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Thyroid follicular neoplasms in cytology

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Lecture overview

- importance of FNAB in assessing thyroid lesions
- follicular thyroid neoplasms
- other follicular-patterned thyroid lesions in cytology and difficulties in their differentiation
- how is The Bethesda system for reporting thyroid cytopathology (TBSRTC) dealing with follicular-patterned lesions
- the role of ancillary techniques



Importance of FNAB in assessing thyroid lesions

- palpable thyroid nodule in 4-10% of the population
- US detected thyroid nodule in up to 27% of the population
- majority benign (app. 1% malignant)
- FNAB is most accurate and cost effective method for triage and management of the patients with thyroid nodules (diagnostic accuracy from 80 to > 95% for representative samples)
- FNAB could be **diagnostic** (papillary, medullary carcinoma,...) or **screening** test (follicular carcinoma)



Follicular neoplasms

- include: - follicular adenoma (FA)
- follicular carcinoma (FC)
- diagnosis of FC based strictly on histological criteria (vascular/capsular invasion)



Follicular adenoma (FA)

- encapsulated benign neoplasm
- several different histomorphologic growth patterns (usually uniform architecture in a single lesion)
- morphologic diversity is the cause for overlapping cytologic patterns in some cases of nodular goiter, follicular adenoma and follicular carcinoma



Morphologic variants of FA

- conventional:
 - macrofollicular (colloid)
 - normofollicular (simple)
 - microfollicular
 - trabecular/solid
- oncocytic
- hyalinizing trabecular
- FA with clear cell change
- FA with papillary hyperplasia
- atypical

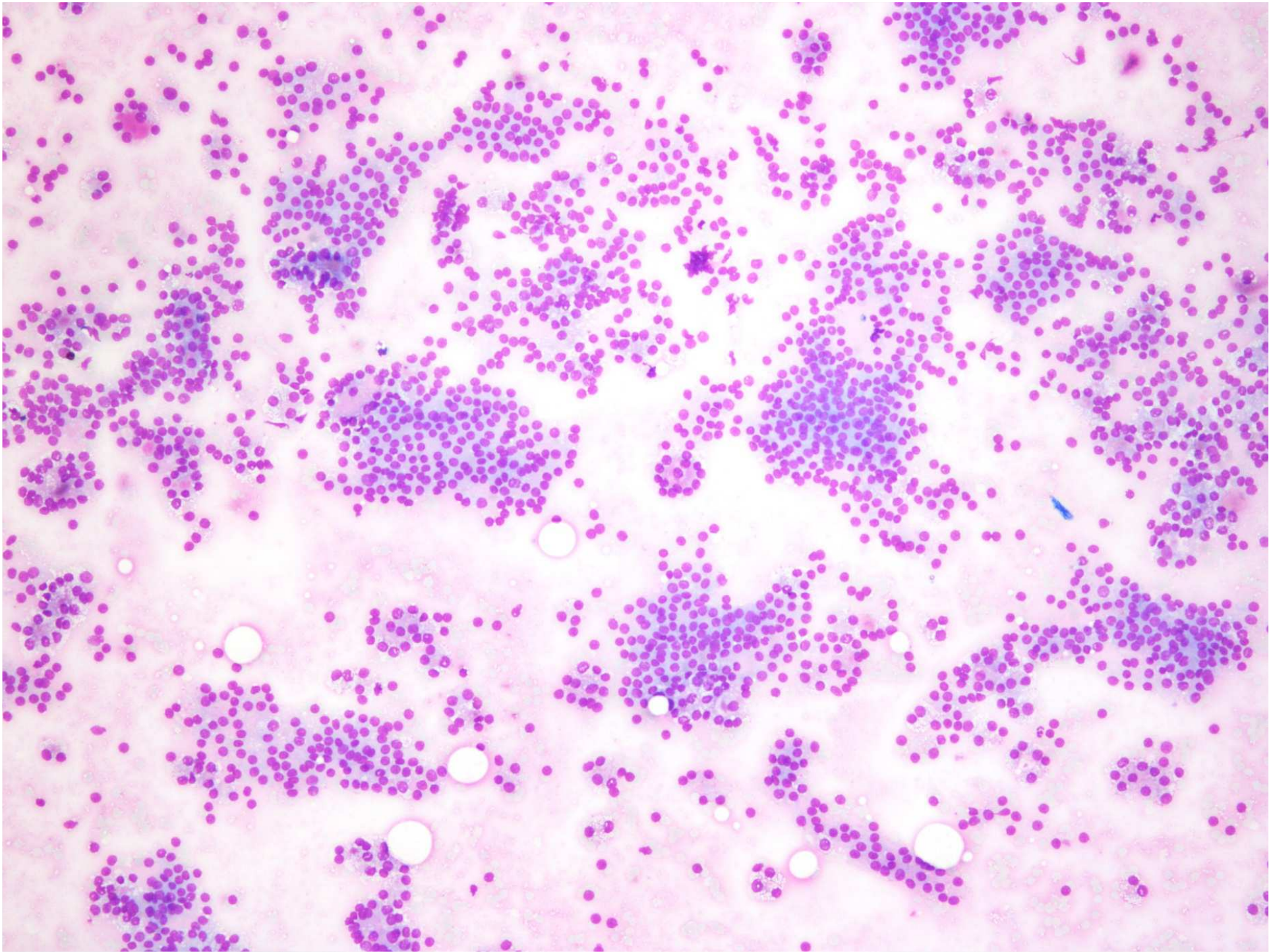


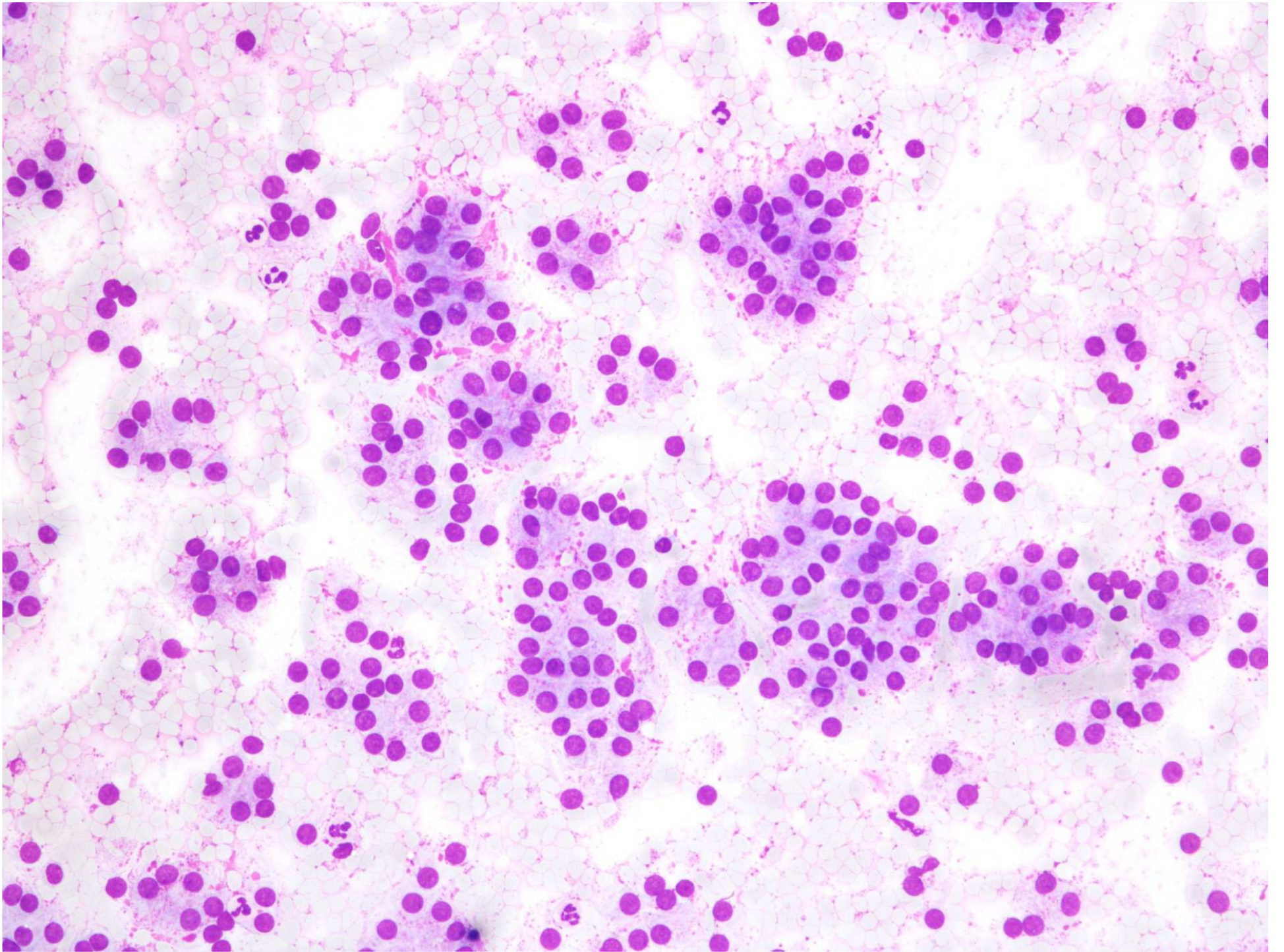
Microfollicular growth pattern

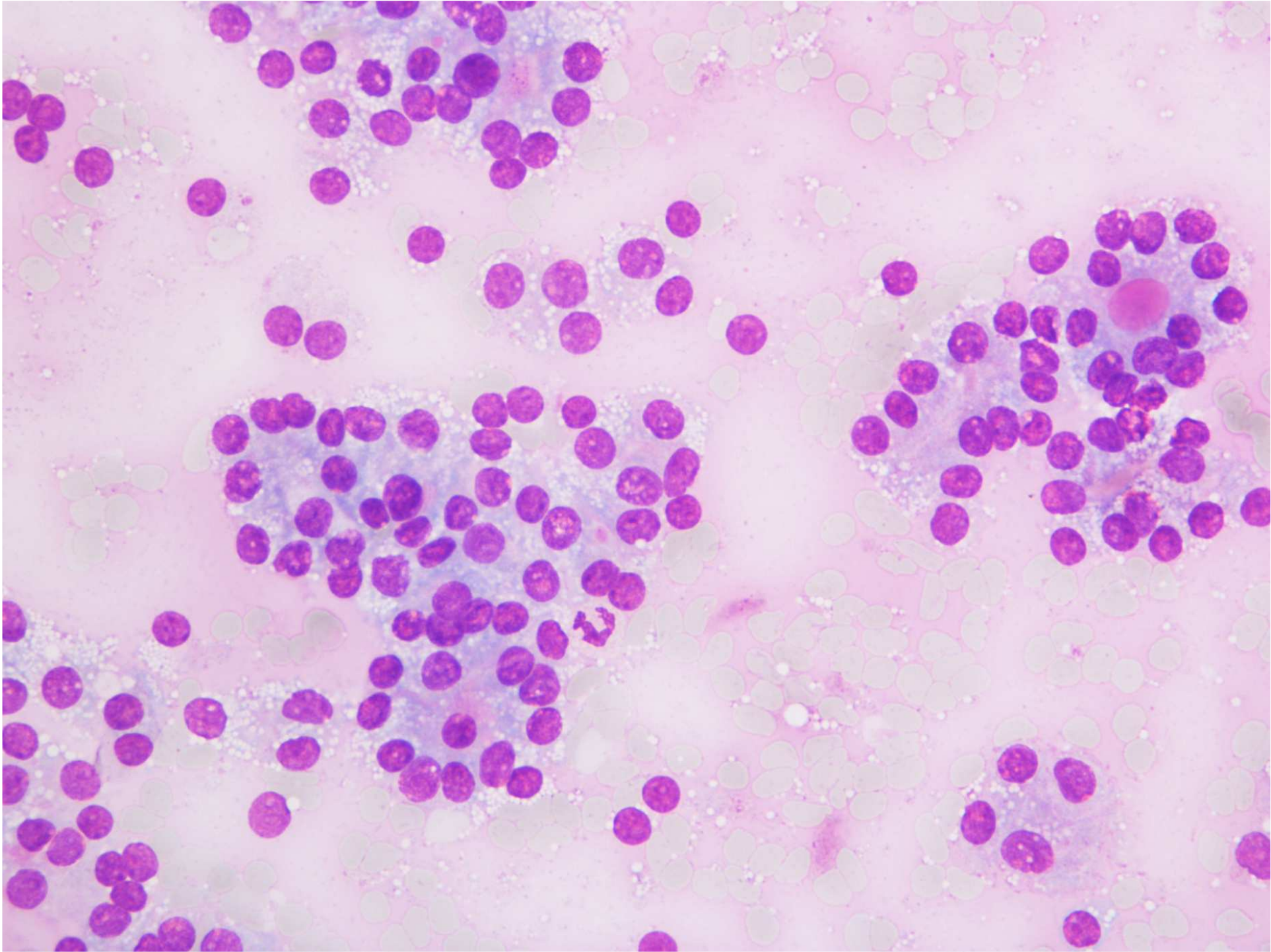
- **architecture**
 - syncytial tissue fragments (mostly follicular pattern)
- **follicular cells characteristics:**
 - uniformly enlarged nuclei
 - fine to coarsely granular chromatin, no nucleoli
- **background:**
 - scant to absent colloid

DD: well differentiated follicular carcinoma







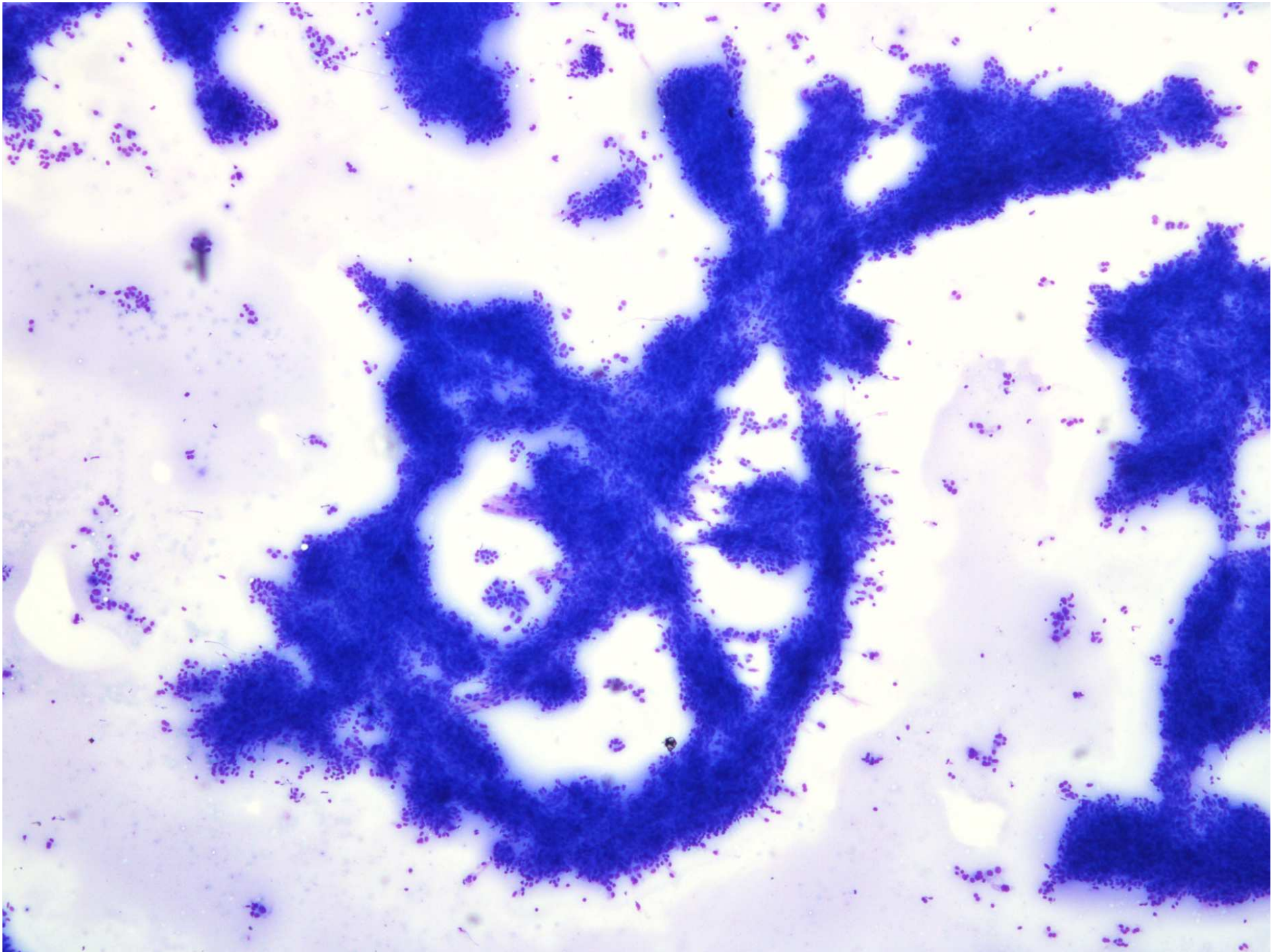


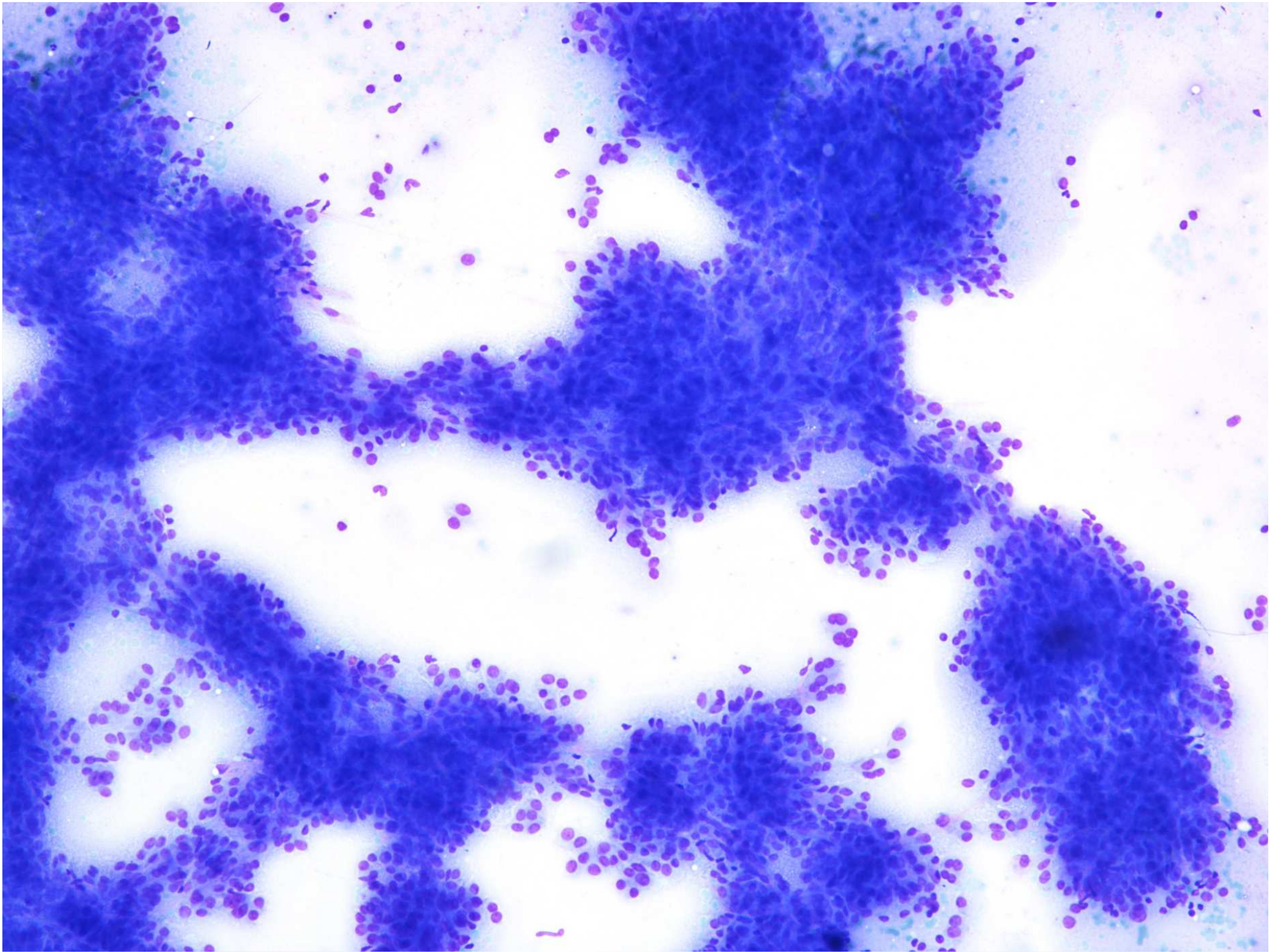
Trabecular/solid growth pattern

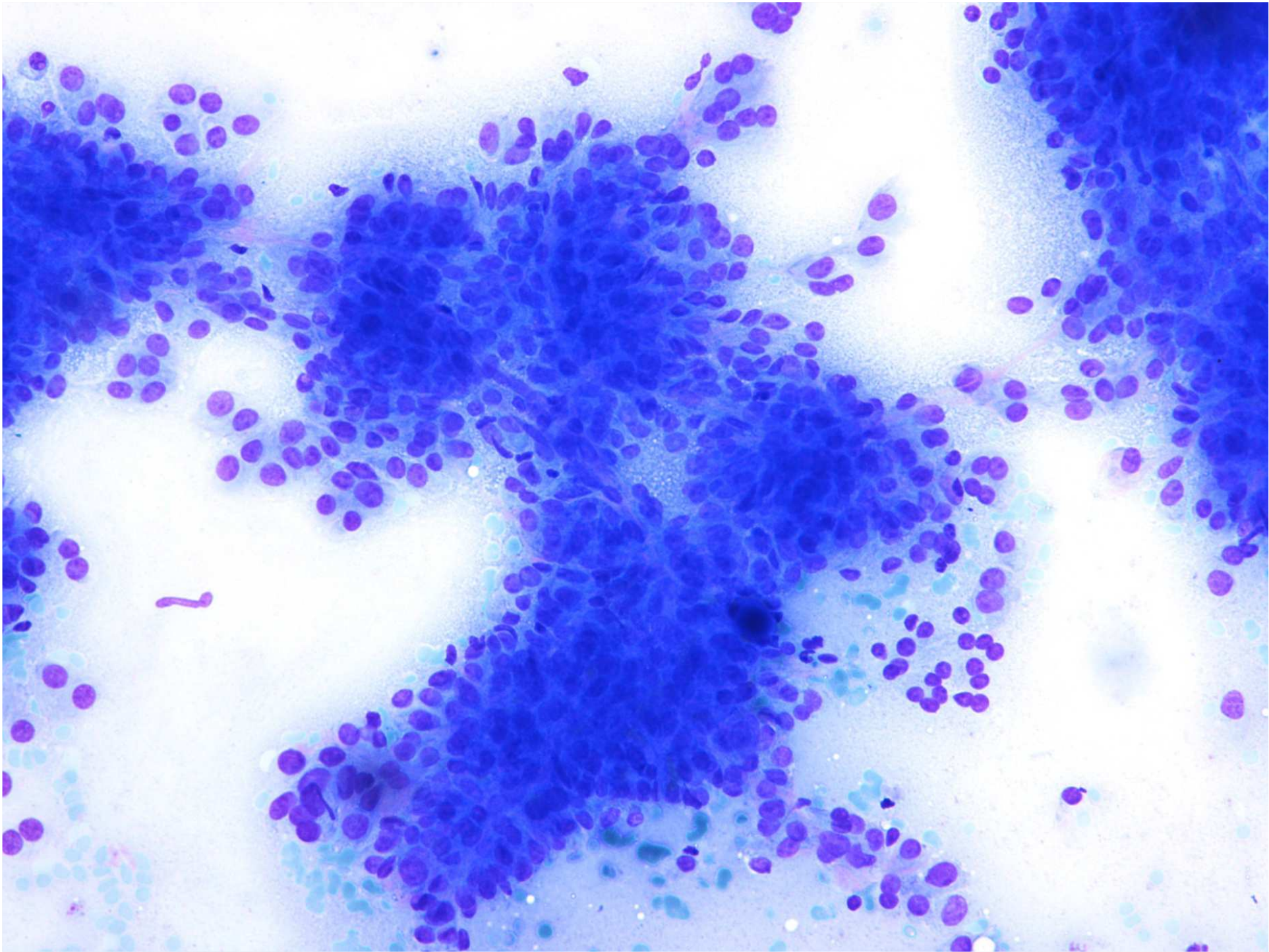
- **architecture**
 - syncytial tissue fragments with mostly trabecular pattern
 - crowding & overlapping of nuclei
- **follicular cells characteristics:**
 - variably enlarged, sometimes pleomorphic nuclei
 - fine to coarsely granular chromatin, no nucleoli
- **background:**
 - scant to absent colloid

DD: well differentiated follicular carcinoma







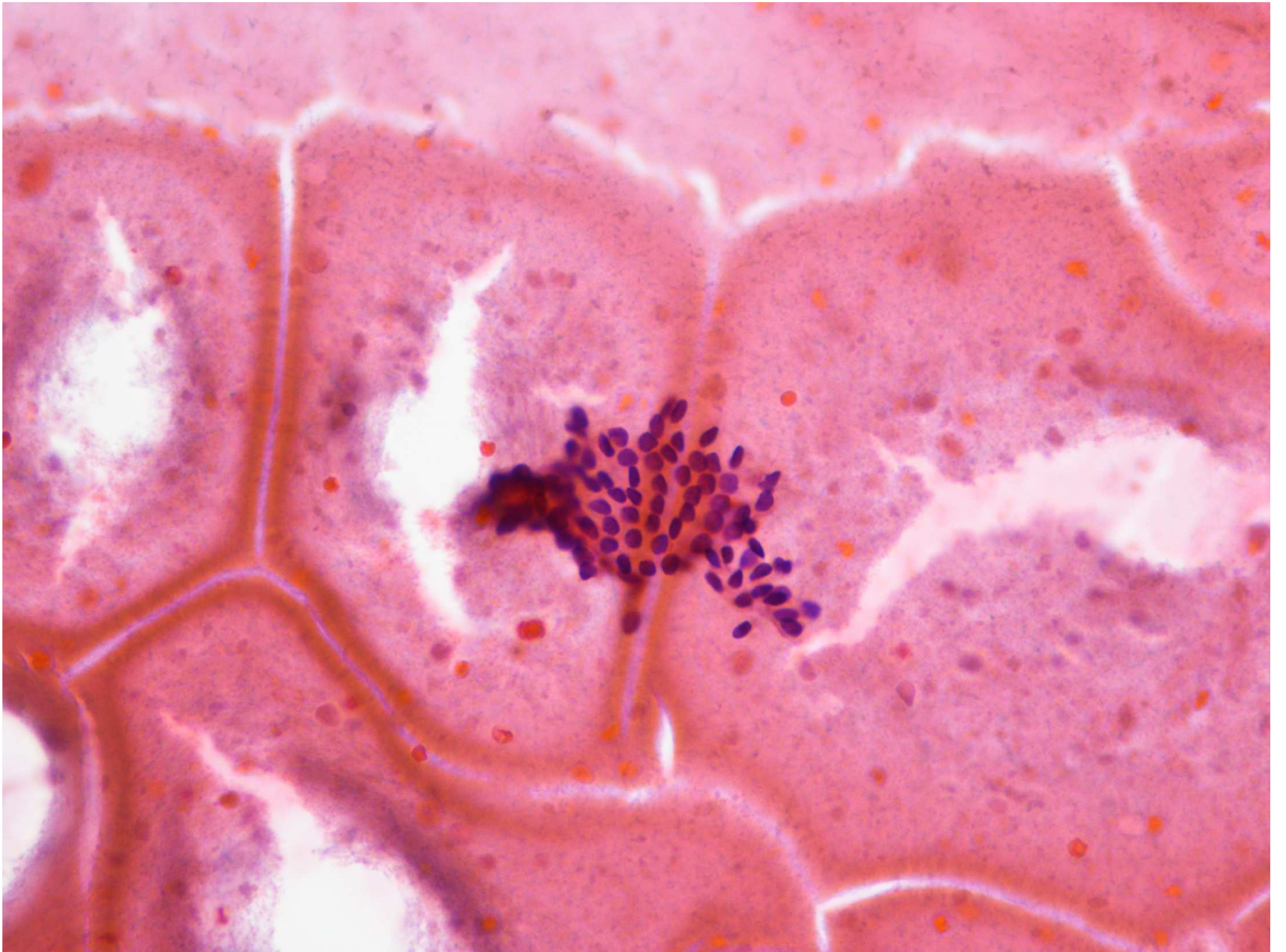


Macrofollicular (colloid) growth pattern

- architecture
 - regular follicles
 - monolayered sheets with honeycomb pattern
- follicular cells characteristics:
 - small picnotic nuclei
- background:
 - abundant colloid
 - bare nuclei of follicular cells

DD: nodular goiter



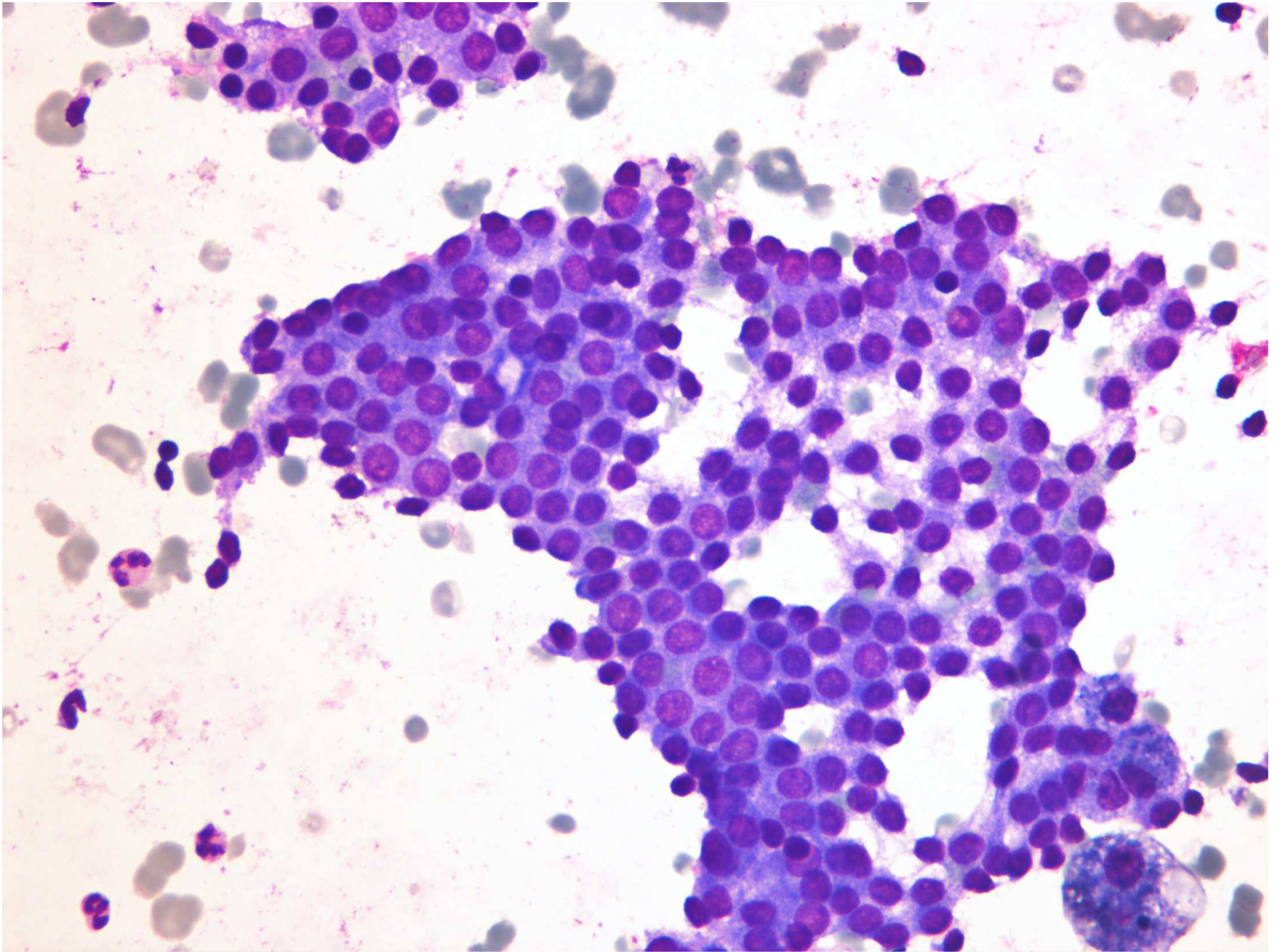


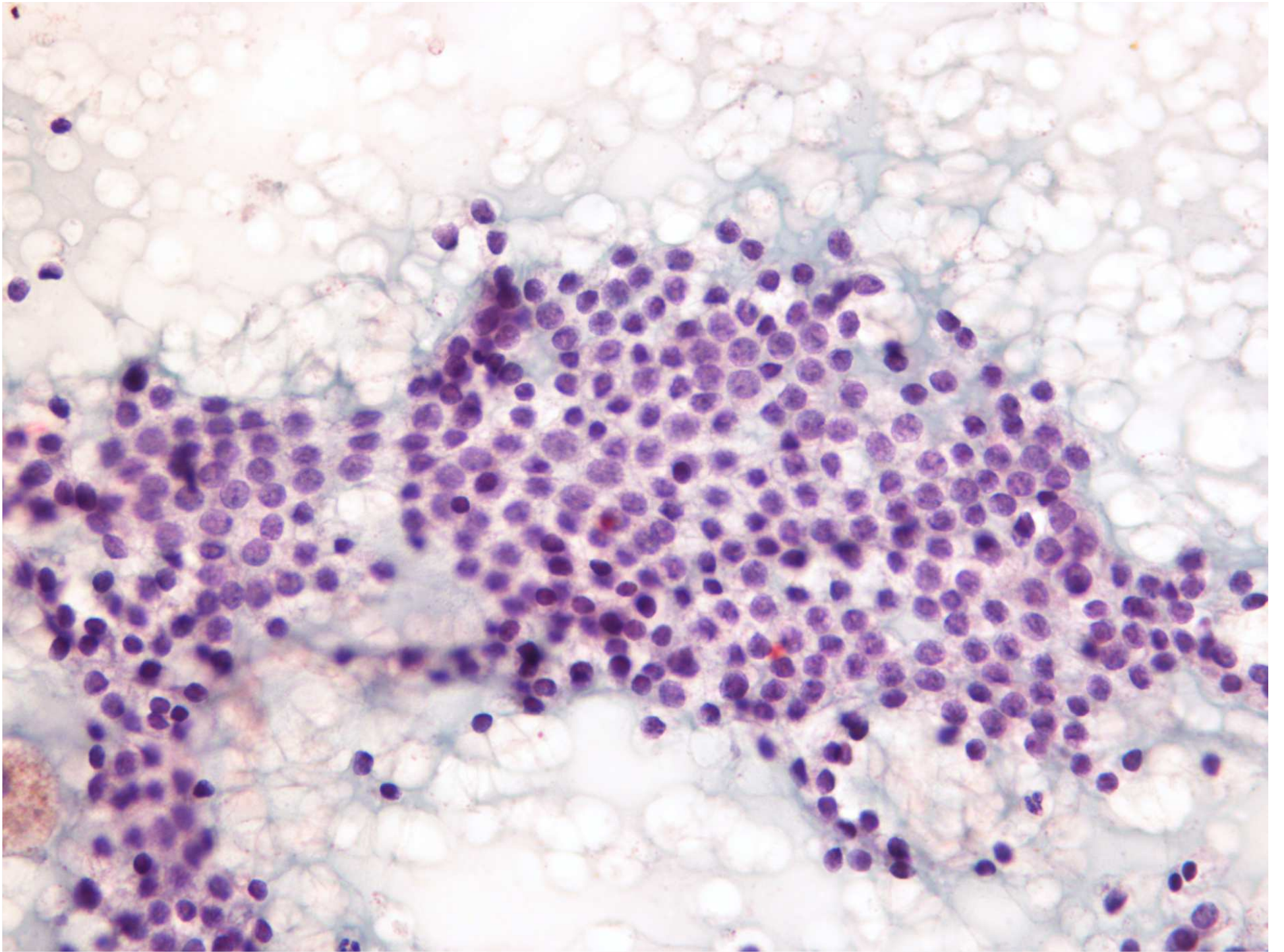
Normofollicular growth pattern

- **architecture**
 - syncytial tissue fragments
 - regular follicles
 - monolayered sheets with honeycomb pattern
- **follicular cells characteristics:**
 - normal sized or slightly enlarged nuclei
 - granular, evenly distributed chromatin, no nucleoli
- **background:**
 - variable amount of colloid

DD: nodular goiter







Follicular carcinoma

- presence of **capsular or vascular invasion** essential for the diagnosis of FC
- different morphologic patterns
- poorly differentiated FC pose no diagnostic problem
- well differentiated FC has overlapping morphologic features with FA

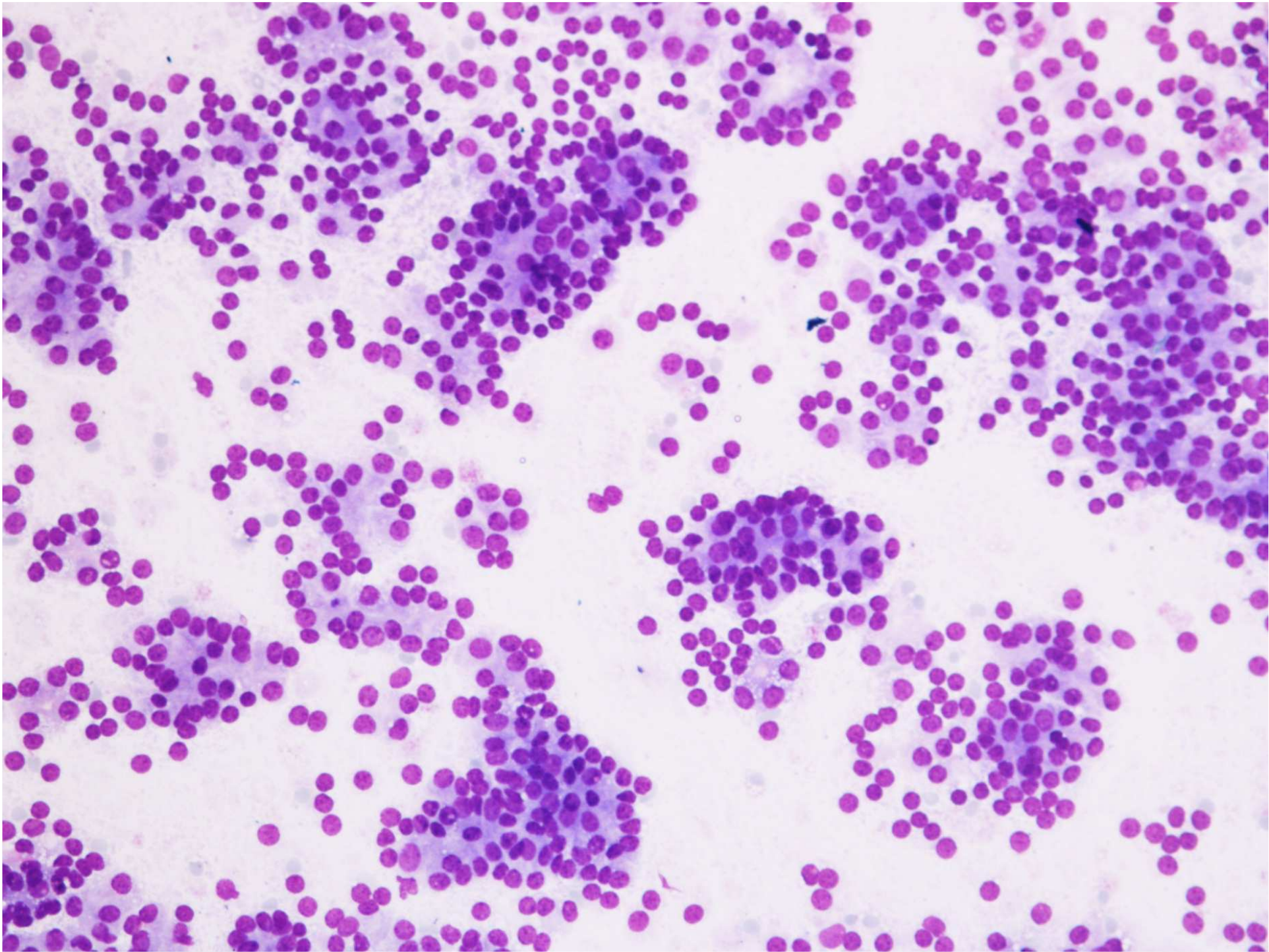


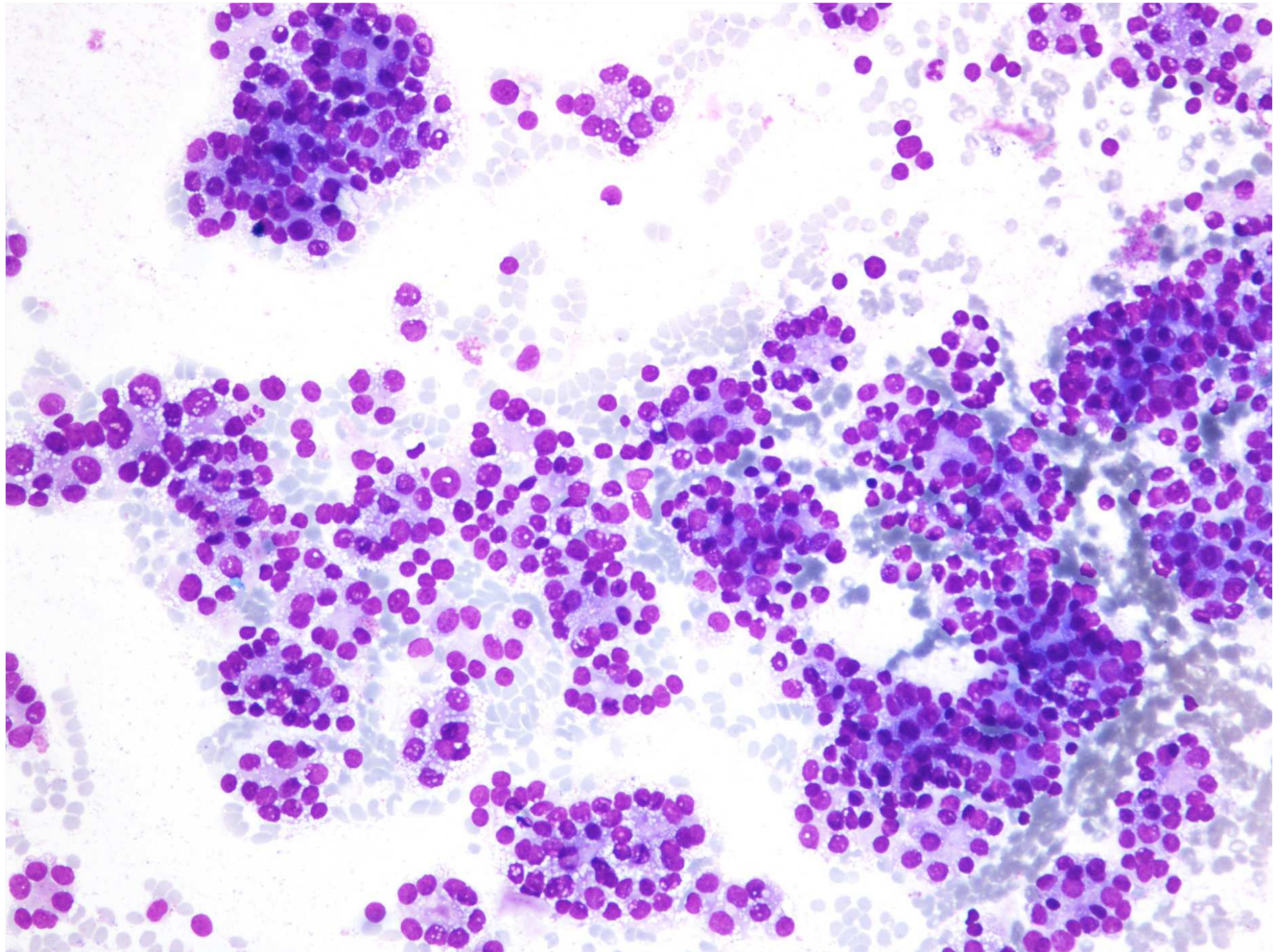
Well differentiated FC

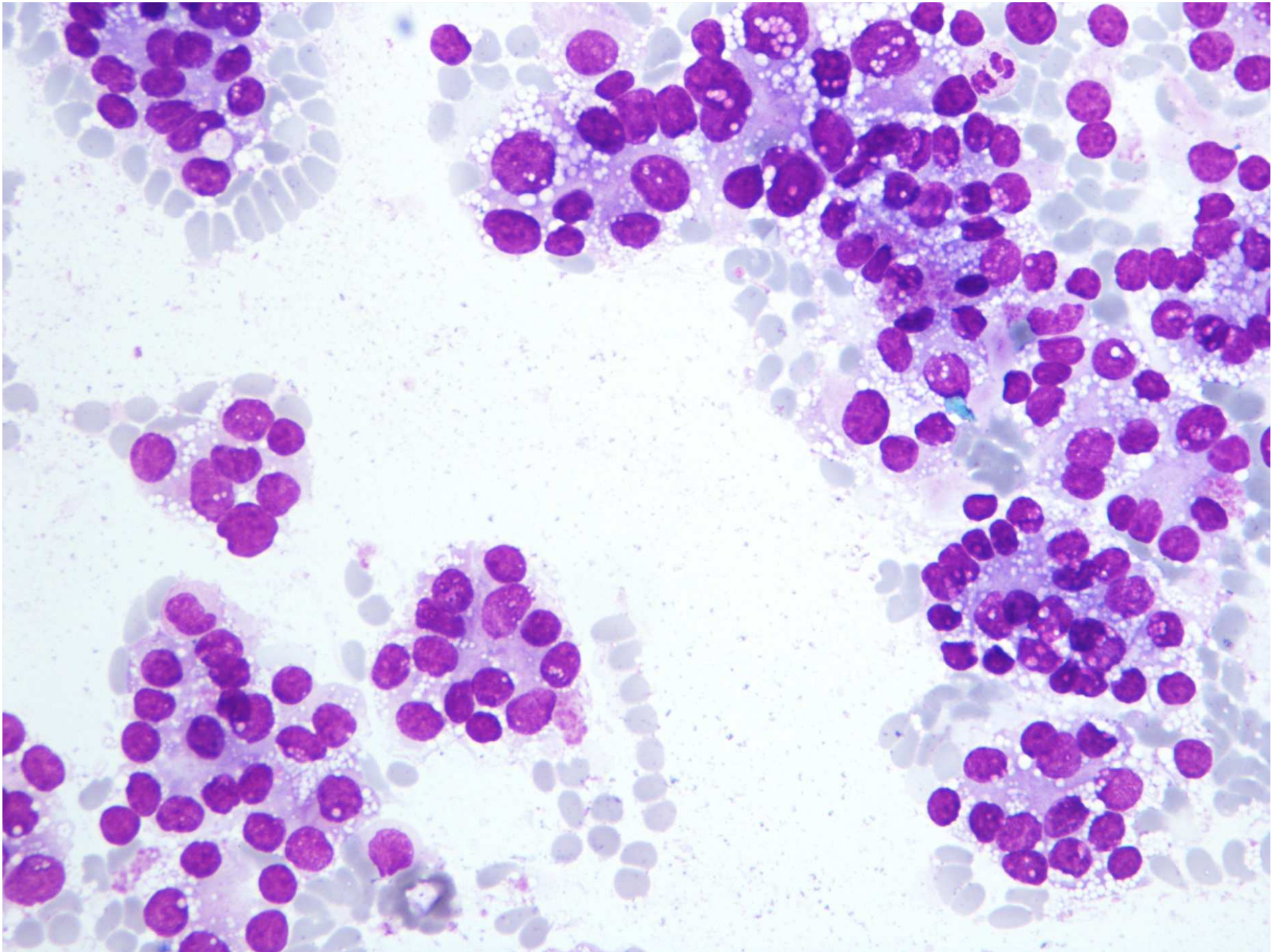
- **architecture**
 - syncytial tissue fragments with or without follicular pattern
 - crowding & overlapping of nuclei
 - irregular follicles
- **follicular cells characteristics:**
 - enlarged, round to oval, uniform or pleomorphic nuclei
 - fine to coarsely granular chromatin, micro and macro nucleoli
 - more cytoplasm than cells of FA, poorly defined cell borders
- **background:**
 - clean, scant or absent colloid

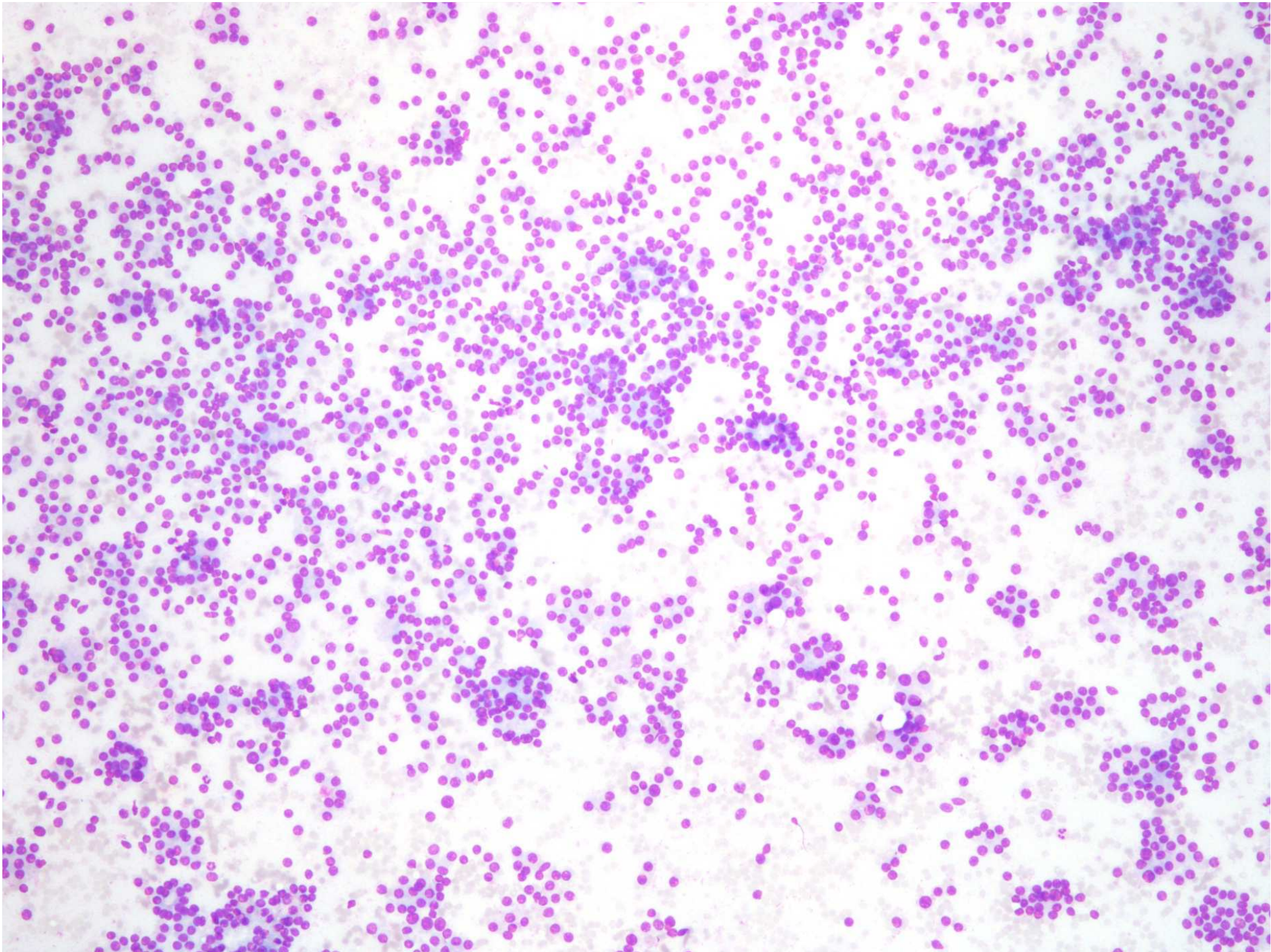
DD: follicular adenoma, FVPC

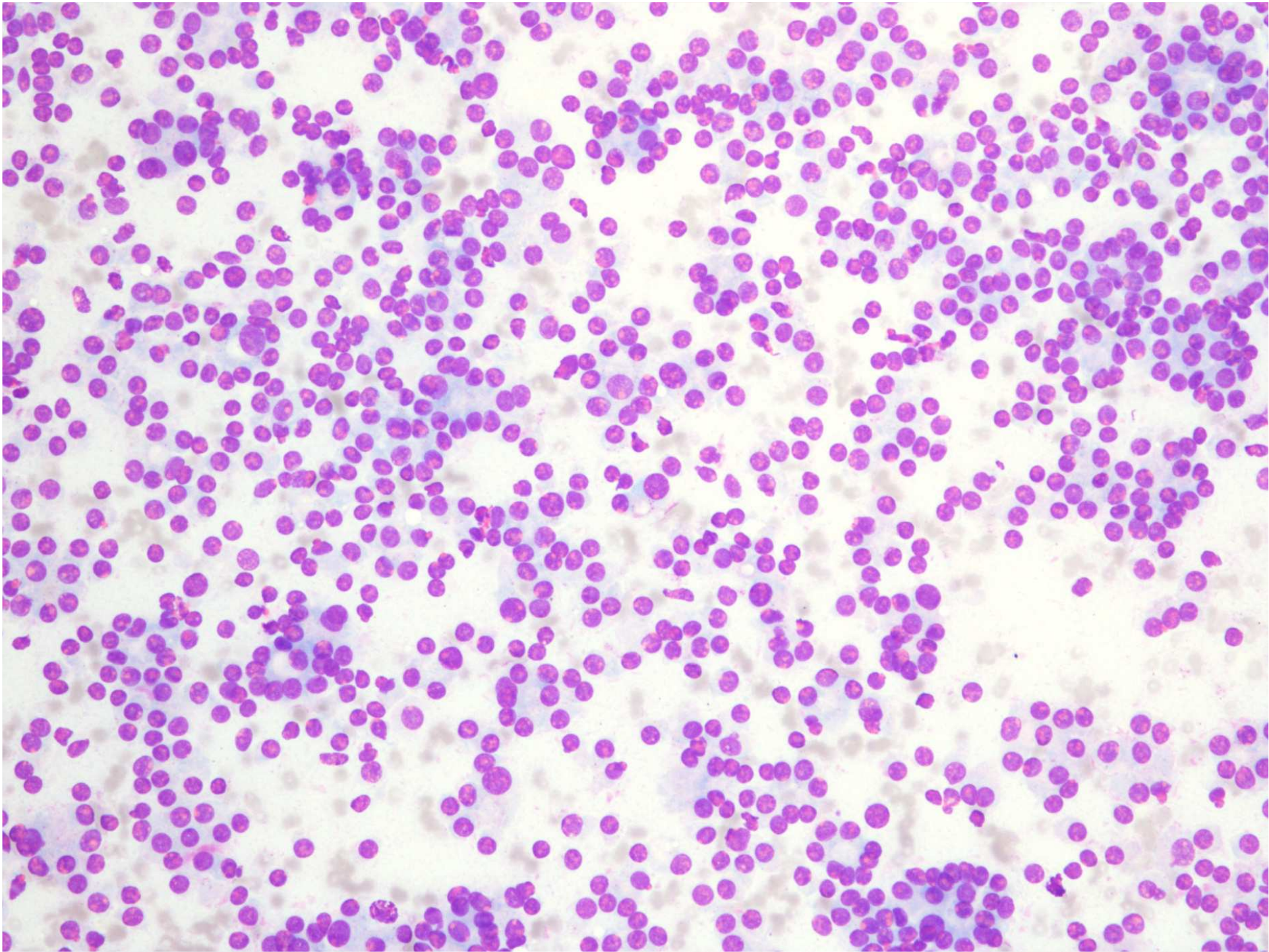


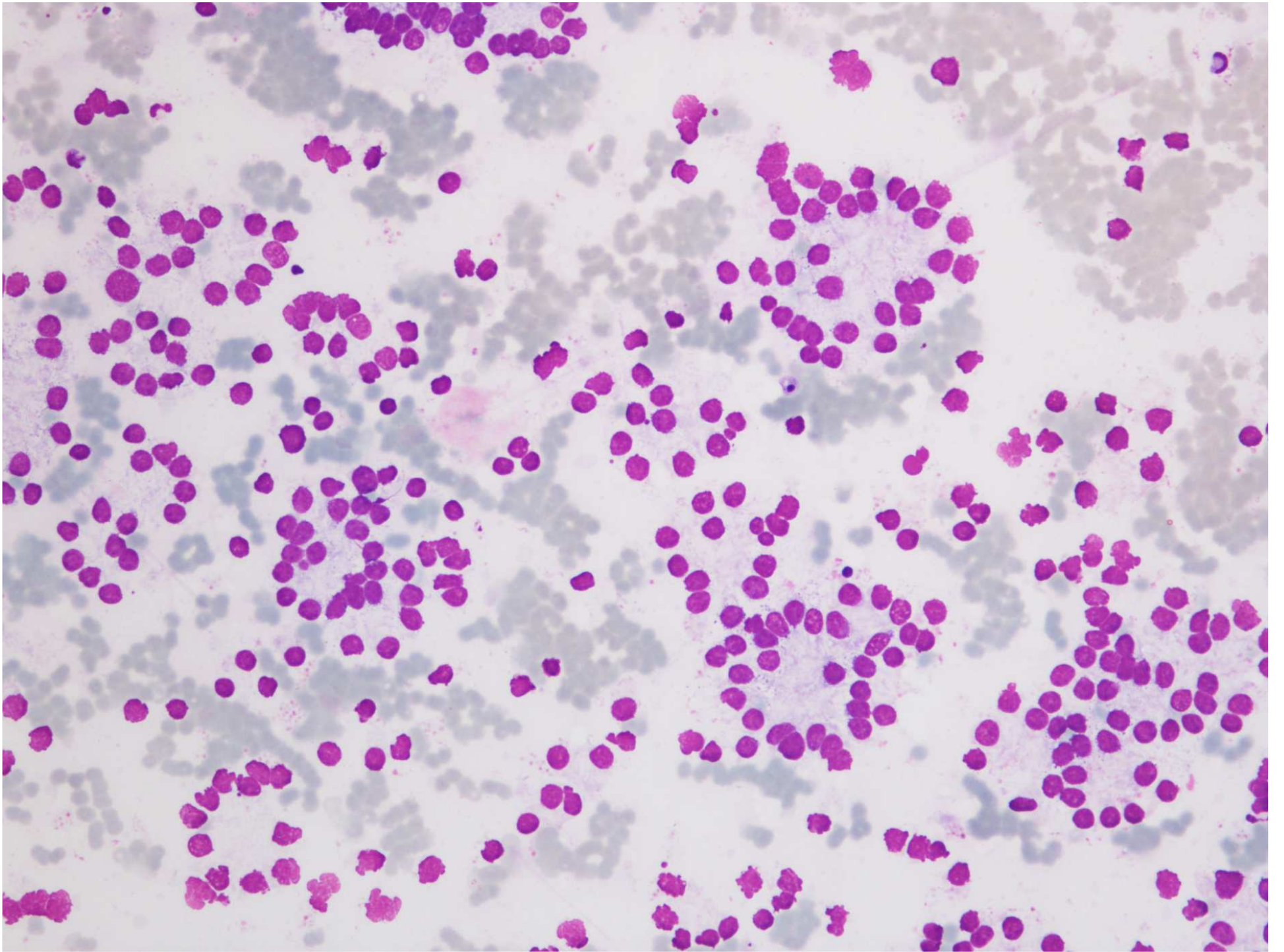


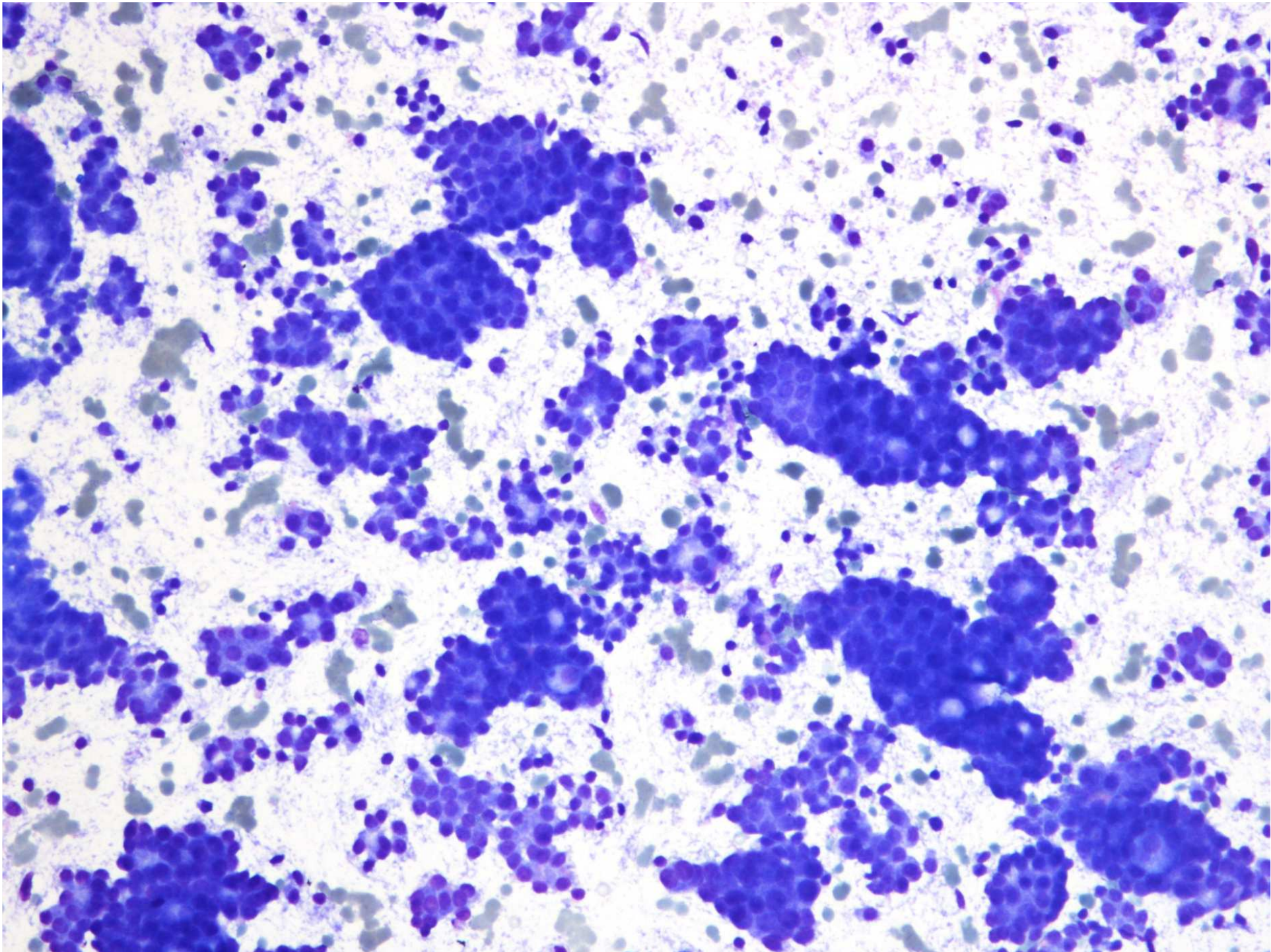


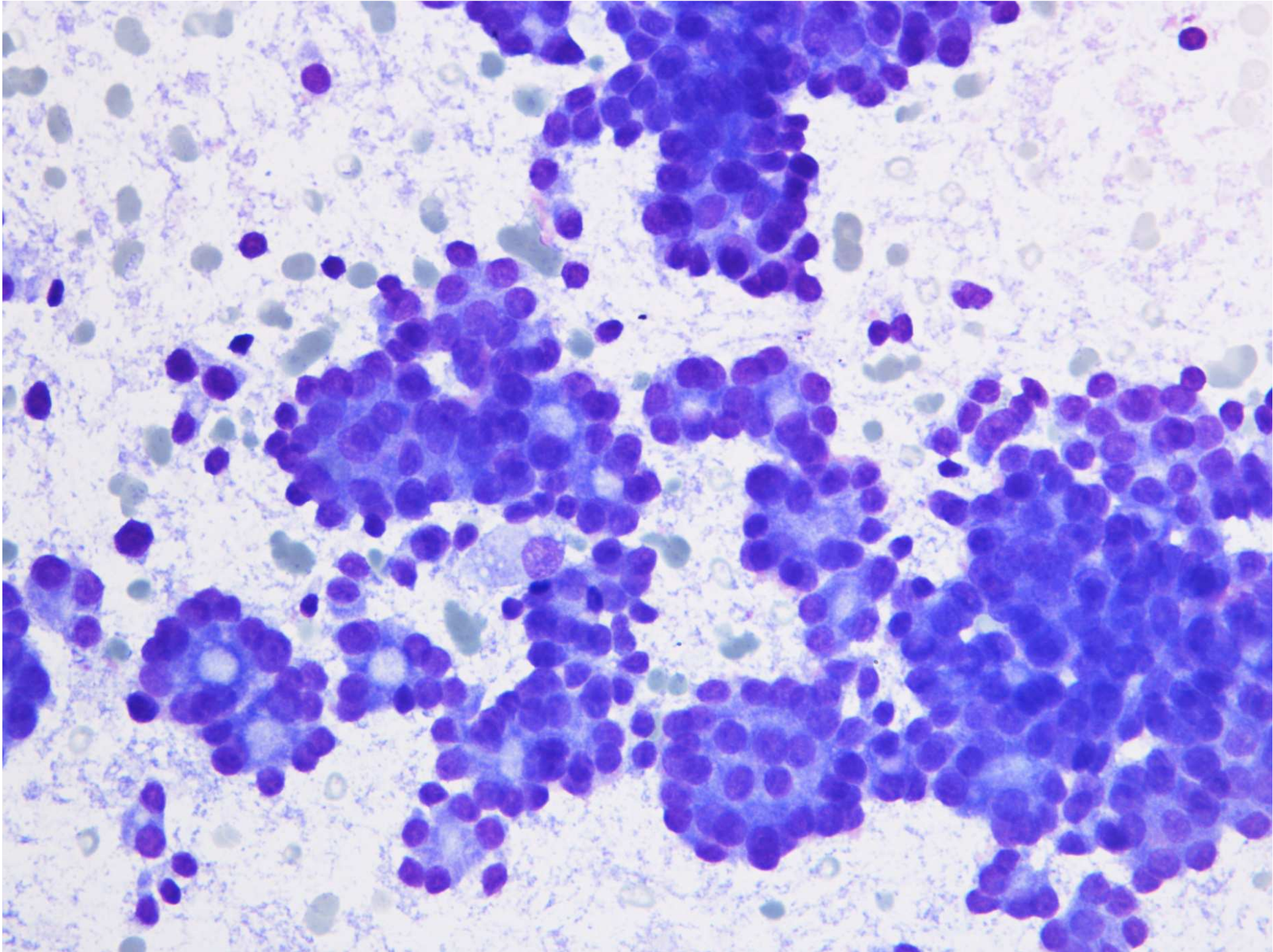








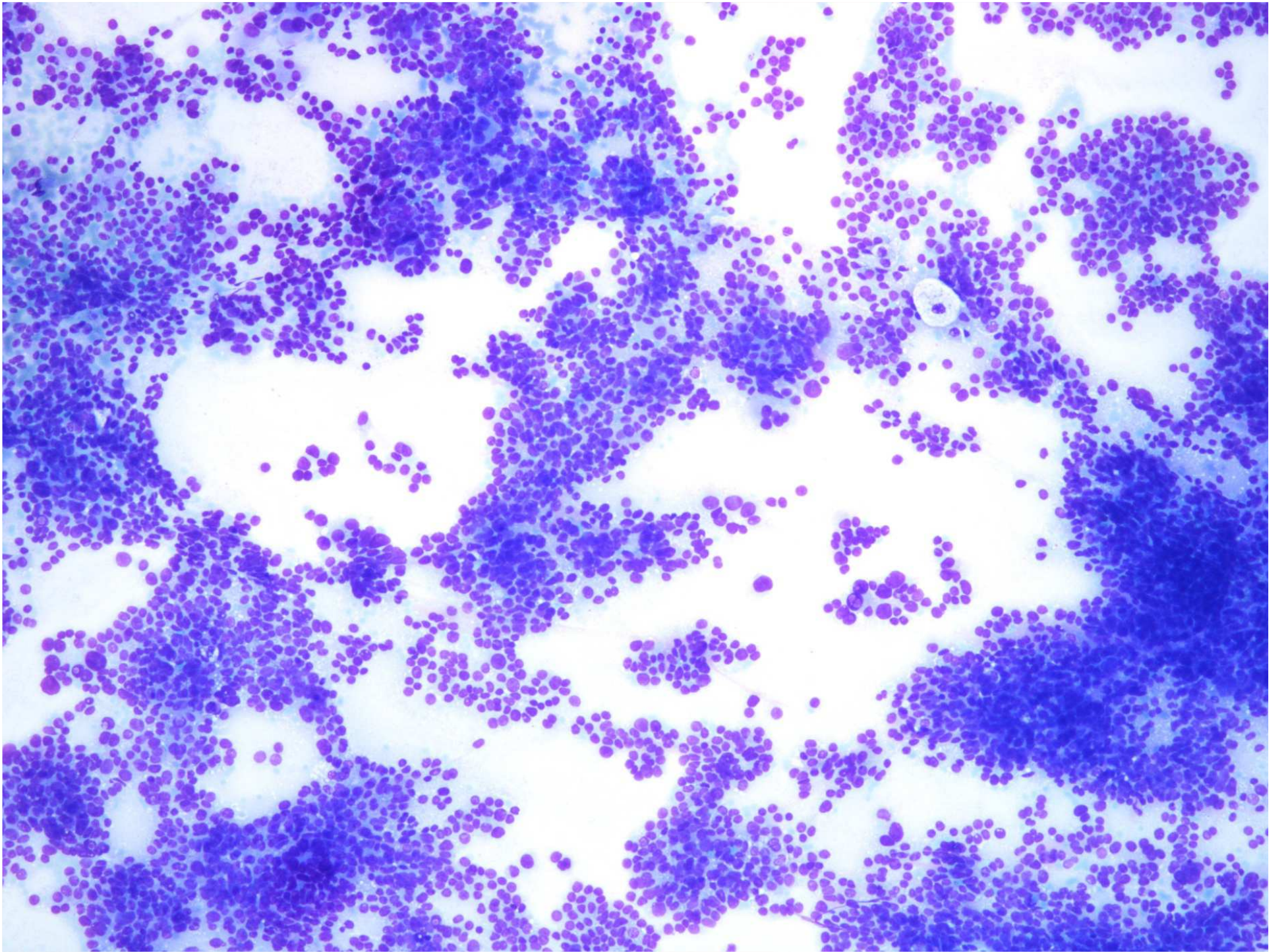


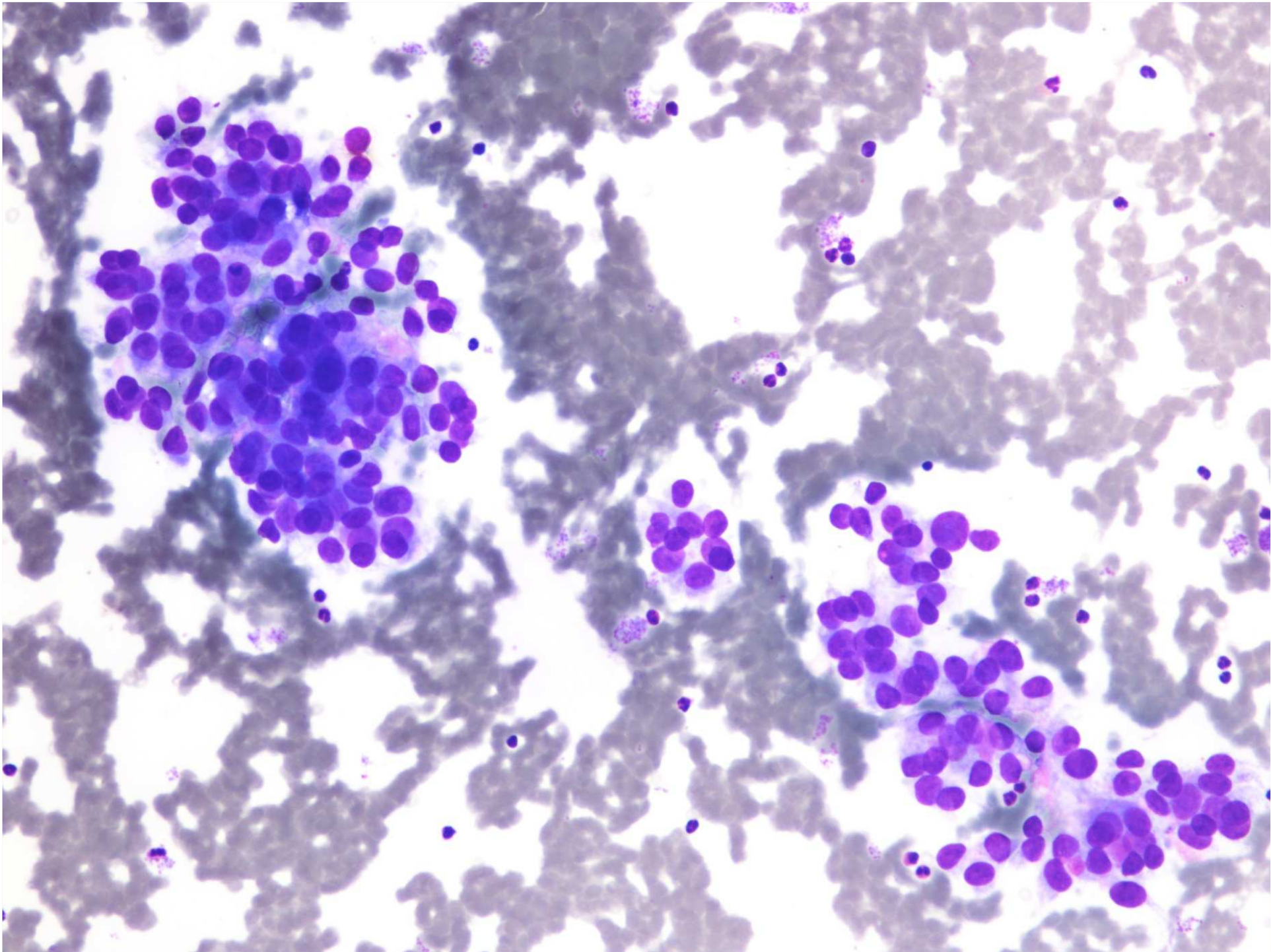


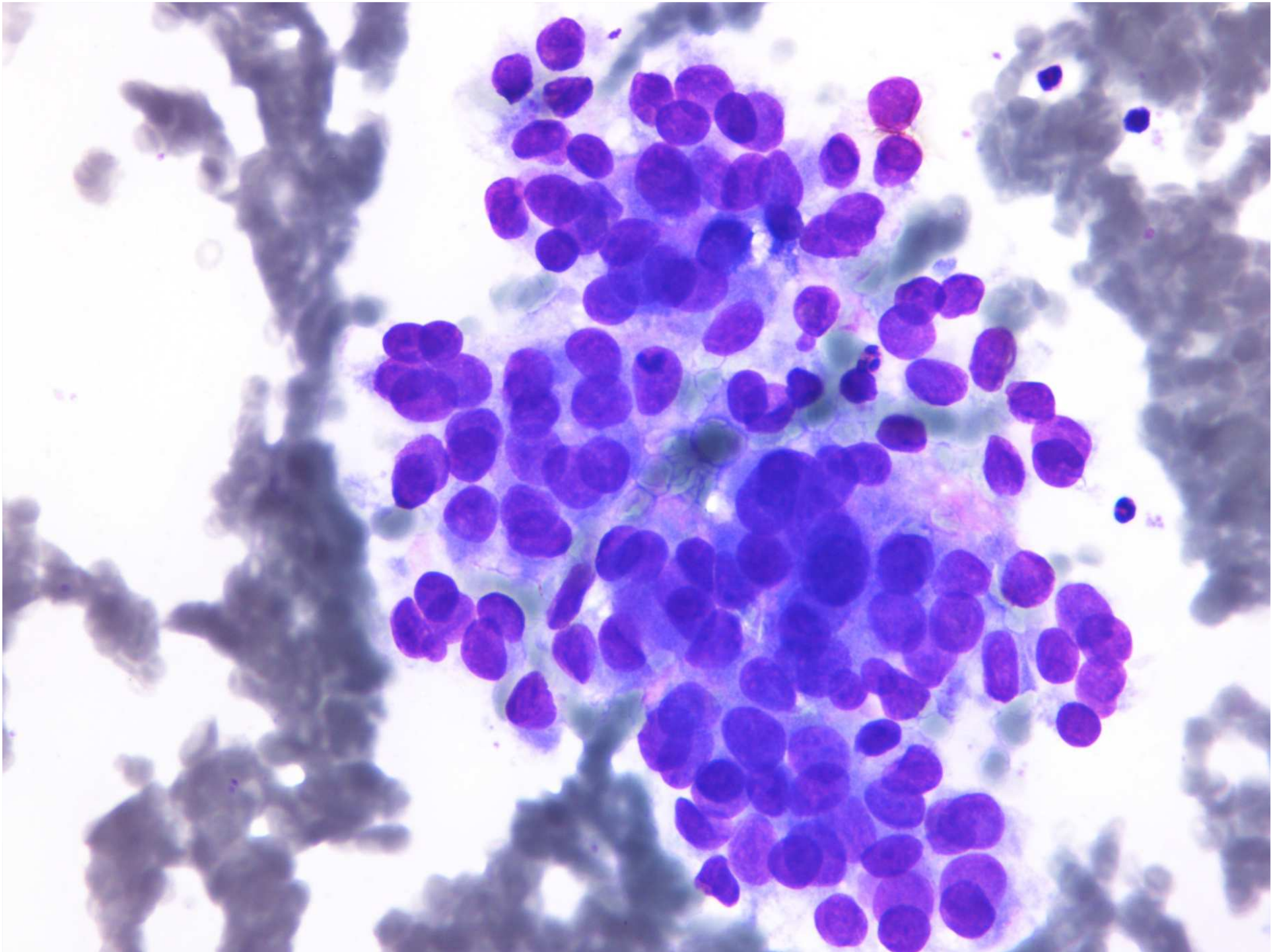
Poorly differentiated FC

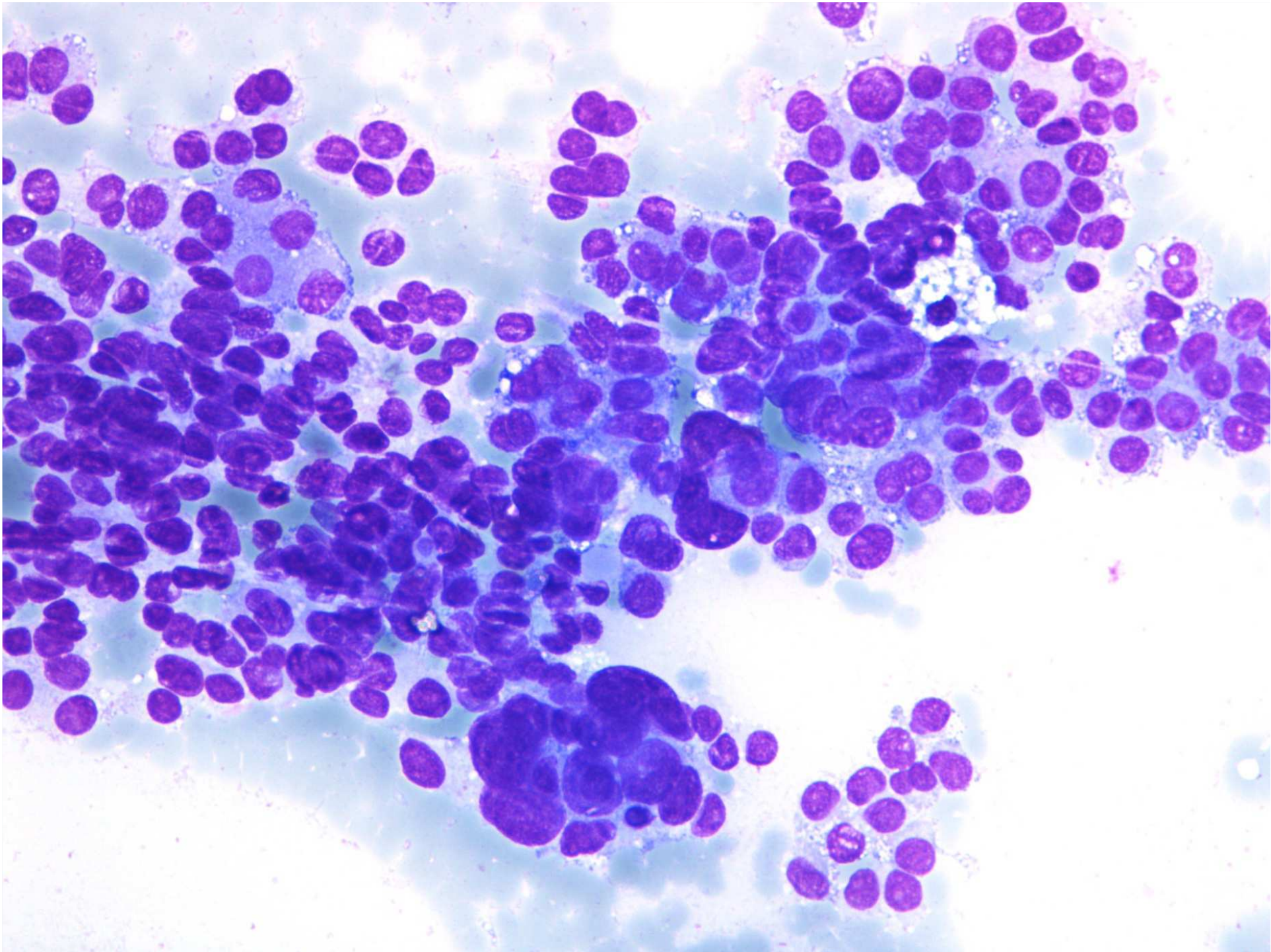
- **architecture**
 - syncytial tissue fragments of malignant cells with or without follicular pattern, solid areas
 - crowding & overlapping of nuclei
- **follicular cells characteristics:**
 - larger than in WDFC, pleomorphic
 - large round nuclei, coarsely granular chromatin, parachromatin clearing, nucleoli
 - pale to dense cytoplasm
- **background:**
 - absent colloid, sometimes necrosis

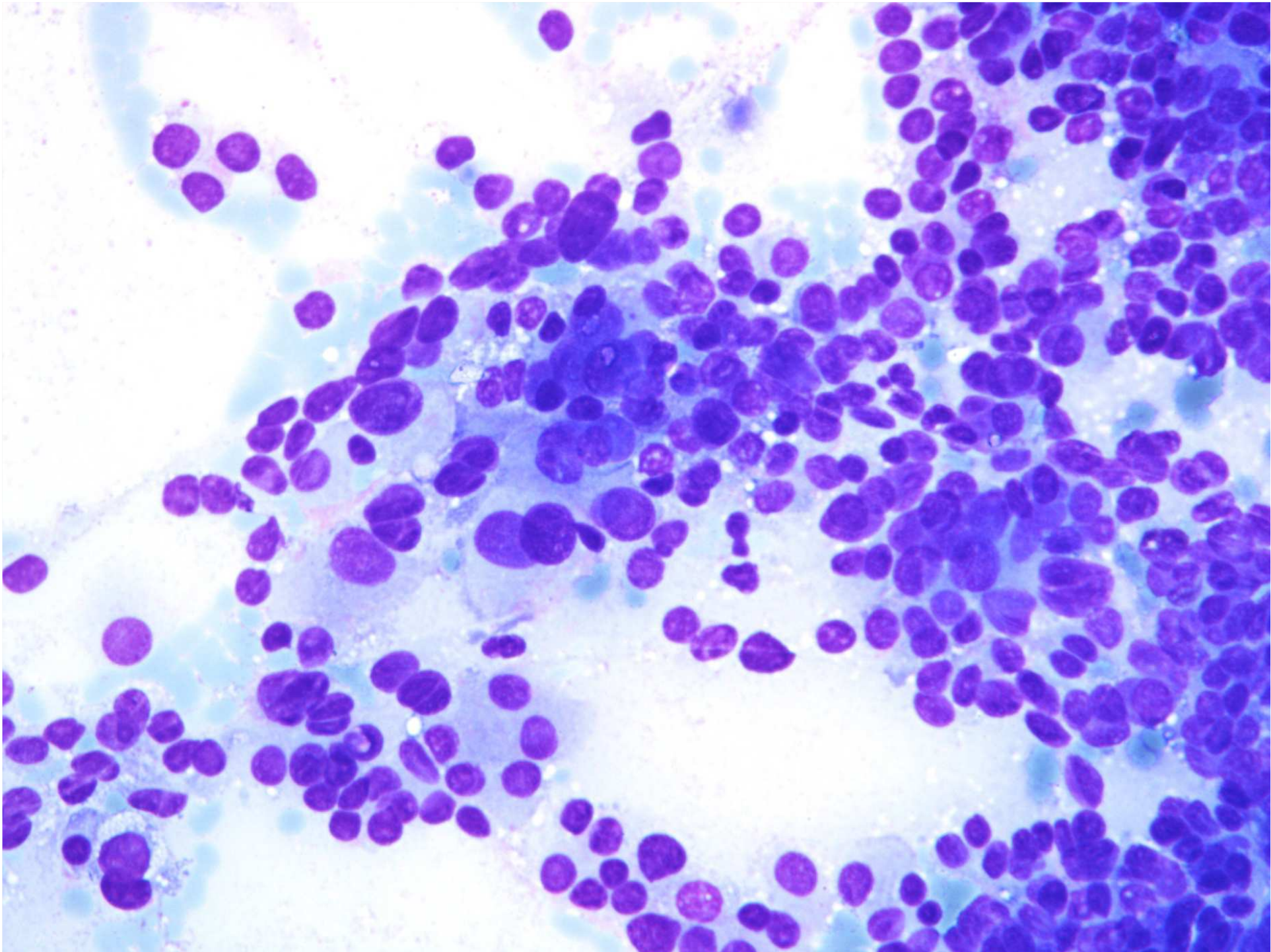












Follicular patterned thyroid lesions

- the most common type of thyroid FNA specimens
- lesions with follicular pattern:

neoplasms:

- follicular adenoma
- follicular carcinoma
- follicular variant of papillary carcinoma

non-neoplastic lesions:

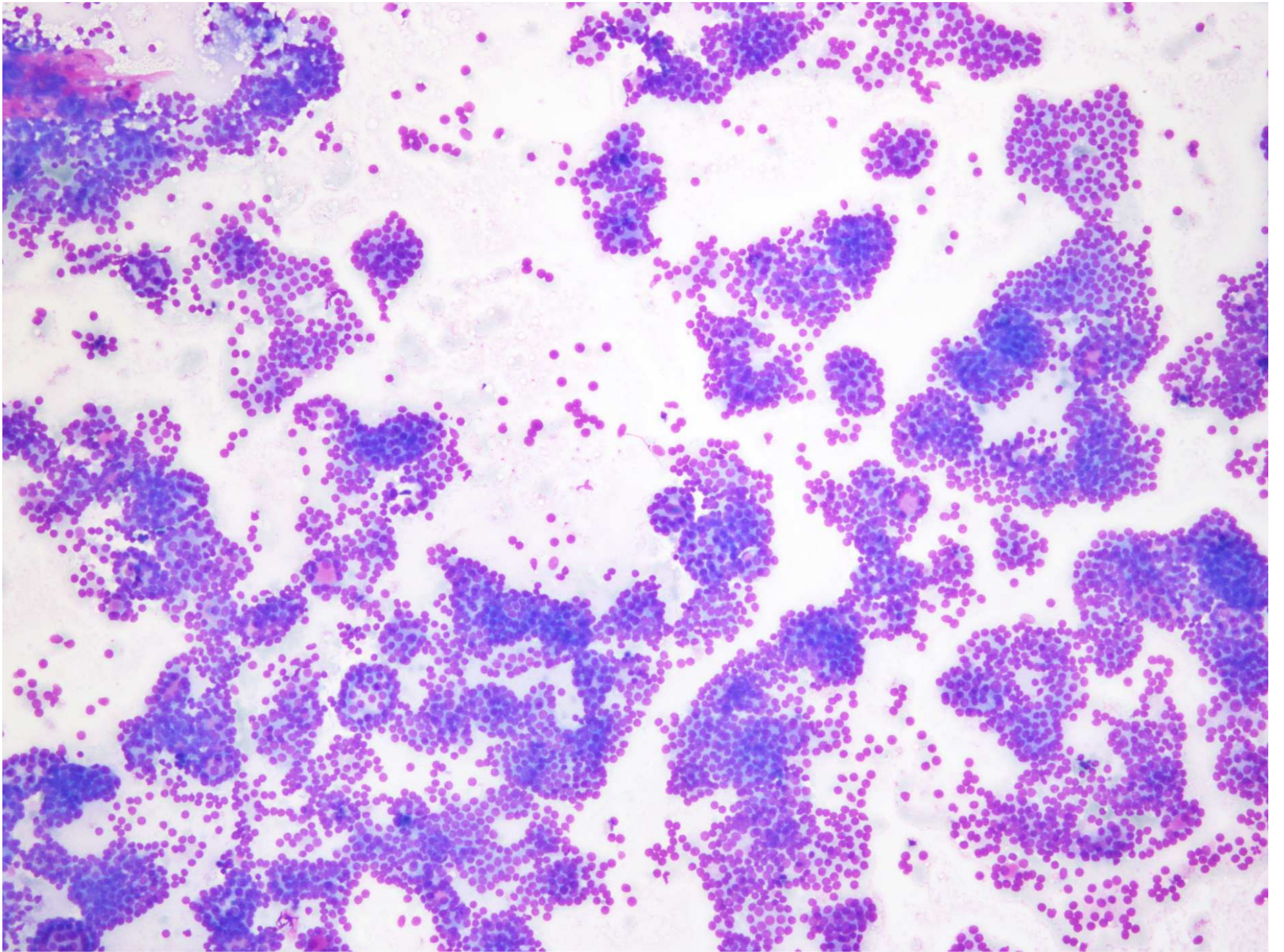
- nodular goiter (nodular hyperplasia)

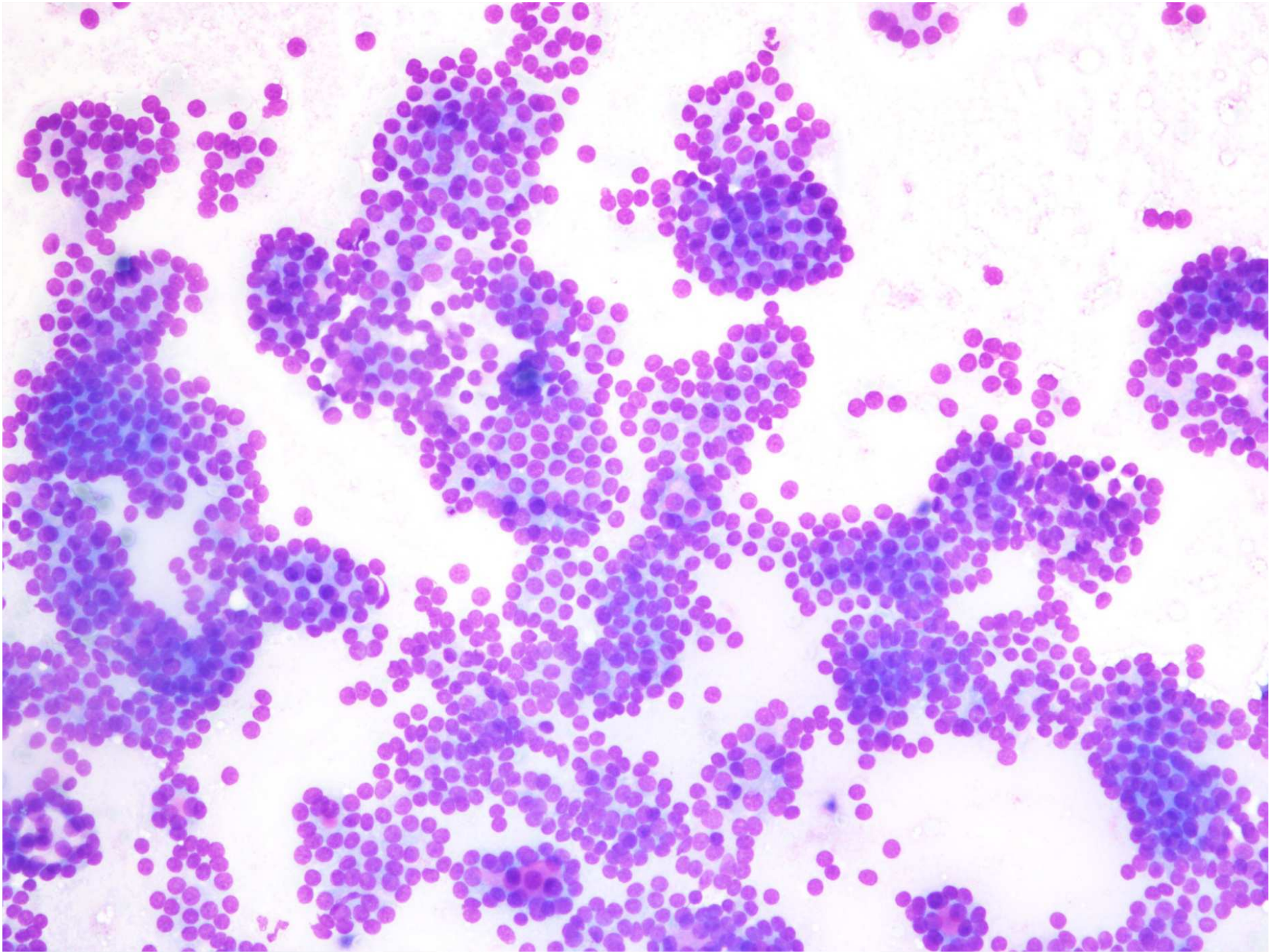


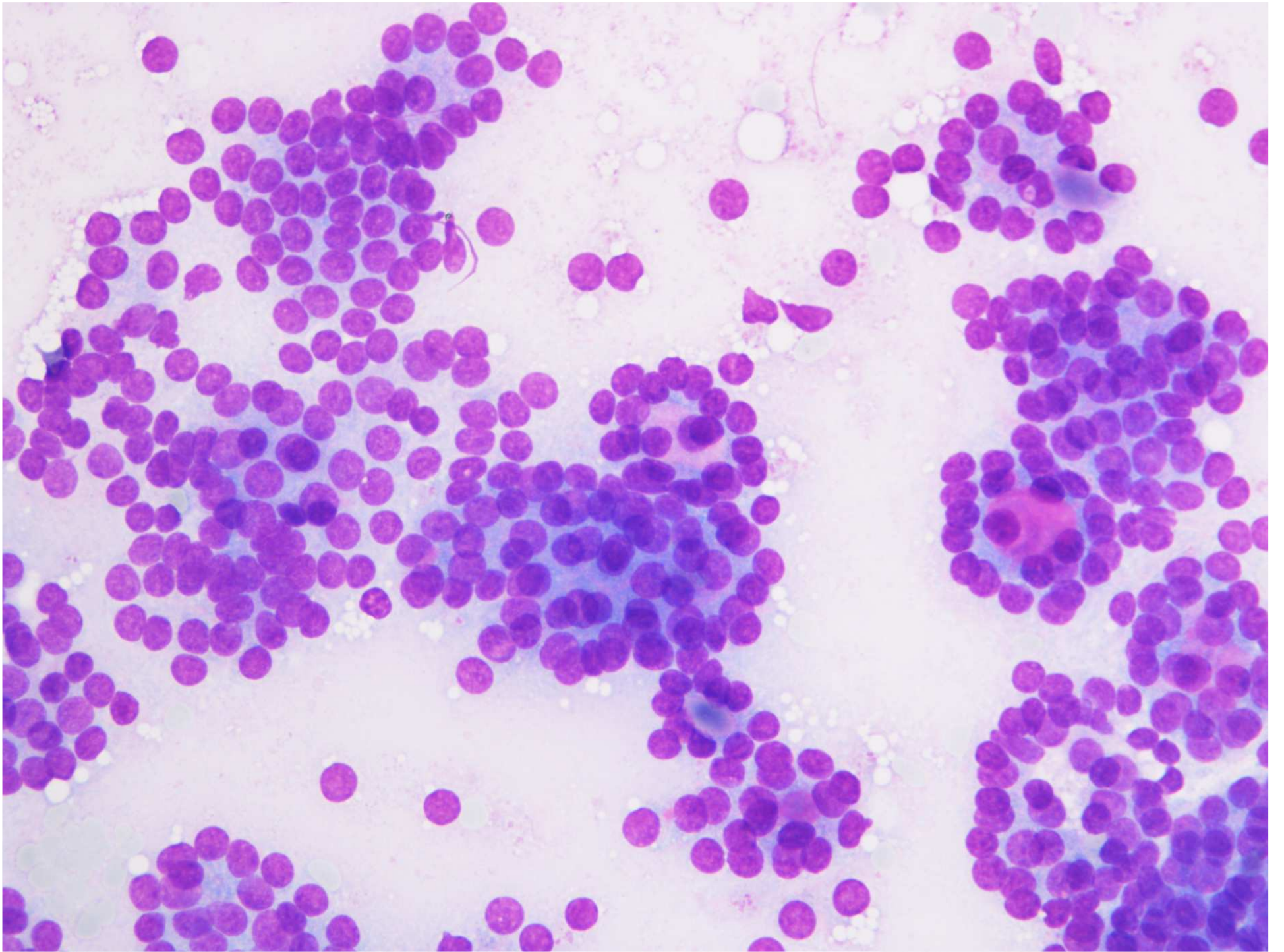
Follicular variant of papillary carcinoma

- **architecture:**
 - syncytial tissue fragments
 - microfollicles
- **follicular cells characteristics:**
 - enlarged nuclei
 - pale chromatin
 - micronucleoli
 - nuclear grooves & pseudoinclusions
- **background:**
 - dense colloid
 - multinucleated giant cells





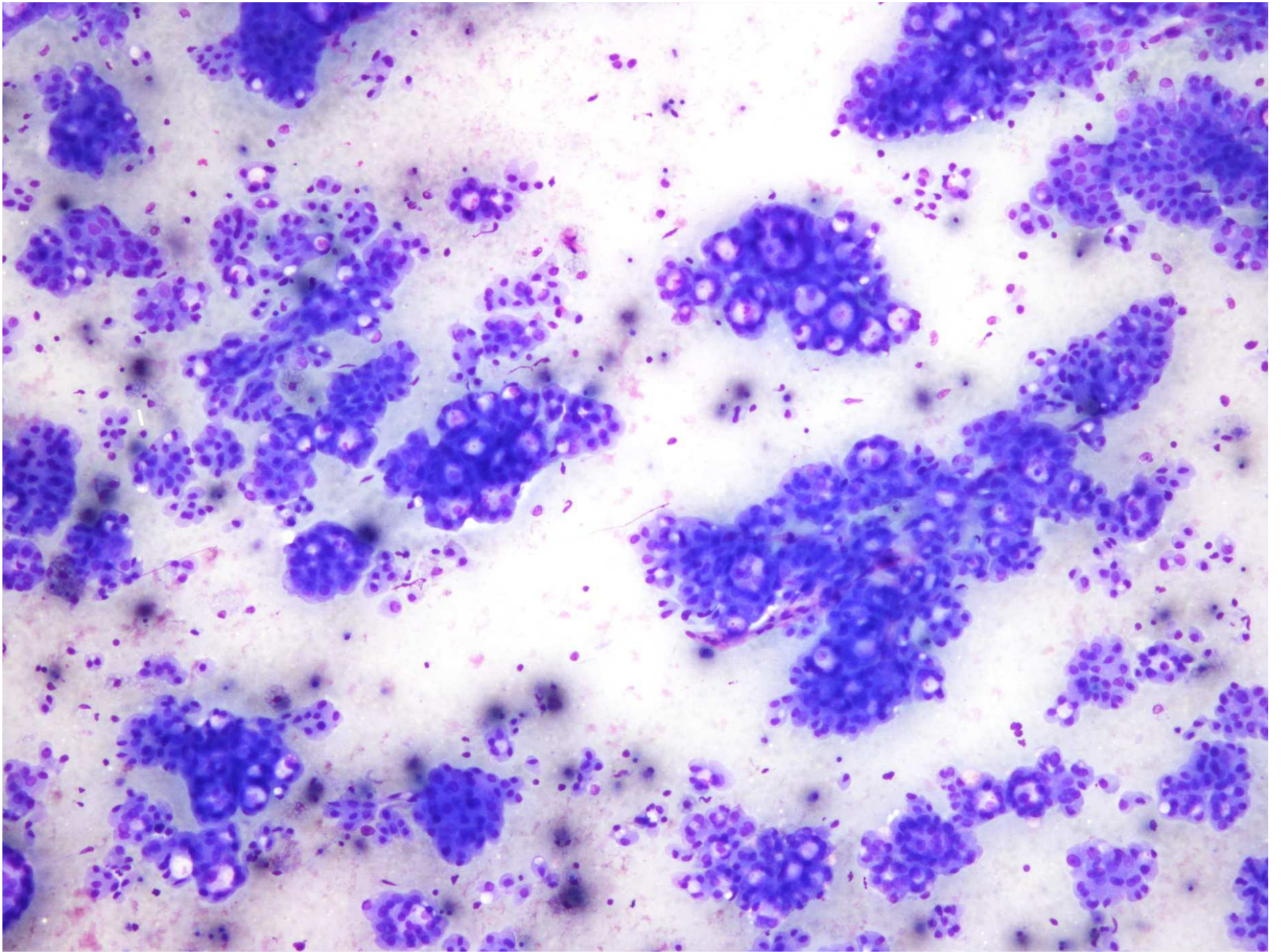


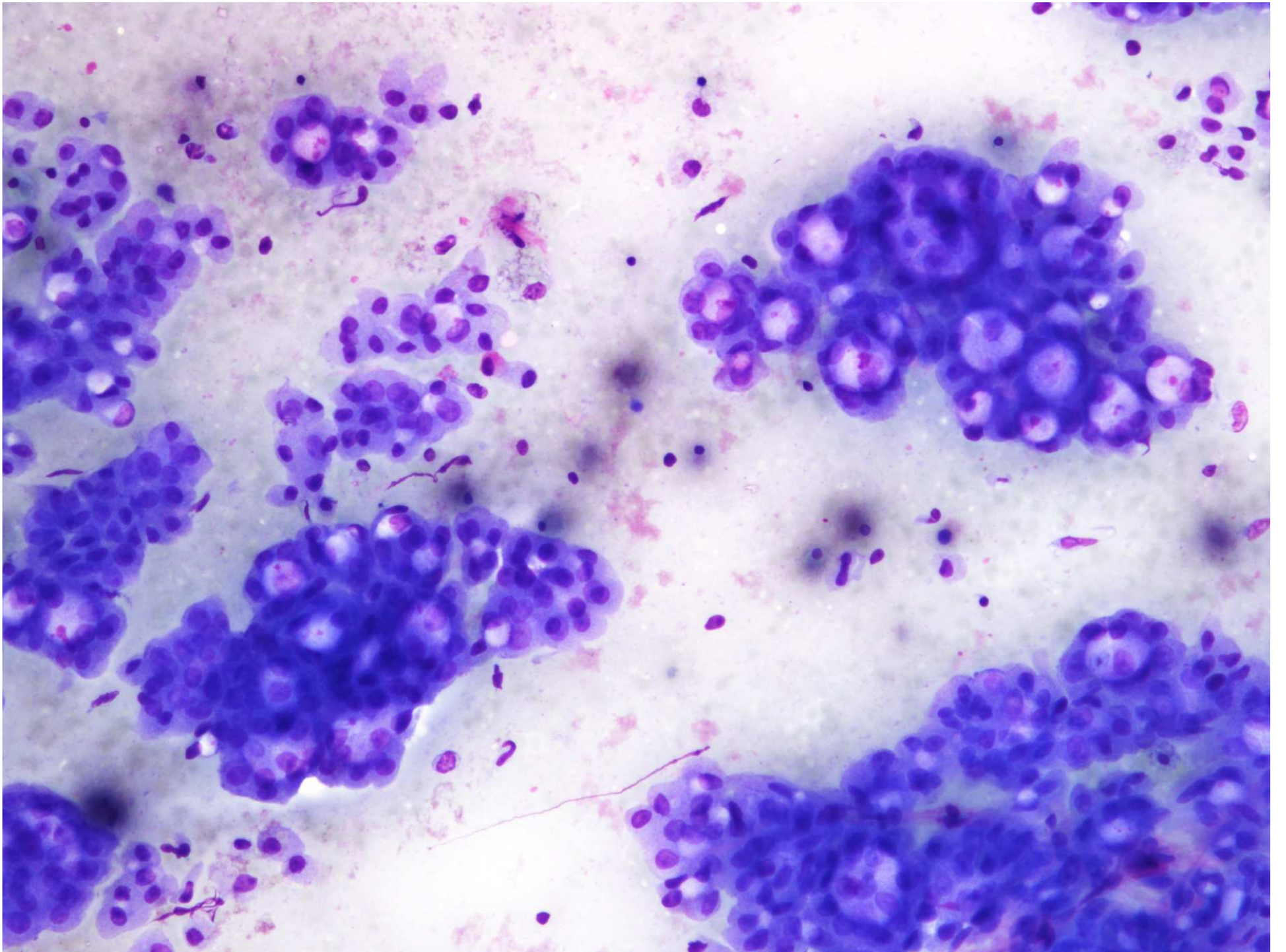


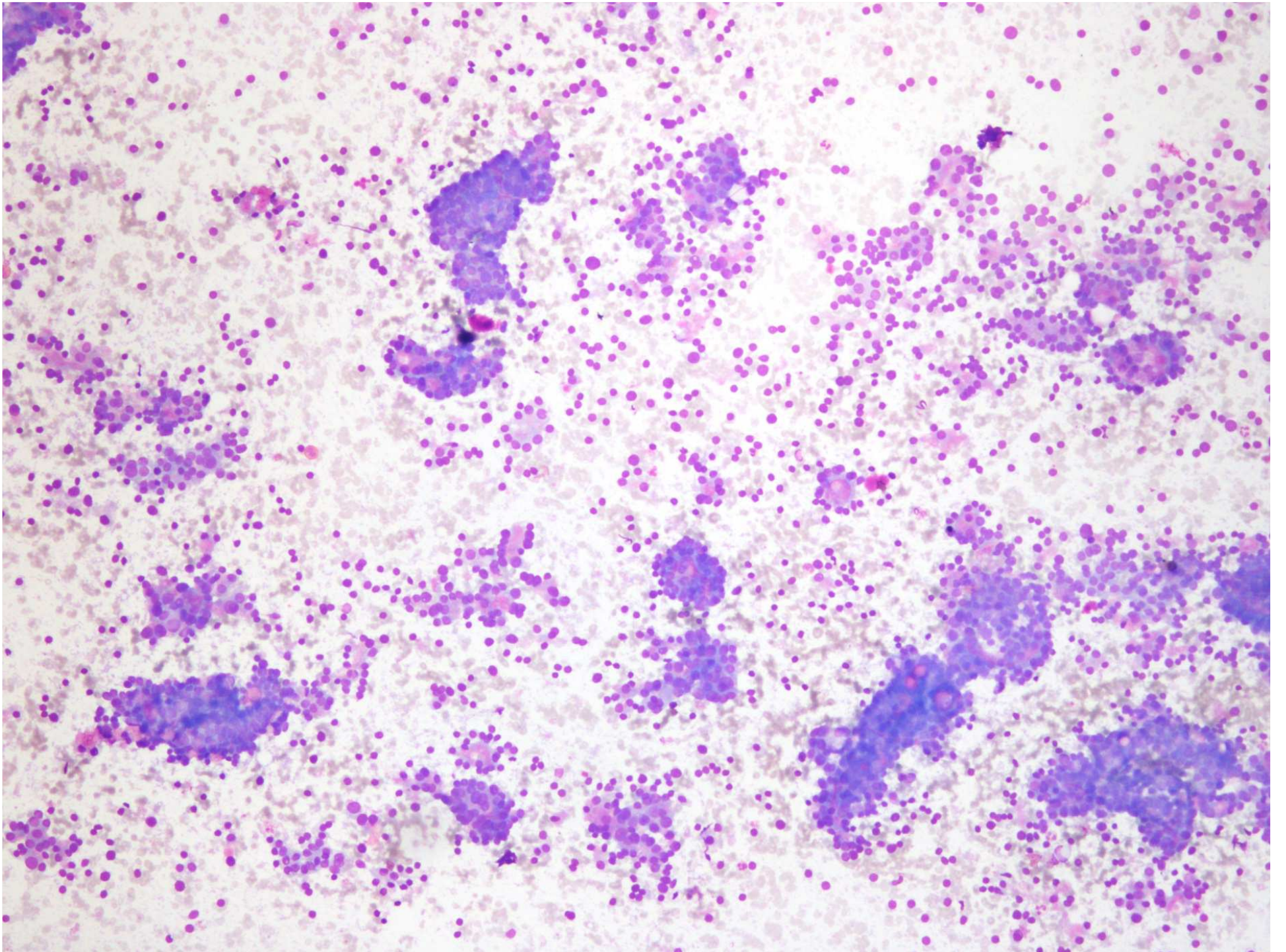
Nodular goiter (nodular hyperplasia)

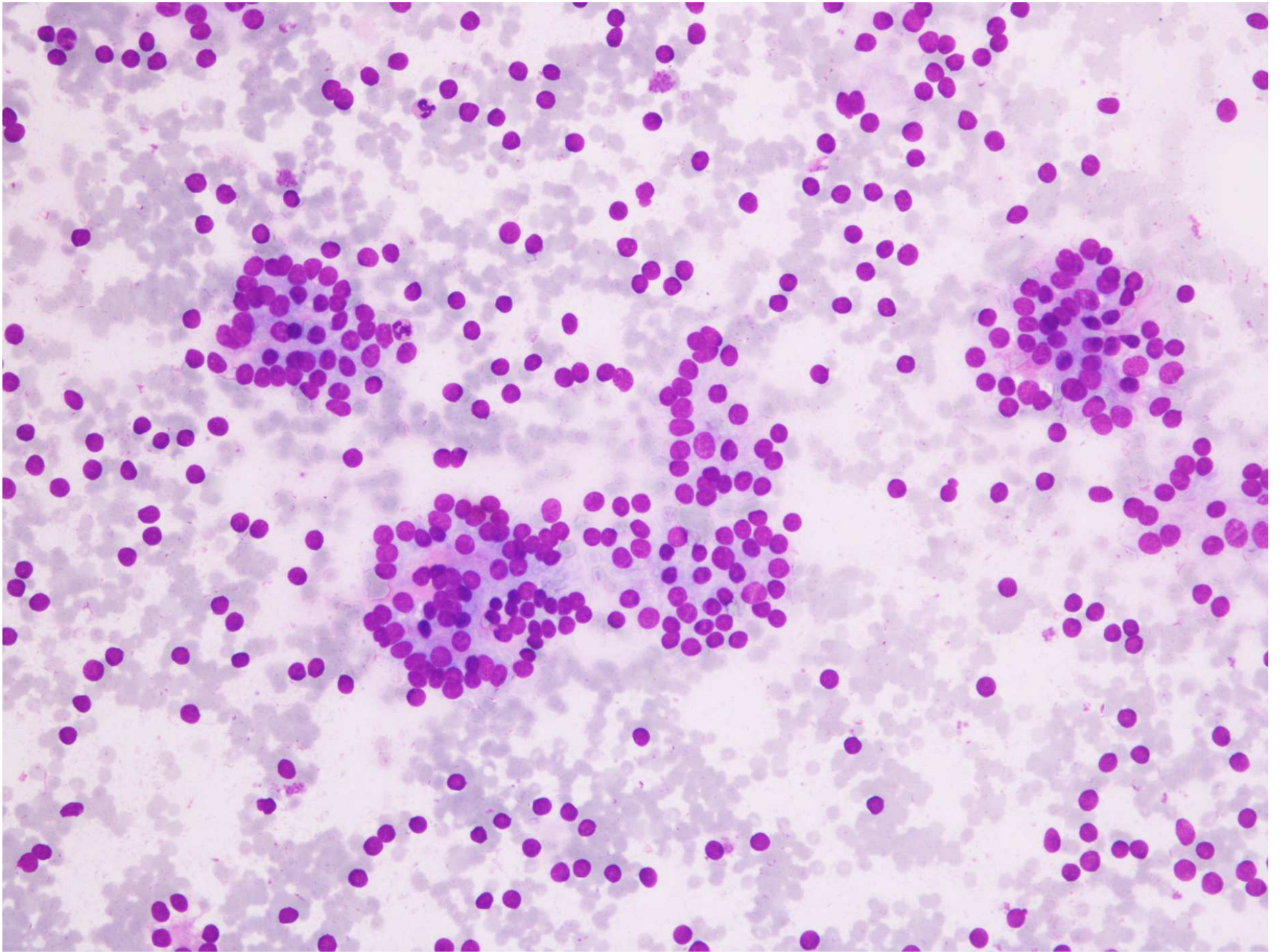
- **architecture:**
 - monolayerd tissue fragments with honeycomb pattern
 - regular follicles
 - pseudopapillary tissue fragments
 - single cells
- **follicular cells characteristics:**
 - small round uniform nuclei
 - compact to finely granular chromatin
- **background:**
 - colloid (variable amount, even absent)

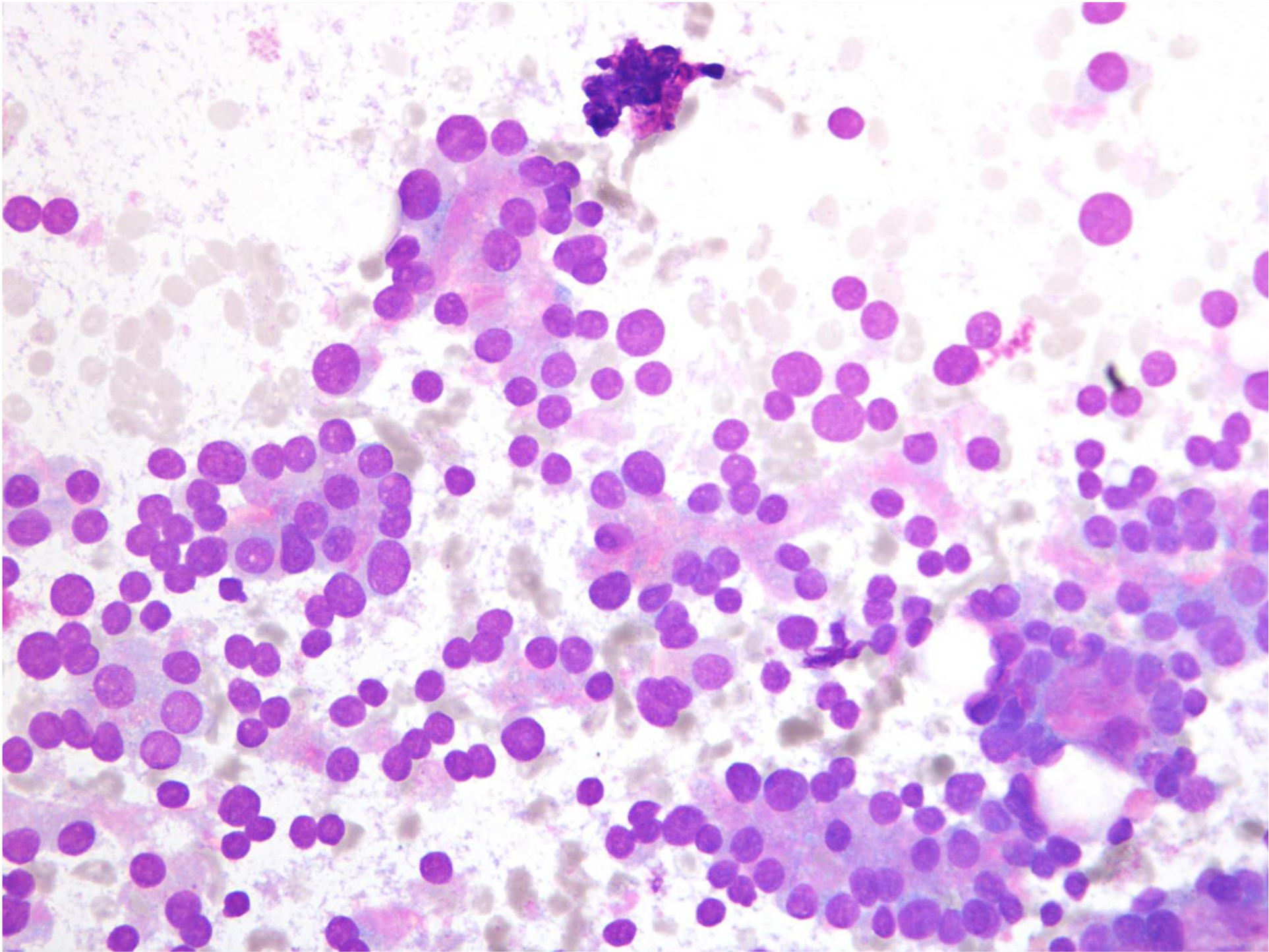


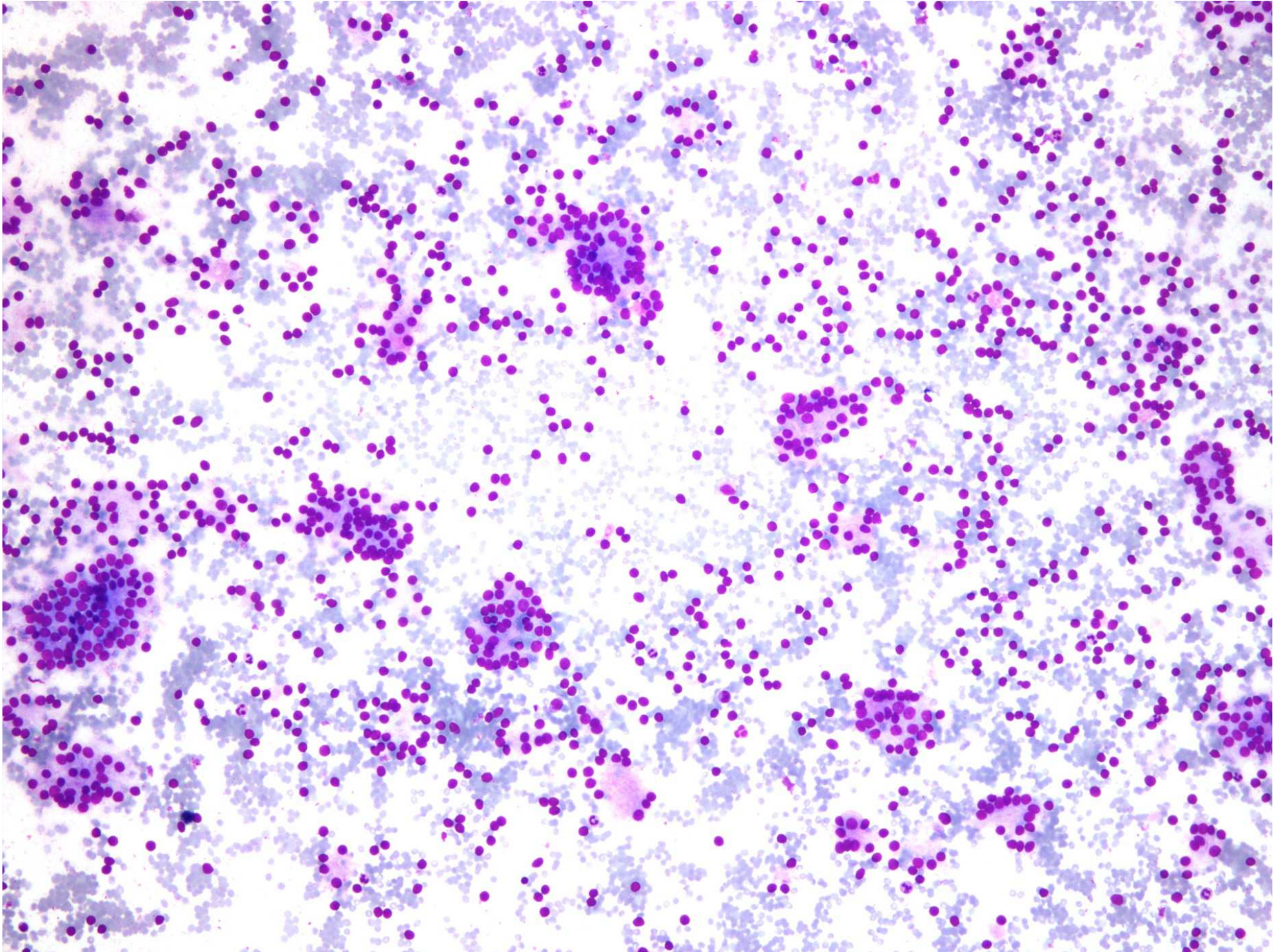


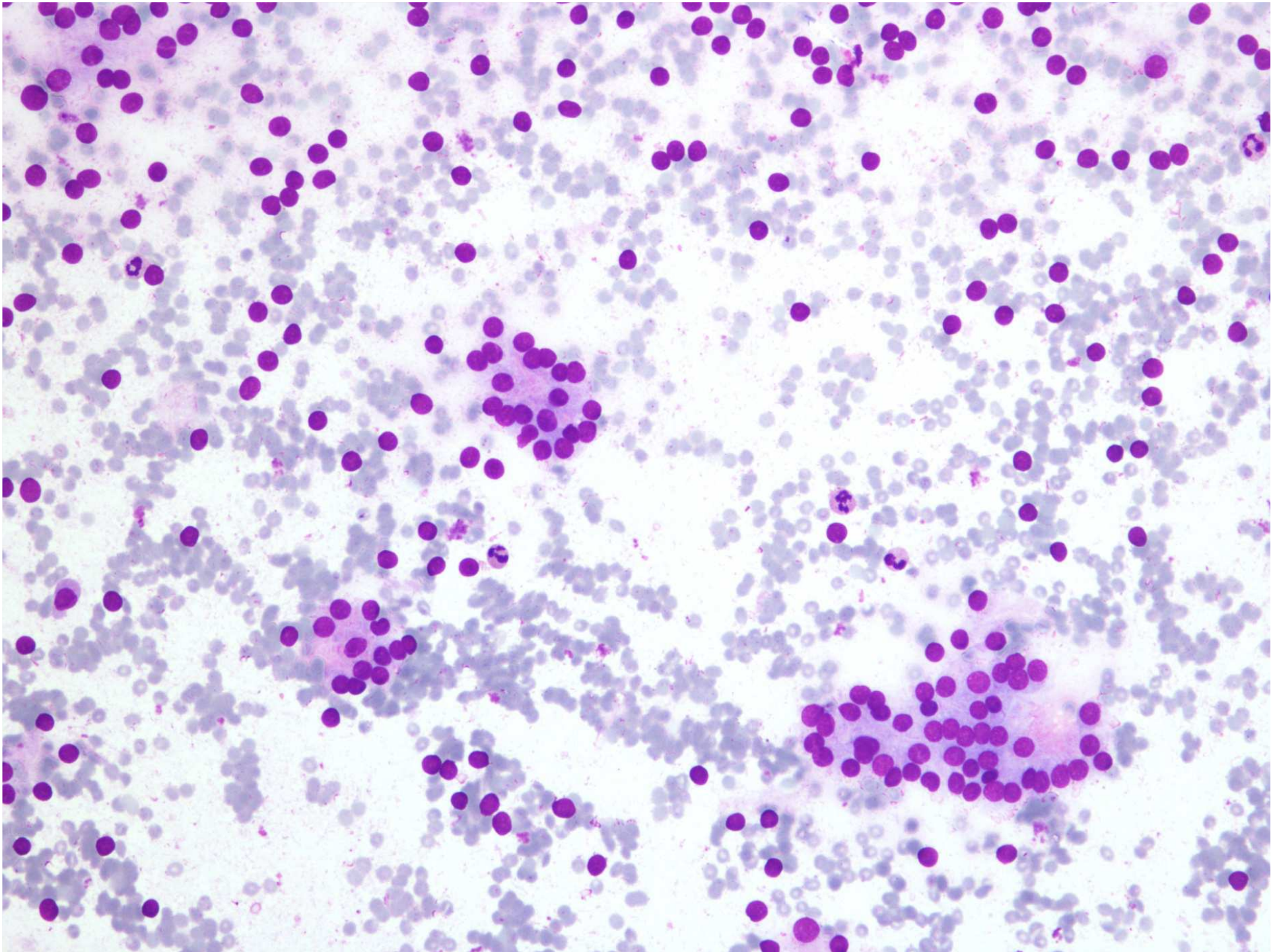












Morphological features that can help in the differentiation of follicular lesions

- amount of colloid
- architectural pattern of tissue fragments
- size and shape of follicular cell nuclei
- changes in chromatin pattern



The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC)

Recommended diagnostic categories:

- nondiagnostic or nonsatisfactory
- benign
- atypia of undetermined significance or follicular lesion of undetermined significance
- follicular neoplasm or suspicious for follicular neoplasm
- suspicious for malignancy
- malignant



The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC)

Advantages:

- standardisation of cytology reports
- each diagnostic category carries the information of:
 - malignancy risk
 - recommended clinical management
- facilitates communication among cytopathologists and clinicians
- facilitates cytologic-histologic correlation



Ancillary techniques in evaluating follicular lesions

- Not very useful:
 - **immunochemistry:**
HBME-1, CD 57, Lactoferrin (malignant vs benign thyroid neoplasms)
 - **DNA ploidy**
- Promising:
 - **molecular techniques:**
 - for detecting somatic mutations (RAS mutations, PAX8/PPARG1 rearrangement)
 - for gene expression profiling (microarrays)



Conclusions

- Follicular thyroid lesions are difficult to evaluate from cytology samples because of variety of their morphological pictures which sometimes overlap between several entities
- TBSRTC enables the standardisation of the thyroid cytology reports, which facilitates the communication between cytologist and referral physician and improve patients care
- cytology will remain a screening and not a diagnostic test for follicular carcinoma until ancillary techniques will be developed that would enable the differentiation between benign thyroid nodules and FC

