour elsewhere
- Underwent vaginectomy
### DIAGNOSIS
- Primary vaginal intestinal-type adenocarcinoma

### VAGINAL INTESTINAL TYPE GLANDULAR LESIONS
- AJSP 2014;38;593-603
- 14 cases- identical features to corresponding large intestinal neoplasms
- Non-neoplastic polyps
- Adenomas
- Adenocarcinomas (often associated with adenoma)
- Often positive with CK7, CK20, CDX2, CEA

### WHO 2014- VAGINAL ADENOCARCINOMAS
- Endometrioid
- Clear cell
- Mucinous (endocervical or intestinal type)
- Mesonephric

### TYPES OF PRIMARY VAGINAL ADENOCARCINOMA
- Clear cell
- Endometrioid
- Serous
- Endocervical-like
- Intestinal
- Gastric-type
- Mesonephric
- Skene’s gland

### PRIMARY VAGINAL ADENOCARCINOMA
- Endometrioid, serous, clear cell, gastric, endocervical-like, mesonephric- always exclude primary elsewhere in female genital tract
- Intestinal- always exclude large intestinal primary (even if confined to surface and seems to be pre-existing adenoma)

### ENDOMETRIOID ADENOCARCINOMA OF VAGINA
- AJSP 2007;31;1490-1501
- 18 cases
- Association with unopposed oestrogens
- No DES history
- Many cases had endometriosis
- Good prognosis
GASTRIC TYPE VAGINAL ADENOCARCINOMA
• 2 cases published as such (1 with uterus didelphys) (others likely described as “mucinous” adenocarcinomas)
• both arose in adenosis (non-DES associated)
• identical to cervical adenocarcinomas of gastric type
• HIK1083 and MUC6 positive
• mutation-type p53
CLEAR CELL

- DES-related
- DES-not related
- Often associated adenosis
- Identical (morphology and immunohistochemistry) to other sites in female genital tract

ENDOCERVICAL-LIKE ADENOCARCINOMA

- HPV related
- Identical to usual (HPV-related) cervical adenocarcinoma
- Need to exclude cervical primary
- p16 diffuse
SKENE’S GLAND ADENOCARCINOMA

- extremely rare
- derived from periurethral Skene’s glands
- female counterpart of prostatic glands
- positive with prostatic markers
- PART OF SPECTRUM OF SKENE’S GLAND LESIONS IN LOWER FEMALE GENITAL TRACT