

子宮頸細胞病理教學手冊

單元 2-1

Atypical Glandular Cells / Hyperchromatic Crowded Group (112 年度)

資料提供：台灣病理學會細胞委員會 / 劉之怡 醫師



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Case #2-1

- 41 y/o lady
- Routine follow-up pap smear in GYN OPD
- Figure 1-2

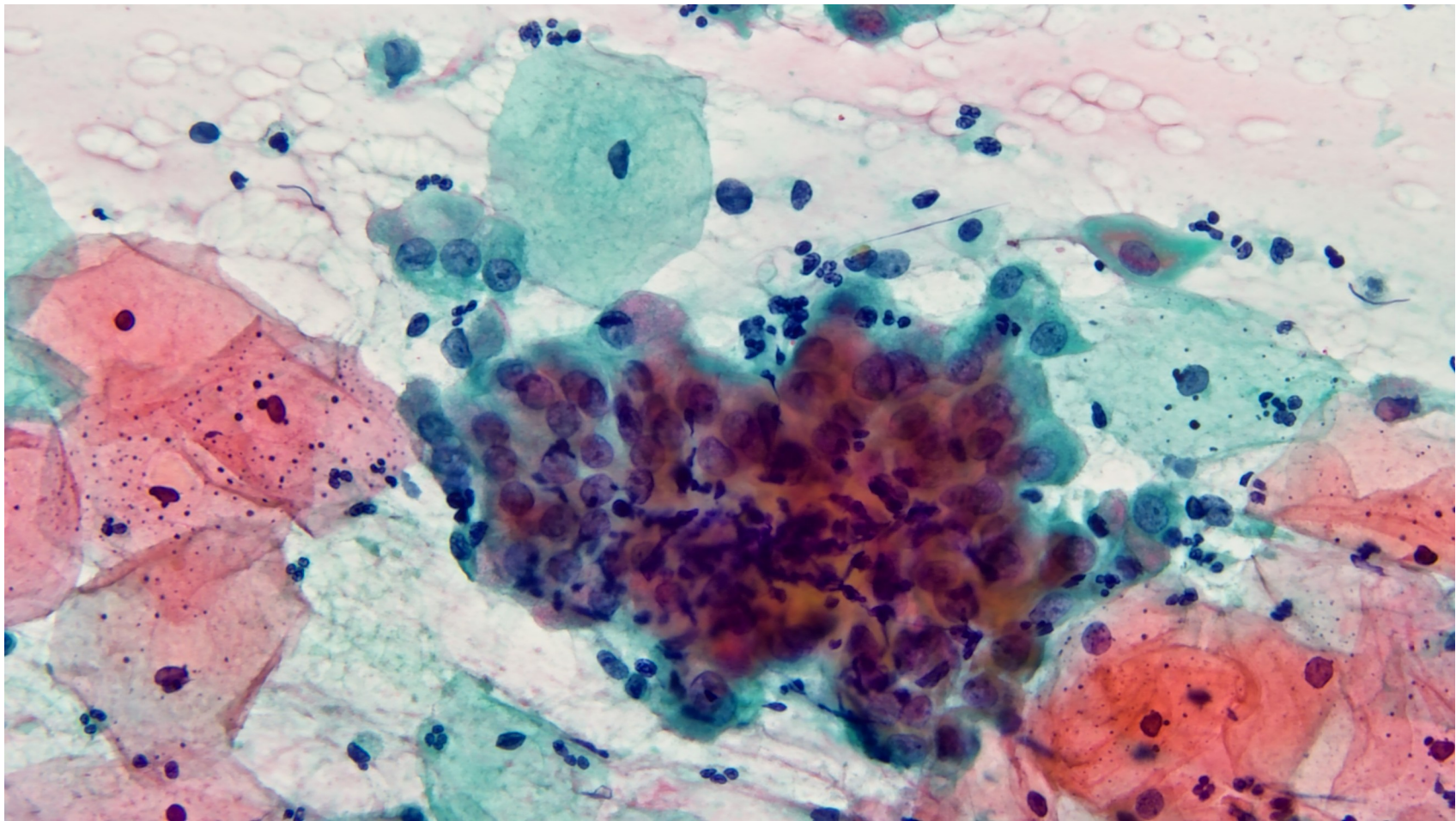


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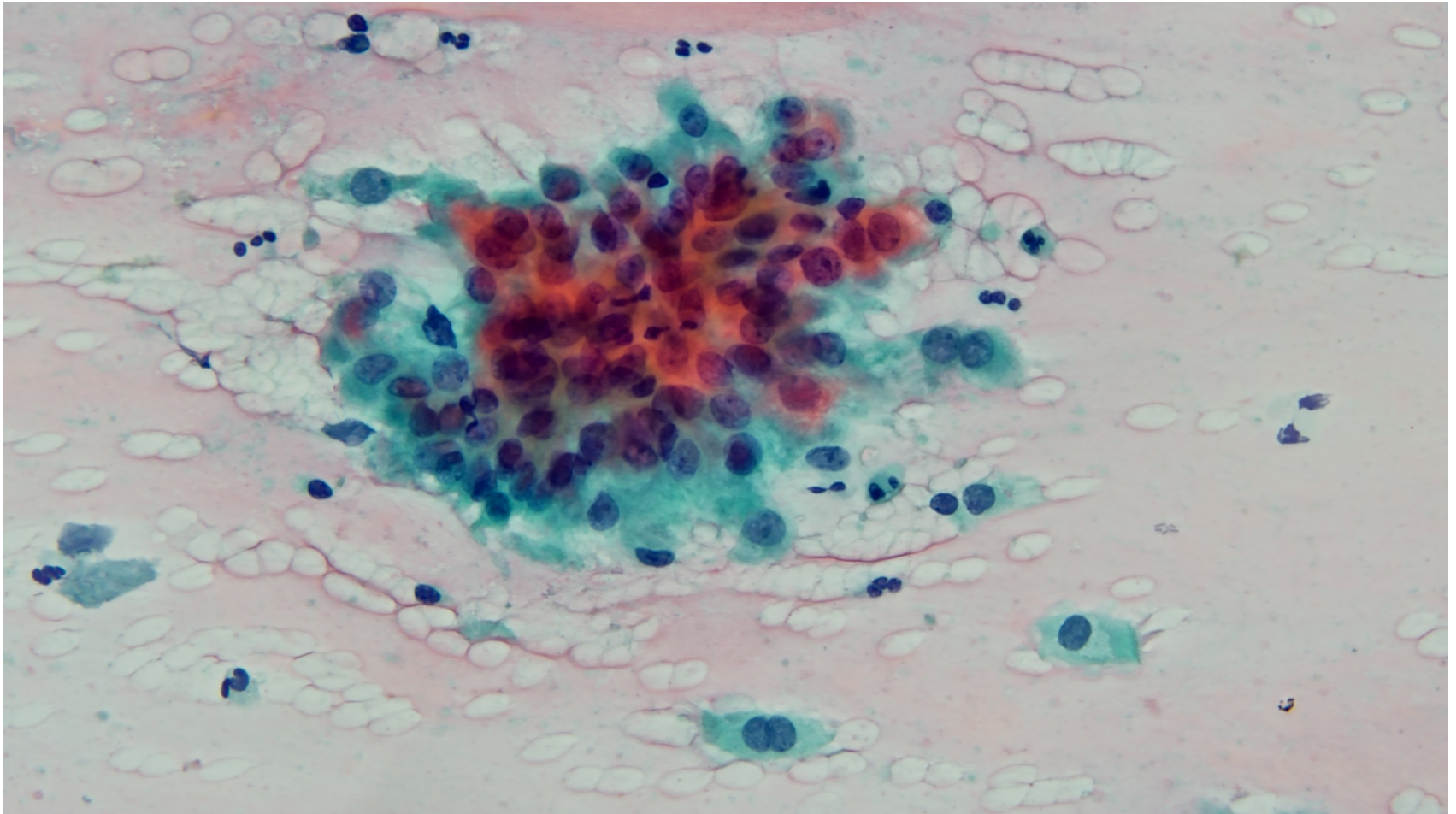


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Case #2-1



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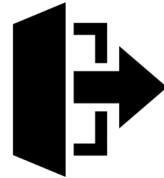
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Case #2-1

Your interpretation ?

please answer via link:



Case #2-2

- 42 y/o lady
- Routine follow-up pap smear in GYN OPD
- Figure 1-3

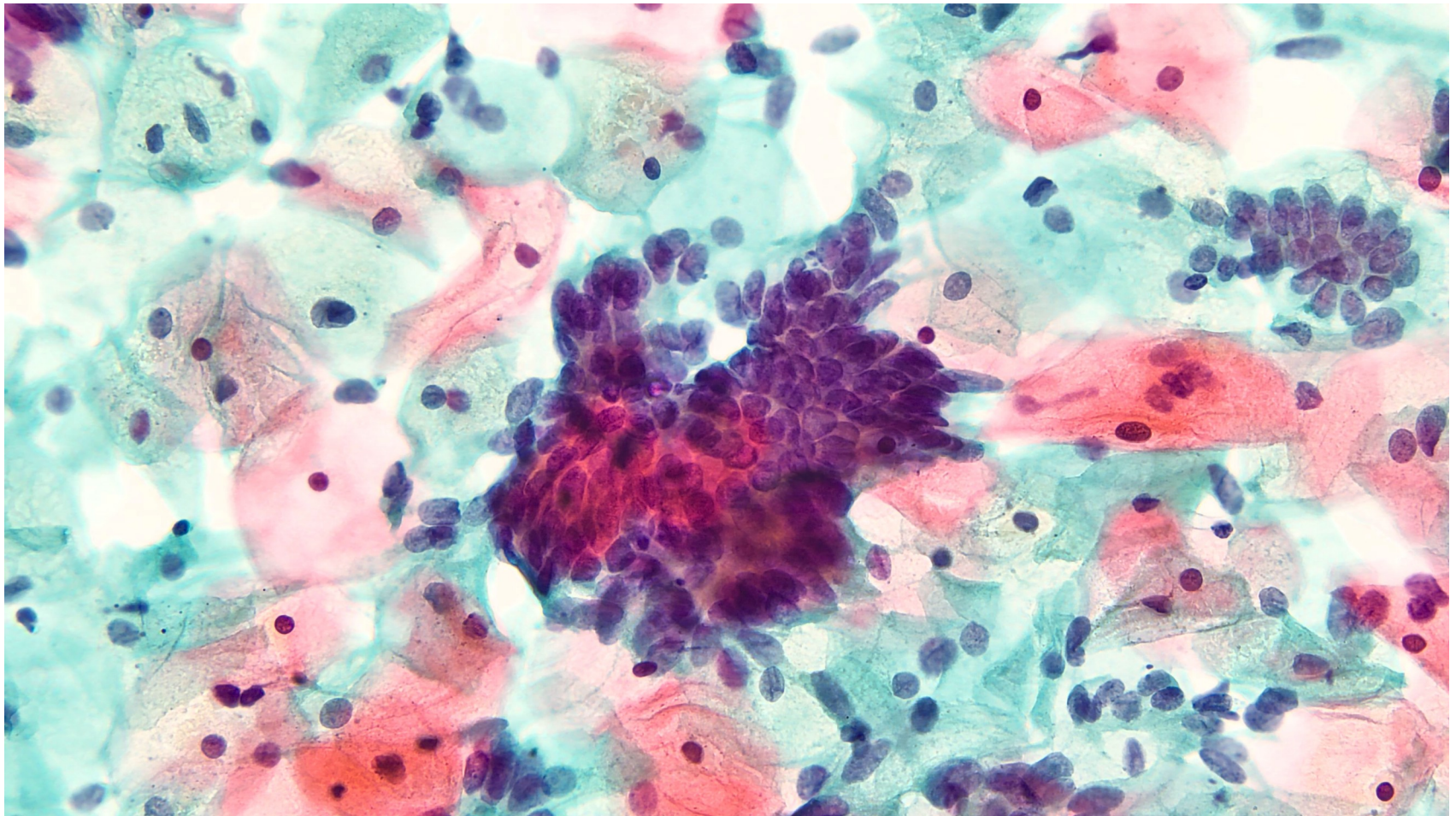


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Case #2-2

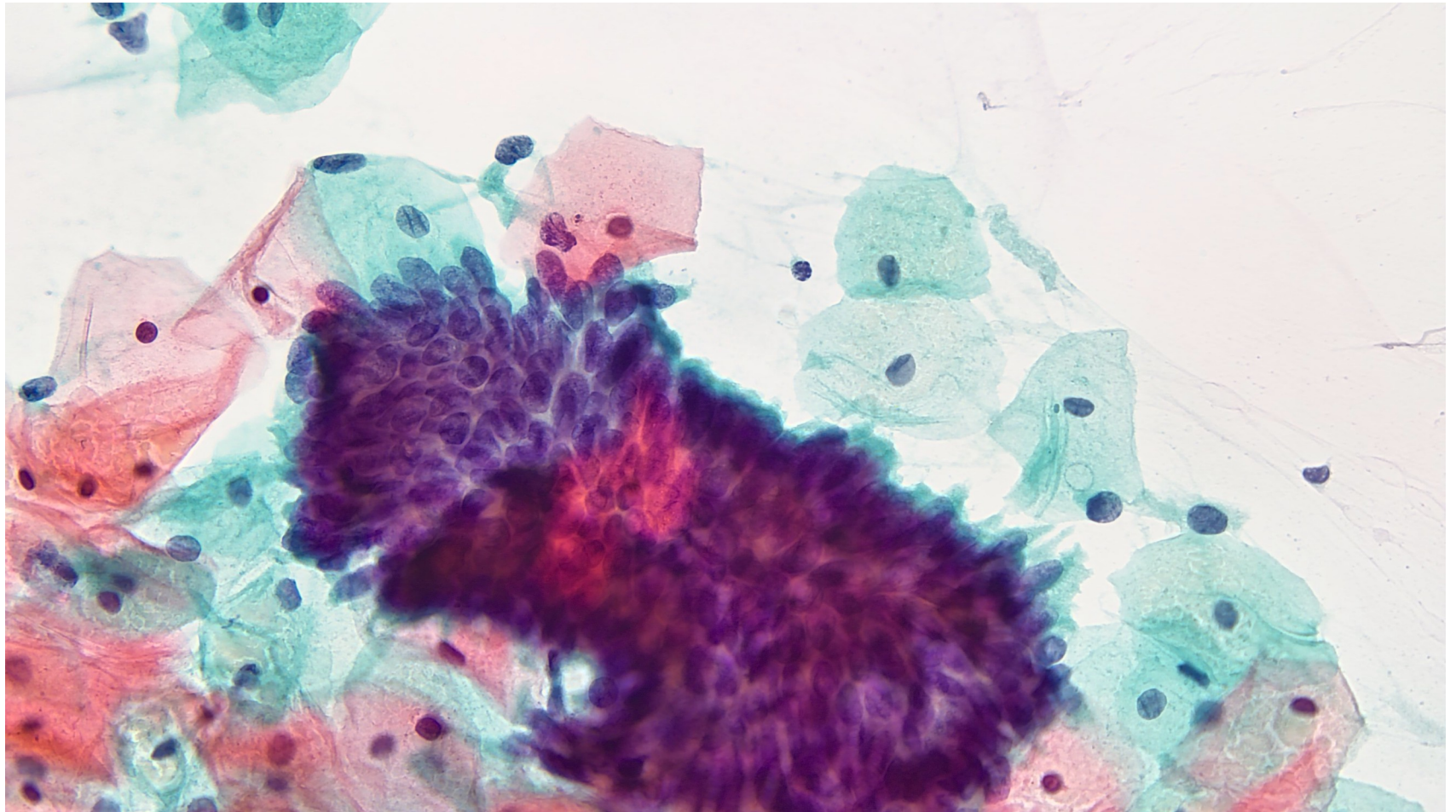


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Case #2-2

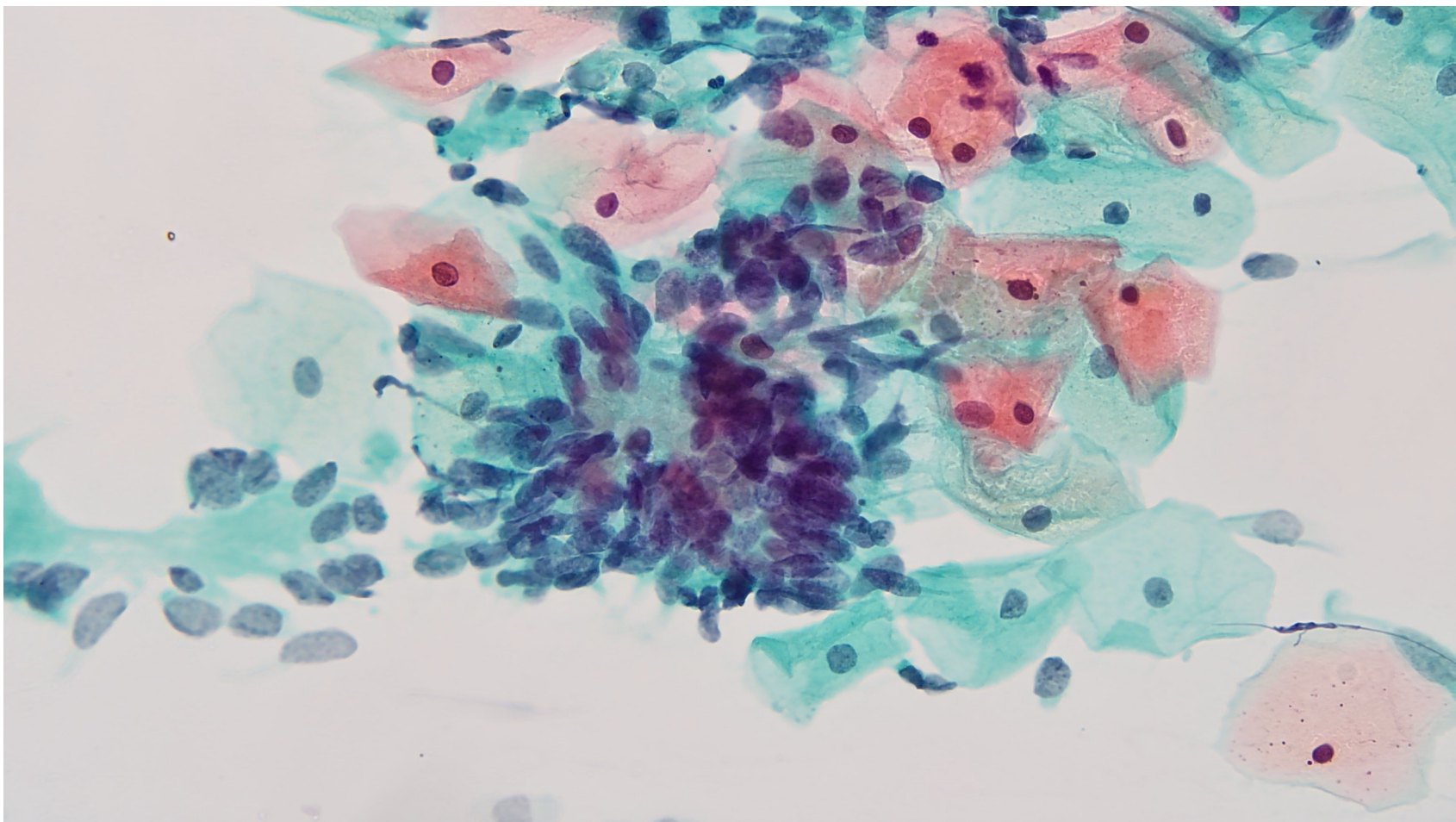


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Case #2-2



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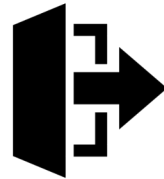
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Case #2-2

Your interpretation ?

please answer via link:



Case #2-3

- 71 y/o lady
- Routine follow-up pap smear in GYN OPD
- Figure 1-3

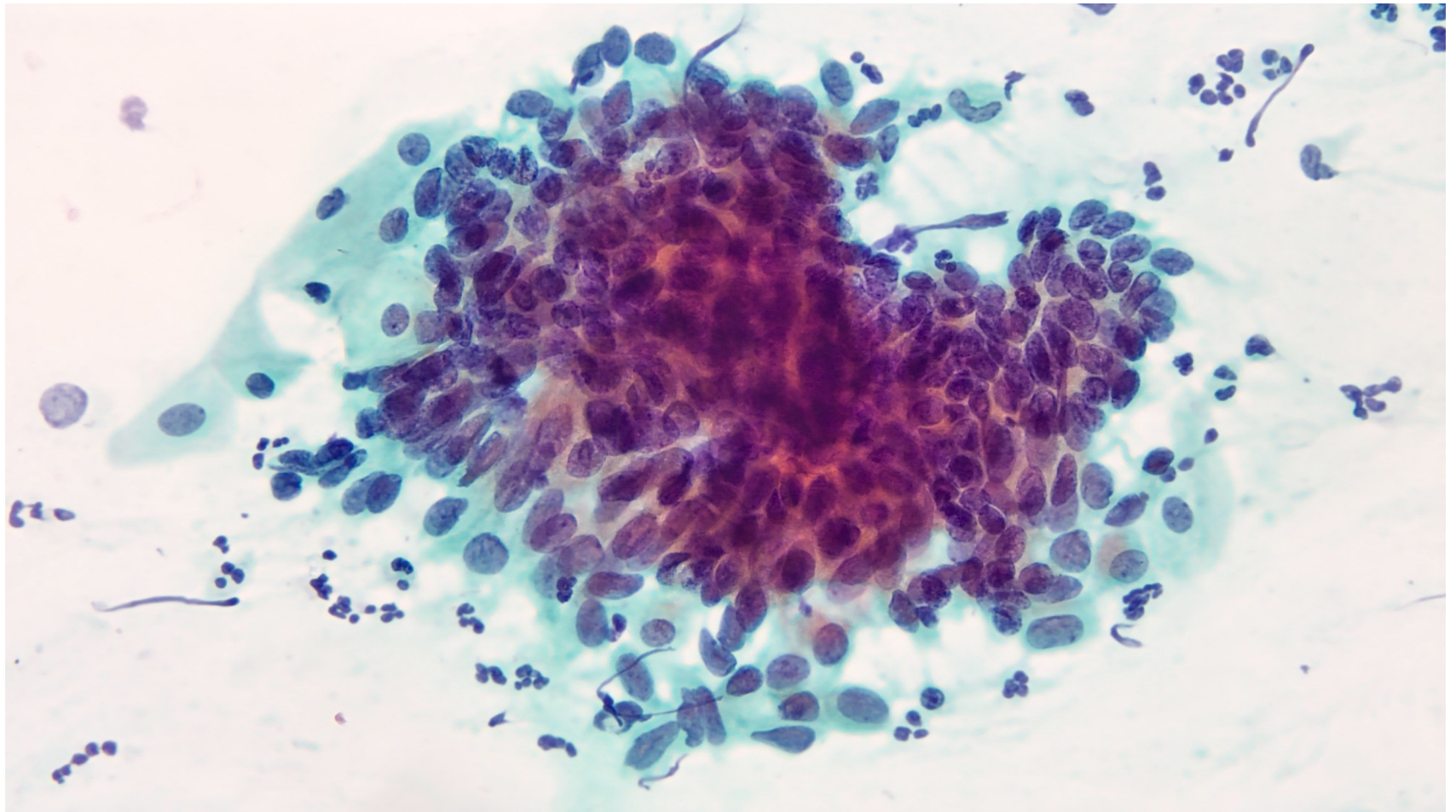


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Case #2-3

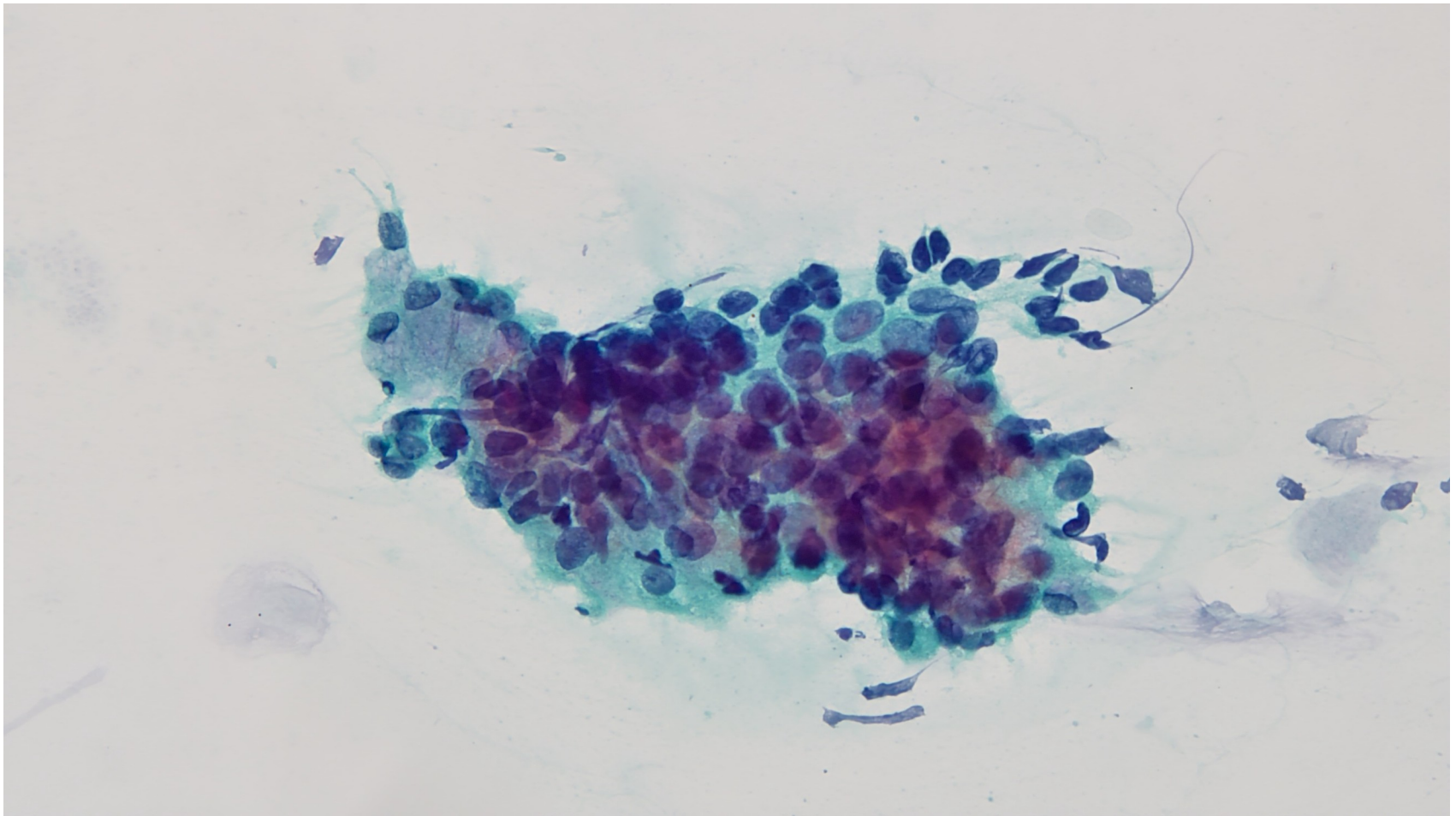


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Case #2-3

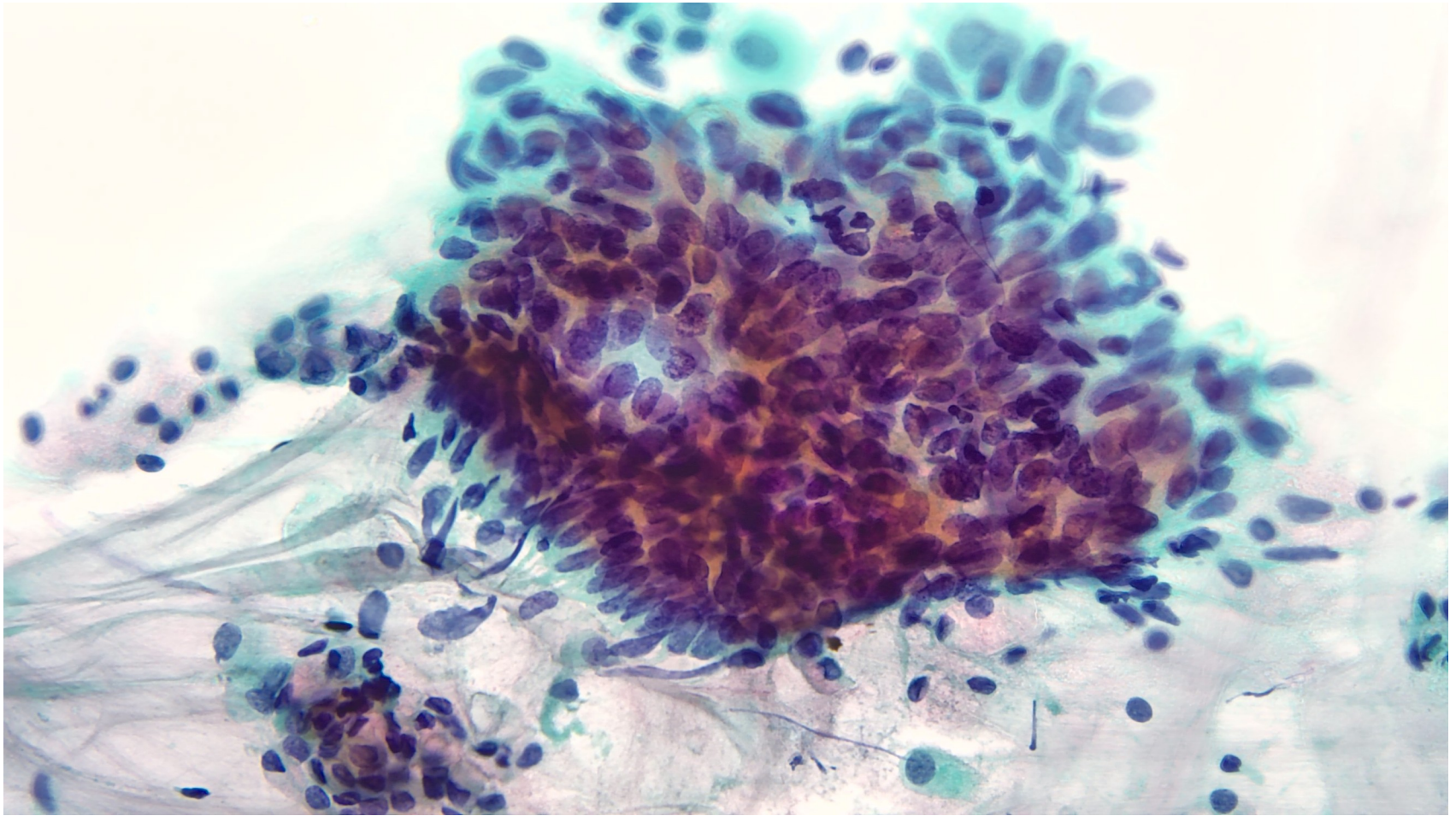


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Case #2-3



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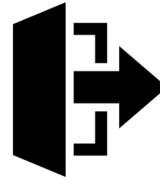
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Case #2-3

Your interpretation ?

please answer via link:



Case #2-1

➤ Cytology result: AGUS? Reactive conditions?

➤ Categories:

Negative for intraepithelial lesion or malignancy / NILM

➤ Diagnosis:

Tubal metaplasia

Case #2-1

Tubal metaplasia

Key points:

- ✓ Small sheets and strips with disoriented nuclei with terminal bars and cilia on every cell
- ✓ Rare strips with nuclear crowding, overlapping, and pseudostratification
- ✓ Nuclei are round to oval with mild hyperchromasia or washed-out chromatin, unlike those of AIS, which are oval to cigar-shaped with coarsely dispersed chromatin
- ✓ When viewed en face, nuclei are generally crowded but without nuclear overlap, mitosis, or apoptosis seen in AIS
- ✓ Usually if cilia is not seen en face, isolated ciliated cell with similar nucleus is seen in immediate vicinity

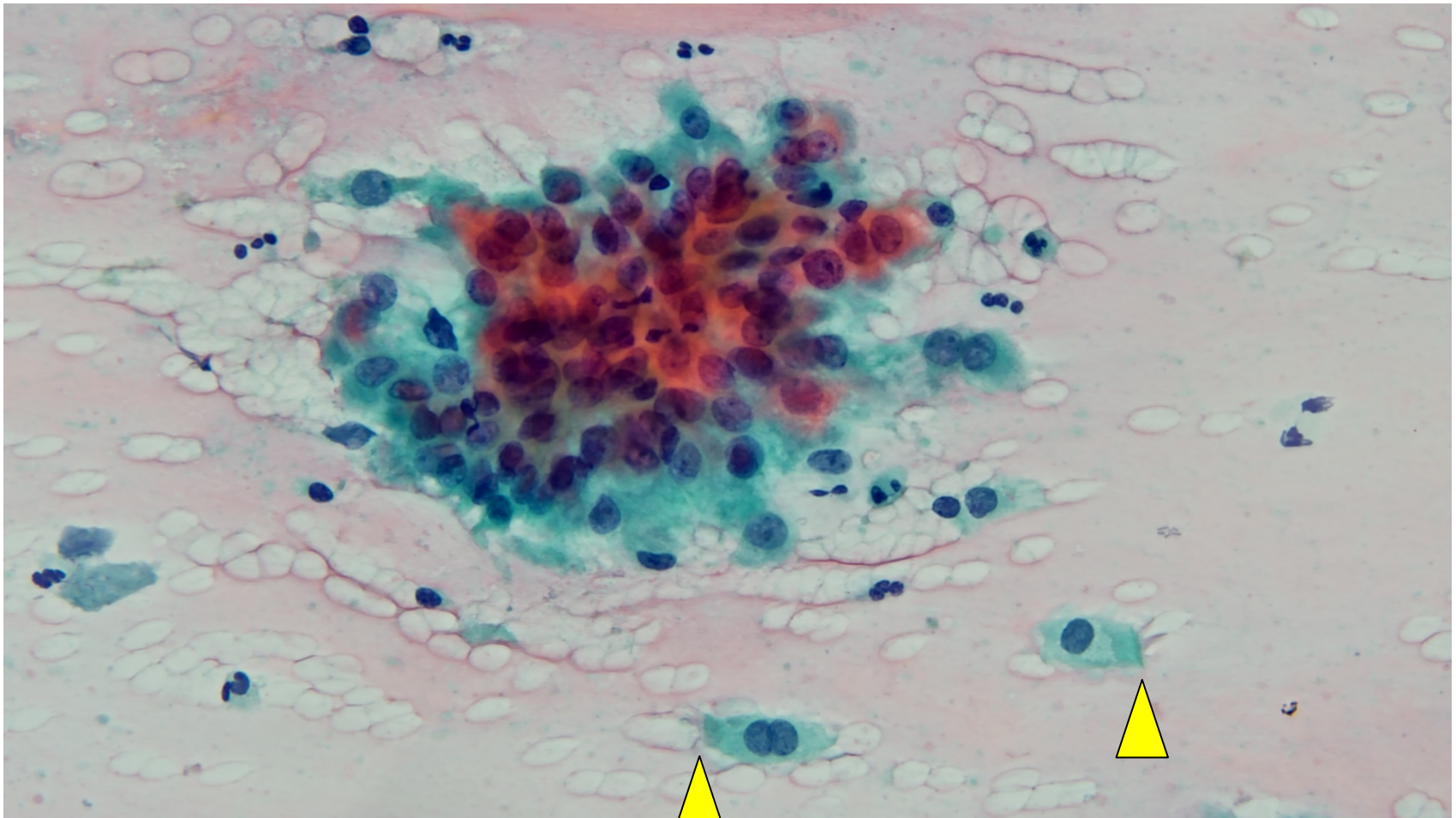


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Case #2-1



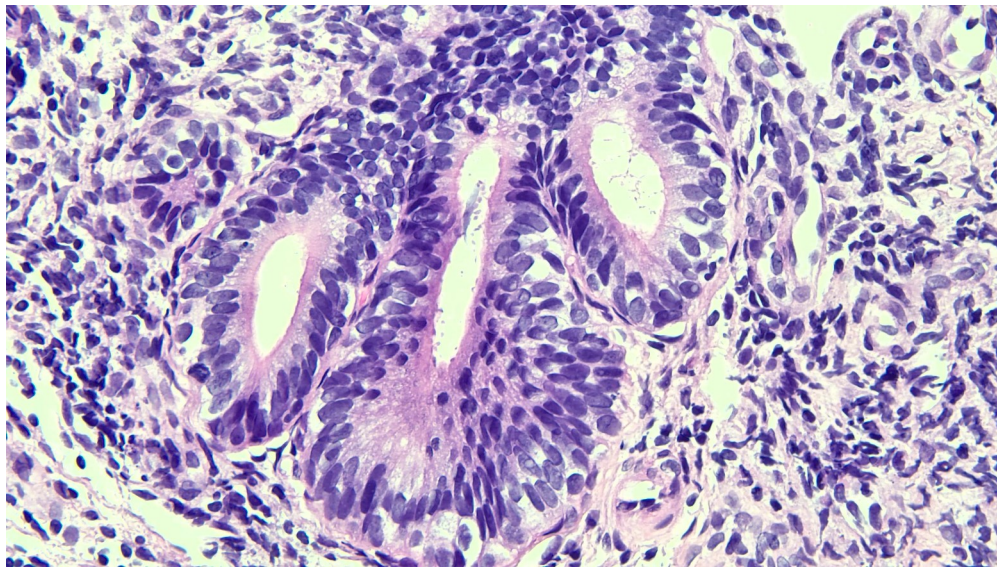
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Case #2-2

- Cytology result: Adenocarcinoma in situ
- Categories:
Epithelial Cell Abnormality / Glandular cells
- Diagnosis:
Endocervical adenocarcinoma in situ



Case #2-2

AIS

Key points:

- ✓ Hyperchromatic nuclei in crowded groups (overlapping nuclei) and strips
- ✓ Peripheral feathering of neoplastic cells
- ✓ May form rosette-like structures
- ✓ Sheet, strips, and torn gland forms with polarization of nuclei perpendicular to circumferential axis
- ✓ Oval or elongated hyperchromatic nuclei with increased N:C ratios and nuclear overlap/crowding
- ✓ Nuclei bulge out from center of cytoplasm, imparting snake egg appearance

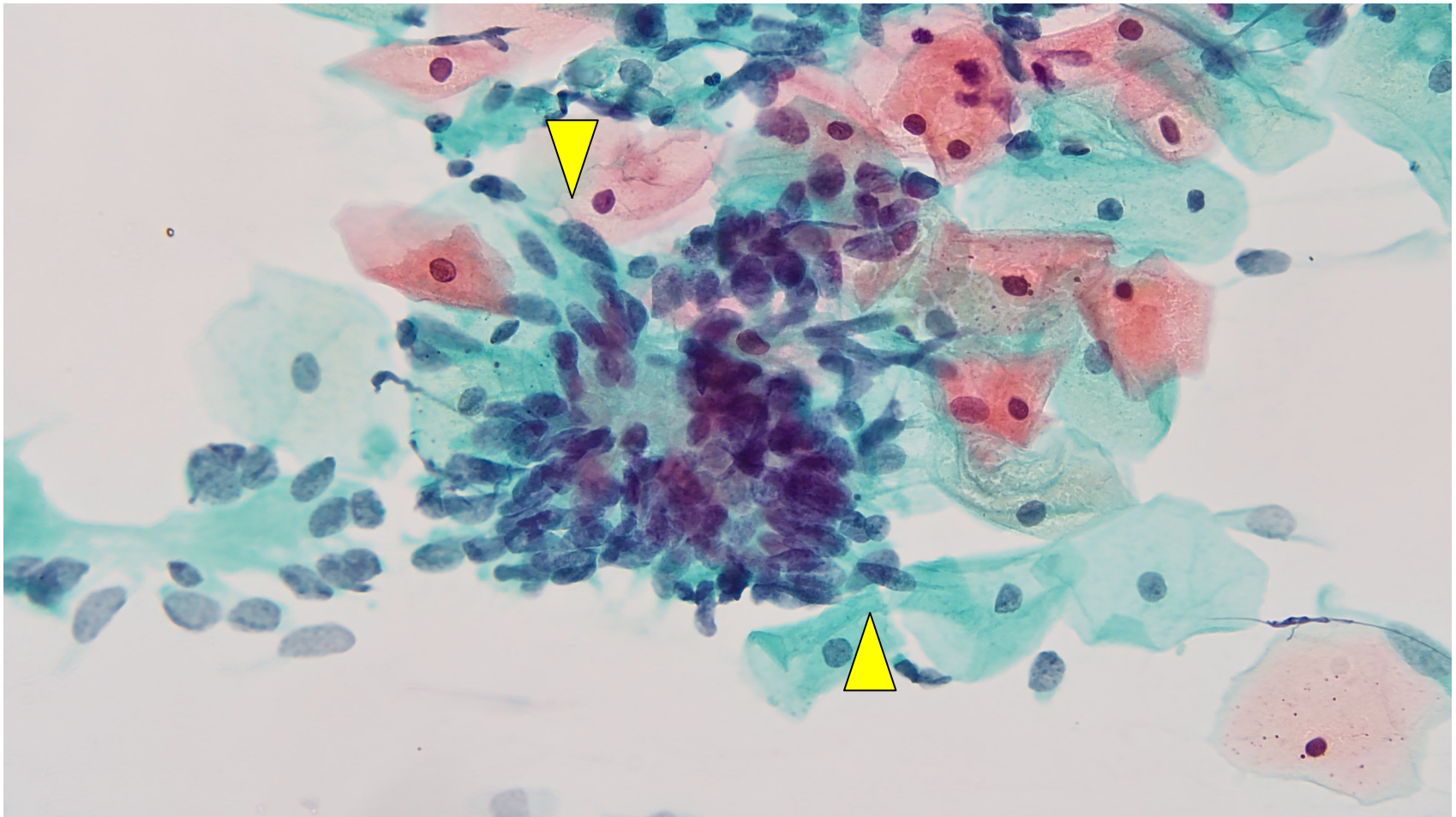


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Case #2-2

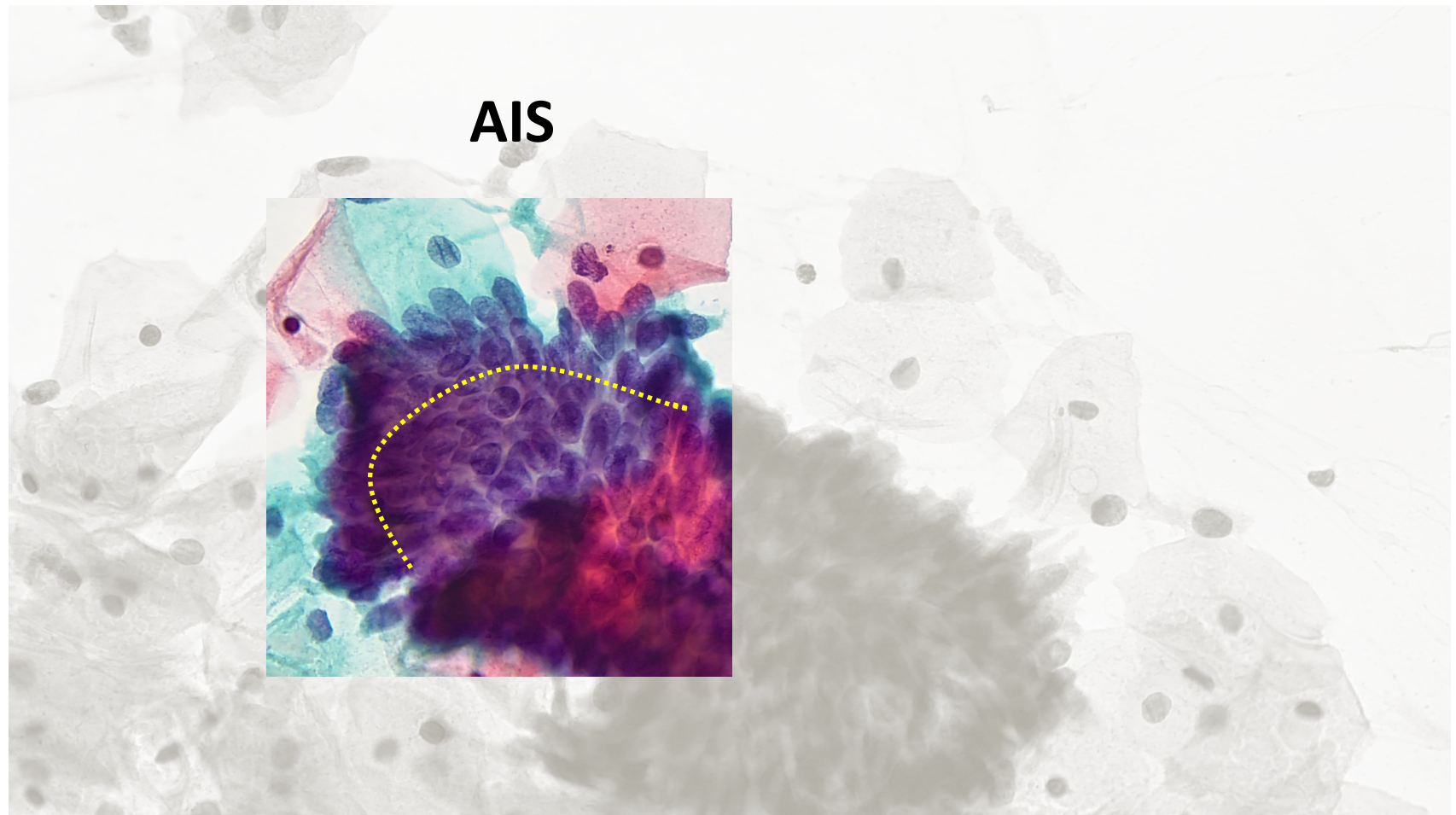


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Case #2-2



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Case #2-3

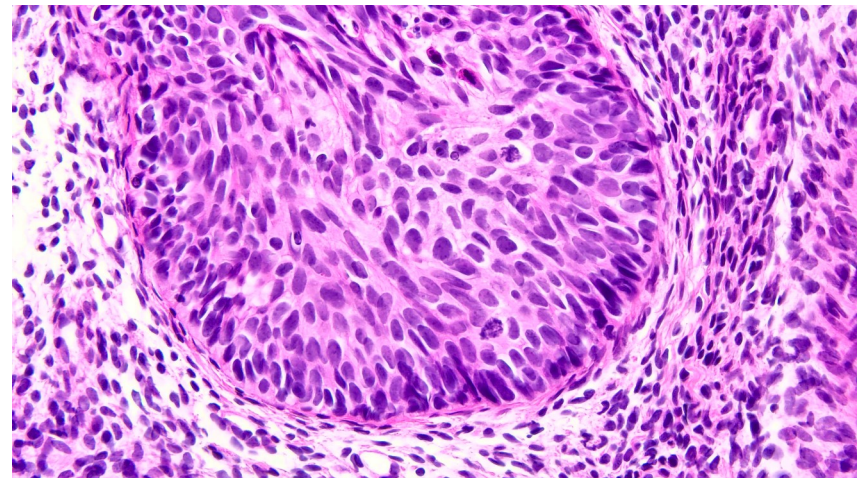
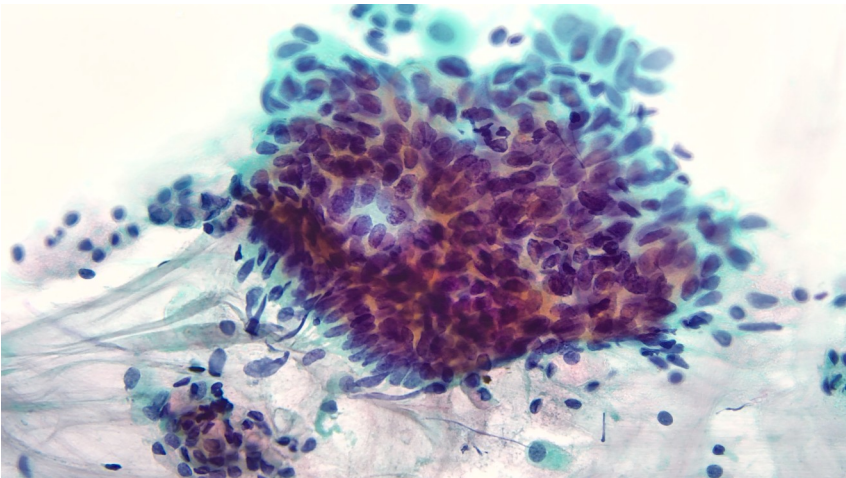
➤ Cytology result: AGUS? AIS? HSIL?

➤ Categories:

Epithelial Cell Abnormality

➤ Diagnosis:

High-grade SIL with glandular involvement



Case #2-3

High-grade SIL

Key points:

- ✓ Hyperchromatic crowded groups (HCGs)
- ✓ Clumps or syncytial aggregates or HCGs if in glands on conventional Paps
- ✓ Affects immature/small cells
- ✓ Cell sizes range from small basal to metaplastic-type cells to larger cells that are closer to intermediate cells but with higher N:C ratio
- ✓ Hyperchromatic nuclei with nuclear contour irregularities due to indentations and grooves

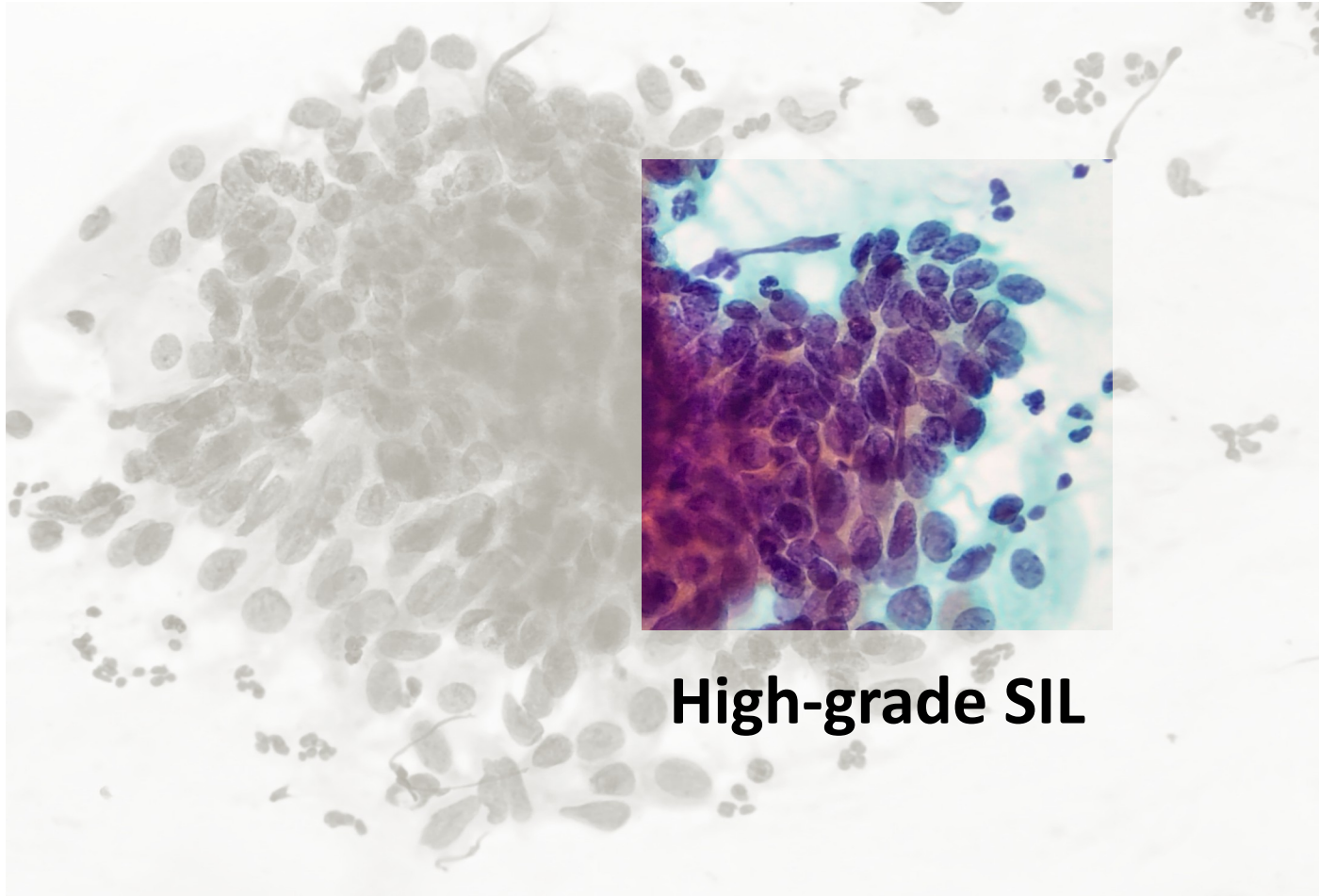


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Case #2-3



High-grade SIL



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Differential Diagnosis of Hyperchromatic Crowded Group

- HCGs are the most important differential with glandular lesions and are one of the significant diagnostic challenges in the cytopathology of Pap smears.
- HCG is specifically defined as dark crowded cell groups of usually more than 15 cells identified at ×10 screening magnification.



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HCG: Tubal metaplasia

- Tubal metaplastic cells may mimic HCG of AGC cells (may be with singly scattered tubal cells in the background)
- Strips of columnar cells with nuclear overlap and pseudostratification (without nuclear feathering)
- Usually cilia or terminal bars are seen
- Round to oval dark nuclei may show size variation with increased N/C ratio
- Lacks: Apoptotic bodies, coarse chromatin, uneven chromatin distribution, and parachromatin clearing



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HCG: HSIL

- The nuclei of HSIL cells do not show easily detectable nucleoli (unless associated with endocervical cells in cases with HSIL with endocervical gland involvement).
- Nuclear-to-cytoplasmic ratio is higher in HSIL compared to AGC
- HSIL nuclear contours are usually irregular as compared to AGC
- HSIL cell cytoplasm is variable but usually “immature” dense, homogeneous cyanophilic, but may be “mature” densely keratinized. Compared to lacy delicate or vacuolated cytoplasm in AGC cells.



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HCG: HSIL or AIS ?

HSIL:

- Nuclei are mostly round to oval (in contrast to elongated, cigar-shaped nuclei in AIS) without palisading and without nuclear feathering
- Degree of nuclear enlargement is more variable.
- Chromatin may be fine or coarsely granular and is evenly distributed.
- Nucleoli are generally absent, but may occasionally be seen along the periphery of groups, particularly when HSIL involves endocervical glands.
- Appearance of the cytoplasm is usually metaplastic, but variable (“immature,” lacy, and delicate or densely metaplastic, occasionally, “mature,” and densely keratinized).

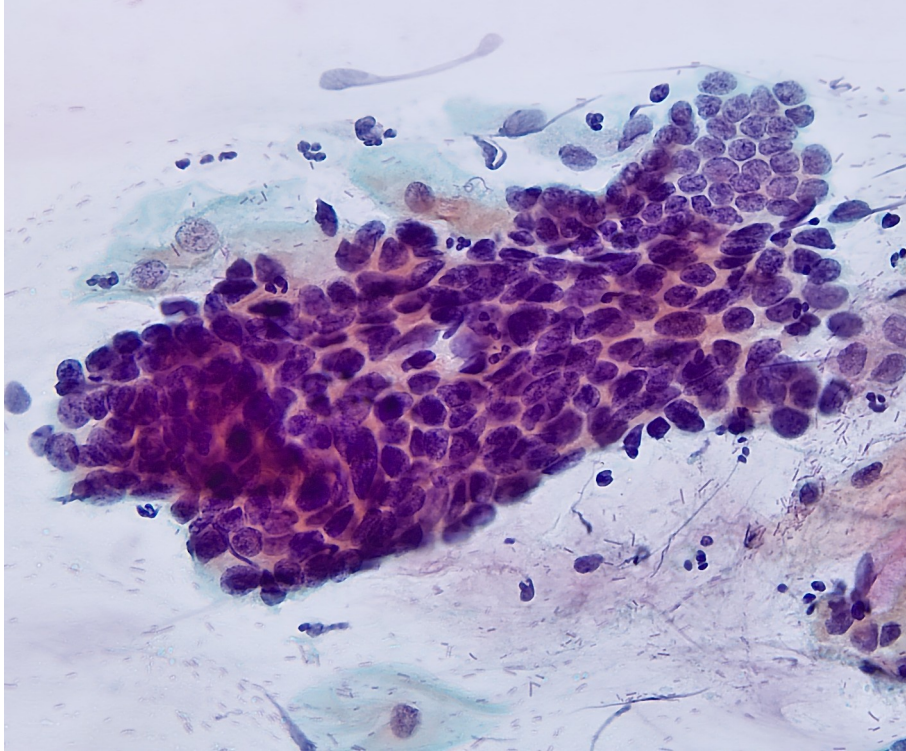


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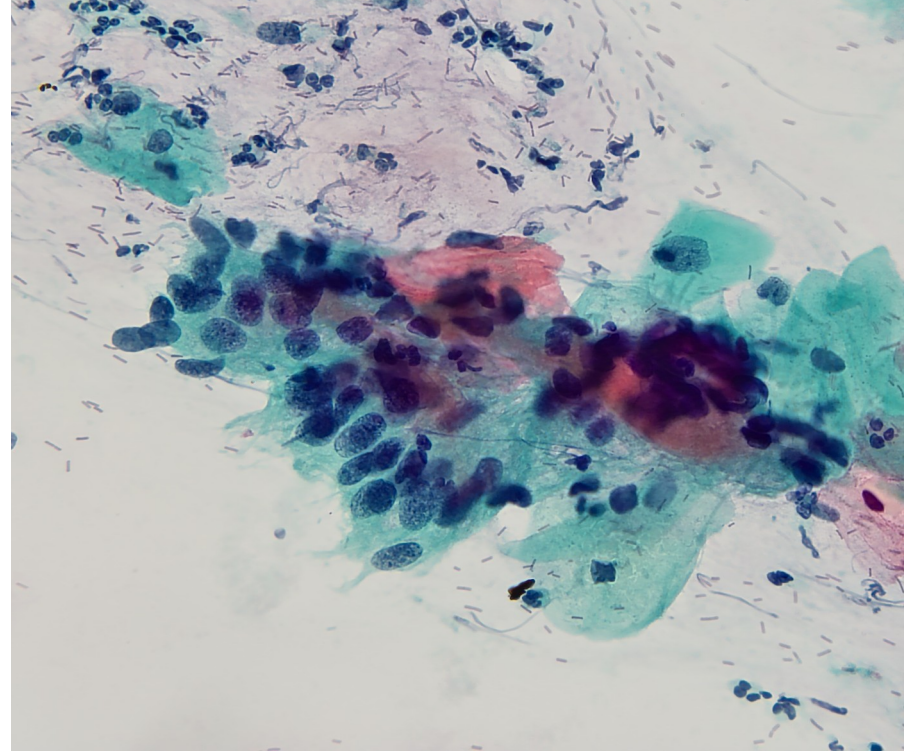
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High-grade SIL



AIS

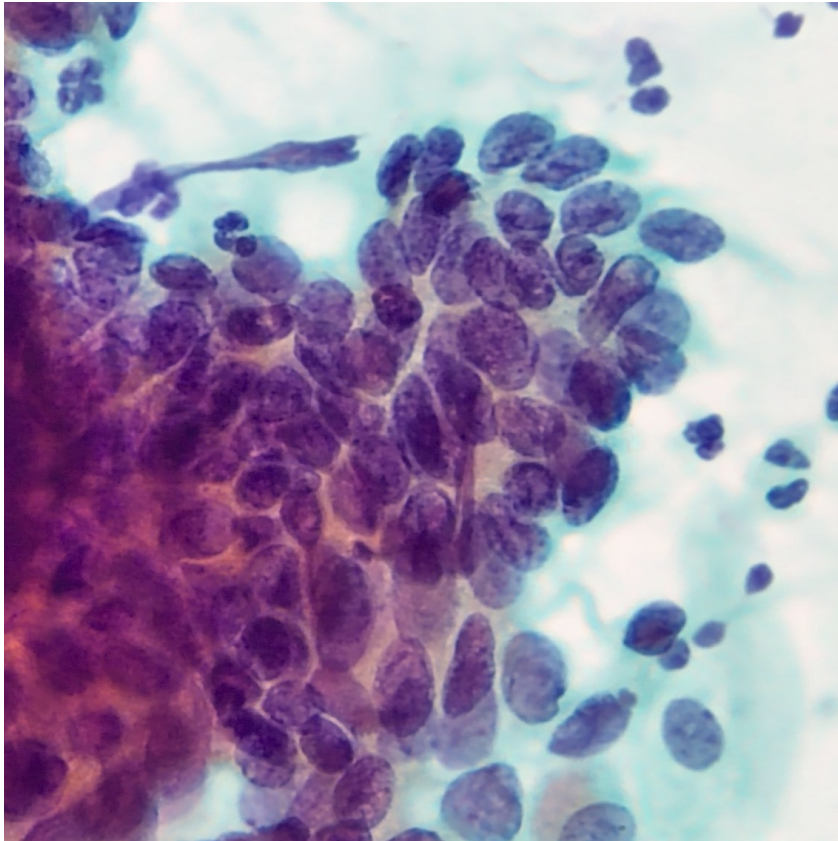


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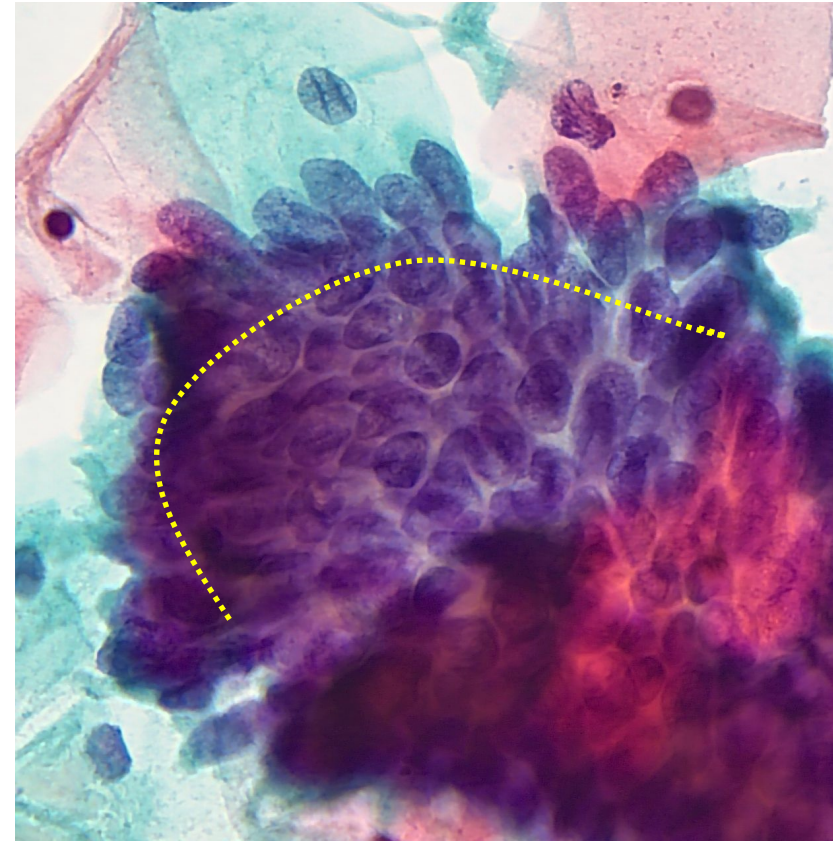
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High-grade SIL



AIS



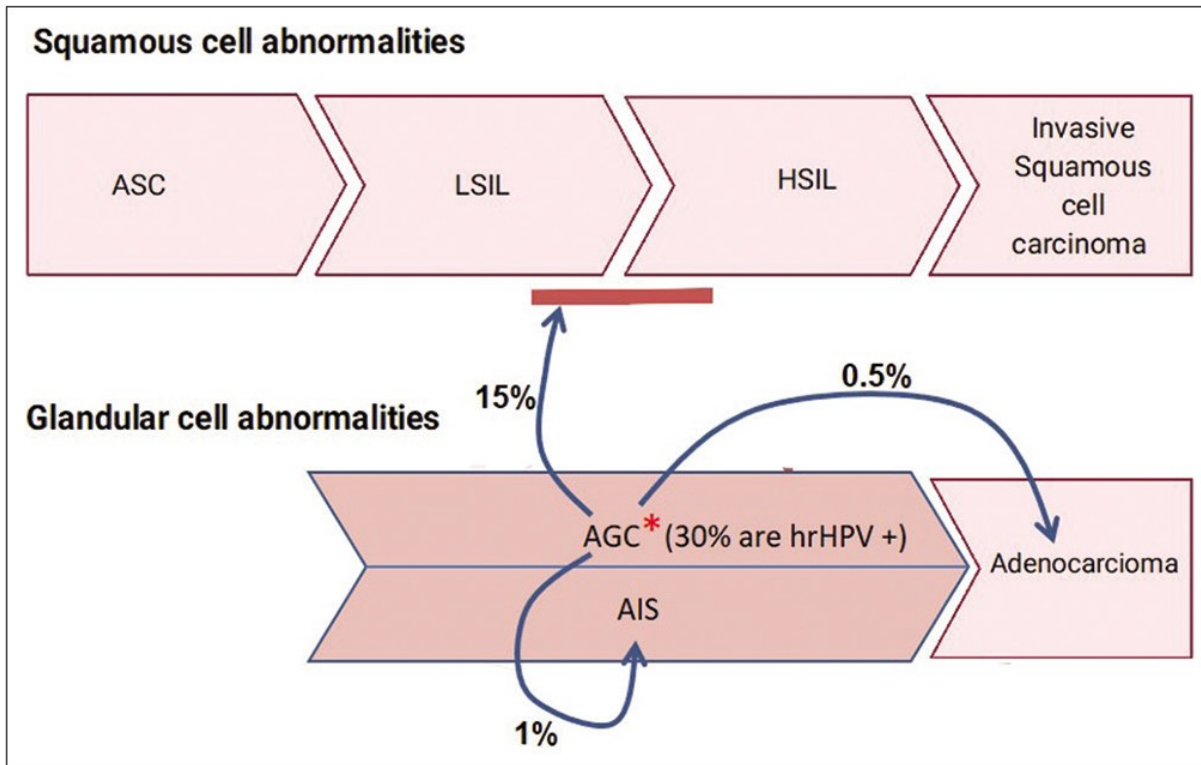
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Atypical glandular cells (AGC)

- The incidence of atypical glandular cells (AGC) is approximately 0.18–0.74% of all cervical smears. Clinical significant lesions is reported in 42-83% of AGCs.
- AGC falls in “high-risk” category because of increased chances of AdCa, AIS, or HSIL on biopsy after AGC on Pap test.
- An overall high risk than ASC-US: Squamous abnormality in 54-88%; glandular abnormality in 12-46%
- A high degree of suspicion, good clinical history, and the presence of diagnostic cytomorphological findings are essential for the proper interpretation of glandular cell abnormalities.



Cyto-histo correlation of AGC: *Around 30% of AGC are High-risk HPV (hrHPV) positive. On cyto-histo correlation about 15% are associated with LSIL or HSIL. 1% are associated AIS and 0.5% with adenocarcinoma.

AGC, endocervical, NOS

- This category includes AGCs with a morphology that is short of adenocarcinoma but overlap with reactive or reparative changes.
- The qualifier “favor reactive” is potentially misleading, and is not included in the current Bethesda terminology.
- “Not Otherwise Specified” (NOS) is recommendation to be used with appropriate comment(s).
- The key for proper designation of atypical endocervical cells lies in the ability to exclude reactive conditions that include repair, tubal metaplasia, radiation, and intrauterine device (IUD) effect.



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References

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- Mody Dina R, Michael J Thrall and Savitri Krishnamurthy. 2022. Diagnostic Pathology (version 3rd ed). Philadelphia: Elsevier.
- Khan, M.Y.A.; Bandyopadhyay, S.; Alrajjal, A.; Choudhury, M.S.R.; Ali-Fehmi, R.; Shidham, V.B. Atypical glandular cells (AGC): Cytology of glandular lesions of the uterine cervix. Cytojournal 19, 31, doi:10.25259/CMAS_03_11_2021.