ESVP – ESVCP Congress
Bordeaux – 2021

MISTERY SLIDES SESSION

- Cytology -

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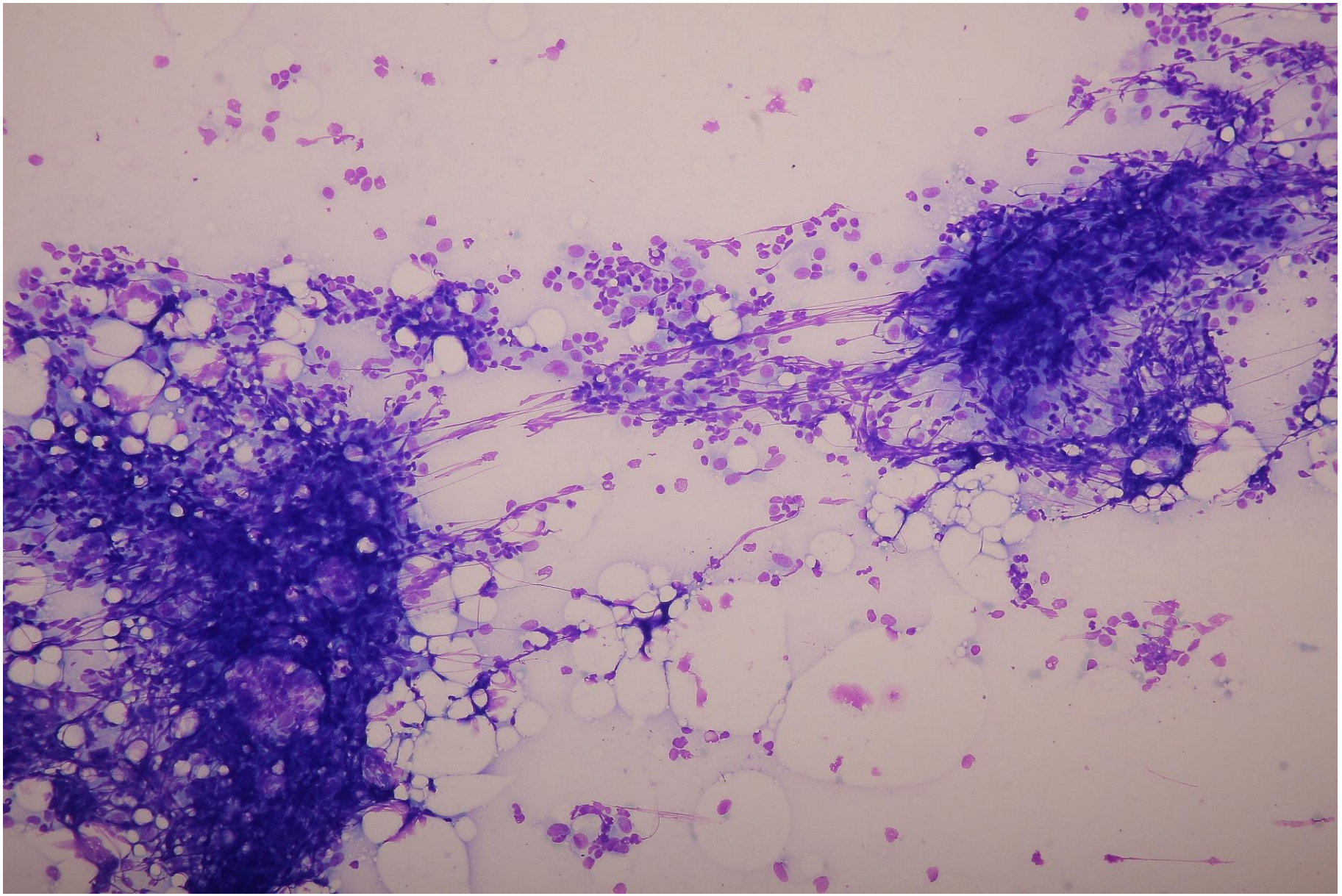
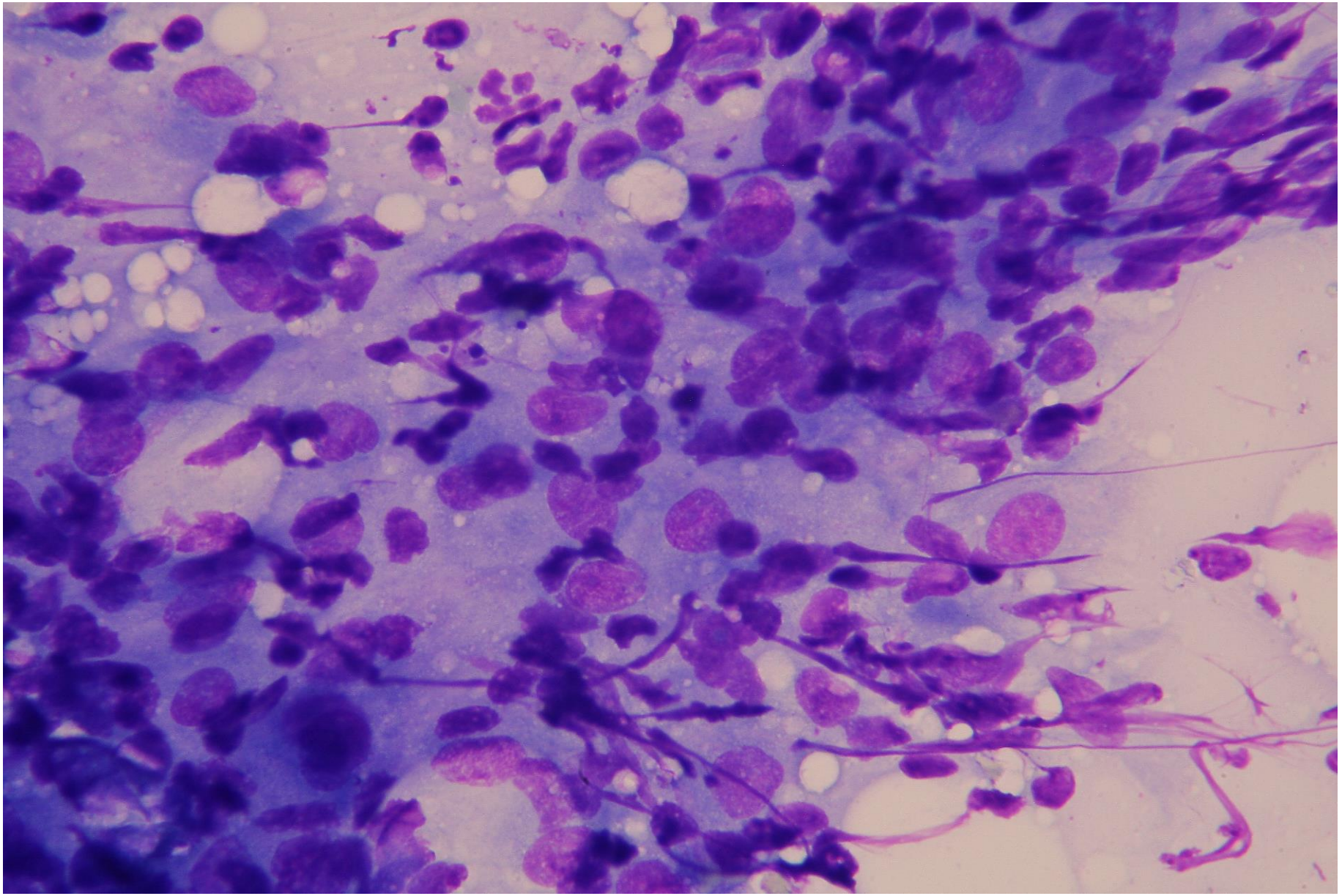
IDEXX LABORATORIES

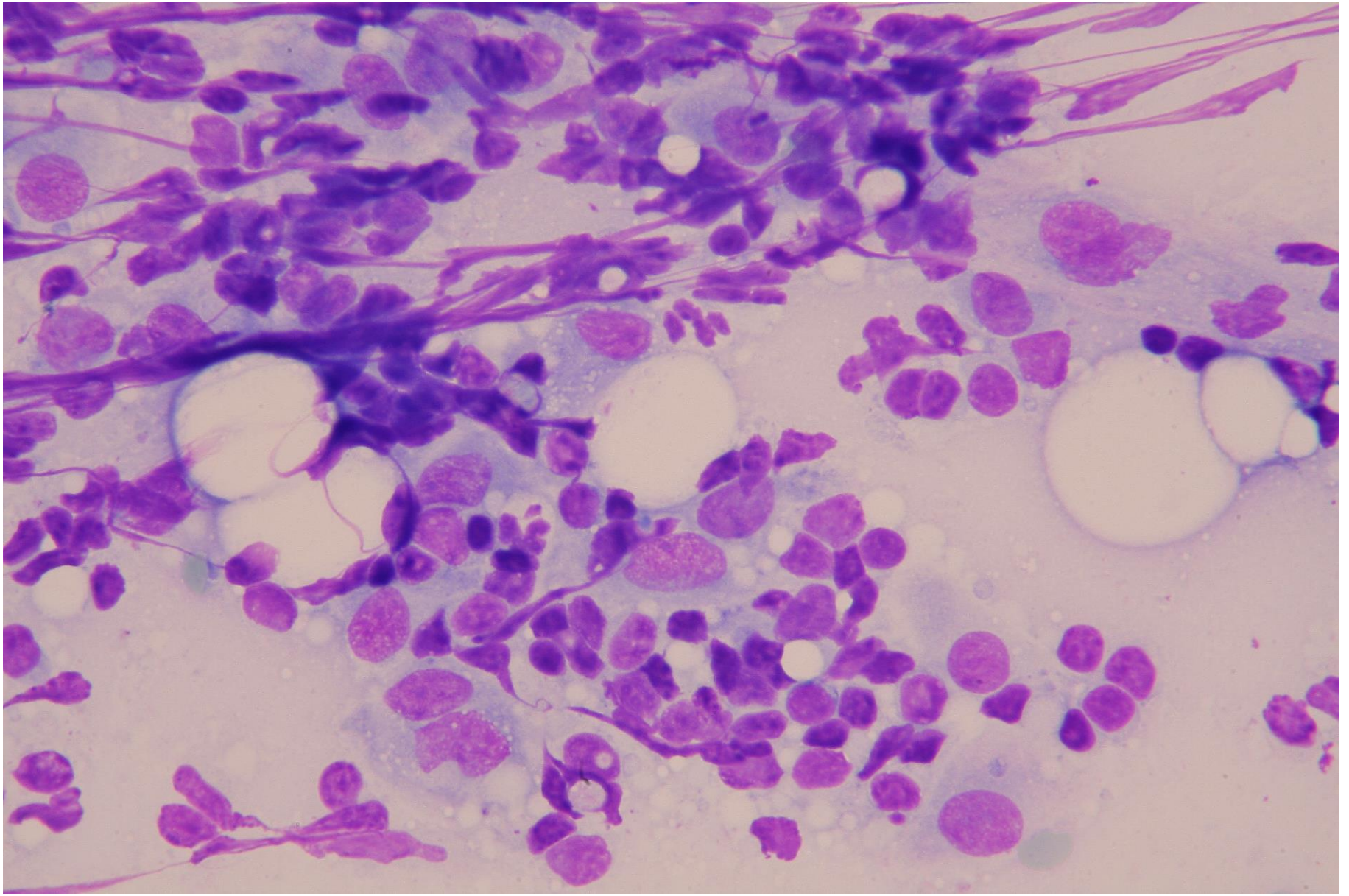
Case #1

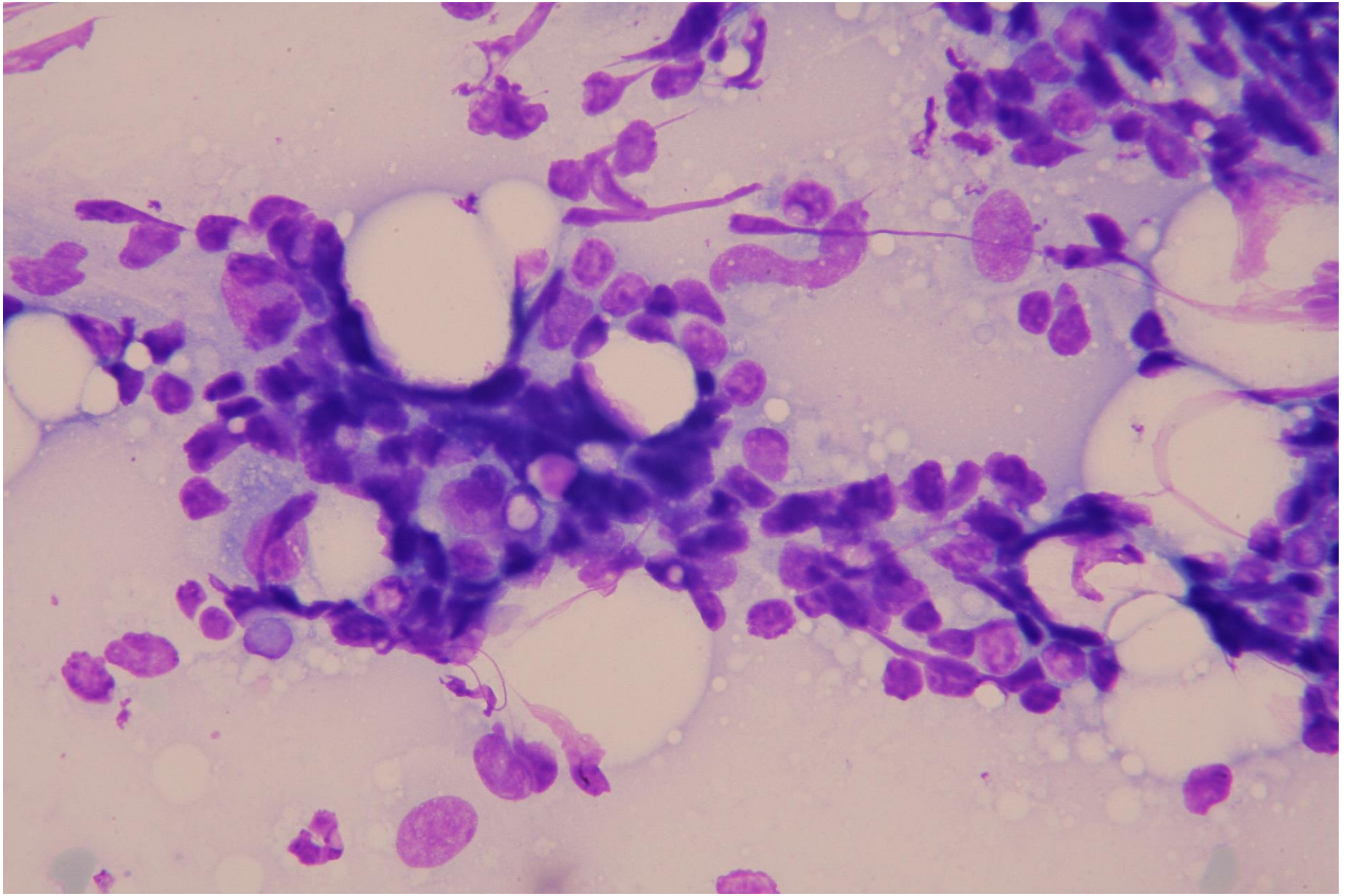
- 9-year-old, female, mixed breed dog.
- Subcutaneous lumps in the sternal and foreleg region.

- FNCS of the lesion
- MGG stain







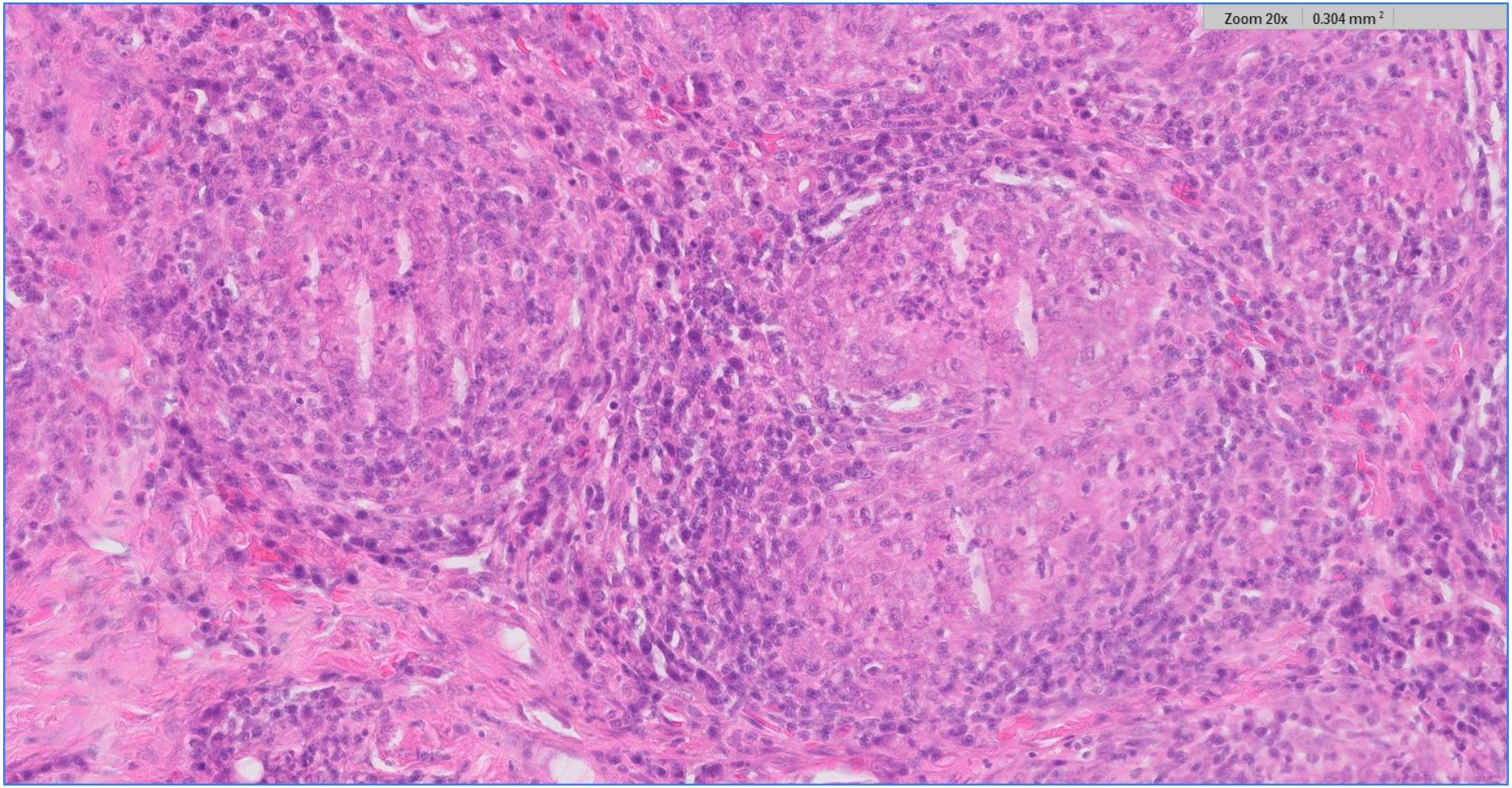


Cytologic findings

- Mild bloody and lipidic background
- Round to spindle cells, mostly in irregular aggregates or dispersed on the background
    - Poor definition of the shape of the cells
    - Histiocytic appearance
- Presence of many small lymphocytes, some plasmacells and a very low number of neutrophils
- Many disrupted cells

Diagnosis

- Cytologic diagnosis:
  - Mixed histiocytic and lymphocytic population; a cutaneous reactive histiocytosis is suspected
- Histological diagnosis:
  - Cutaneous reactive histiocytosis


Zoom 20x
0.304 mm²

Discussion

- Reactive histiocytosis
  - Cutaneous
    - Multiple nodules and plaques, dermal and subcutaneous in location
    - Muzzle, nose, eyelid, scrotum, trunk and extremities
  - Systemic
    - Involvement of internal organs
- Cause: putative deregulation of the immune system of unknow origin
  - Defective interaction of dendritic and T lymphocytes

Discussion

- Cytological findings depend on the stage of the disease
  - Early stage: very low cellularity
  - Advanced stage: moderate to high amount of cells
- Histiocytic cells are frequently disrupted and difficult to be recognized
- Lymphocytes always present, mostly well preserved
- Diagnosis is based on clinical presentation and cytological features

Albanese, 2017

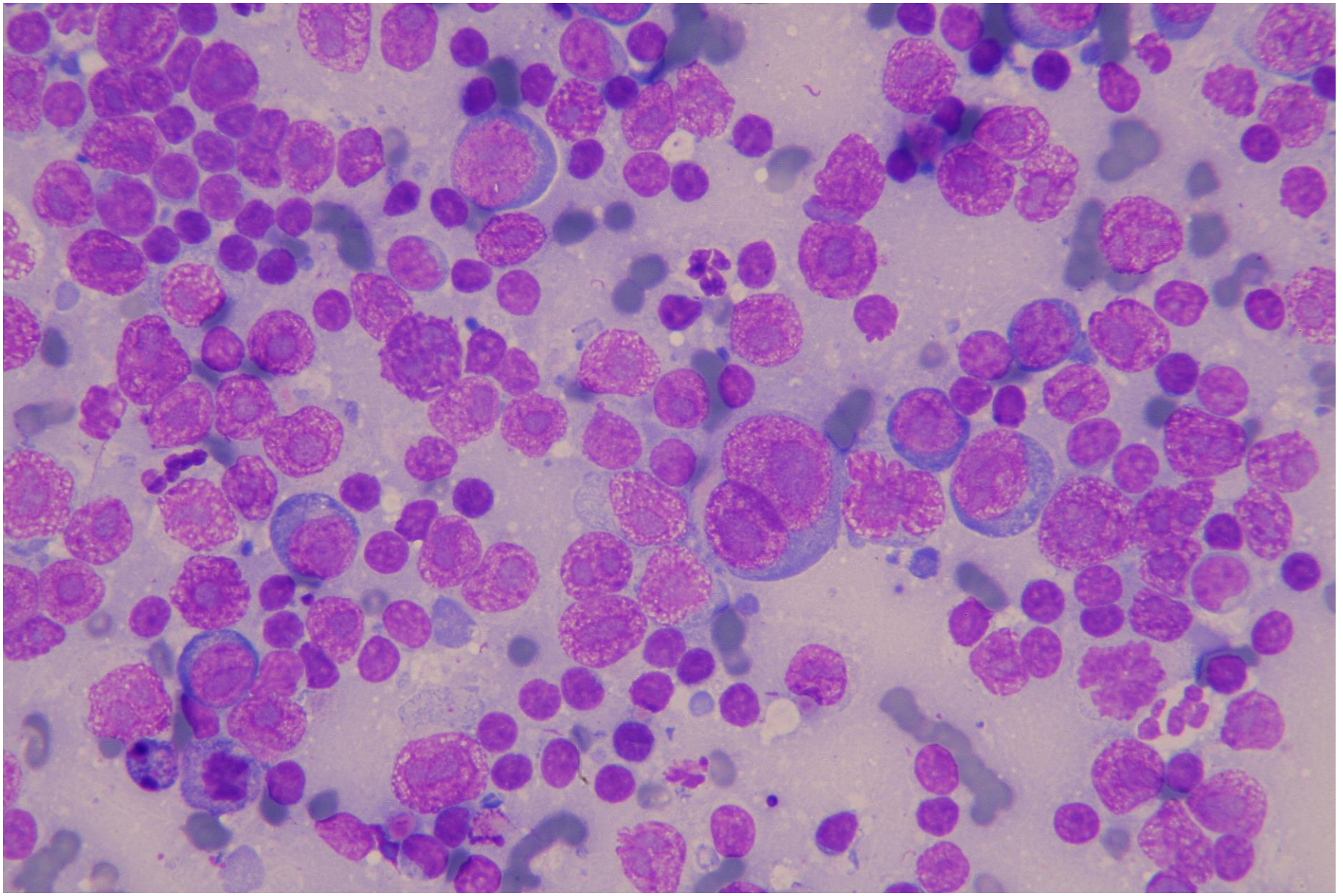
Discussion

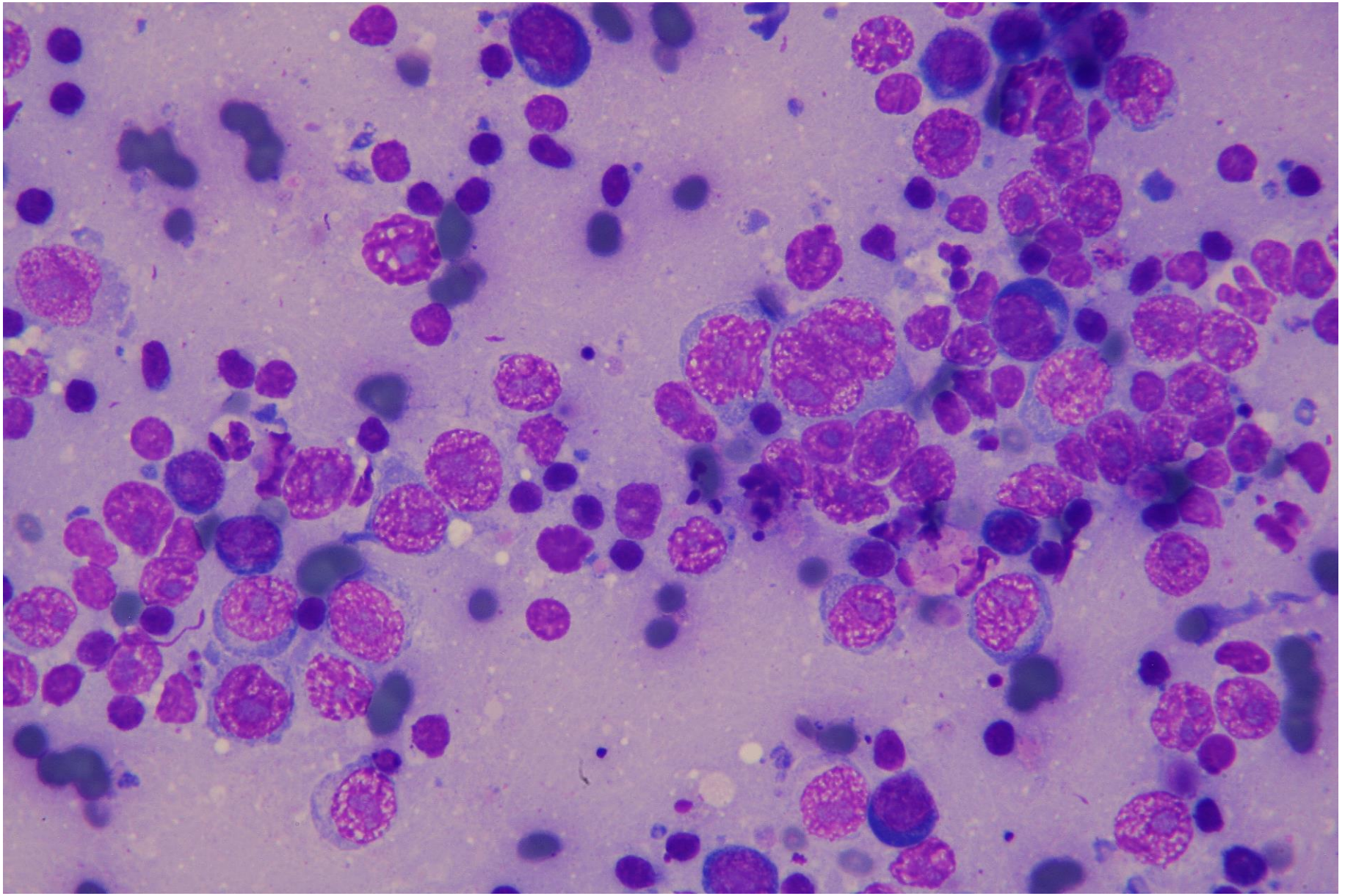
- Differential diagnosis
  - Infectious diseases
    - Cytology much more able to recognize infectious agents than histology
    - No evidence of bacteria or fungi
    - Is a Leishmania infection possible???
  - Sterile granuloma or pyogranuloma syndrome

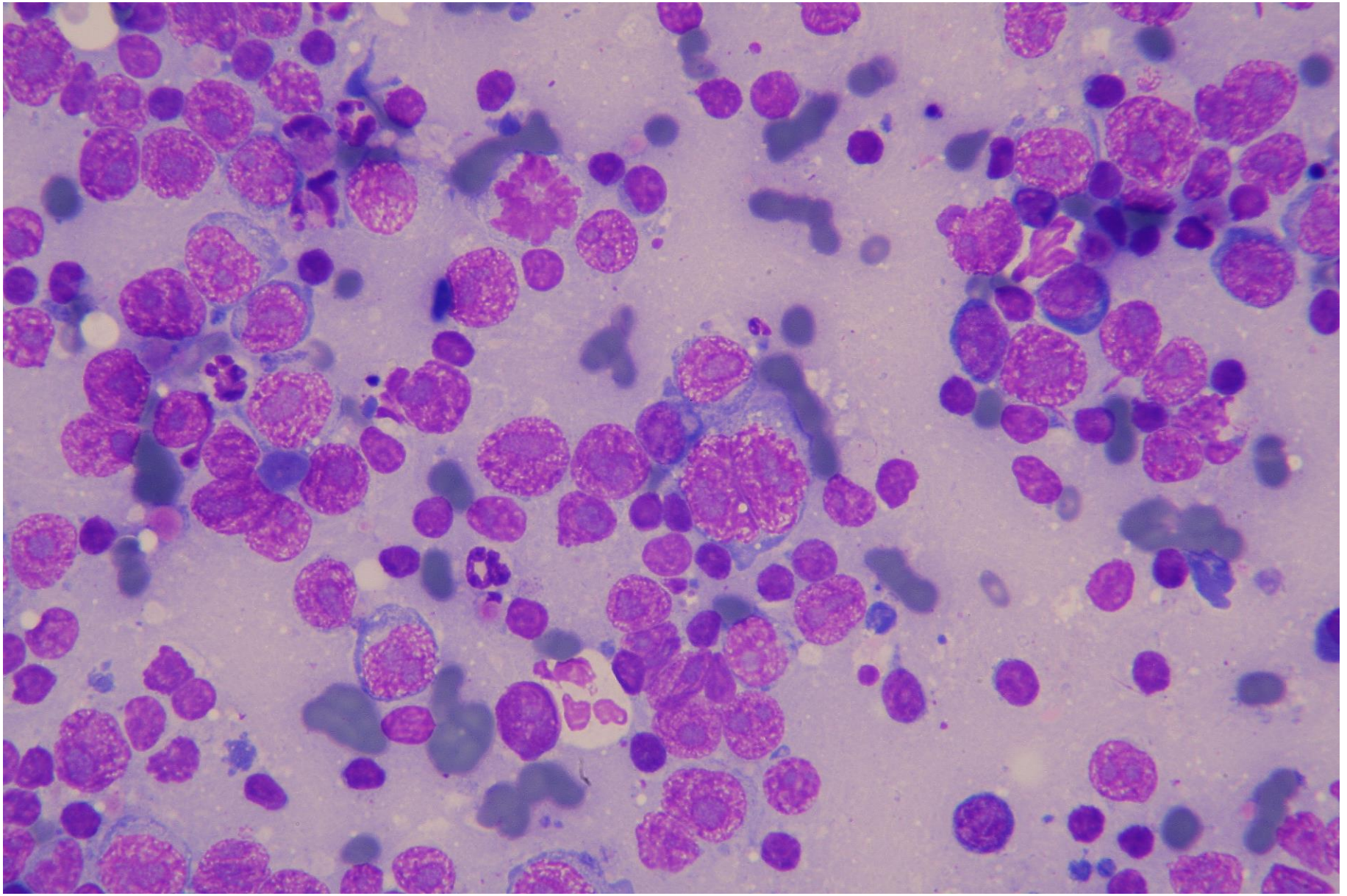
Case #2

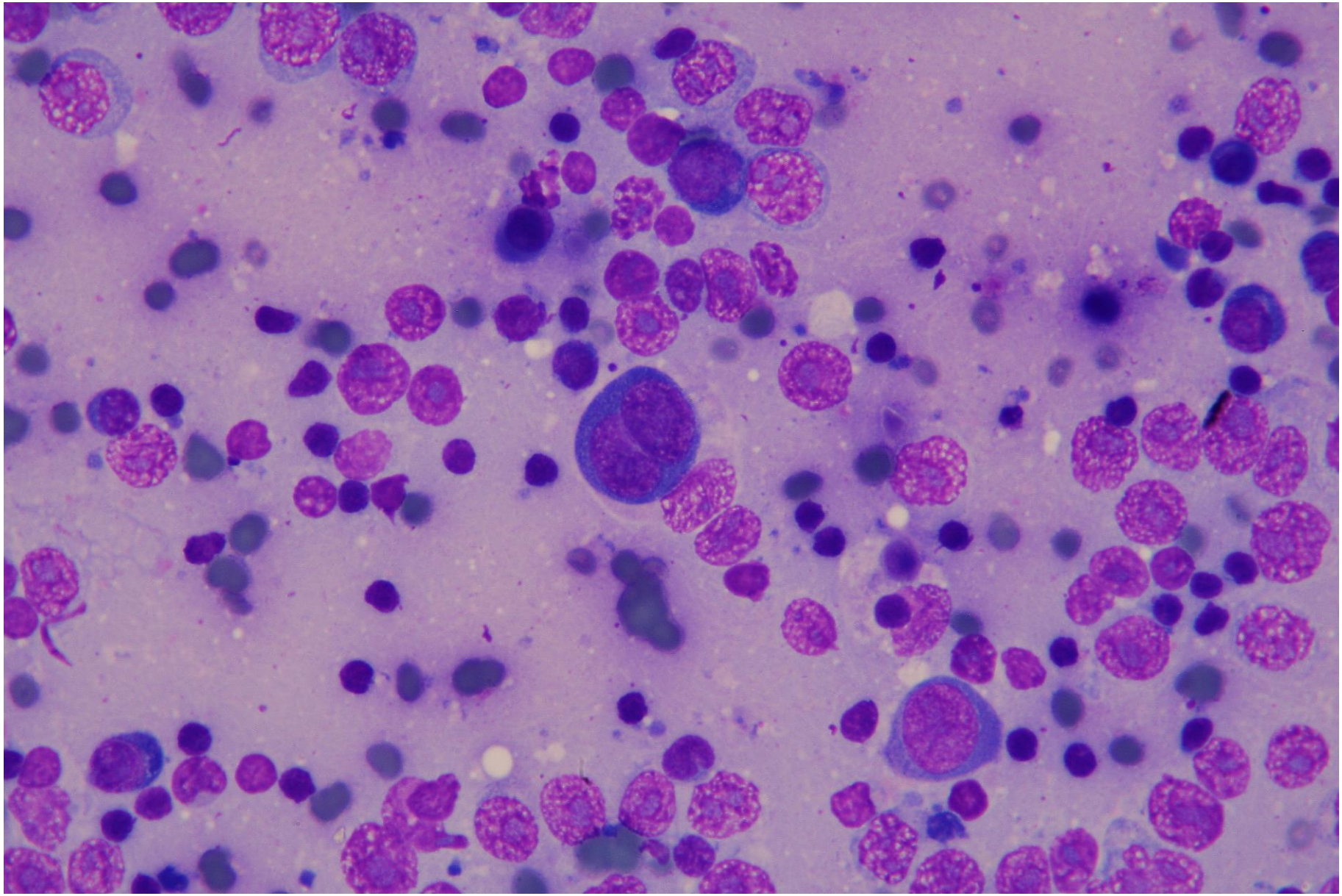
- 5-year-old, neutered male, Persian cat.
- Enlarged mandibular lymph node.

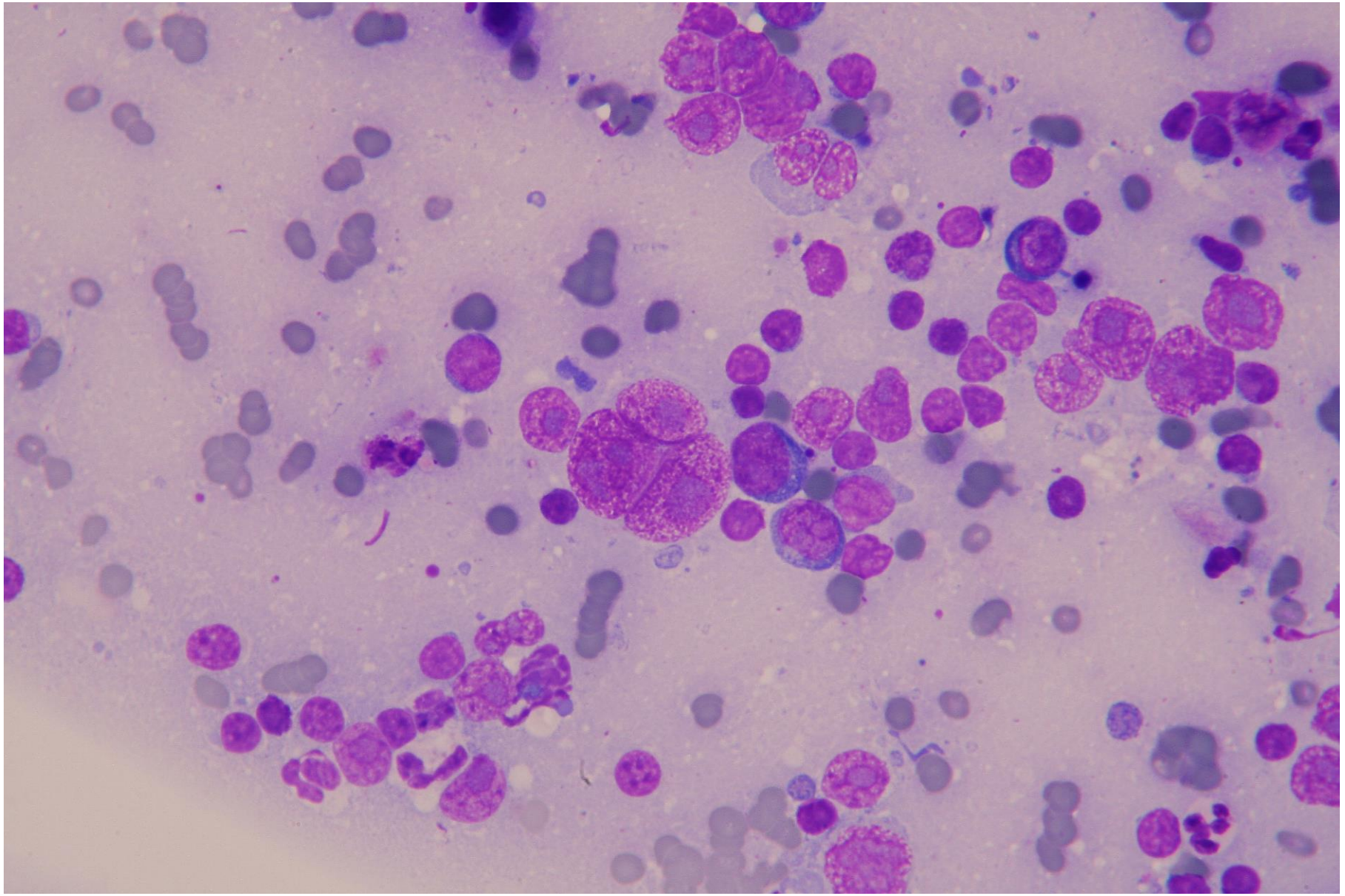
- FNCS of the lesion
- MGG stain.

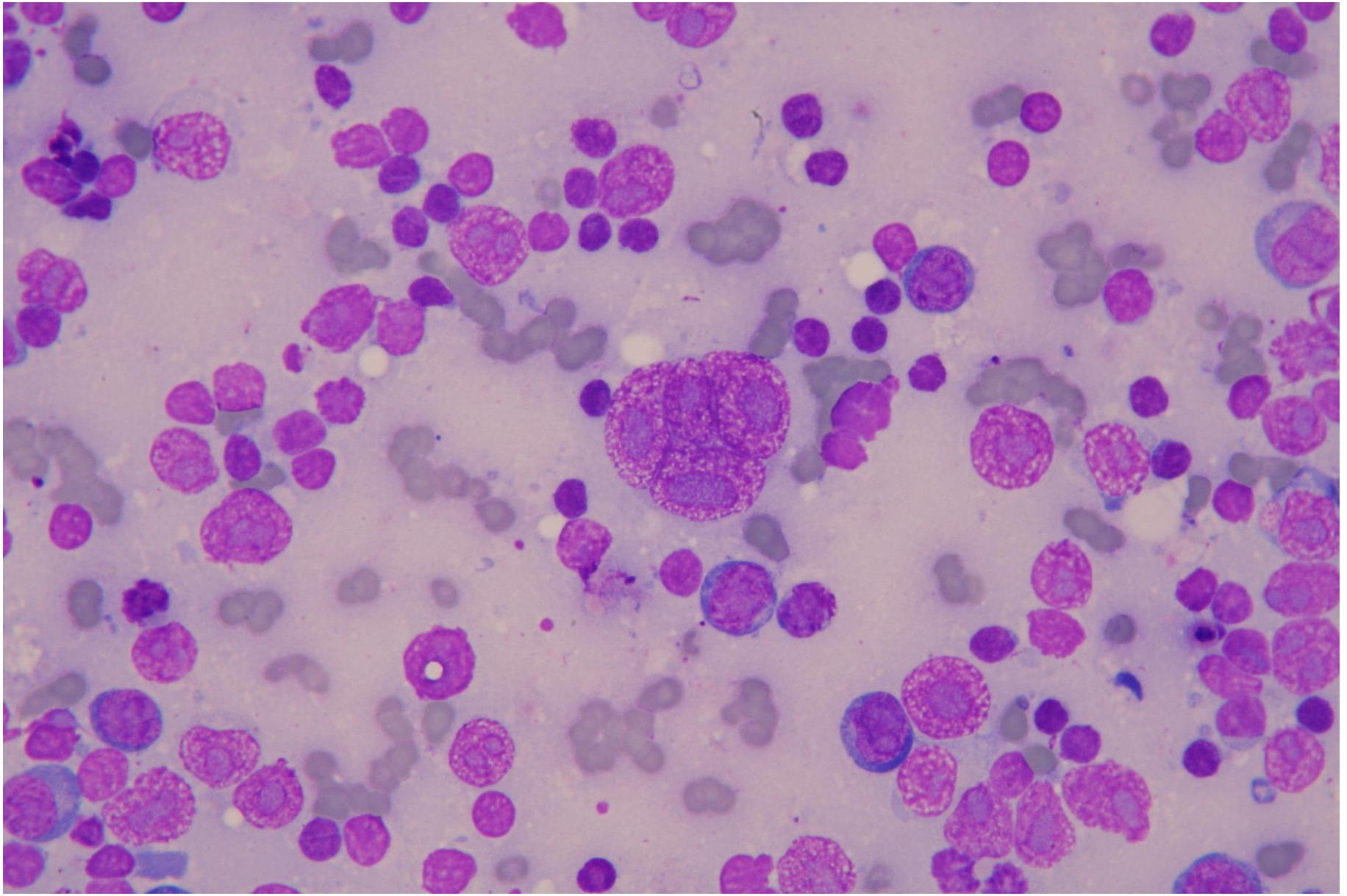












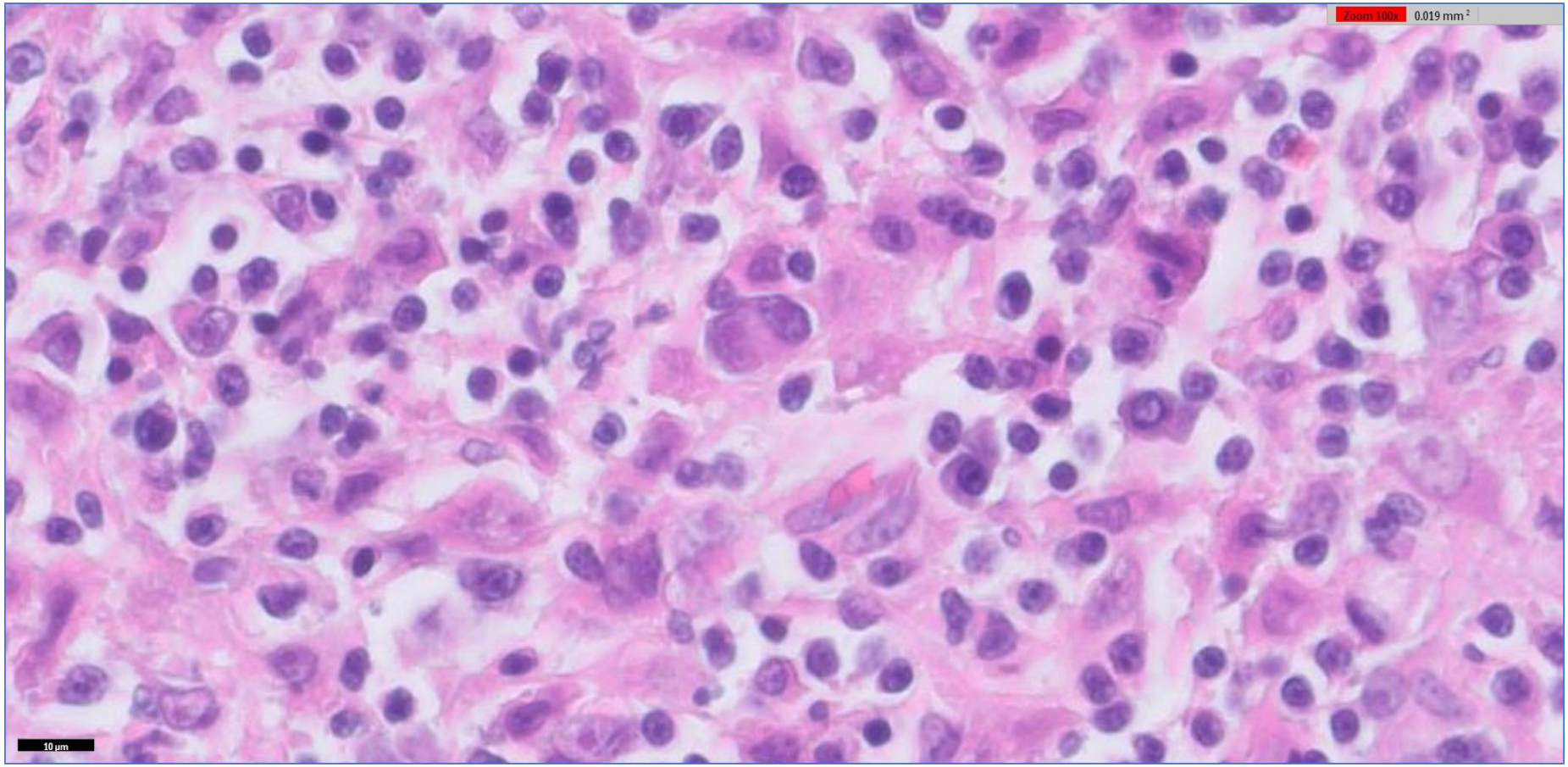
Cytologic findings

- Mixed polymorphic lymphoid population
- High number of large cells with basophilic cytoplasm (B cell appearance) and round nuclei with clumped chromatin and prominent nucleolus
- Some large (20-40 µm) round cells with two nuclei and prominent nucleoli, resembling Reed-Sternberg-cells, as described in human being
- Population of small to intermediate-sized lymphocytes

Diagnosis

- Cytological diagnosis
  - T cell-rich large B-cell lymphoma (TCRLBCL)
  - Also called «feline Hodgkin's disease»

- Histological diagnosis
  - T cell-rich large B-cell lymphoma (TCRLBCL)
  - IHC not done



- Normal architecture effaced
- Presence of mixed population of lymphoid cells
- Large Reed-Sternberg-like cells much more difficult to be recognized

Discussion

- My interpretation:
- Based on the presence of two distinct population
  - Small to intermediate-sized lymphocytes
  - Large cells with round nucleus
- Presence of Reed Sternberg-like cells
    - Large B cells with marked anisokaryosis (CD20+/-; CD79a+/-)
    - Large nucleus with clumped chromatin and central nucleolus
    - Often binucleated, sometimes 3-4 nuclei
    - Sometimes pyknotic nucleus

Discussion

- Early TCRLBCL may have 80-90% small to intermediate-sized non neoplastic T cells, with the rest of the cells being neoplastic large B cells and histiocytes
- Neoplastic B cells gradually increase in number
- The pattern seen with IHC are unusual because of the heterogeneity of cells:
  - Large B cells: CD20+; CD79a+/-
  - Smaller T cells: CD3+
- How can be useful the recognition of Reed-Sternberg cells in early diagnosis?
- It is IHC necessary for diagnosis?

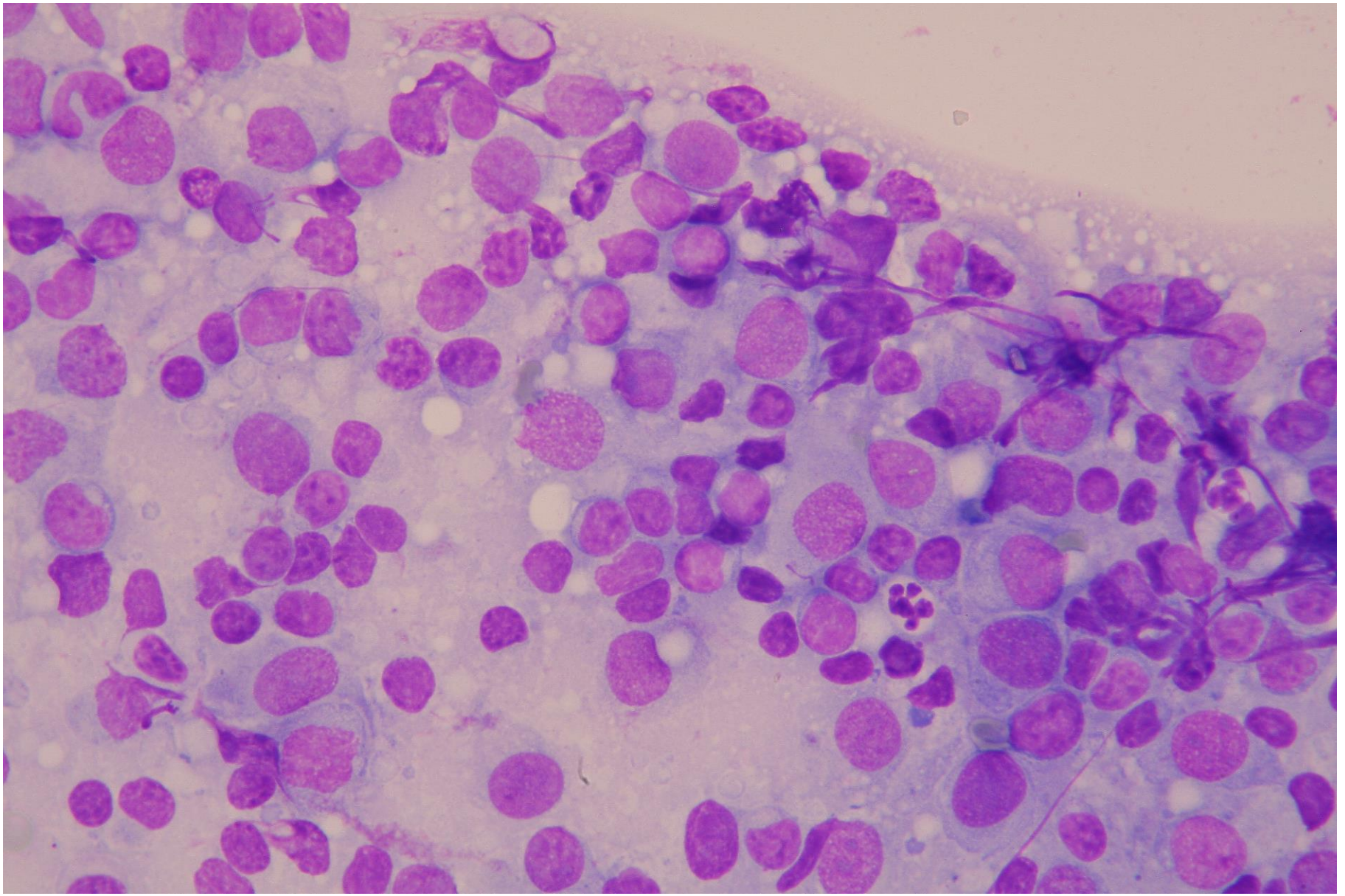
Discussion

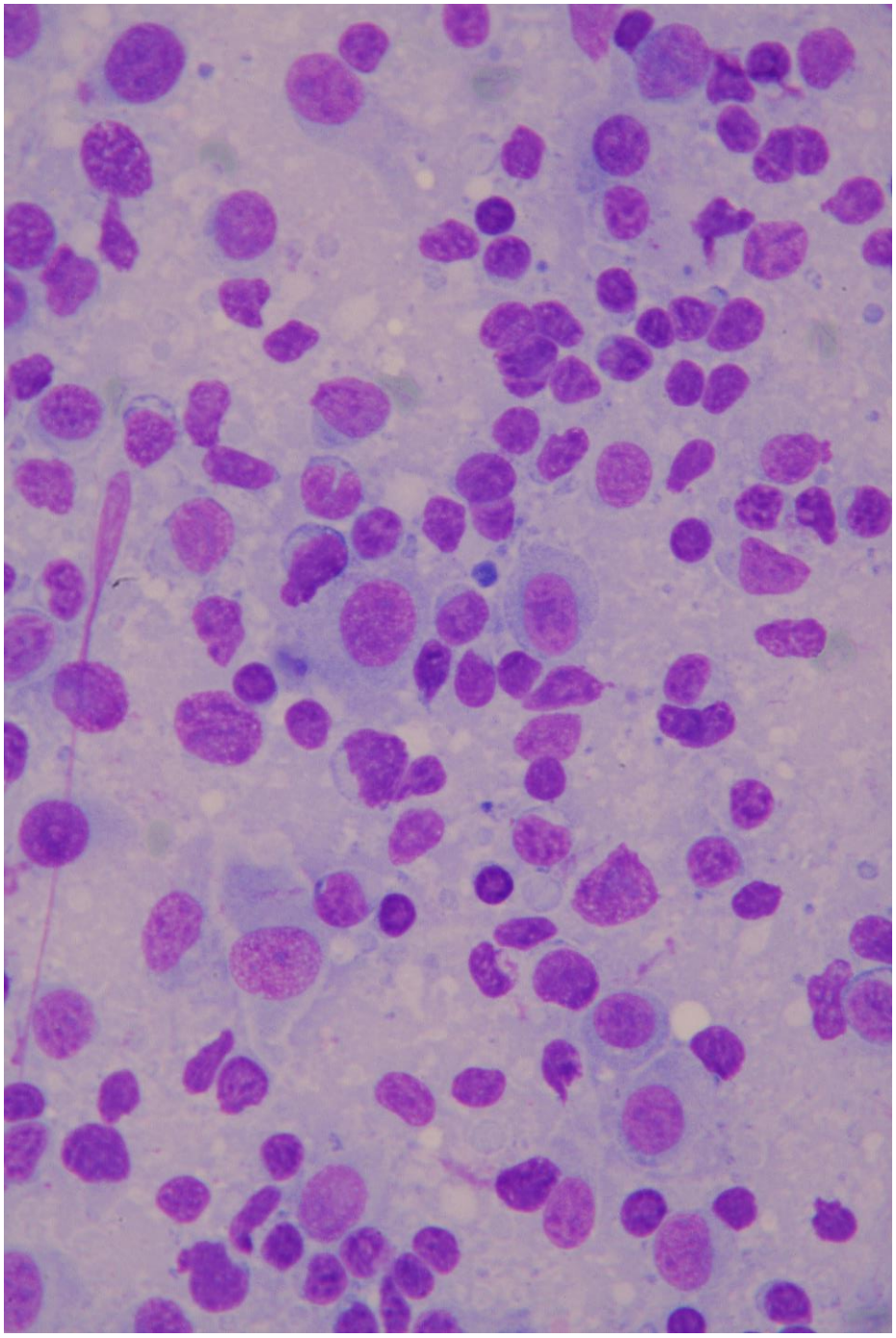
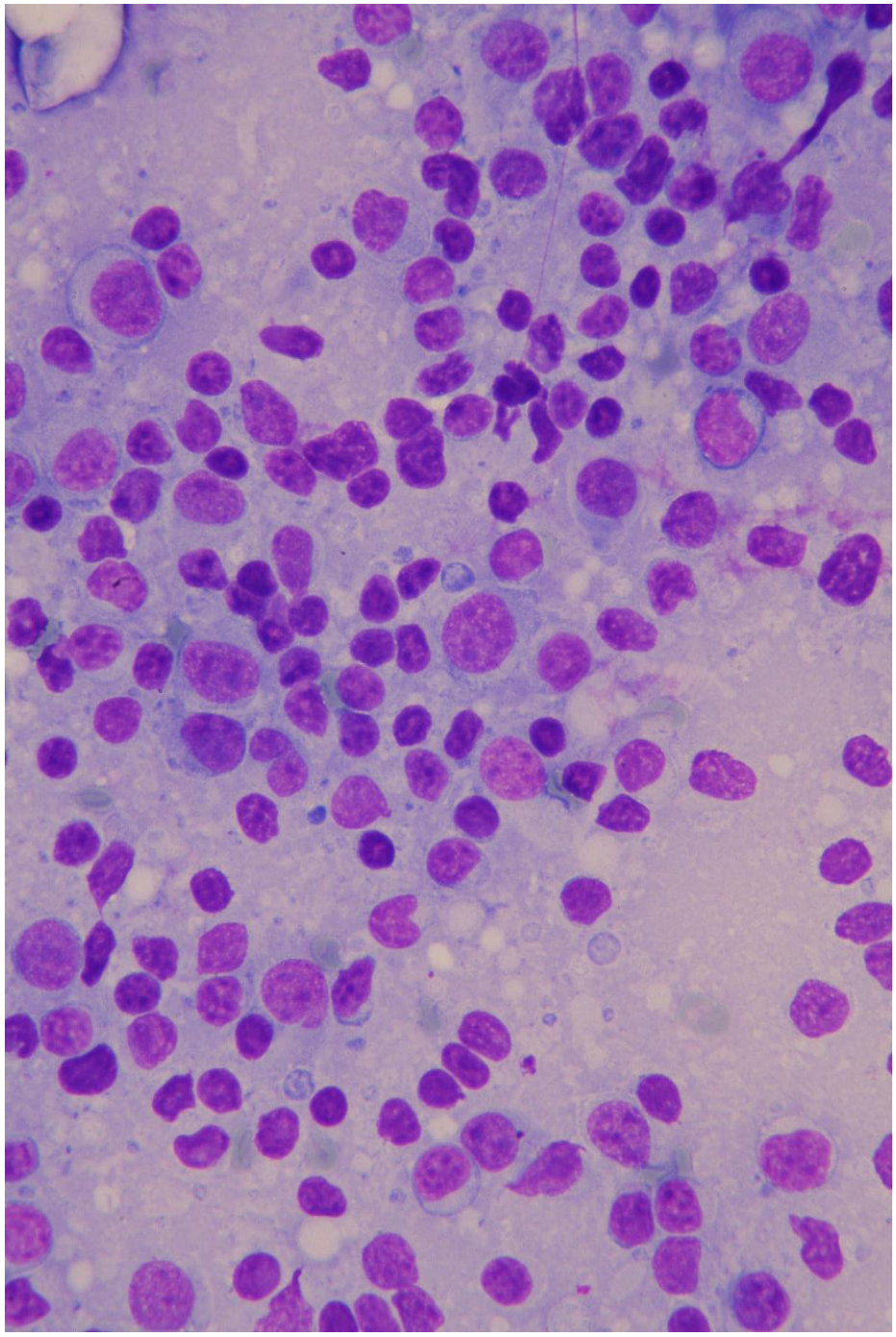
- TCRLBCL constitutes about 10% of all feline lymphomas
  - Also described in dog(+/--), horse (++), killer whale, skunk and rat
- Most cats are generally in good body condition
- Generally a single enlarged lymph node in the neck area
- 25% of the cats may presents multicentric localization of the disease.
  - Need for staging

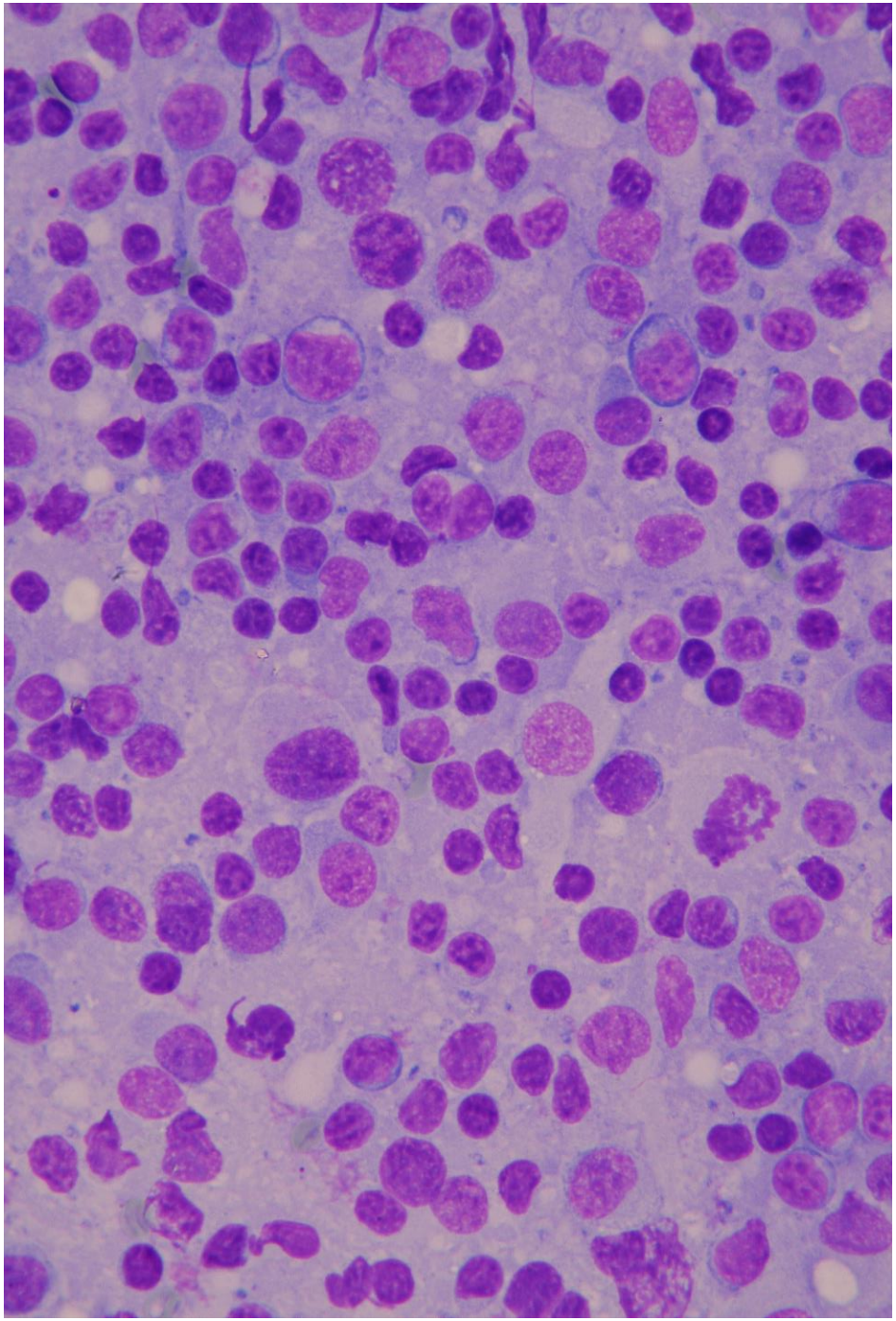
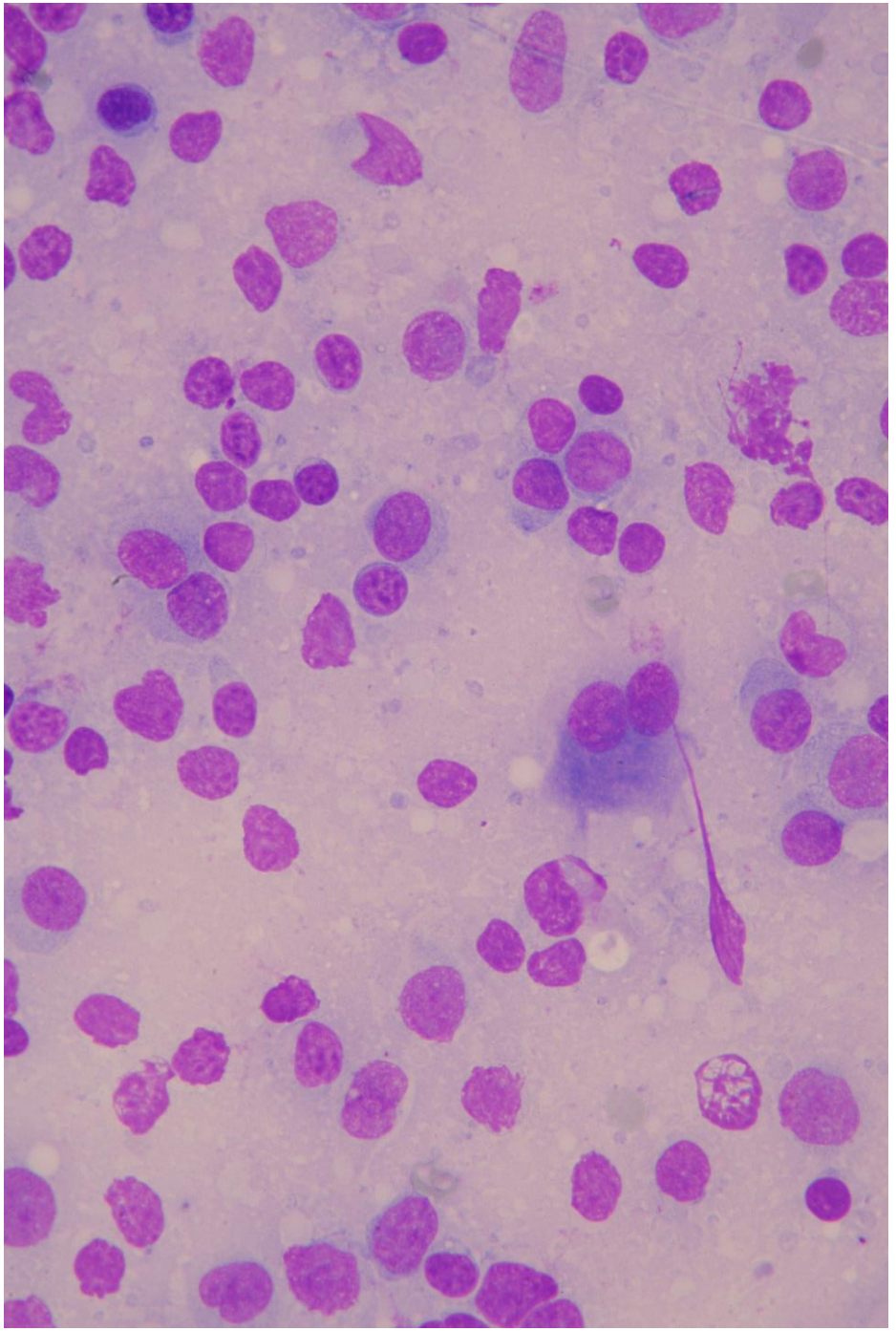
Case #3

- 10-year-old, male, Boxer dog.
- Cutaneous nodule on the eyebrow

- FNCS of the lesion
- MGG stain



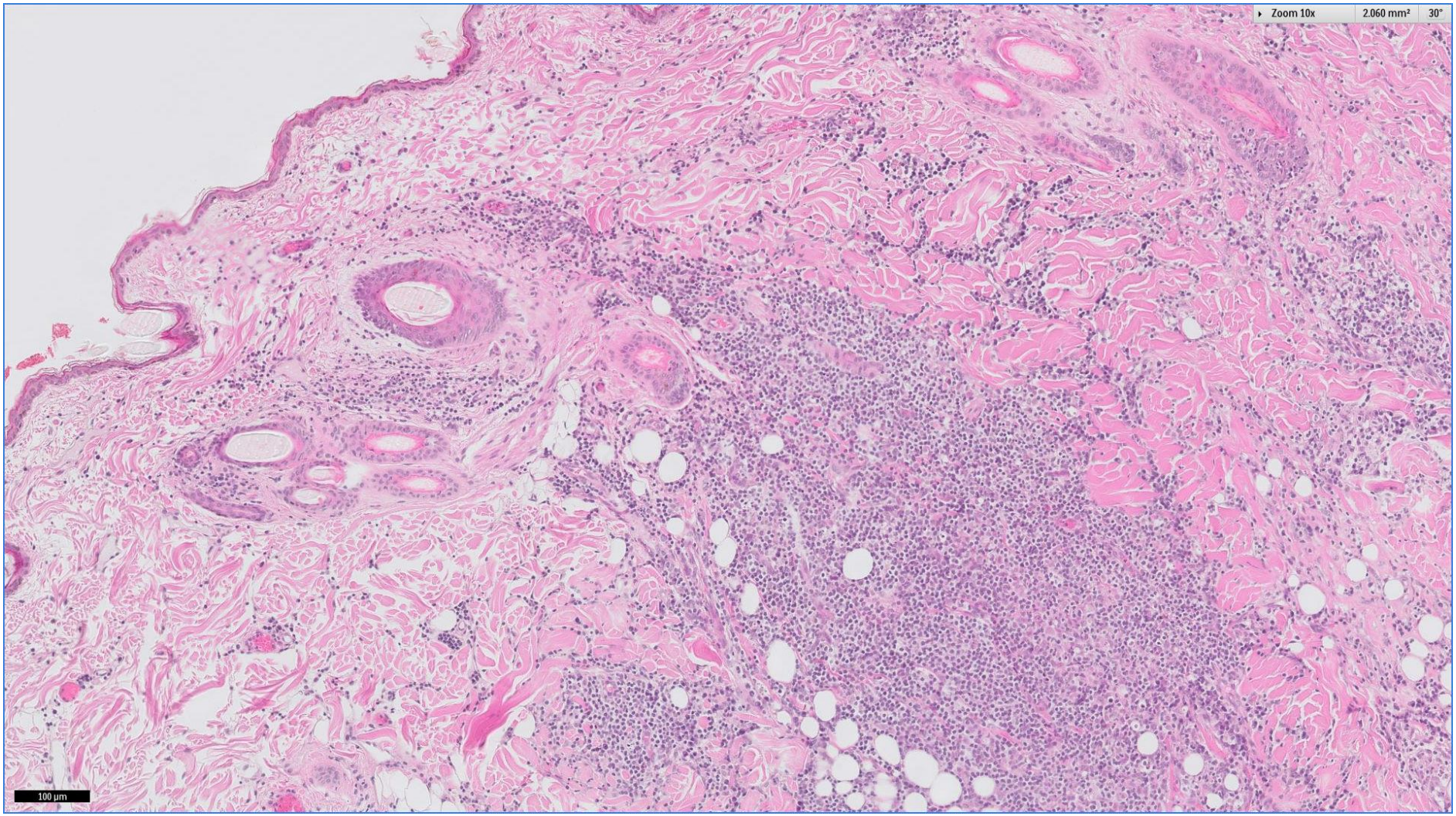



Cytologic findings

- Large round to polygonal, sometimes spindle cells
- slightly basophilic cytoplasma
- Large nucleus with finely distributed chromatin
- Large amount of mixed lymphocytes
- Rare plasma cells

Diagnosis

- Cytological diagnosis:
  - Regressing histiocytoma
    - DD: mixed lymphocytic/histiocytic inflammation
- Histological diagnosis:
  - Regressing histiocytoma


Zoom 10x
2.060 mm²
30°
100 µm

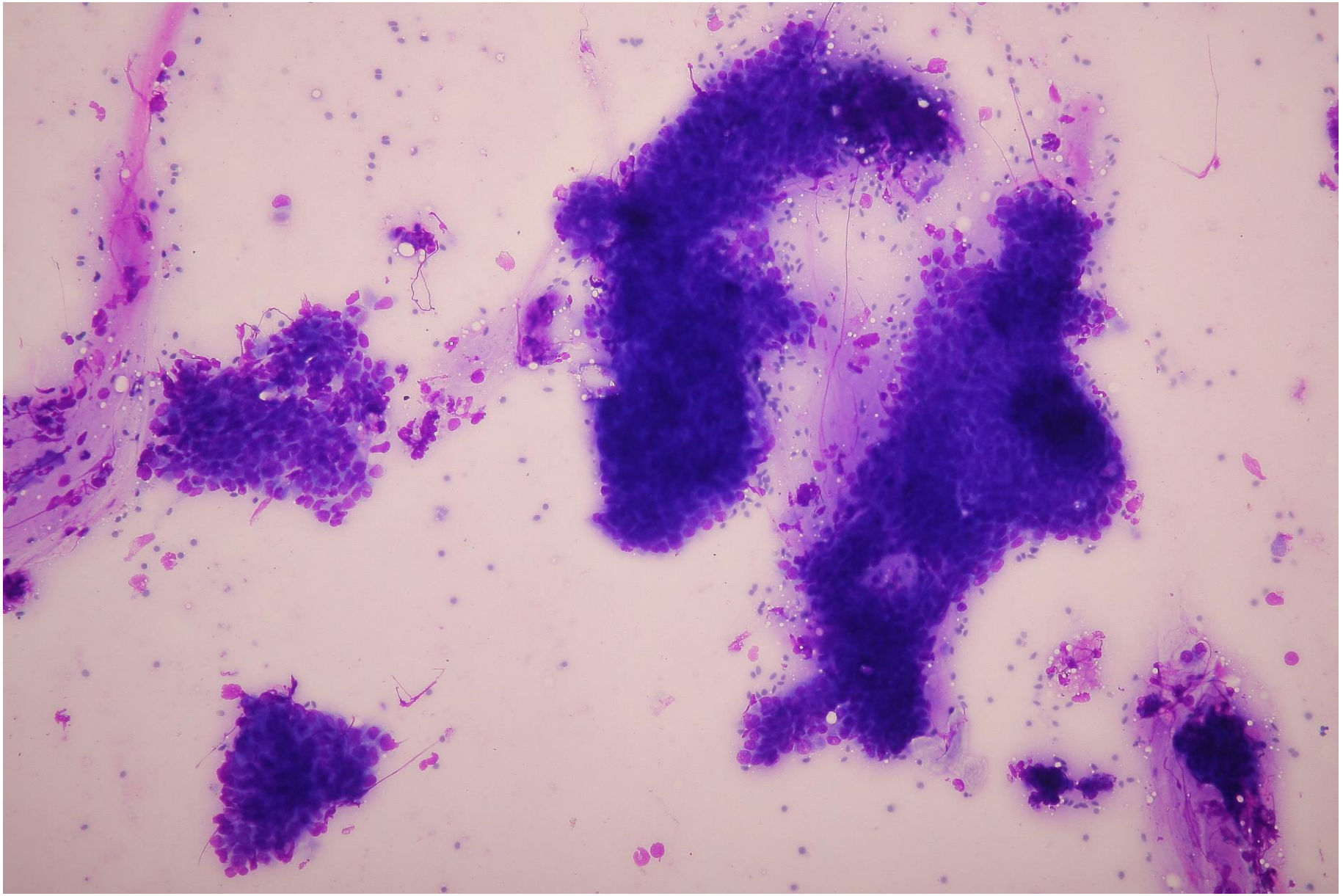
Discussion

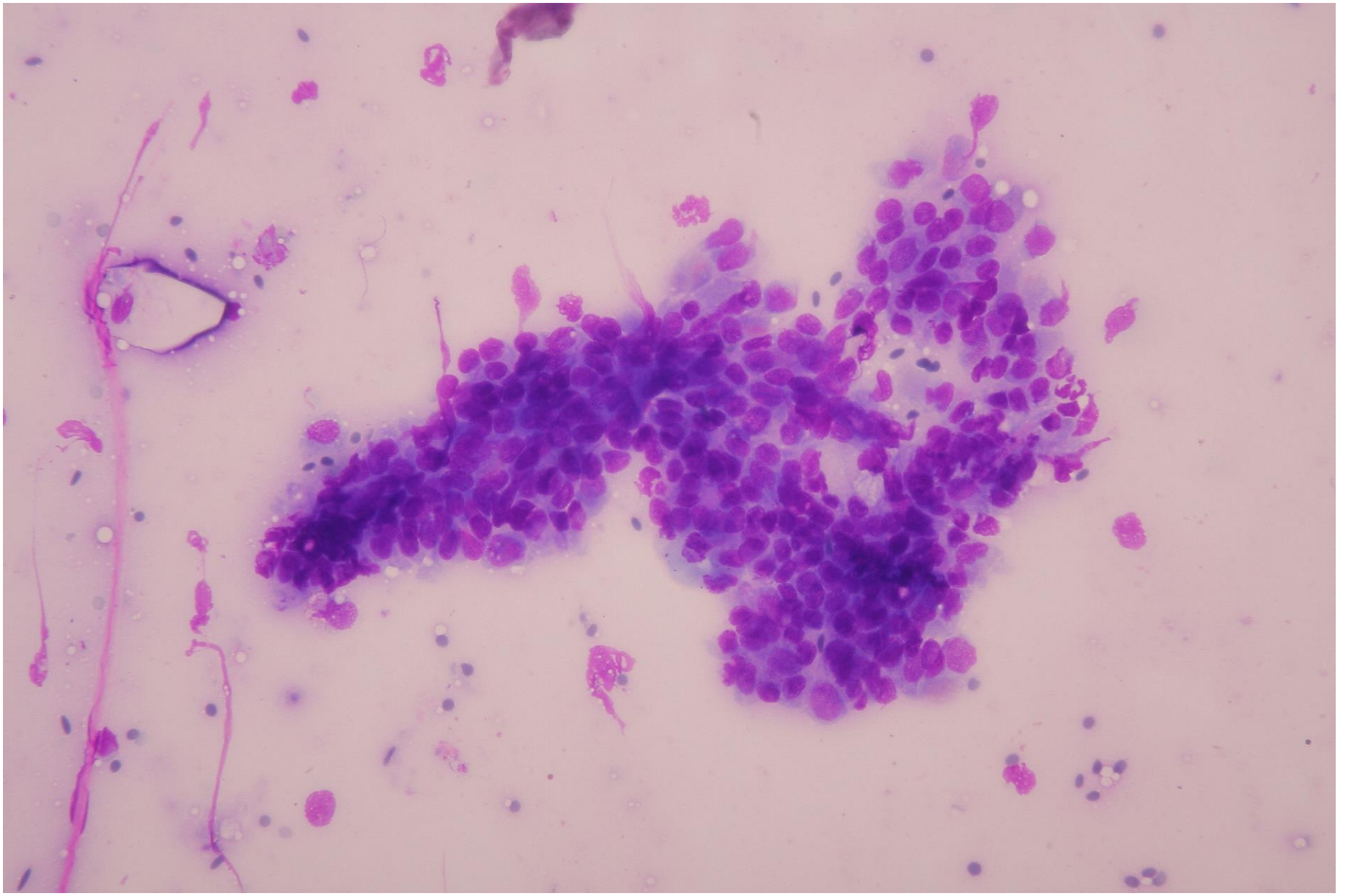
- Some doubts in diagnosis because the age of the dog
- Histiocytoma is much more frequent in young-middle aged dog but also described in old dog
- The lesion undergo spontaneous regression
  - CD3/CD8+ cytotoxic T cells

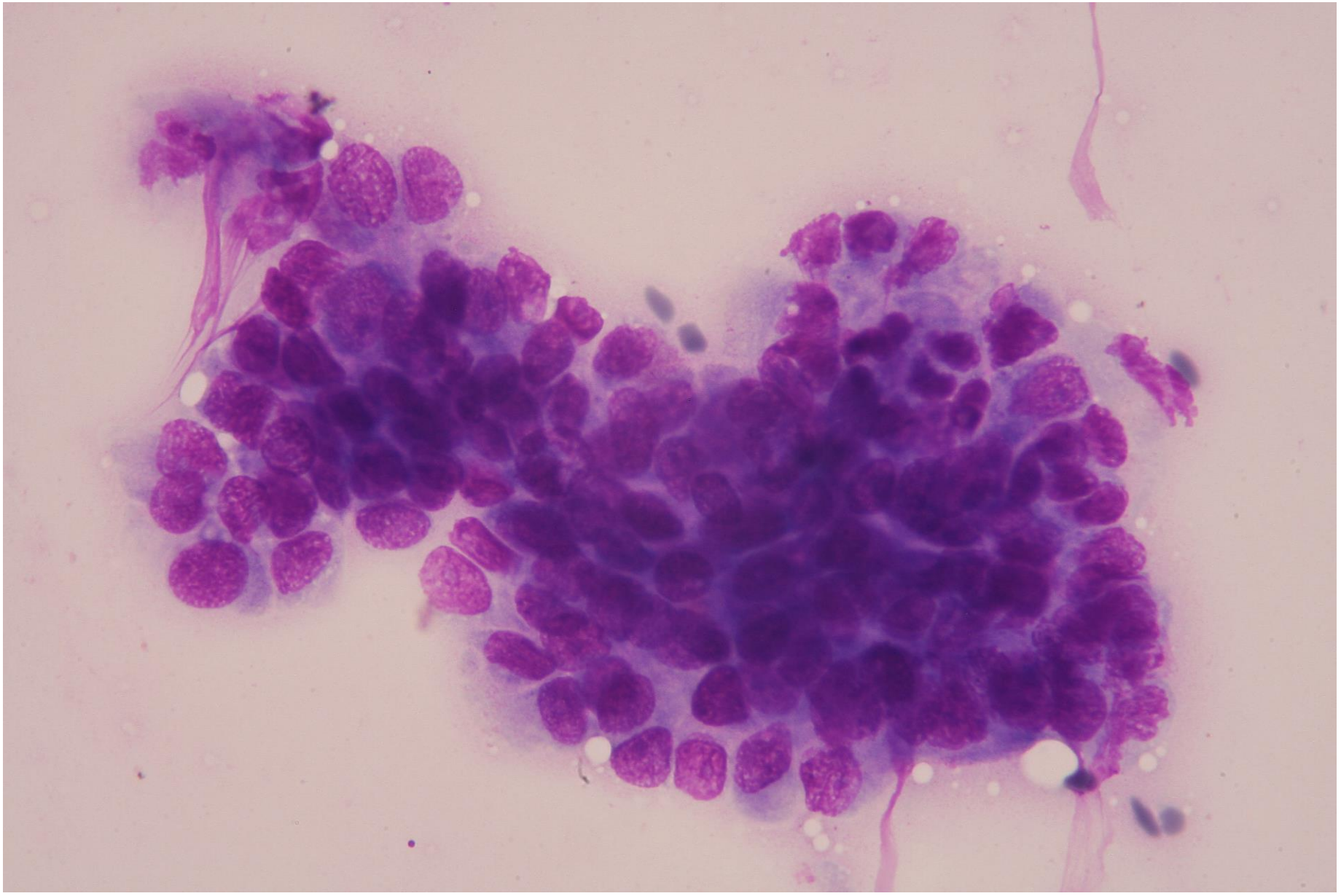
Case #4

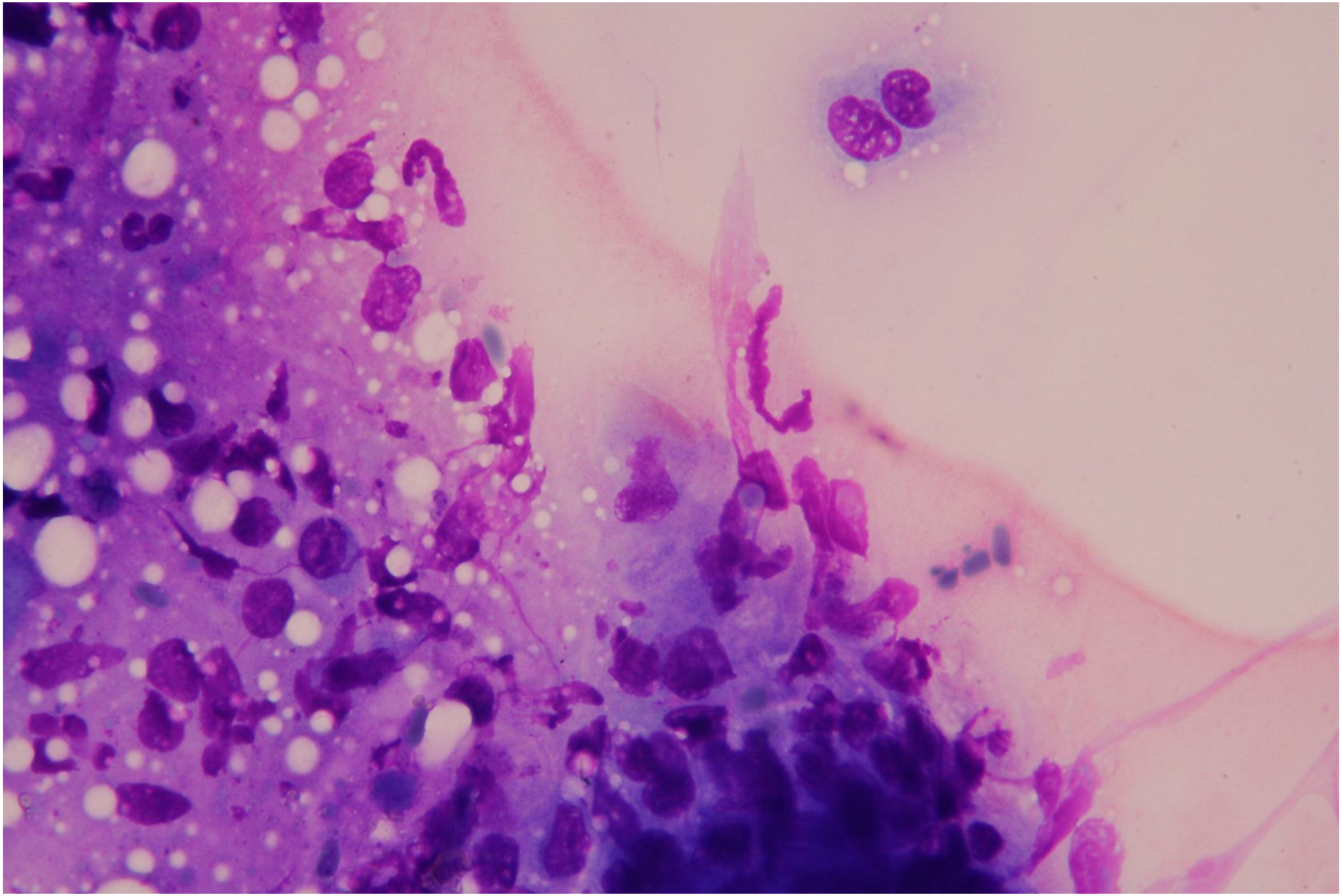
- 10-year-old, male, DSH cat.
- Nodule on a toe.

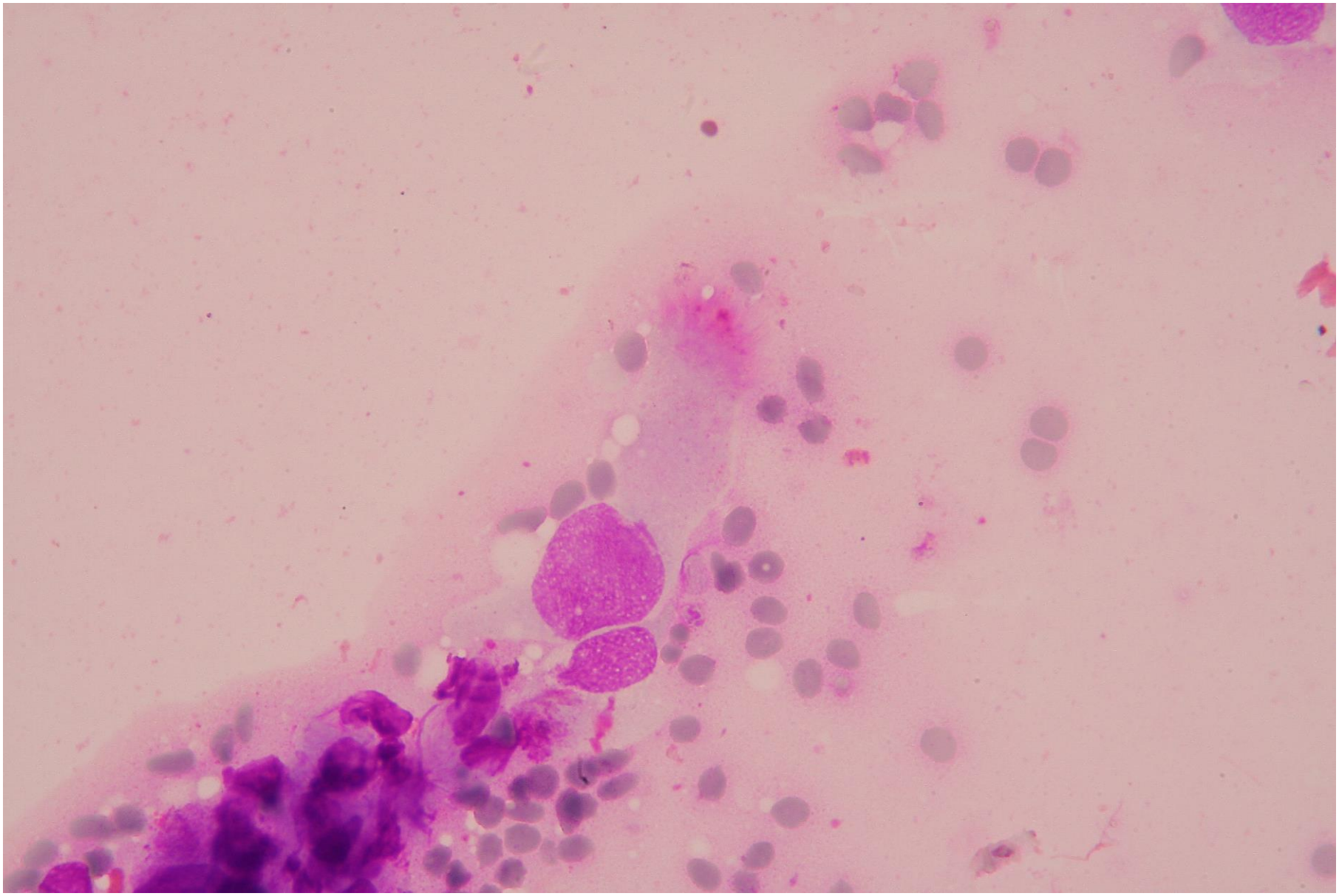
- FNCS of the lesion
- MGG stain











Cytological findings

- Bloody and proteinaceous background
- Many epithelial cells
  - Round to columnar shape;
  - Anisokariosis and anisocytosis moderate
  - Some ciliated cells
- Rare mixed inflammatory cells

Diagnosis

- Cytological diagnosis:
  - Malignant epithelial neoplasm
    - Suspected metastasis of primary pulmonary carcinoma (Lung & Digit Syndrome)
- Histological diagnosis
  - Malignant infiltrative epithelial neoplasm;
  - Possible Lung & Digit Syndrome

100 µm
Zoom 10x
2.860 mm²
300°

Zoom 60x
0.057 mm²
300°
20 µm

Follow-up

- RX: nodular mass into the lung
- Presence, in some weeks, of others small nodules in the skin of the fingers

Discussion

- Lung & Digit Syndrome
- Unusual pattern of metastasis that is seen with various types of primary lung tumours
    - Bronchial and bronchioalveolar adenocarcinoma.
- Tumour metastases are found at atypical sites, notably the distal phalanges of the limbs.
    - Direct arterial embolisation from the tumour.
- Other sites of metastases skin, eyes, skeletal muscle and bone, as well as multiple thoracic and abdominal organs.

Goldfinch, 2012

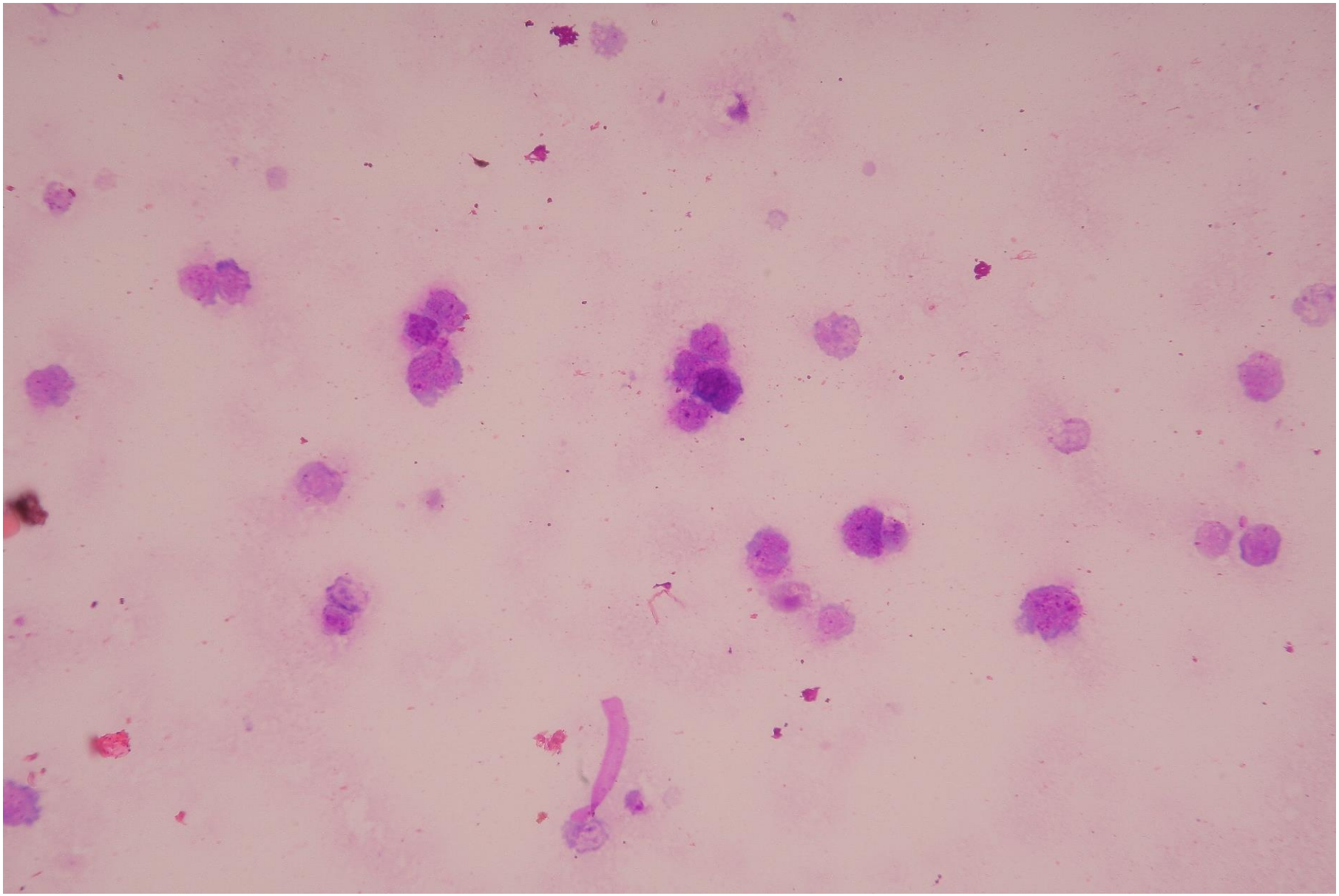
Discussion

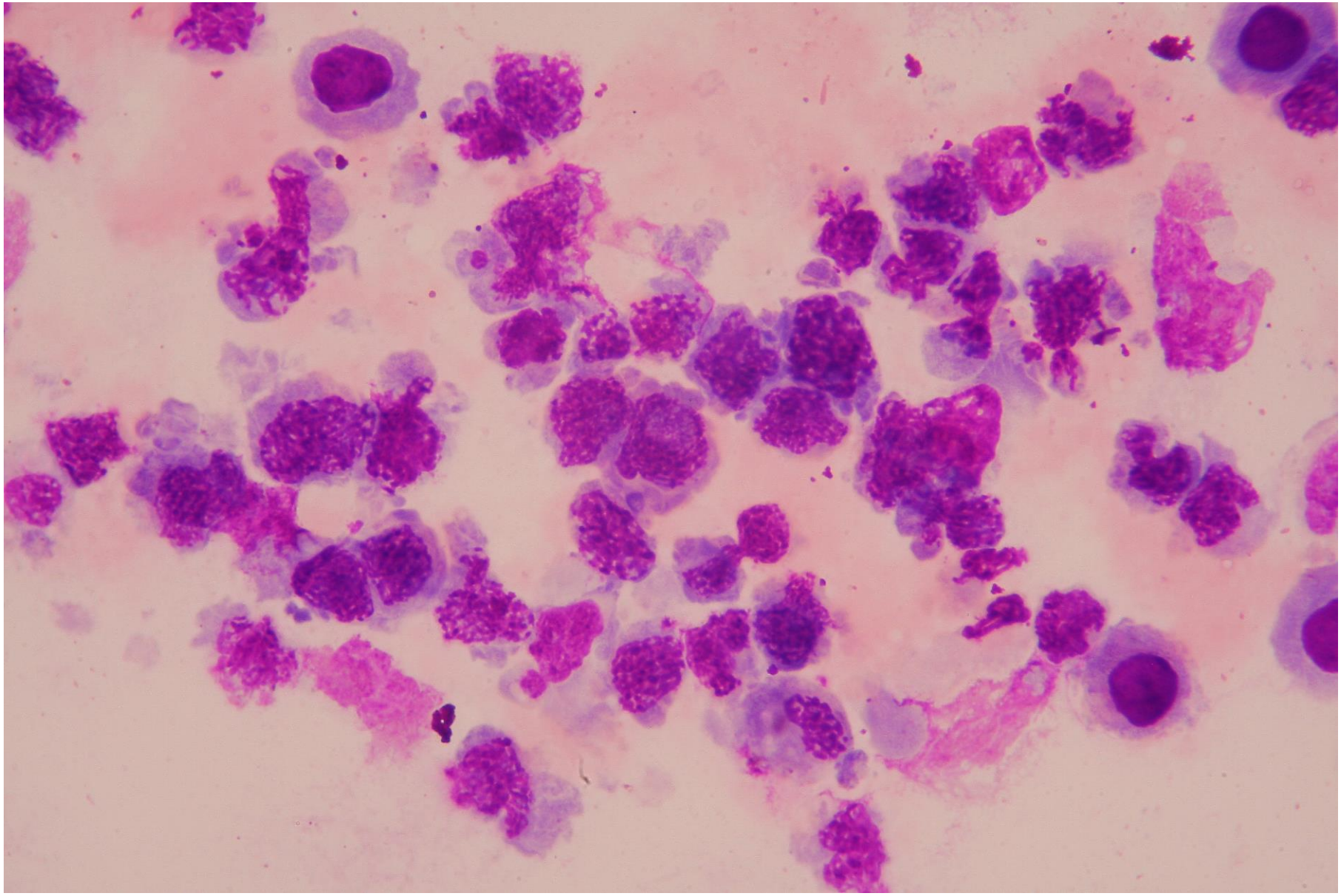
- Presence of ciliate cells into the tumor as morphologic hallmark
- The high digital blood flow and weight bearing favors metastasis to the digits, but the exact pathophysiology is unknown

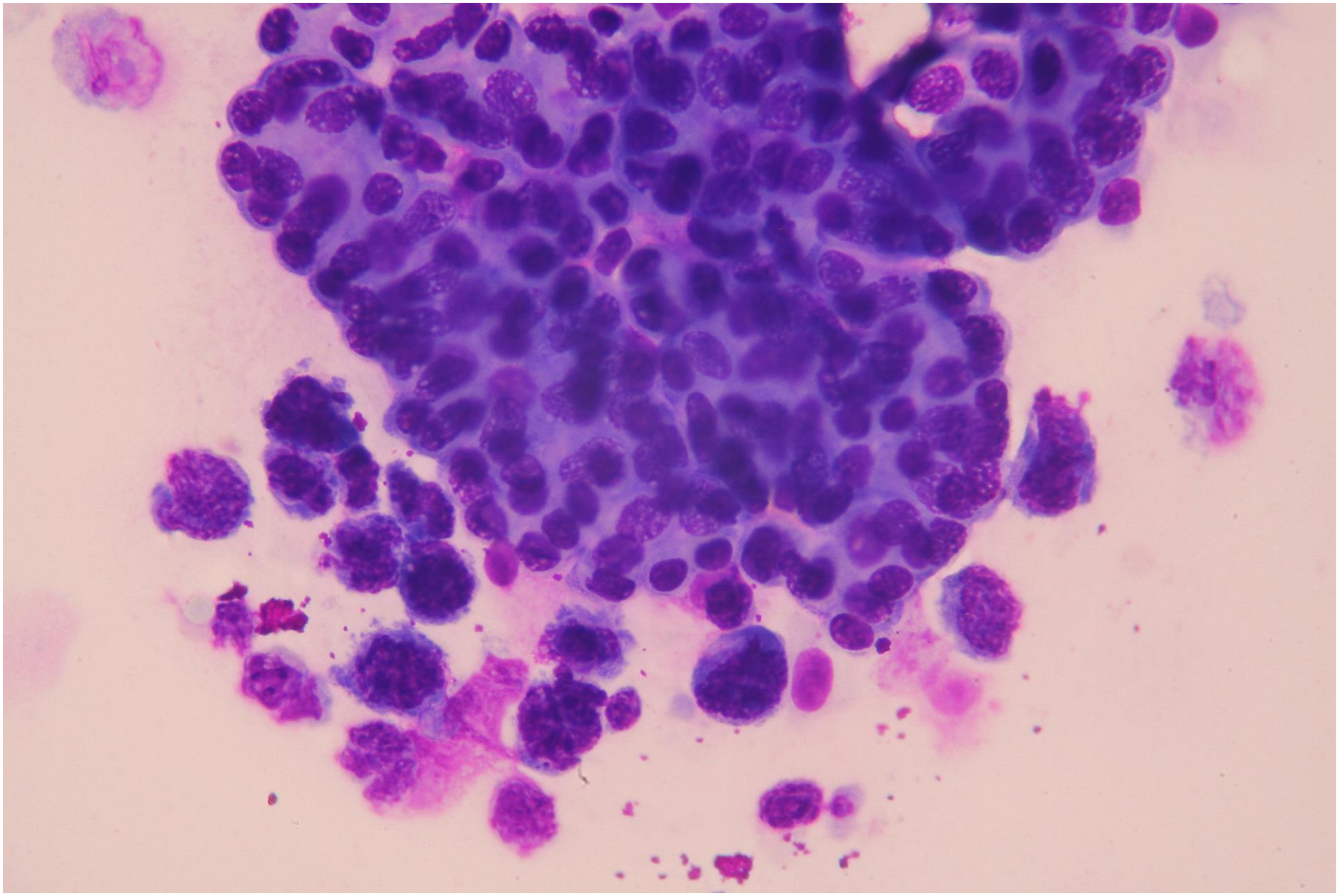
Vobornik, 2014

Case #5

- 14-year-old, male, mixed breed dog.
- Haematuria
  - Thickening of wall bladder on US
  - Presence of suspended material, adherent to bladder surface
- Smear of urine sediment
- MGG stain







Cytologic findings

- Medium, large-sized round cells
  - Small amount of slightly basophilic cytoplasm
  - Round to irregularly folded nucleus
  - Clumped chromatin, rare nucleoli
- Cells are frequently disrupted
- Rare epithelial (transitional) aggregates

Diagnosis

- Cytologic diagnosis
  - Bladder lymphoma
- Histological diagnosis:
  - Not done

Staging and follow-up

- No evidence for US changes in other organs
- No evidence, by FNCS, for involvement of lymph nodes, spleen or liver parenchyma

- After 5 weeks the dog developed fever, anorexia and peripheral lymph nodes enlargement
- Large cells lymphoma

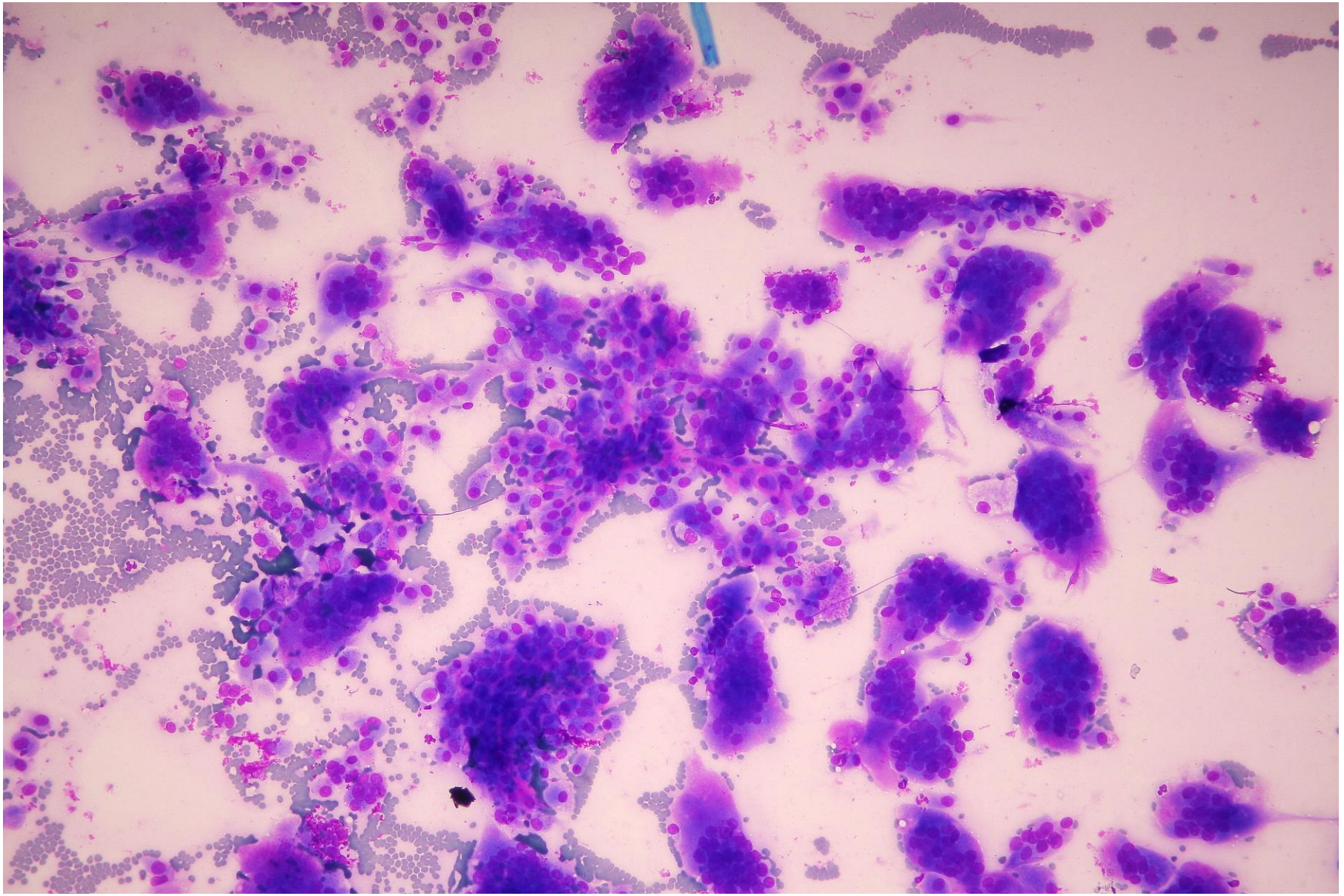
Discussion

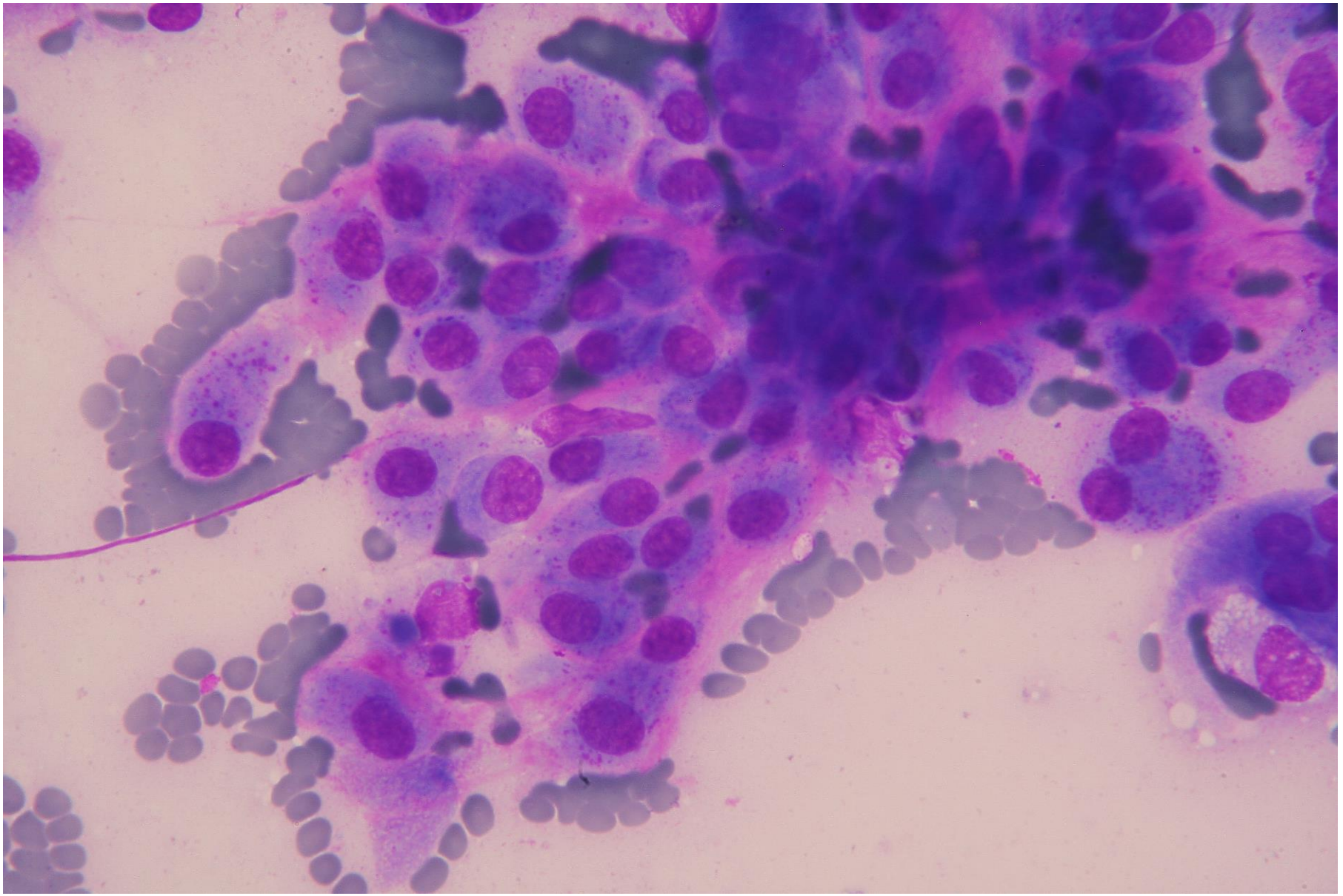
- Bladder lymphoma:
  - Extremely rare as primary disease
  - In veterinary medicine, only 8 cases have been reported
    - 2 in dogs
  - Primary disease, part of a multicentric lymphoma or extension from other sites?
- Need for complete staging

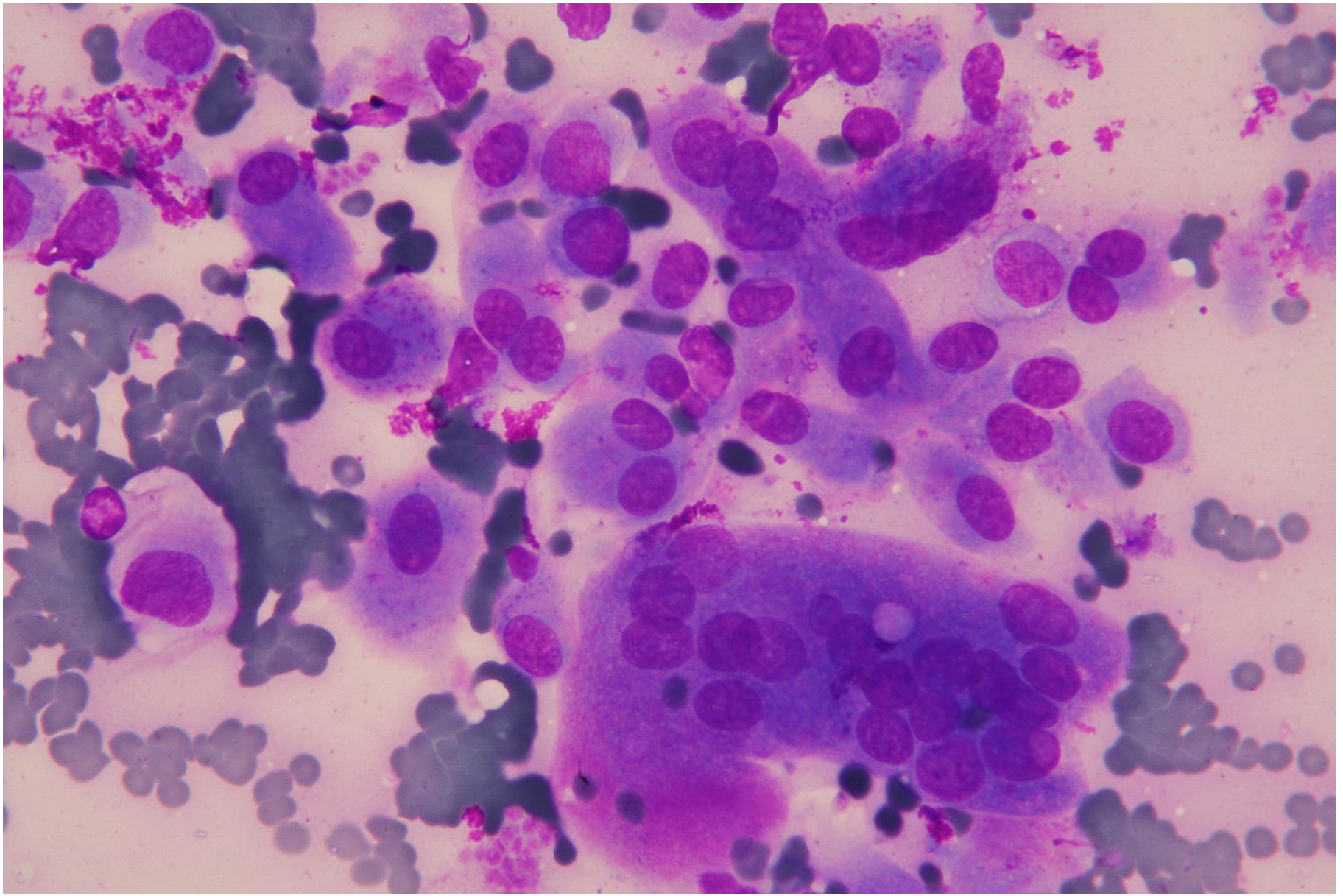
Case #6

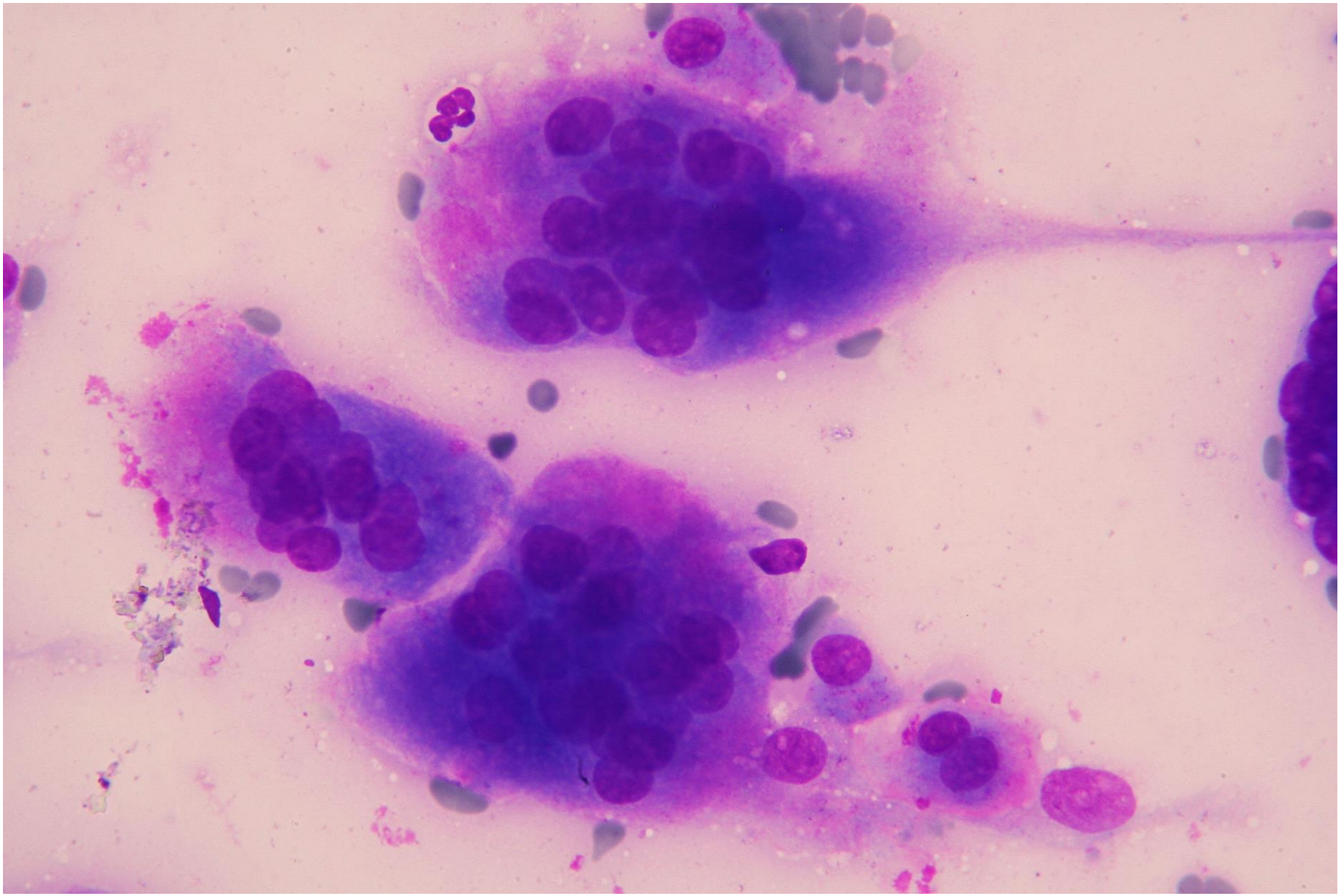
- 10-year-old, neutered female, DSH cat.
- Subcutaneous lump on the nasal planum, near the eye; radiographic evidence of osteolysis

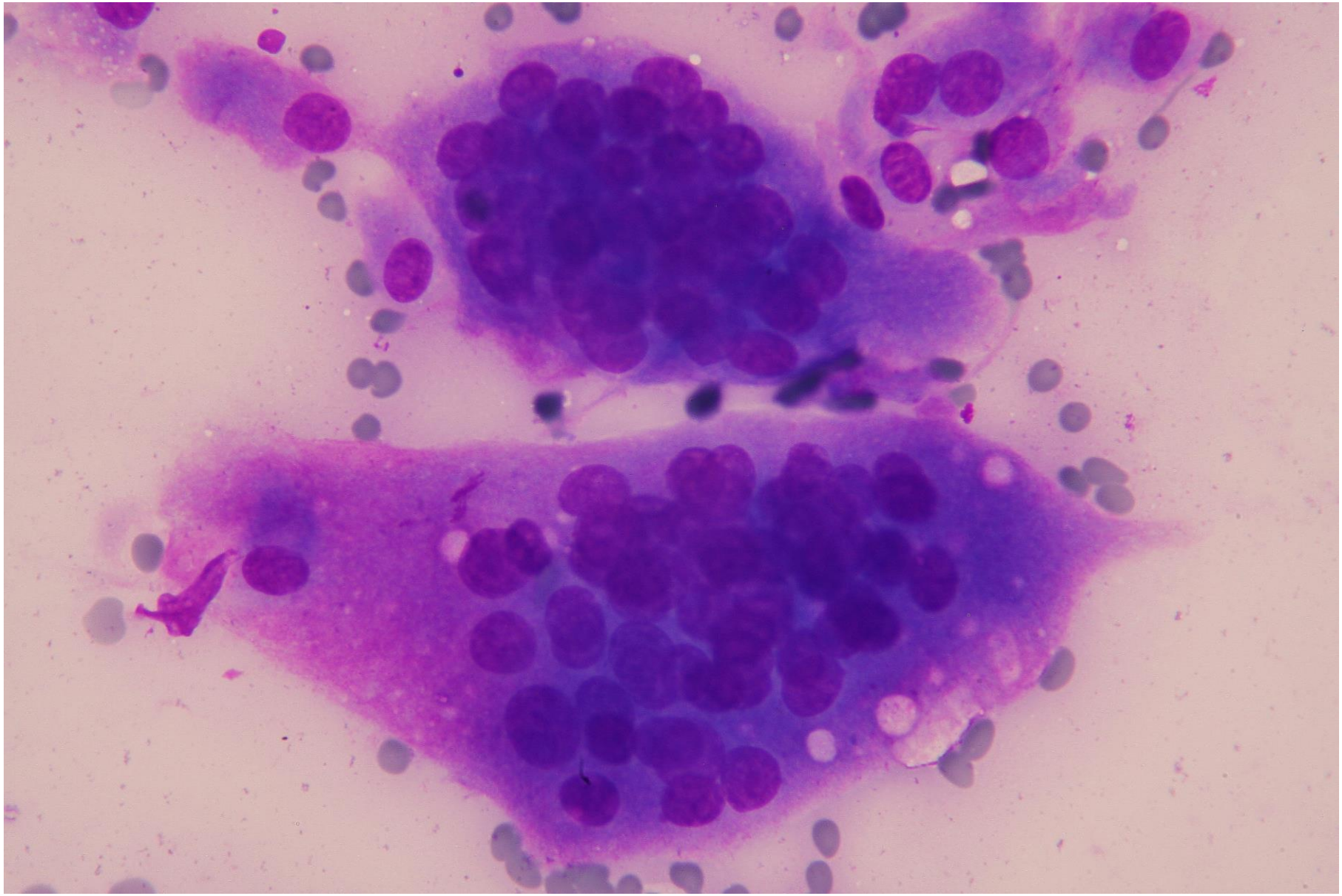
- FNCS of the lesion
- MGG stain









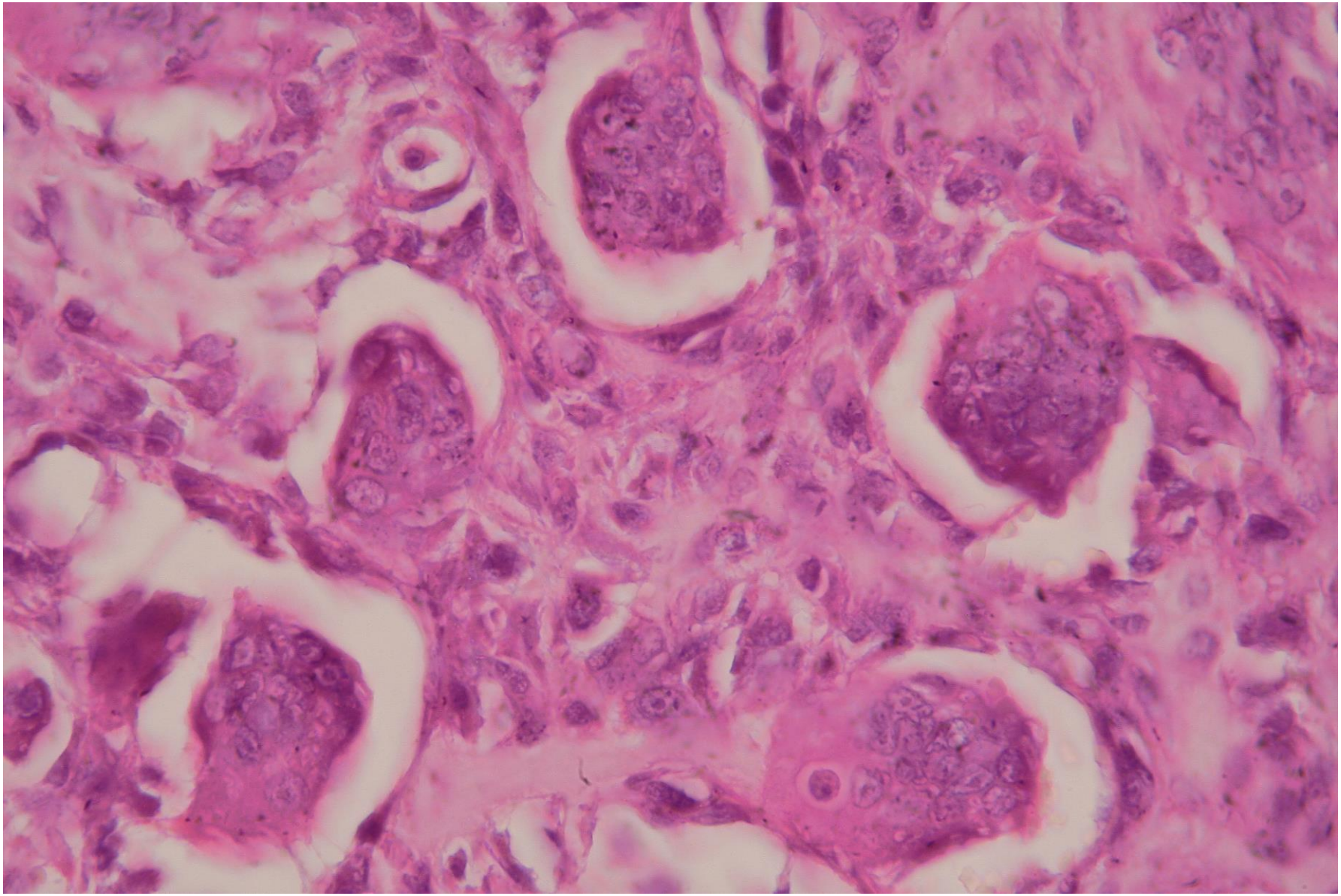


Cytologic findings

- Very high number of giant multinucleated cells with osteoclast-like appearance
  - Polar distribution of nuclei
  - Membrane discontinued by small eosinophilic granules (acid phospatase)
- Presence of round to spindle cells with eosinophilic cytoplasm, filled with magenta globule
  - Round to ovoid nuclei
  - Aniskaryosis moderate
- Macrophages

Diagnosis

- Cytologic diagnosis
  - Suspected multinucleated giant cell tumor
    - DD:
      - Multinucleated giant cell sarcoma or osteosarcoma
      - Less likely: aneurysmal bone cyst
- Histological diagnosis:
  - Multinucleated giant cell tumor of bone



Discussion

- «This tumor is rare in animals; isolated cases reported in dogs, cats and horses»
- «Most reported giant cell tumors in animals have occurred near joints in long bones, but they are also reported occasionally in the cranium, ribs and vertebrae»
- «Benign and malignant forms are reported in animals, the former being most common»

Thompson KJ, 2017

- Always to compare the morphological data with radiographic features!!!

Discussion

- «Giant cell tumor of bone has traditionally been described histologically as comprising large number of multinucleated giant cells resembling osteoclasts closely associated with a second population of neoplastic mononuclear cells
  - Mononuclear cells: spindle-shaped, fibroblast-like cells of **putative** osteoblastic lineage
  - Giant cells: mononuclear lineage is responsible for recruiting monocytes, promoting their fusion into osteoclast-like cells by producing a variety of cytokines and differentiation factors

Thompson KJ, 2017

Discussion

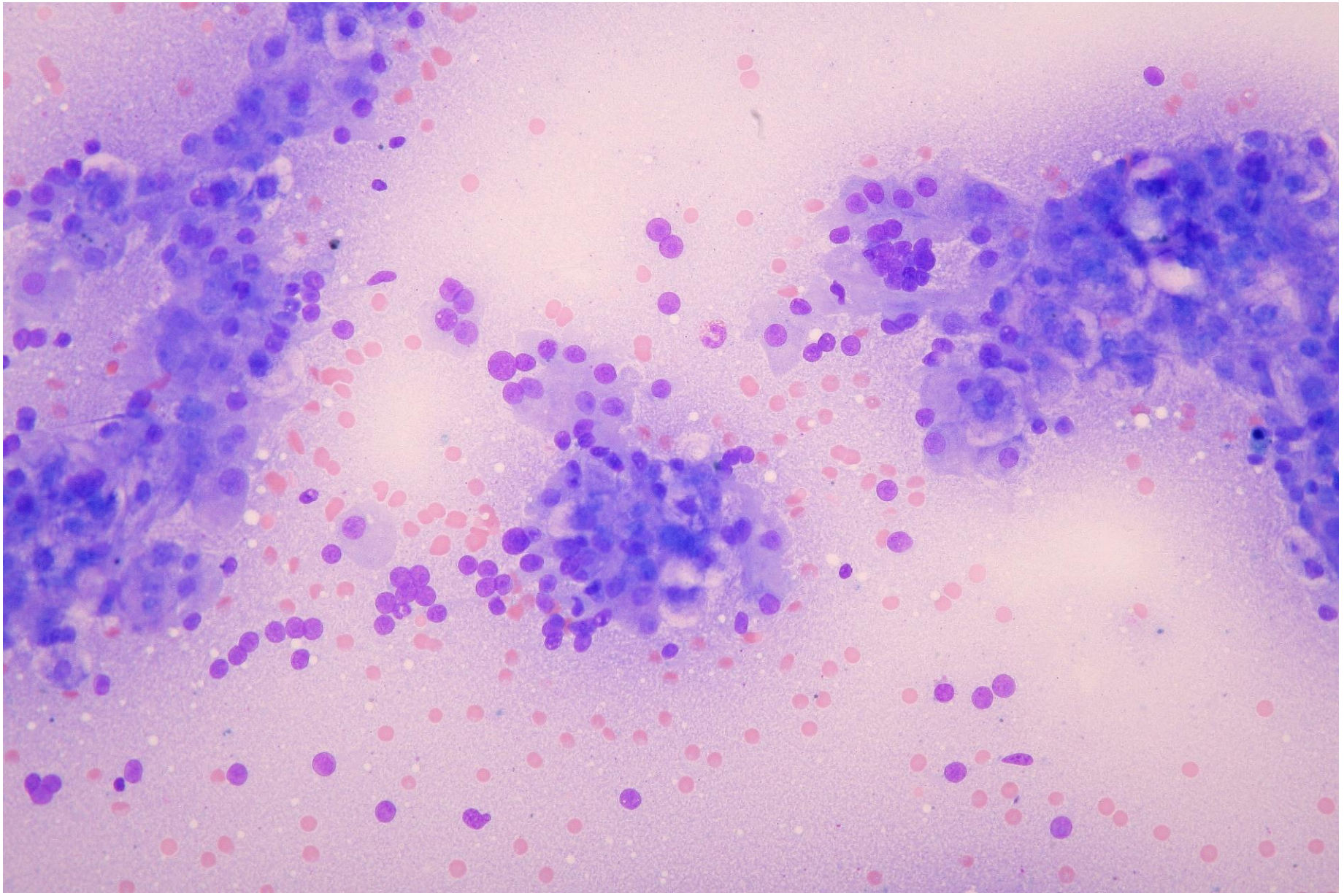
- «Cytologically examination of fine needle aspirates may be helpful in the diagnosis of giant cell tumors as the giant cells are so easy to recognize»
- «The presence of relatively high percentage of multinucleated giant cells among mononuclear cells that vary from spindle-shaped to round to ovoid suggests the possibility of giant cell tumor»
- «Giant cell tumors can also be feature of osteosarcoma, chondrosarcoma and even fibrosarcoma but their prevalence in GCT is much higher»

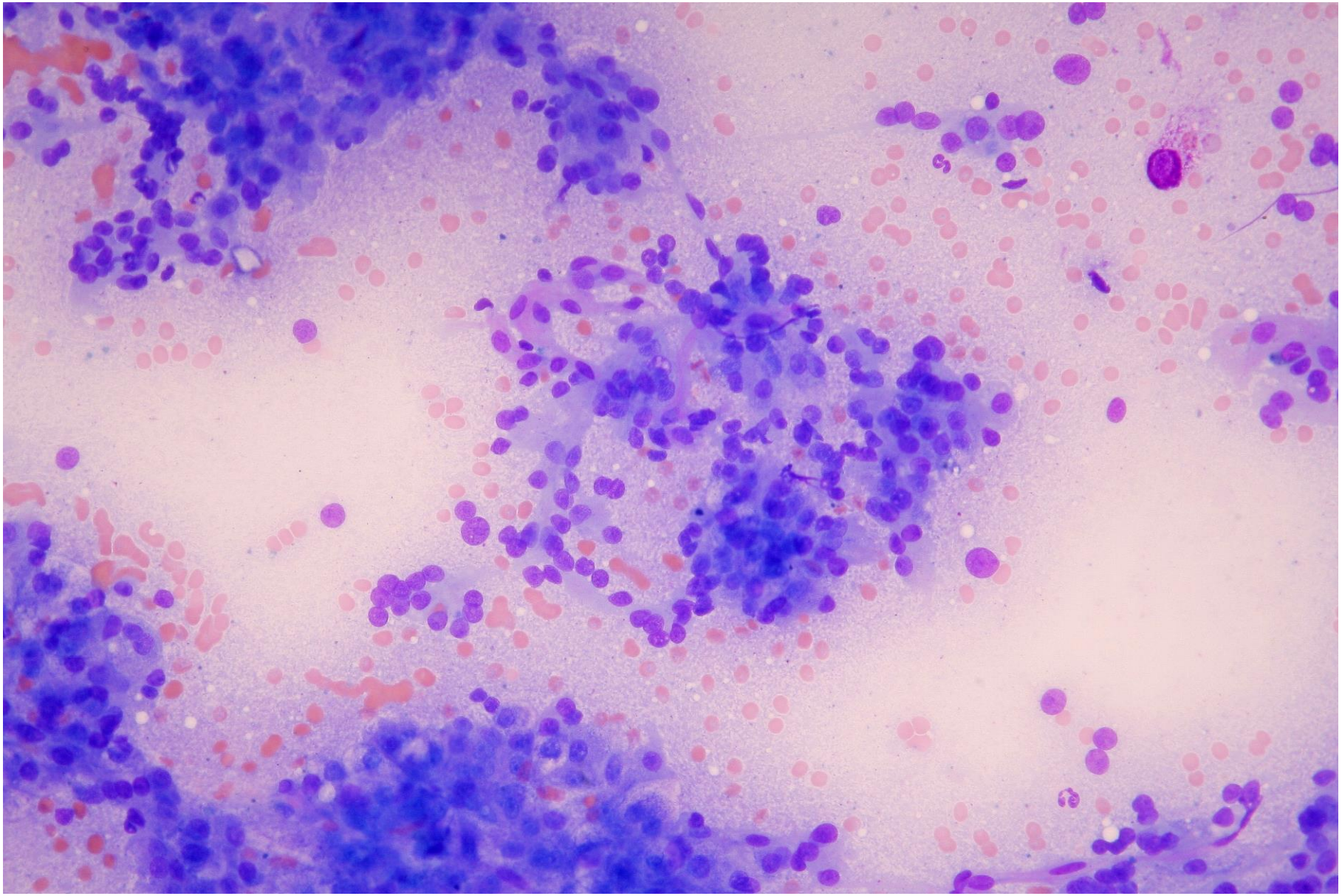
Thompson KJ, 2017

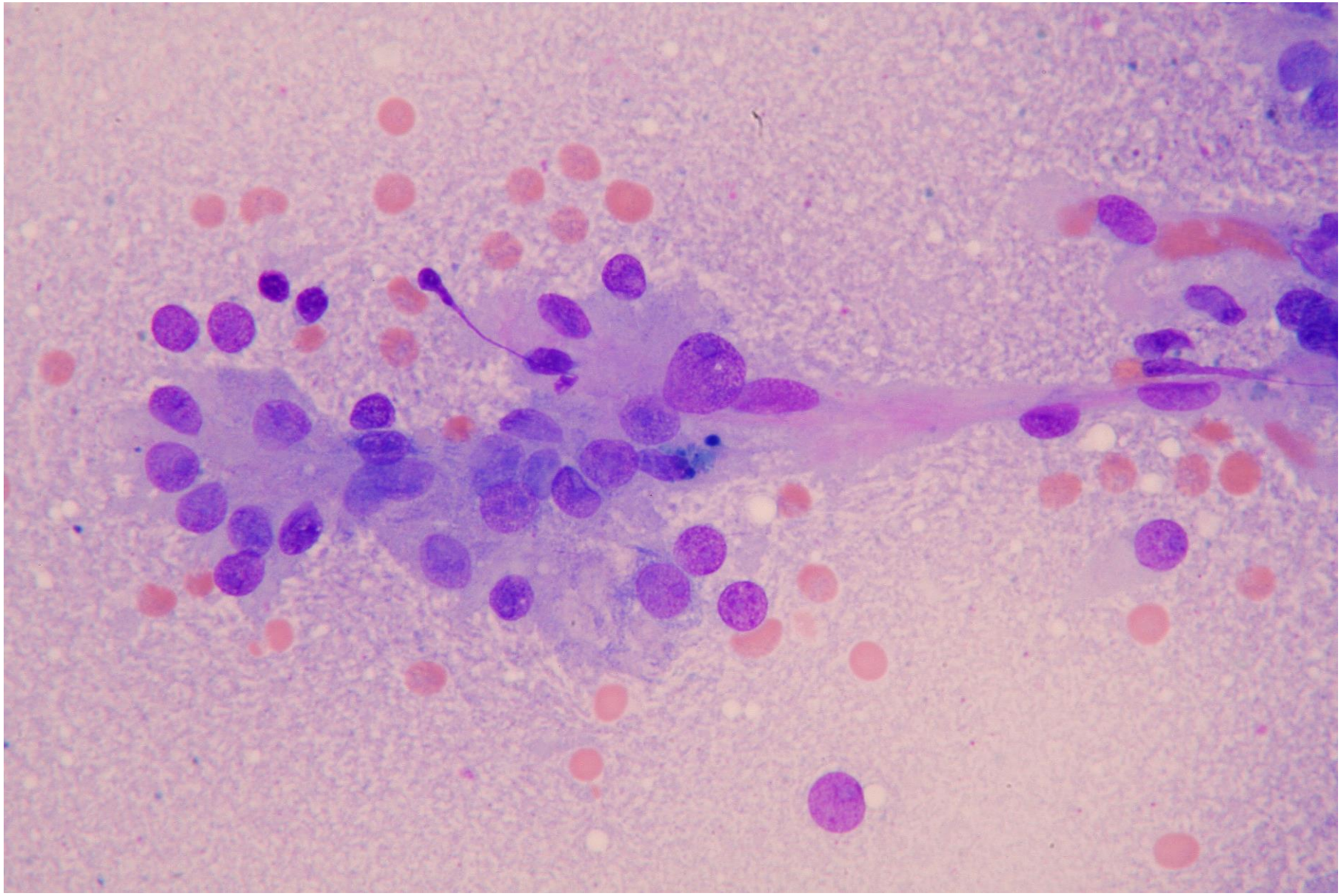
Case #7

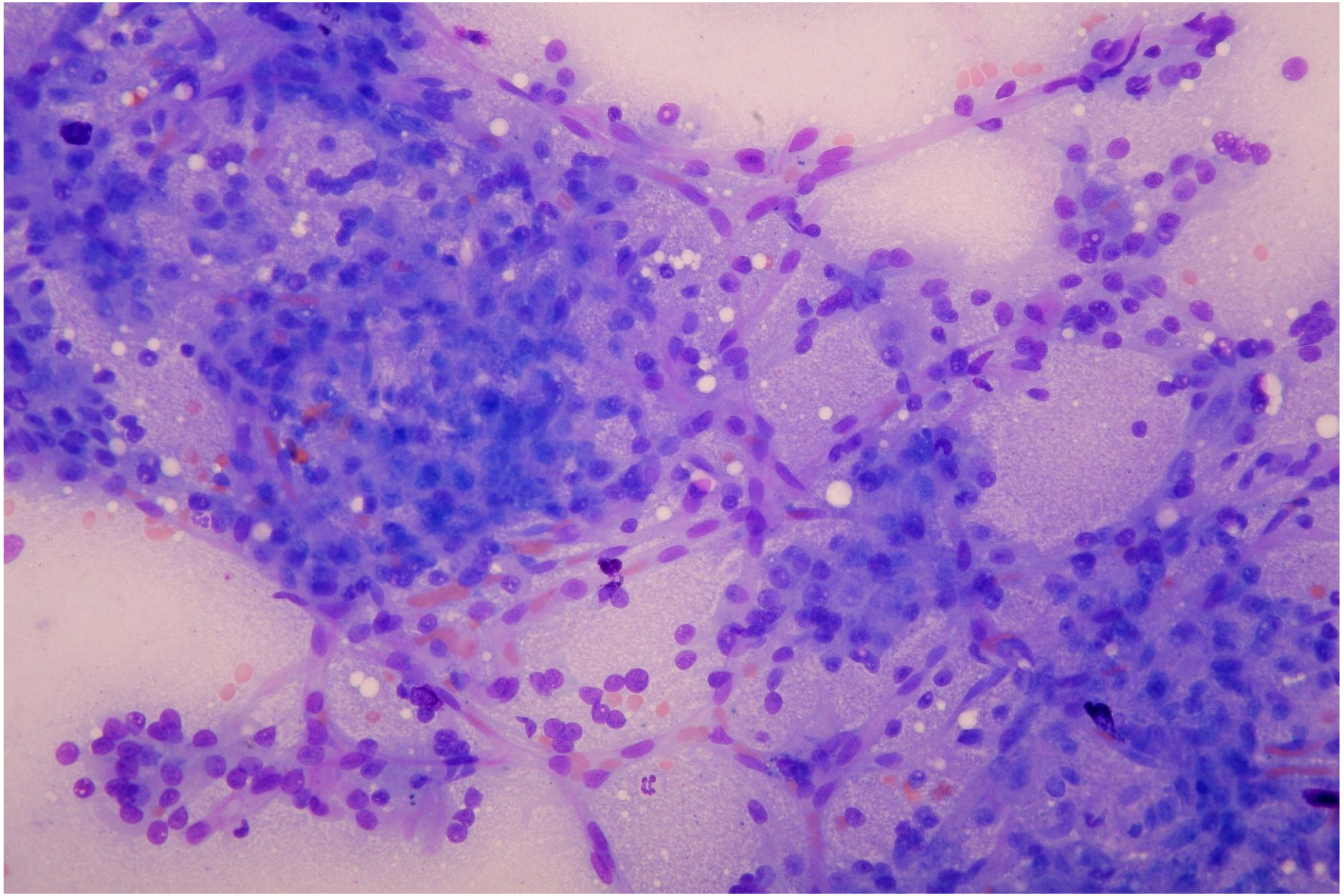
- 12-year-old, female, German Pinscher dog.
- Mass in the liver.

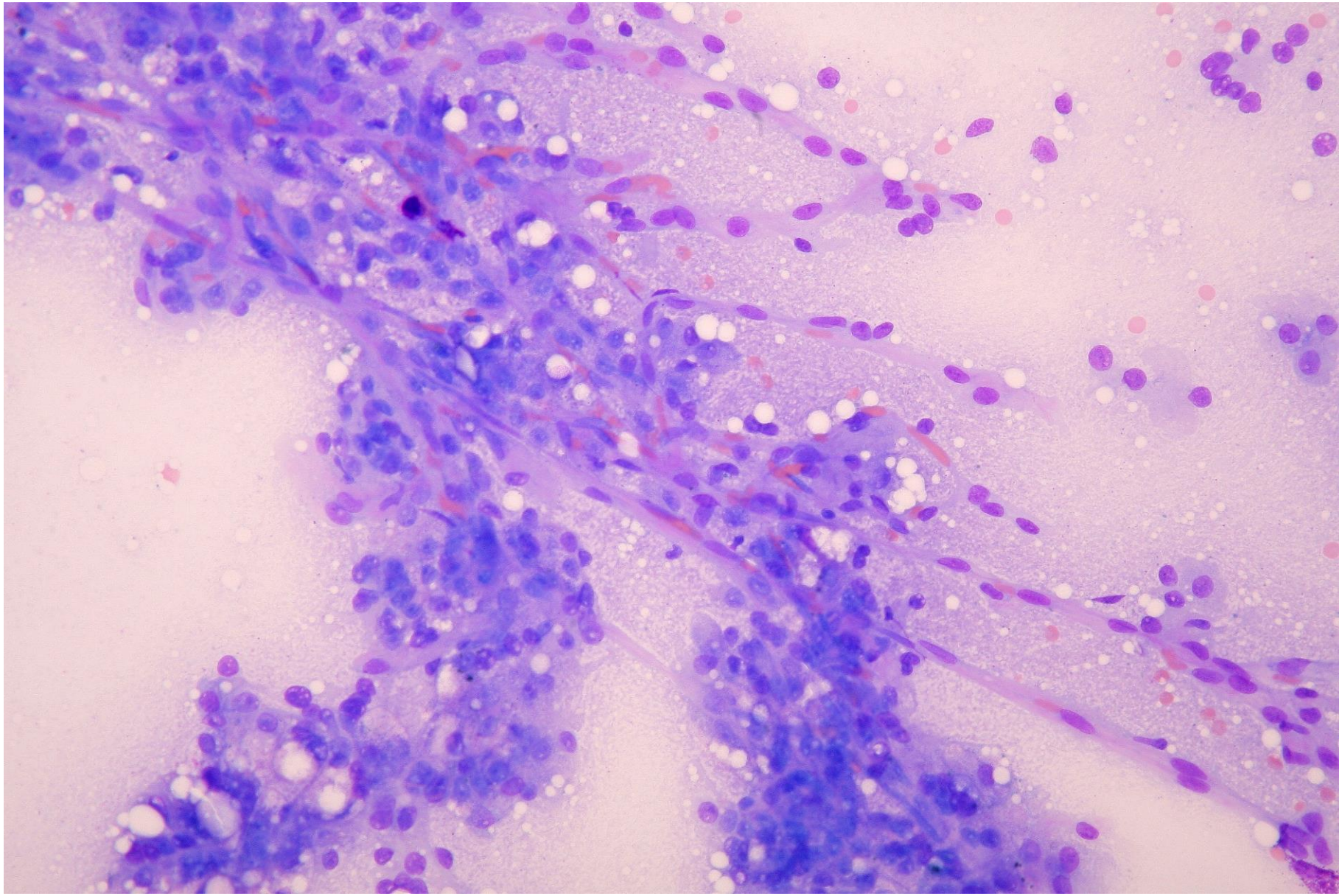
- FNCS of the lesion
- MGG stain

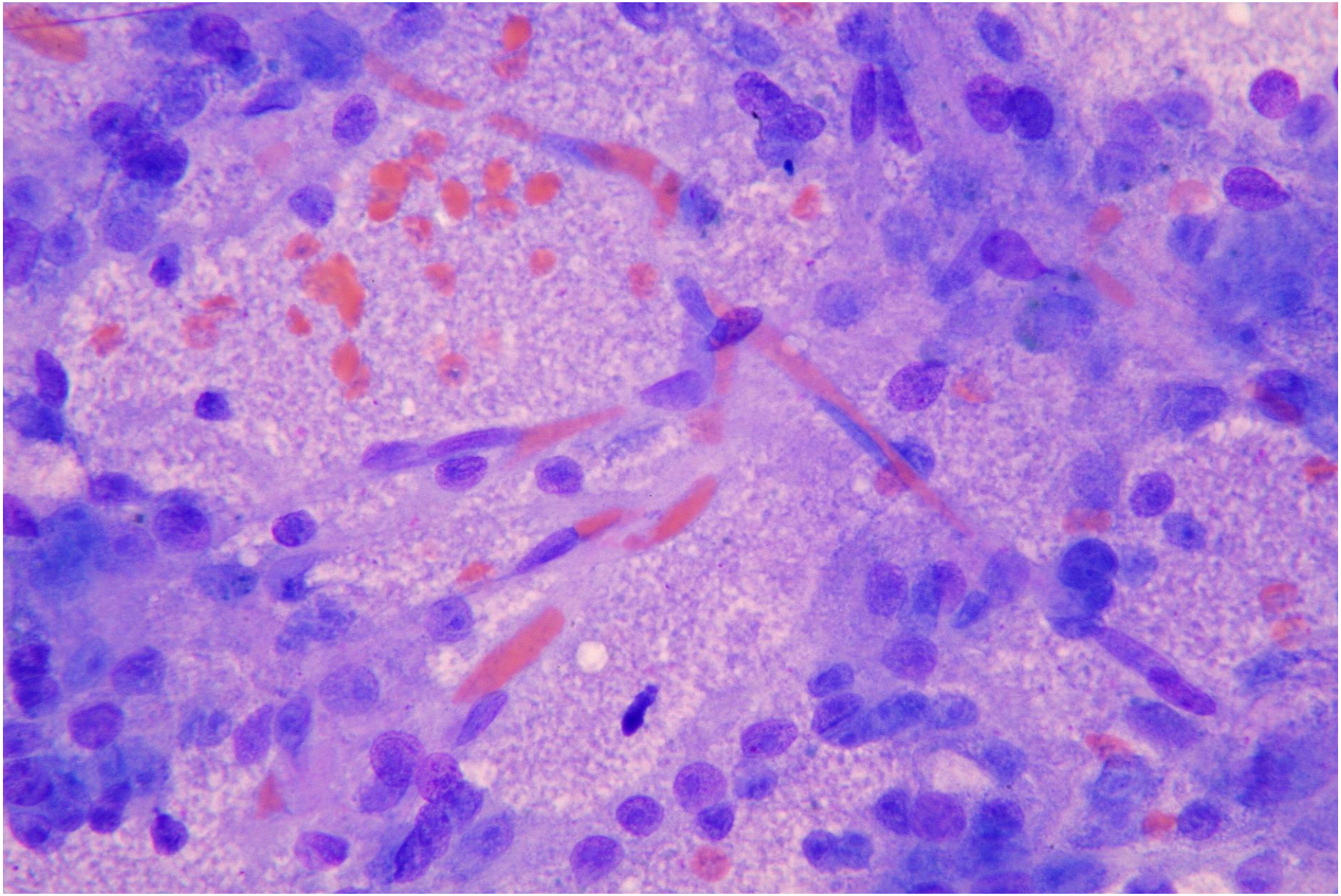


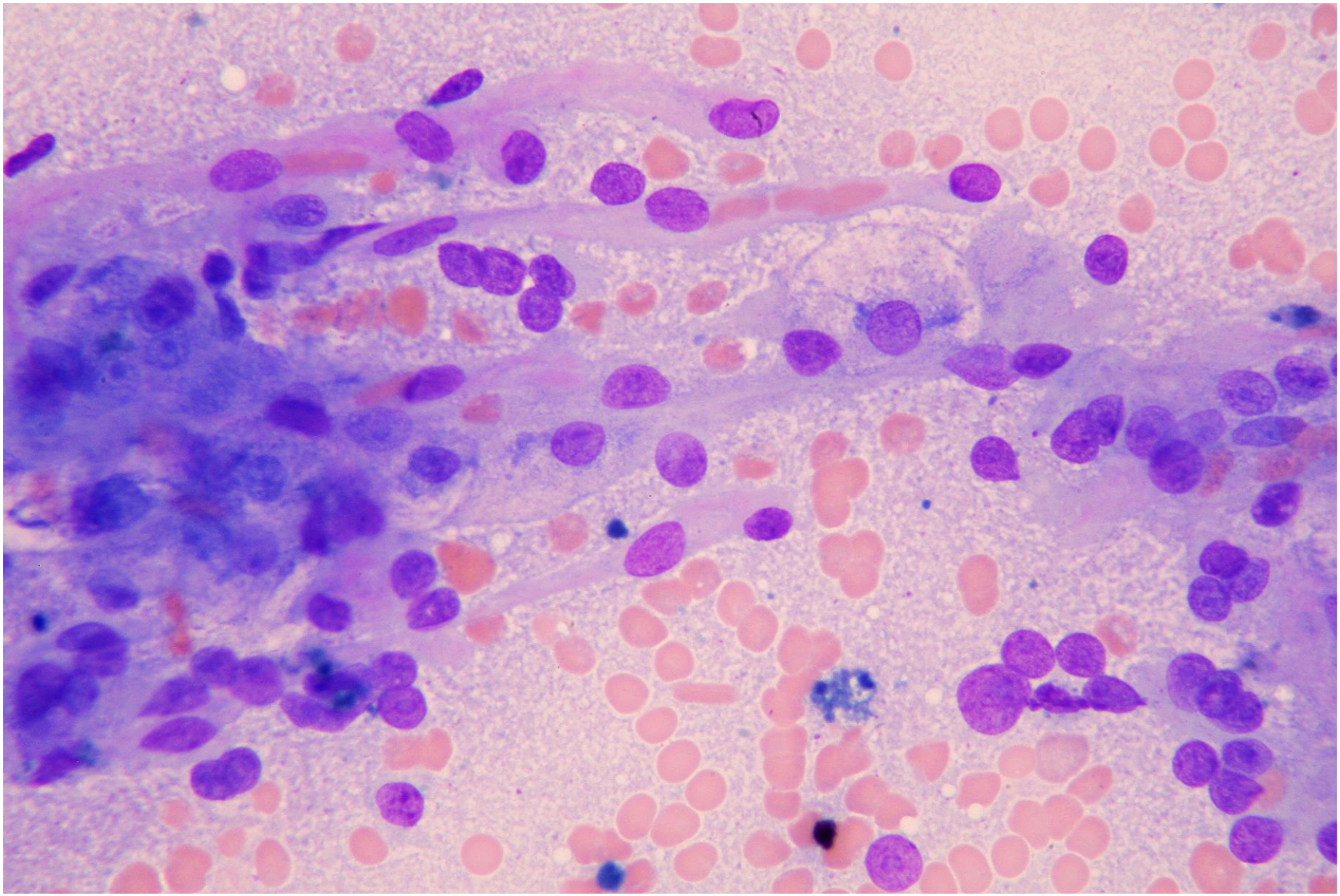










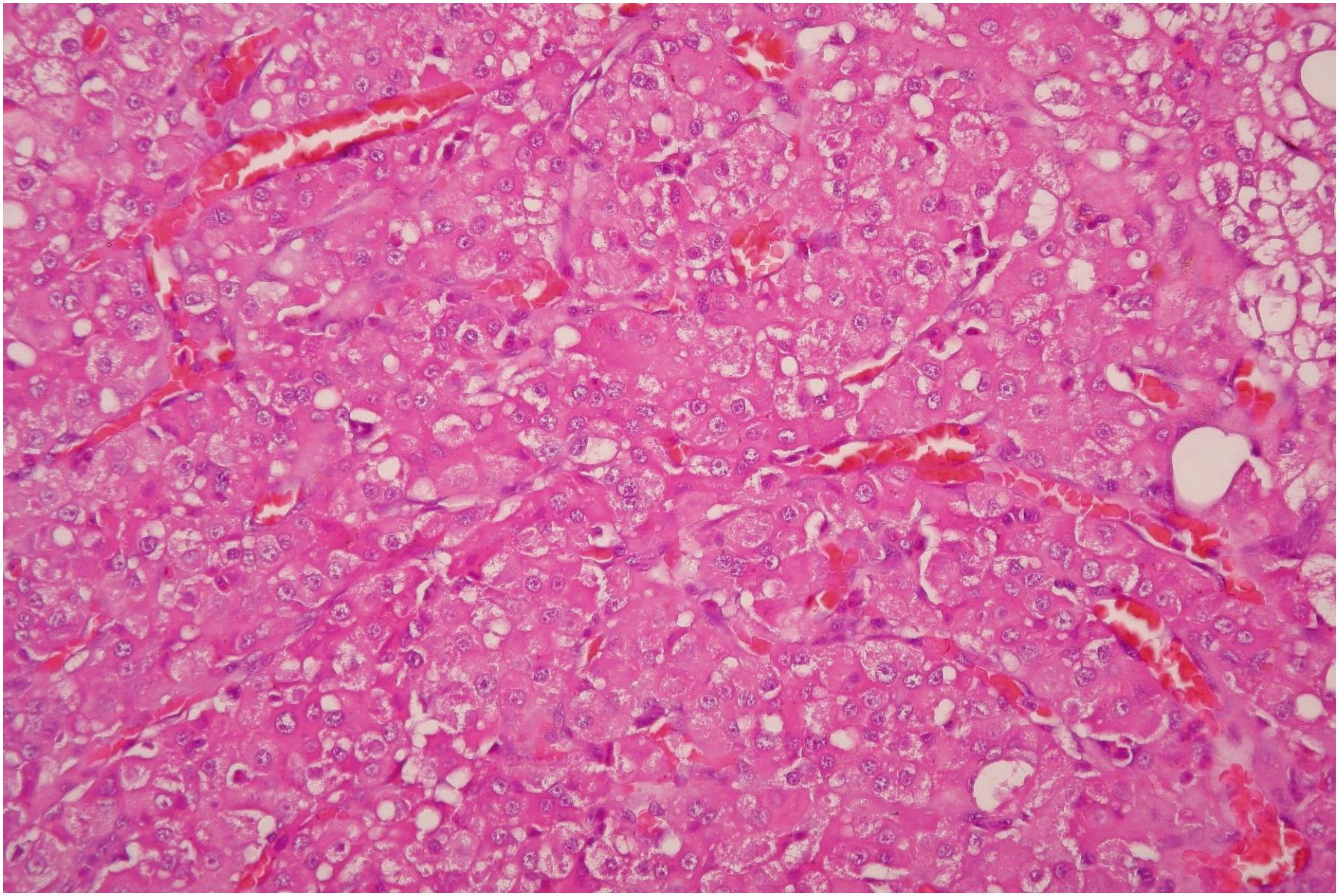


Cytologic findings

- Epithelial cells, hepatocytic origin
- Anisokaryosis and anisocytosis mild to moderate
- Naked nuclei around the epithelial clusters
- Many linear or branched capillaries

Diagnosis

- Cytologic diagnosis
  - Hepatocellular carcinoma
- Histological diagnosis:
  - Fibrolamellar hepatocarcinoma



Comments

- Criteria for diagnosis:
  - Overlapping
  - Anisokaryosis, anisocytosis
  - Naked nuclei
  - Perivascolar pattern

Comments

- Perivascolar pattern:
- «The typical fenestration of normal sinusoidal endothelial cells is lost. Also, unlike the normal pattern for sinusoidal endothelial cells, there is deposition of basement membrane material beneath the endothelial cells in hepatocellular carcinoma»

Cullen, 2017. Tumors of Domestic Animals

- «Some of the large, tightly packed clusters of malignant cells are sharply outlined and are surrounded by a layer of spindle-shaped cells with small elongated nuclei, presumably of endothelial origin».

Koss, 1984. Aspiration Biopsy – Cytologic Interpretation and Histologic Bases

Veterinary Clinical Pathology ISSN 0275-6382

ORIGINAL RESEARCH

Retrospective study of cytologic features of well-differentiated hepatocellular carcinoma in dogs

Carlo Masserdotti[1], Michele Drigo[2]

Vet Clin Pathol 41/3 (2012) 382–390

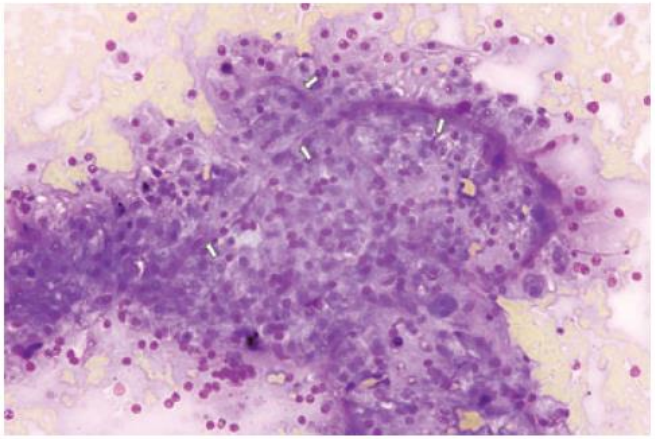


Figure 4. Fine-needle aspirate of a well-differentiated hepatocellular carcinoma in a dog. A large cluster of neoplastic hepatocytes is traversed by a long capillary (arrows) with RBCs in the lumen. May–Grünwald Giemsa, ×40 objective.

Although present in low numbers in WD-HCC, capillaries were absent in smears from non-neoplastic liver and likely represent increased vascularization of the tumor, rather than sinusoidal dilation, due to neoangiogenesis.[19] Similar findings have been reported in people, and the observation of vessels traversing tissue fragments is a useful criterion in the diagnosis of WD-HCC.[20]

Table 2. Scores for 33 cytologic features evaluated in fine-needle aspirates of 15 hepatocellular carcinomas and 15 samples from non-neoplastic, non-nodular liver in dogs.

		Score					
Cytologic Feature	Diagnosis	0	1	2	3	*U**	*P*†
Capillaries	WD-HCC	10 (66.7%)	3 (20%)	1 (6.7%)	1 (6.7%)	75	**.016**
	Control	15 (100%)	0	0	0		

	Score			
Cytologic Feature	0	1	2	3
Capillaries	None	1/HPF	2-5/HPF	> 5/HPF