Gynaecological Cytology Interesting Case Study

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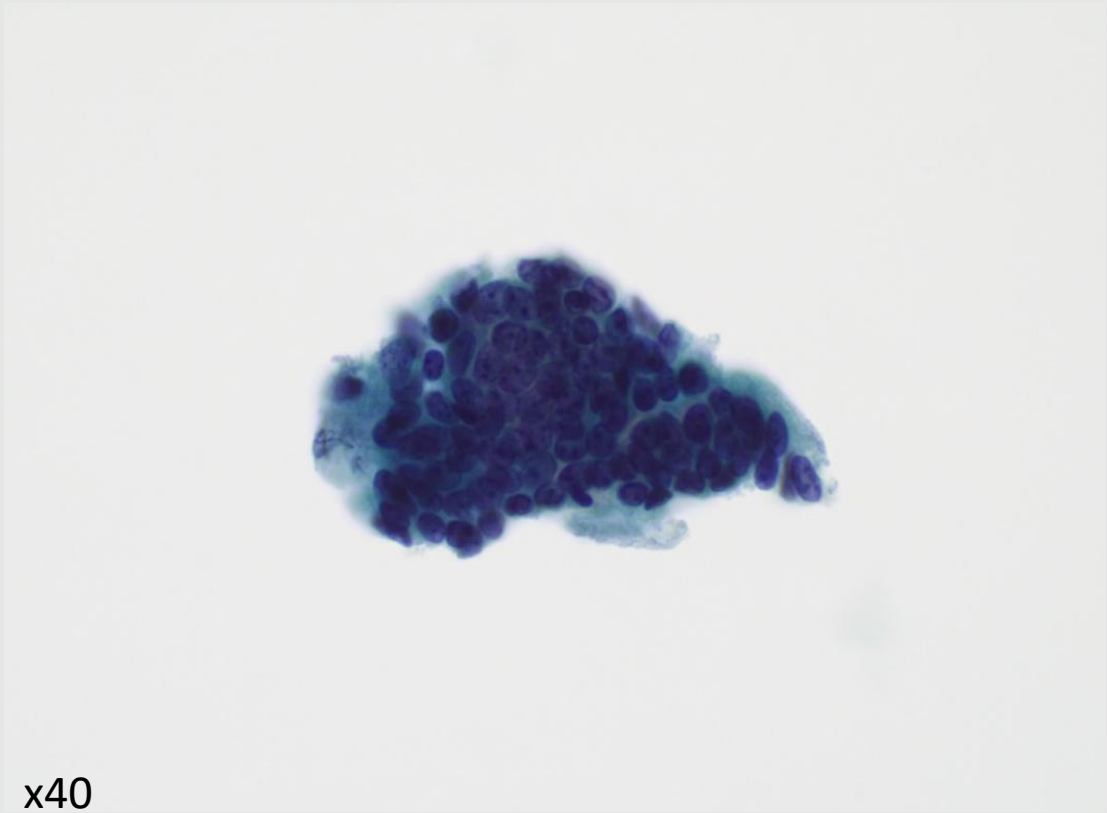
Clinical History

- Age 48
- Previous hysterectomy for CIN in 2015
- Vault sample taken in Gynae' outpatients
- Aceto-white change
- Previous vaginal adenosis diagnosis
- Last vaginal cytology = HPV+/cytology –ve.
- One year prior, HPV-ve/cytology unsatisfactory
- Cervex brush and endocervical brush samplers used

Long cytology history

- Alternating borderline glandular cells and low grade dyskaryosis reports for several years then lost to follow up until HPV+ve/cyto-ve sample showing changes consistent with vaginal adenosis 3 years previously.

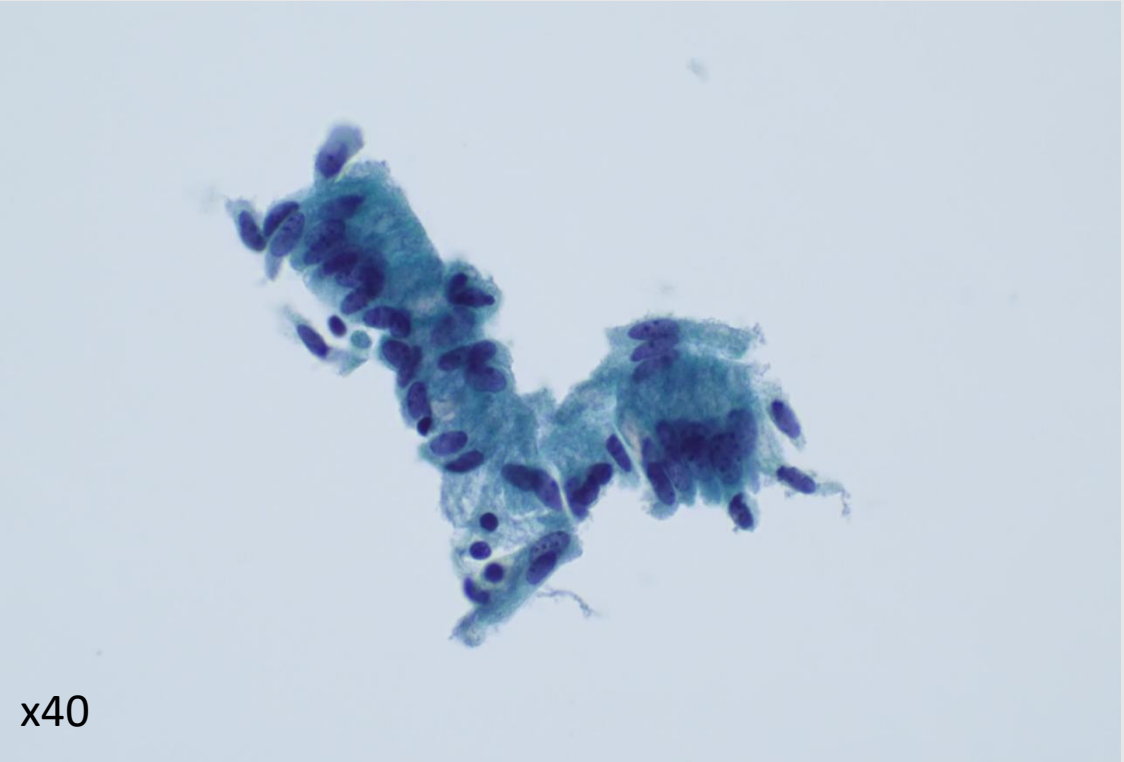
2020 Vaginal adenosis



x40

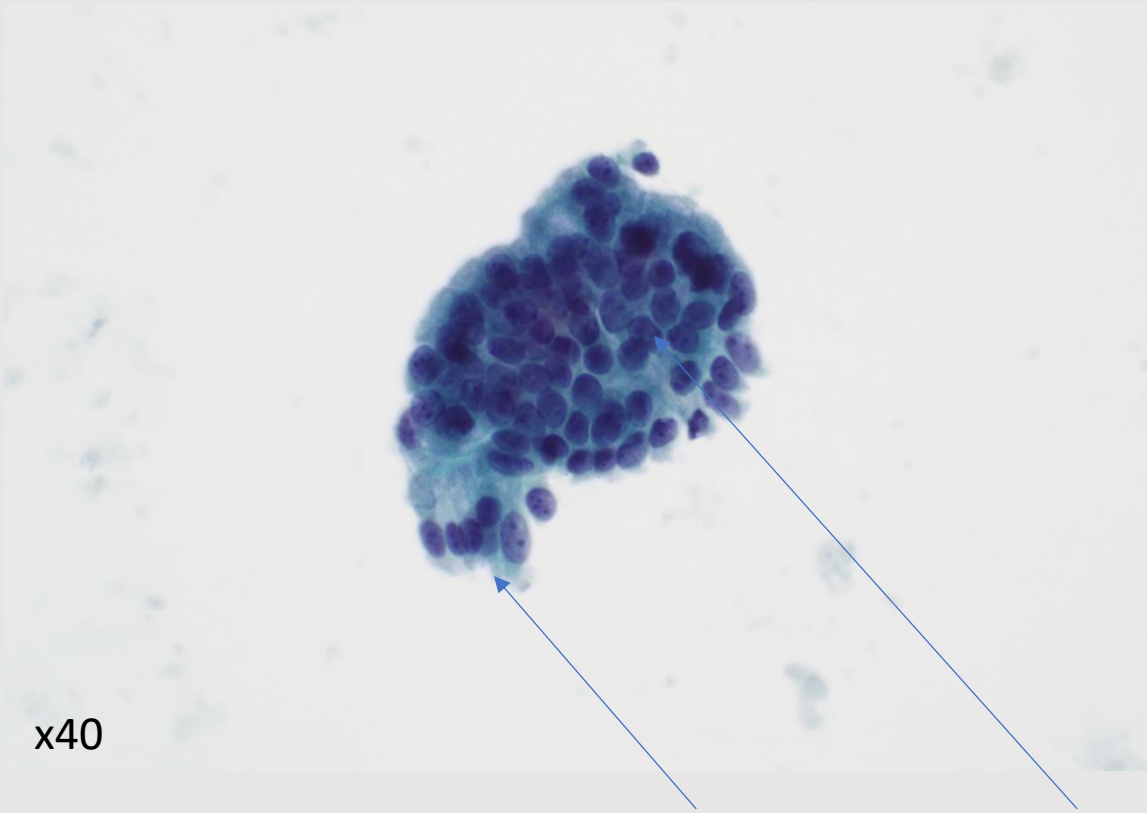
Hyperchromatic group of small regularly arranged cells in sheet formation

2020 Vaginal adenosis



Slender columnar cells arranged within regular palisade

2020 Vaginal adenosis

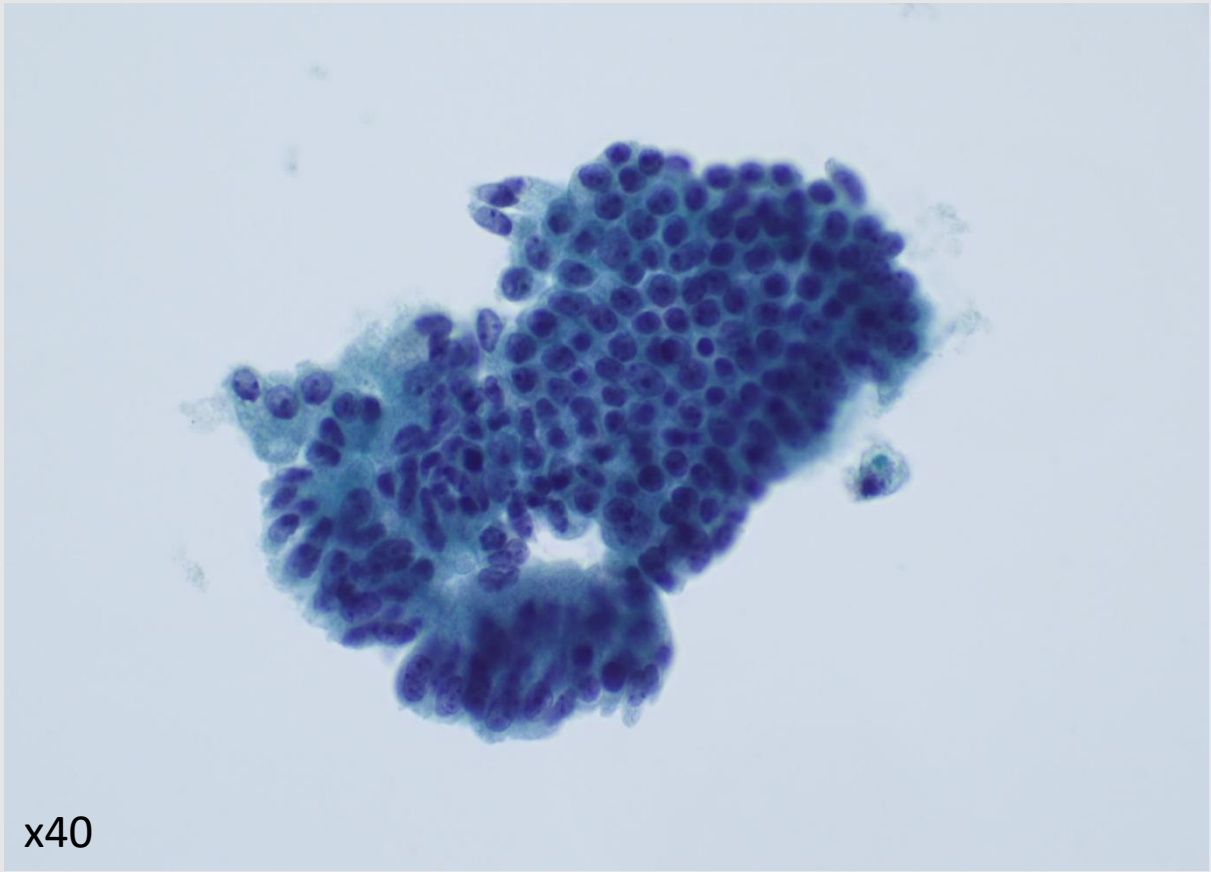


Glandular cell group showing both palisade and honeycomb pattern with bland nuclear chromatin

2021 Vaginal adenosis

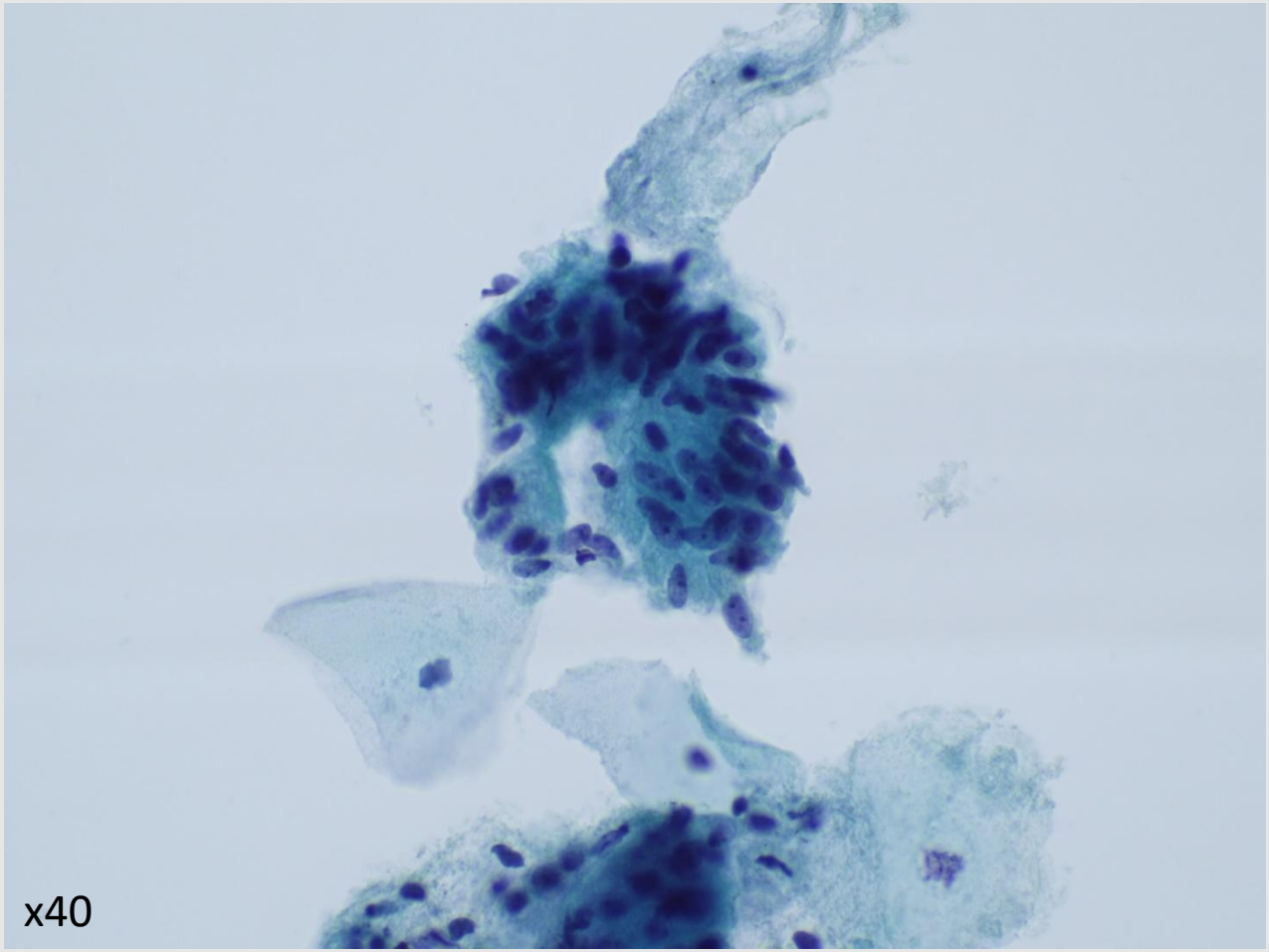
Palisade and mucin

2021 Vaginal adenosis



Regular glandular cell arrangement

2021 Vaginal adenosis

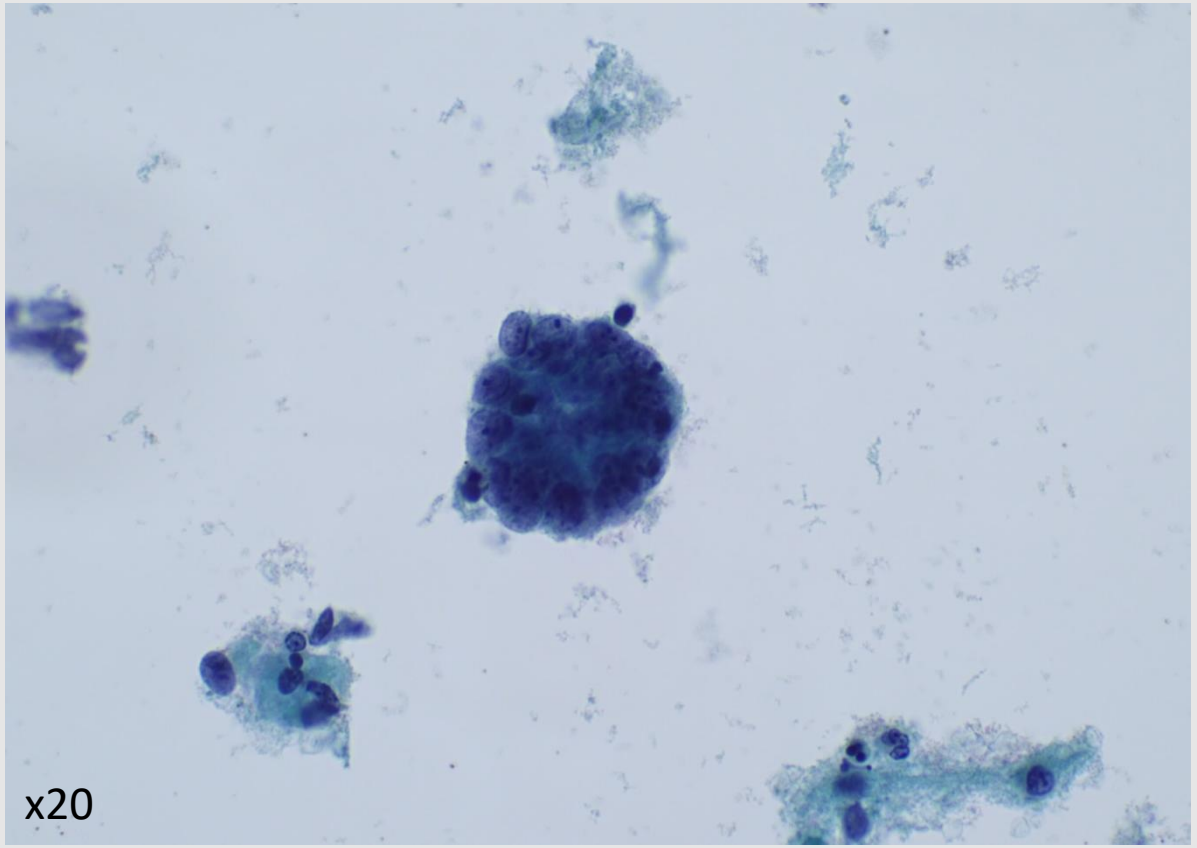


Columnar cells

2021 vault sample

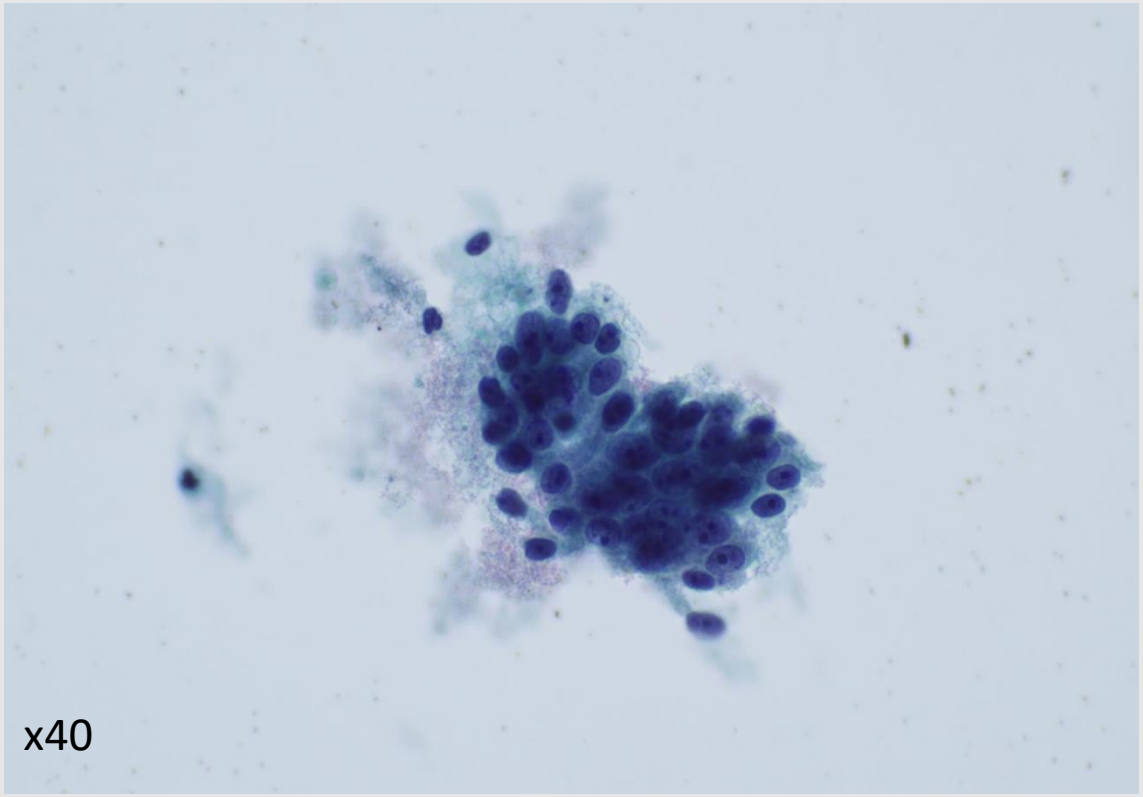
- HPV +ve.
- A negative cytolysed vault sample with scanty squamous cells and chiefly comprised of endocervical-type cells arranged in regular sheets and palisades. The appearances are consistent with those of vaginal adenosis.

2024. AWE seen



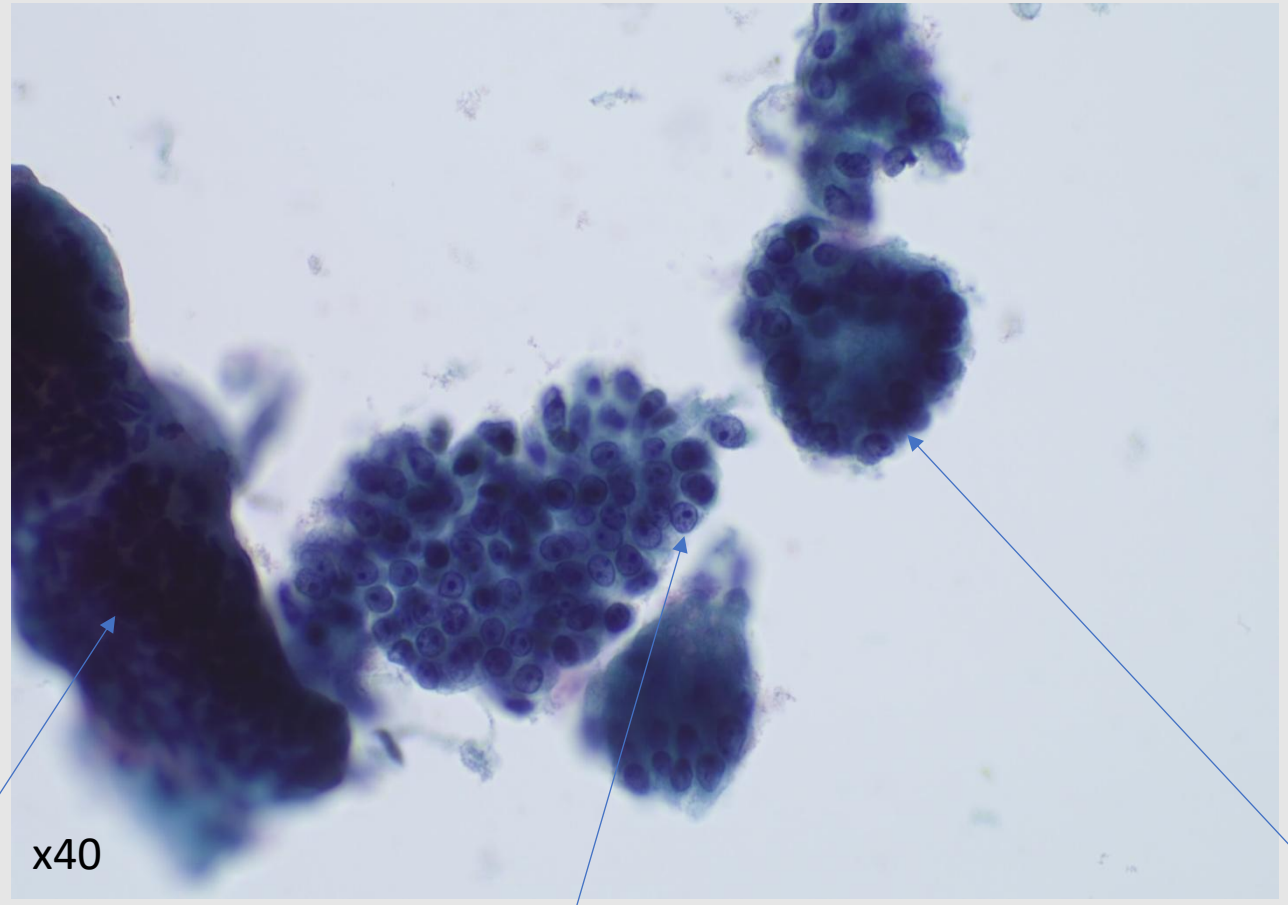
Glandular cells in tight cluster formation, minimal cytoplasm and eccentric nuclei showing a hint of scalloping

2024



Disorganised hyperchromatic glandular cell group

2024



Hyperchromatic crowded cell group (HCG)

Prominent nucleoli, minimal cytoplasm and disorganised arrangement

Group hyperchromatic cell cluster

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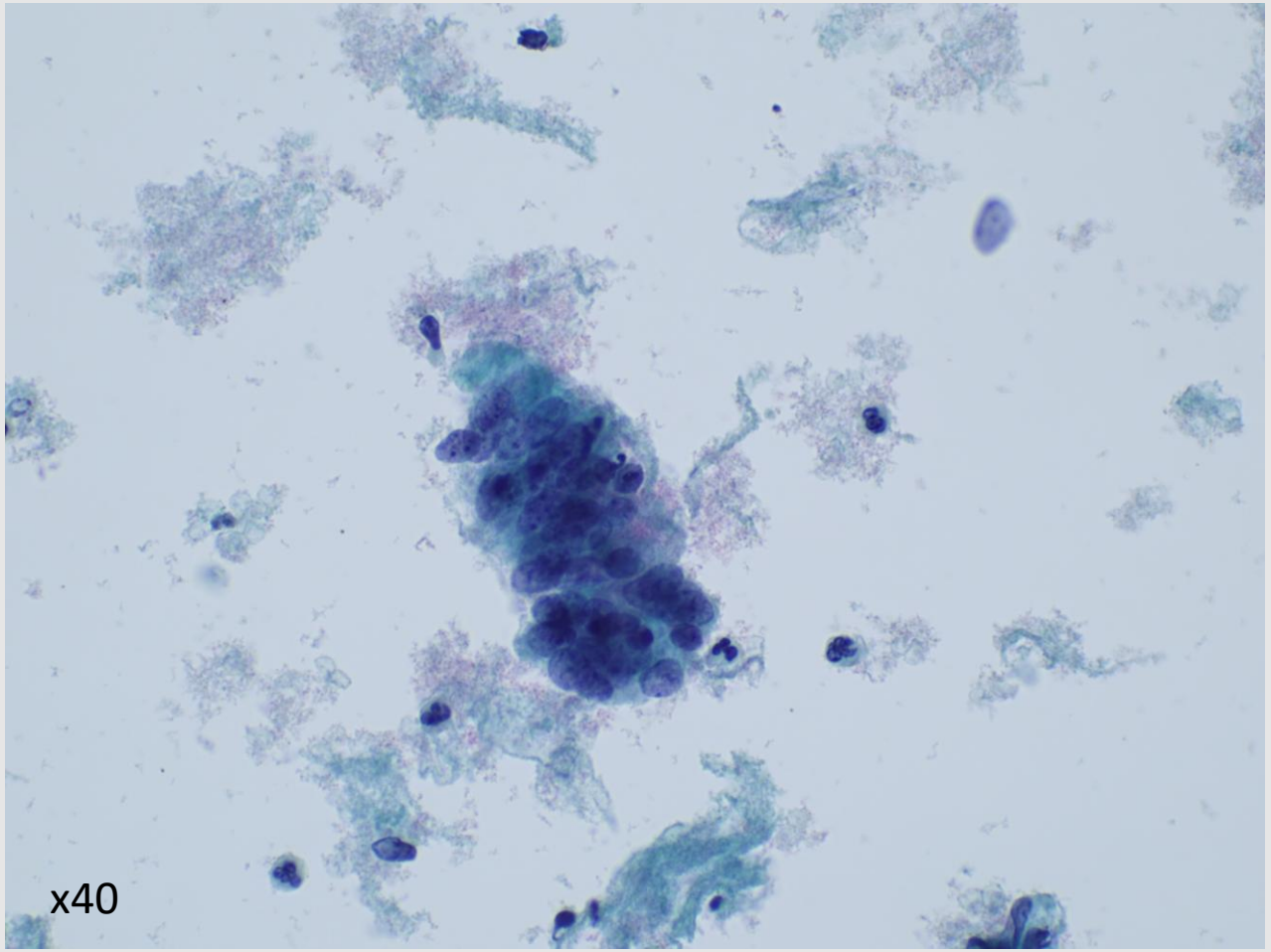
2024



Pseudostratified strip of columnar cells

Cytology report

- HPV +ve.
- Vault sample chiefly consists of columnar glandular cells. Appearance in keeping with known history of vaginal adenosis. However, occasional groups show prominent nucleoli and some with slightly atypical architecture and are therefore best regarded as **borderline changes in glandular cells** and a re-assessment at Colposcopy advised.
- NB. Given the challenge of interpreting these cytological features, clinical follow-up may be appropriate in future.

Reporting limitations within Scottish Cervical Call Recall System

Only diagnosis options for reporting in SCCRS:

1. Borderline nuclear changes (BNC) in glandular cells
2. Glandular abnormality of endocervical type

Therefore, opted for 1. because sample = a vault sample and so changes not sampled from an abnormality within the endocervical canal

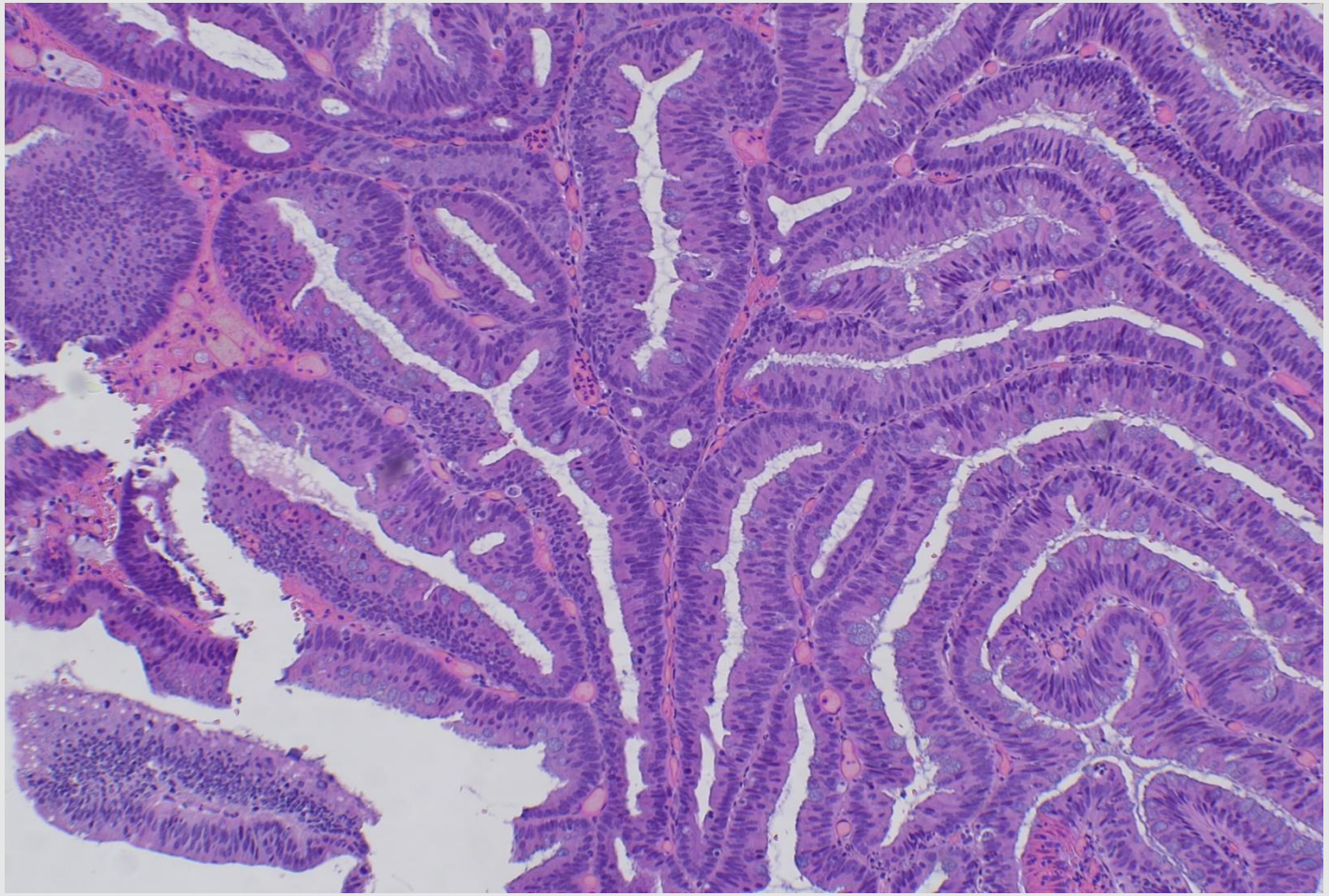
NB. 2nd Cons opinion sought due to reporting as BNC glandular as Scottish Cervical Screening Programme, Nationally Agreed Procedure.

Histology findings

Clinical history:

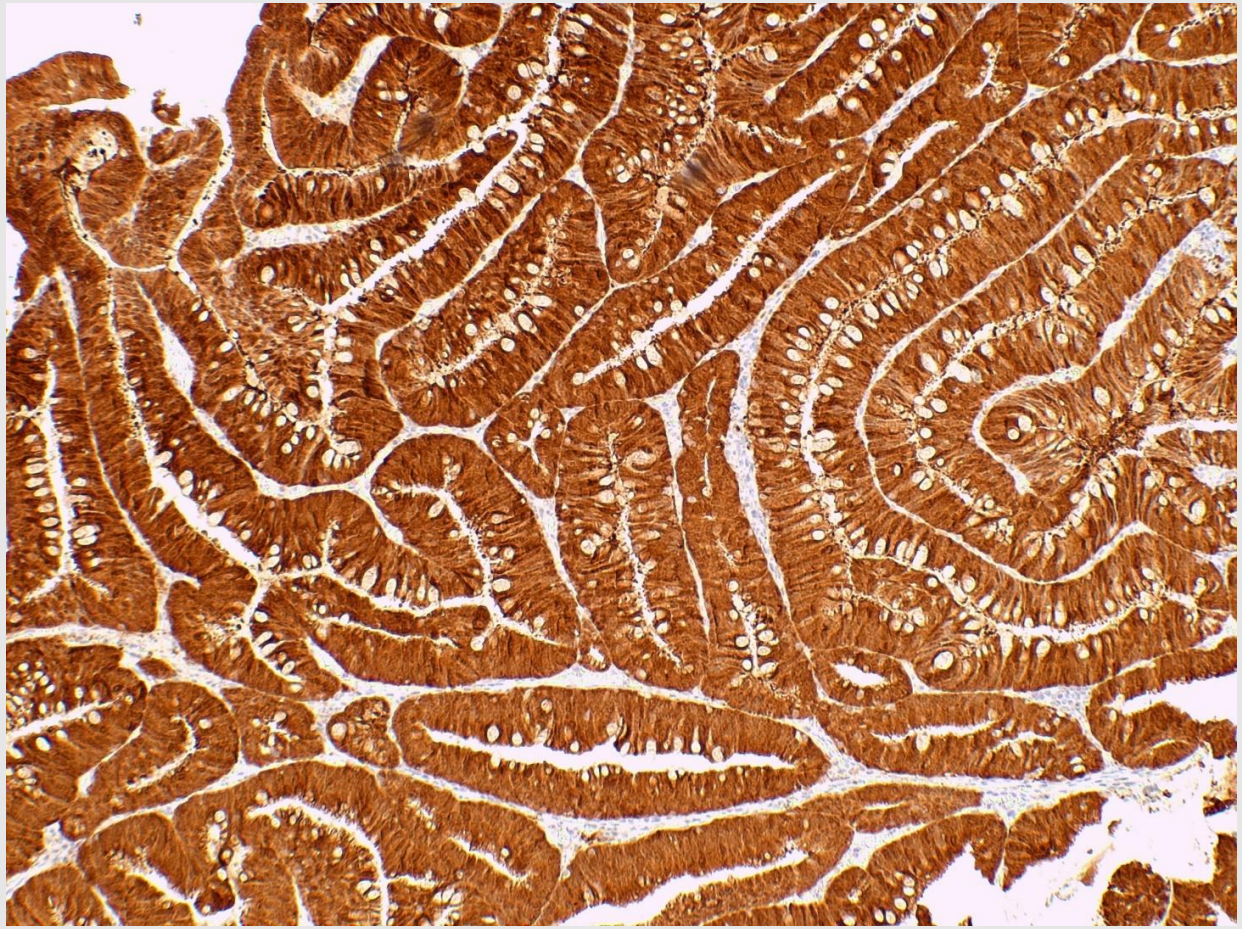
- Known vaginal adenosis.
- Black discharge
- Leucoplakia sampled to confirm no malignancy
- 4x vaginal biopsies:
  - Right vaginal biopsy
  - Right vaginal fornix biopsy
  - Left vaginal fornix biopsy
  - Introital lesion

Vaginal biopsy – Well differentiated HPV-associated adenocarcinoma



H&E

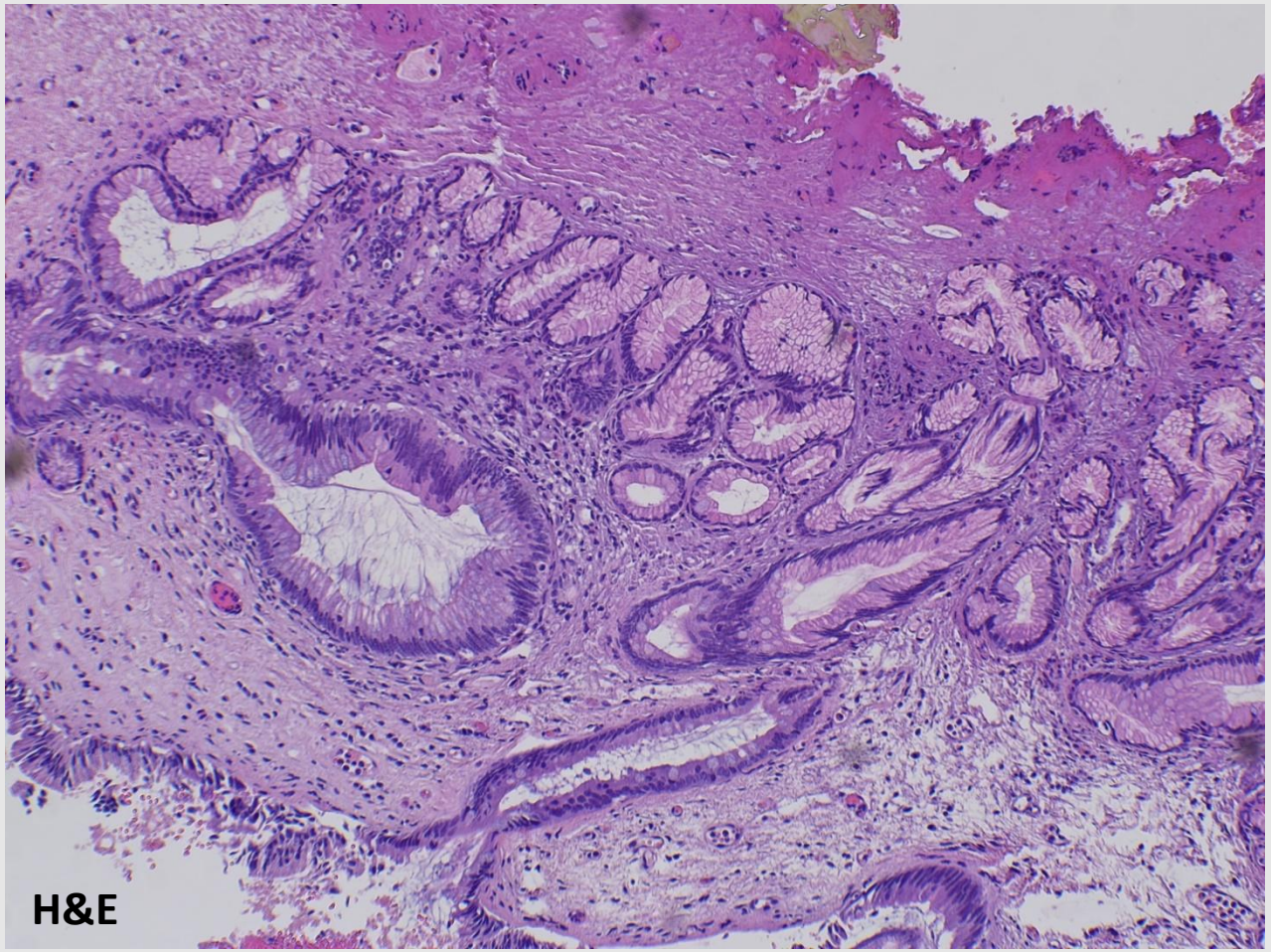
IHC p16



Diffuse, strong p16 staining.

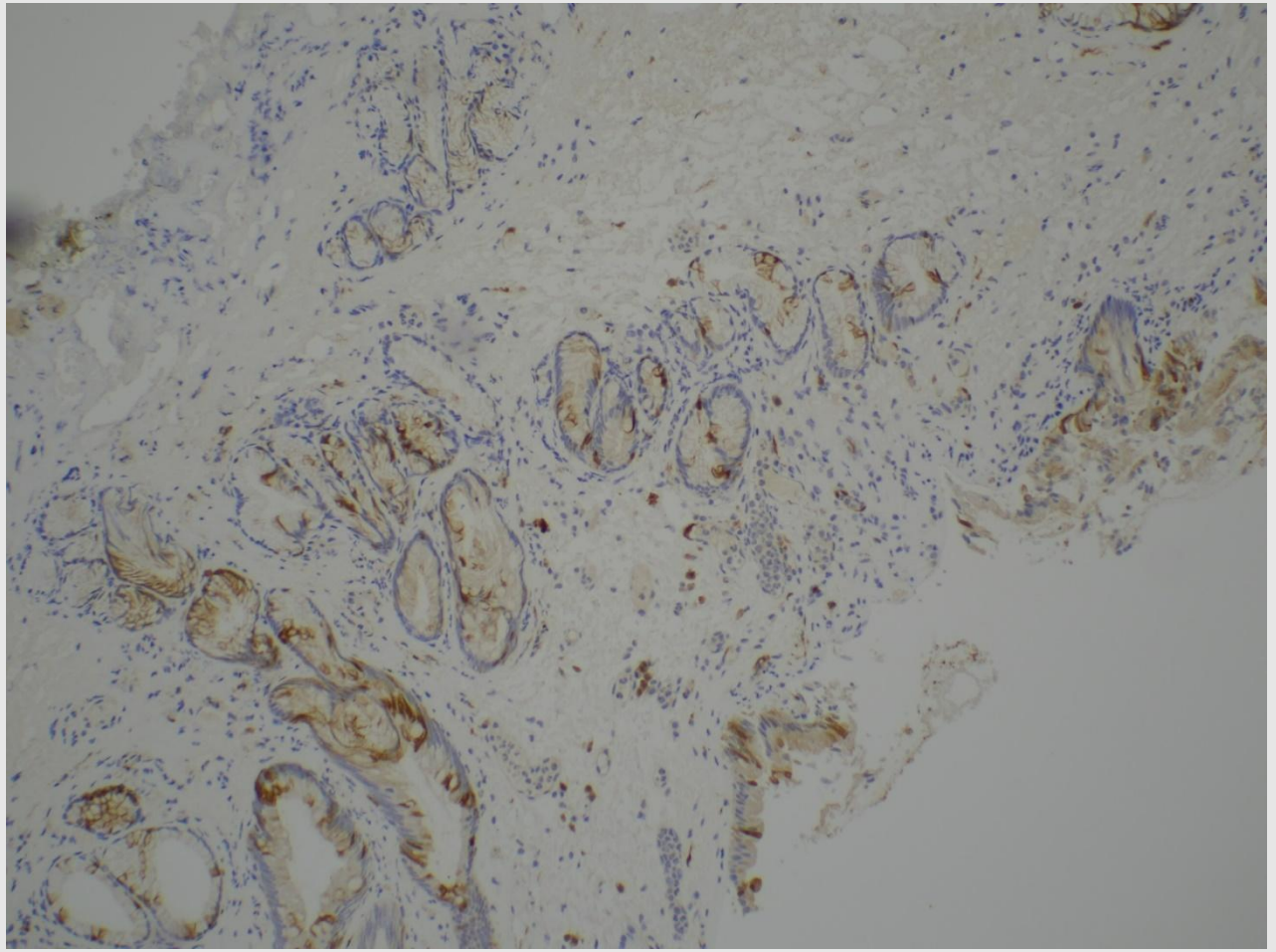
p16 = surrogate marker for high-risk HPV infection

Vaginal adenosis area



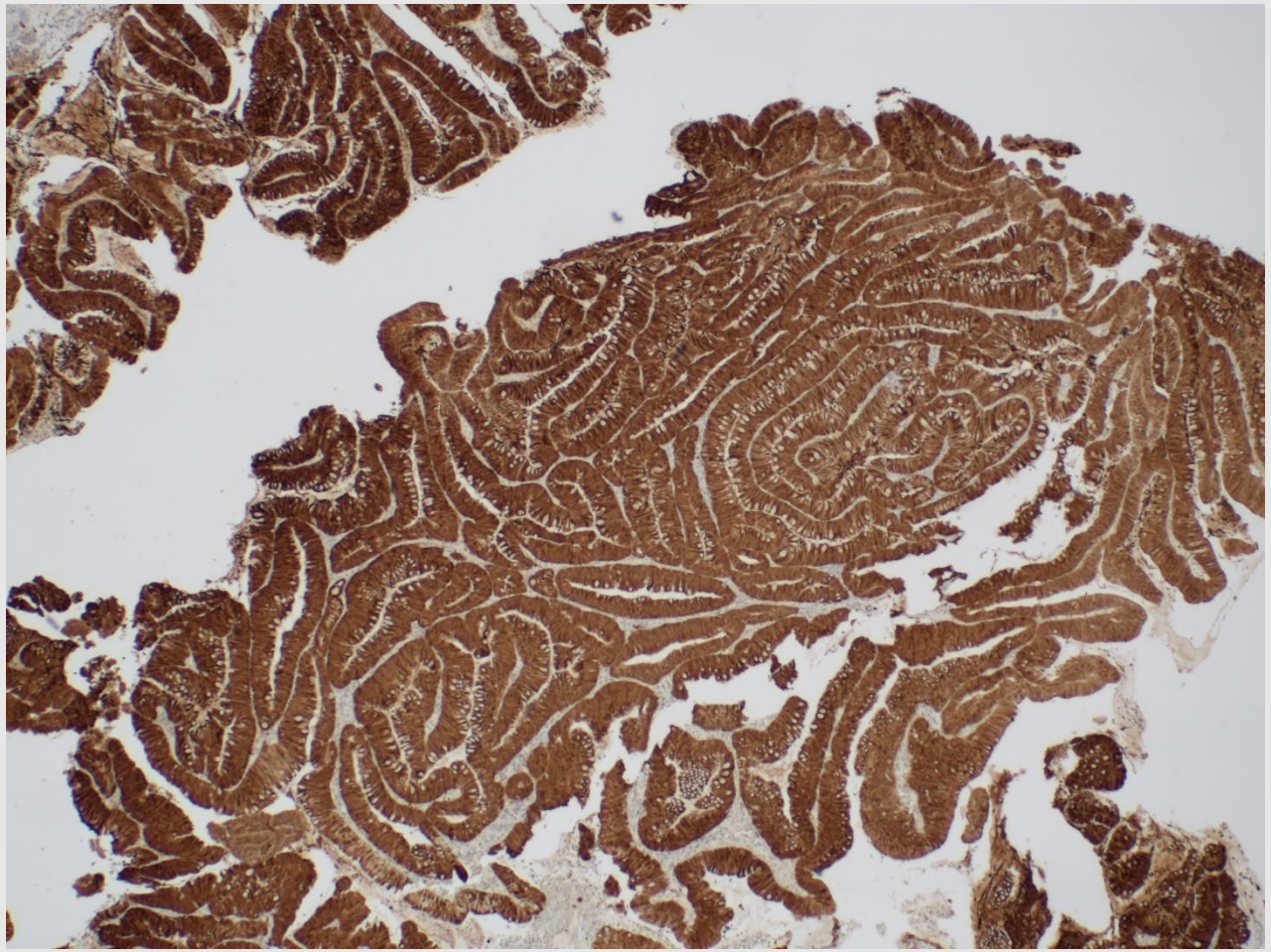
Some mucinous endocervical-like glands

Vaginal adenosis area



P16 patchy staining only

Exophytic region of tumour



Diffuse, strong p16 +ve

Vaginal biopsies report

- Vaginal fibrosis containing abundant mucinous glands.
- In some areas bland glands demonstrating features consistent with vaginal adenosis
- Other areas mucinous glands consist of tall, atypical columnar cells forming complex glandular architecture.
- **HPV-associated well differentiated adenocarcinoma arising in a background of vaginal adenosis.** Mostly exophytic nature

Immunohistochemistry

- Mucinous benign glands: **CK7+** , **CDX2+** and focal **CK20**+. **Patchy p16**+.
- Atypical glands: **diffuse strong p16+. PAX8 & ER** –ve. **p53** wild-type pattern.
- **HPV genotyping** carried out and Hr-HPV type 18 detected.

Subsequent history findings

- TAH in Morecombe Bay 10 years before
- Previous LLETZ showed CGIN not CIN as stated in history provided.
- No known exposure to DES.

Treatment and follow-up

- Treated with radiotherapy and chemotherapy
- Followed up with regular surveillance including vaginoscopy
- Subsequent residual HPV associated adenocarcinoma on biopsy
- More recently 2 occasions of HPV-associated adenocarcinoma in-situ on biopsies
- Severe ongoing vulvodynia and cutaneous reaction to treatment
- Symptoms reduced after antibiotic and steroid treatment
- Discussed extensively at MDM and with colleagues at Imperial College London

Background vaginal adenosis

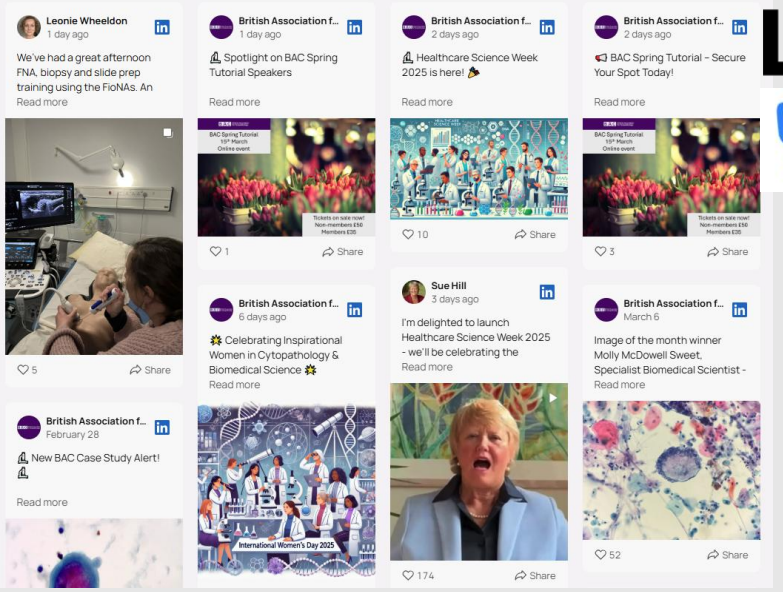
- 1st described in 1877 by von Preuschen
- Benign abnormality
- Asymptomatic or abnormal mucinous vaginal discharge
- Characterized by the presence of Műllarian glandular or metaplastic glandular epithelium in the vagina.
- Often associated with in utero exposure to diethylstilbestrol (DES)
- Vaginal application of 5-fluoruracil and vaginal CO2 laser therapy (common treatments for condyloma acuminata) are 2 known non-DES causes for vaginal adenosis.
- Women are at risk of neoplasia, including clear cell adenocarcinoma as well as squamous dysplasia

Vaginoscopic appearance

- It presents with similar appearance to columnar epithelium on the cervix
- It can be discovered as nodules or cysts on the vaginal tube, with biopsy needed for further diagnosis
- More common in upper region of vagina
- Vaginal mucosa displays red granular spots or patches and is iodine negative.

References

- Vaginal adenosis has also been reported in 2 - 10% of non DES-exposed females (Eur J Gynaecol Oncol 2001;22:260)
- 2 adult (differentiated) forms of adenosis have been described:
  - Mucinous: most common type of adenosis (62% of biopsy specimens); characterized by mucinous columnar cells resembling normal endocervical mucosa
  - Tuboendometrial: (21% of specimens); glands lined by light and dark cells, often ciliated. Resemble fallopian tube and endometrial gland cells



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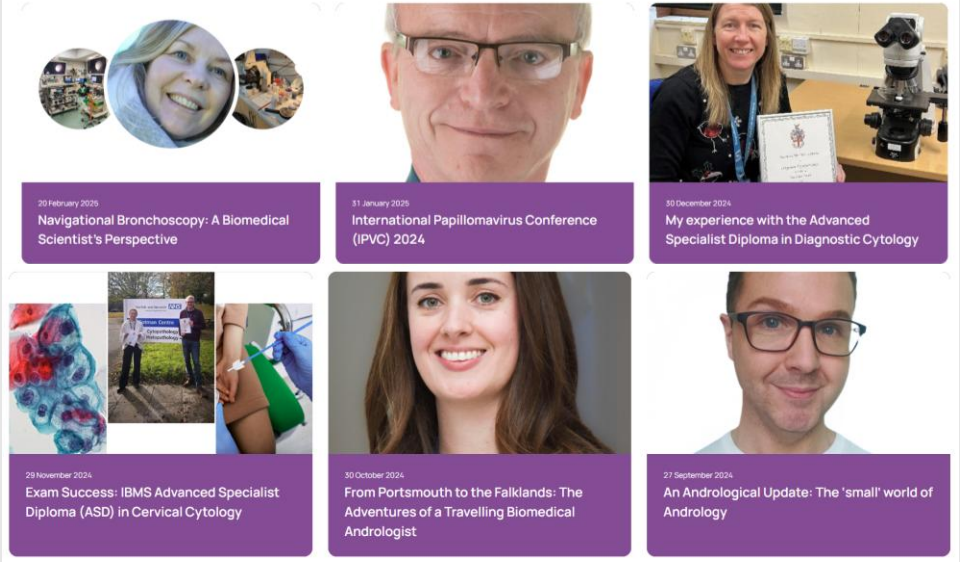

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