

**ESVP – ESVCP Congress
Arnhem 2019**

**MISTERY SLIDES
SESSION**

- Cytology -

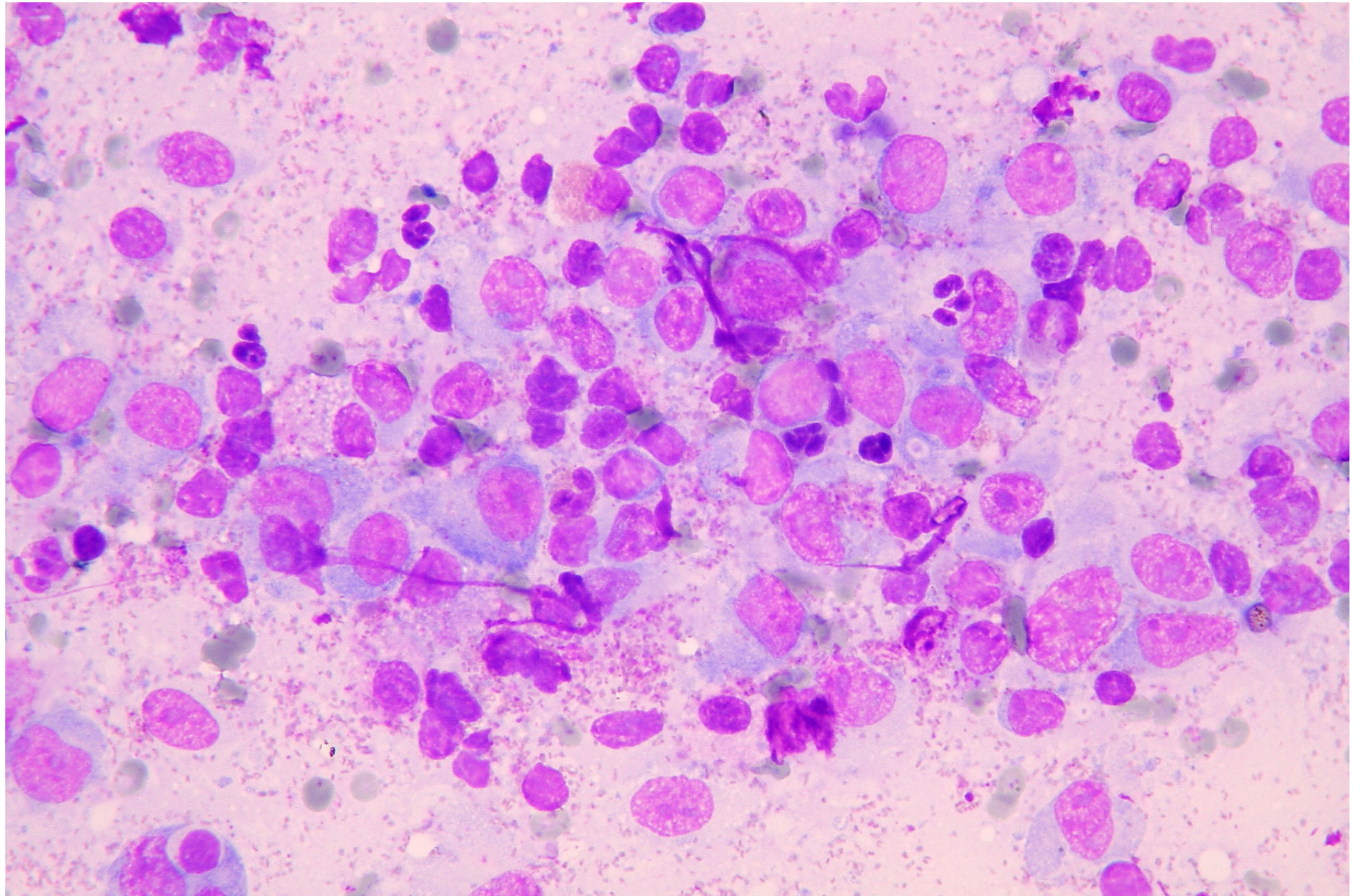
**Carlo Masserdotti DVM,
DipIECVCP, Spec Bioch Clin IAT
Brescia**

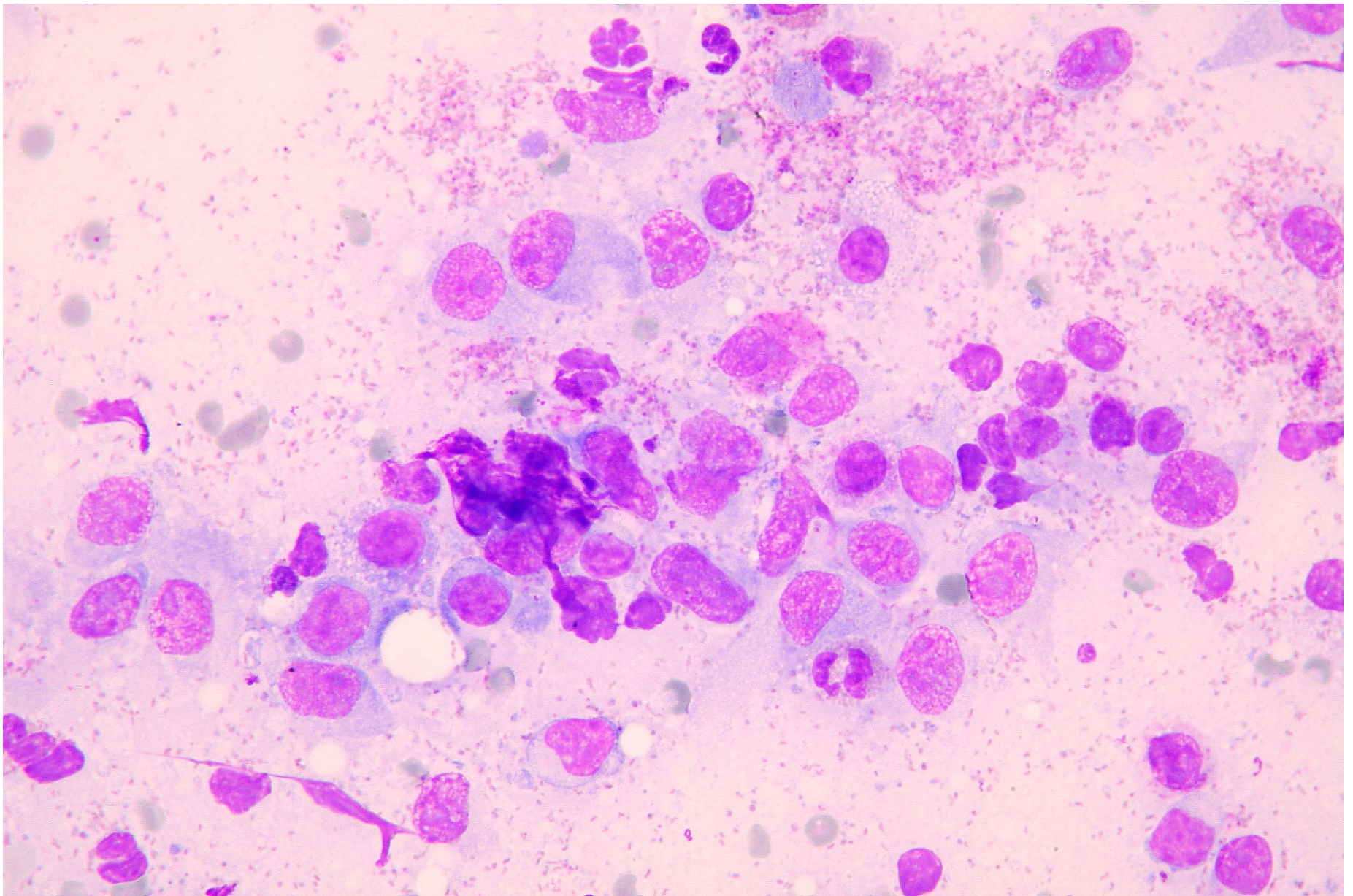


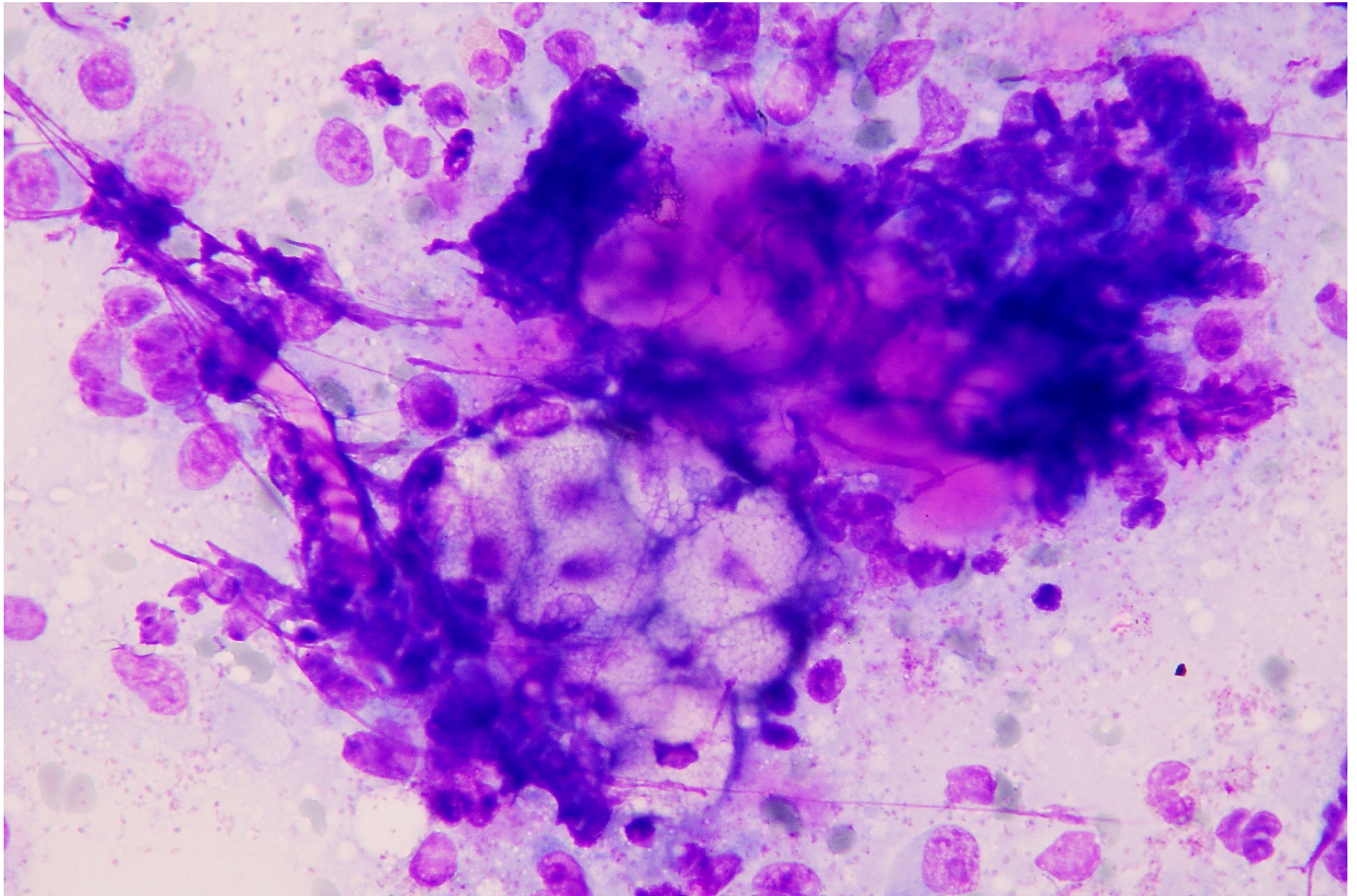
Case #1

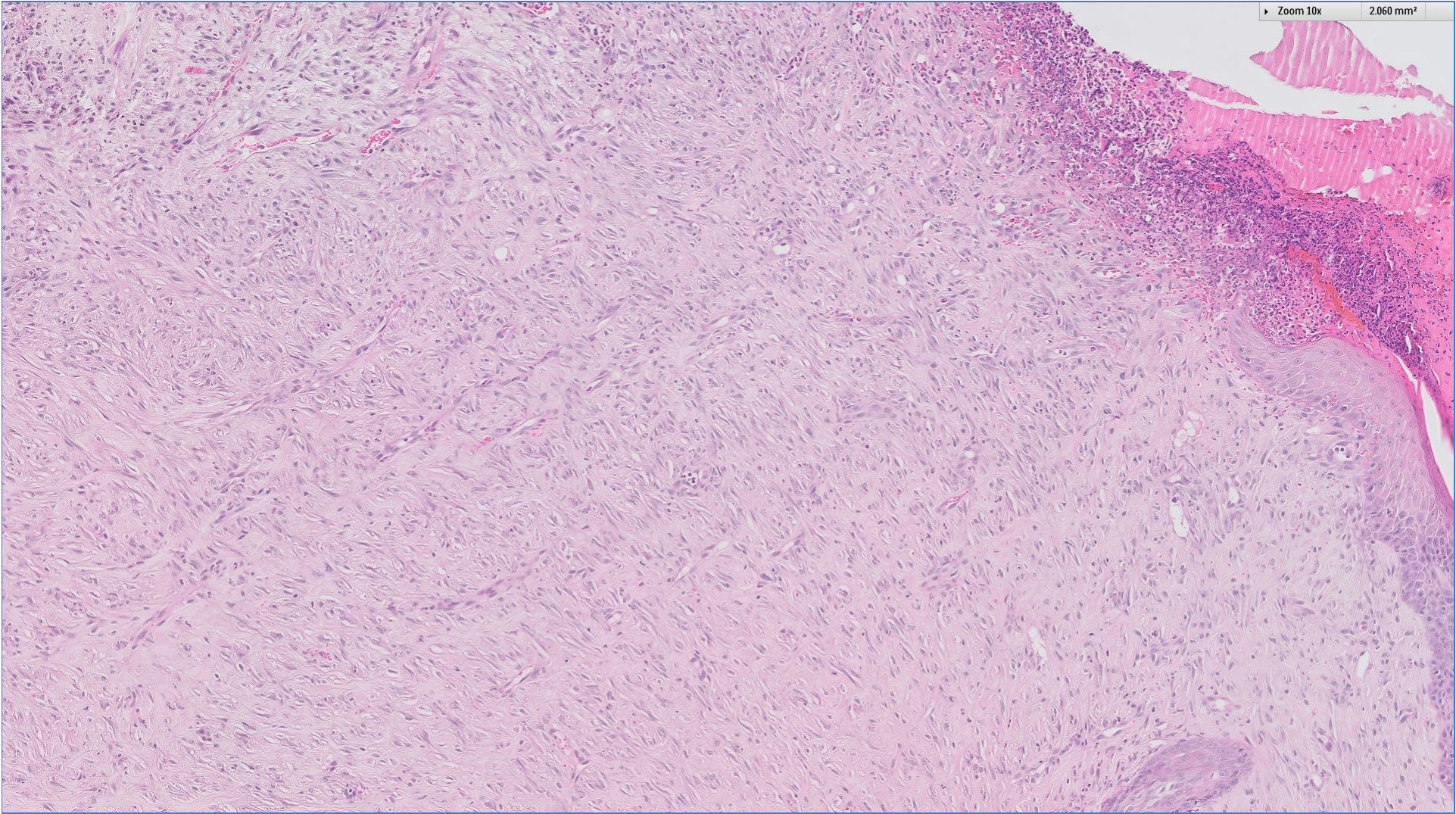
- Cat, DLH, 1-year old;
- Multiple cutaneous lumps on the back
- Sample: FNCS
- Stain: MGG

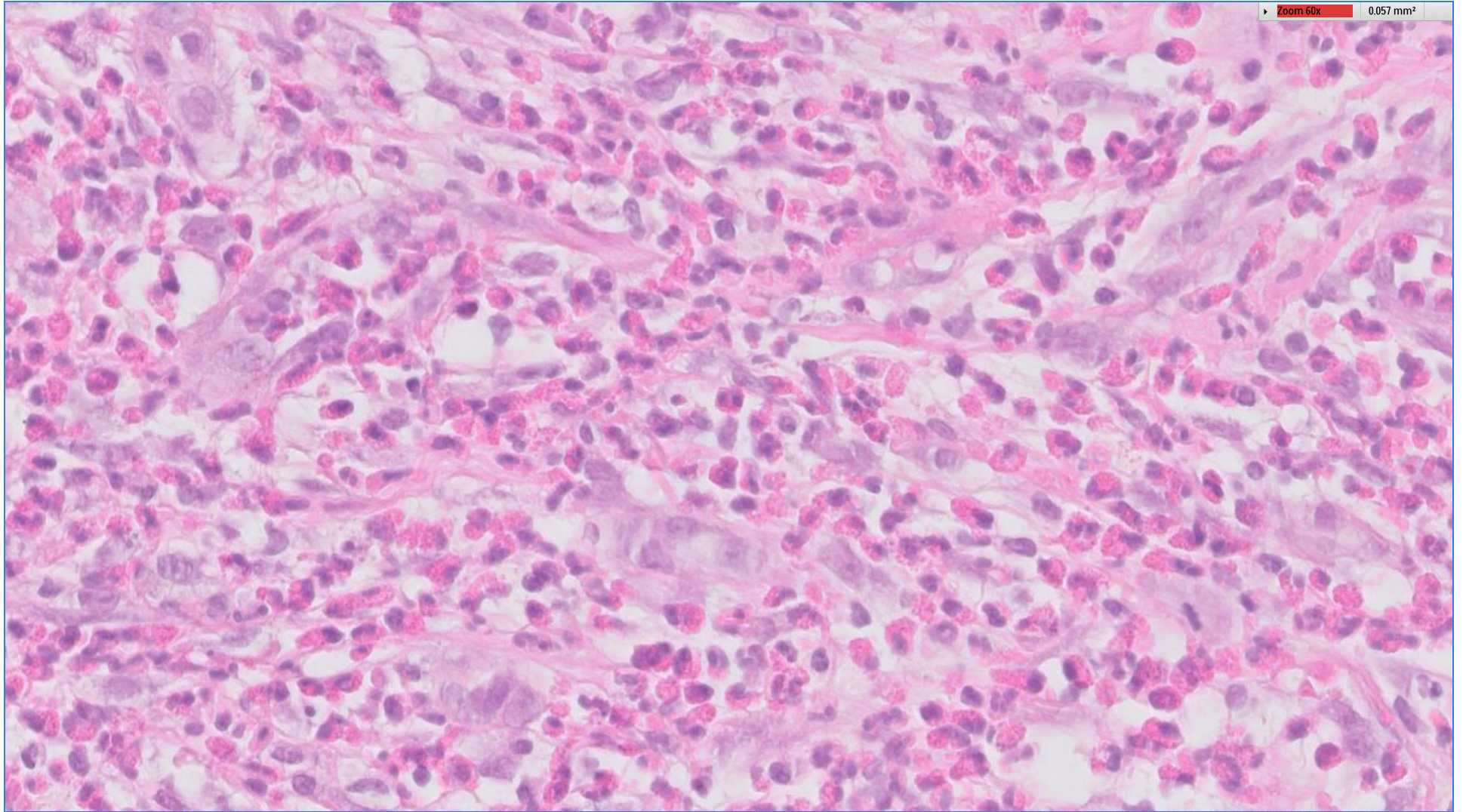












Cytologic findings

- **Spindle cells**
 - Scattered on the background
 - Sometimes entrapped in eosinophilic material
- **Inflammatory cells**
 - Mostly eosinophils
 - Lymphoplasmacytic cells



Diagnosis

- Cytologic diagnosis:
 - Spindle cells, probably reactive proliferation, with eosinophilic inflammation
 - DD: well-differentiated sarcoma with secondary inflammation
- Histological diagnosis:
 - Reactive fibroplasia with eosinophilic inflammation



Discussion

- Eosinophilic inflammation in cats:
 - Feline herpesvirus ulcerative dermatitis
 - Feline eosinophilic granuloma
 - Feline eosinophilic plaque
 - Feline indolent ulcer
 - Feline hypereosinophilic syndrome
 - Insect bite granuloma
- Fibroplasia is described mostly in chronic arthropod bite reaction



Discussion

- Eosinophils and fibroplasia in cat

- Feline gastrointestinal eosinophilic sclerosing fibroplasia (FGESF)
 - thick dense collagen trabeculae and predominantly eosinophilic inflammation within the intestine and lymph nodes
 - [Linton M](#) et al. Feline gastrointestinal eosinophilic sclerosing fibroplasia: 13 cases and review of an emerging clinical entity. [J Feline Med Surg](#). 2015 May;17(5):392-404.
- Feline gastrointestinal eosinophilic sclerosing fibroplasia limited to mesentery
 - [Kambe N](#) et al. A case of feline gastrointestinal eosinophilic sclerosing fibroplasia limited to the mesentery. [J Small Anim Pract](#). 2018 Apr 30.
- Chronic feline asthma (?)
 - The amount of fibrosis depends on the age and severity of the lesion
 - Numerous eosinophils infiltrate the epithelium (Jubb)



Discussion

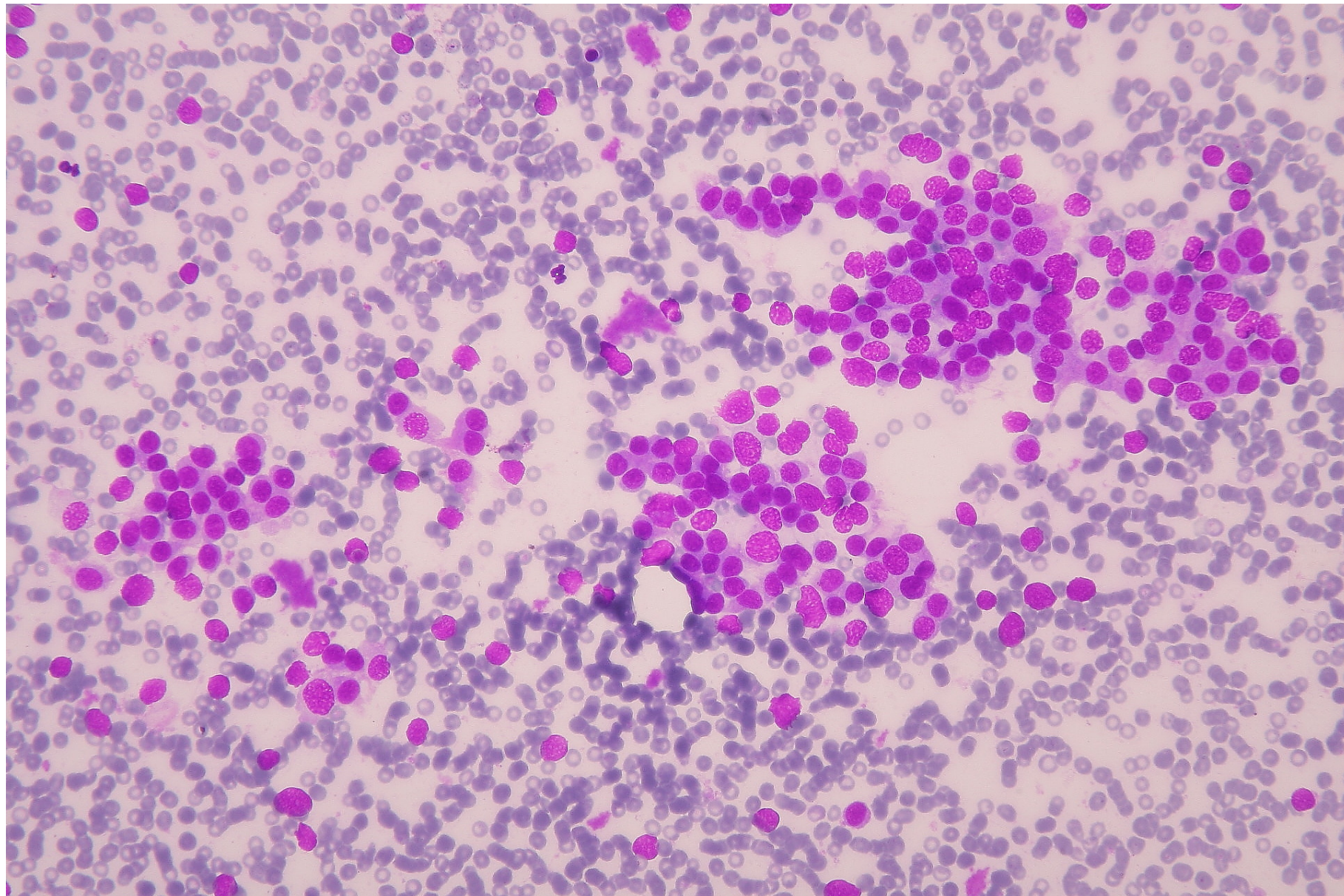
- My opinion about this case:
 - Primary eosinophilic inflammation
 - Primary allergic disease?
 - Chronicization of the inflammatory process
 - Fibrosis (not described in books, but most likely process)
- Is inflammation enough to exclude a sarcoma?

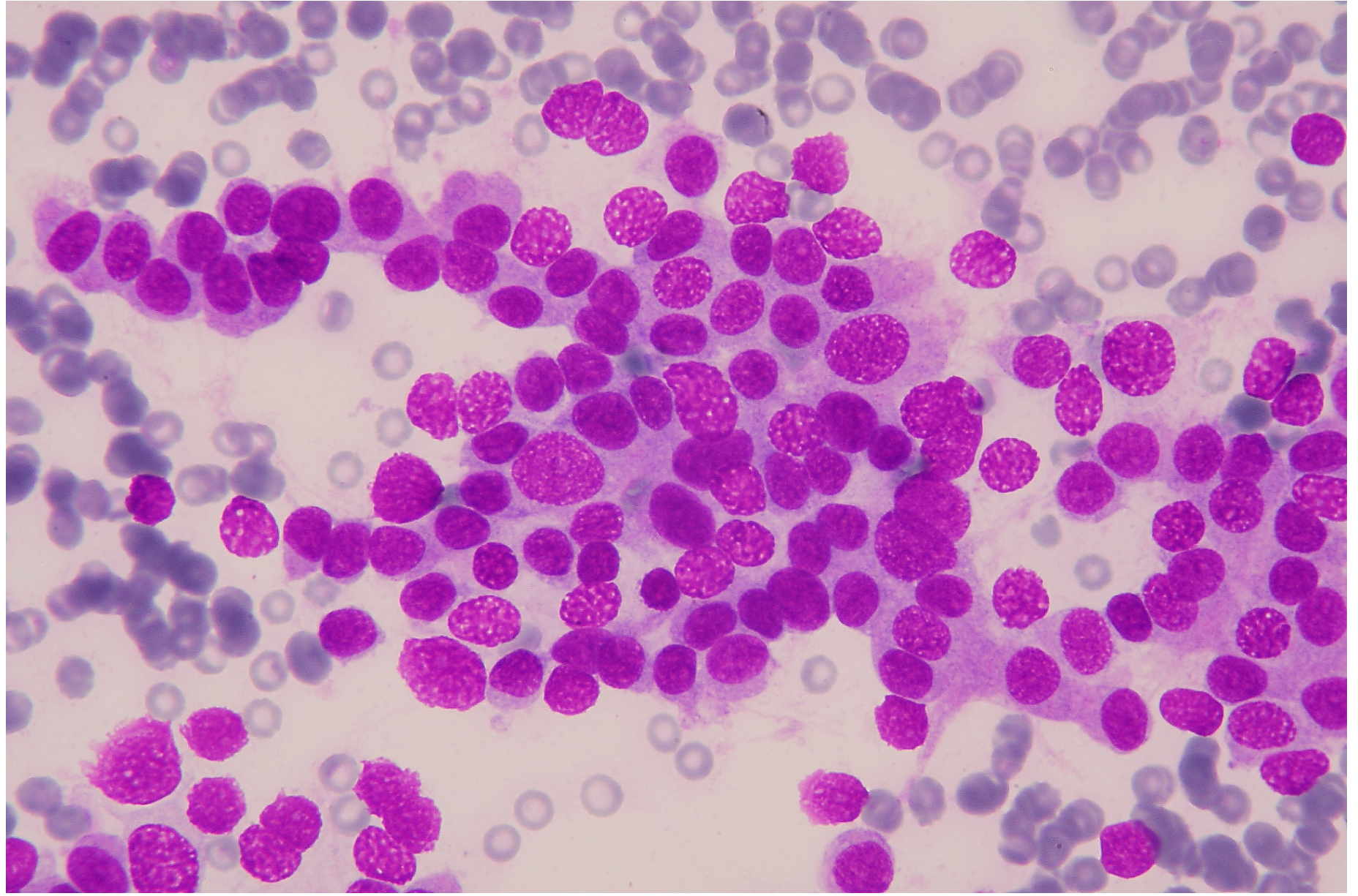


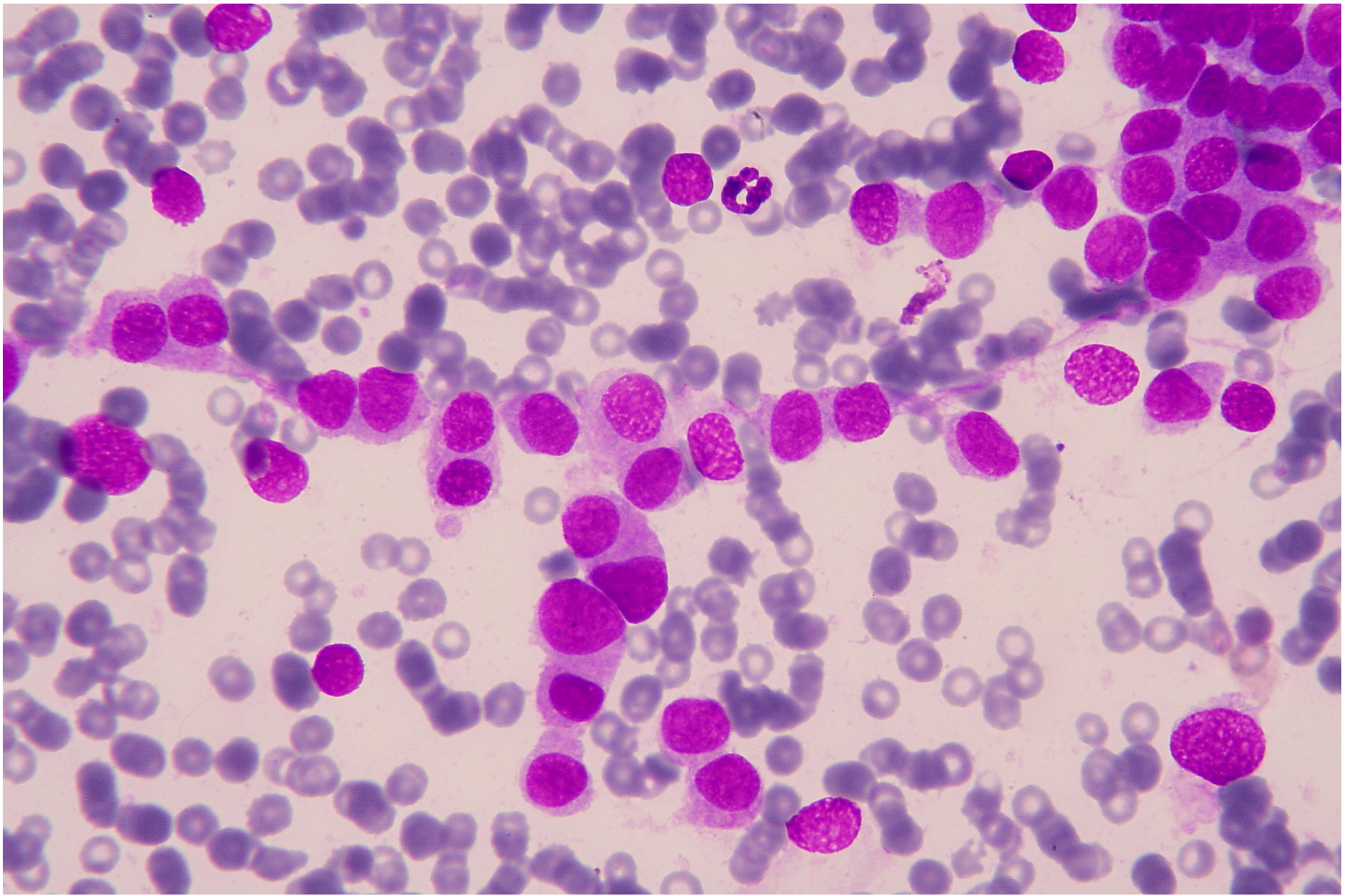
Case #2

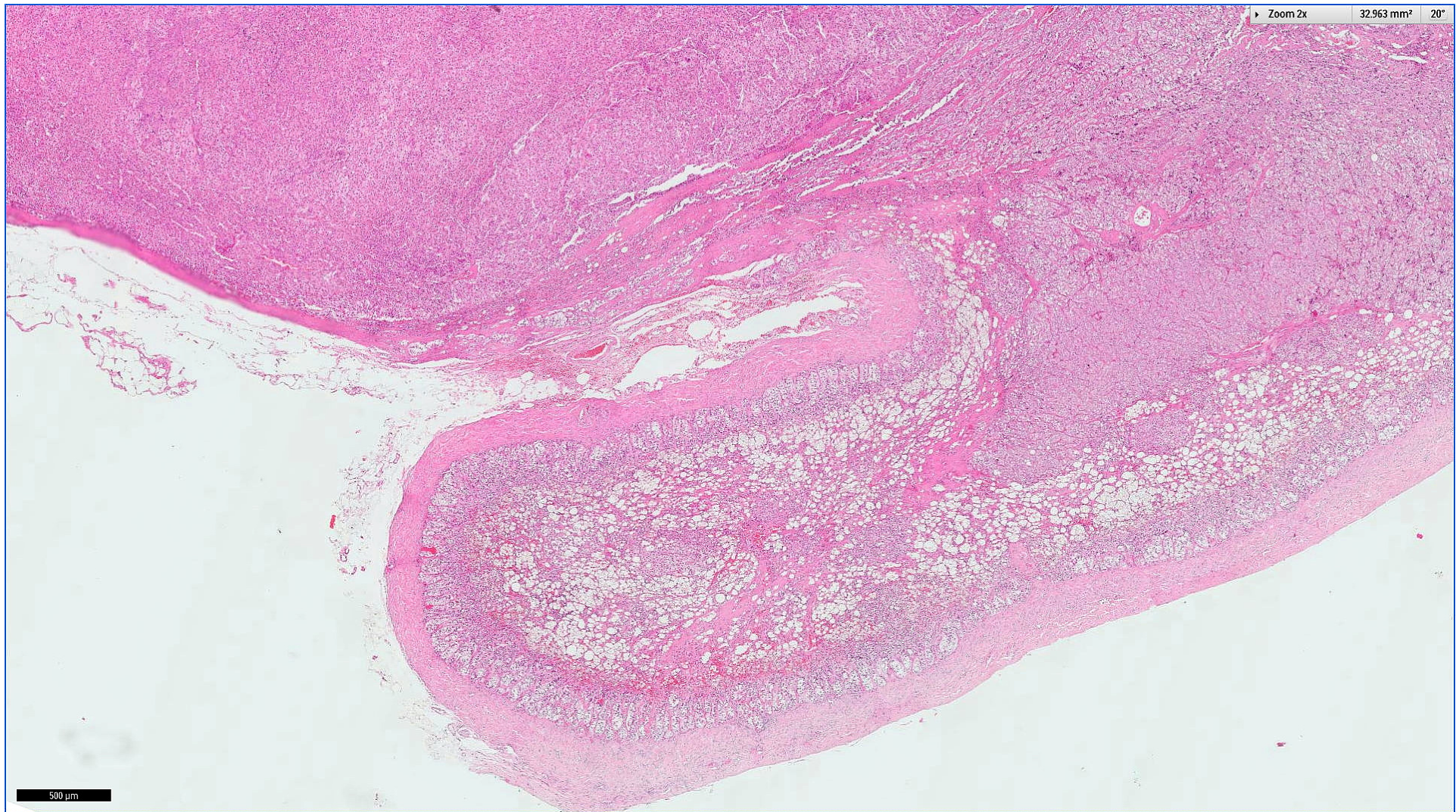
- Dog, Shih-Tzu, 10-year old, female, neutered
 - Adrenal mass.
-
- Sample: FNCS of the mass
 - Stain: MGG











Cytologic findings

- Epithelial cells
- Rows arrangements
- Small, round, eosinophilic cytoplasm
- Round to ovoid nuclei
- Granular chromatin
- Slight to moderate anisokaryosis and anisocytosis
- Small number of naked nuclei



Diagnosis

- Cytological diagnosis:
 - Epithelial proliferation, morphology suggestive of pheochromocytoma
- Histological diagnosis:
 - Pheochromocytoma



ORIGINAL RESEARCH

Accuracy of cytology in distinguishing adrenocortical tumors from pheochromocytoma in companion animals

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Key Words

Cats, Cushing disease, dogs, hyperadrenocorticism, hyperaldosteronism

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Background: The distinction between adrenocortical tumors and pheochromocytoma can be challenging using clinical findings, diagnostic imaging and laboratory tests. Cytology might be a simple, minimally invasive method to reach a correct diagnosis.

Objectives: The purpose of this study was to assess the accuracy of cytology in differentiating cortical from medullary tumors of the adrenal glands in dogs and cats.

Methods: Cytologic key features of adrenocortical tumors and pheochromocytoma were defined by one reference author. Cytologic specimens from primary adrenal tumors were submitted to 4 cytopathologists who were asked to classify the tumors based on the previously defined key features without knowledge of previous classification.

Results: Twenty specimens from histologically confirmed adrenal tumors (Group 1) and 4 specimens from adrenal tumors causing adrenal-dependent Cushing's syndrome (Group 2) were evaluated by the 4 cytopathologists. Accuracy in differentiating cortical from medullary origin ranged from 90% to 100%, with a Kappa coefficient of agreement between cytopathologists of 0.95.

Conclusions: The origin of an adrenal tumor can be easily determined by cytology alone in many cases. However, cytology was not reliable in distinguishing benign from malignant neoplasia. Additional studies are needed to assess possible risks and complications associated with fine-needle biopsy of adrenal tumors in dogs and cats.

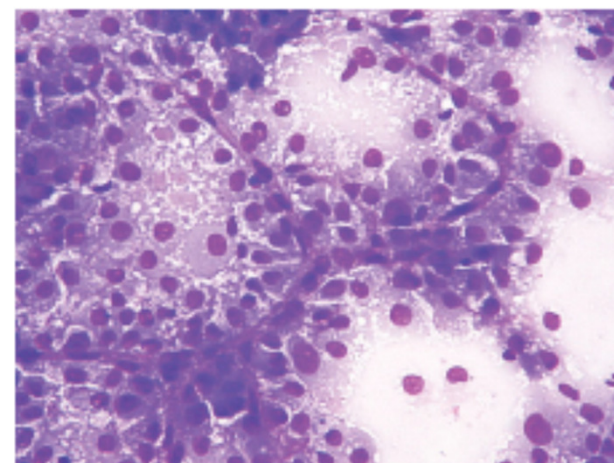


Figure 3. A group of cortical cells from an adrenal cortical tumor in a dog, showing a perivascular arrangement. May-Grünwald-Giemsa. $\times 40$ objective.

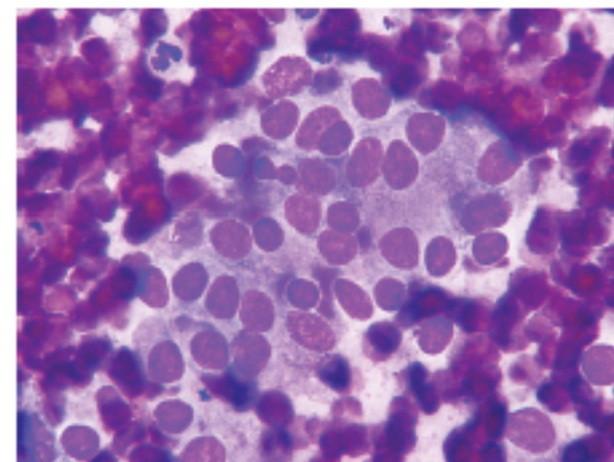


Figure 6. A rare cluster of intact cells from a canine pheochromocytoma. Cells show a high nuclear to cytoplasmic ratio, a small amount of slightly basophilic cytoplasm, uniform round to oval nuclei with fine chromatin and indistinct nucleoli. May-Grünwald-Giemsa. $\times 100$ objective.

Discussion

- **Pheochromocytoma**
 - Most common tumor in adrenal medulla
 - Potential excessive catecholamine secretion
 - Tachycardia
 - Hypertension
 - Cardiac hypertrophy
 - Edema
 - Macroscopic criteria of malignancy
 - Size
 - Invasion into the posterior vena cava
 - Microscopic criteria of malignancy
 - Invasion through the adrenal capsule
 - Cells could be more pleomorphic than benign tumor



Discussion

- Clinical implications
 - Need to compare cytological/histological features with infiltrative activity
 - Imaging
 - Need of early recognition of pheochromocytoma
 - Prevention or therapy for catecholamine activity



Discussion

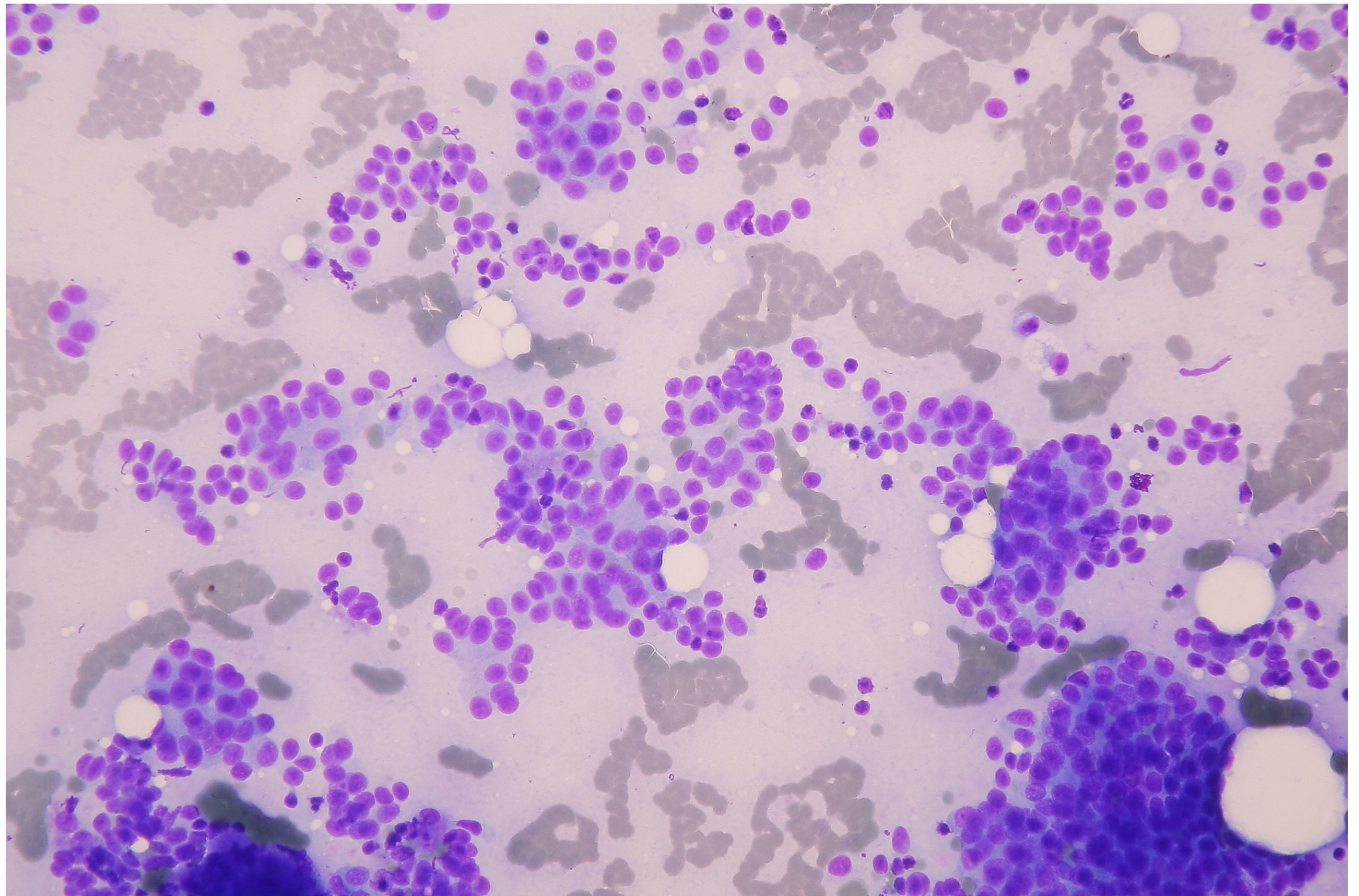
- Need to differentiate pheochromocytoma from other adrenal tumor
 - Risk factor for poor short-term survival
 - Pheochromocytoma [Barrera JS](#) et al. Evaluation of risk factors for outcome associated with adrenal gland tumors with or without invasion of the caudal vena cava and treated via adrenalectomy in dogs: 86 cases (1993-2009). [J Am Vet Med Assoc](#). 2013 Jun 15;242(12):1715-21.
 - Adrenal neoplasm
 - Postoperative management of hypoadrenocorticism [Zini E](#) et al. Pheochromocytoma in Dogs Undergoing Adrenalectomy. [Vet Pathol](#). 2019 May;56(3):358-368.
- Pheochromocytoma
 - Pheochromocytoma-associated catecholamine-induced cardiomyopathy (anesthetic risk) [Edmondson EF](#) et al. Pathologic and cardiovascular characterization of pheochromocytoma-associated cardiomyopathy in dogs. [Vet Pathol](#). 2015 Mar;52(2):338-43.

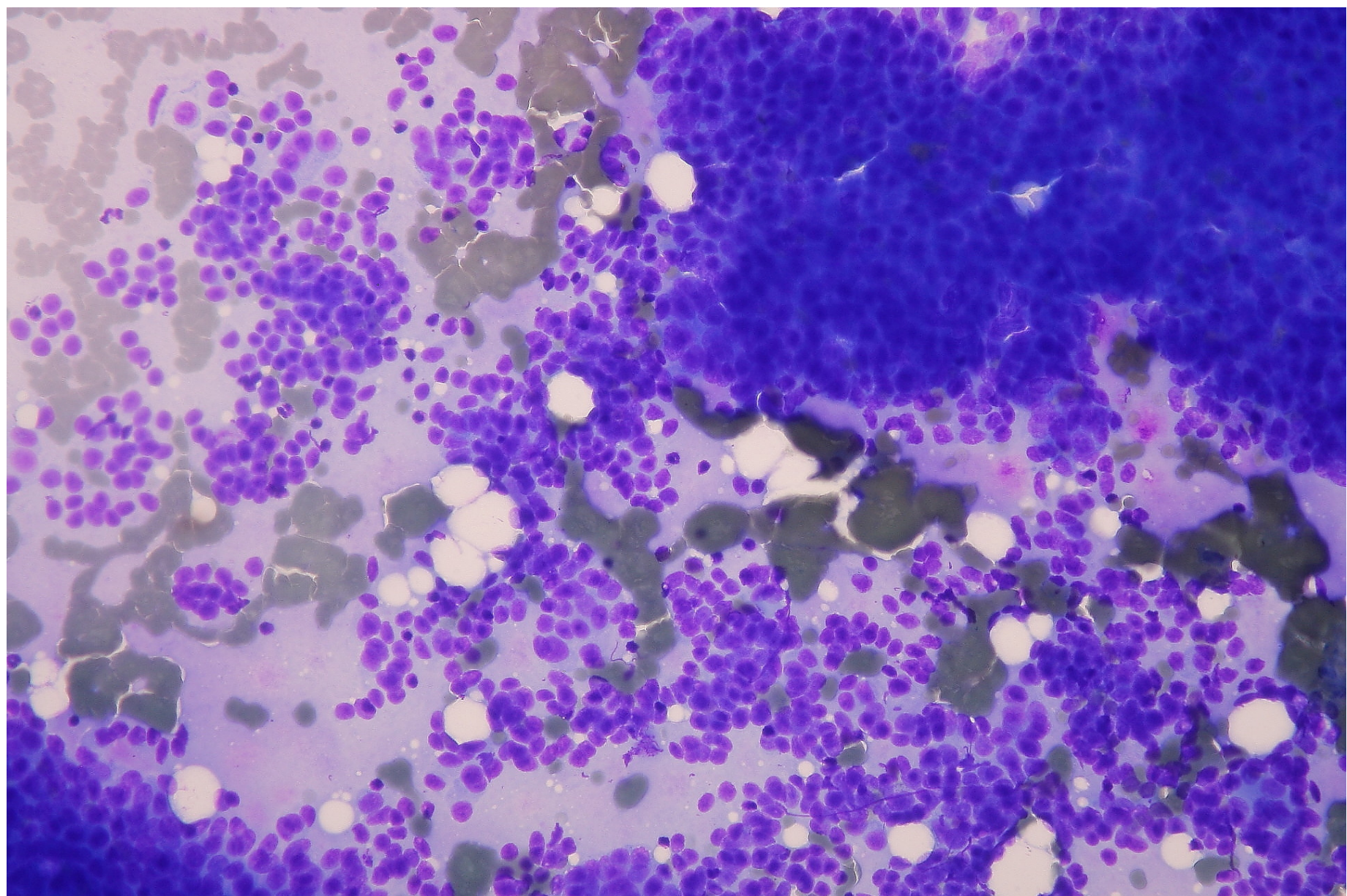


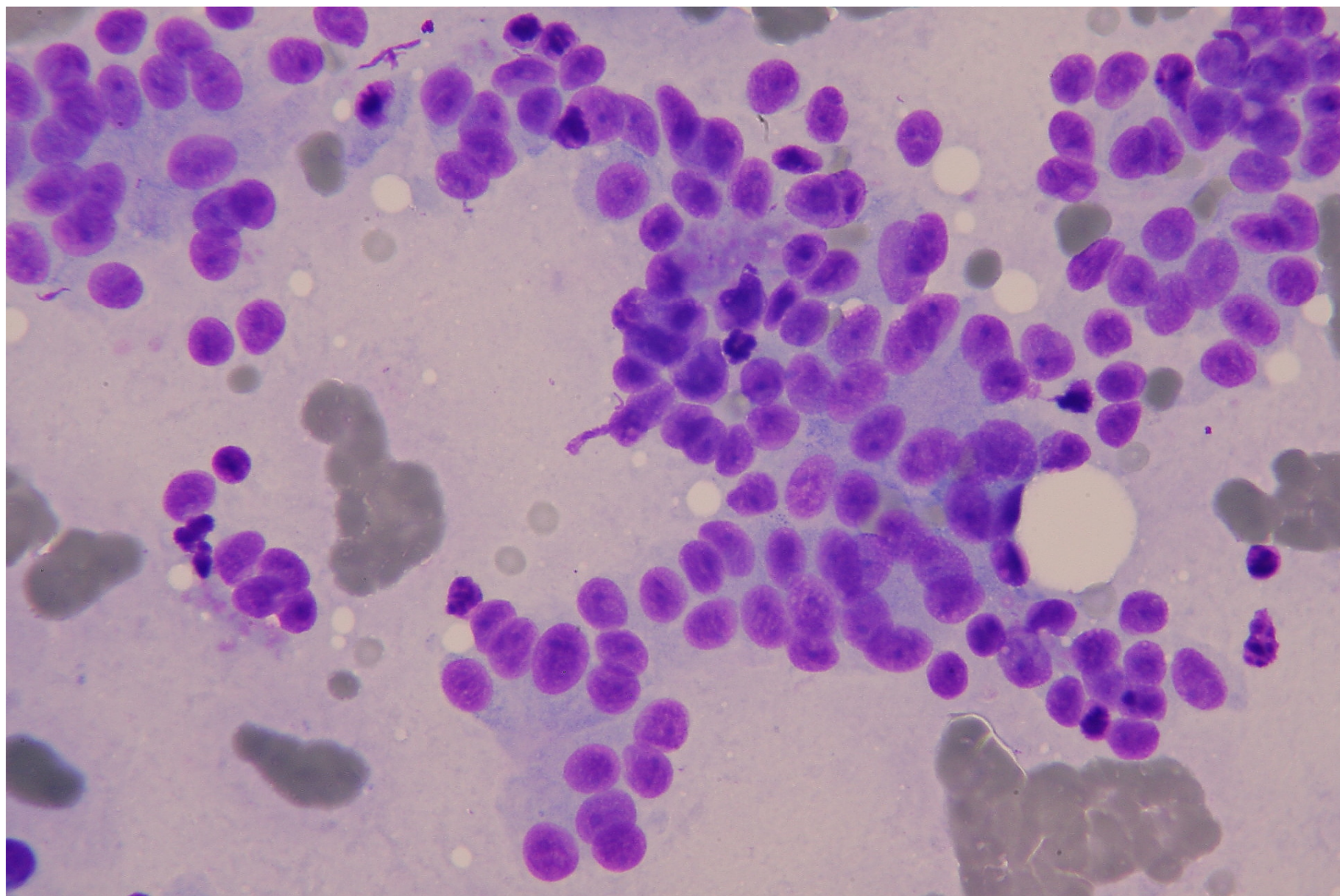
Case #3

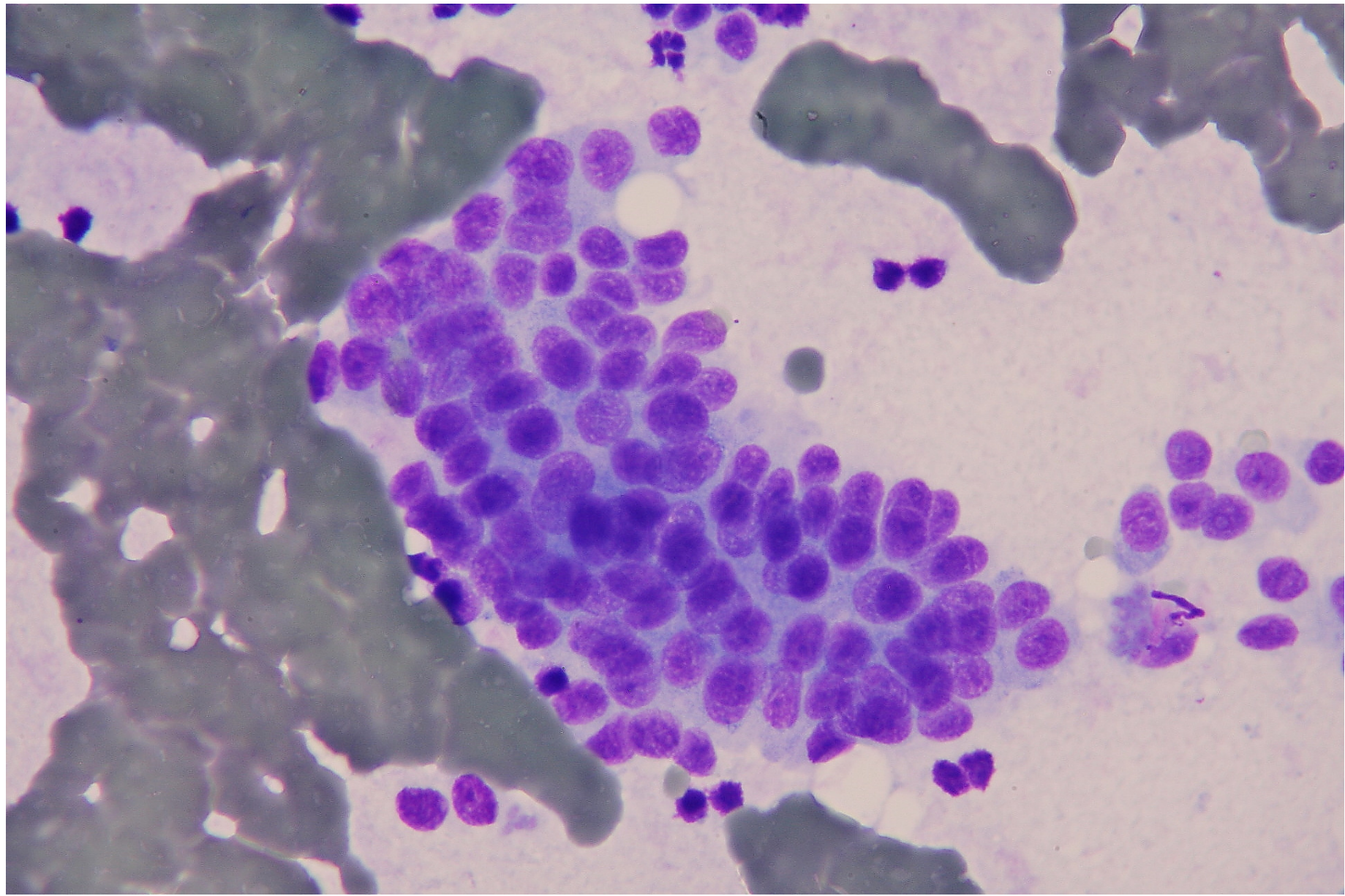
- Cat, DSH, 12-year old, female, neutered
- Thickening of intestinal wall
- Sample: US-guided FNCS
- Stain: MGG

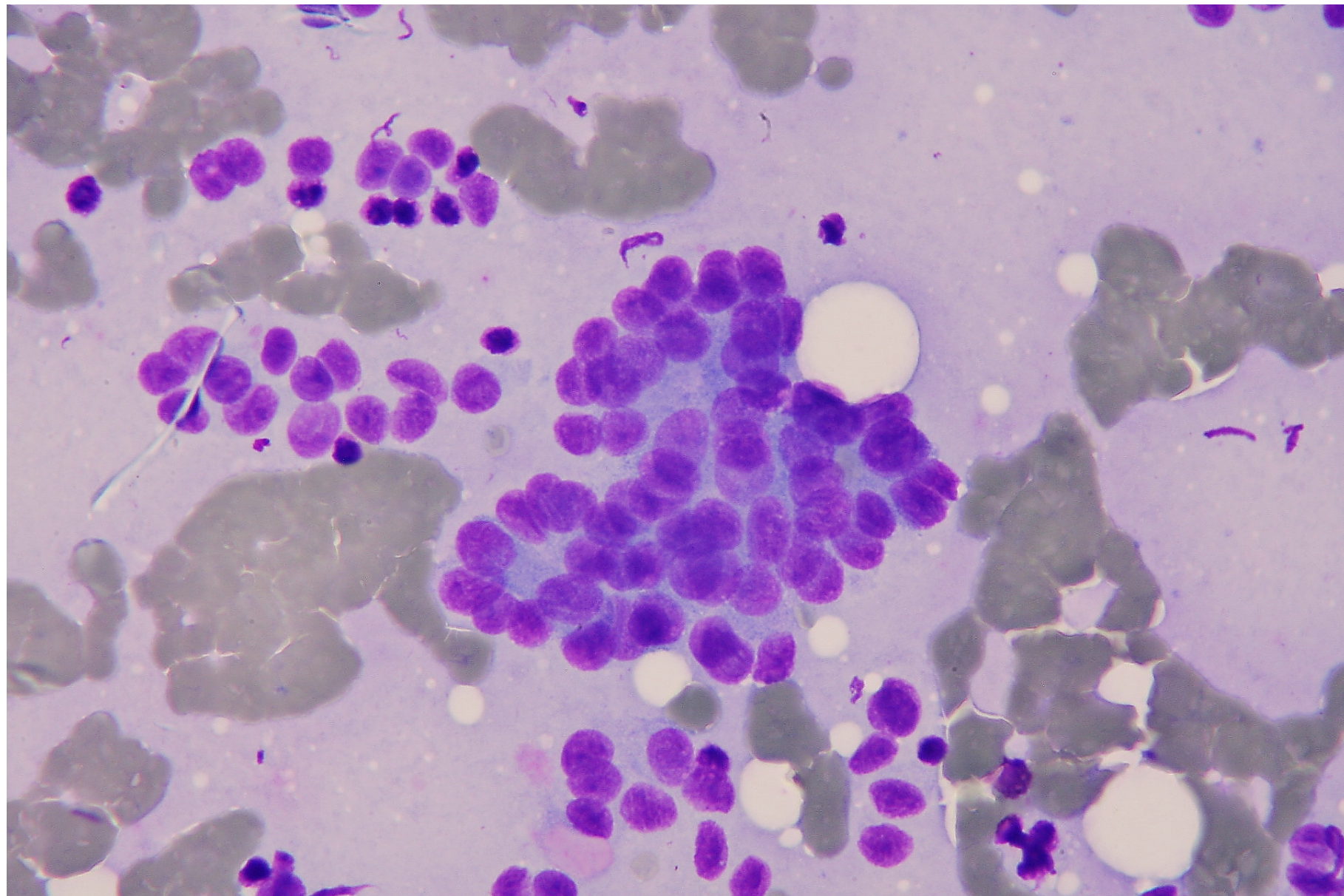












Cytologic findings

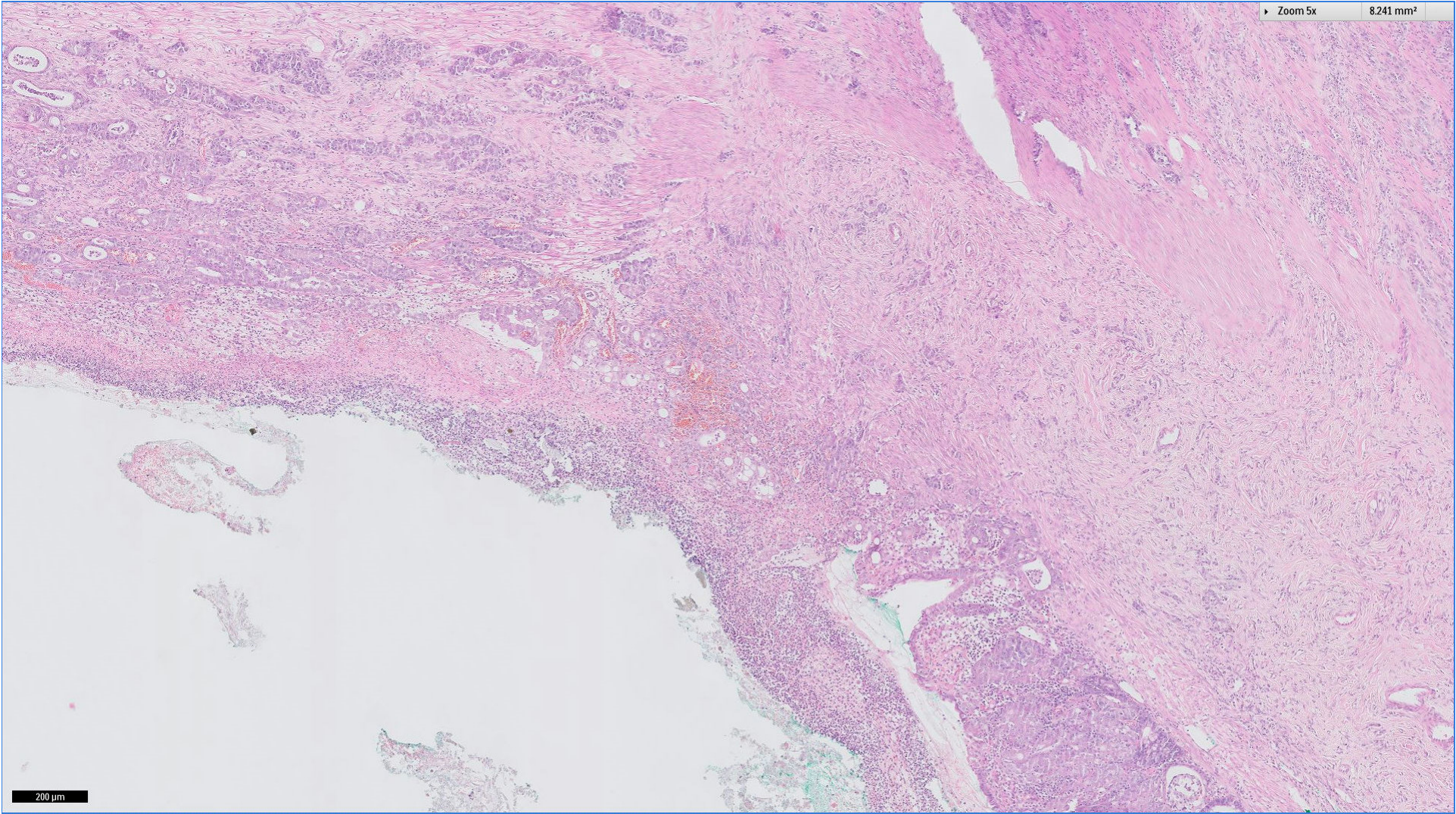
- Epithelial cells
 - Small amount of indistinct cytoplasm
 - Round to ovoid nuclei
 - Finely stippled chromatin
- Arrangements:
 - Dischoesive clusters
 - Rows
 - Microacini

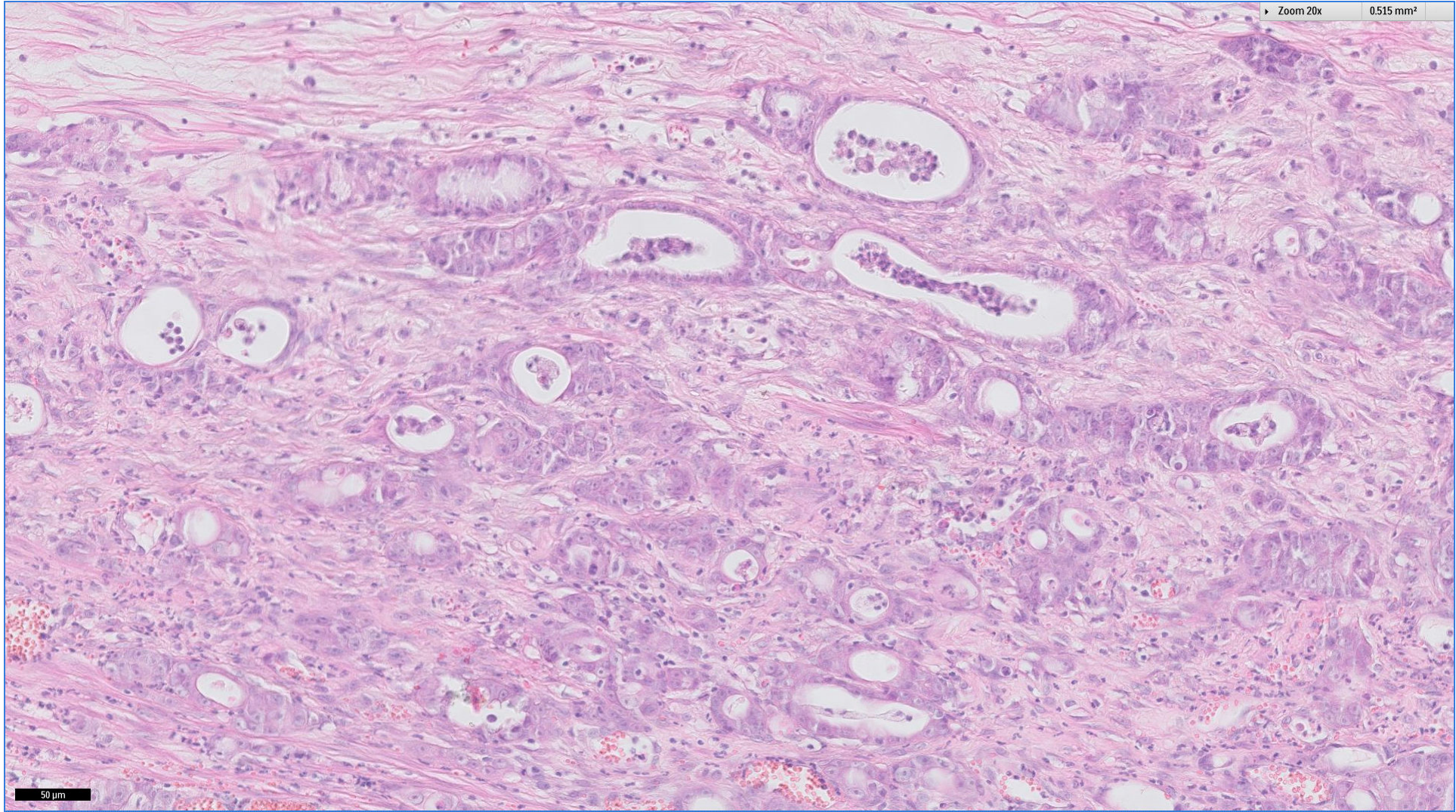


Diagnosis

- Cytological diagnosis:
 - Epithelial malignant neoplasm
 - Neuroendocrine carcinoma
- Histological diagnosis:
 - Intestinal adenocarcinoma







Discussion

- Cytological criteria for carcinoid:
 - Dischoesive aggregates
 - Rows (ok)
 - Rosette (microacini – ok)
 - Small indistinct cytoplasm (ok)
 - Round nuclei (ok)
 - **Naked nuclei (no!)**



Discussion

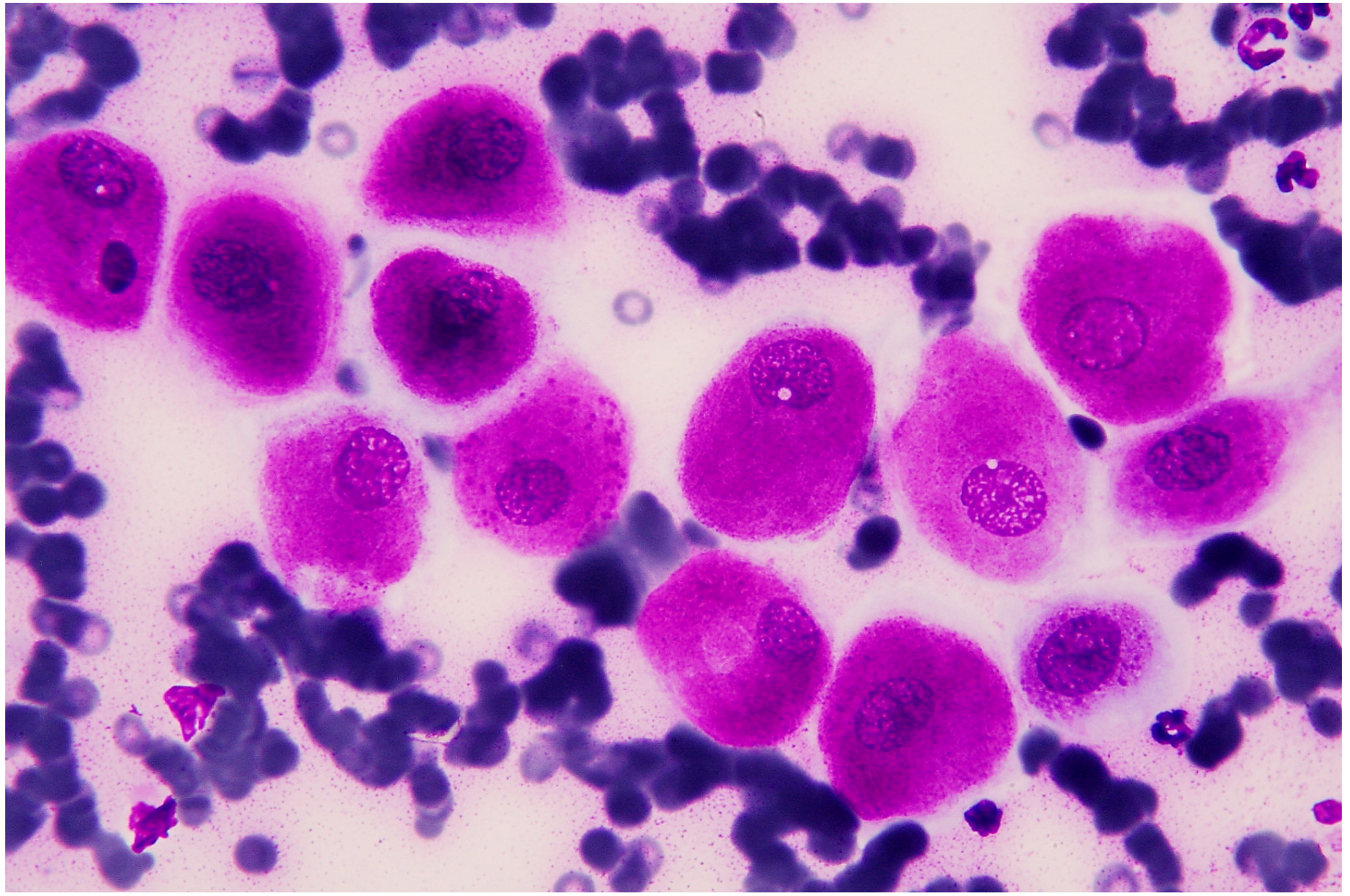
- How much disease incidence should affect diagnosis ?
 - Intestinal adenocarcinoma: frequent
 - Intestinal carcinoid: uncommon (in dog and cat)
- Can anatomical location help?
 - Intestinal adenocarcinoma: small intestine
 - Carcinoid: proximal jejunum and duodenum (in dog) Munday in Meuten
- Influence of diagnosis in clinical outcome:
 - Intestinal adenocarcinoma: «metastasize rapidly»
 - Carcinoid: «aggressive behaviour and widespread metastasis»

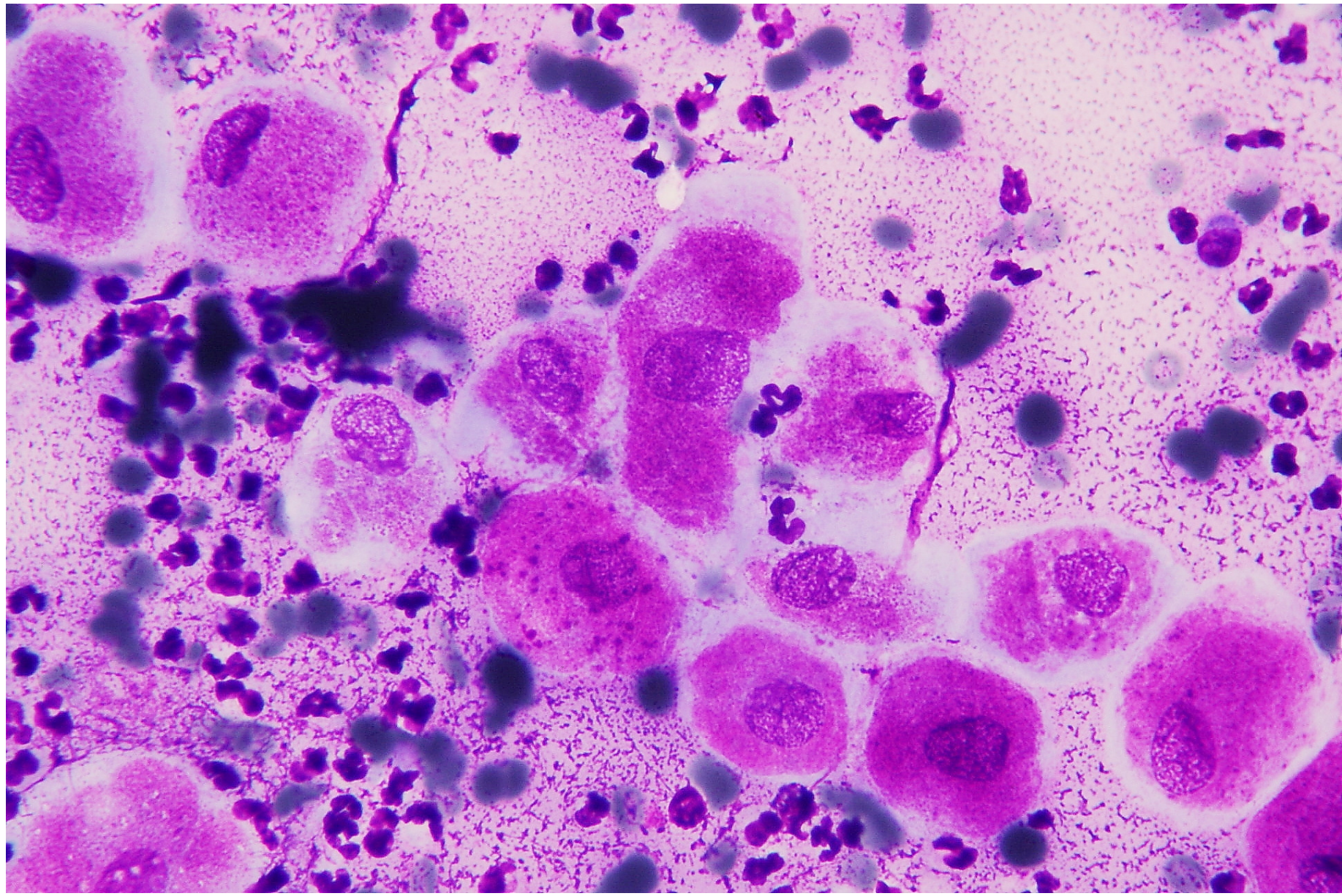


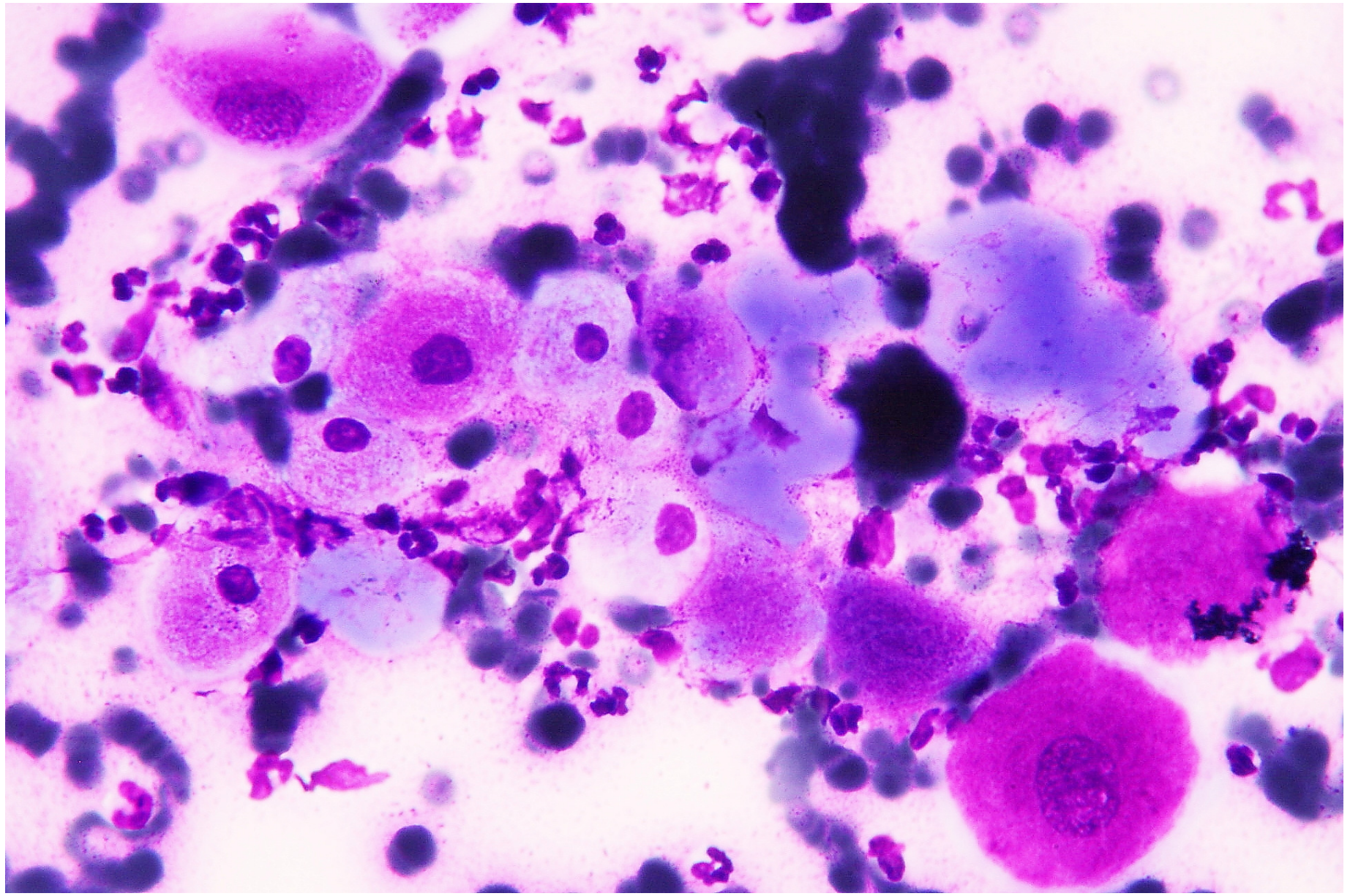
Case #4

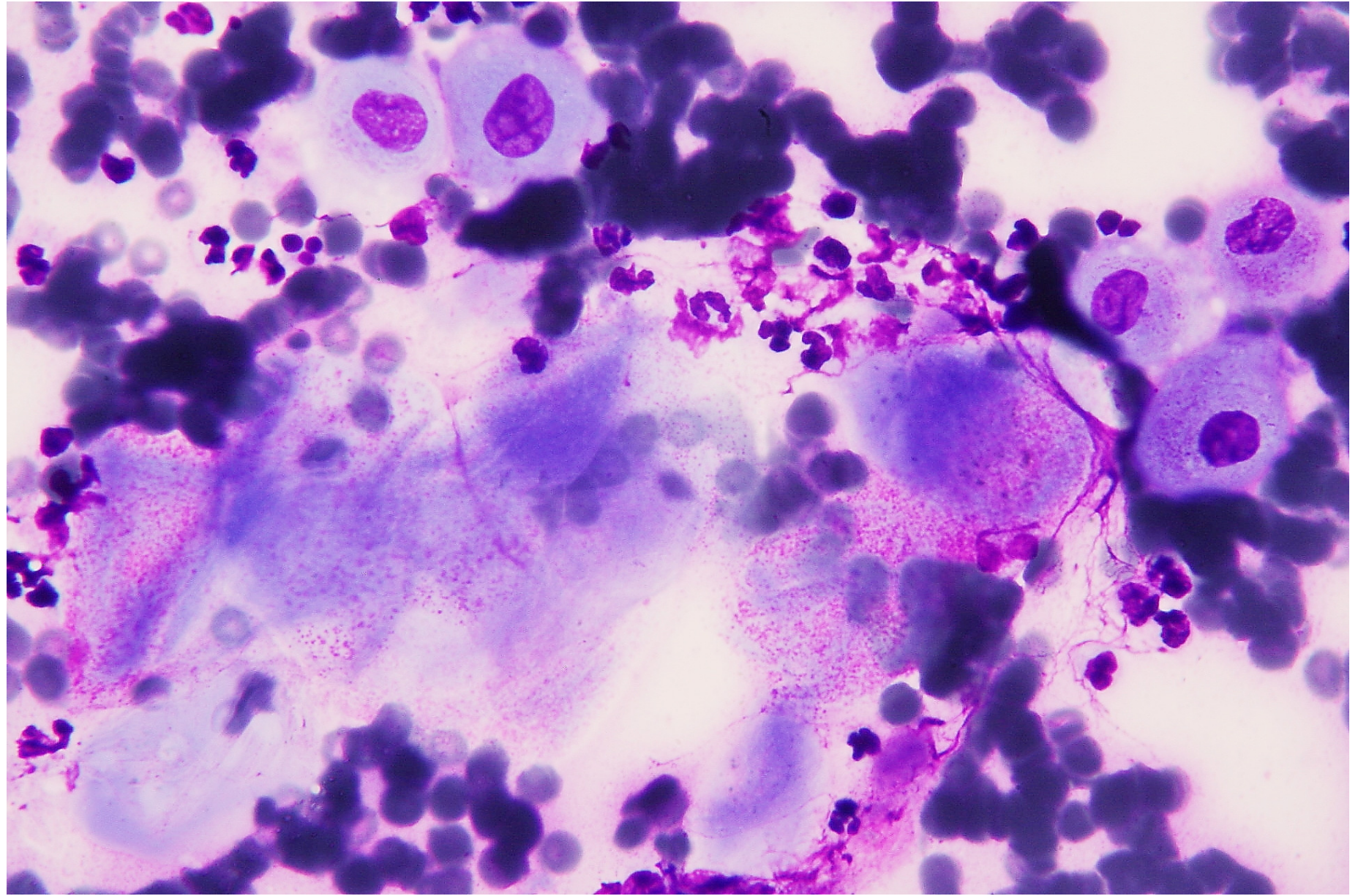
- Dog, mongrel, 16-year old, female
 - Small exophytic neoplasia in the external ear canal (neoplasia?)
 - Chronic otitis.
-
- Sample: cotton swab
 - Stain: MGG











Cytological findings

- Epithelial cells
 - Round to polygonal shape; sometimes mature keratinocytes
 - Small eosinophilic cytoplasmic granules
 - Round nucleus
 - Granular chromatin
- Inflammatory cells
 - Mostly well-preserved neutrophils



Diagnosis

- Cytological diagnosis:
 - Dysplasia ?
 - Abnormal cornification/keratinization?
 - Keratohyaline granules???



Discussion

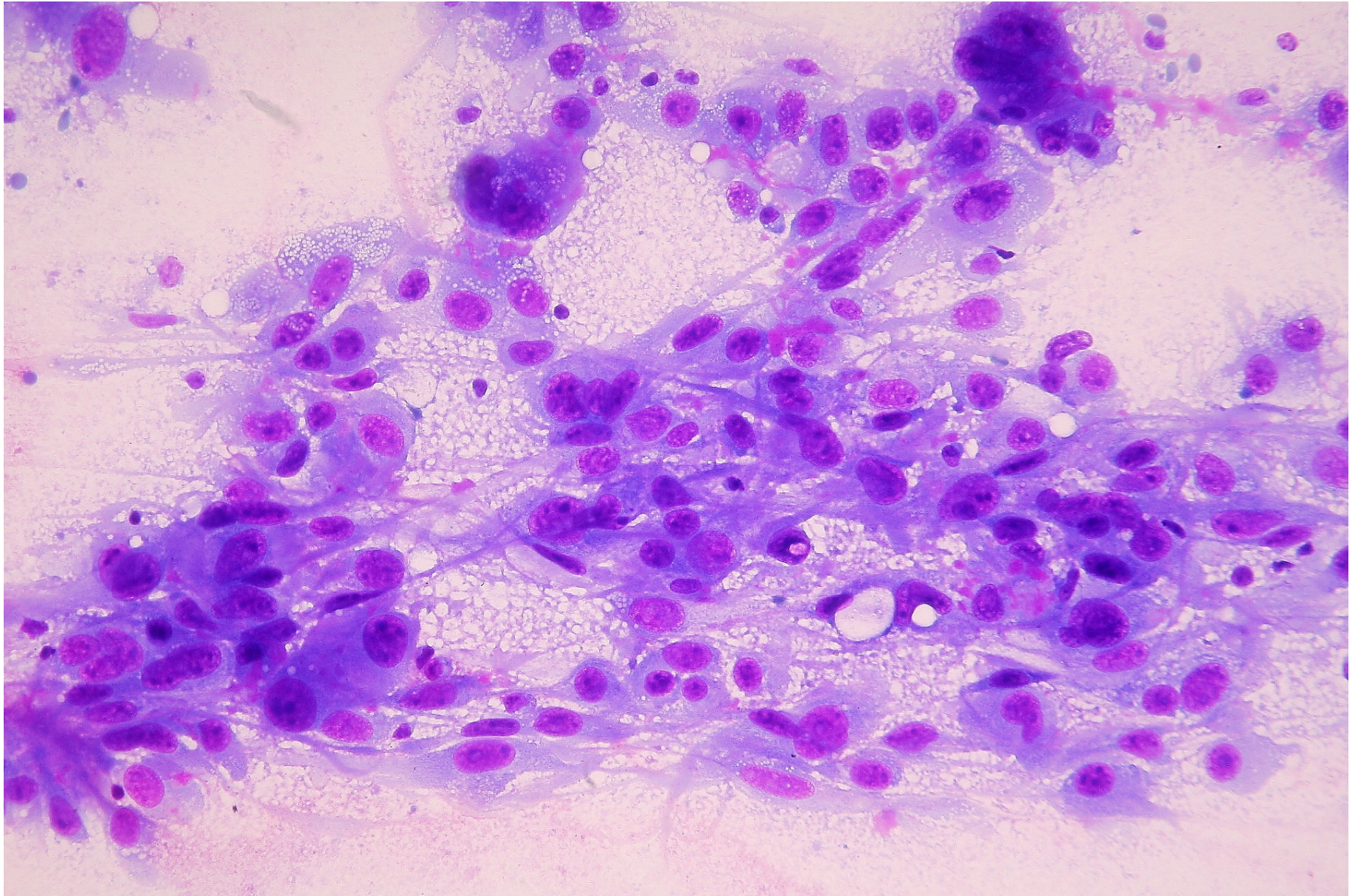
- Too small to be keratohyaline granules??
 - Consequence of dysplasia due to the inflammation?
 - Consequence of a primary, hidden lesion (non representative sample)?
 - Papillomavirus?
-
- The dog recovered after symptomatic therapy...
 - 030 9780153

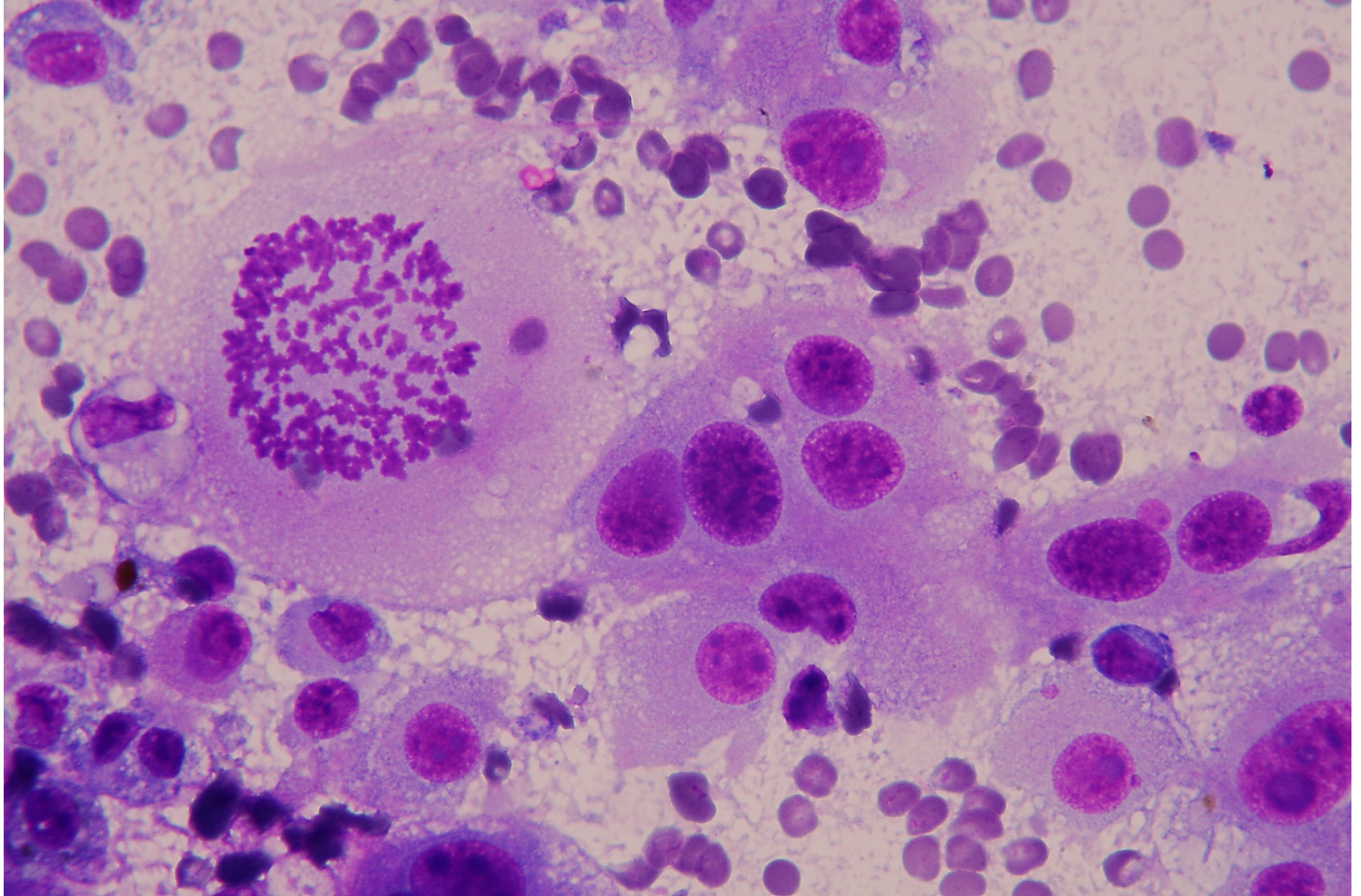


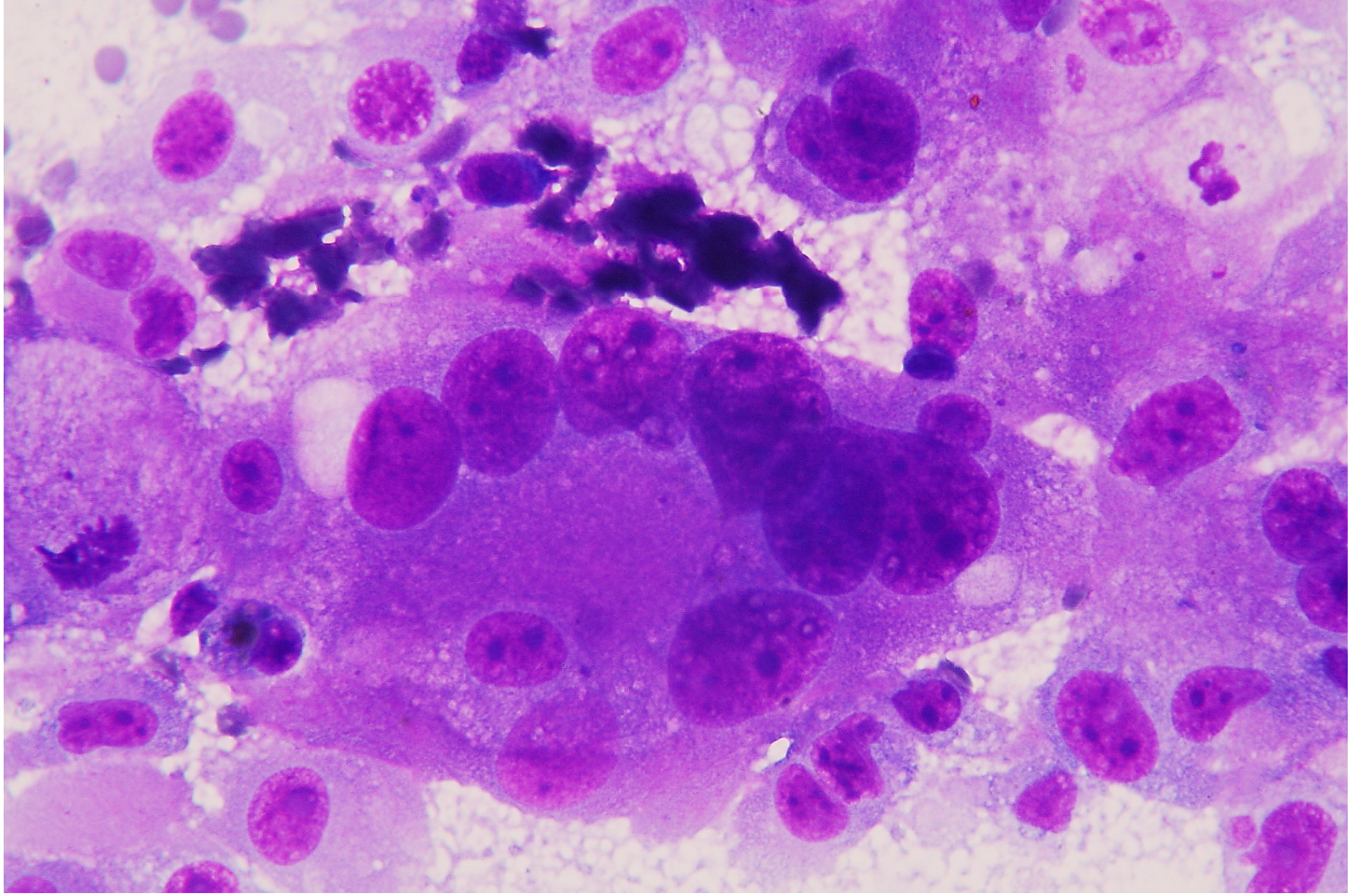
Case #5

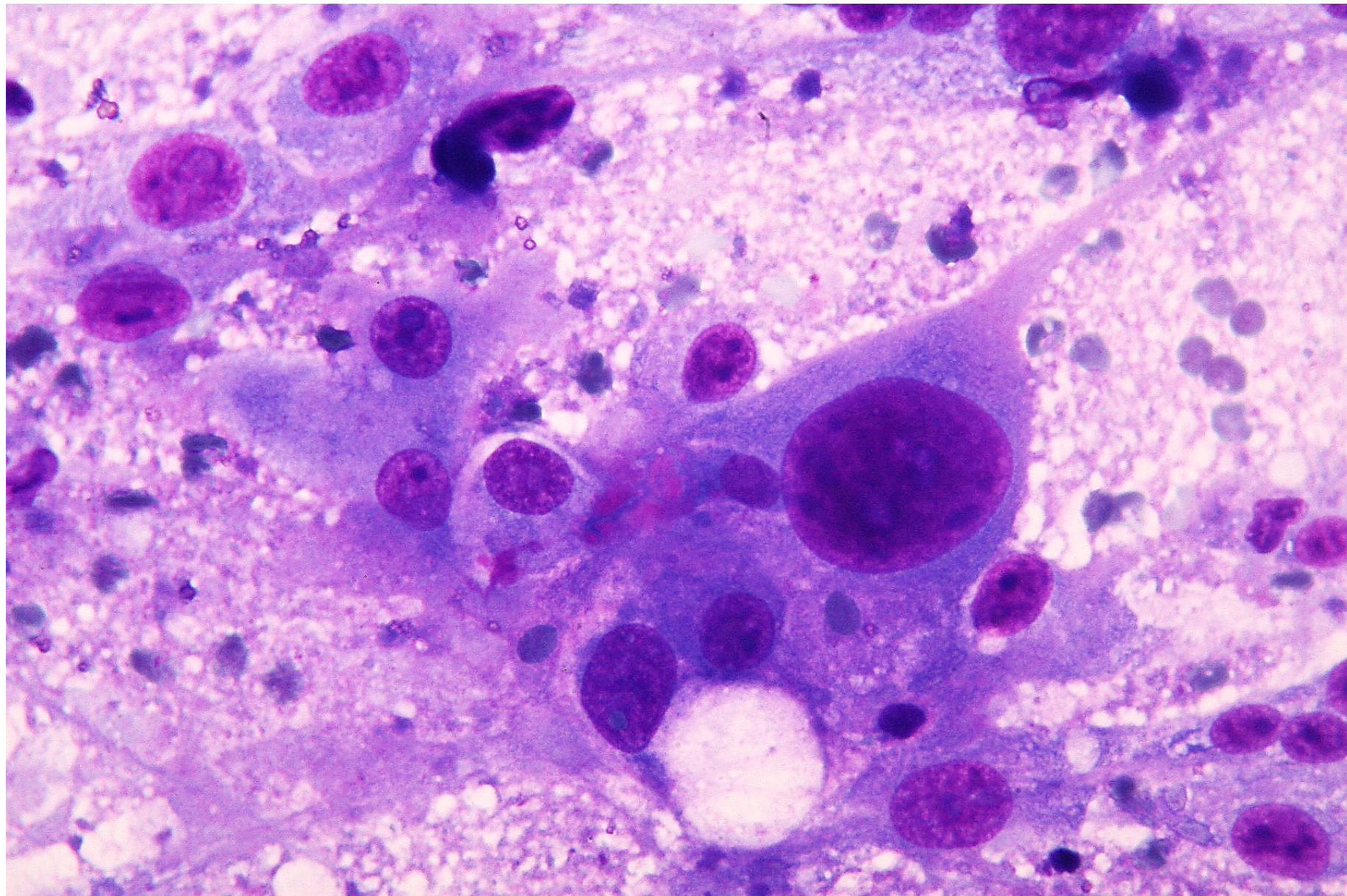
- Dog, Dobermann, 8.5-year old, male.
- Mass on the back
- Sample: FNCS
- Stain: MGG

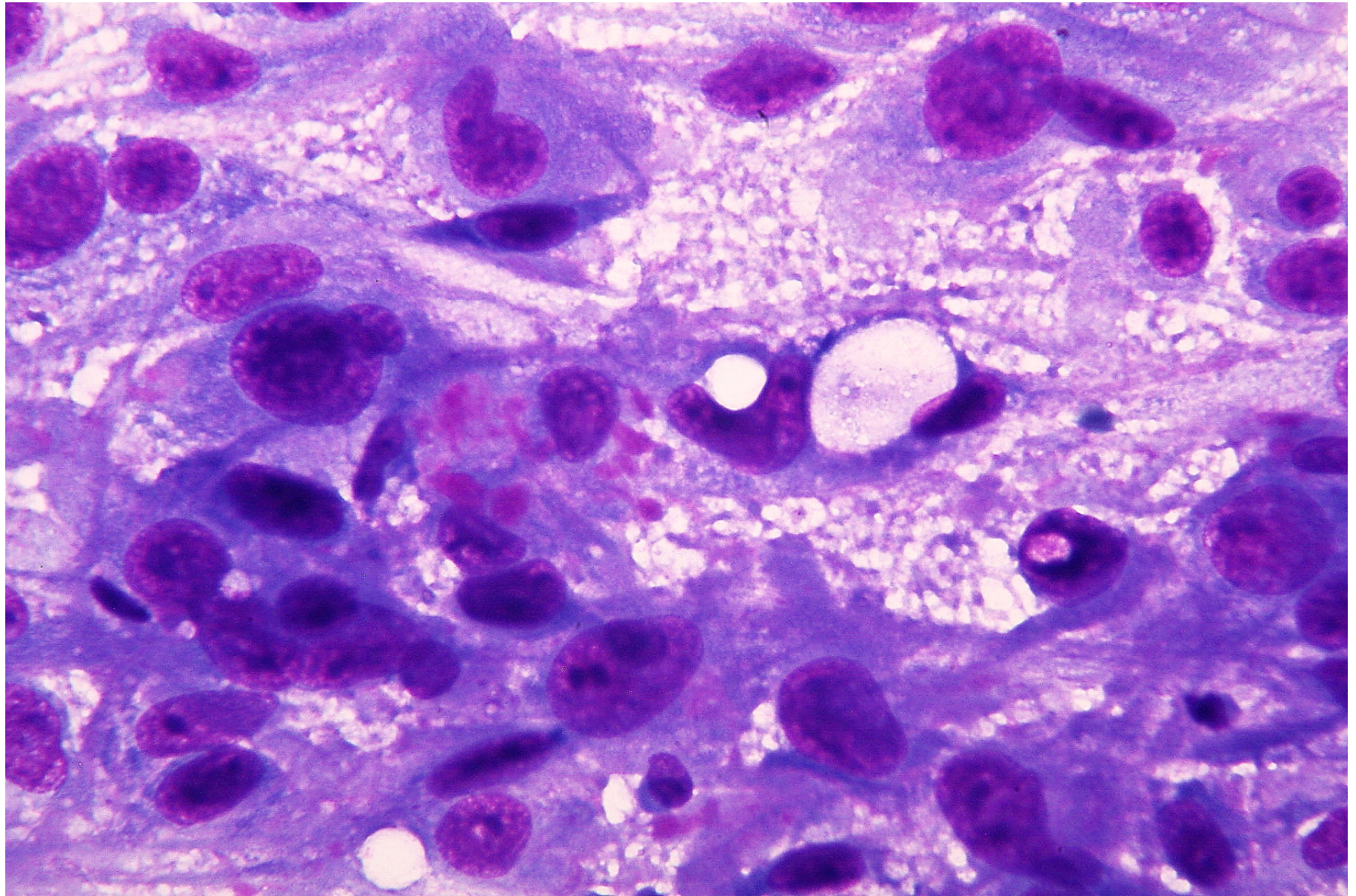


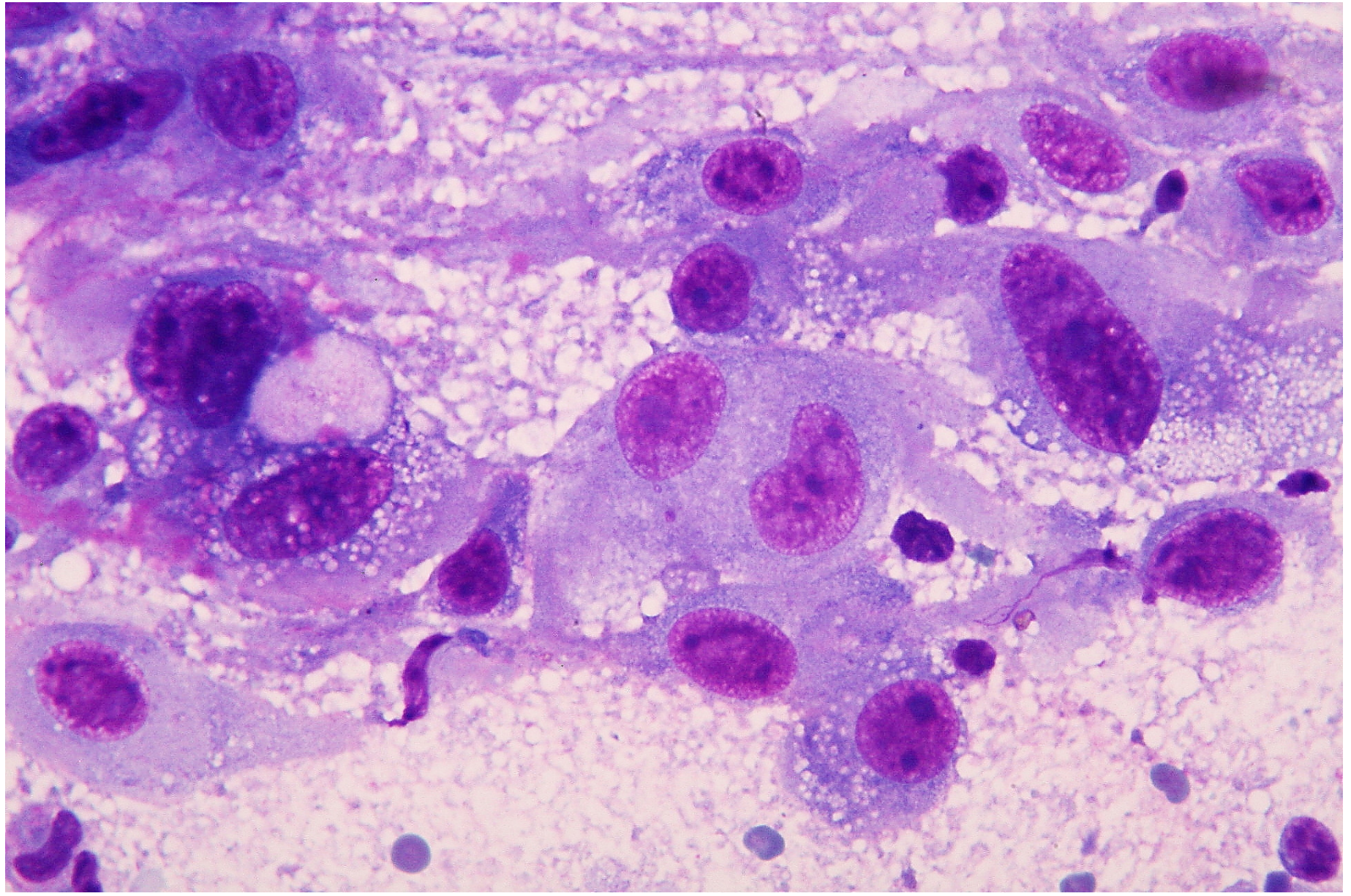


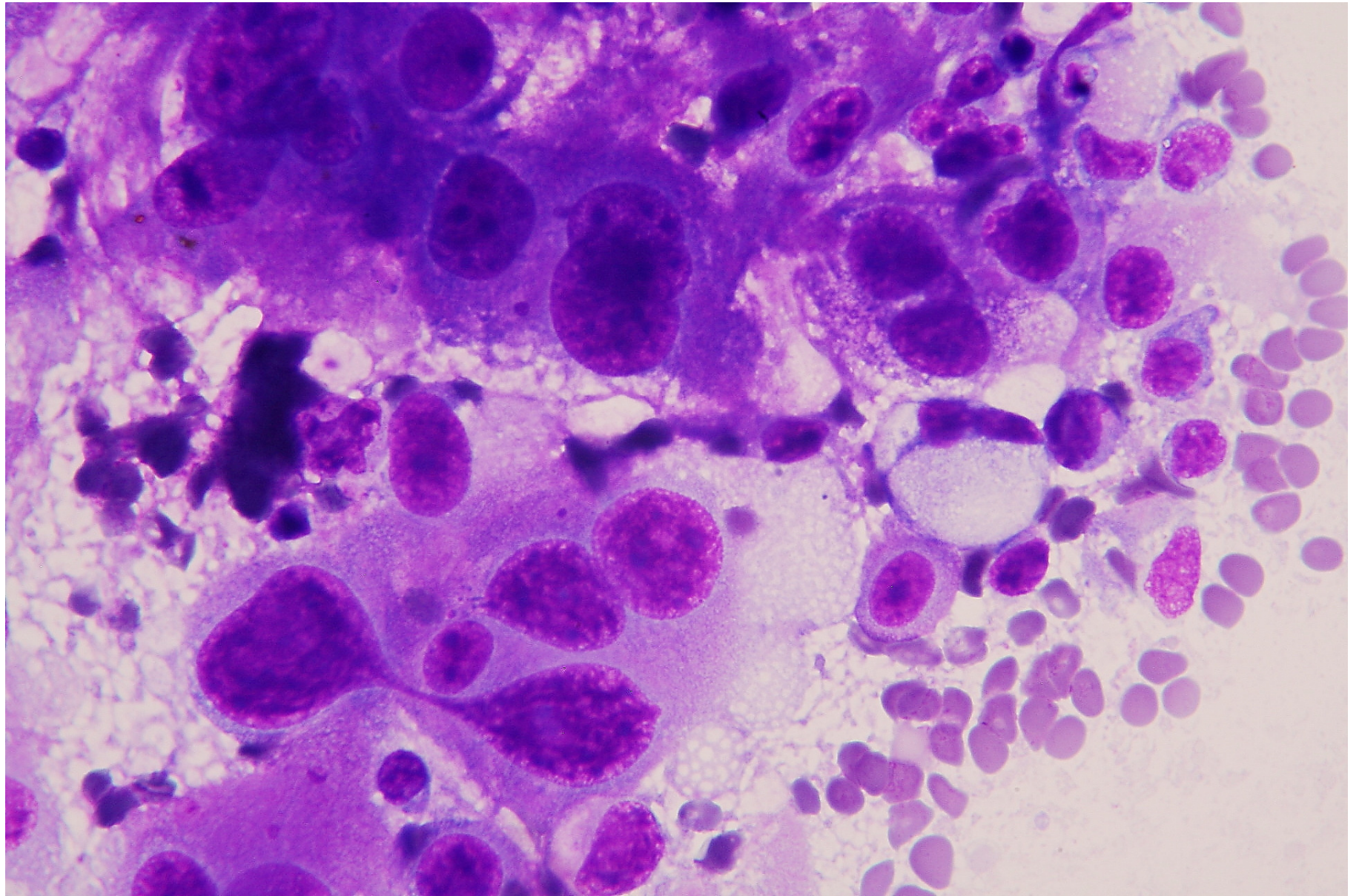








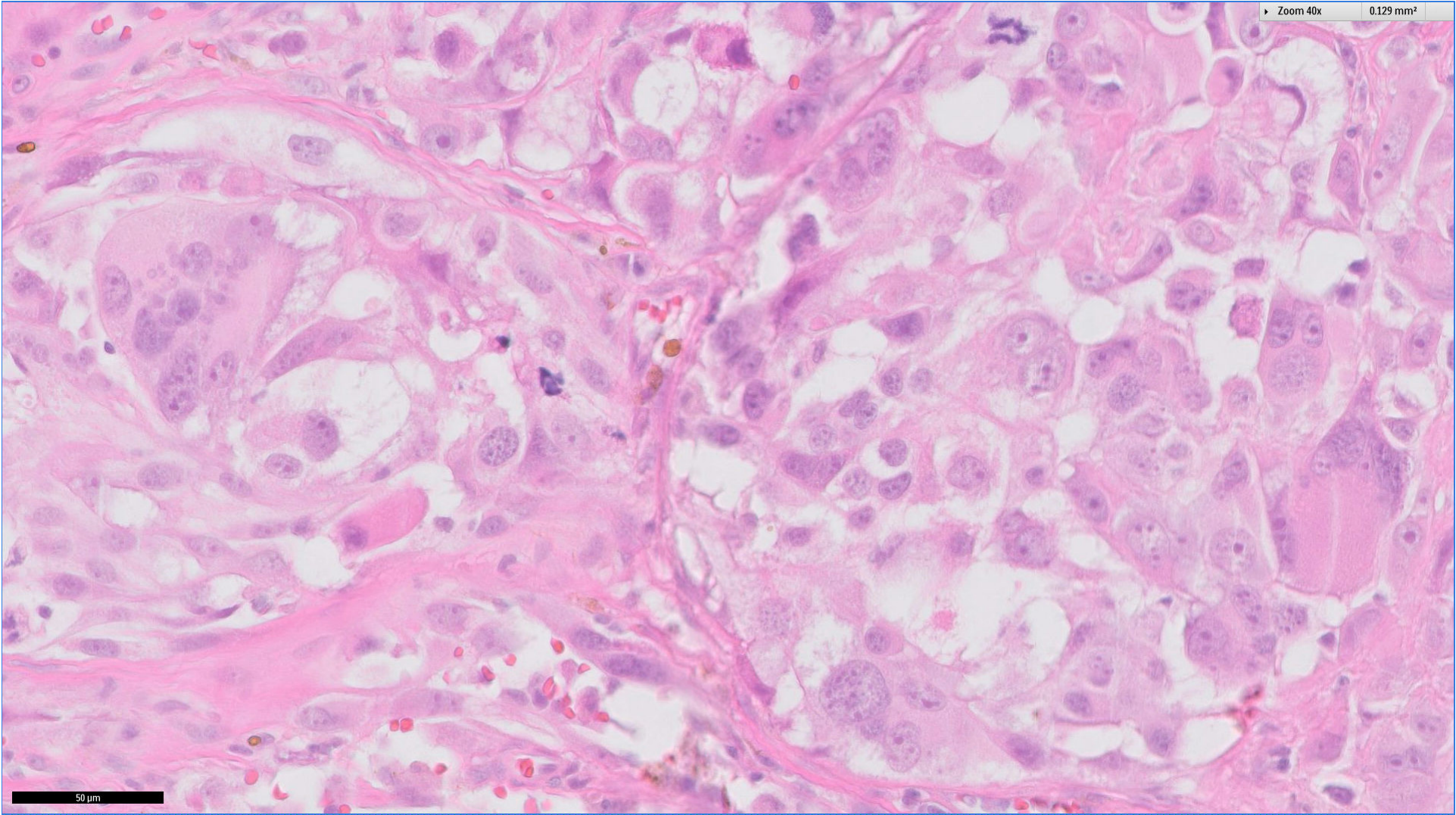


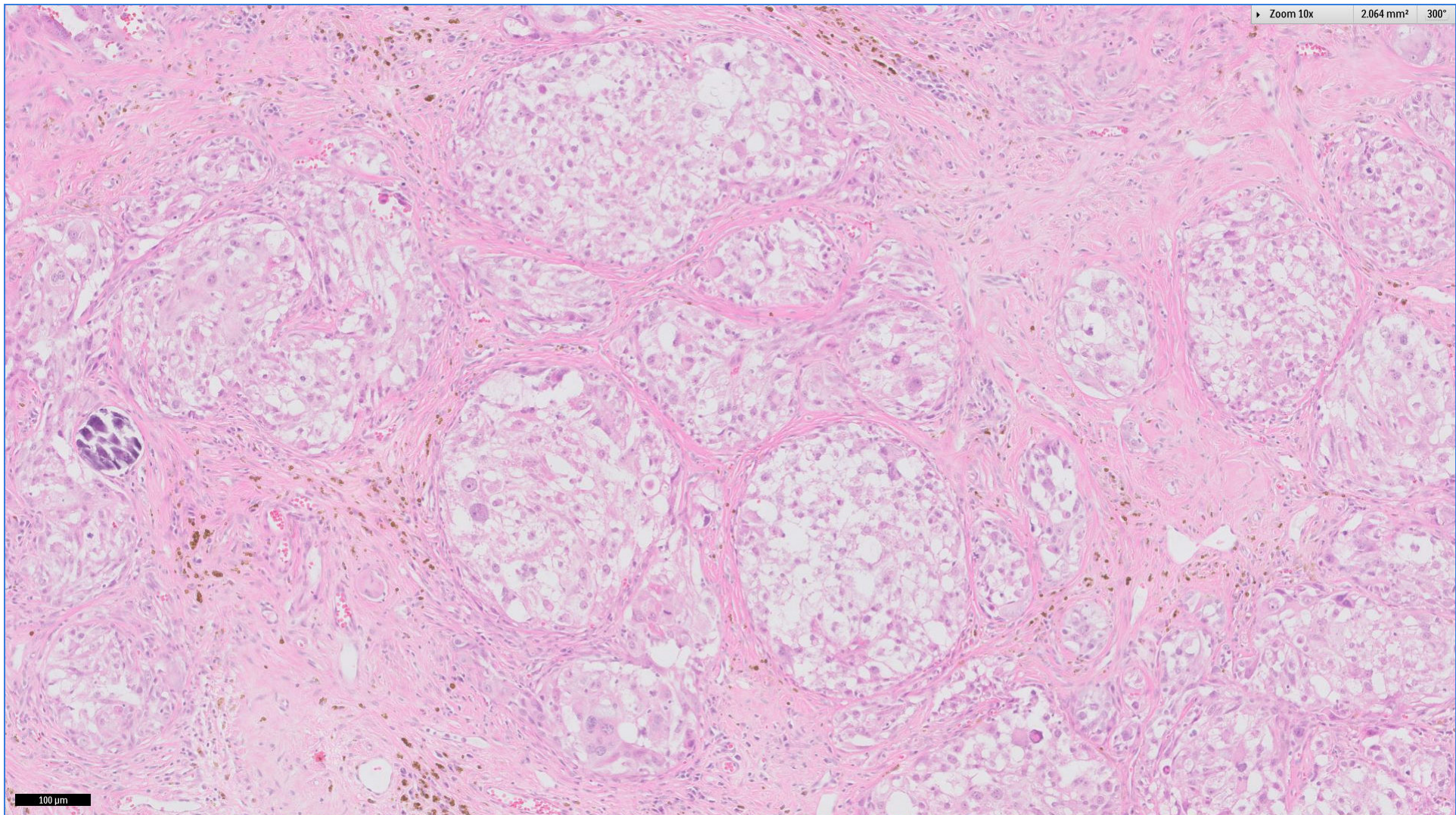


Cytologic findings

- Spindle cells
 - Basophilic cytoplasm
 - Sometimes filled with large lipid globules
 - Large round to ovoid nuclei
 - Peripheral displacement of nucleus
 - Deformed nucleus shape
 - Severe anisokaryosis and anisocytosis
- Presence of rare lipoblasts
- Multinucleated giant cells







Diagnosis

- Cytological diagnosis: poorly differentiated liposarcoma
- Histological diagnosis: pleomorphic liposarcoma



Discussion

- Cytological criteria for diagnosis:
 - Lipoblasts
 - Lipid globules that displace the nucleus



Discussion

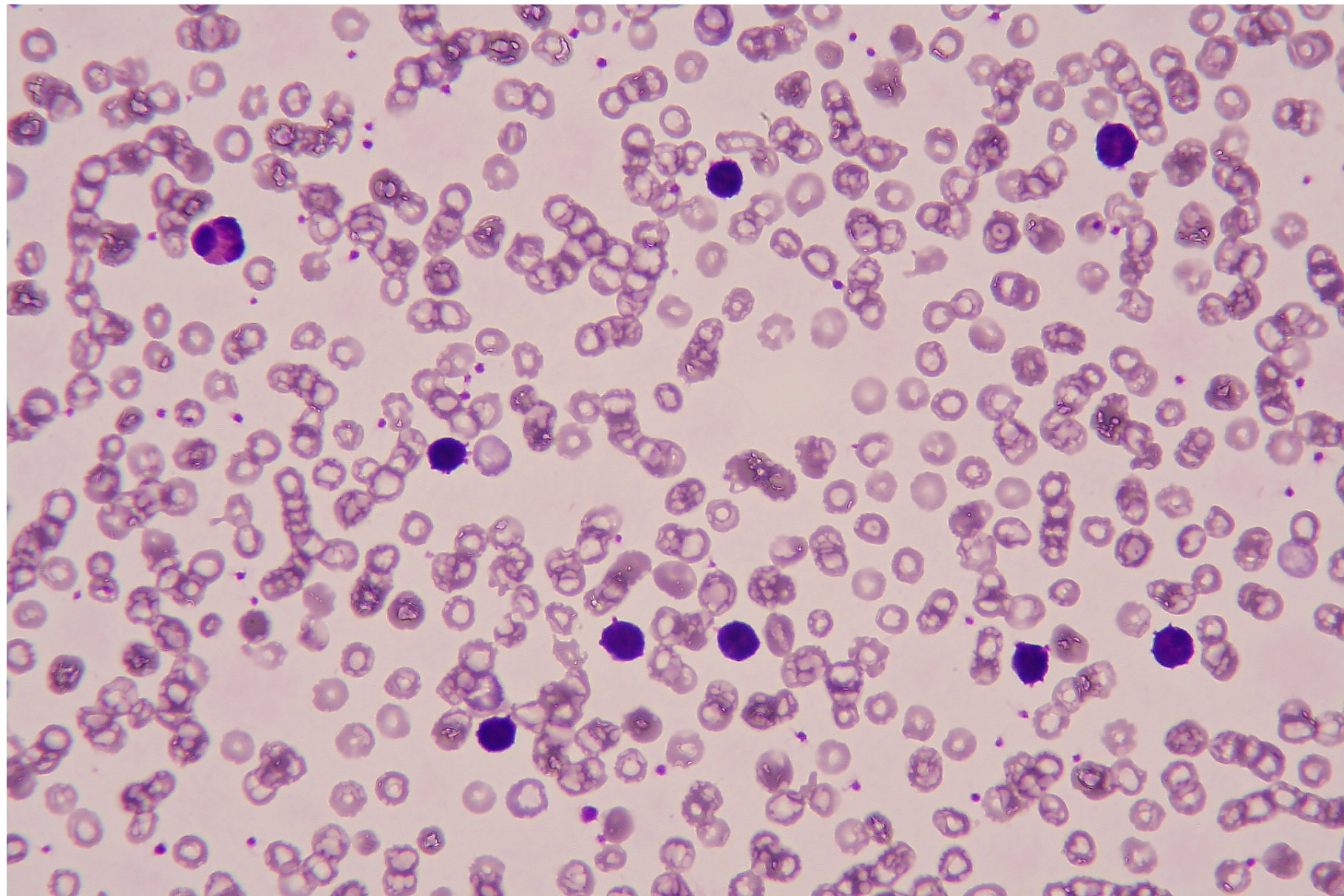
- **Liposarcoma** (Gross):
 - Atypical lipoma
 - Well differentiated liposarcoma
 - Myxoid liposarcoma
 - Pleomorphic liposarcoma
 - Rare variant
 - Giant cells common
 - Lipid vacuoles present in a small number of neoplastic cells
 - Nuclei exhibit marked variability in size and shape

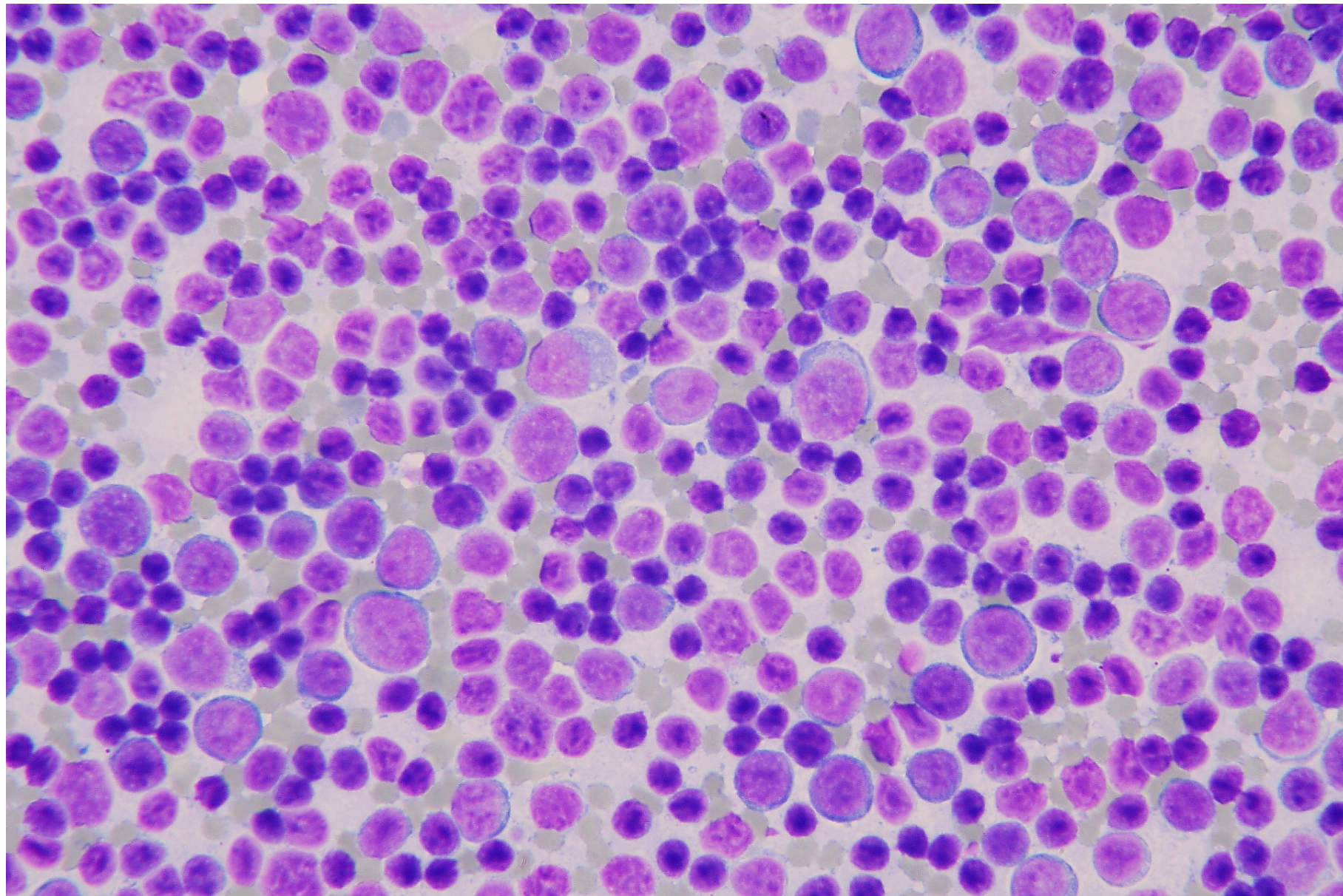


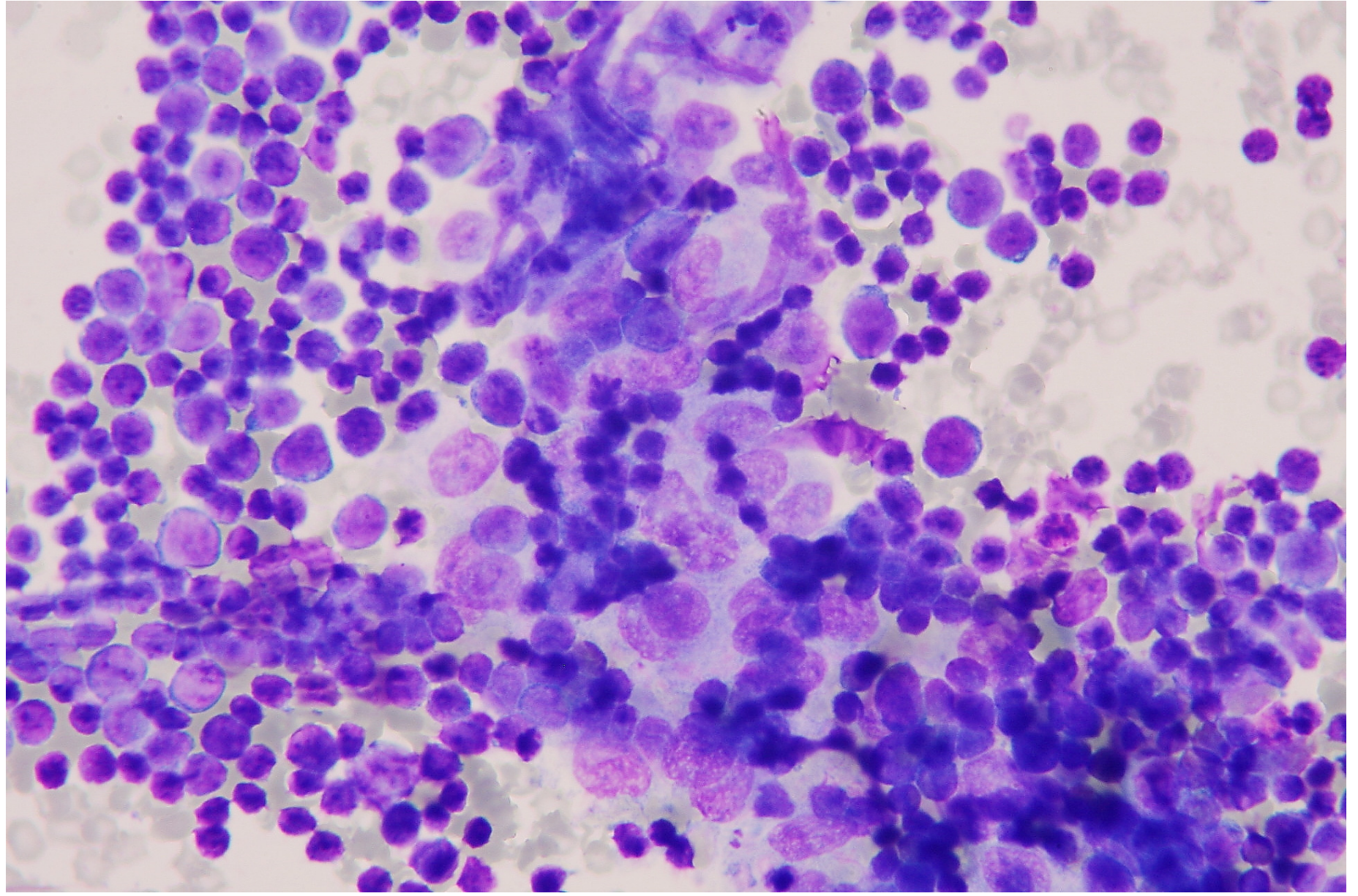
Case #6

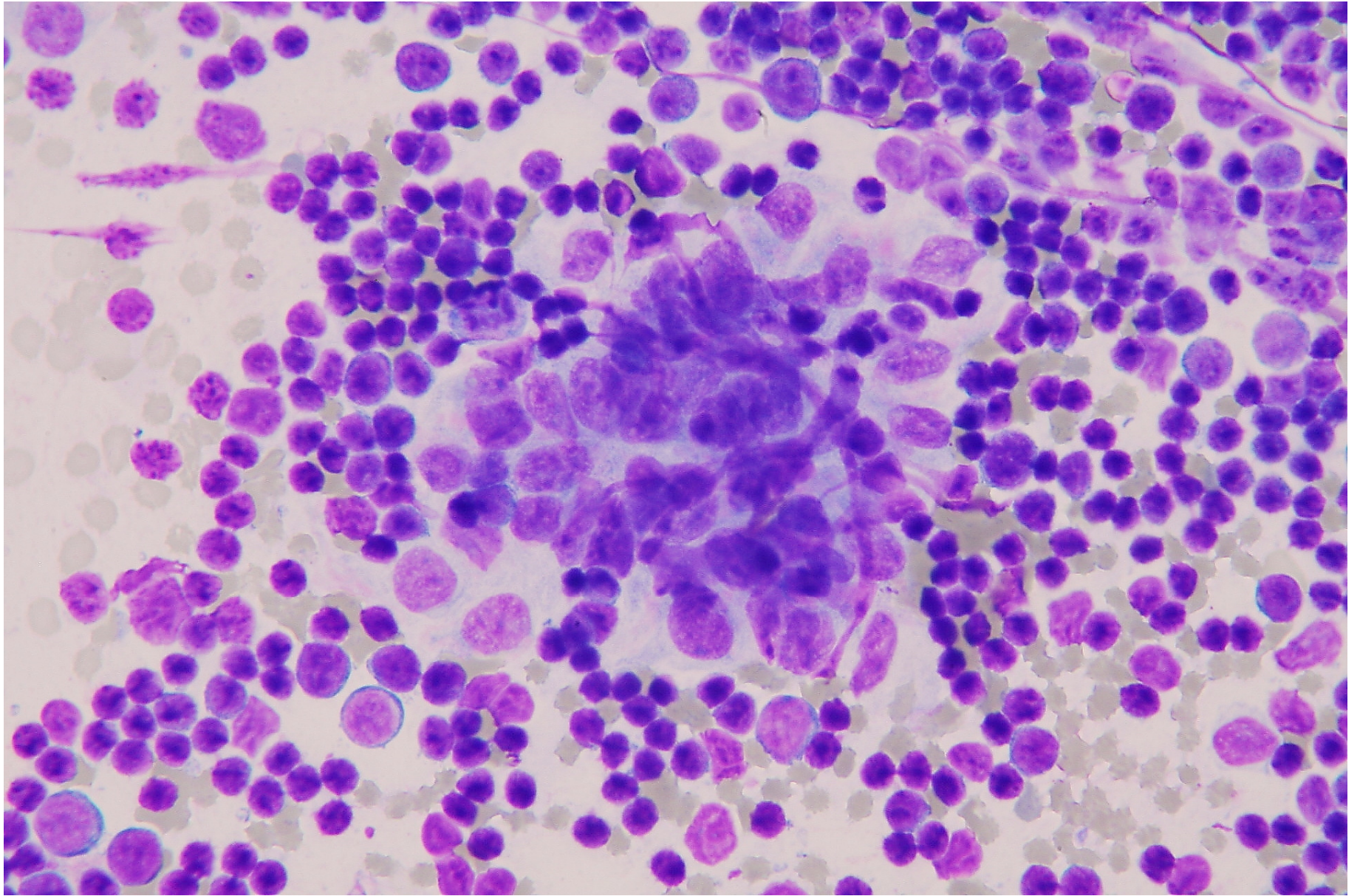
- Dwarf rabbit, 4-year old, male
 - Dispnoea
 - Mediastinal mass
 - Peripheral blood
- Sample: US-guided FNCS of mediastinal mass
- Blood: 35000 WBC
- Stain: MGG

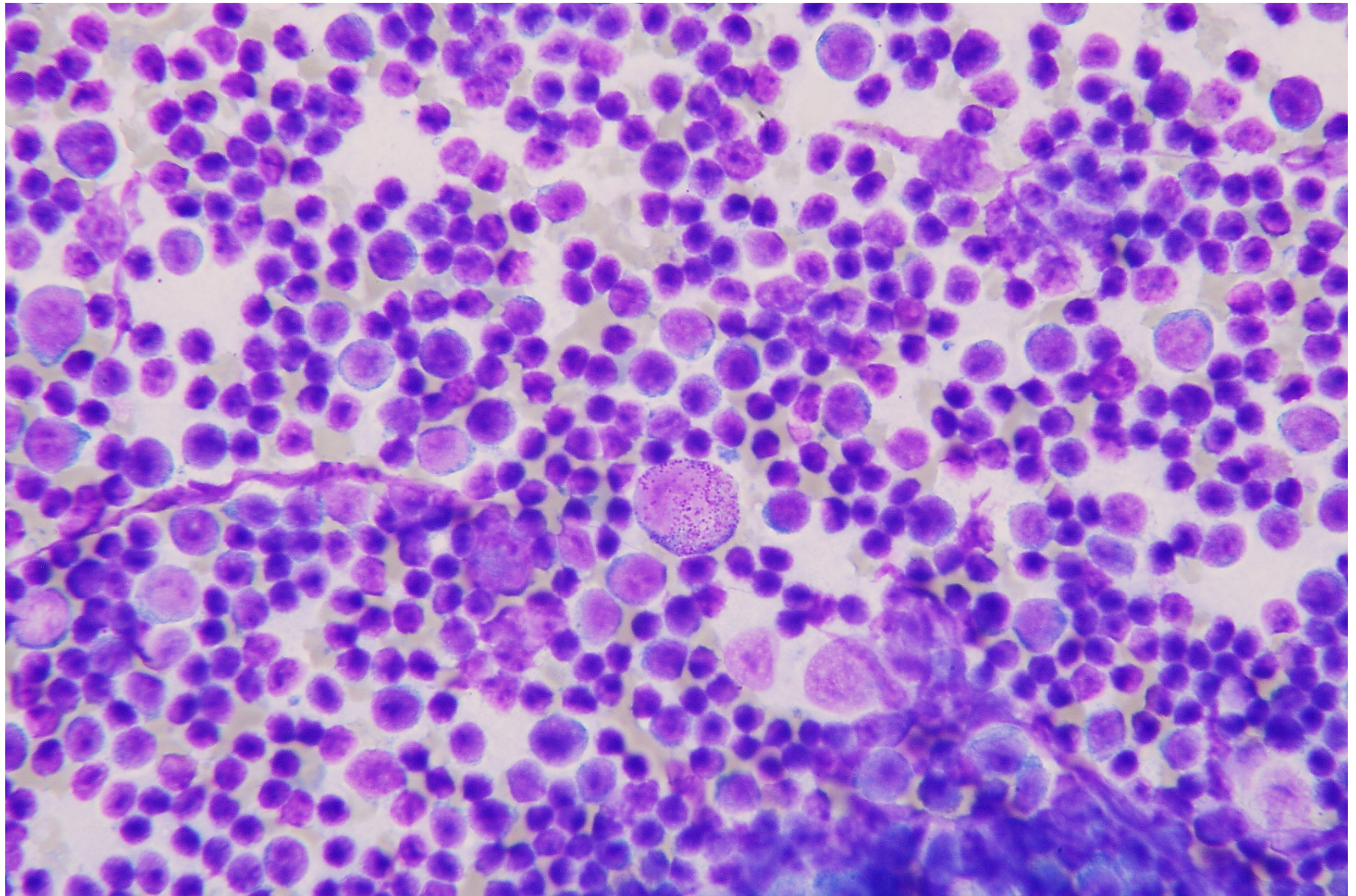








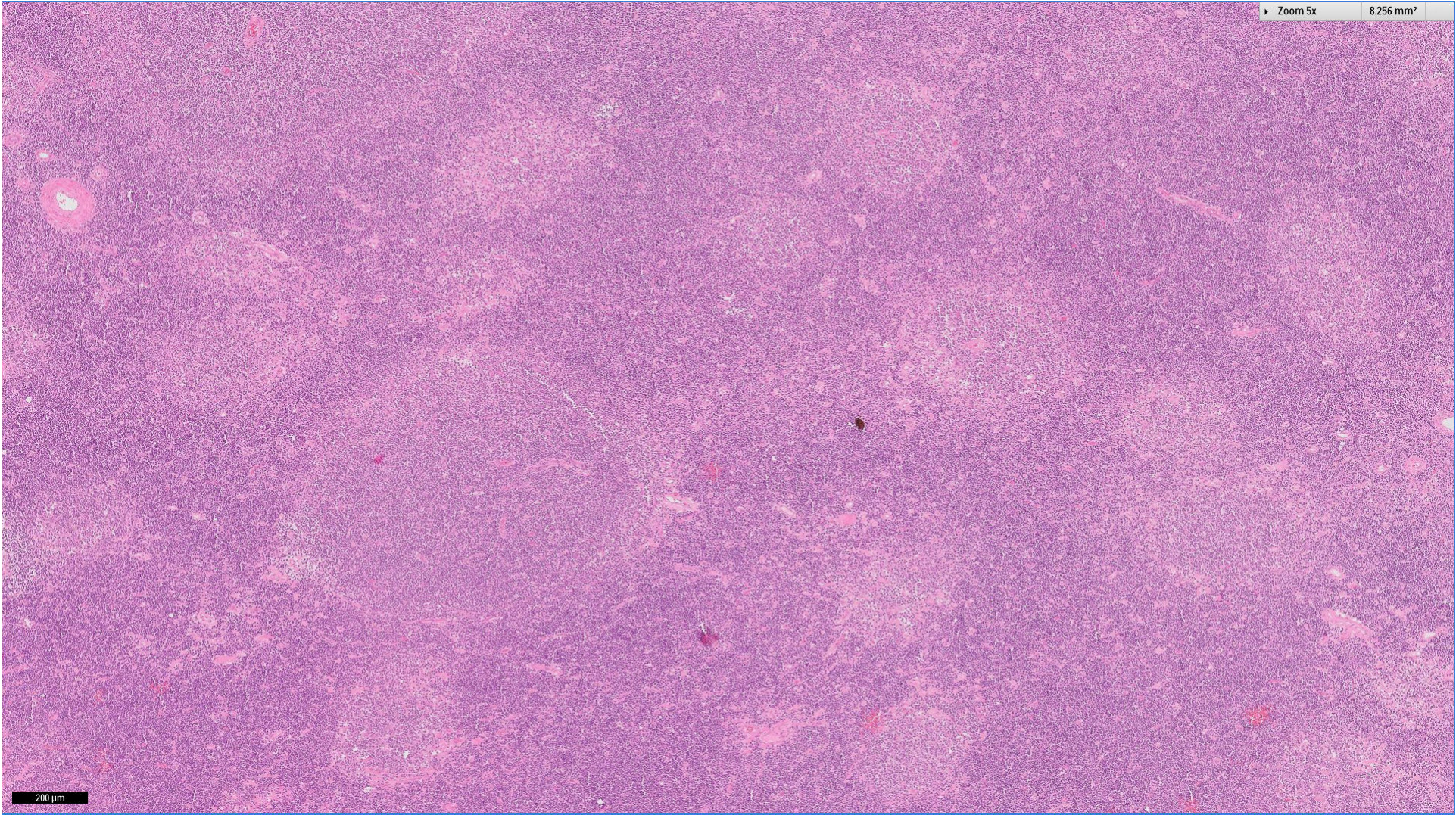


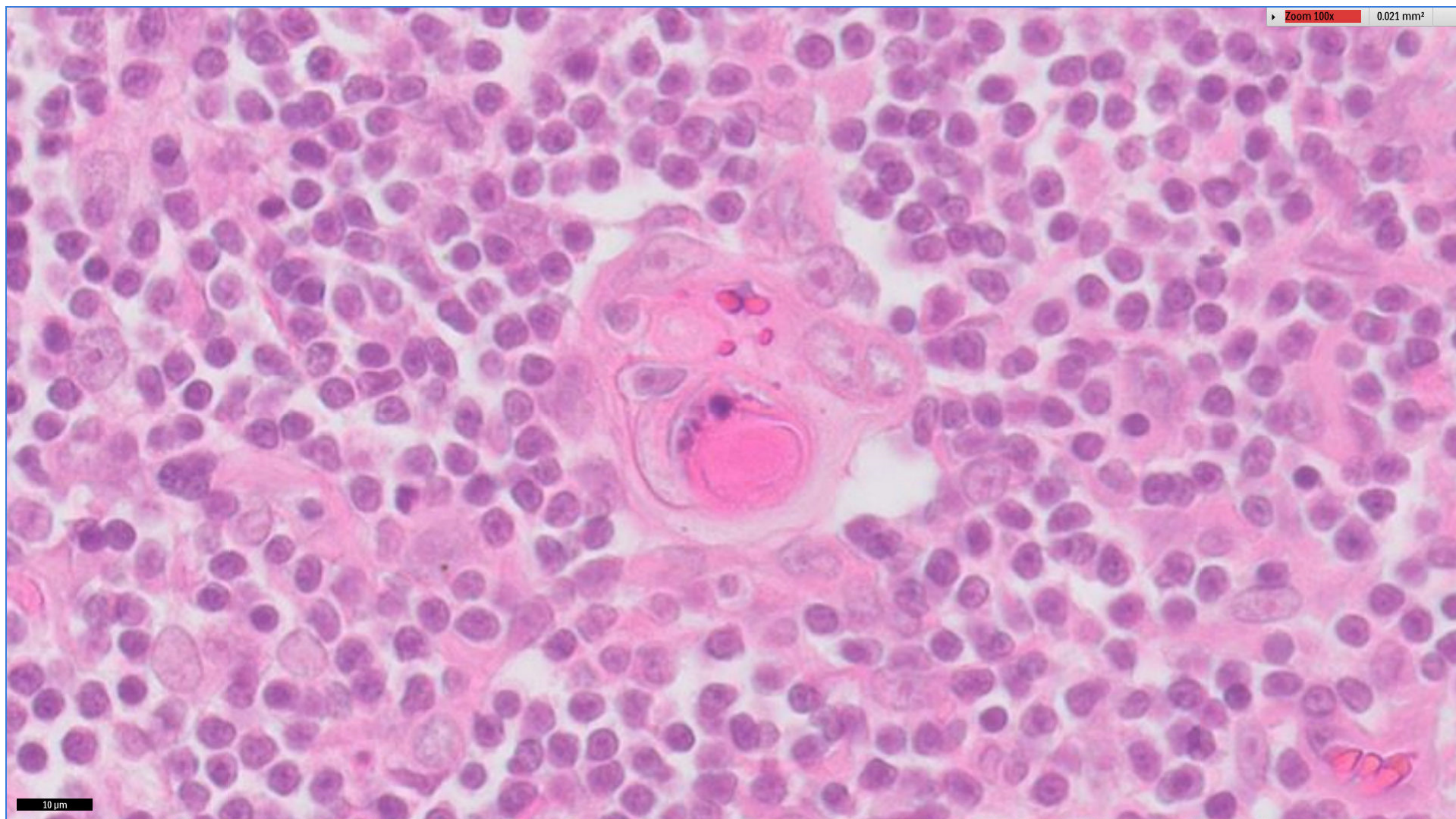


Cytologic findings

- Blood: lymphocytosis
 - Small mature lymphocytes
- Mediastinal mass
 - Polymorphic lymphoid population
 - Small aggregates of epithelial-like cells
 - Rare mast cells







Diagnosis

- Cytological diagnosis: thymoma, lymphocyte predominant
- Histologic diagnosis: thymoma



Discussion

- Künzel F et al. Thymomas in rabbits: clinical evaluation, diagnosis, and treatment. J Am Anim Hosp Assoc. 2012 Mar-Apr;48(2):97-104.
- Cytological criteria for diagnosis of thymoma Künzel, 2012
 - Mixed population of small, intermediate and large lymphocytes
 - Variable amount of epithelial cells (Hassal corpuscles)
 - Mast cells (?)
- Blood
 - 4/8 rabbits with leukocytosis
 - 4/8 rabbits with lymphocytosis



Discussion

- Mediastinal mass in rabbit:
 - Thymoma
 - Thymic lymphoma
 - Mediastinal abscess

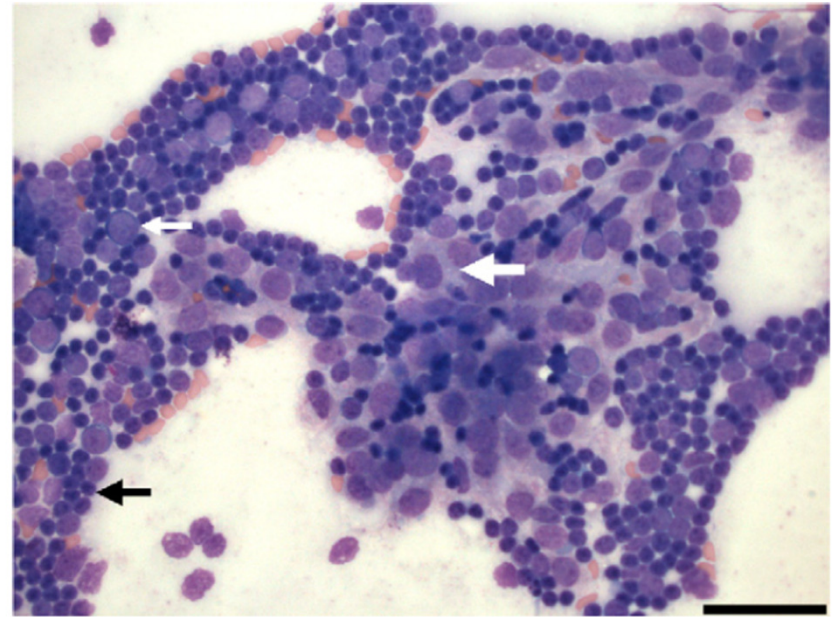


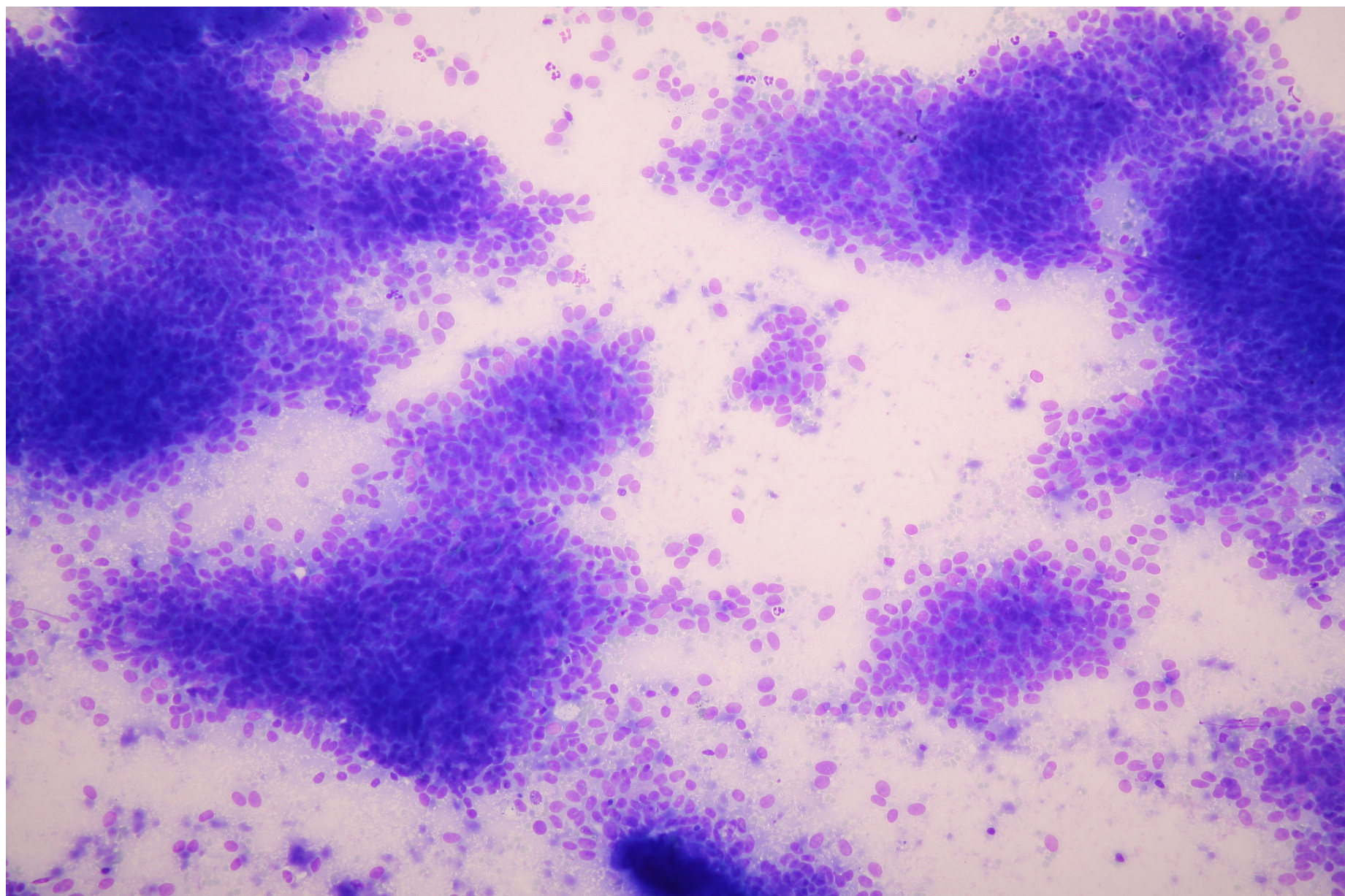
FIGURE 4 Cytology of a thymoma. Note the cluster of thymic epithelium (large white arrow) surrounded by a mixed population of large (thin white arrow) and small (black arrow) lymphocytes. The presence of a heterogeneous lymphocytic population differentiates thymomas from thymic lymphomas. Diff-Quick staining, original magnification $\times 400$.

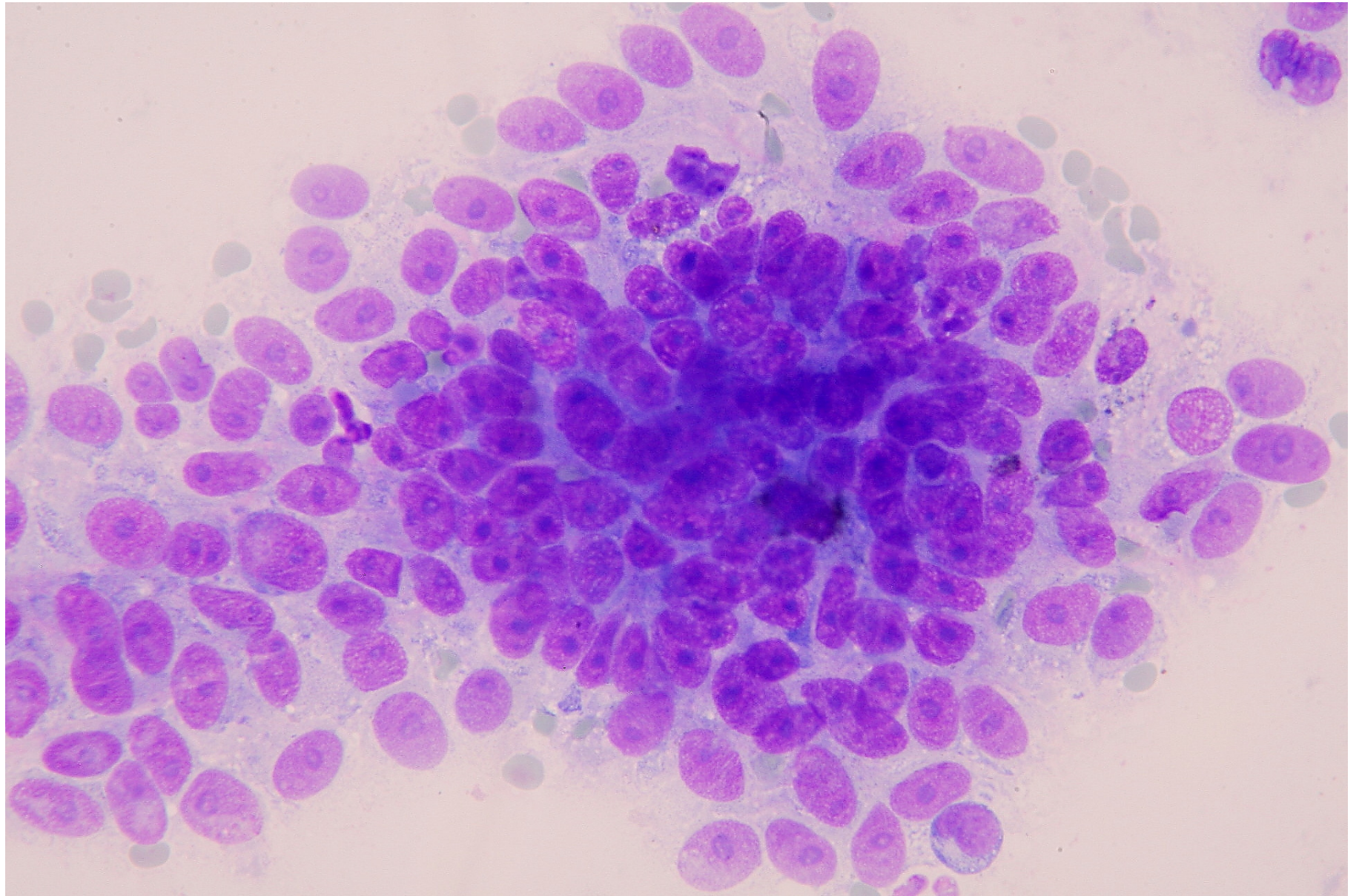


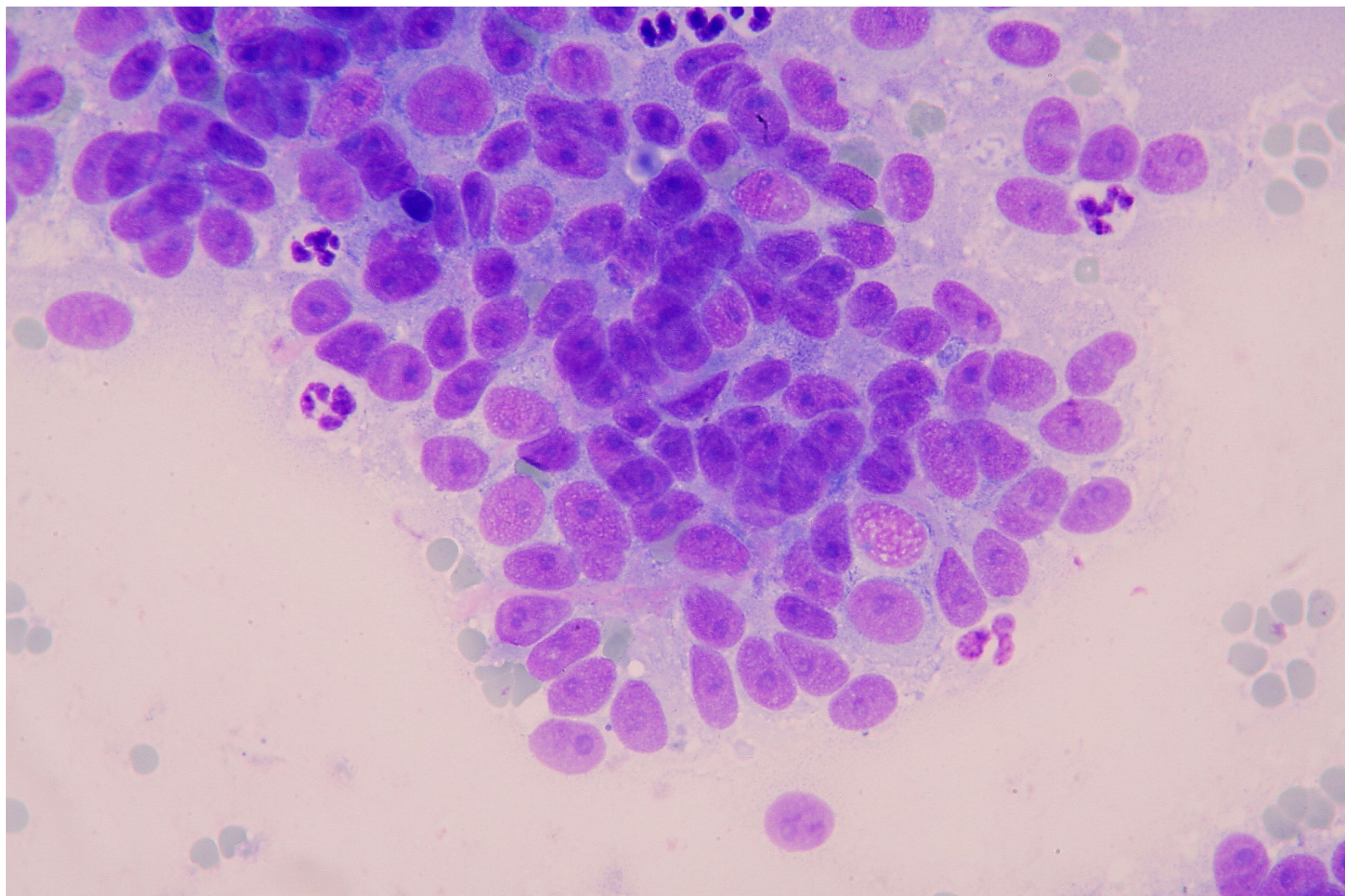
Case #7

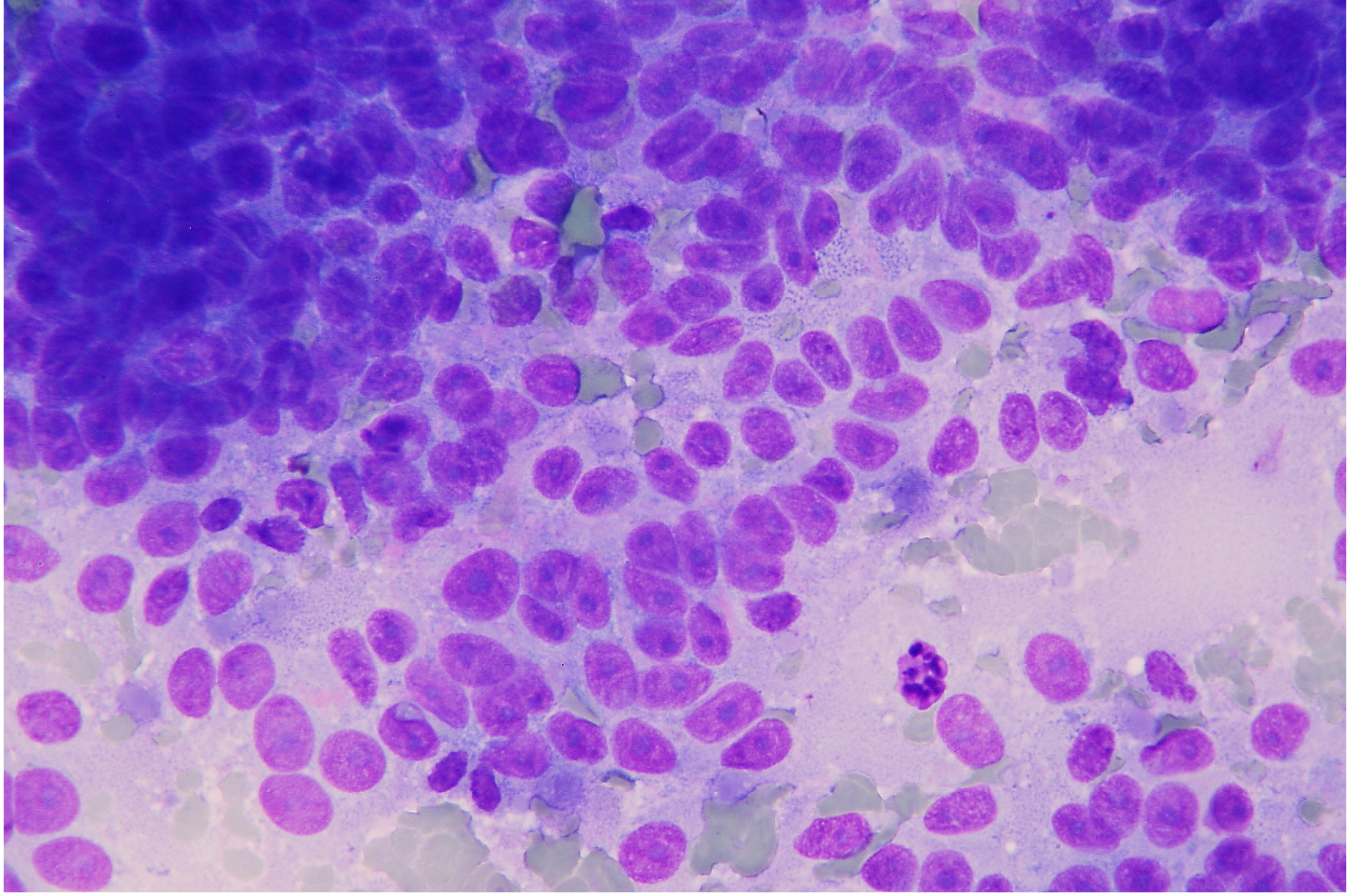
- Cat, DSH, 18-year old, female
 - Mass in the anterior chambers of eye.
-
- Sample: FNCS
 - Stain: MGG







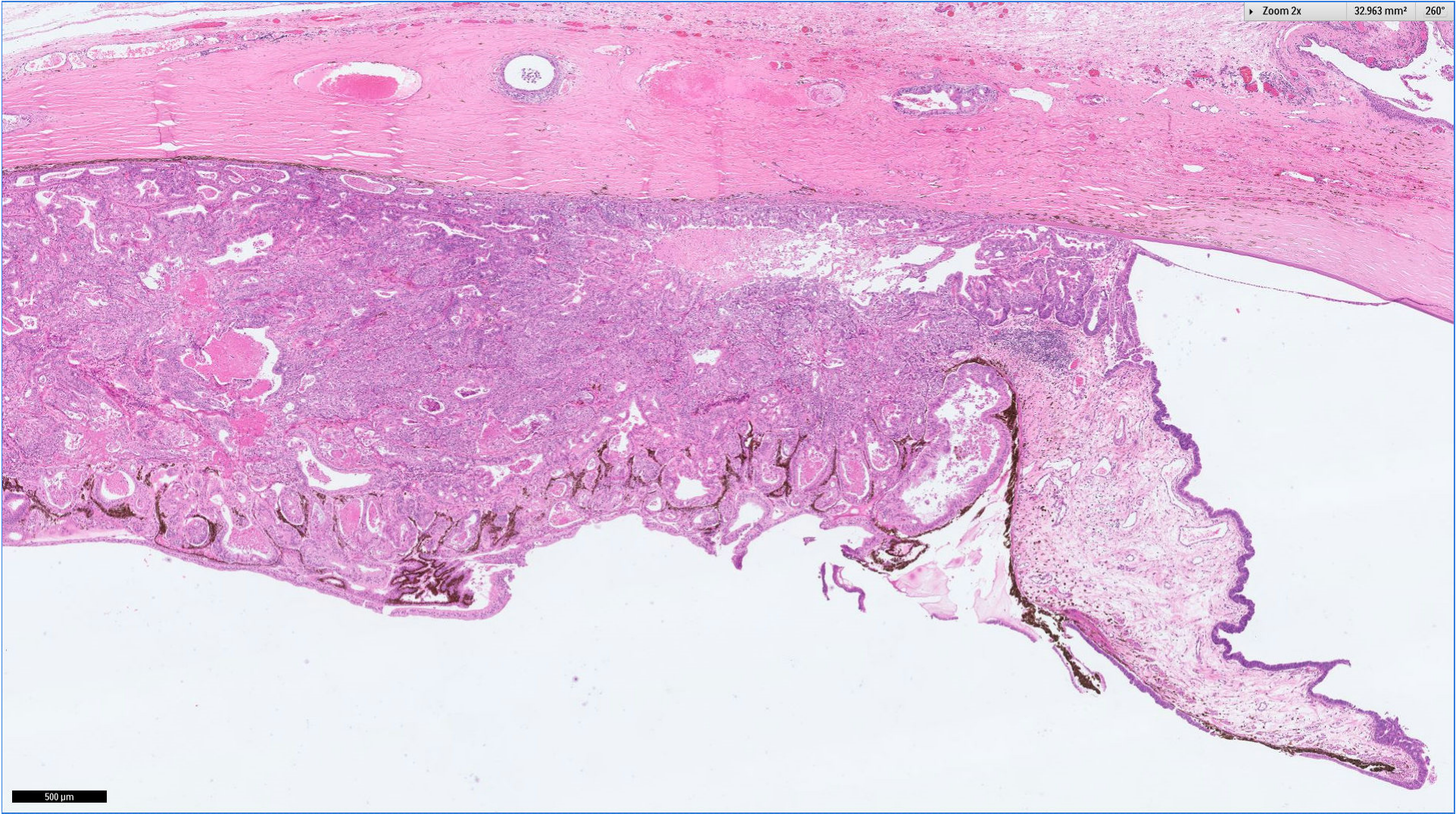


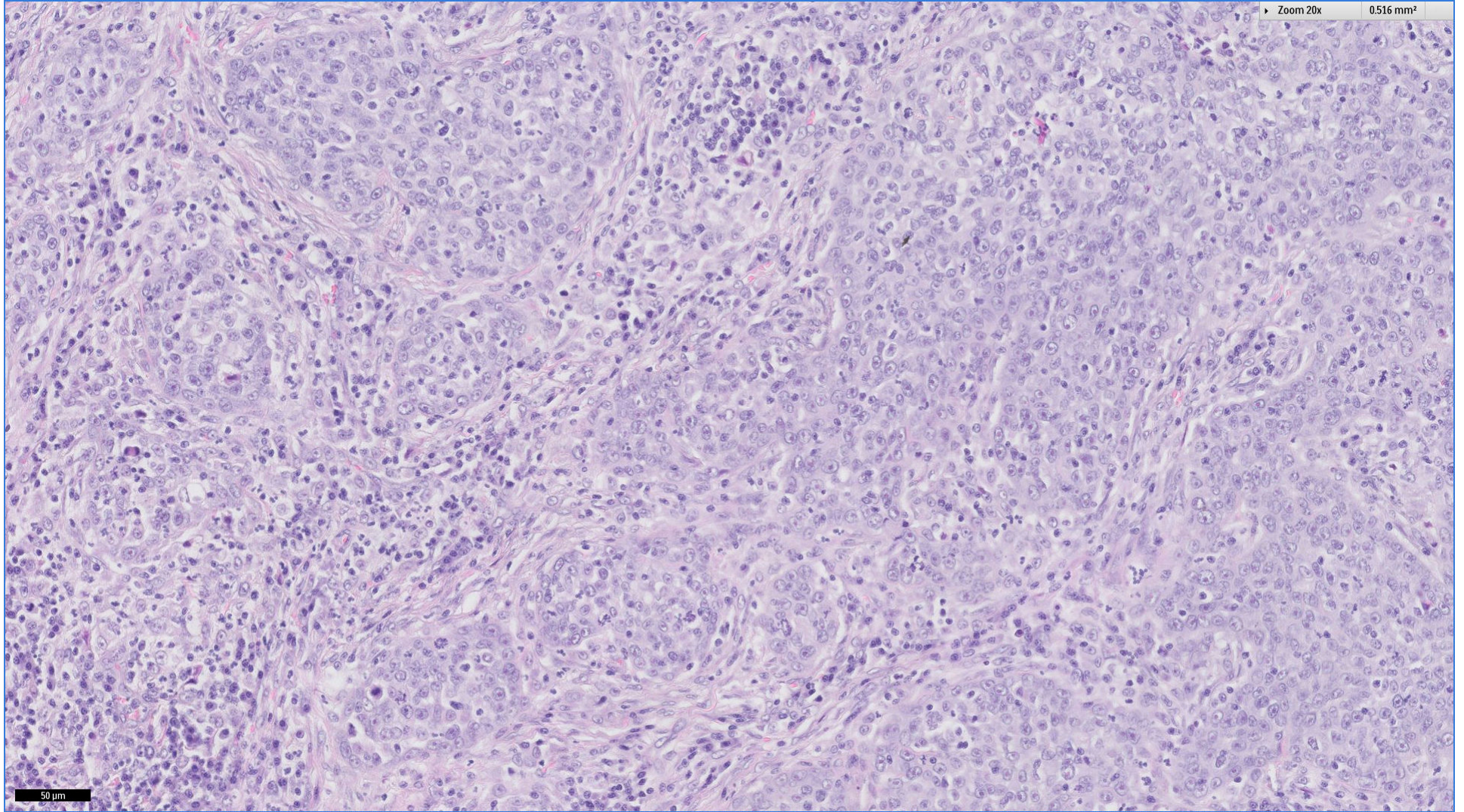


Cytologic findings

- Large clusters of epithelial cells
 - Indistinct, slightly blue cytoplasm
 - Round to ovoid nuclei
 - Anisocytosis and anisokaryosis slight to moderate
- Arrangements:
 - Acinar
 - Rows to tubular







Diagnosis

- Cytological diagnosis: malignant epithelial neoplasia, suggestive of iridociliary carcinoma
- Histological diagnosis: iridociliary carcinoma



Discussion

- Iridociliary carcinoma

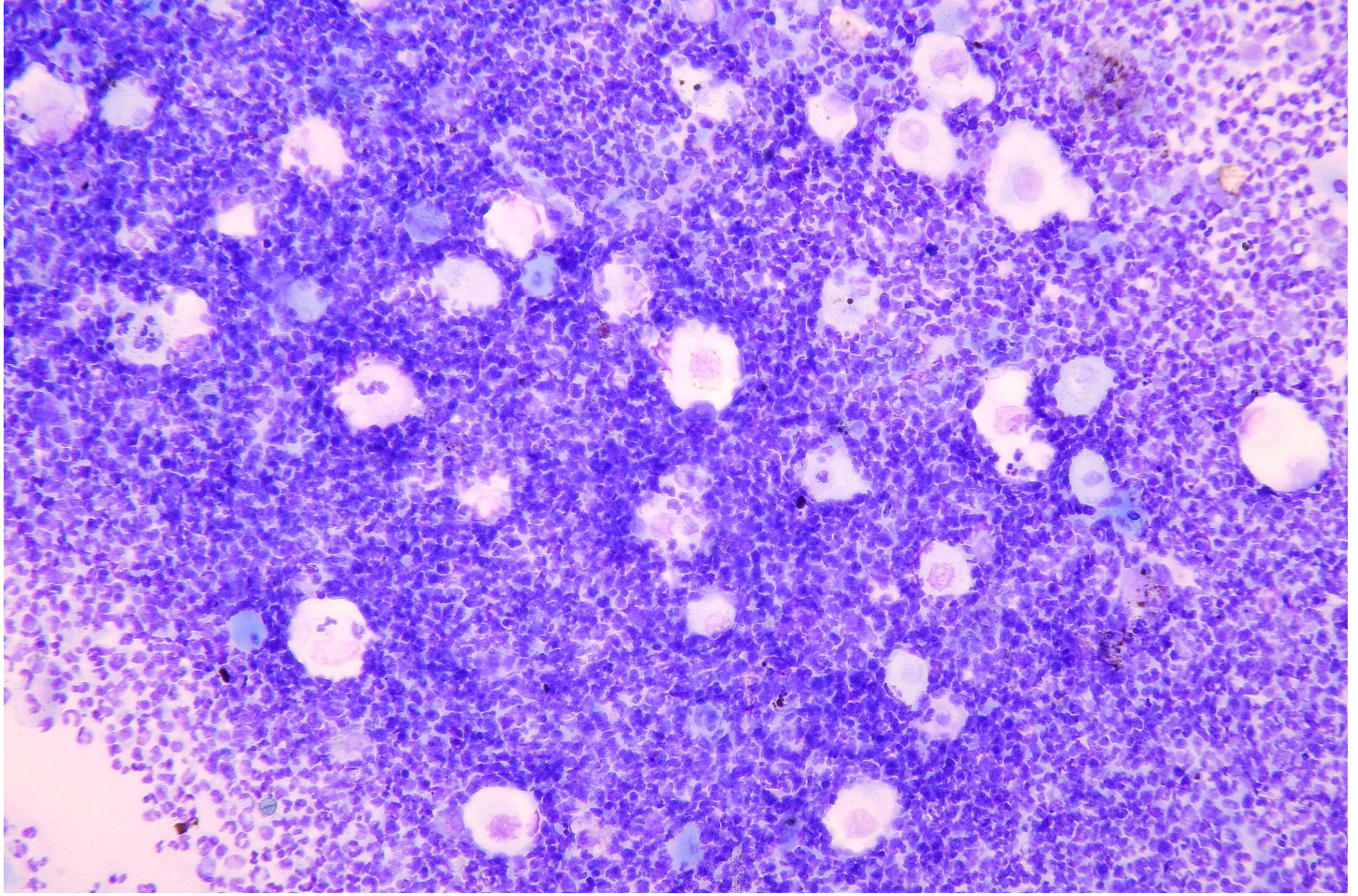
- [Dubielzig RR](#) et al. Iridociliary epithelial tumors in 100 dogs and 17 cats: a morphological study. [Vet Ophthalmol.](#) 1998;1(4):223-231.
- Rare tumor, but second most common primary intraocular tumor in dogs and cats
- It arise from pigmented and non-pigmented epithelial cells
 - Positive staining for vimentin, S-100, and NSE
- In cat less common
 - All of the feline tumors were nonpigmented and 14 of 16 feline tumors were solid and two of the tumors were papillary

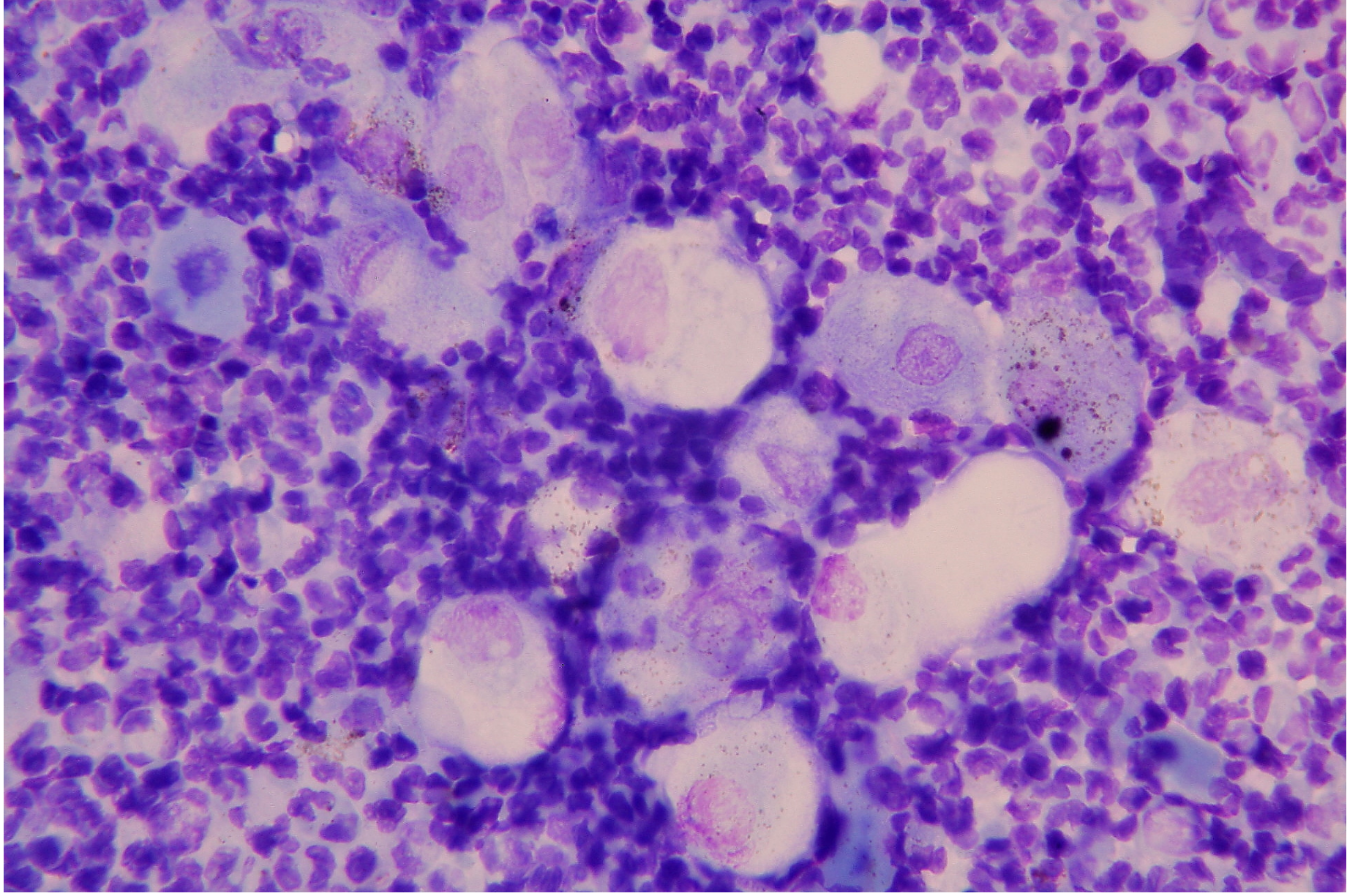


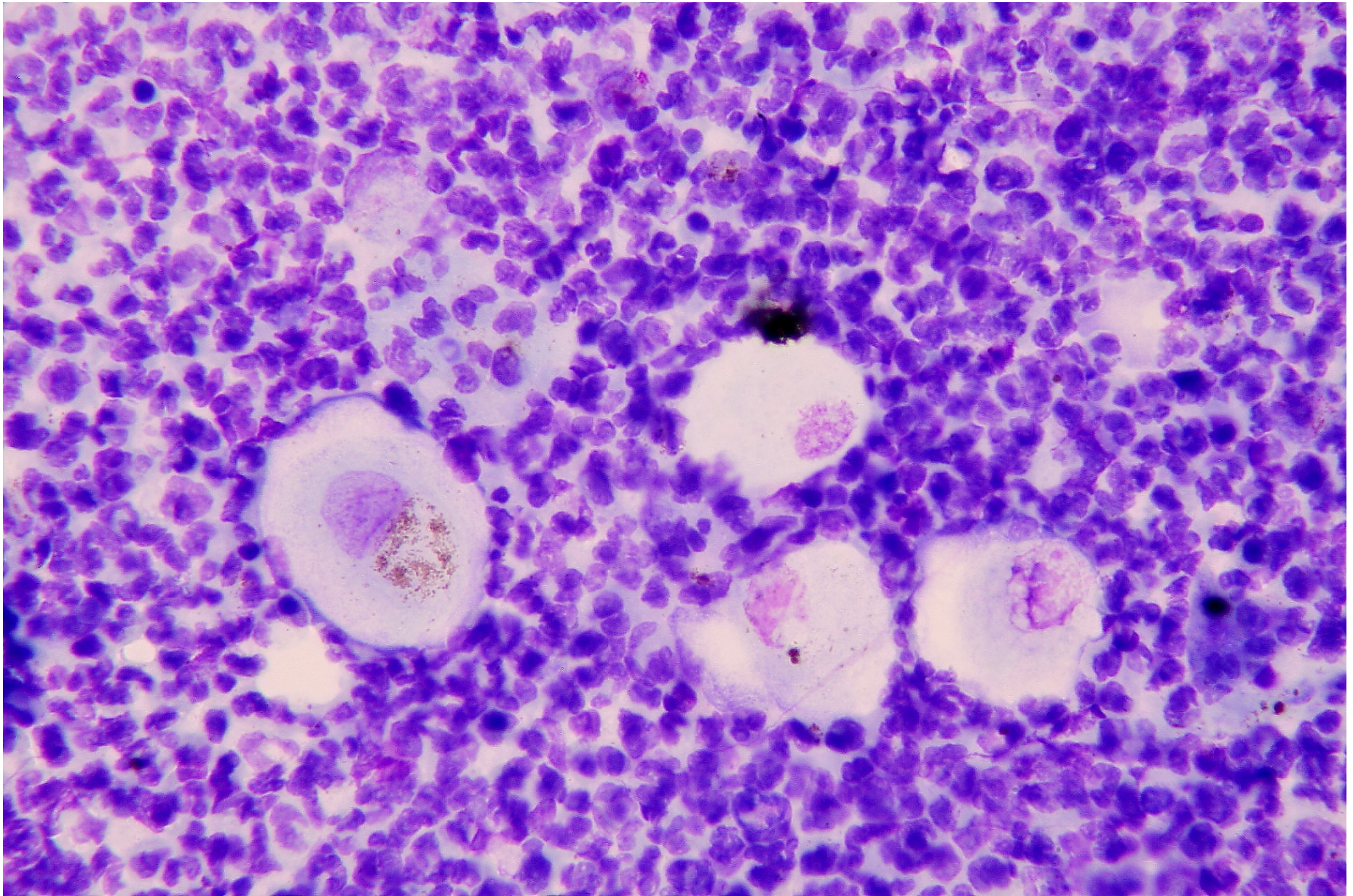
Case #8

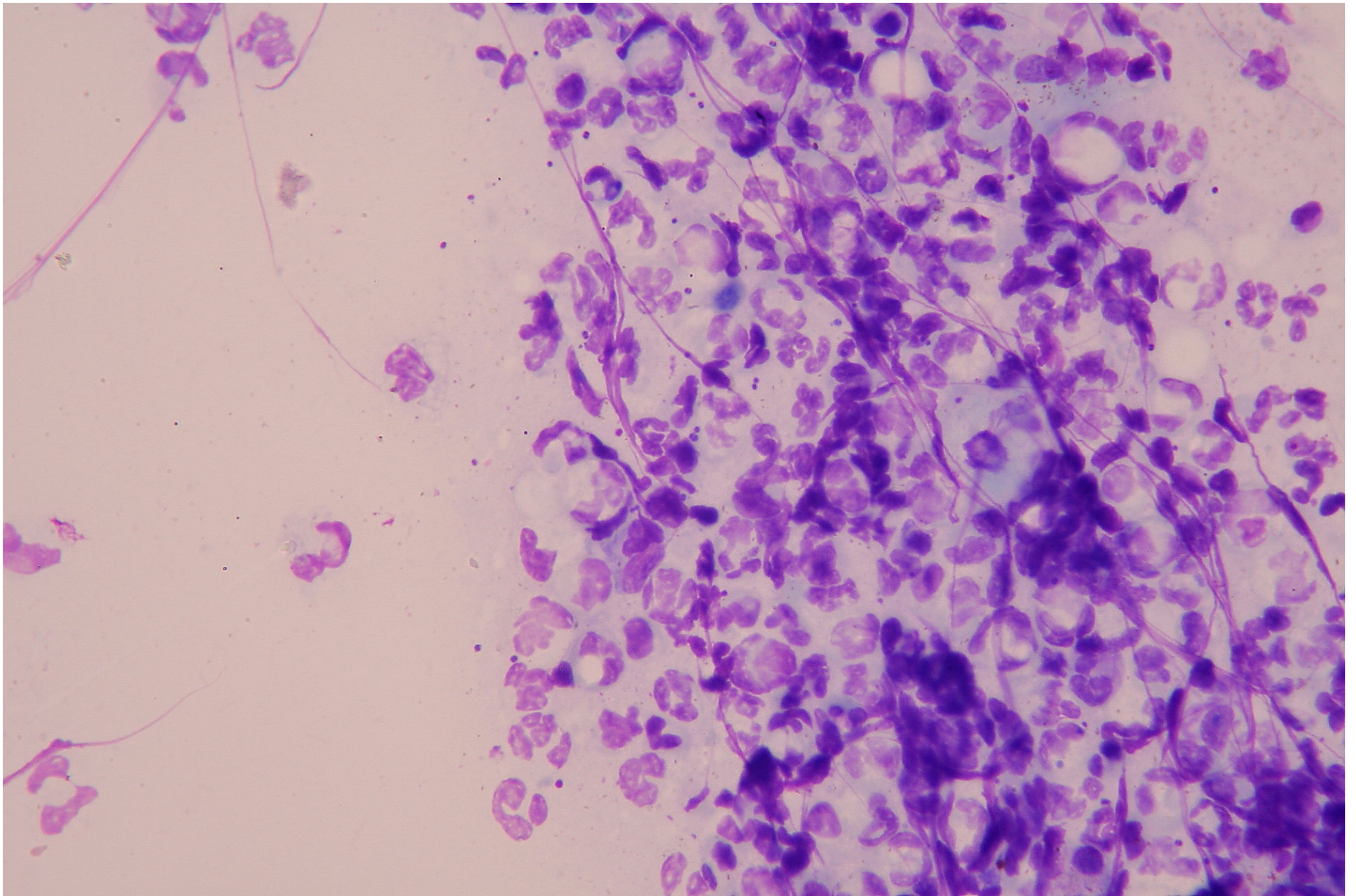
- Cat, Persian, 11-year old, female, neutered
- Generalized crusts
- Sample: impression smears
 - apposition of crusts and after removal of a crust
- Stain: MGG

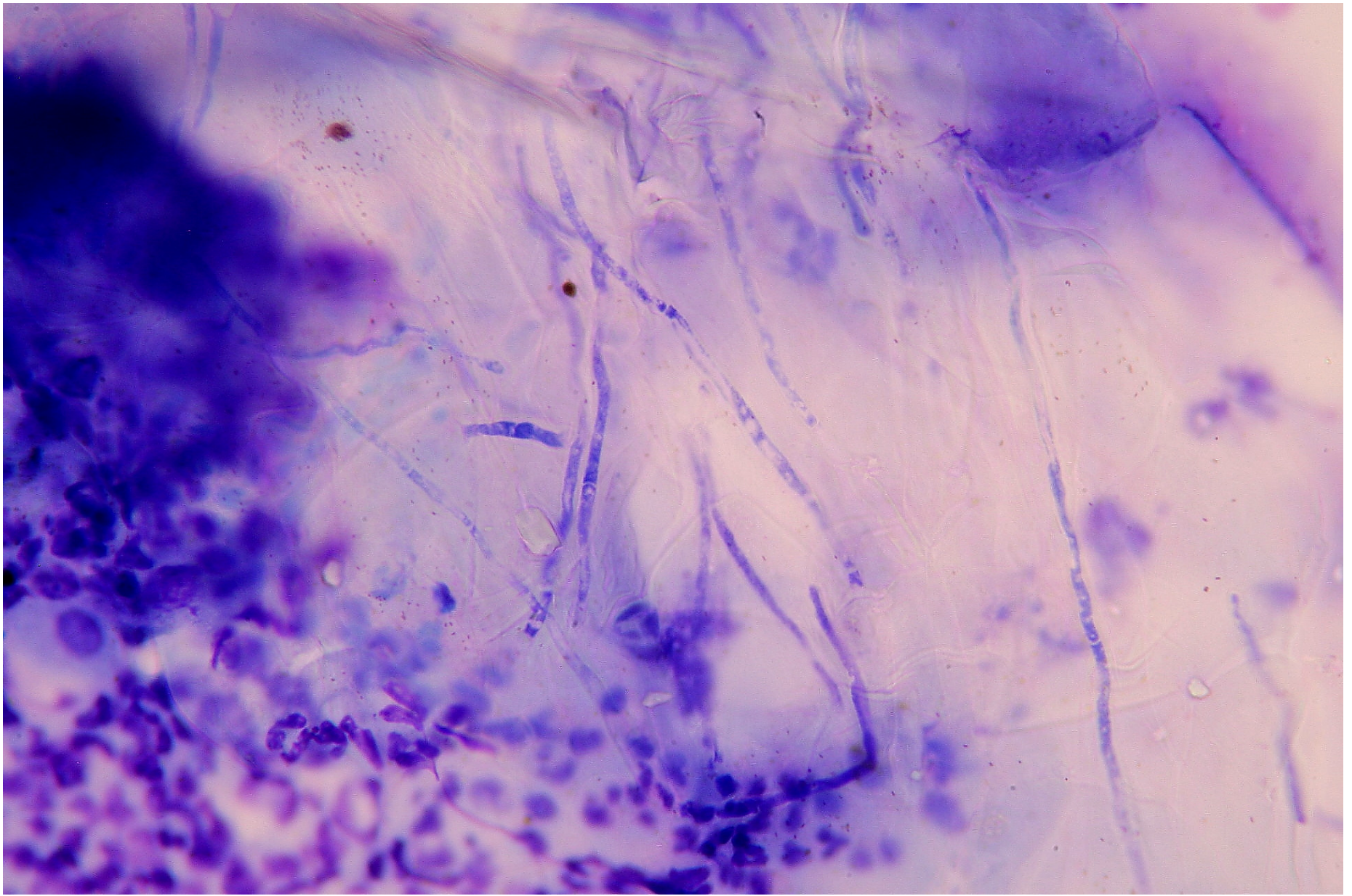


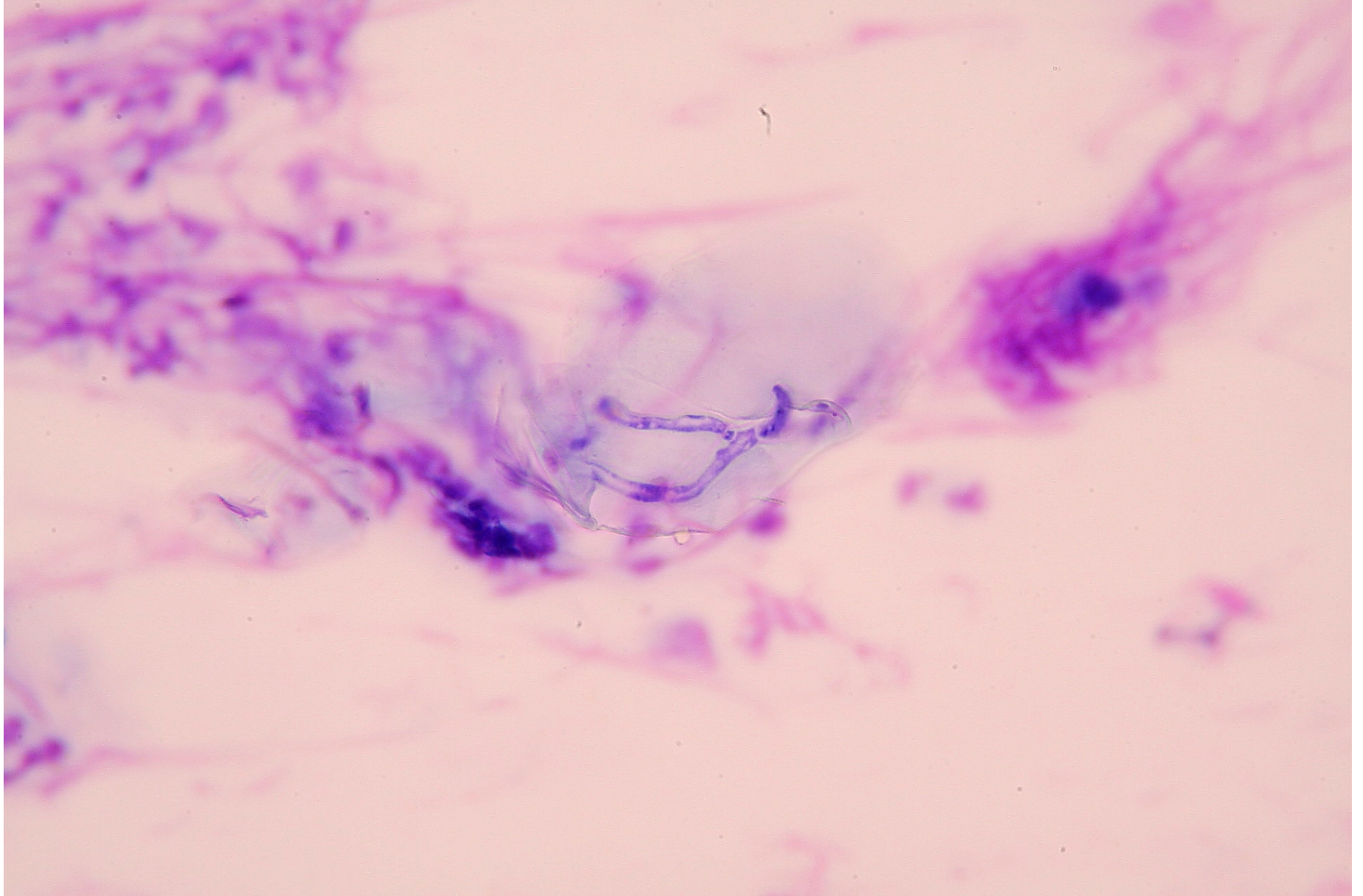


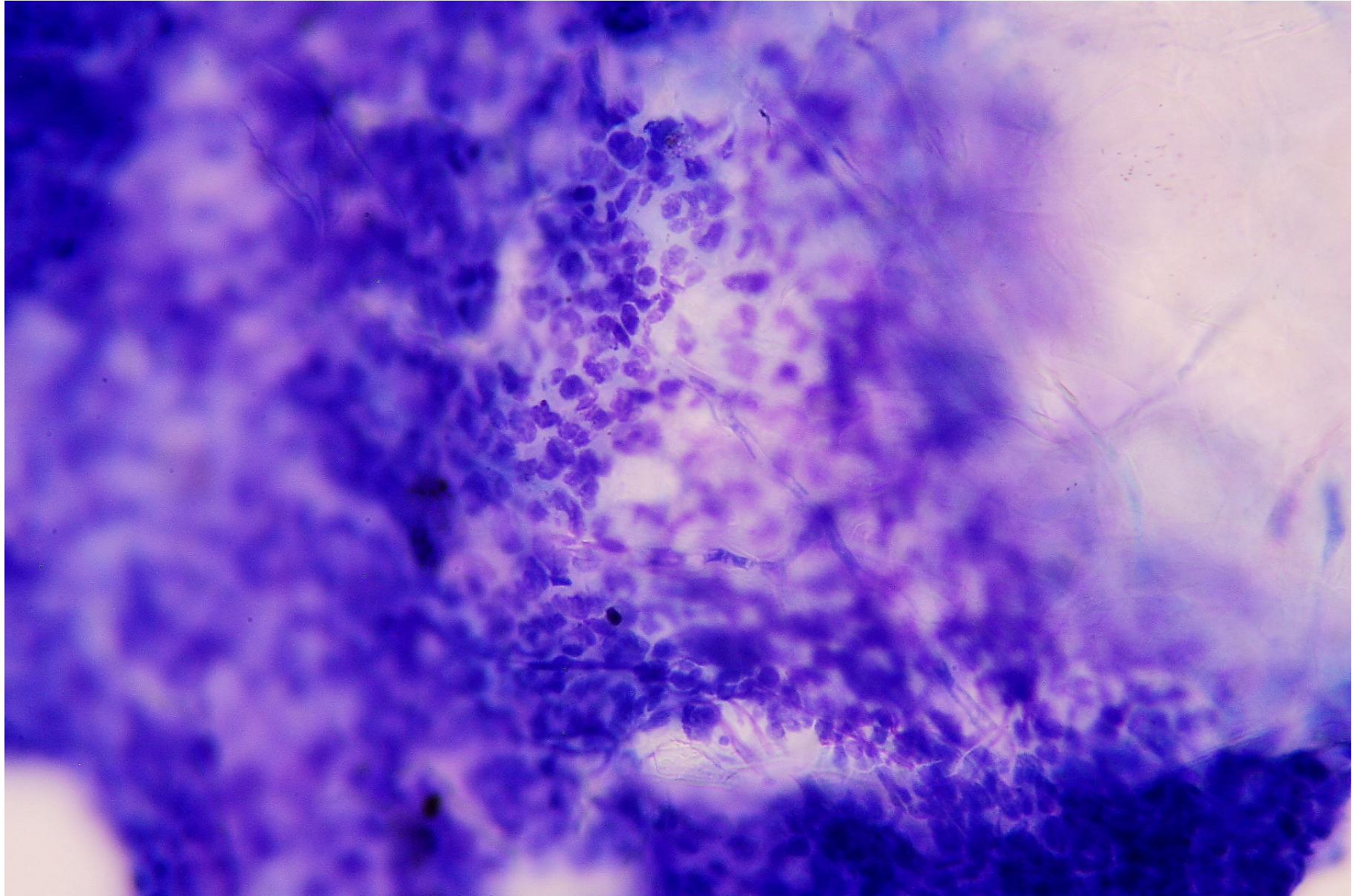


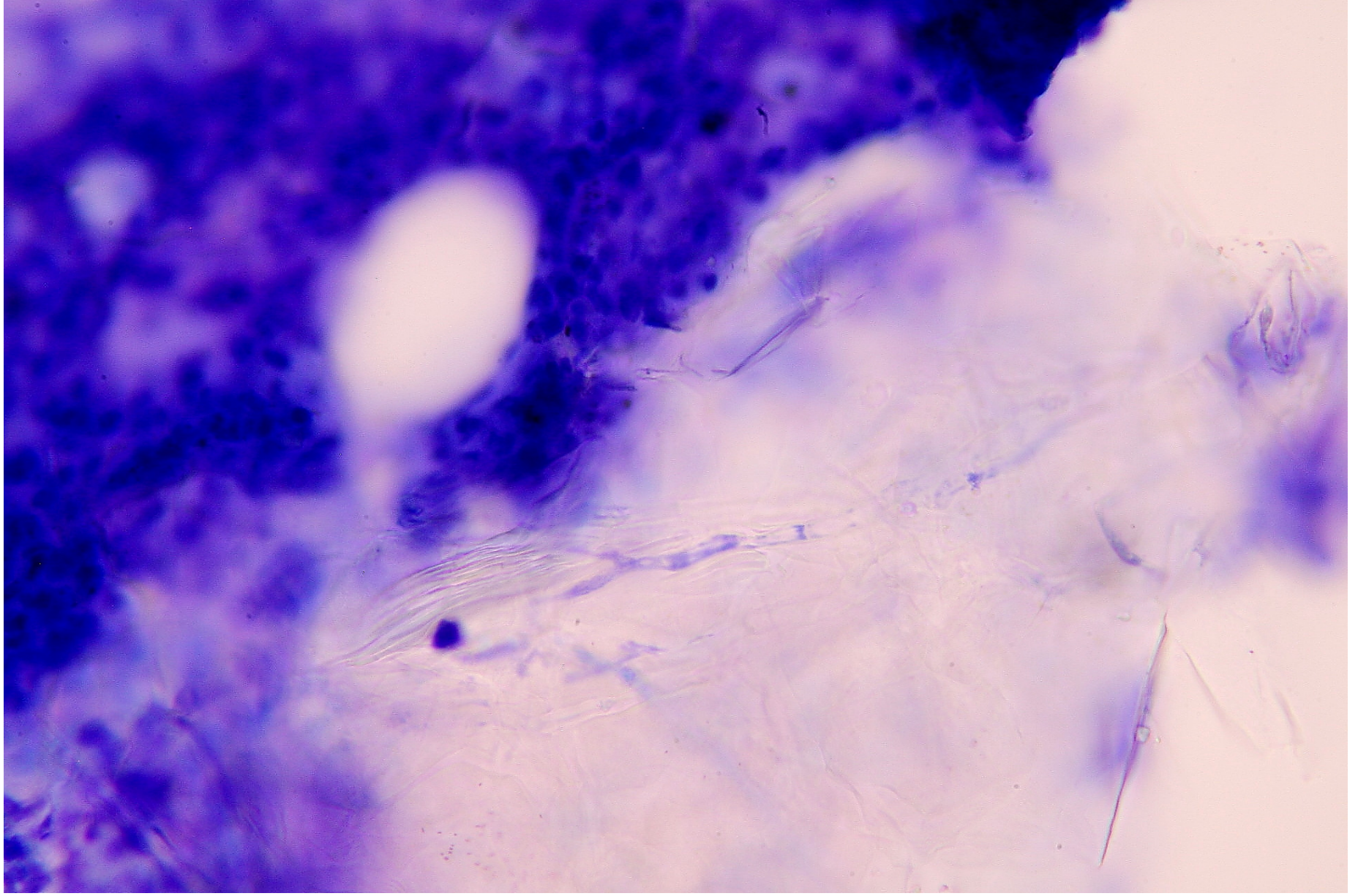










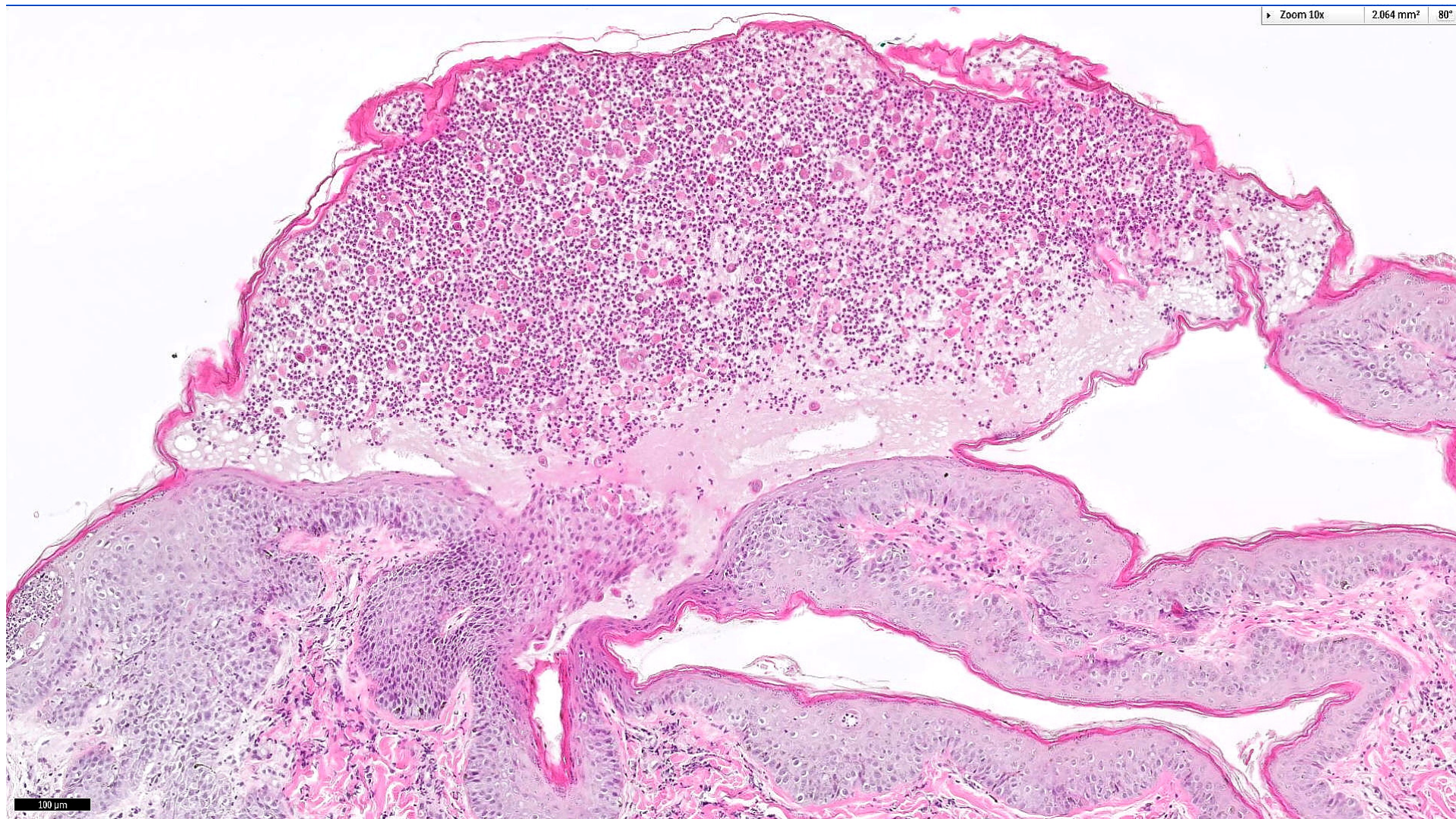


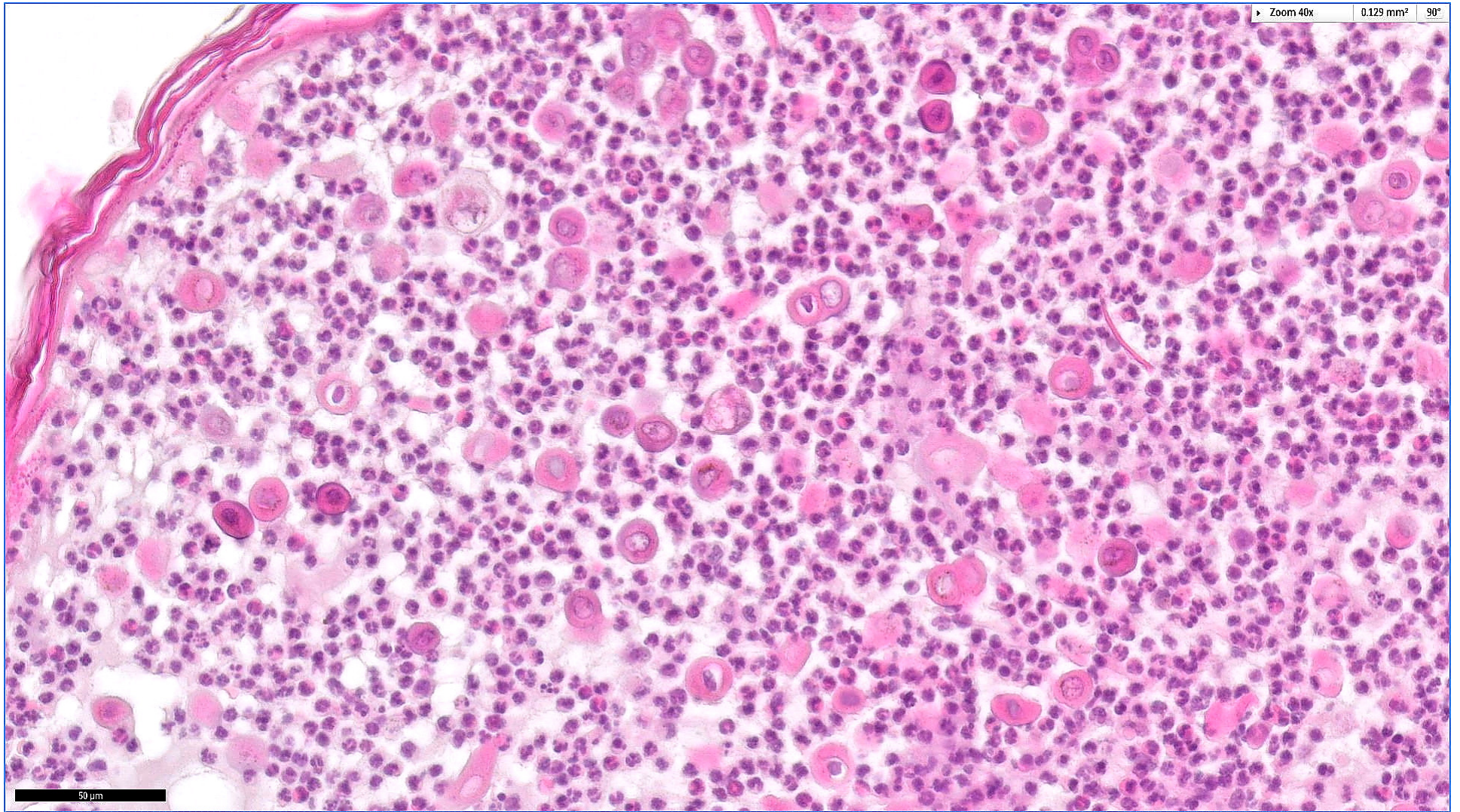
Cytologic findings

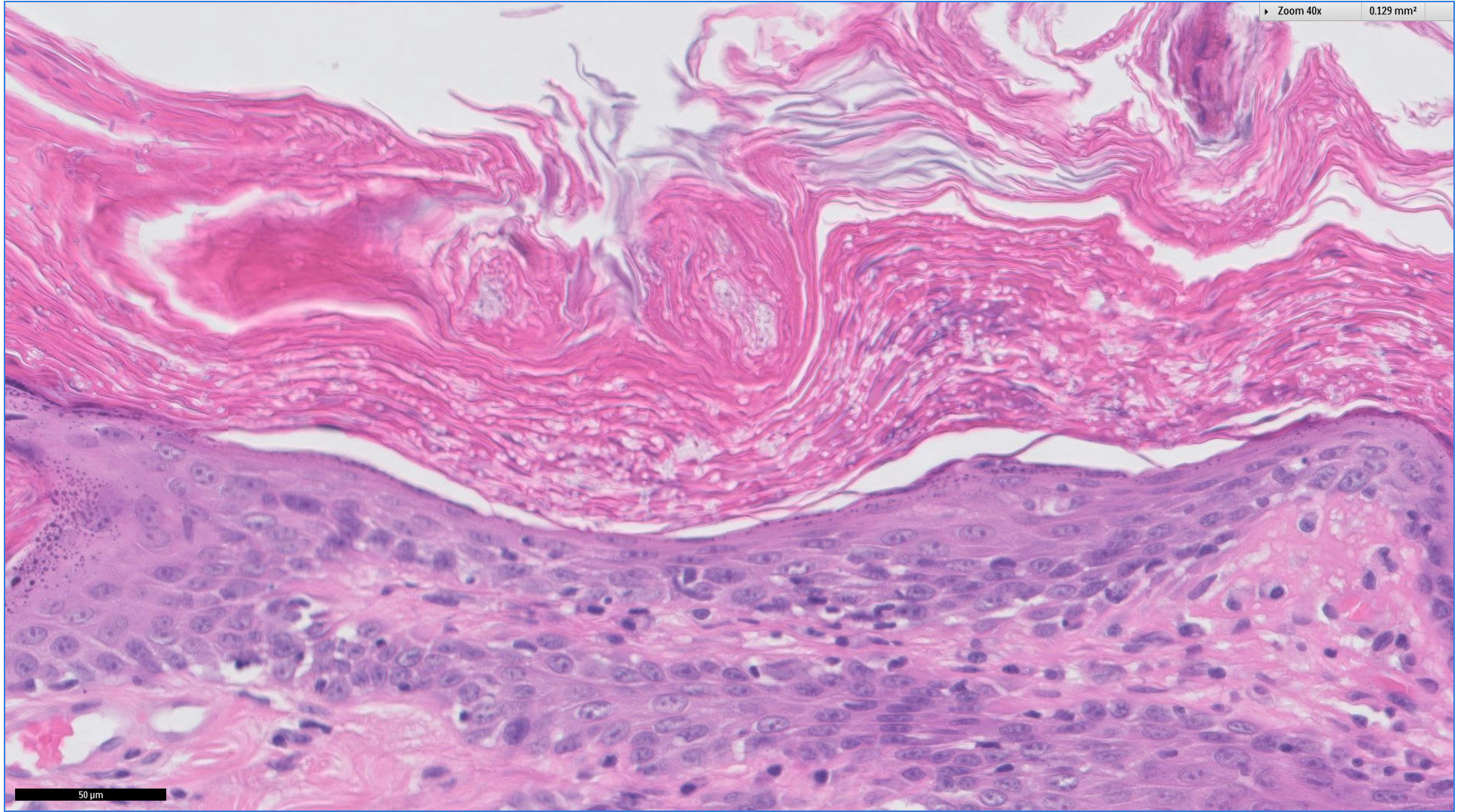
- Many inflammatory cells
 - Mostly segmented neutrophils
 - Occasional phagocytosis of coccoid bacteria
- Round, nucleated epithelial cells
- Sometimes surrounded by
 - Acantholytic cells (?)
- Fungal hyphae adherent to epithelial cells



Zoom 10x 2.064 mm² 80°







Diagnosis

- Cytologic diagnosis: suppurative inflammation; fungal (and bacterial) infection; acantholysis
- Histological diagnosis: superficial pustular dermatophytosis



Discussion

- Superficial pustular dermatophytosis
- Superficial epidermal pustules
- Almost most often small, they may be large and broad
- The degree of acantholysis relatively mild in most cases
- In some canine cases it may be prominent
- SDP with minimal to no acantholytic cells has been seen in cats



Discussion

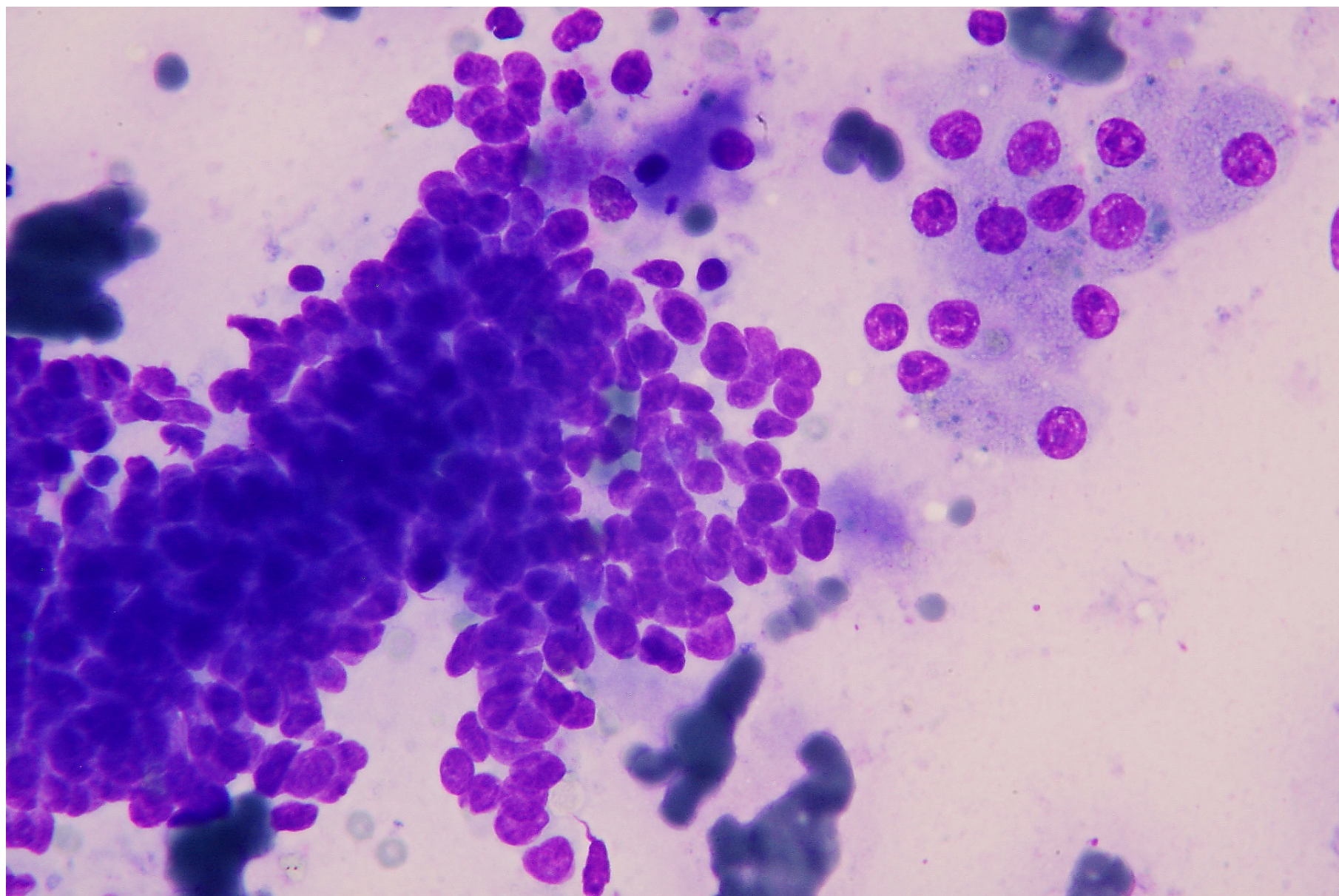
- Keratin-colonizing dermatophytes:
 - Trichophyton mentagrophytes (+++)
 - Microsporum persicolor (+)
 - Epidermophyton floccosum (+)
- Acantholysis:
 - Result from complement-mediated, transepidermal neutrophilic chemotaxis, as well as proteolytic enzymes secreted by dermatophytes
 - Dermatophytes may be less well adapted to canine and feline hosts and thus induce a more florid cell-mediated response

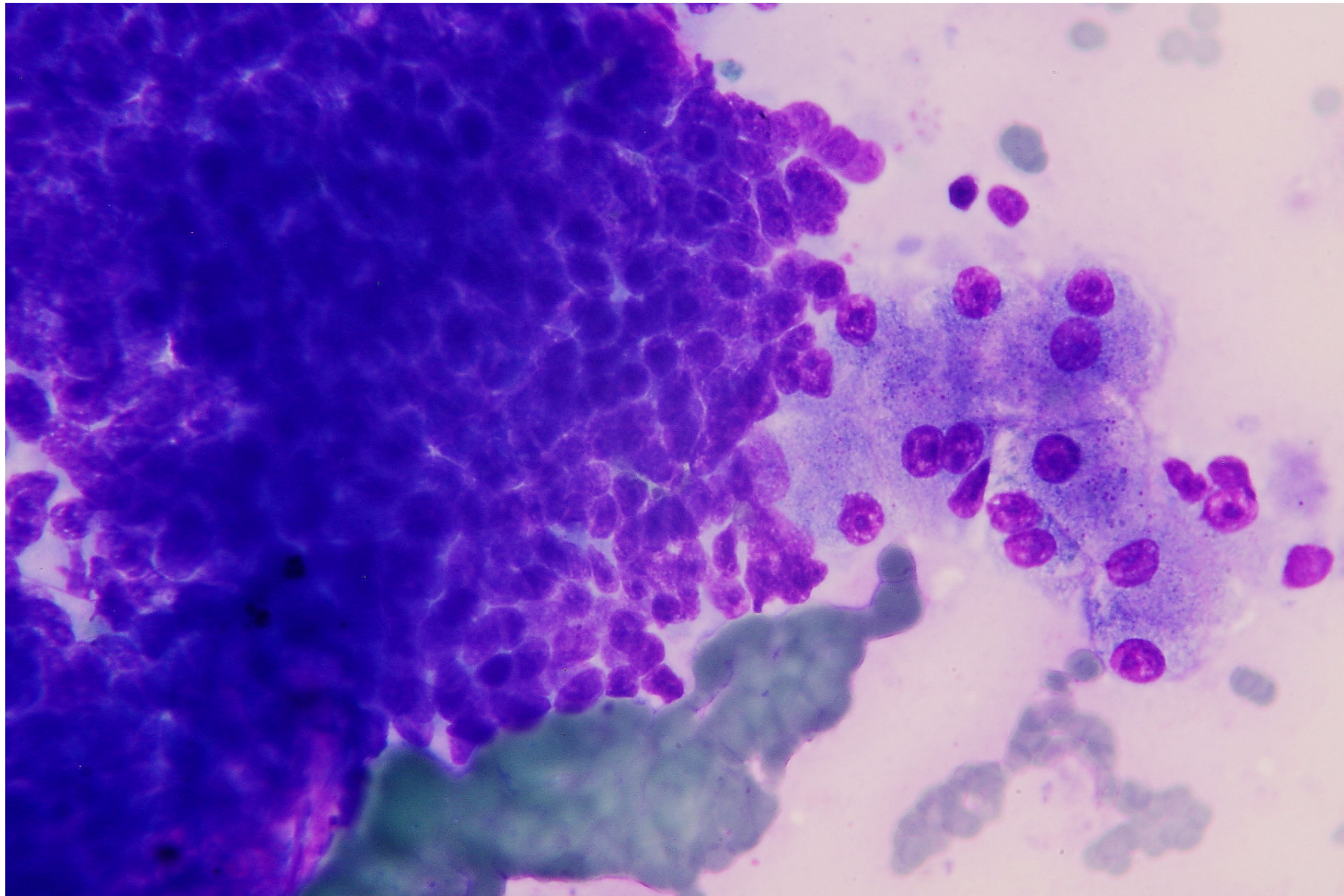


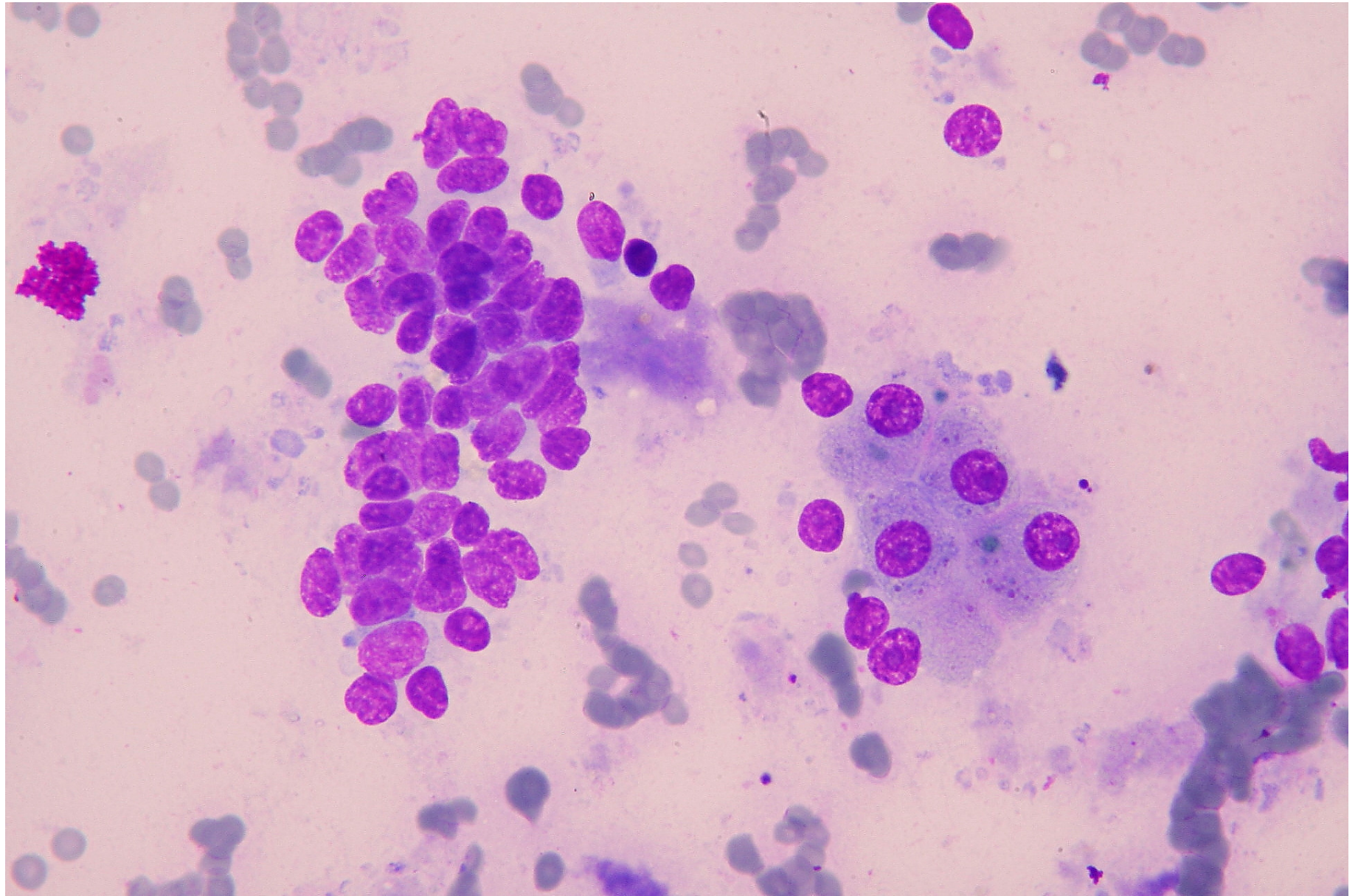
Case #9

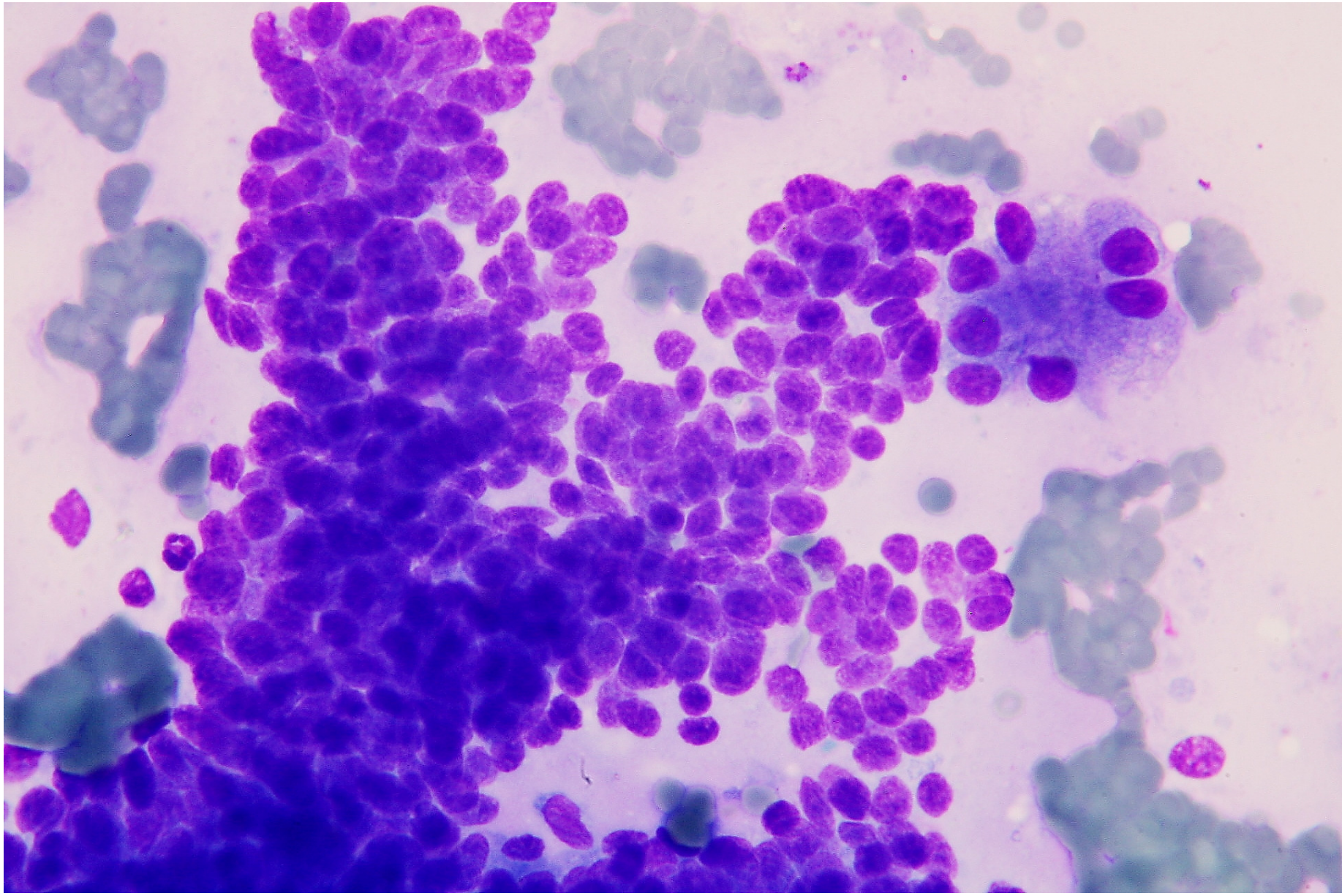
- Cat, DSH, 14-year old, male neutered
- Hepatic mass.
- Sample: FNCS
- Stain: MGG

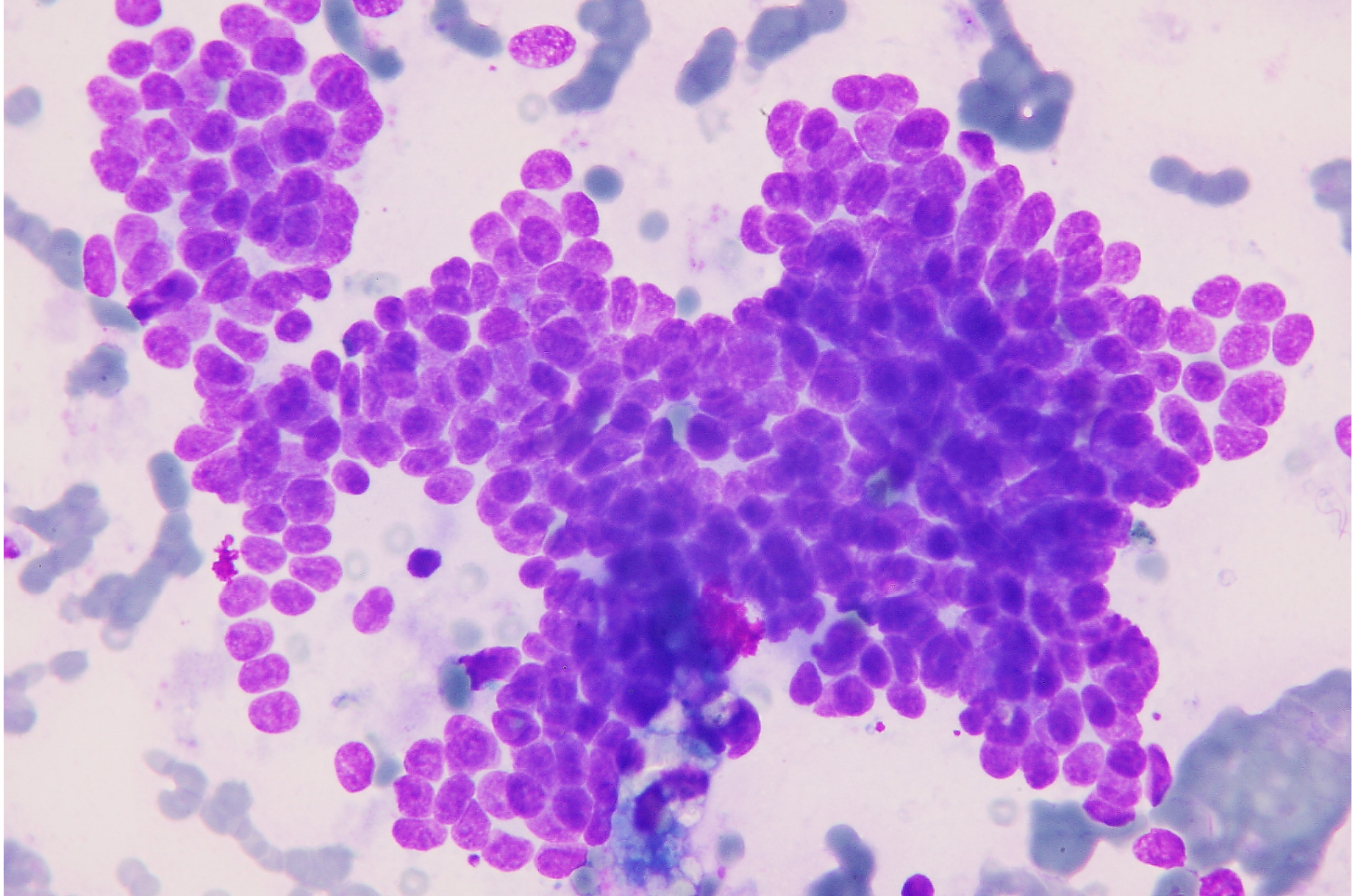


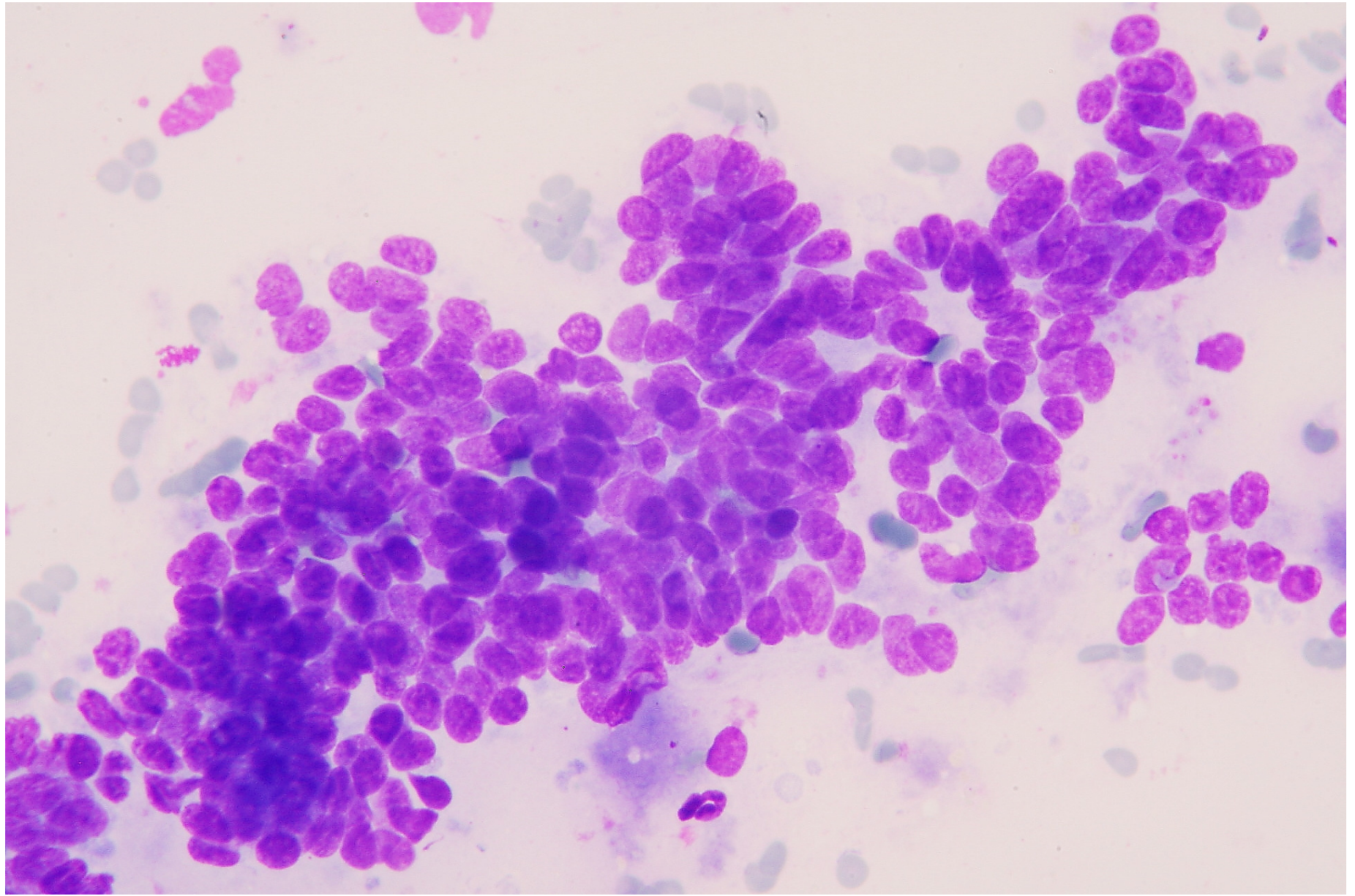












Cytologic findings

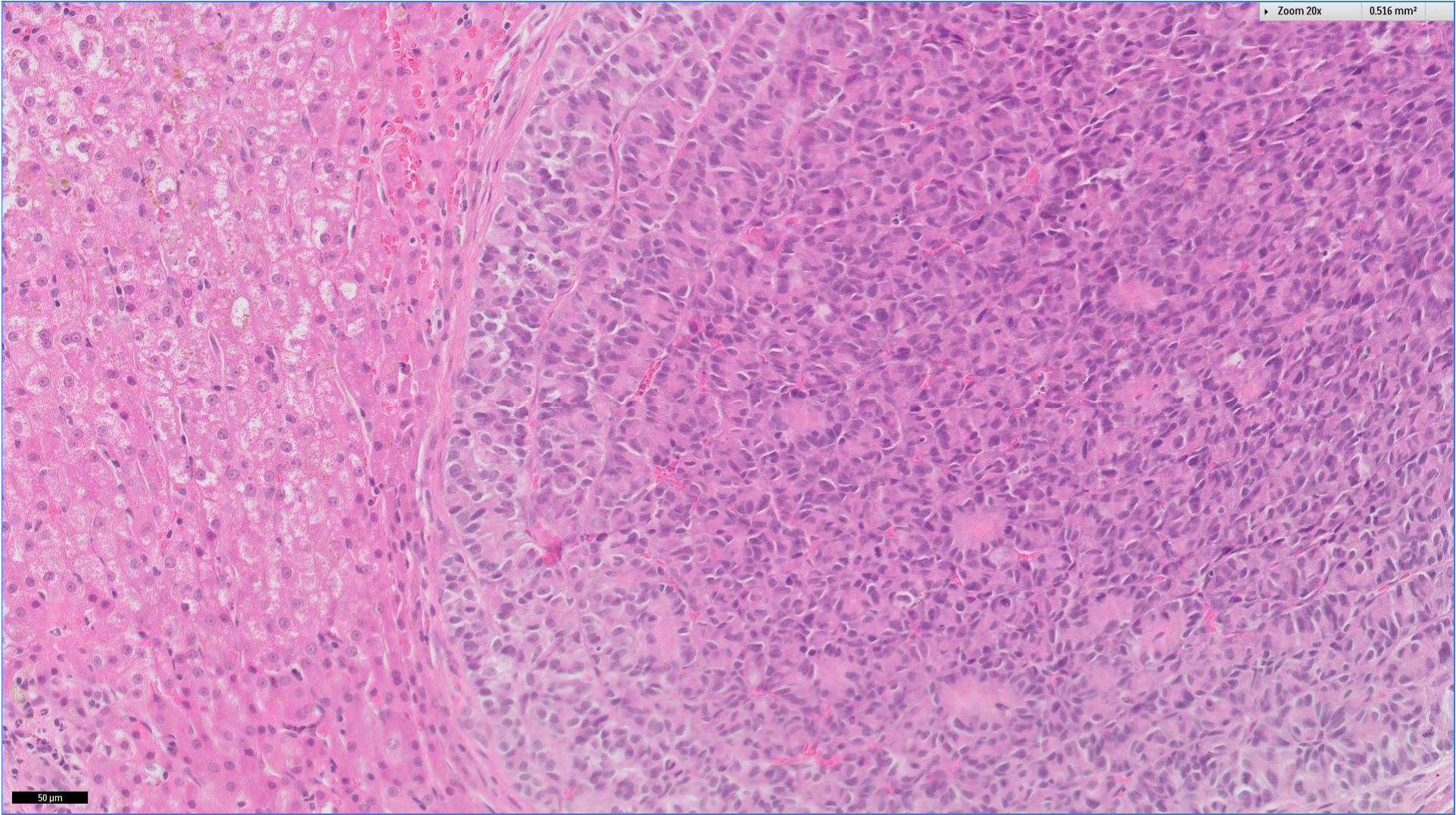
- Epithelial cells
 - Small, indistinct cytoplasm
 - Round to ovoid nuclei
 - Granular to compact chromatin
- Arrangements:
 - Rare microacinar
 - Rare rows
- No (rare) naked nuclei!!!



Diagnosis

- Cytologic diagnosis: neuroendocrine neoplasm, suggestive of carcinoid
 - DD: cholangiocarcinoma (???)
- Histological diagnosis: hepatic carcinoid

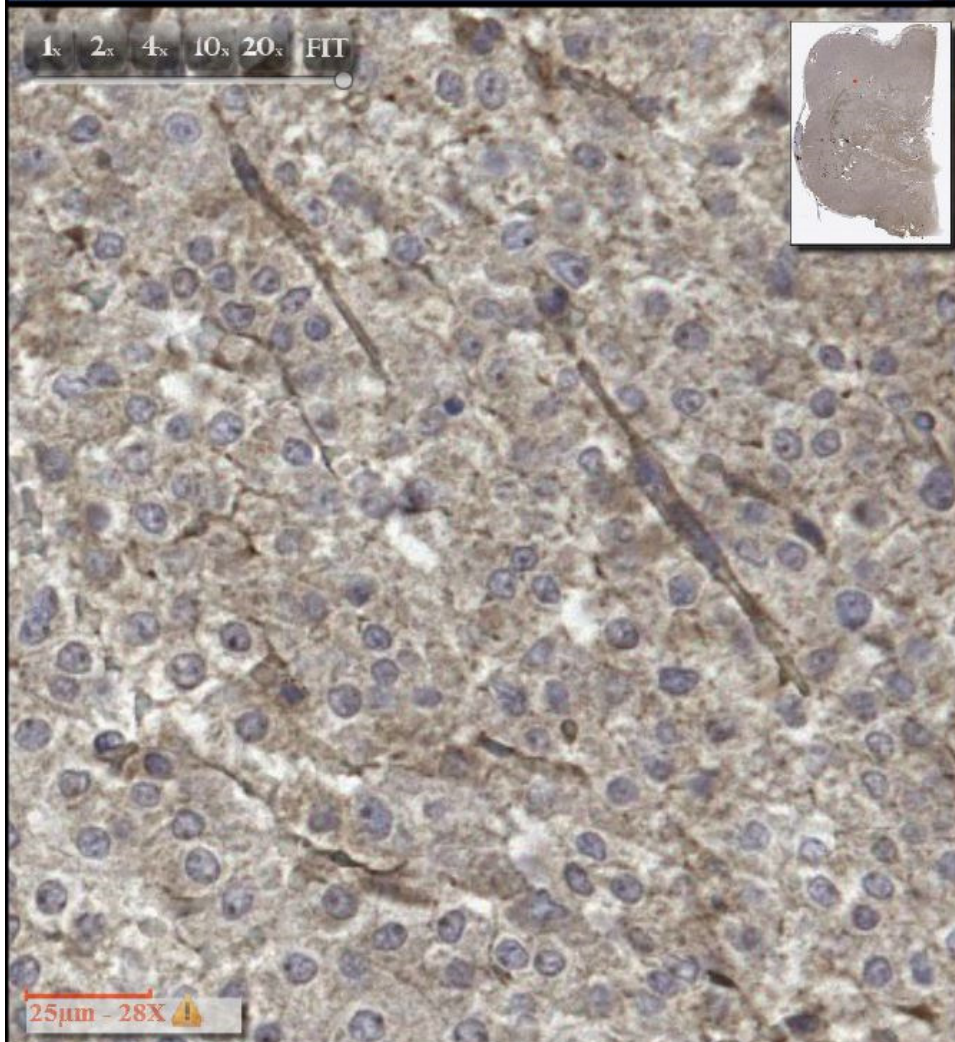




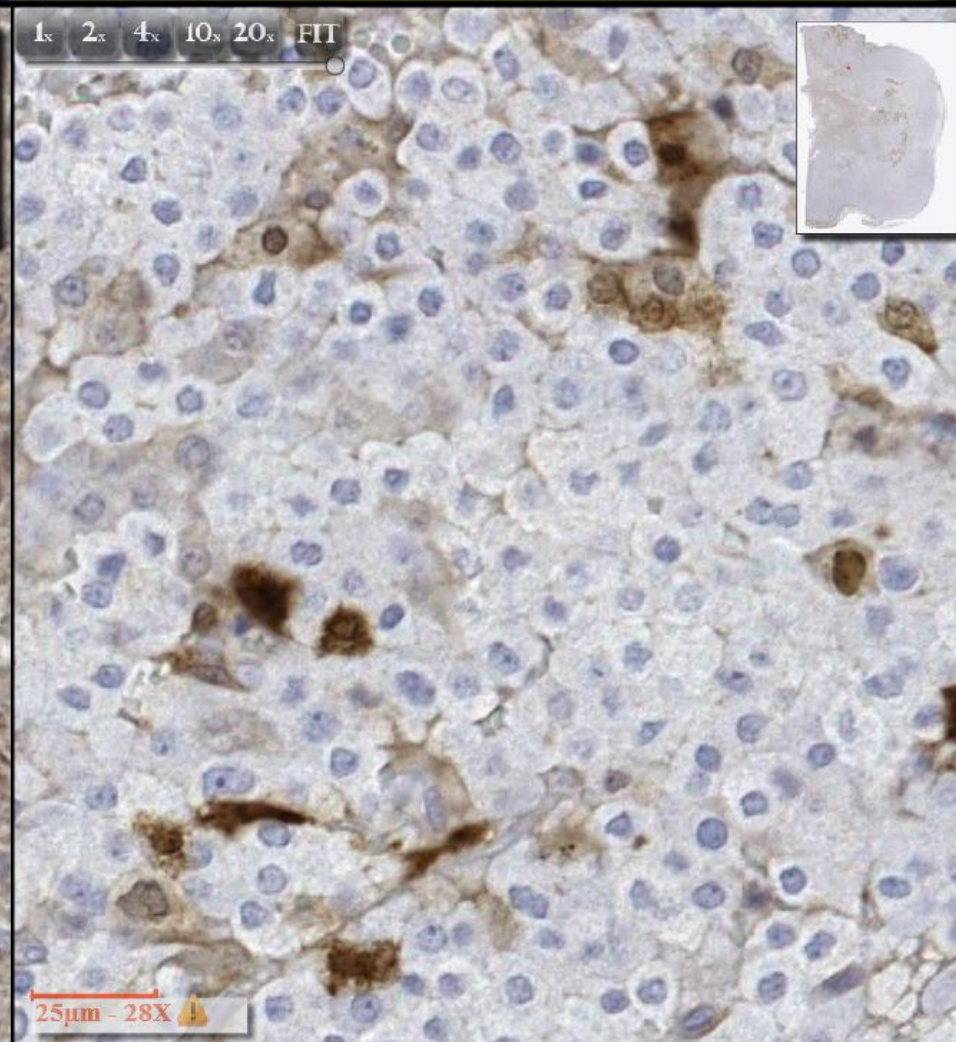
► Zoom 20x 0.516 mm²

50 µm

Slide CROMO, Region 1



Slide n-NSE, Region 0



Discussion

- Cytologic criteria for diagnosis:
- Small size
- Indistinct cytoplasm
- Round to ovoid nuclei
- Minimal anisokaryosis and anisocytosis
- Naked nuclei (?)



Discussion

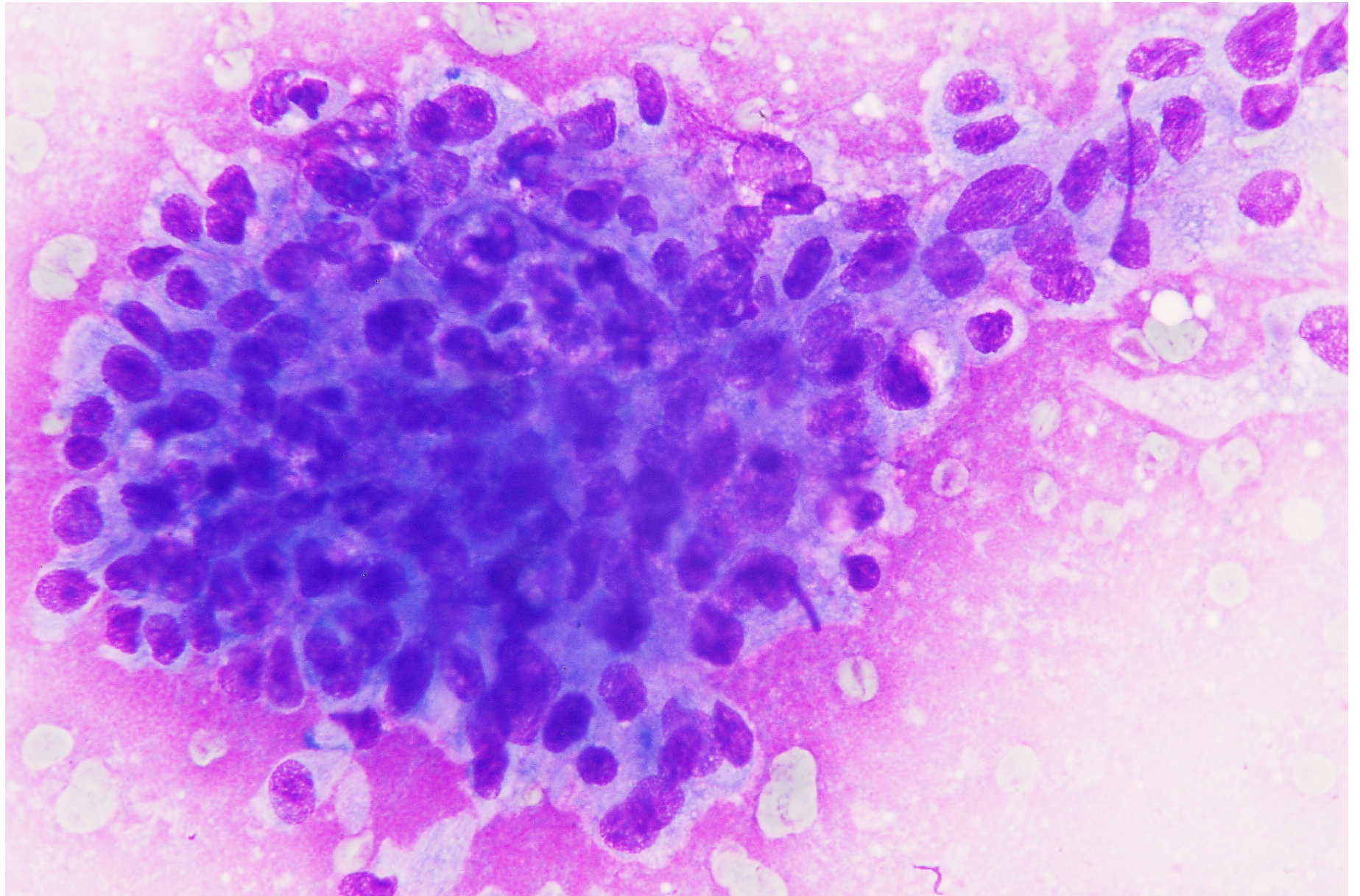
- Hepatic carcinoid:
 - HC are believed to originate from the diffuse neuroendocrine cell population distributed throughout the biliary epithelium
 - Clinical signs are aspecific
 - Increased activity of liver-related enzymes but no specific pattern
 - From large, single bulging mass to multiple nodules

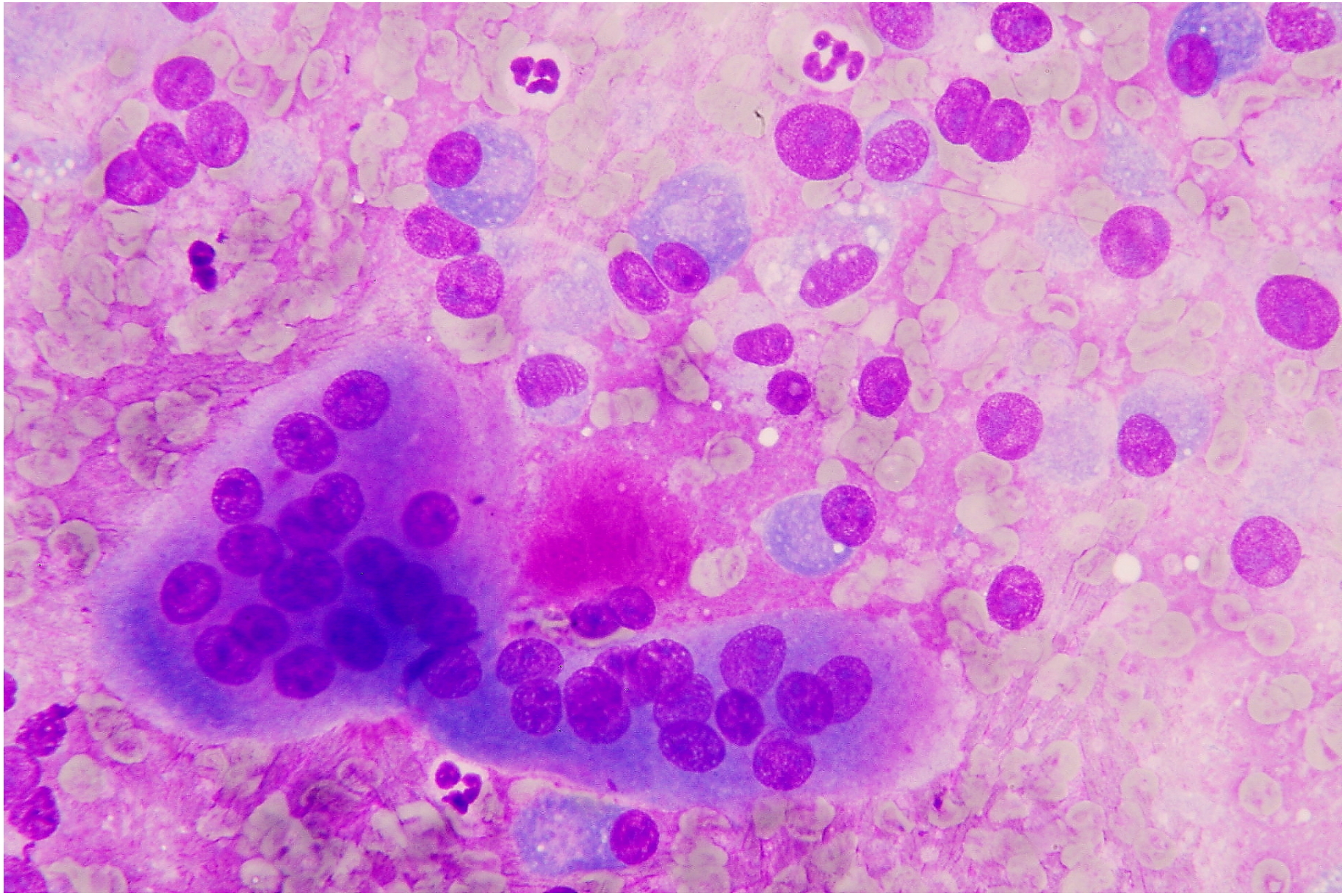


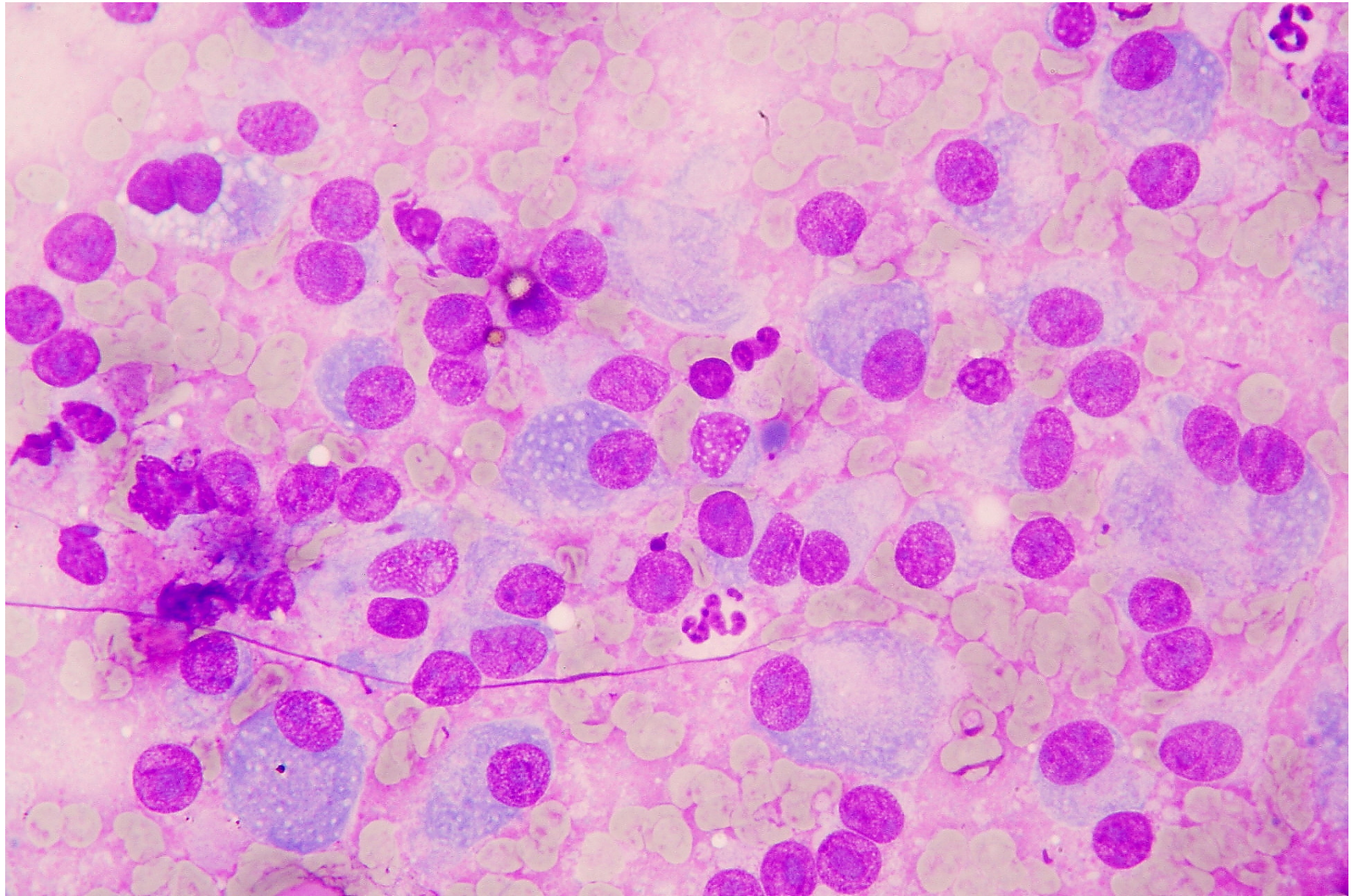
Case #10

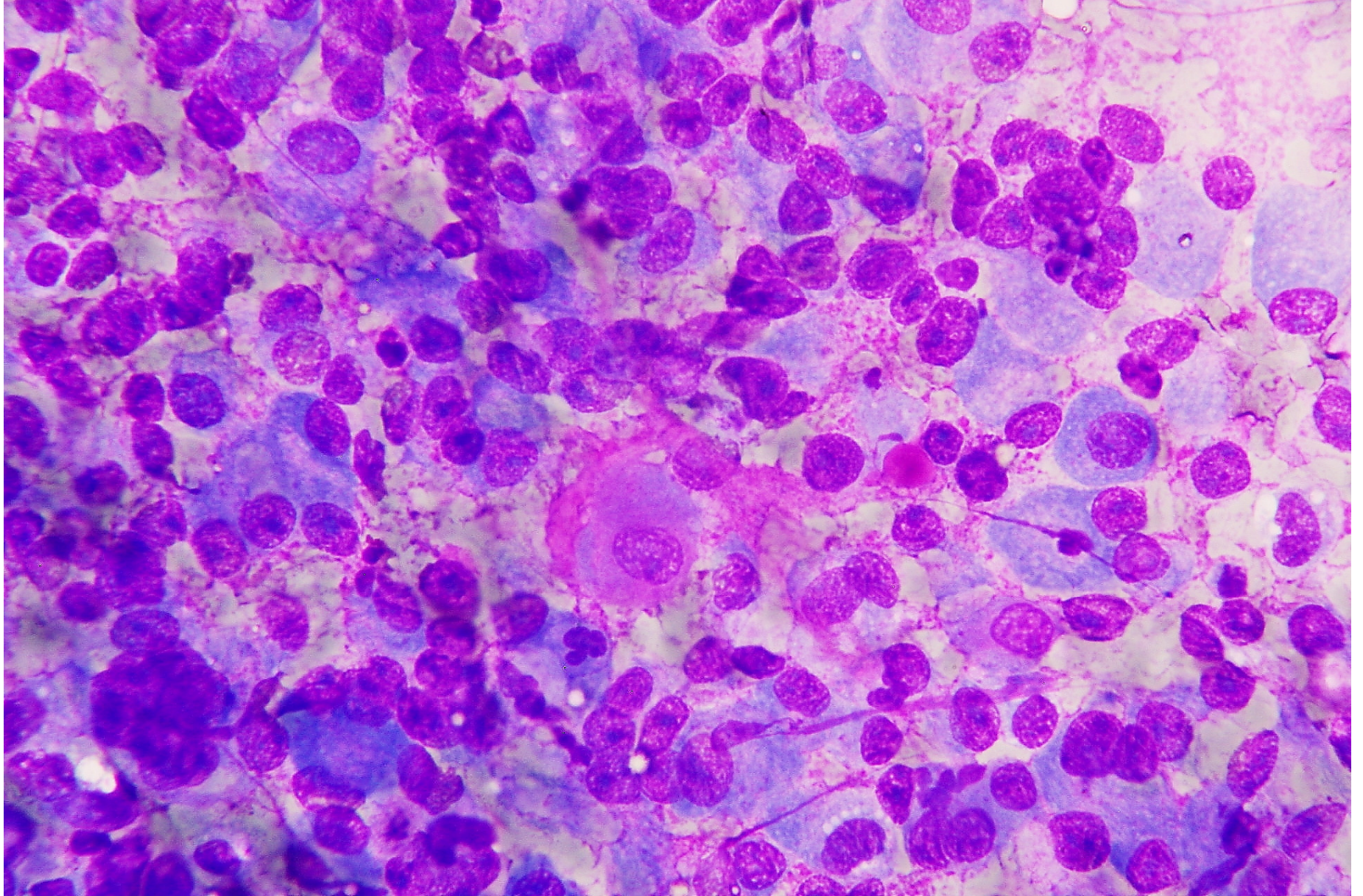
- Dog, Poodle, 10-year old, female, neutered
- Mammary lump.
- Sample: FNCS
- Stain: MGG







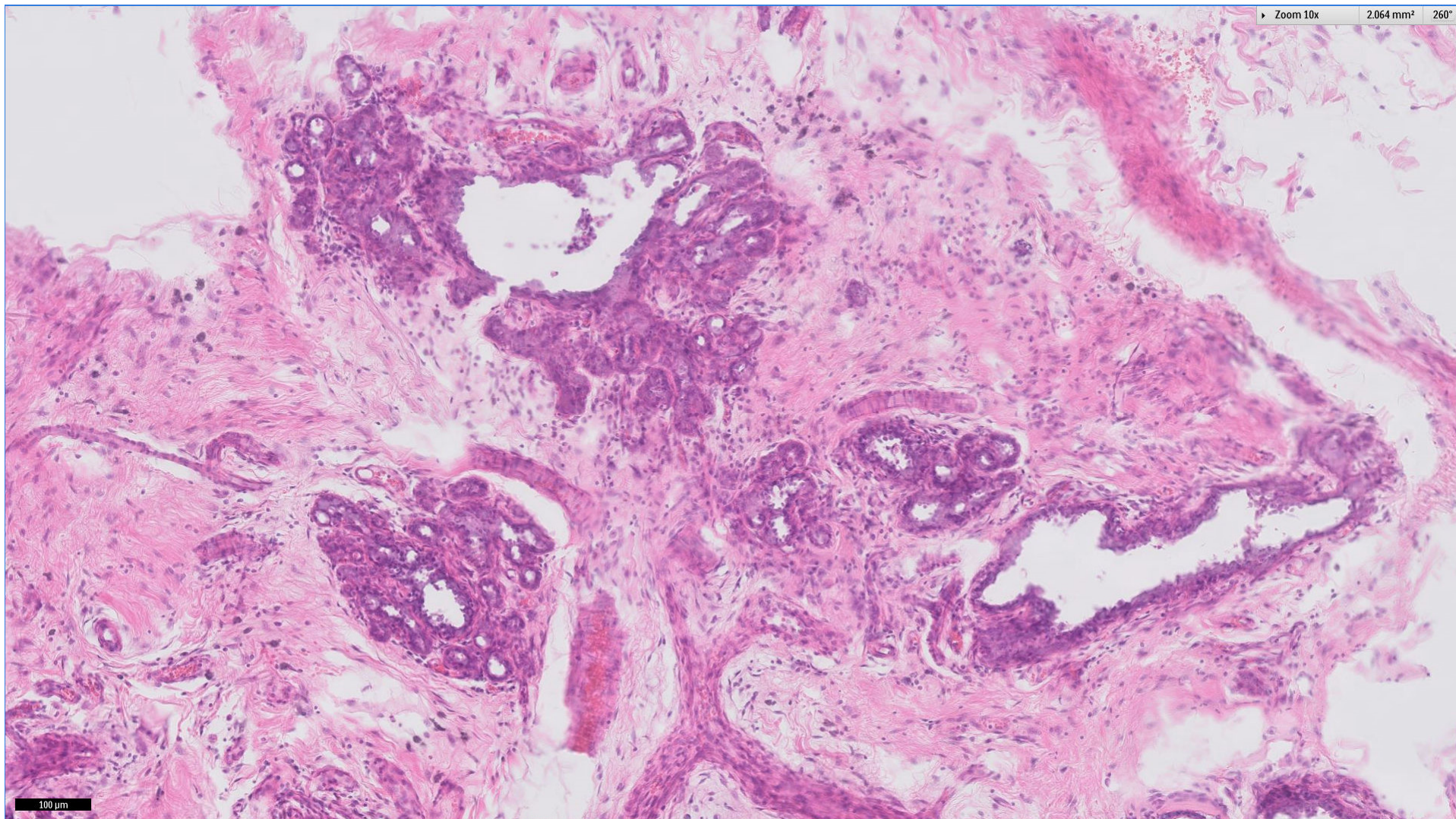


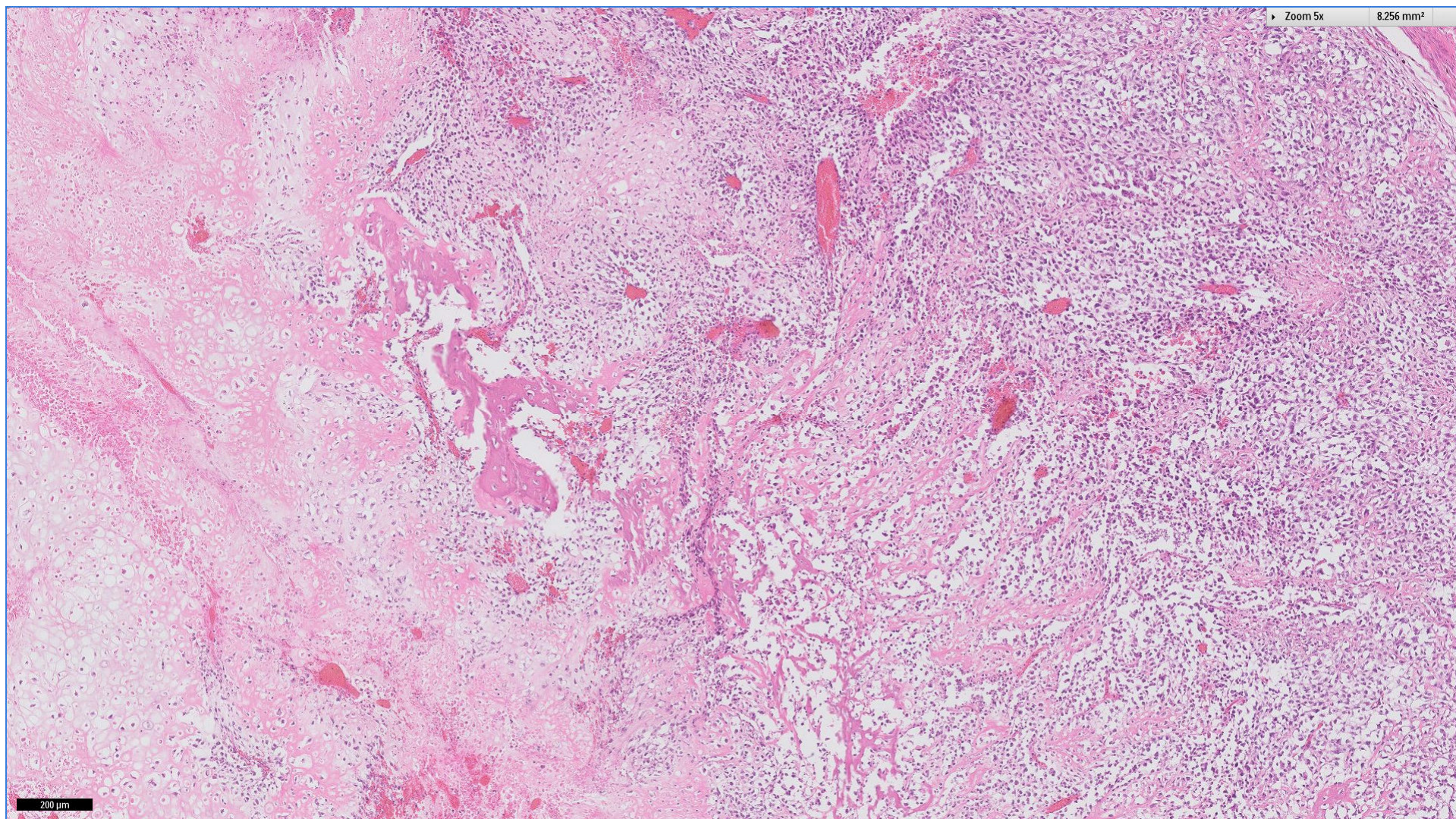


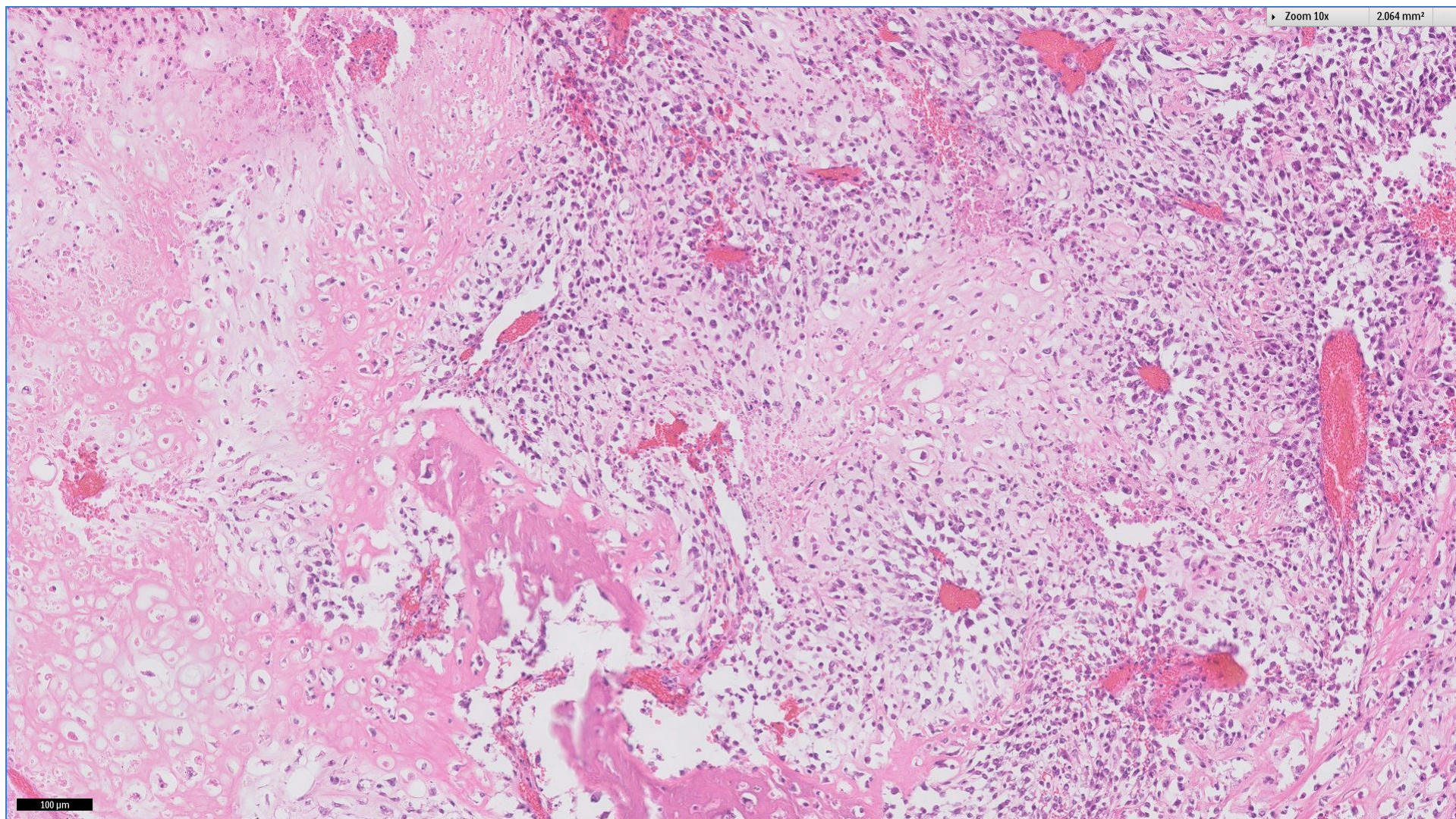
Cytologic findings

- Rare epithelial aggregates
 - Cuboidal to round, bluish cytoplasm
 - Round to ovoid nuclei
 - Slight to moderate anisokaryosis and anisocytosis
- Round discrete cells
 - Large size
 - Bluish, at times plasmocytoid in appearance (of the cytoplasm)
 - Very eccentric, round nucleus
- Multinucleated giant cells (osteoclasts)









Diagnosis

- Cytological diagnosis: osteosarcoma
 - DD: carcinosarcoma
- Histological diagnosis: mammary osteosarcoma



Discussion

- **Mammary osteosarcoma** Goldschmidt 2011
 - The most common mesenchymal neoplasm of the canine mammary gland
 - Biological behaviour is similar to that of osteosarcomas at other sites, with metastases via the hematogenous route
 - Lungs





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