

Cervical Cytology Case Study

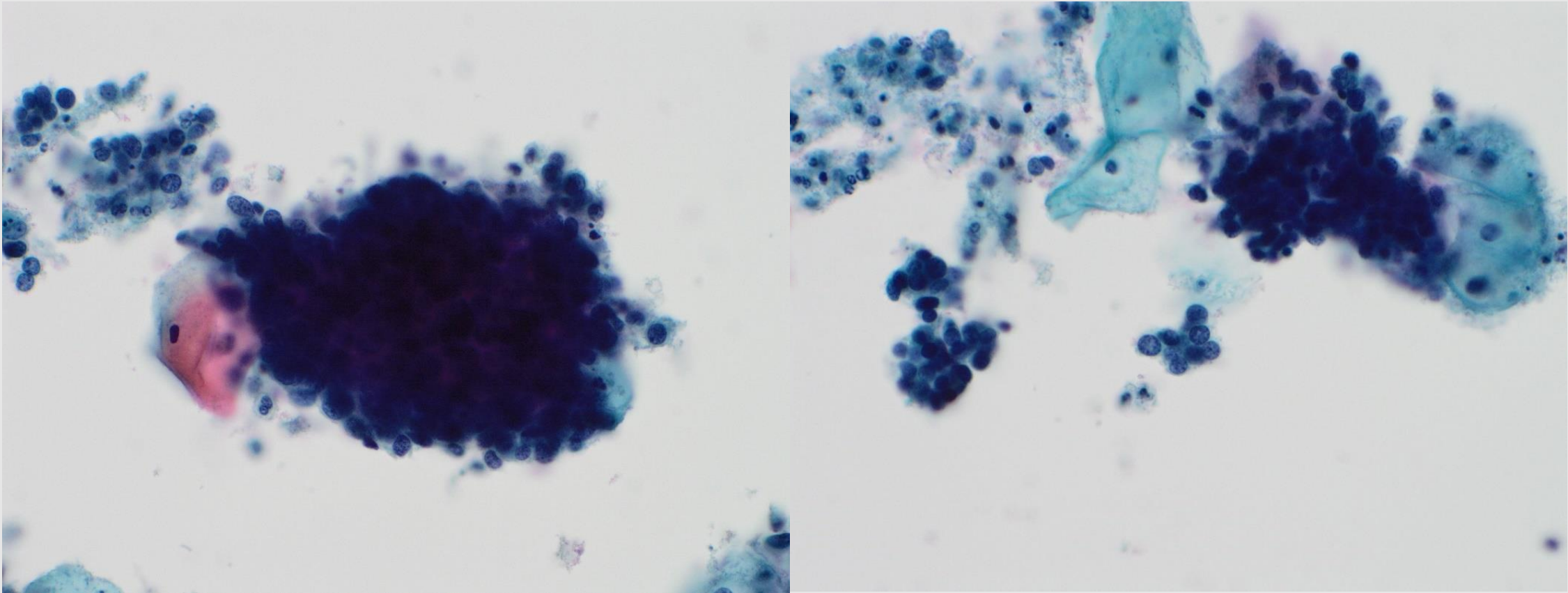
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Clinical History

- 32 year old patient
- Last cervical screen 12months ago, HPV positive/Cytology negative
- Mirena Coil
- Small ectropion, bled on contact
- HPV test – positive, slide made for cytology screening

Sample contained numerous hyperchromatic crowded groups of cells



What do you think?

Abnormal?

HG Severe

Cervical Glandular Neoplasia (CGIN)

Squamous Cancer

Other?

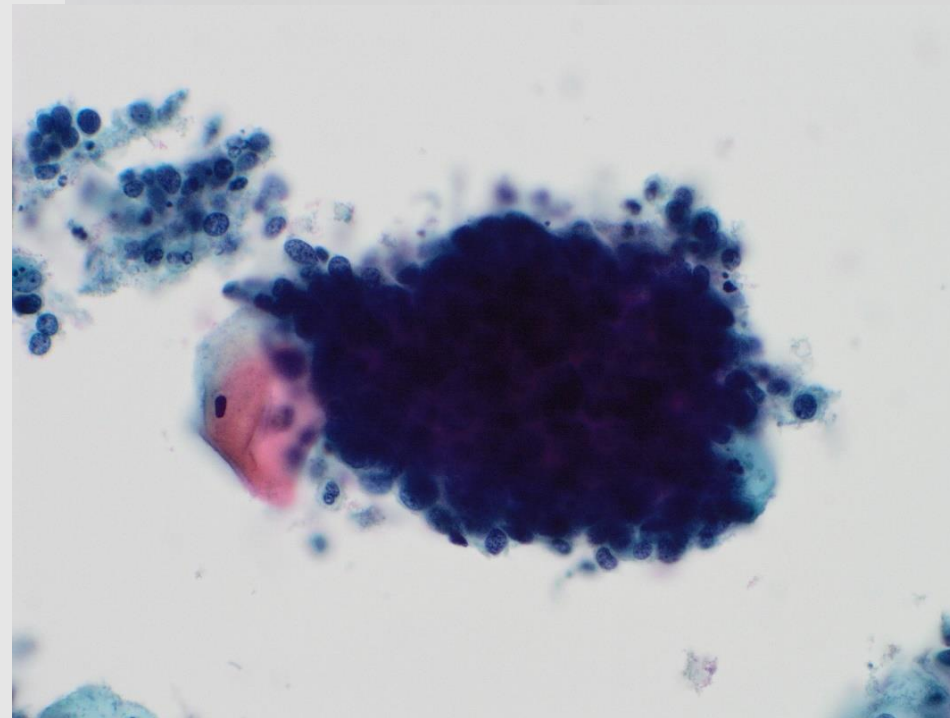
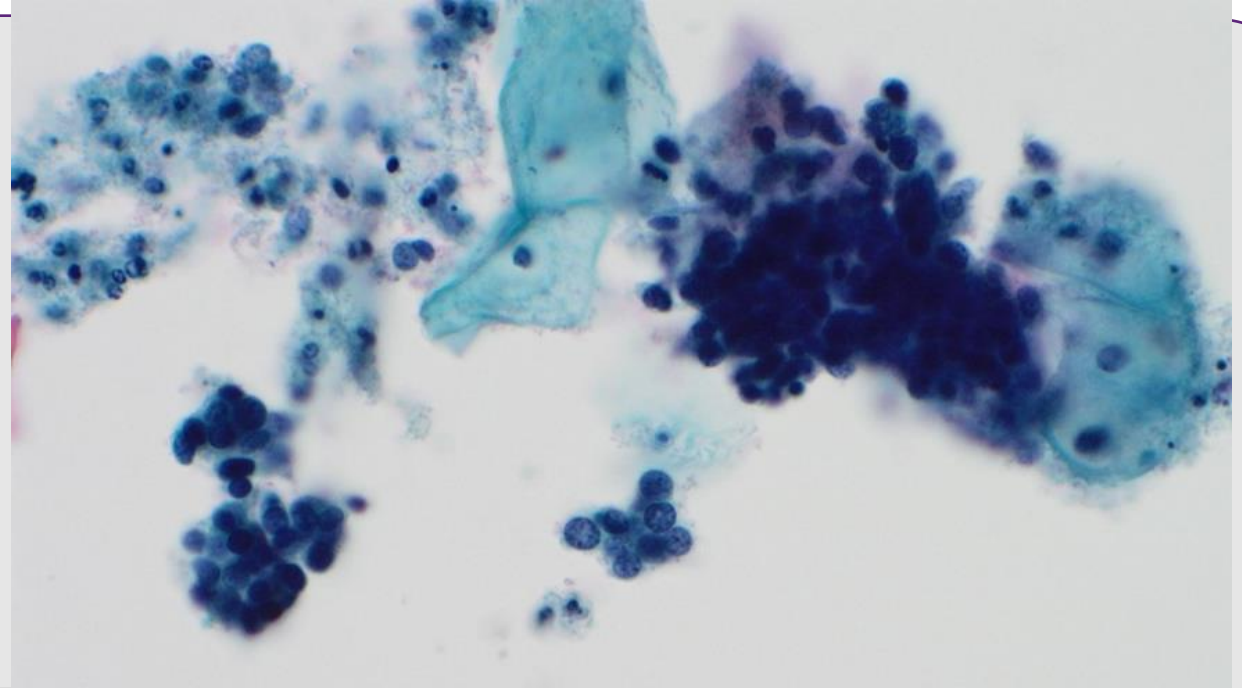
Normal?

Endometrial cells

TEM

Follicular cervicitis

Other?



Cytology Report

- Screened/checked and reported as ?Cervical Glandular Neoplasia

- Report comments:

This sample is mainly composed of abnormal endocervical cells both in clusters and as numerous poorly differentiated single cells in a background of blood and polymorphs. Invasive disease cannot be ruled out.

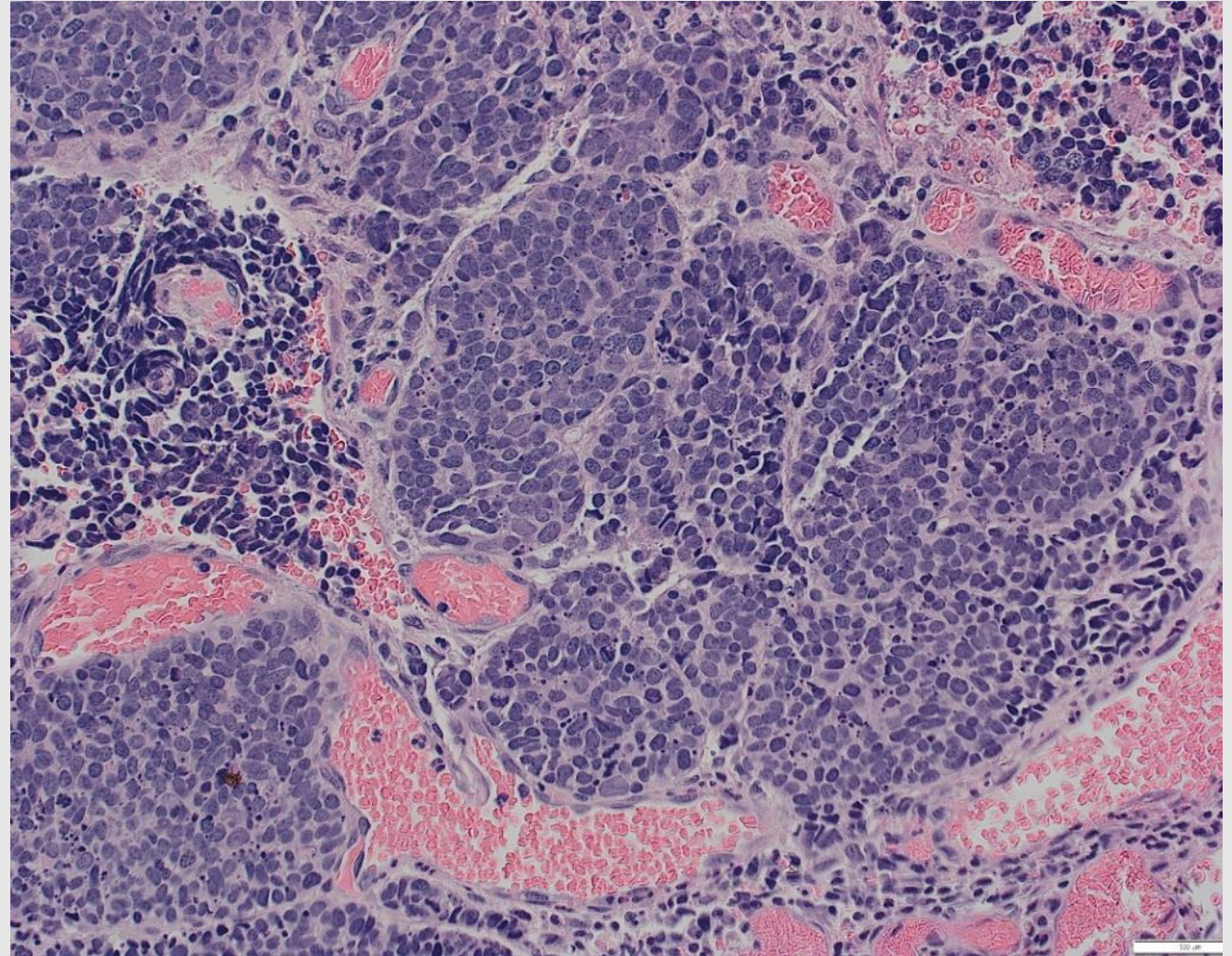
- Urgent referral to colposcopy advised

Histology: Small Cell Neuroendocrine Cancer

Wedge biopsy 17x11x7mm of the cervix shows a high grade neuroendocrine tumour of the cervix, of small cell type. Biopsy is diffusely infiltrated by an ulcerated basaloid malignant neoplasm growing in solid sheets. The cells have a high N:C ratio and stippled chromatin with focal nuclear moulding. Mitoses and apoptotic bodies are very frequent.

Immunohistochemistry was positive for synaptophysin (a marker for neuroendocrine tumours) and High risk HPV.

No CIN or CGIN identified.



Representative section of H&E showing nests of small cell carcinoma

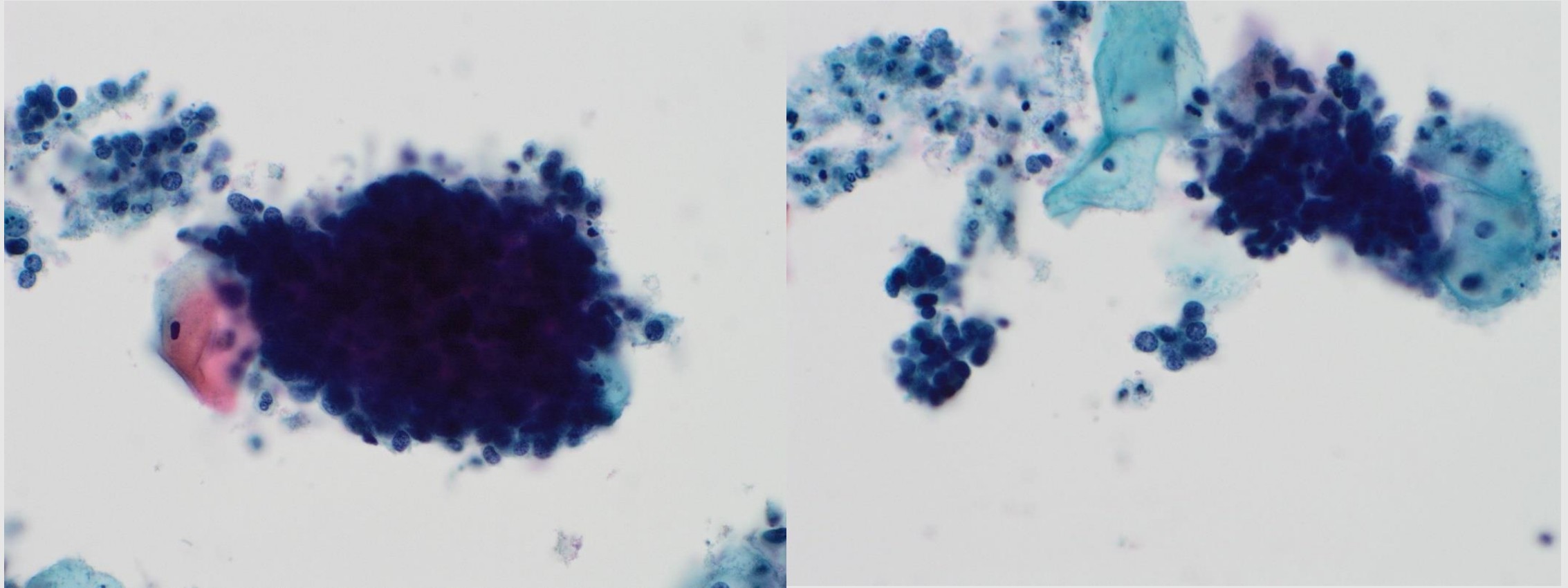
Small Cell Neuroendocrine Cancer

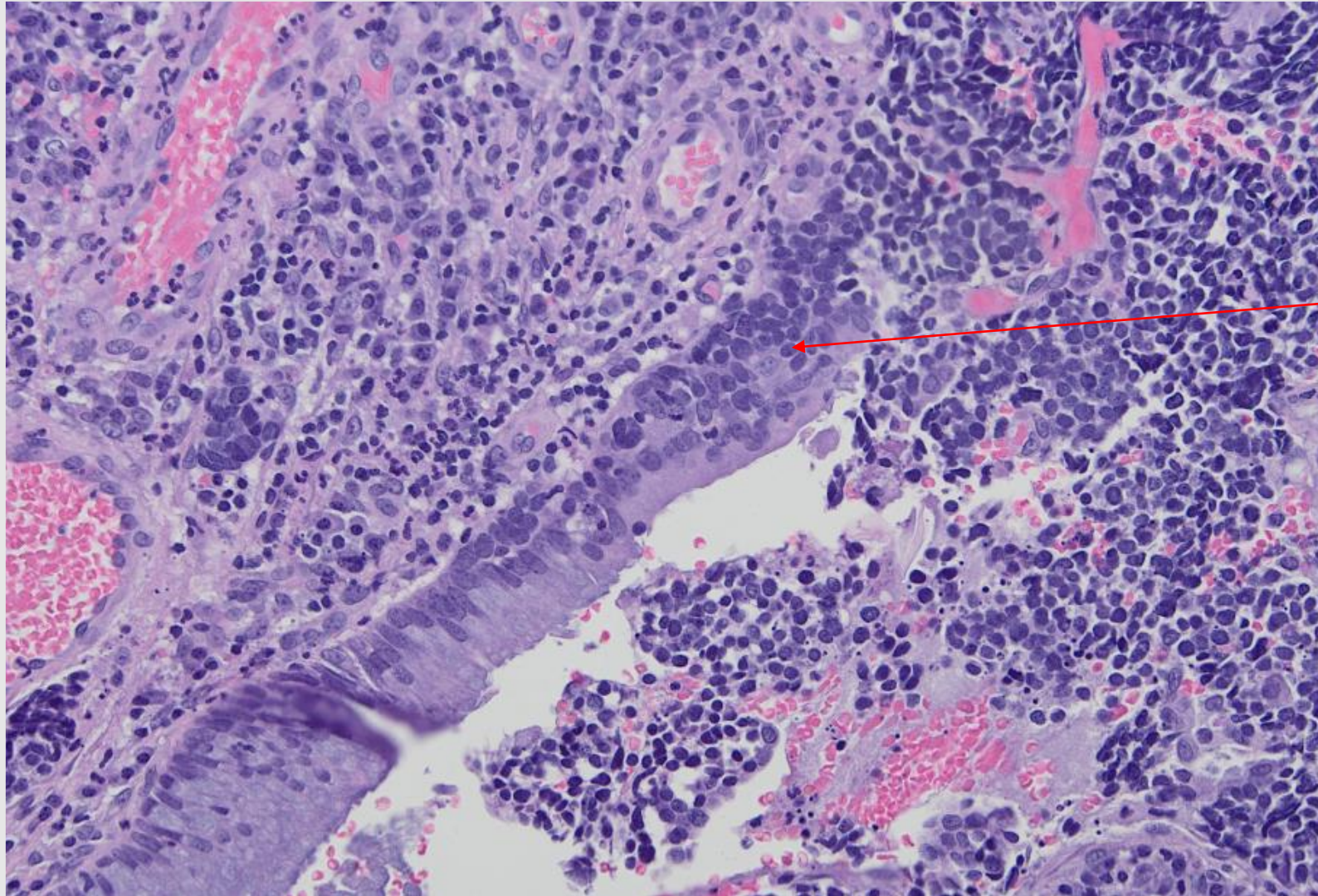
- Neuroendocrine neoplasms are aggressive malignancies derived from neuroendocrine cells and originate from the embryonic neuroectoderm
- Rare, account for 2% of cervical cancer
- Usually HPV positive
- Most common in females in their 30's and 40's
- The tumour cells typically express positivity for neuroendocrine markers such as synaptophysin, neuron-specific enolase (NSE), chromogranin, and CD56

Cytological features of Small cells neuroendocrine tumours

- Presence of small tumour cells with high NC ratios
 - Chromatin pattern is typically granular/stippled
 - Inconspicuous nucleoli
 - Nuclear moulding can sometimes be seen
-
- Review of cytology with knowledge of outcome...

- In retrospect, the abnormal cells are small with high n/c ratio, stippled chromatin, inconspicuous nucleoli, hint of moulding? But there is also an edge of atypical endocervical cells which is misleading and likely led to the report of CGIN. Are they endocervical?





H&E slide showing malignant cells abutting on glands. Glands show apparent pseudostratification which may explain the cytological appearance of ?CGIN

Conclusion

- A case of small cell neuroendocrine cancer, in retrospect some typical features can be seen
- These cancers are rarely seen in cervical samples and therefore easily misinterpreted as glandular abnormalities when nearby glands are associated with the abnormal cells
- The previous cervical samples will be reviewed as part of cervical cancer audit

Further Reading

- Gordhandas, S. Schlappe, BA. Qin Zhou, AI. Leitao, MM. Park, JK. de Brot, L. Alektiar, KM. Sabbatini, PJ. Aghajanian, CA. Friedman, C. Zivanovic, O. O'Cearbhaill, RE. Small cell neuroendocrine carcinoma of the cervix: Analysis of prognostic factors and patterns of metastasis. *Gynecologic Oncology Reports*. 2022 Volume 43, 101058. DOI: [10.1016/j.gore.2022.101058](https://doi.org/10.1016/j.gore.2022.101058)
- Tempfer, C.B., Tischoff, I., Dogan, A. *et al.* Neuroendocrine carcinoma of the cervix: a systematic review of the literature. *BMC Cancer* 2018; 18: 530 DOI: [10.1186/s12885-018-4447-x](https://doi.org/10.1186/s12885-018-4447-x)
- Gupta, P, Gupta, N, Suri, V, Rai, B, Rajwanshi, A. Cytomorphological features of cervical small cell neuroendocrine carcinoma in SurePath™ liquid-based cervical samples. *Cytopathology*. 2021; 32: 813– 818 DOI: [10.1111/cyt.13030](https://doi.org/10.1111/cyt.13030)