

Case Study – Cervical cytology

Andrea Taibi

Trainee consultant BMS, North Bristol NHS Trust

Date

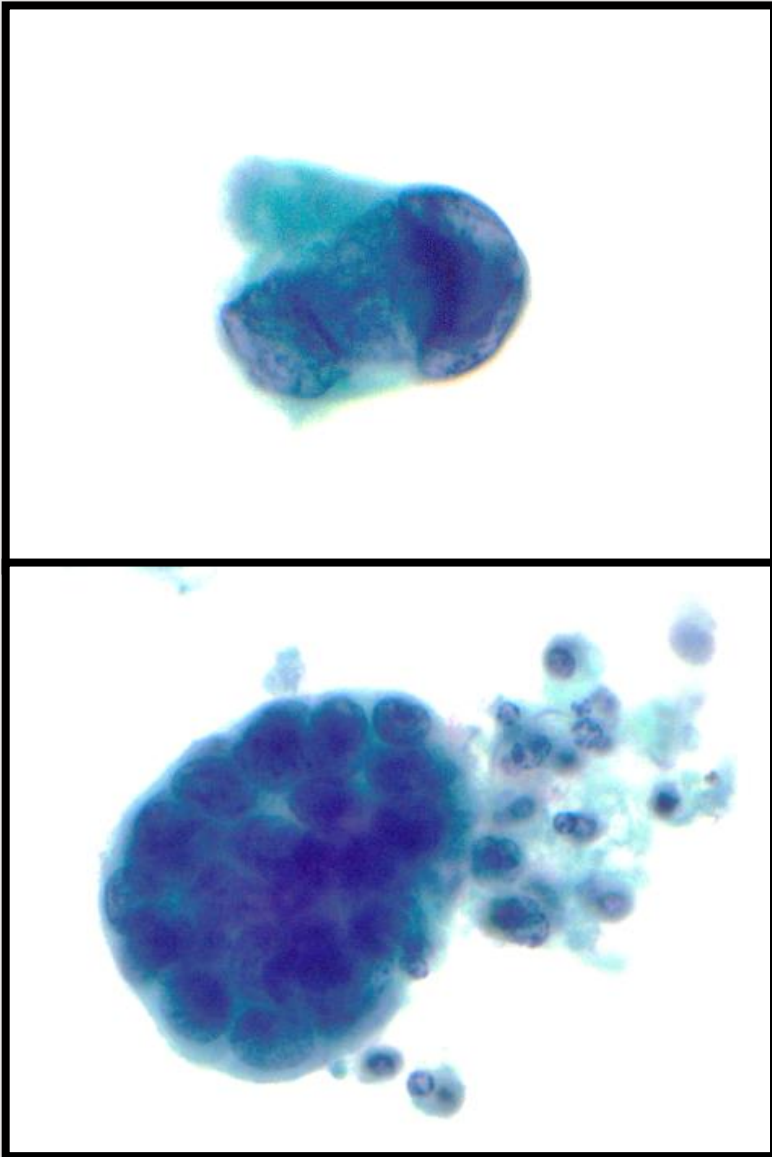
Clinical information

- 45-year-old female patient presented with vaginal bleeding and purulent discharge from cervix
- No previous cervical screening history
- Co-current cervical biopsy and cytology sample was taken in colposcopy (non-colposcopy) clinic
- HPV test was positive

Cervical cytology

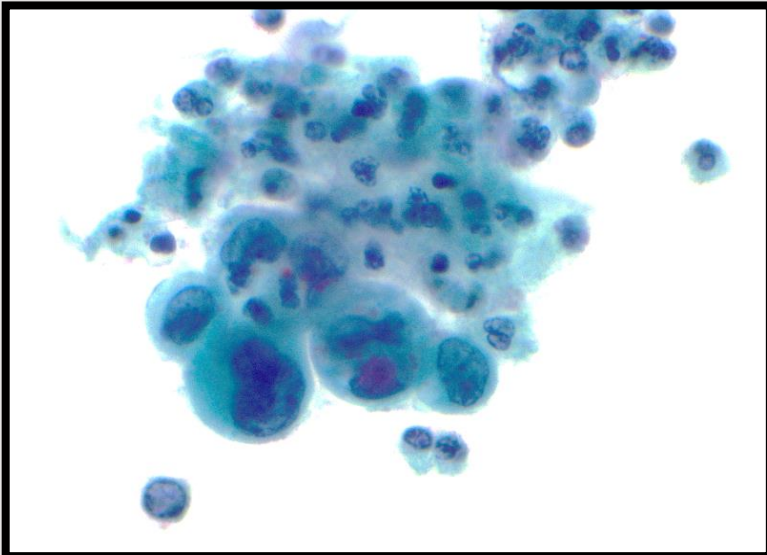
- The cervical cytology slide showed numerous neutrophils mixed with blood, atypical hyperchromatic groups with increased nuclear to cytoplasmic ratio, abnormal coarse chromatin and hyperchromasia.

Cervical cytology

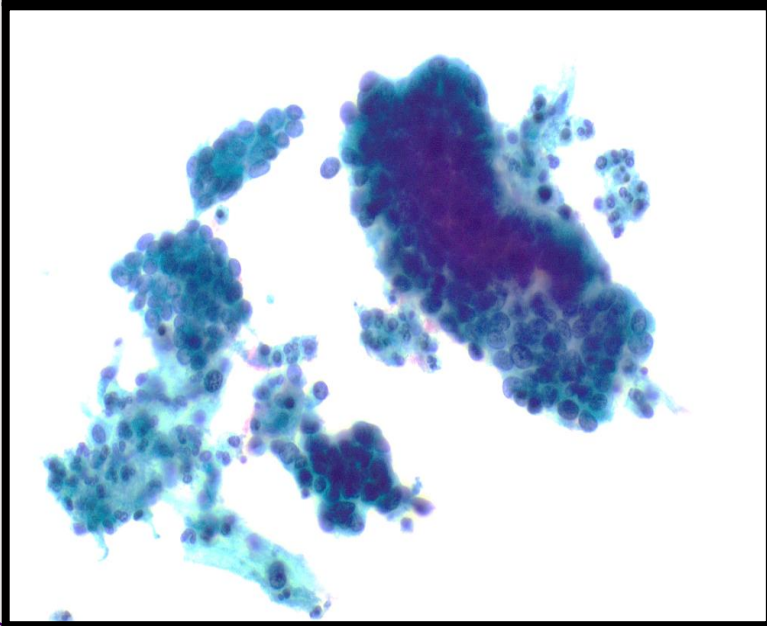


- Atypical glandular cells are present in sheets, clusters and as single abnormal cells
- Clusters showing nuclear crowding, nuclear hyperchromasia with evenly dispersed, coarsely granular chromatin. Nuclei are enlarged and variably sized.
- No tumour diathesis, but inflammatory debris is present

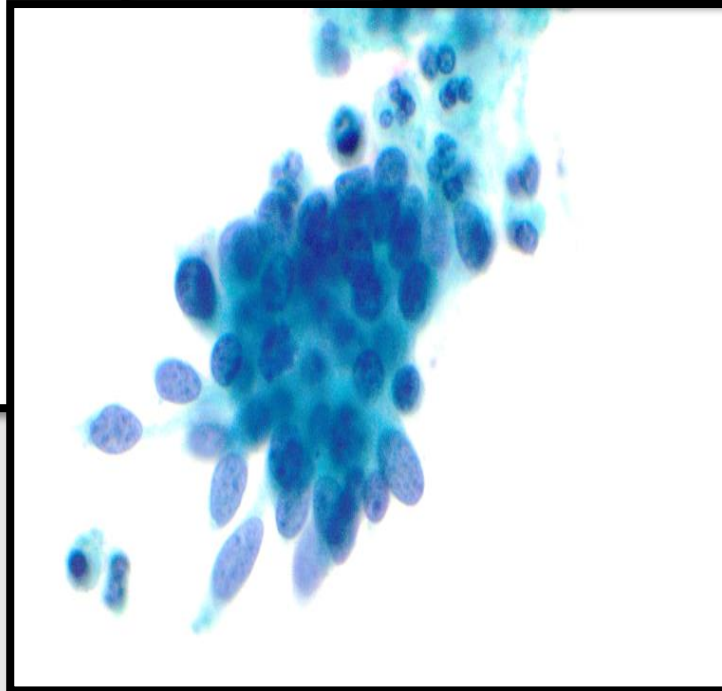
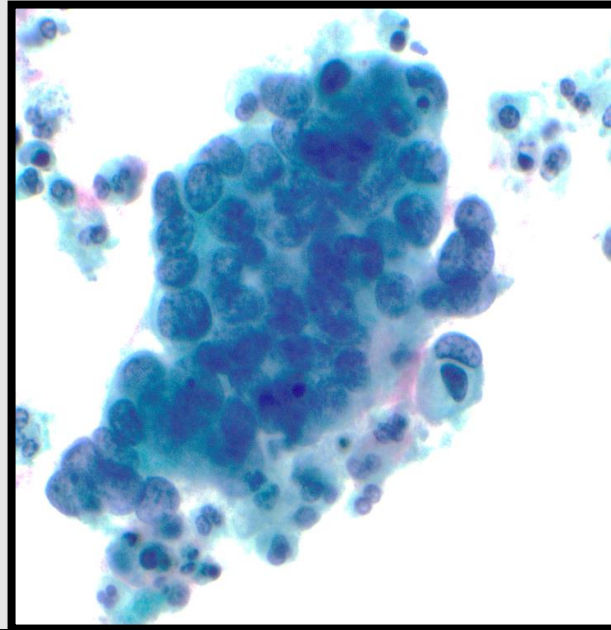
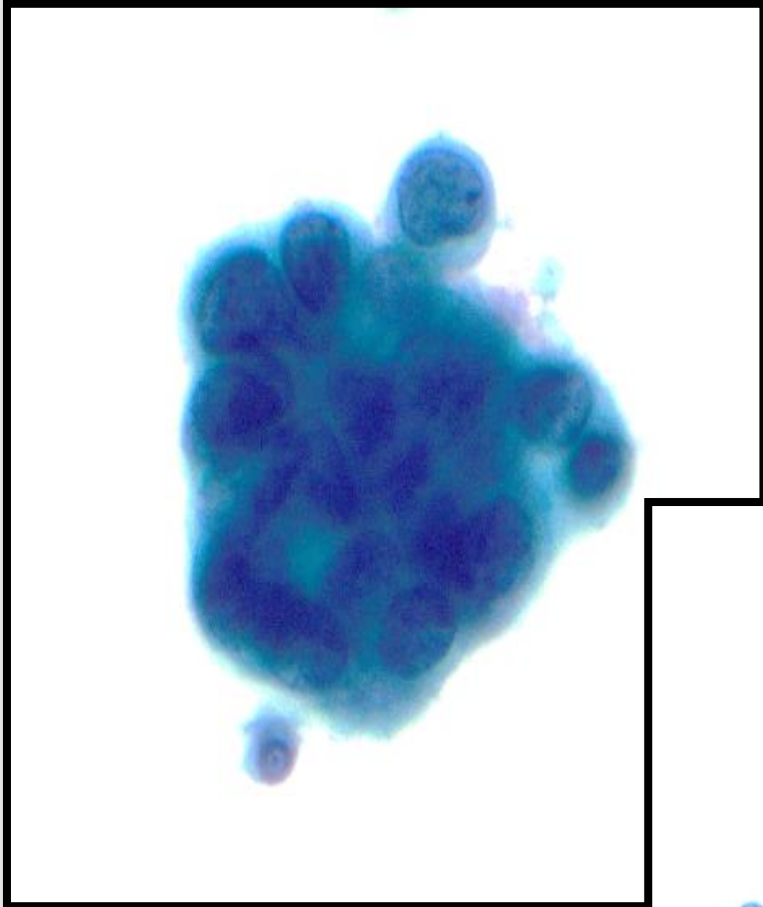
Cervical cytology



- Atypical three-dimensional cell groups showing increased nuclear to cytoplasmic ratio, coarse granular chromatin and nuclear pleomorphism.



Cervical cytology



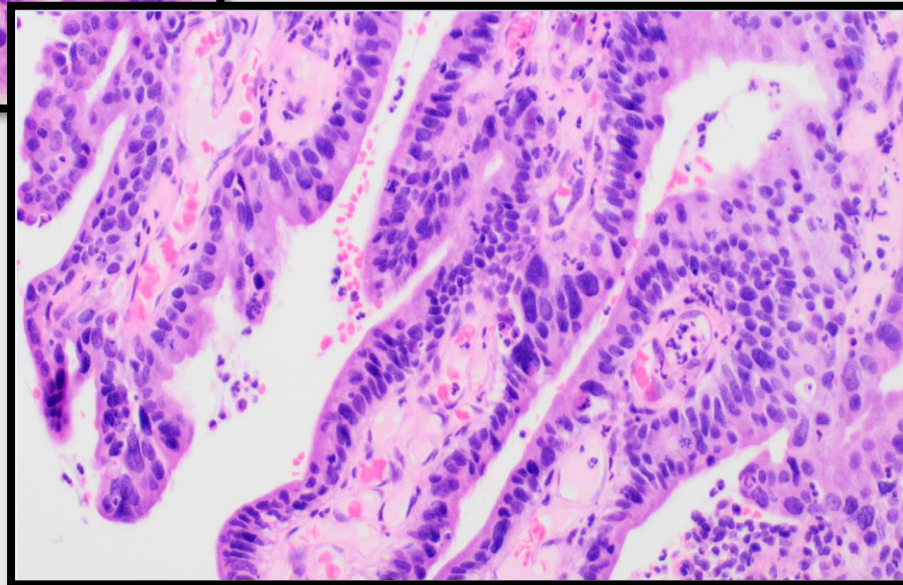
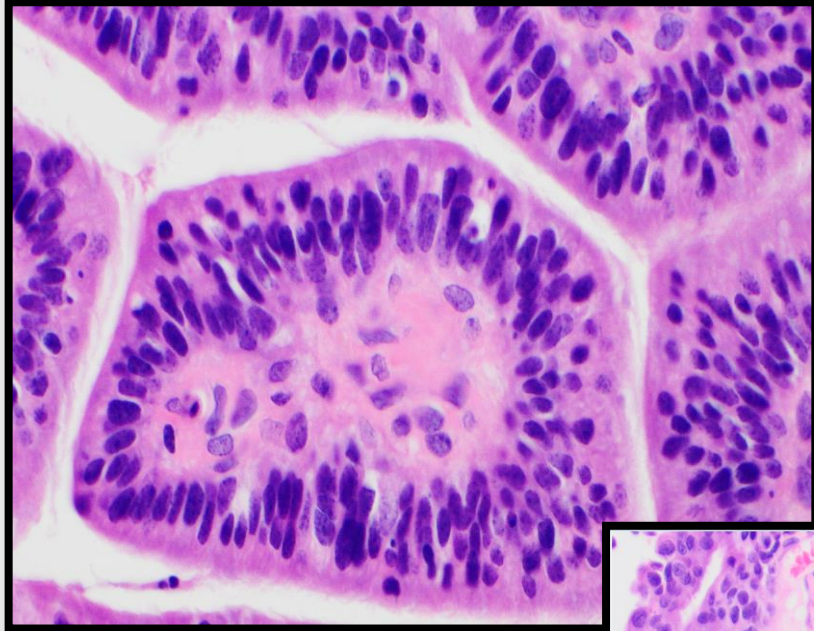
- Nuclear feathering and cell strips have more subtle presentation
- Prominent nuclear pleomorphism is visible within the glandular clusters

Cervical cytology report

- Primary screener report - High grade dyskaryosis (severe)
- Checker and consultant BMS – ?glandular neoplasia, endocervical.

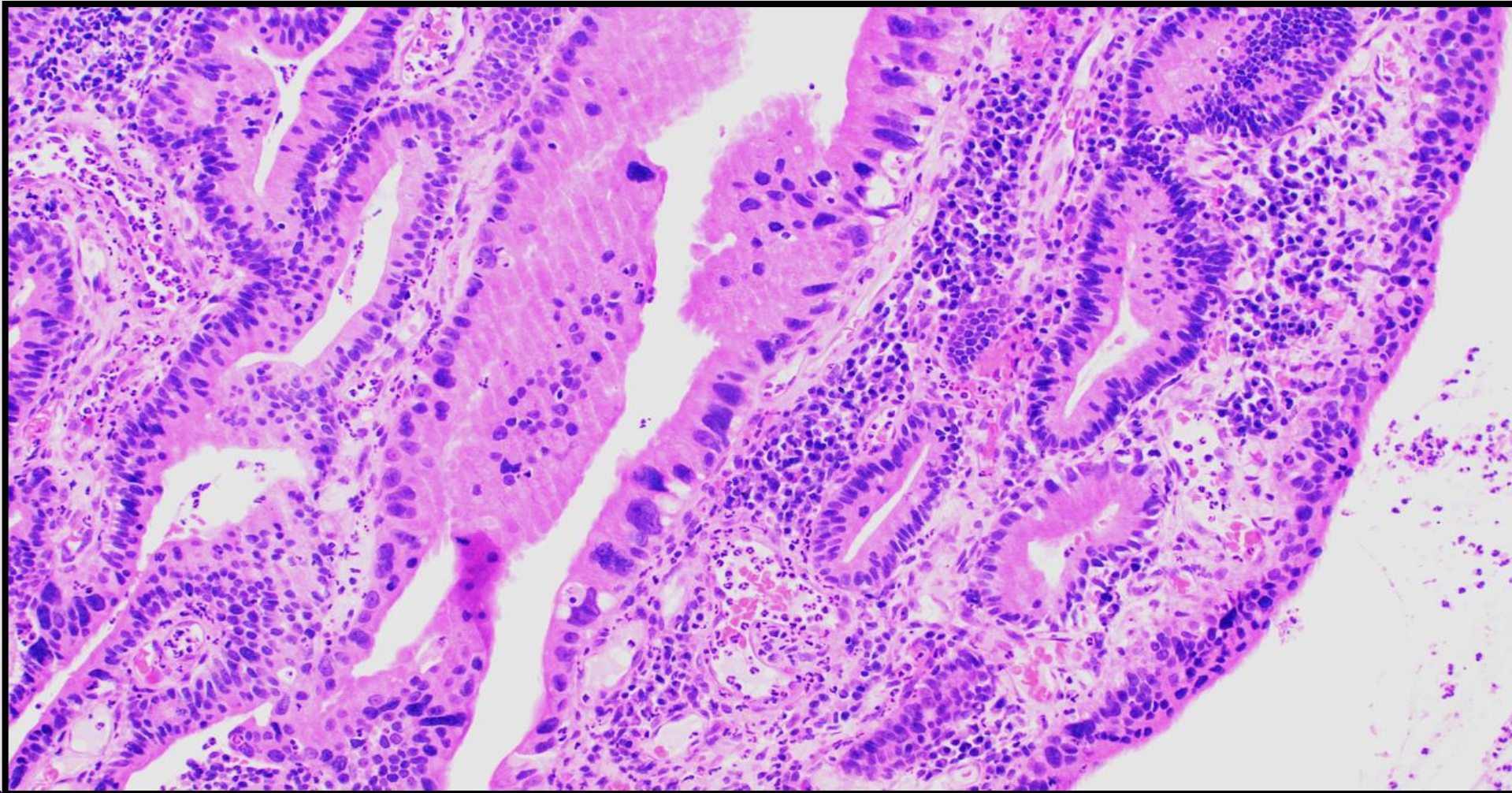
Report comment – this is suspicious for adenocarcinoma and a squamous element cannot be excluded.

Cervical biopsy



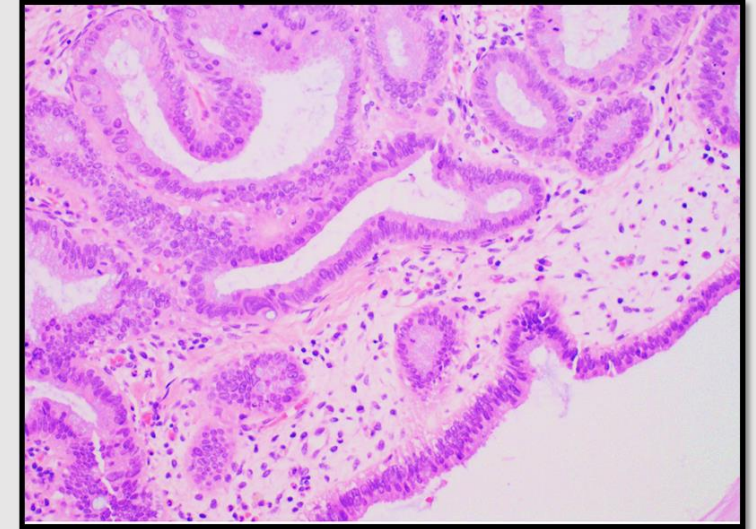
- Multiple irregular fragments were received, the largest measured 7 mm
- The cervical biopsy showed an exophytic lesion with high grade cervical glandular intraepithelial lesion (CGIN)

Cervical biopsy

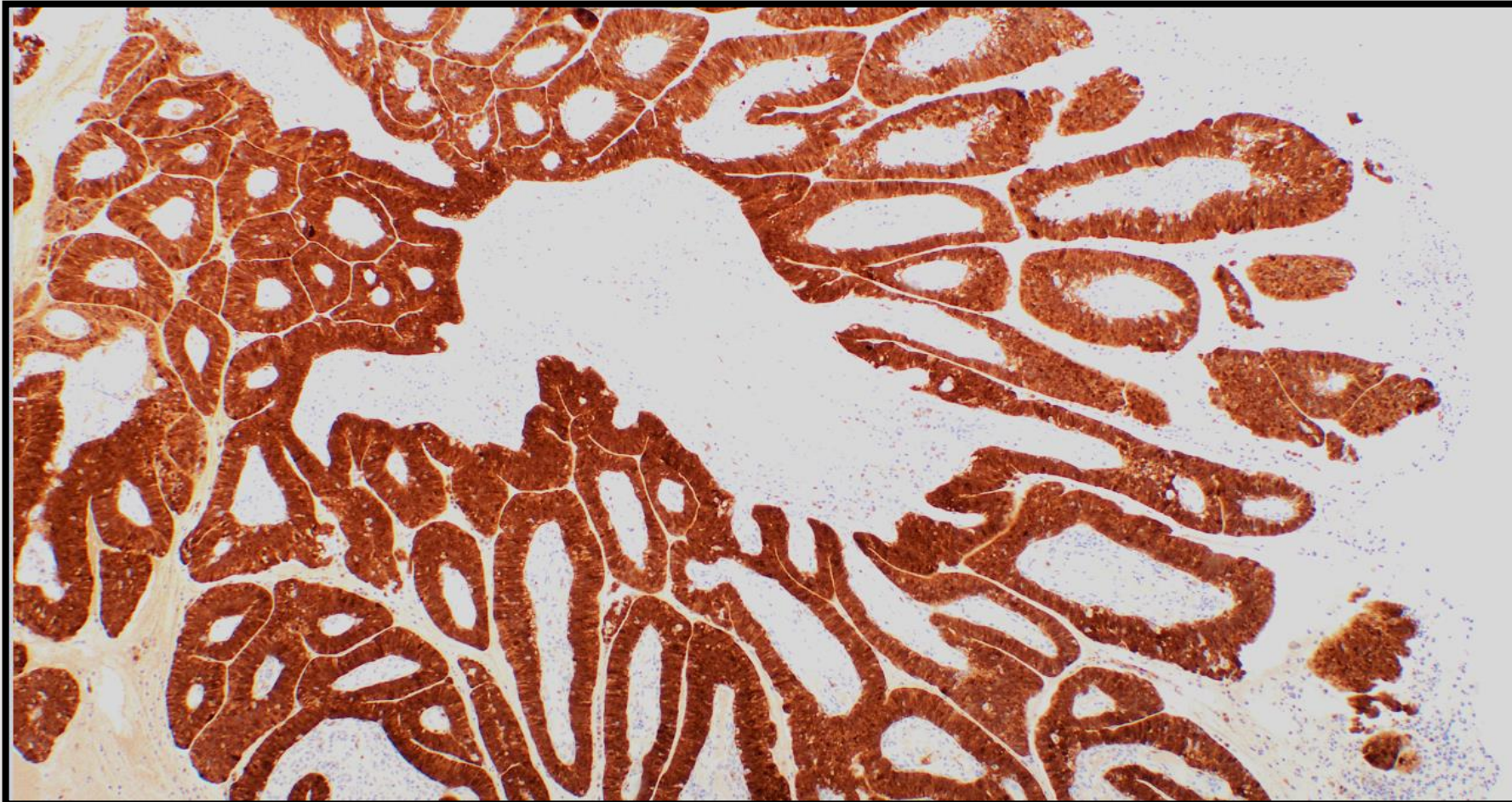


Large Loop Excision of the Transformation Zone (LLETZ)

- 6 friable pieces of tissue were received, largest piece was measuring 20x10x10 mm. Orientation of the sample was not possible. No obvious squamous epithelial surface was seen.
- Microscopy report showed predominantly glandular tissue and few strips of squamous epithelium. The squamous component showed HPV related change and no cervical intraepithelial neoplasia (CIN). The glandular component was entirely composed of neoplastic glandular epithelium with a surface villoglandular/papillary architecture. Some of the glandular component may represent cervical glandular intraepithelial neoplasia (CGIN), but most of the tissue showed complexity amounting to adenocarcinoma (predominantly Silva pattern A, but there are some foci of Silva pattern C. FIGO stage 1B2. No lymphovascular invasion was noted. Tumour exceeded to the edges of all pieces.
- Report comment - This is a diagnostic sampling not an attempt for excision



LLETZ – p16 positive



Differential diagnosis

- The histological differential diagnosis of cervical adenocarcinoma includes benign glandular lesions for example tunnel clusters, microglandular hyperplasia, lobular endocervical glandular hyperplasia, diffuse laminar endocervical glandular hyperplasia, deep Nabothian cysts, Arias-Stella reaction, mesonephric remnants and atypical oxyphilic metaplasia. The features including superficial location, lack of deep infiltration, well defined margins, bland nuclear features, inconspicuous mitotic and apoptotic activity, and absence of stromal reaction support the diagnosis of benign glandular lesions.
- Metastatic carcinomas involving cervix arise most commonly from gastrointestinal tract, ovary breast and bladder
- Endometrial adenocarcinoma extending to the endocervix

Endocervical Adenocarcinoma

In developed countries, adenocarcinoma currently accounts for 20-25% of all carcinomas of uterine cervix.

Cervical adenocarcinoma start in the endocervical canal and often show a papillary exophytic growth at the time of diagnosis.

Most endocervical adenocarcinomas are associated with high-risk oncogenic human papillomavirus, mostly 16 and 18. Approximately 15% of all endocervical carcinomas are not associated with HPV and contain distinct molecular alterations, which was addressed in the updated 2020 WHO categorization of endocervical adenocarcinomas.

Endocervical adenocarcinoma classifications according to the WHO 2020 and The International Endocervical Adenocarcinoma Criteria and Classification (IECC) classification systems:

HPV associated endocervical adenocarcinoma

Usual type

Mucinous (not otherwise specified, intestinal, signet ring cell, invasive stratified mucinous carcinoma)

Adenocarcinoma (not otherwise specified)

HPV – independent endocervical adenocarcinomas

Gastric type

Mesonephric type

Endometrial type

Clear cell type

Adenocarcinoma (not otherwise specified)

Modified from Stolnicu *et.al* (2021)

Endocervical Adenocarcinoma

- The endocervical adenocarcinoma is increasing in younger patients of a reproductive age and therefore individual patient treatment options must be considered.
- Pattern based histopathological classification for invasive cervical adenocarcinoma - Silva pattern system has been proposed for assessment of clinical and pathological features to provide targeted clinical management and individualised treatment, especially in patients who wish to preserve their fertility.
- The Silva system categorises cervical adenocarcinomas into 3 patterns; A,B or C based on the morphological features seen under the microscope. It has been developed to predict lymph node status as well as prognosis.
- Conservative treatment is recommended for patients with pattern A with negative margins, including preservation of uterus and no need for lymphadenectomy.

Silva pattern-based classification for HPV-associated invasive adenocarcinoma (Modified from Diaz de Vivar *et al.* (2013))

PATTERN A

No destructive stromal invasion
Well-demarcated glands with rounded contours, commonly forming groups
No single cells or cell detachment
Complex intraglandular growth allowed (i.e. cribriform, papillae), < a 4× field (5 mm in diameter)
No solid growth or high-grade cytology
No lymphovascular invasion
Irrelevant relationship to large cervical vessels or depth of the tumour

PATTERN B

Localized (limited, early) destructive stromal invasion arising from well-demarcated glands (pattern A-like glands)
Individual, ragged glands or small clusters of tumour cells, separated from the rounded glands, usually in an inflamed or desmoplastic stroma
Foci may be single, multiple, or linear at the base of the tumour, < a 4× field (5 mm in diameter)
No solid growth
Lymphovascular invasion present/absent

PATTERN C

Diffuse destructive invasion
Infiltrative glands that are variable in shape and size, often angulated or interconnected
Confluent growth
Glands or papillary structures with little intervening stroma or mucin lakes with tumour cells within the cervical stroma and filling a 4x field (5mm)
Solid
Poorly differentiated component (architecturally high grade) with sheets of large malignant cells
Extensive linear destructive
Diffuse laminar EACs ≥5 mm. Tumour cells or individual glands are present in a desmoplastic stroma at the base of the tumour
Band-like lymphocytic infiltrate
Superficial prominent band-like lymphoid infiltrate that obscures the neoplastic aggregates
Micropapillary
Numerous small clusters of tumour cells
Lymphovascular invasion present/absent

Endocervical Adenocarcinoma

- The treatment of endocervical adenocarcinoma is subject to FIGO staging and clinical presentation. The treatment can include surgery, chemotherapy, radiation and immunotherapy and combination of these. Most patients undergo radical hysterectomy and pelvic lymphadenectomy.
- The features, which influence prognosis are histological grade, tumour size, depth of invasion, lymphatic-capillary space involvement, stage, age and lymph node status, ratio of mitotic index to apoptotic index.
- The 5-year survival for adenocarcinoma according to stage is follows:
stage 1a1 – 100%, stage 1a2 – 93%, stage IB – 83%, stage II – 37-63%, stage III – 13-31%, stage IV – 0-6%.

References

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