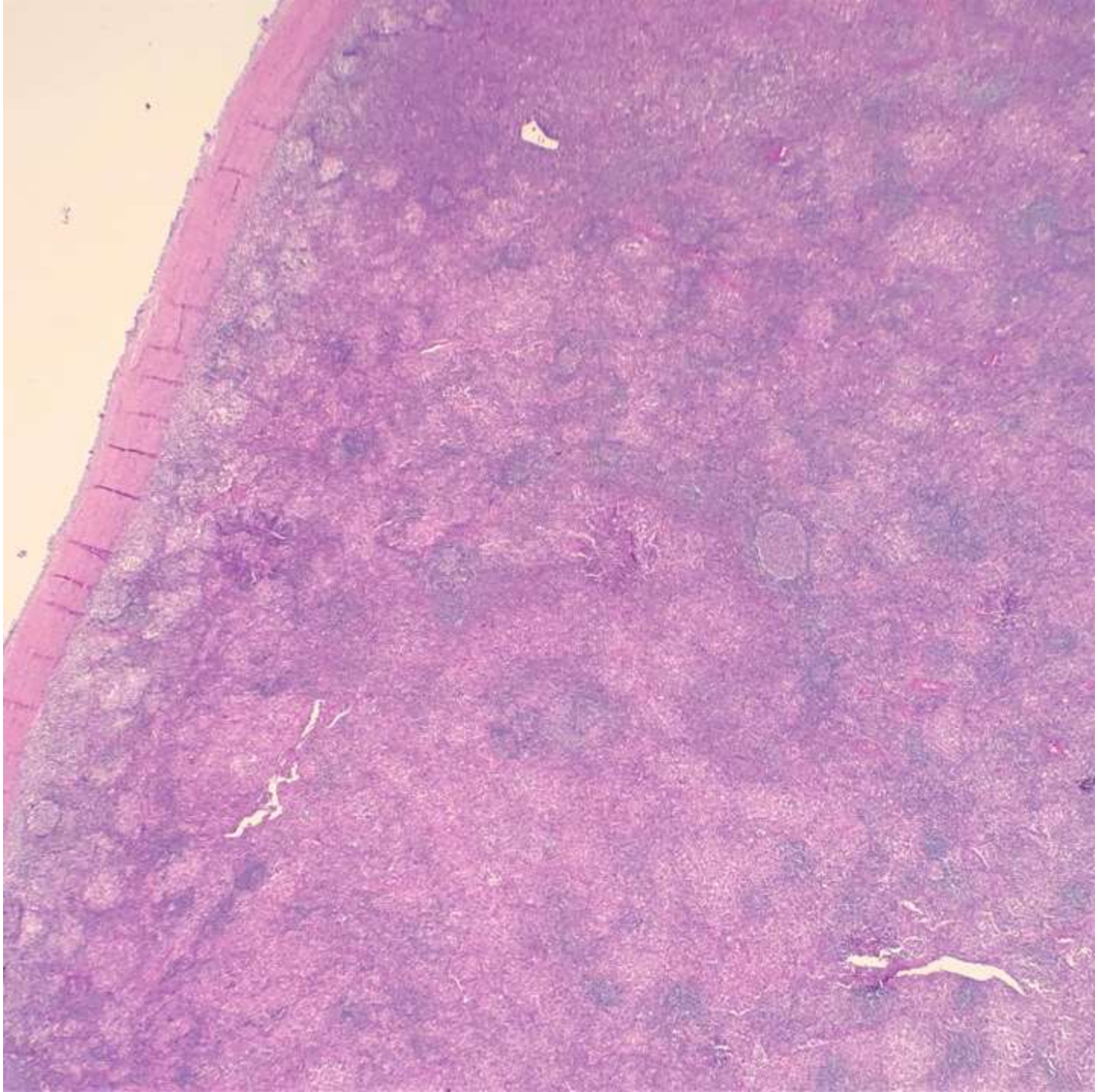
June 2019 DIAGNOSIS LIST

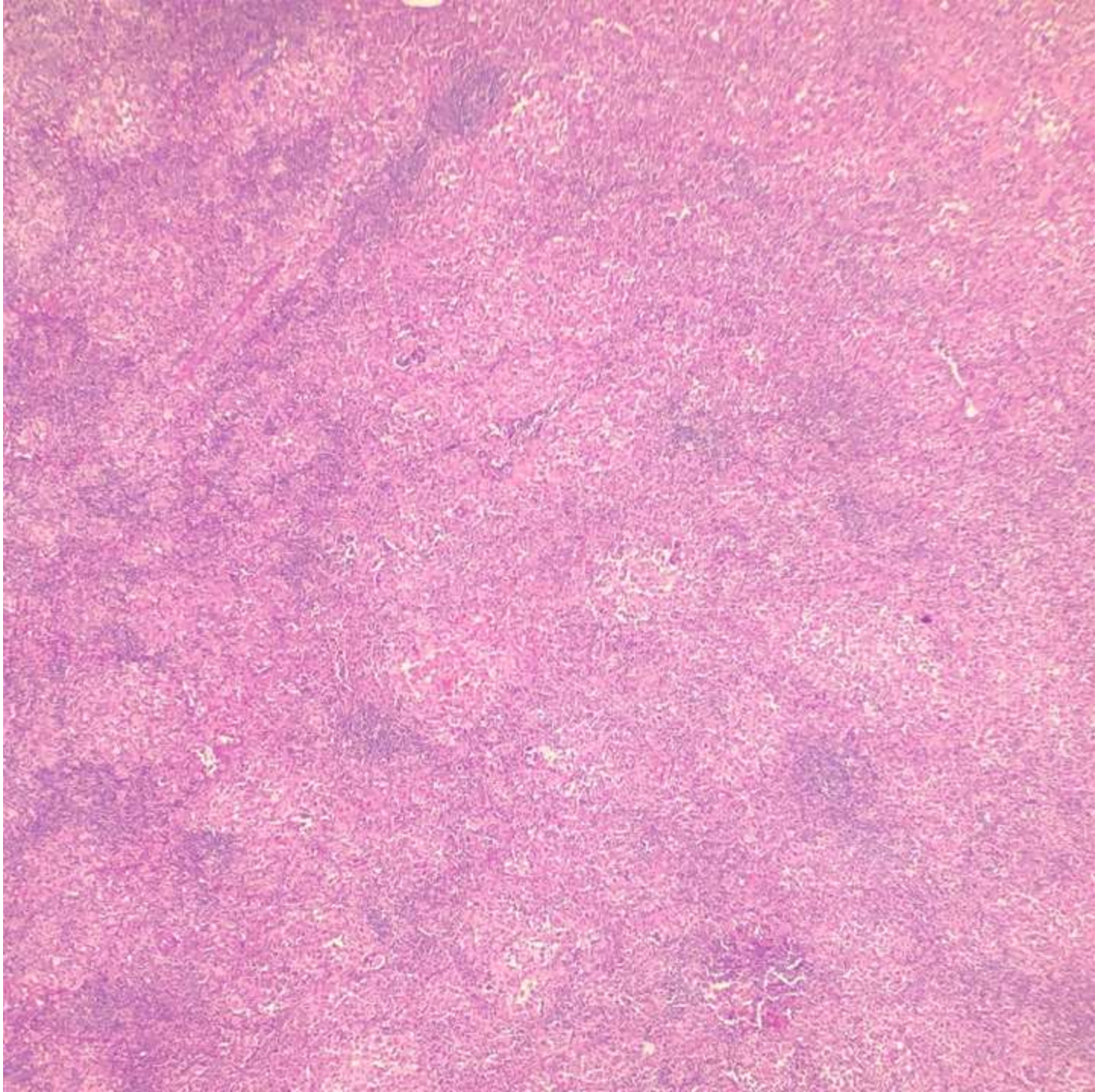
19-0601: Langerhans cell histiocytosis and Rosai-Dorfman disease [lymph node/hematopathology]
19-0602: Kaposi sarcoma [stomach/GI pathology+ID pathology]
19-0603: cutaneous pleomorphic liposarcoma [skin/soft tissue pathology]
19-0604: Melamed-Wolinska bodies [urine/GU pathology]
19-0605: metastatic prostatic adenocarcinoma with neuroendocrine differentiation [pleural fluid/GU pathology]
19-0606: papillary thyroid carcinoma with adenoid cystic-like pattern [thyroid/h&n pathology)
19-0607: metastatic sertoli cell tumor [lymph node/GU pathology]
19-0608: Wilms tumor [kidney/GU pathology]
19-0609: anaplastic oligodendroglioma [brain/neuropathology]
19-0610: Doxycycline-related gastric injury

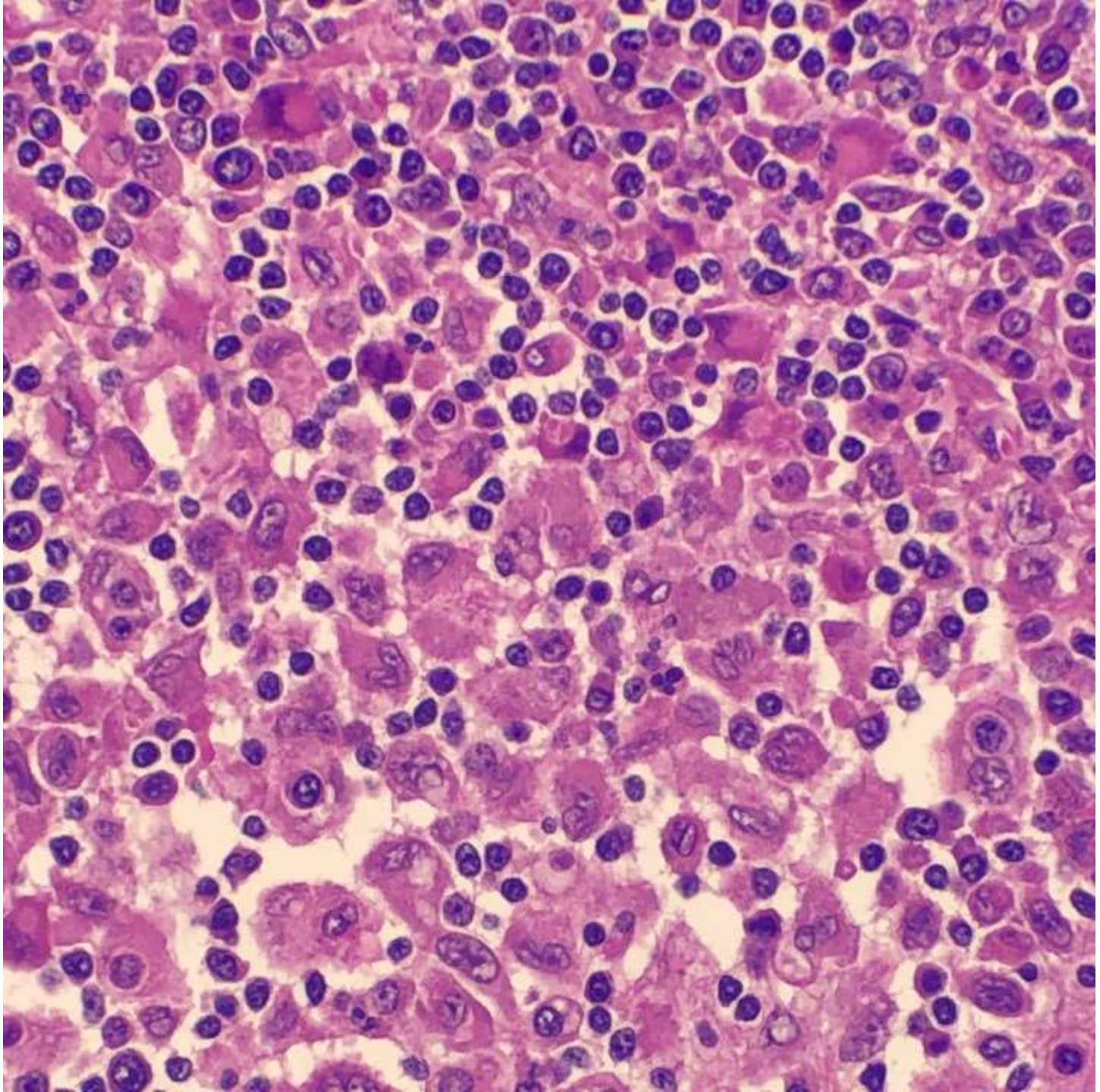
19-0601

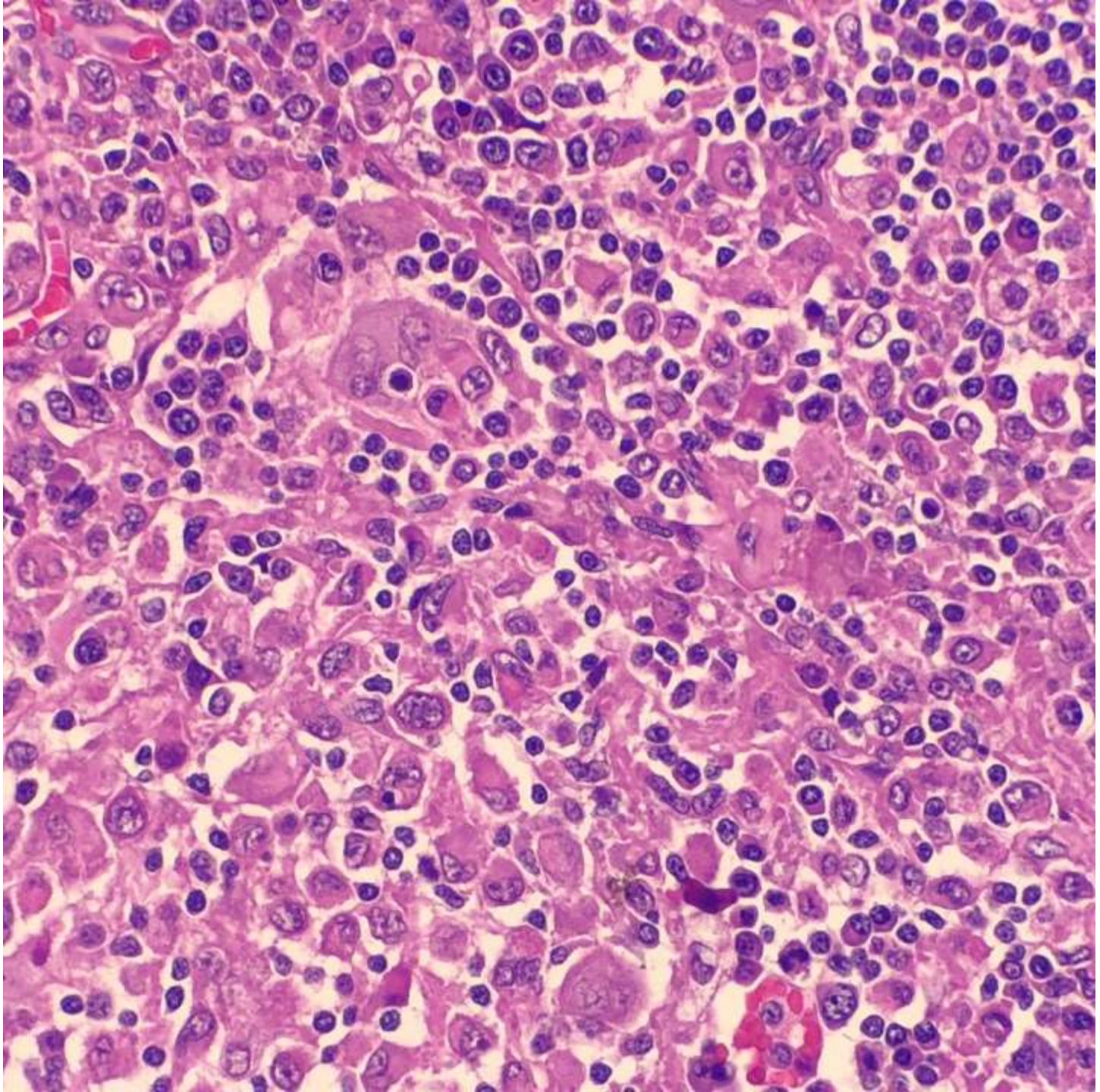
Llara Lezama/Jenny Hoffman/Dita Gratzinger; Stanford

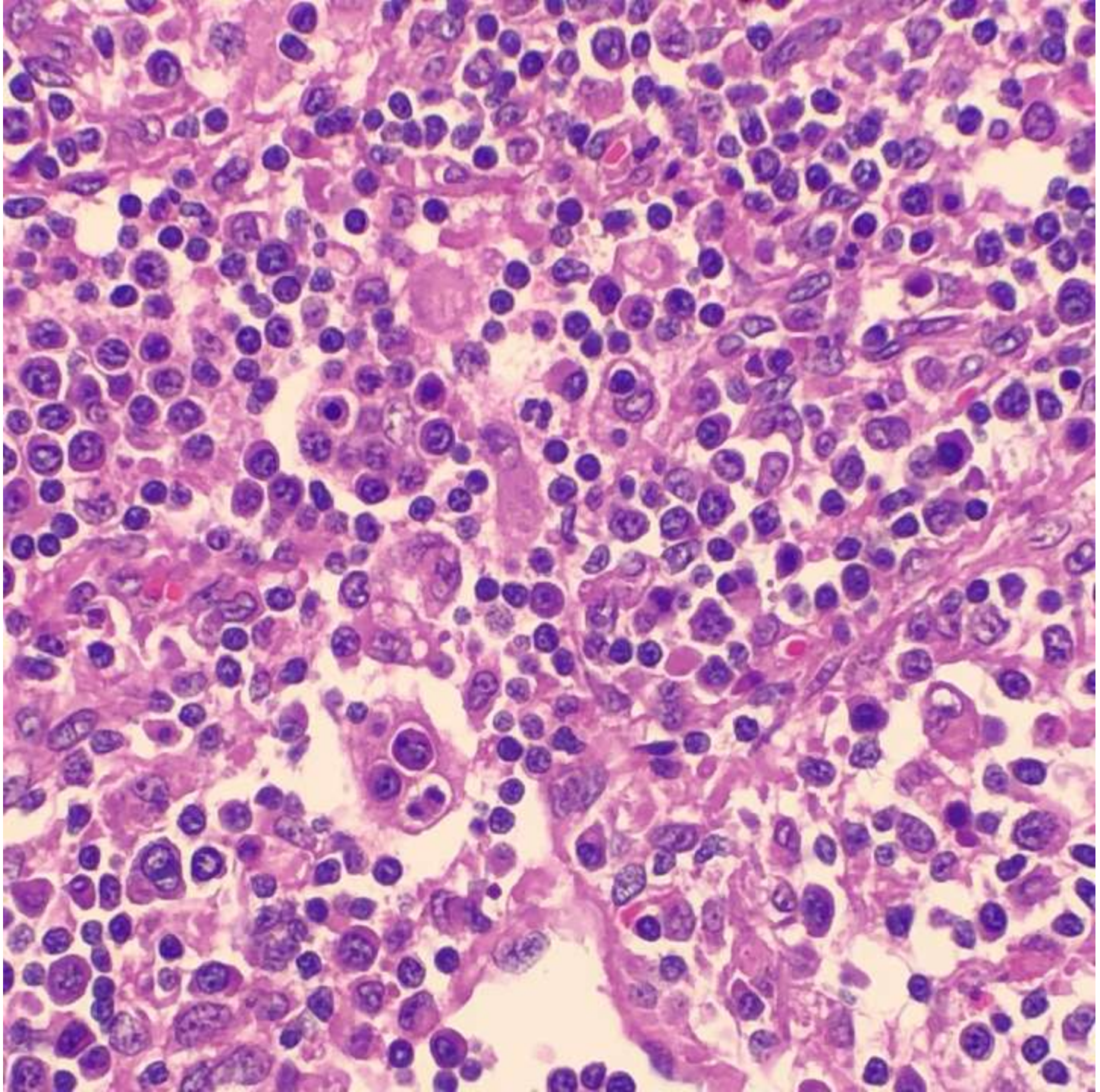
1-year-old male with progressive bilateral cervical lymphadenopathy evolving for 2 months with mild fever.

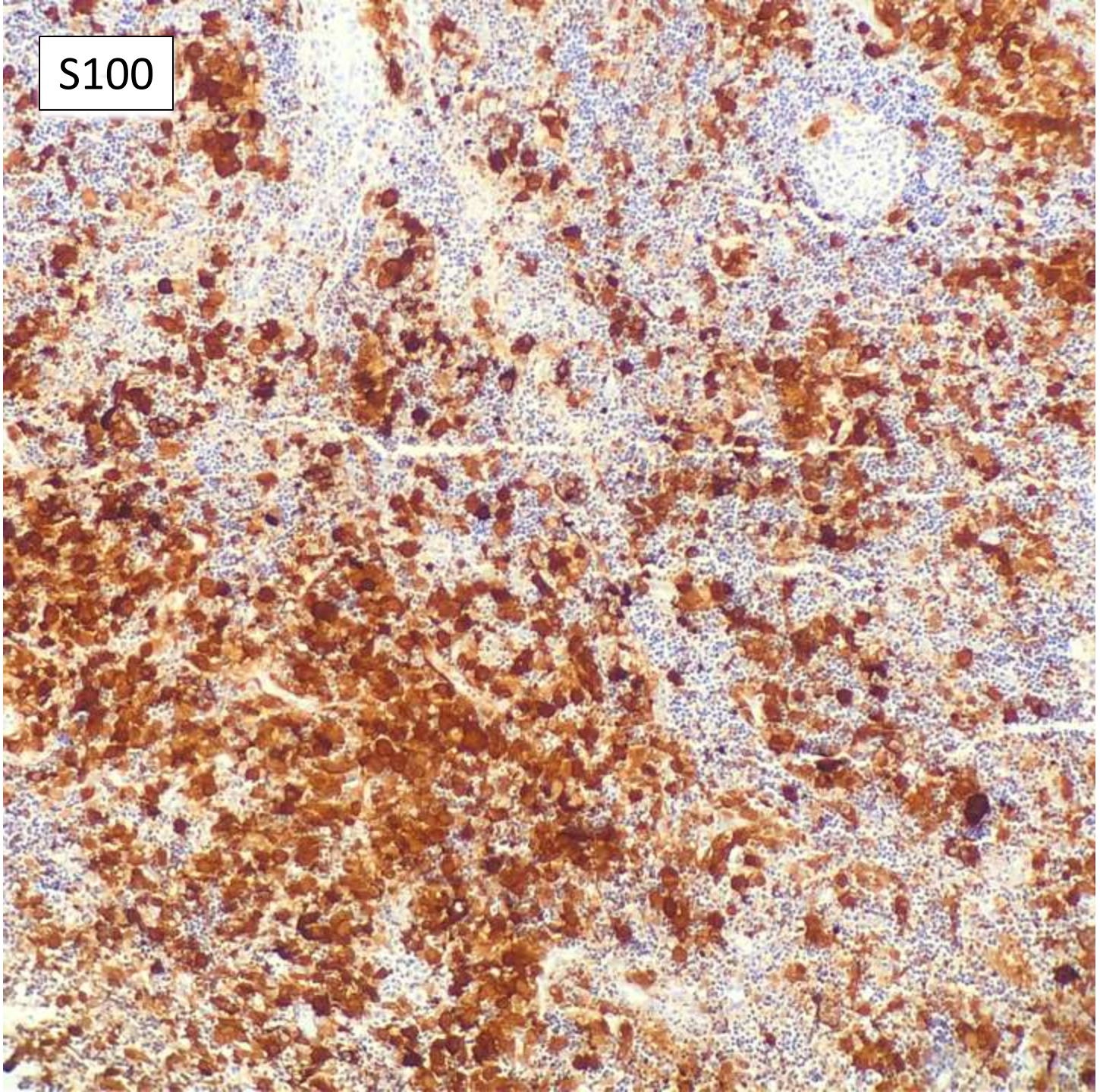








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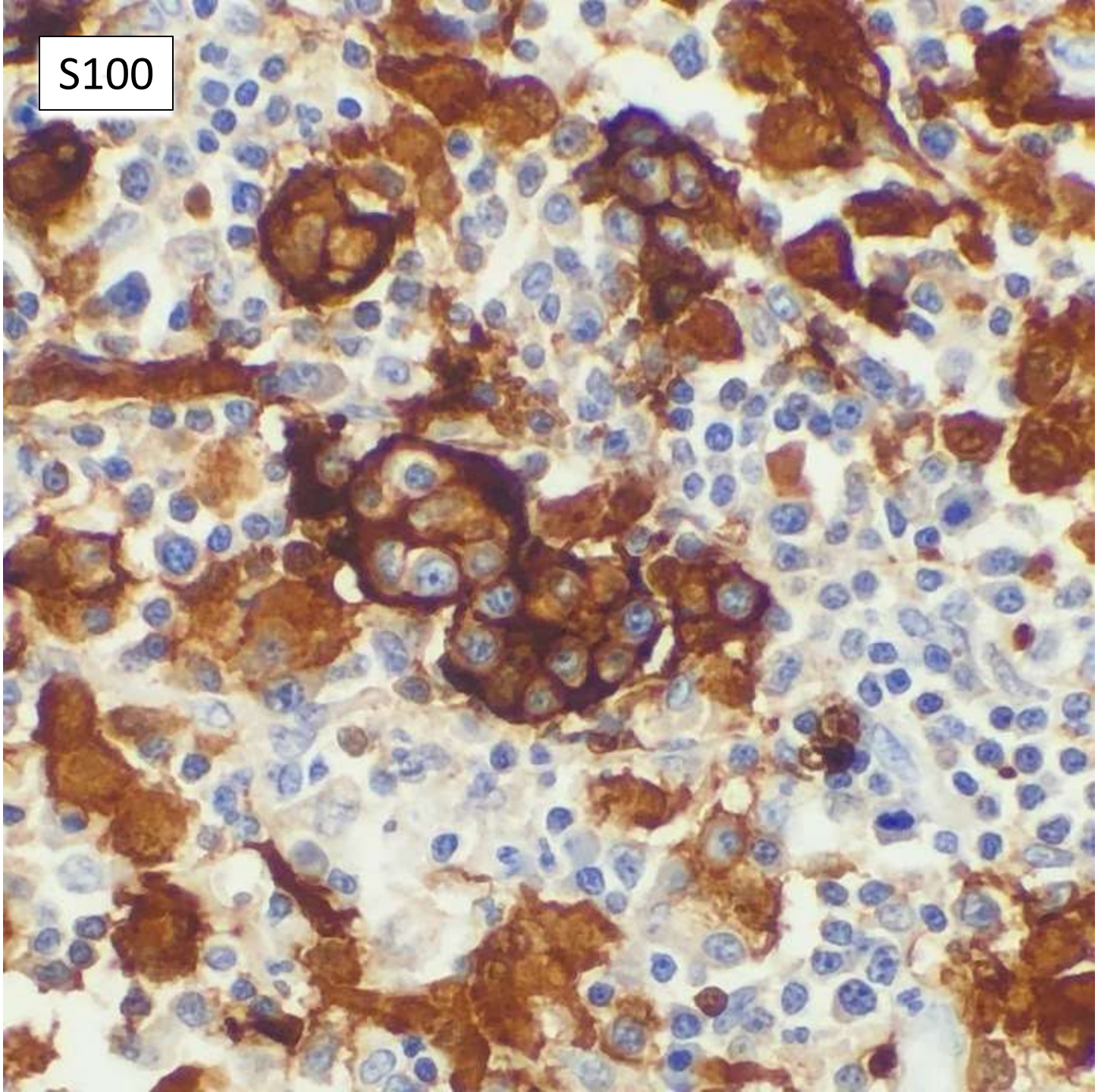
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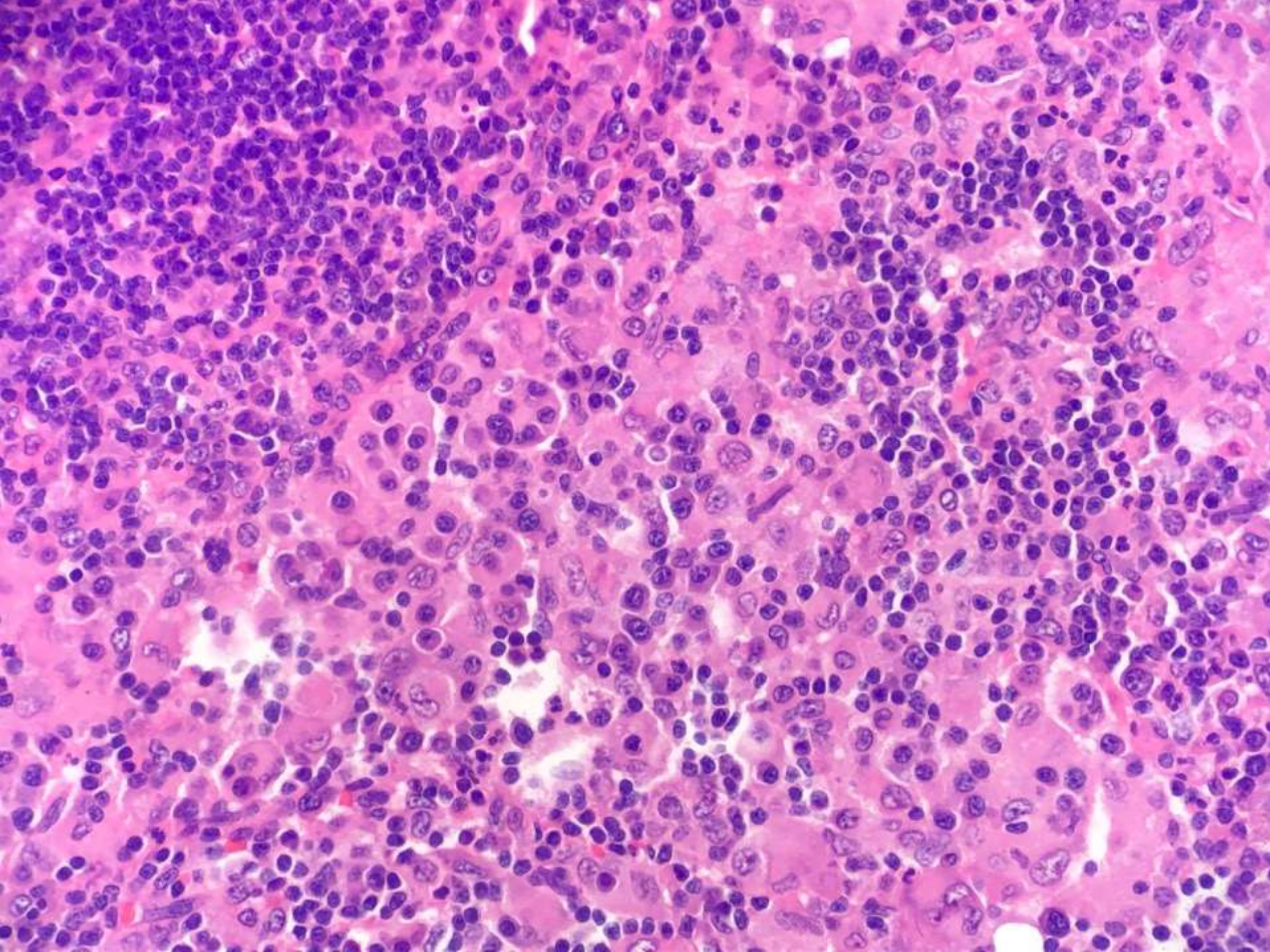
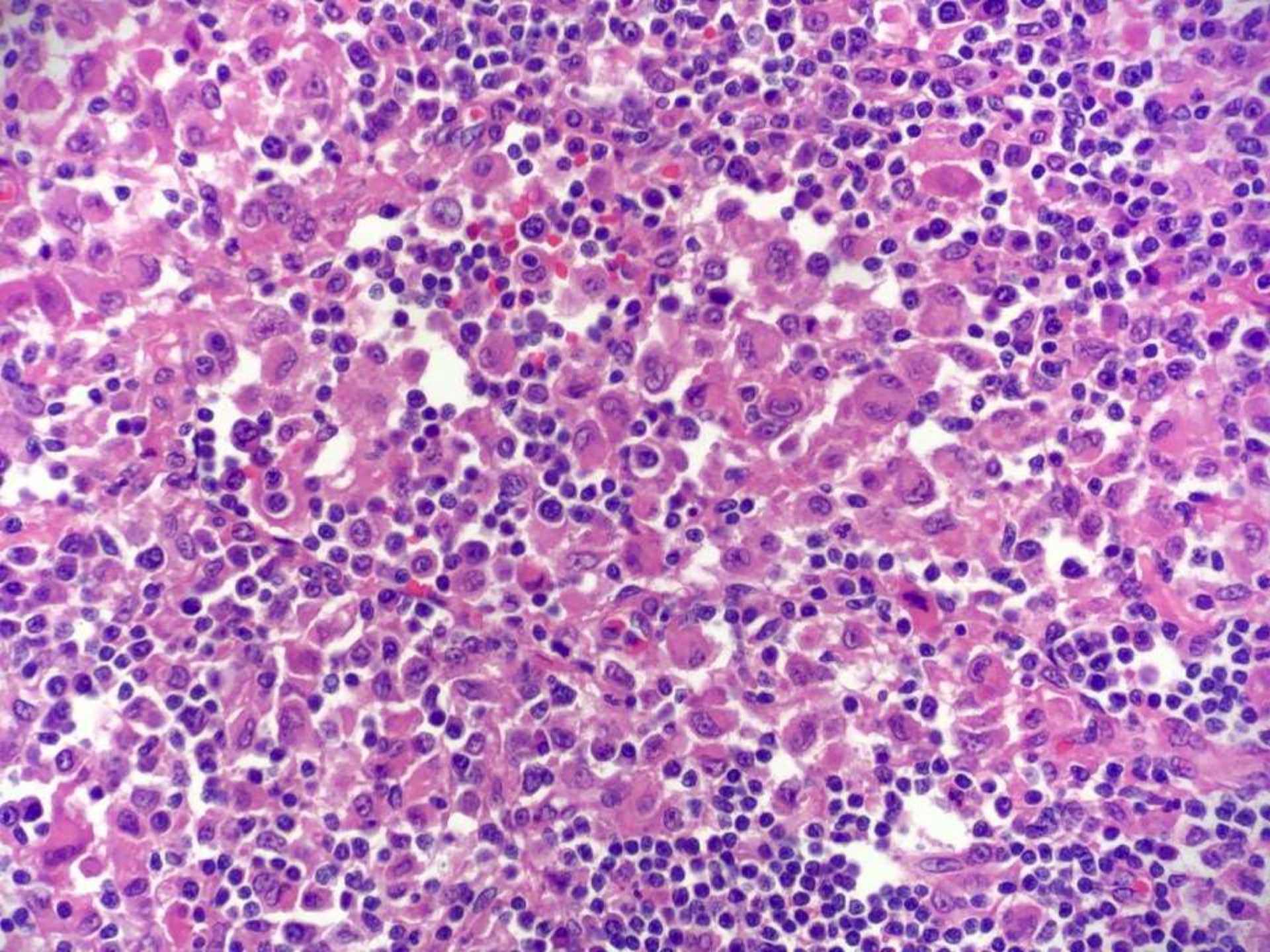
SB 19-0601

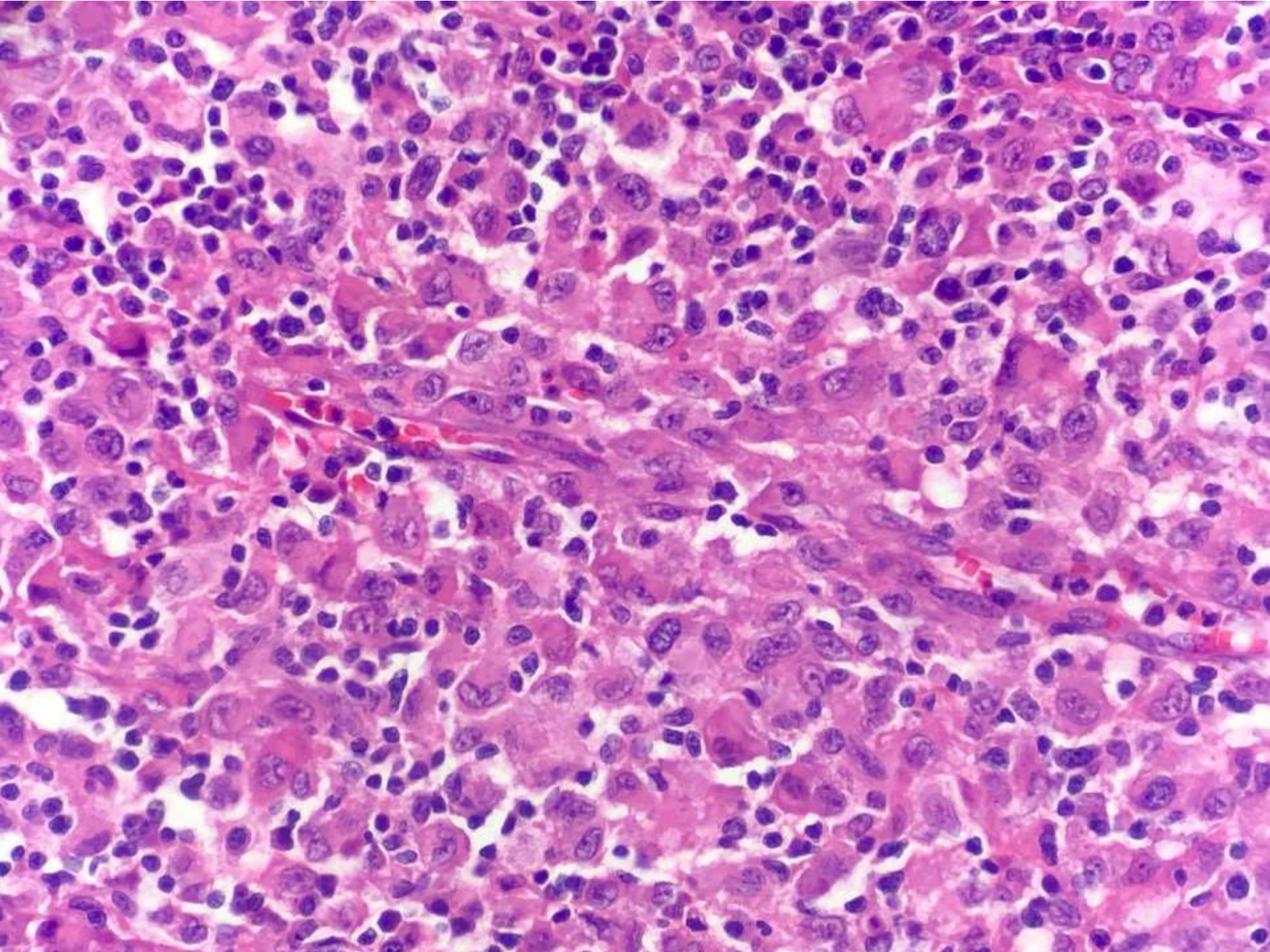
June 2019

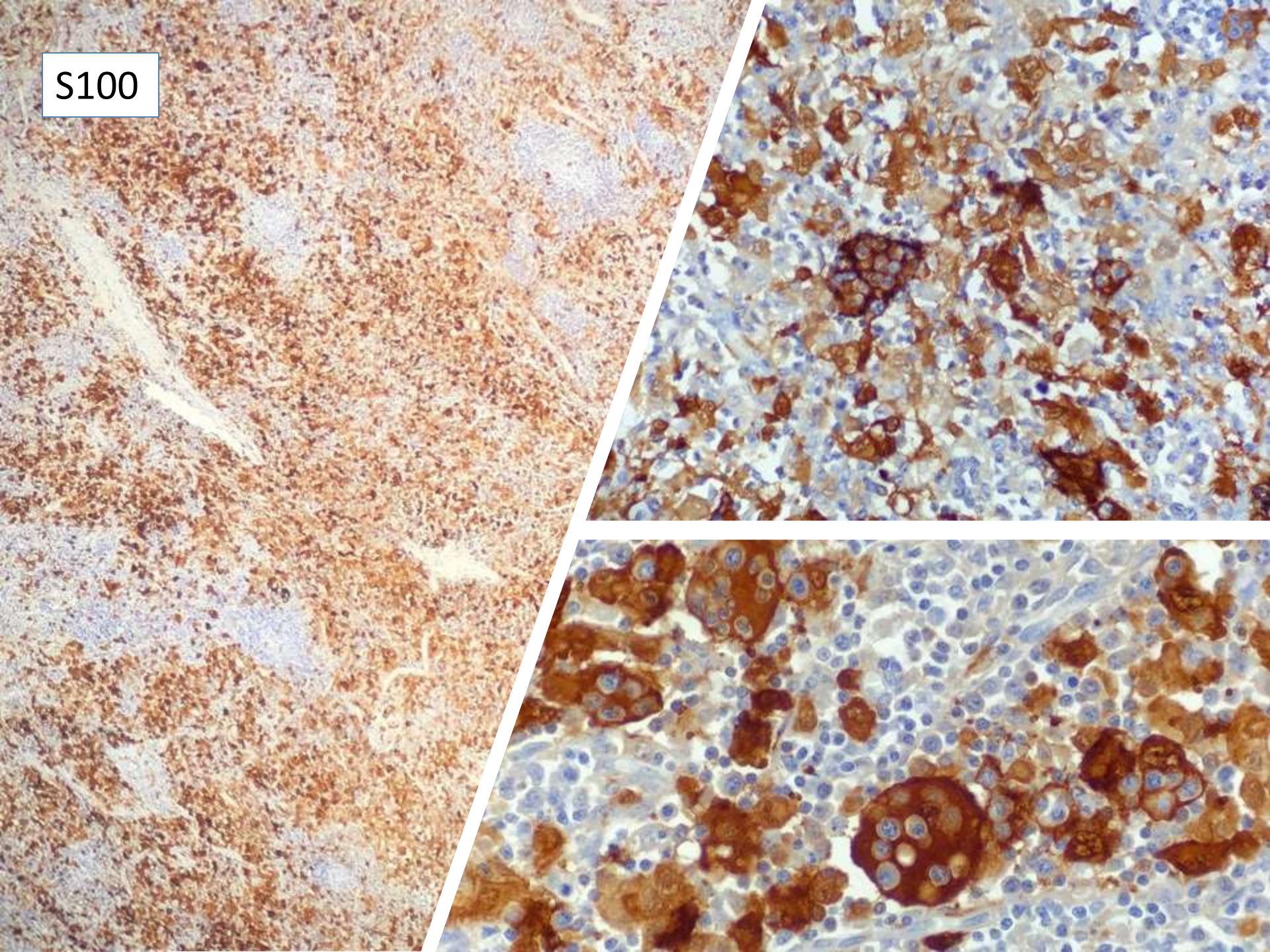
Lhara Lezama MD (PGY-5)

Stanford MEDICINE





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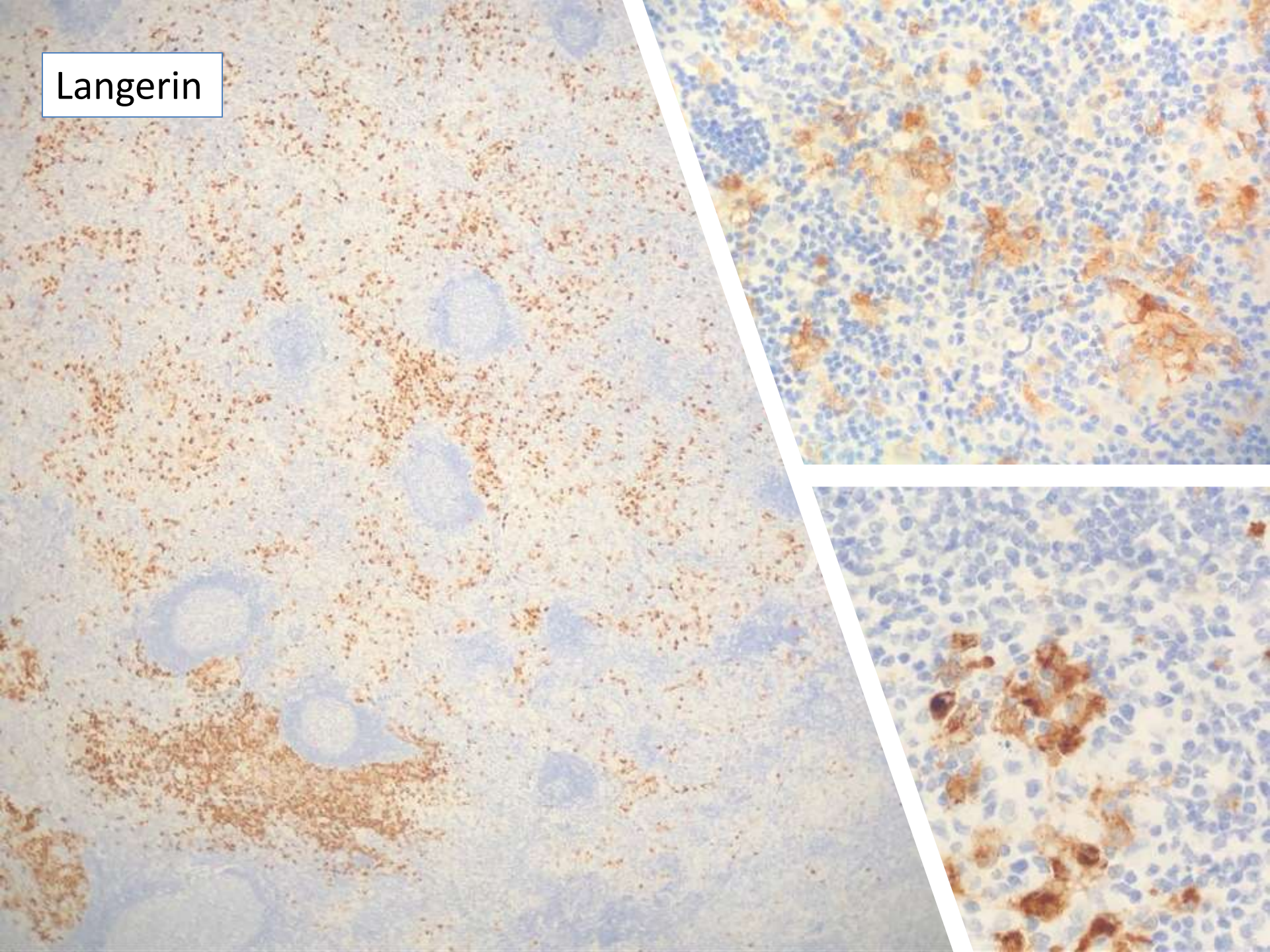
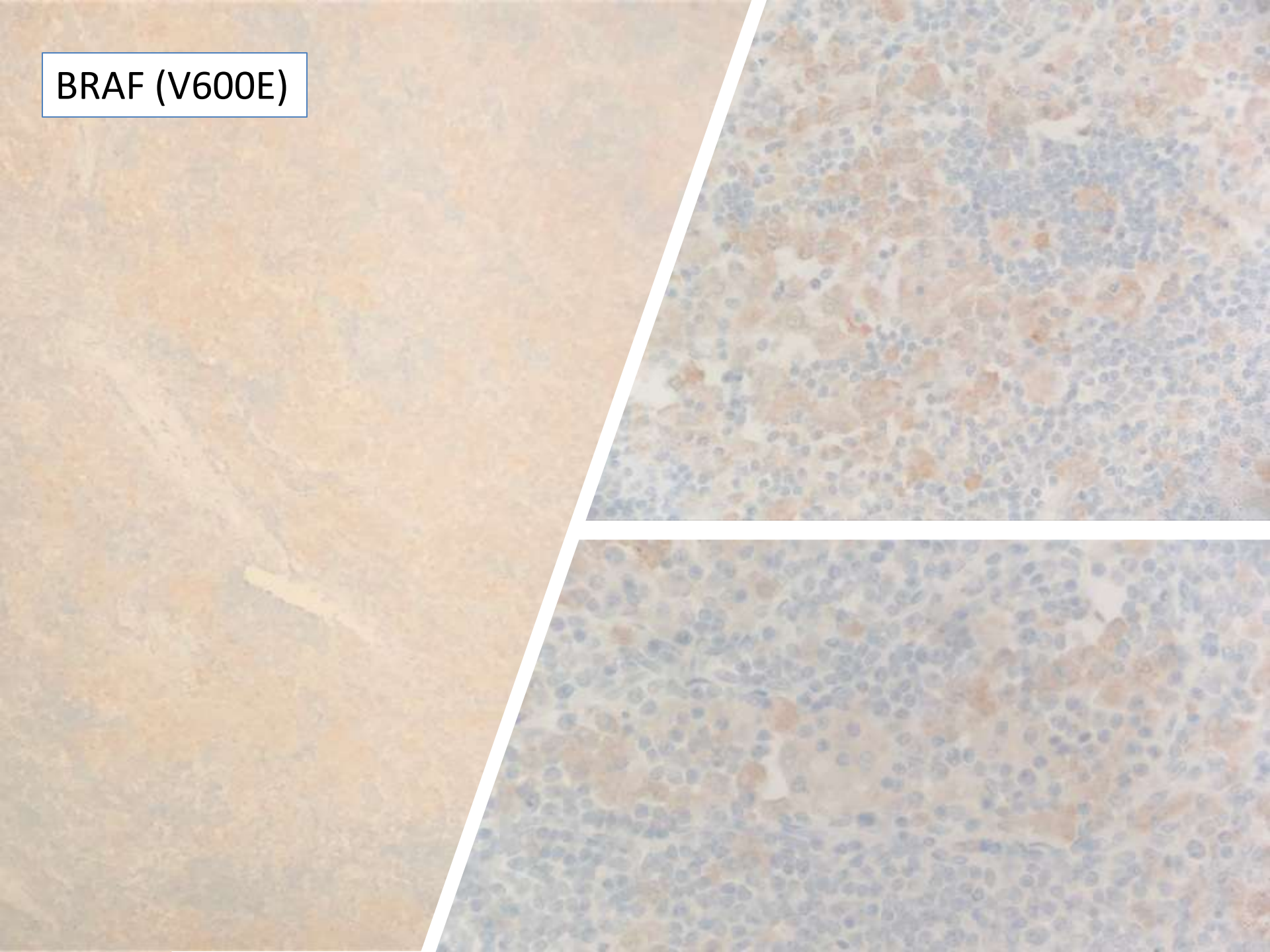

Langerin

BRAF (V600E)



Diagnosis:

CONCURRENT LANGERHANS CELL HISTOCYTOSIS AND ROSAI-DORFMAN DISEASE

HEME-STAMP

HEME-STAMP (Heme Stanford Actionable Mutation Panel), identified a BRAF V600E mutation (VAF 3%).

British Journal of Dermatology 2002; **147:** 770–774.

CASE REPORT

Coexistence of localized Langerhans cell histiocytosis and cutaneous Rosai–Dorfman disease

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**Department of Pathology, Taipei Medical University Hospital, Taipei, Taiwan*
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Accepted for publication 27 February 2002

Summary Rosai–Dorfman disease (RDD; sinus histiocytosis with massive lymphadenopathy) and Langerhans cell histiocytosis (LCH) are two different yet pathogenetically related histiocytic disorders. While systemic and localized forms have been identified in both diseases, each has its own characteristic histological, immunohistochemical and ultrastructural profile. Rarely, either RDD or LCH can also occur in the context of certain malignant neoplasms. However, the coexistence of RDD and LCH has never been described. We report a case of cutaneous RDD in which a focus of LCH was found. Clinical and laboratory examinations revealed no evidence of extracutaneous involvement of RDD or LCH. We believe that this is the first report of such a coexistence, and the possible pathogenesis is discussed.

Key words: Langerhans cell histiocytosis, Rosai–Dorfman disease

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Abstract: Rosai-Dorfman disease (RDD) is a reactive multisystem histiocytosis that typically presents with cervical lymphadenopathy and systemic symptoms. Cutaneous involvement occurs in approximately 10% of cases, and 3% of cases are limited to the skin without nodal or other extranodal involvement. Langerhans cell histiocytosis (LCH) is a clonal histiocytosis with a wide spectrum of presentations ranging from isolated skin or bone disease to multisystem involvement. Rare case reports have identified concomitant presentation of RDD and LCH; however, most of these reports have involved LCH and RDD occurring concurrently but at separate sites. We present a rare case of concurrent RDD and LCH presenting within a single skin nodule. The patient did not have any evidence of systemic involvement and has remained stable without additional treatment. We also review the literature on this unusual co-presentation and suggest possible underlying mechanisms. Finally, we recommend baseline laboratory and imaging studies and discuss treatment options based on the available evidence.

Key Words: Rosai-Dorfman disease, Langerhans cell histiocytosis, histiocytosis

(*Am J Dermatopathol* 2015;37:936–939)

MODERN PATHOLOGY (2010) 23, 1616–1623

Rosai–Dorfman disease and Langerhans cell histiocytosis are both disorders of accessory immune cells. Two cases have been previously reported of concurrent Langerhans cell histiocytosis and Rosai–Dorfman disease. In this report, we characterize the findings and selected molecular studies in nine additional cases. Histology was reviewed. Immunohistochemical stains were performed on all cases in which slides or blocks were available. A combination of CD1a, S-100, CD3, CD20, langerin, CD68, CD163, CD21, CD35 and CD123 immunohistochemical stains were performed. High-resolution array comparative genomic hybridization was performed on six samples from five cases. In these cases, seven were female and two male, with an average age of 25 years (15 months–59 years). A majority of the cases were identified in lymph node. Areas of Langerhans cell histiocytosis had a typical appearance with the existence of bland 'coffee-bean' nuclei, clear cytoplasm and associated eosinophils. The immunophenotype was typical, including expression of CD1a, S100, CD68 and langerin. In areas of Rosai–Dorfman disease, there was emperipolesis seen in all cases. Cells were intermediate-large in size with large round nuclei and ample clear or pale cytoplasm. The lesional cells were positive for S100, CD68, CD163, without expression of langerin or CD1a. Array comparative genomic hybridization showed gains and/or losses in four of the six samples. One case showed no gains or losses and one additional case showed gains and losses in the Langerhans cell histiocytosis, while no abnormalities were discovered in the Rosai–Dorfman disease component. These findings are comparable to those seen in previous studies of Langerhans cell histiocytosis. We report the clinical and pathologic findings of the combination of Langerhans cell histiocytosis and Rosai–Dorfman disease. Furthermore, we suggest on the basis of evidence from our cases that, when simultaneous, the two entities may be pathophysiologically related.
Modern Pathology (2010) **23,** 1616–1623; doi:10.1038/modpathol.2010.157; published online 20 August 2010

Case follow-up

Serie Osea: No se observan lesiones líticas.
Hematologia:

Globulos Blancos	13,000
Neutrofilos	8,000.
Linfocitos	4,000.
Hgb	9
Hct	29
Plaquetas	505

Tratamiento

Vincristina, Prednisona SEMANA 1
Vincristina, Prednisona SEMANA 3

Comentario: Paciente con difícil apego y seguimiento por lugar de origen. Actualmente sin adenopatías, ni otros hallazgos al examen físico únicamente fallo de medro.

References

- O'Malley DP, Duong A, Barry TS, Chen S, Hibbard MK, Ferry JA, Hasserjian RP, Thompson MA, Richardson MS, Jaffe R, Sidhu JS, Banks PM. Co-occurrence of Langerhans cell histiocytosis and Rosai-Dorfman disease: possible relationship of two histiocytic disorders in rare cases. Mod Pathol. 2010 Dec;23(12):1616-23.

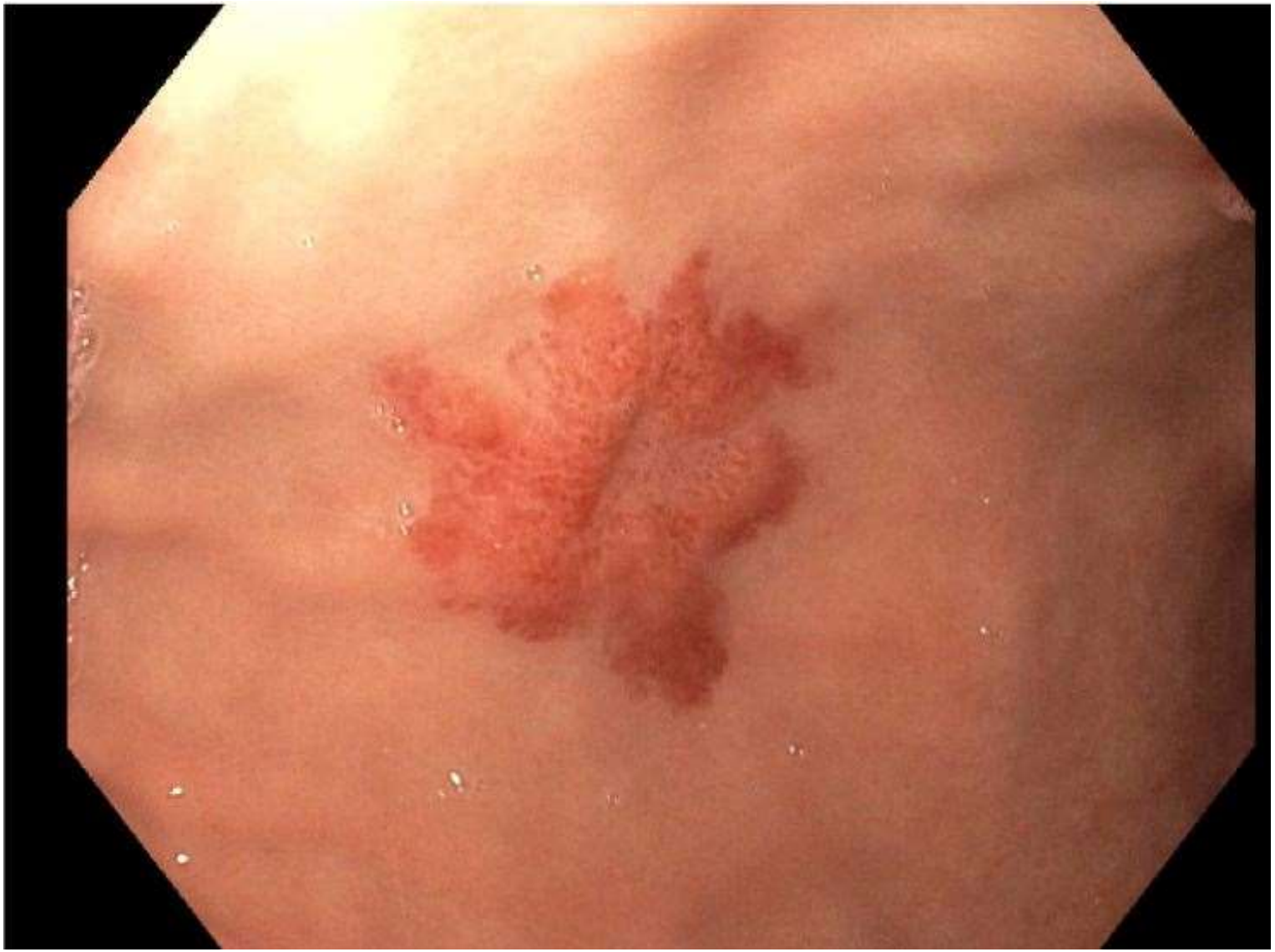
- Wang, K. , Cheng, C. , Hu, C. and Lee, W. (2002), Coexistence of localized Langerhans cell histiocytosis and cutaneous Rosai–Dorfman disease. British Journal of Dermatology, 147: 770-774.

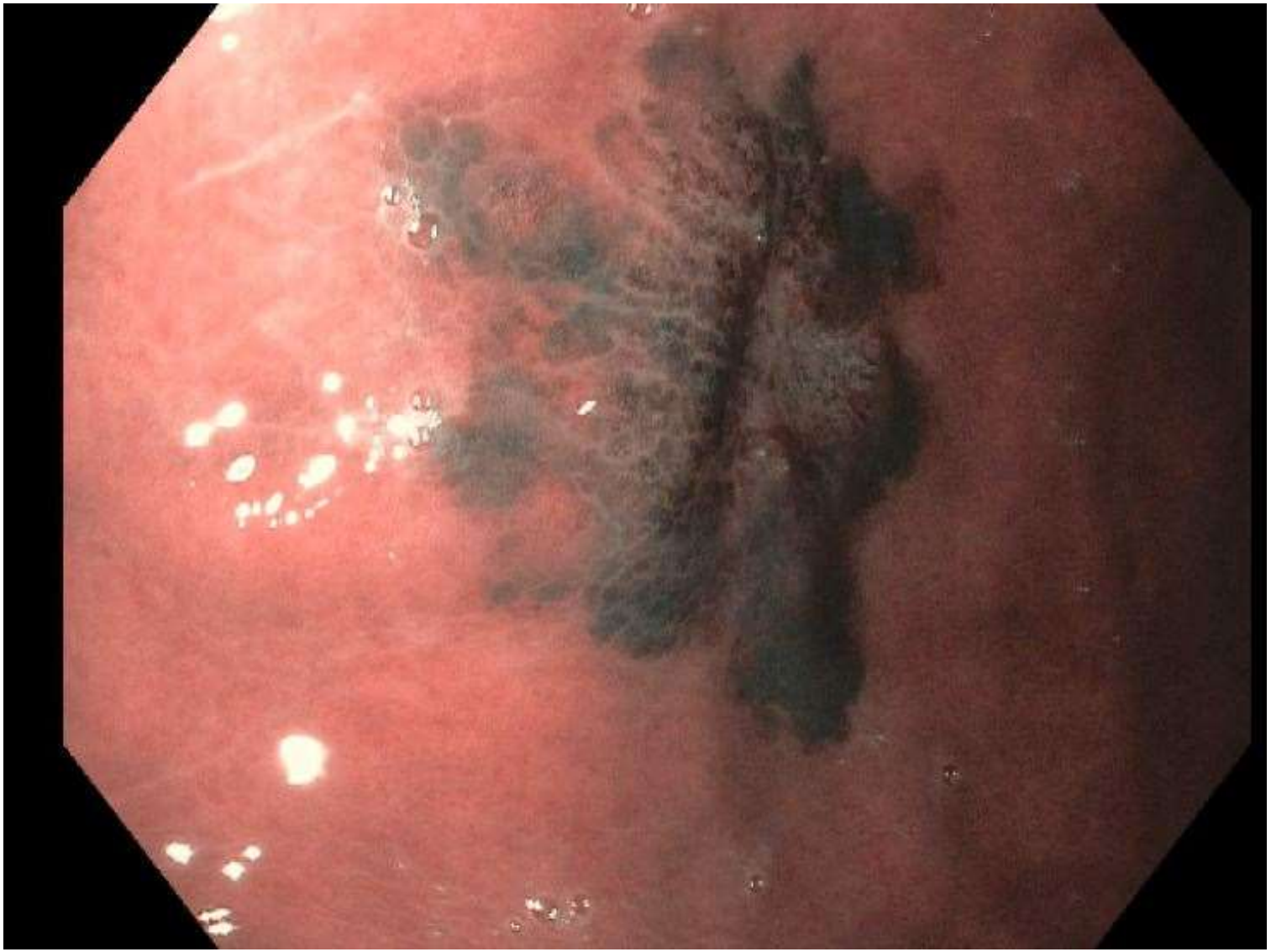
- Litzner BR, Subtil A, Vidal CI. Combined Cutaneous Rosai-Dorfman Disease and Localized Cutaneous Langerhans Cell Histiocytosis Within a Single Subcutaneous Nodule. Am J Dermatopathol. 2015;37(12):936-9.

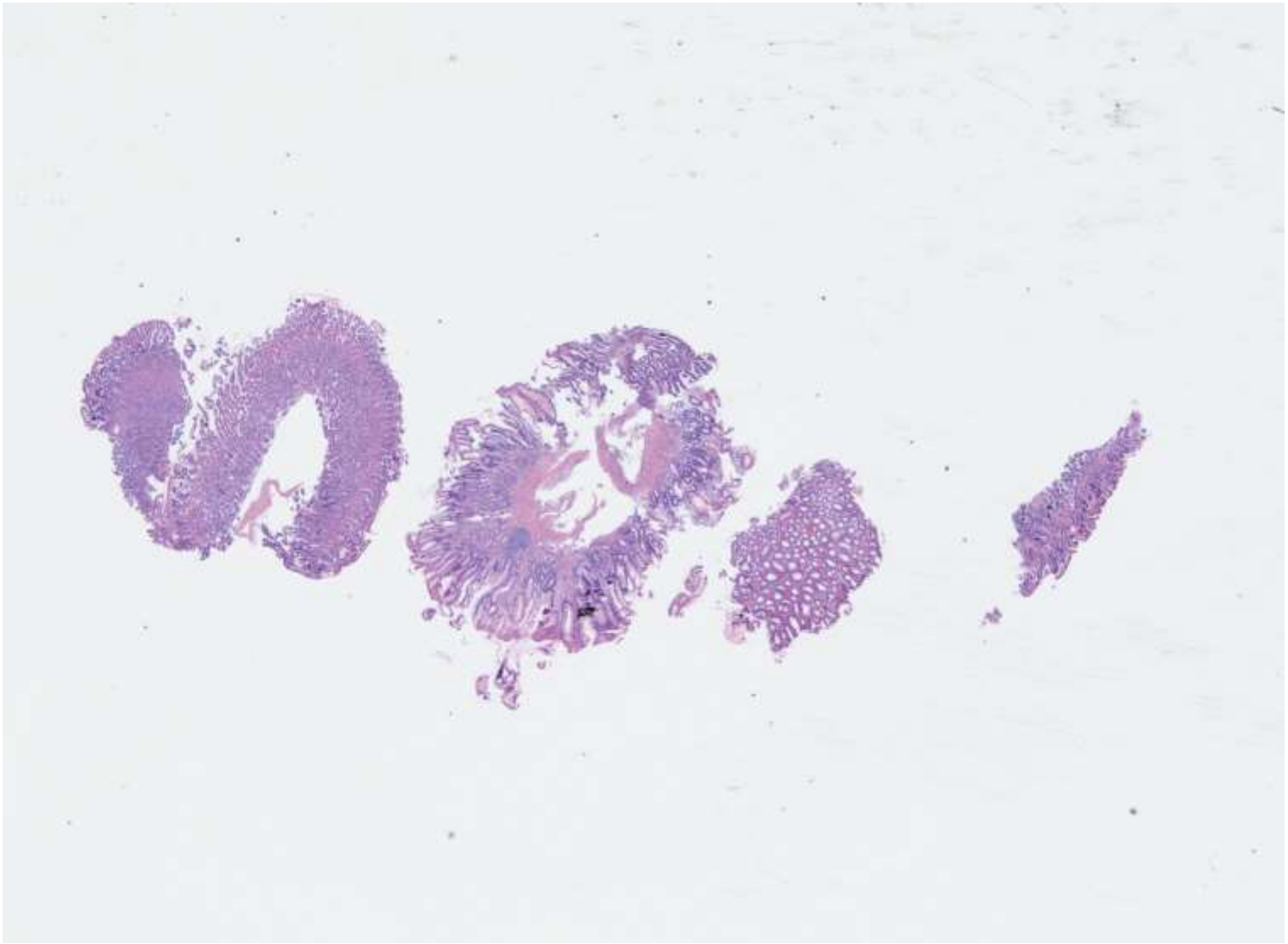
19-0602
(scanned slide available)

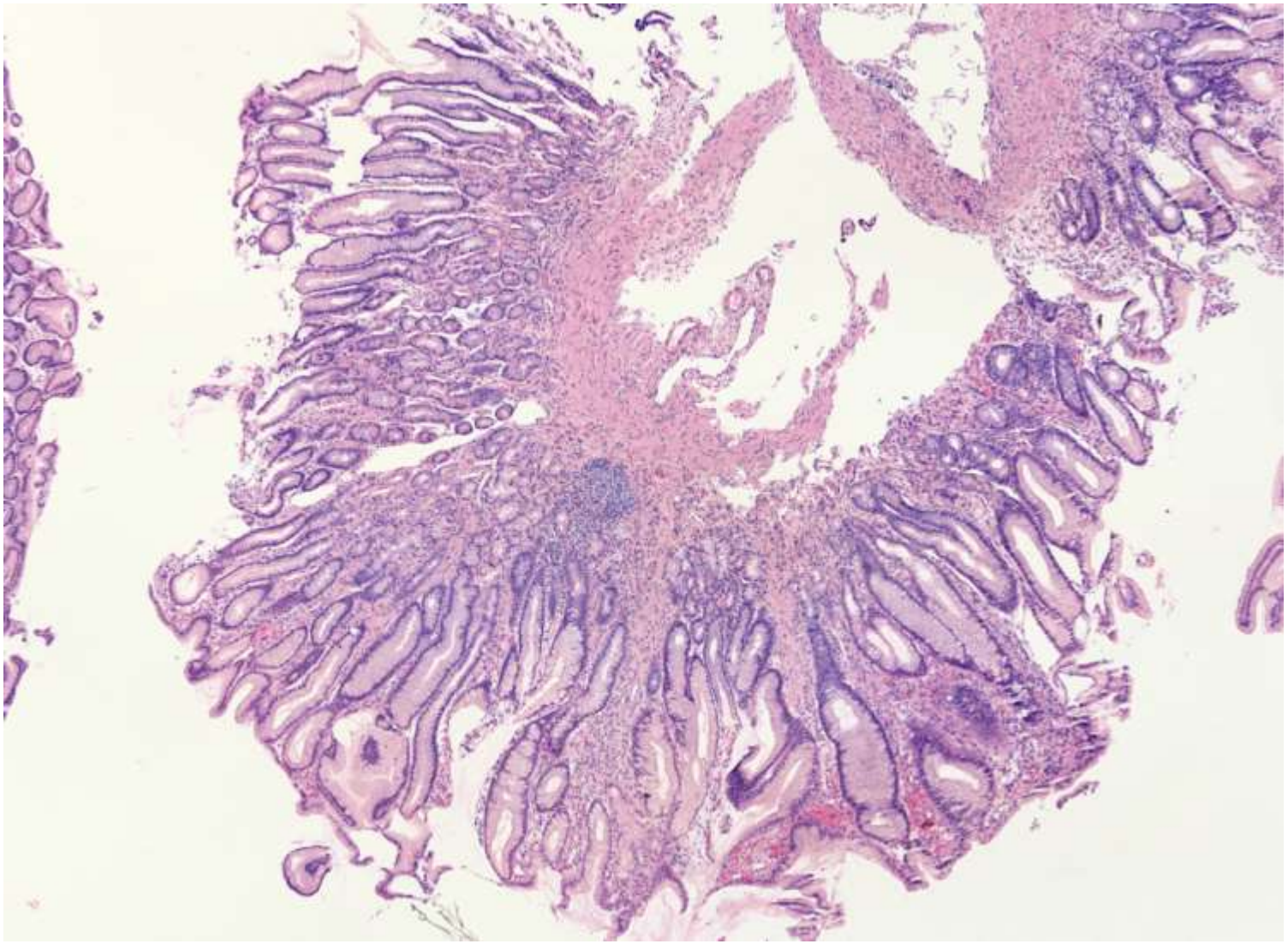
Jing Zhang/Christine Louie; Palo Alto VA

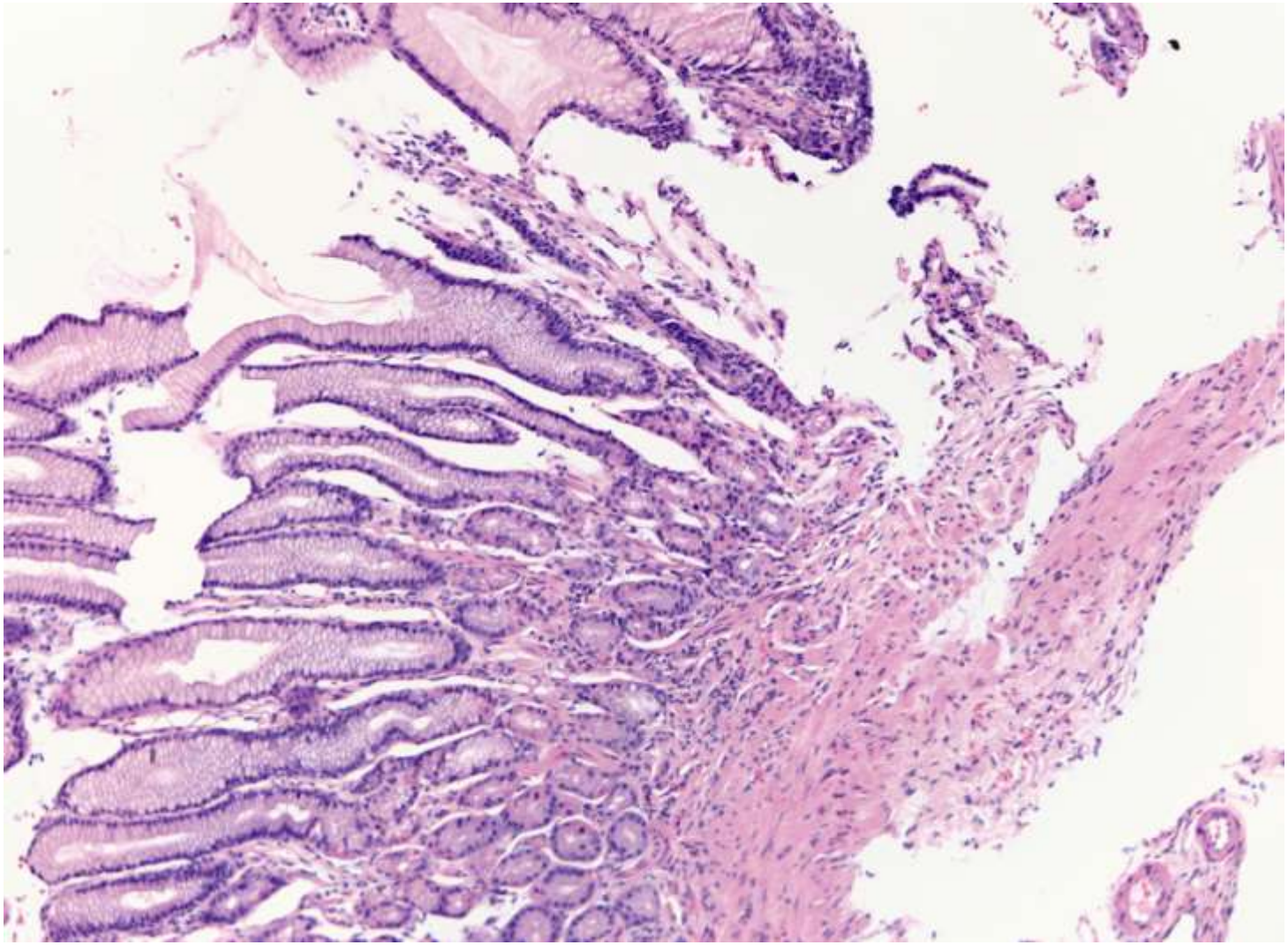
45-year-old male with HIV. Gastric biopsy performed.

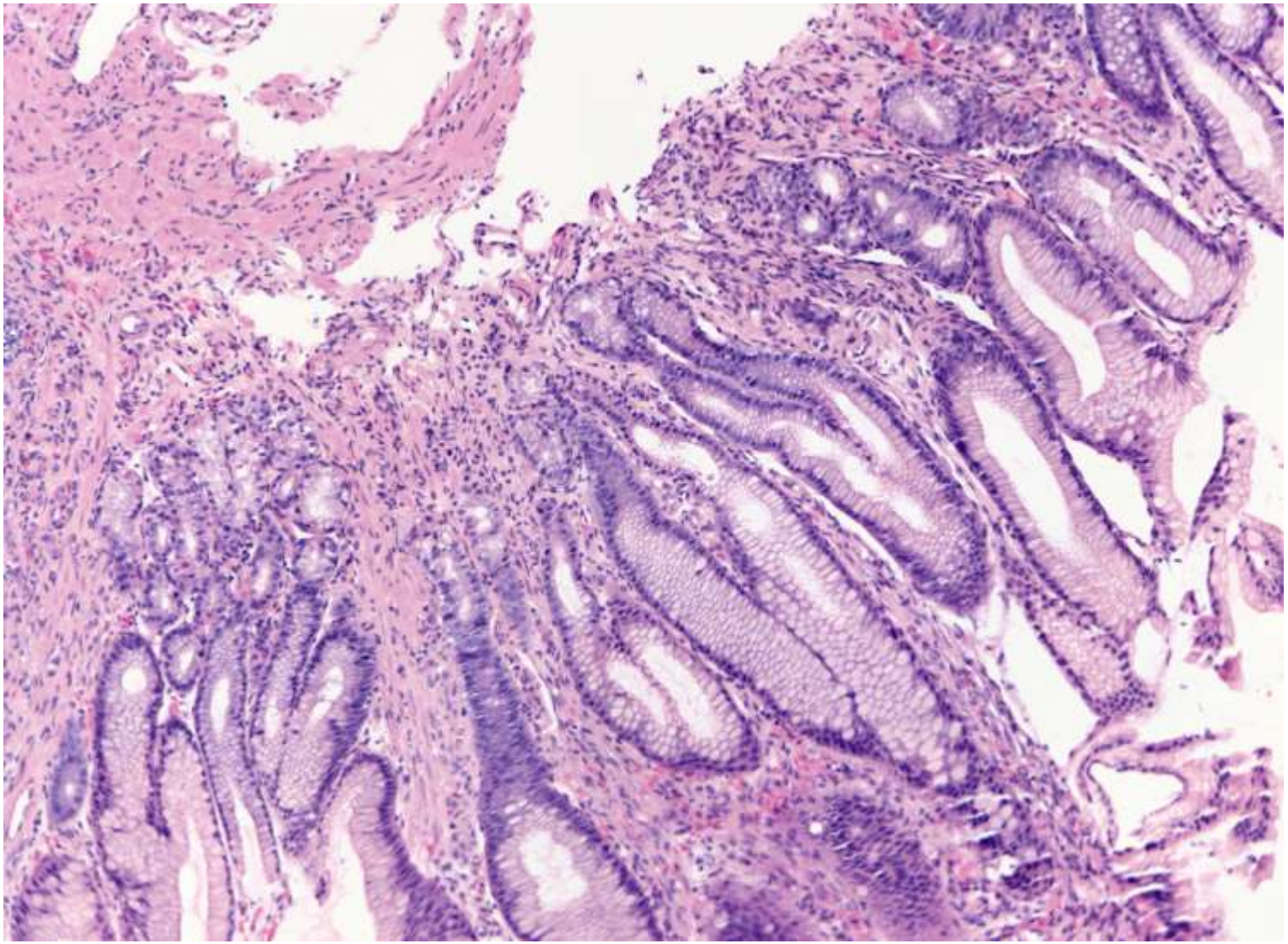


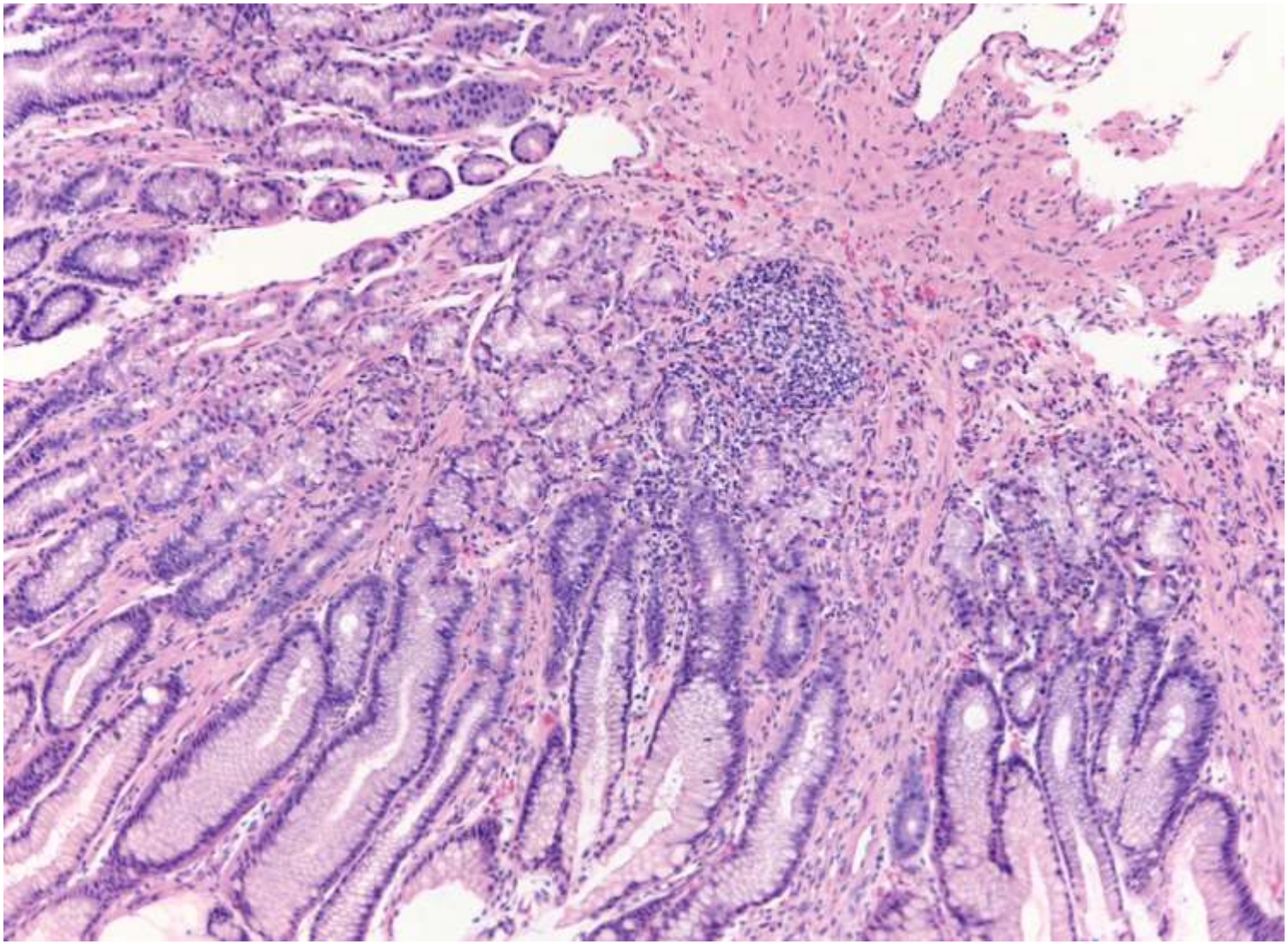


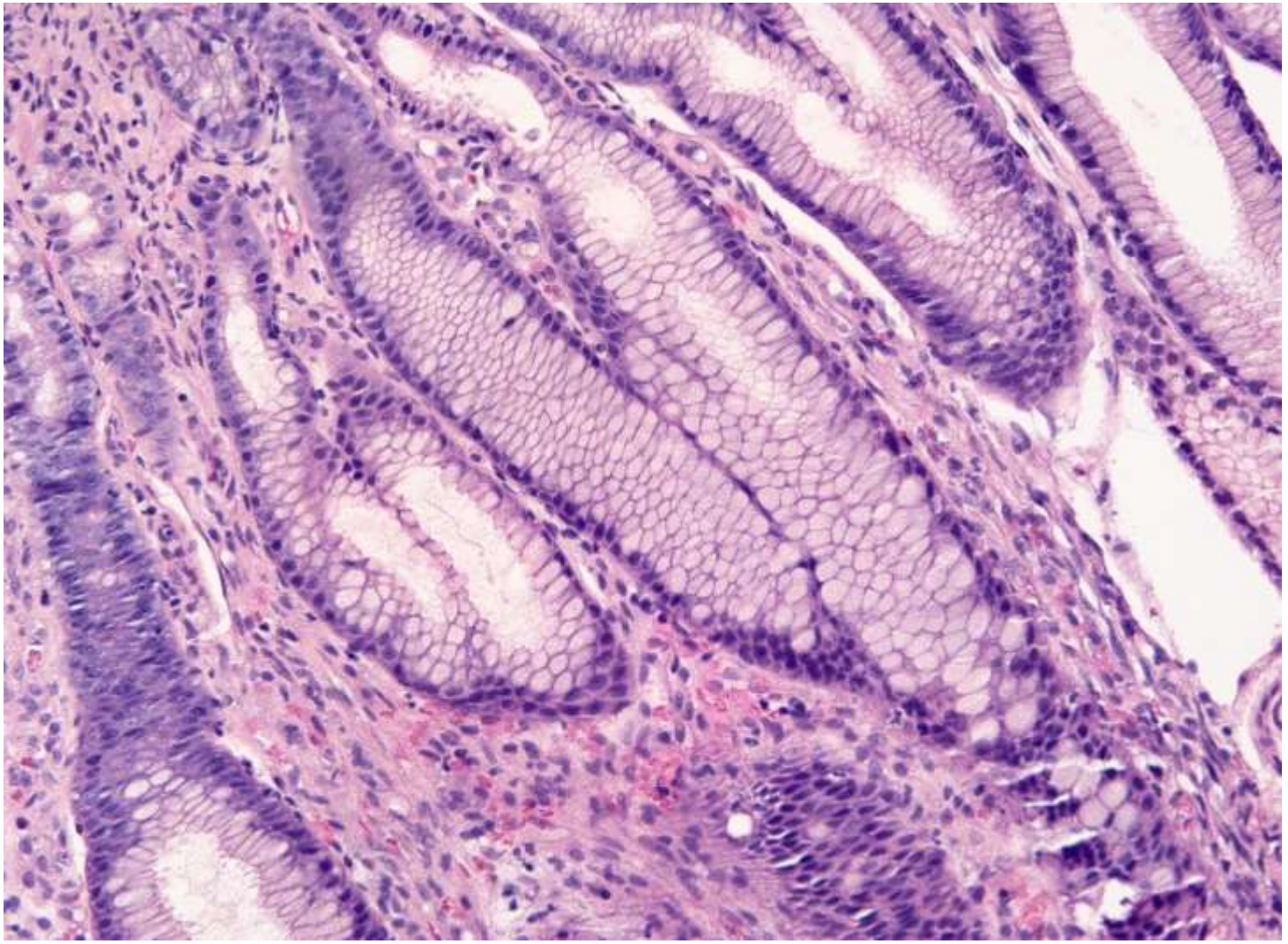


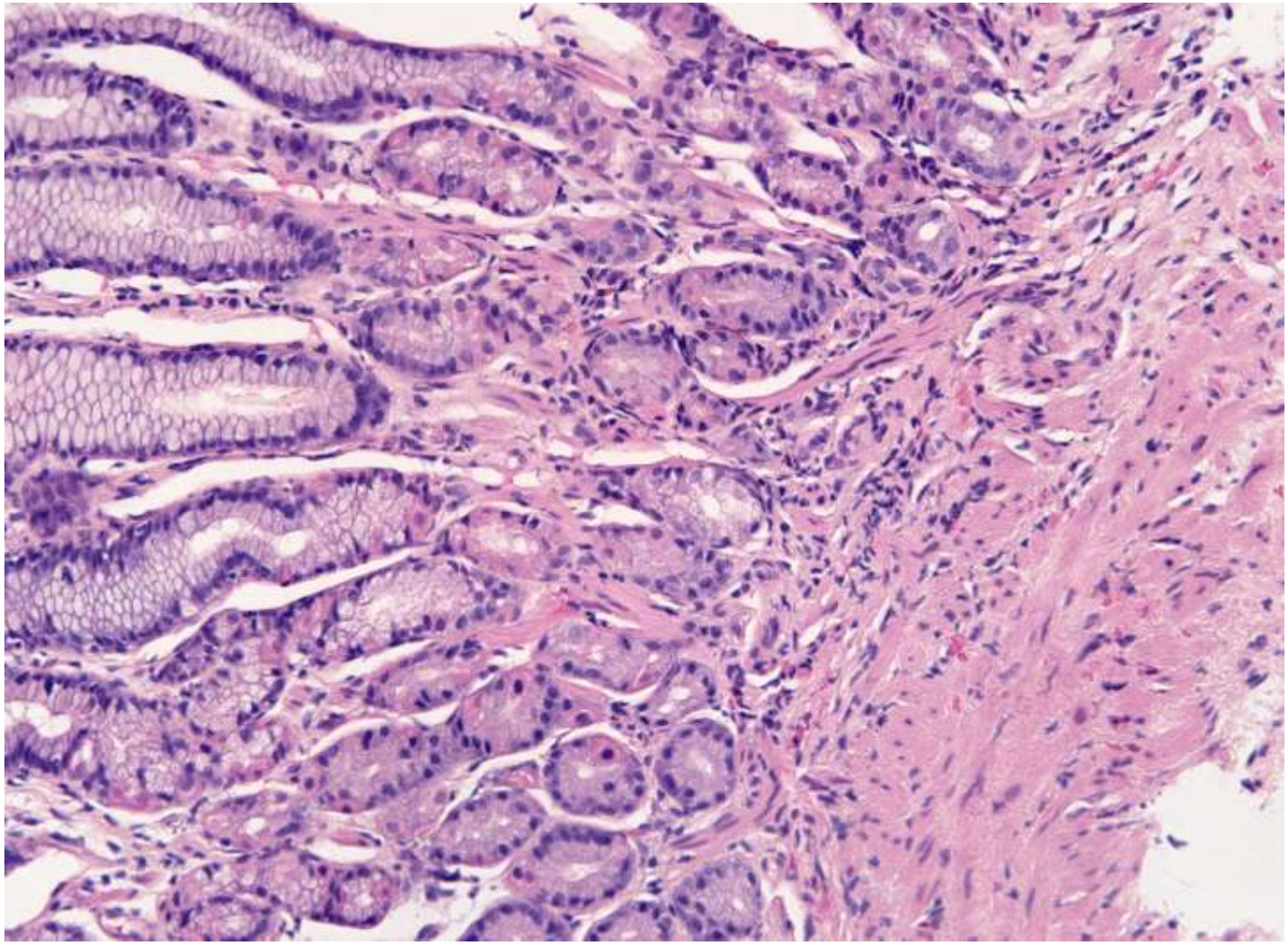








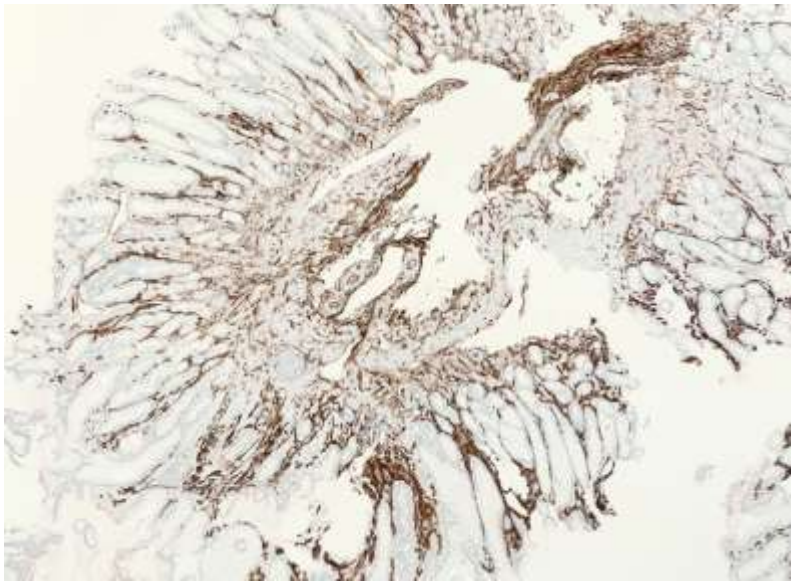


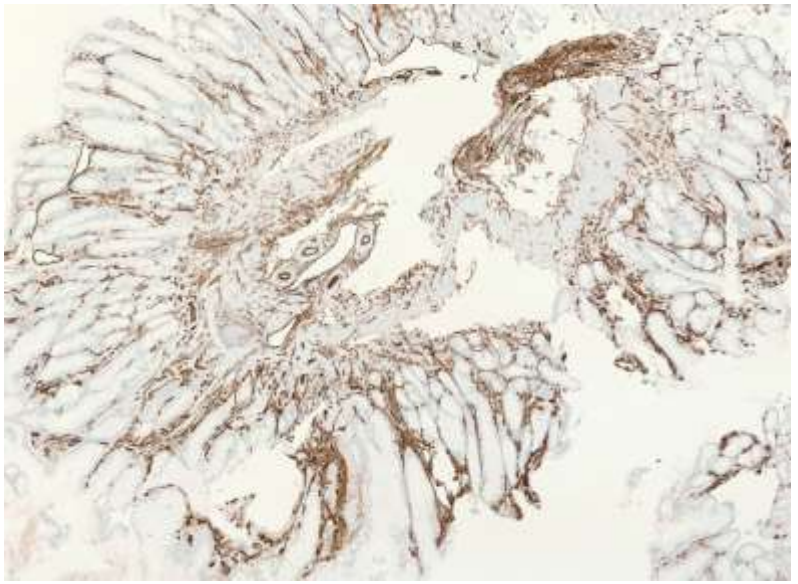


CD34

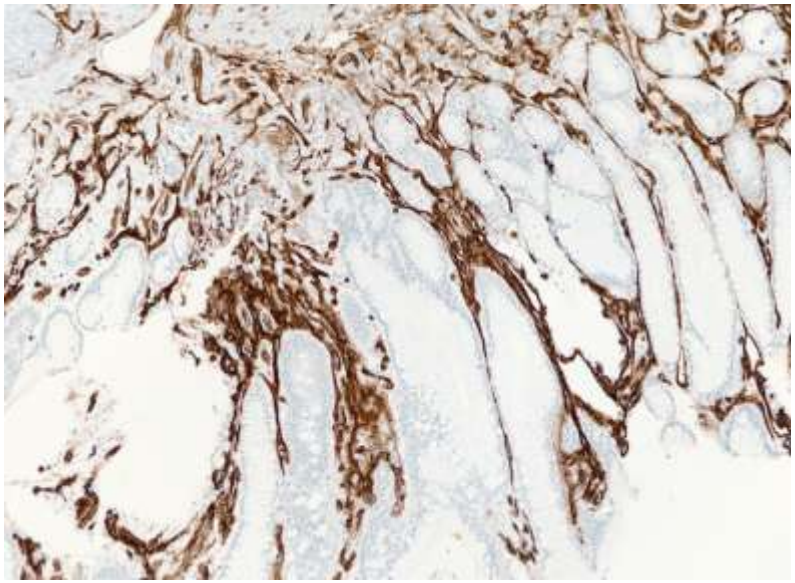
CD31

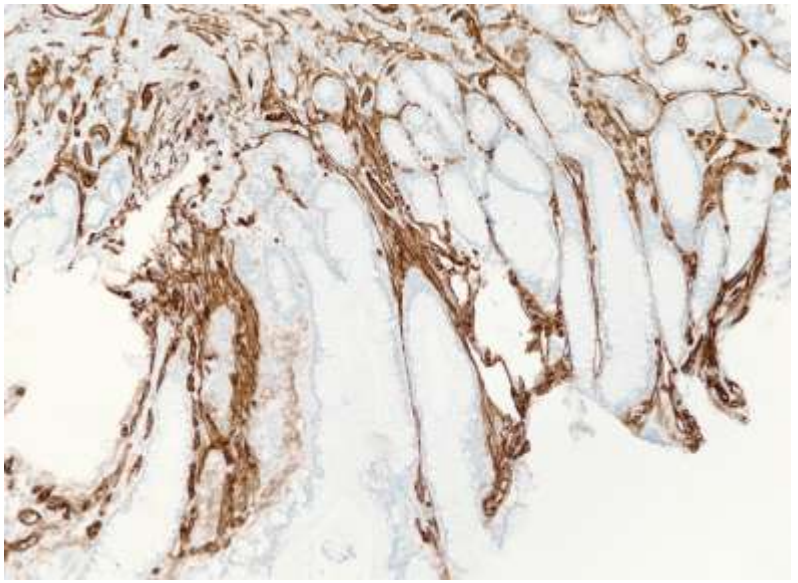
4x



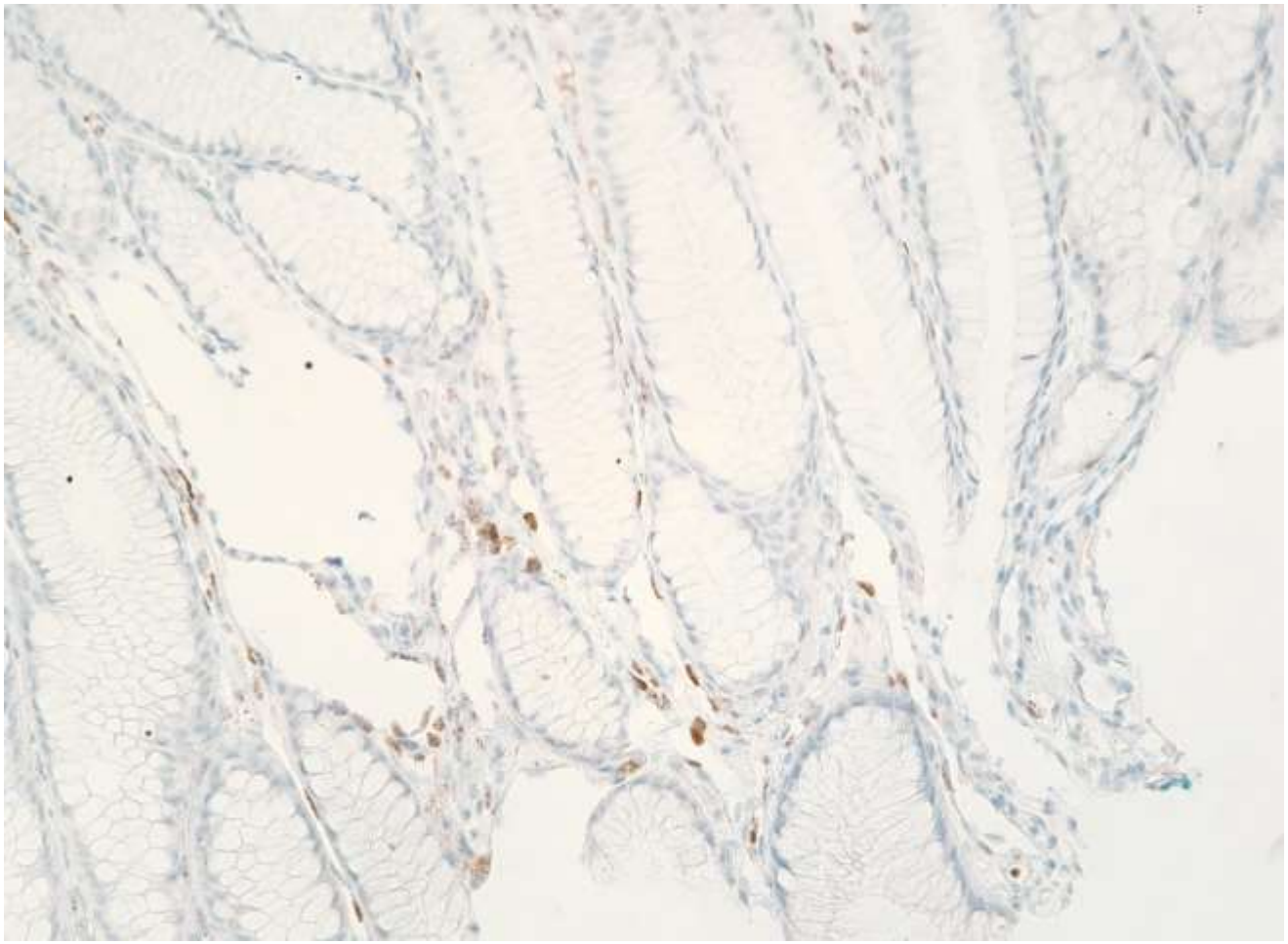


10x





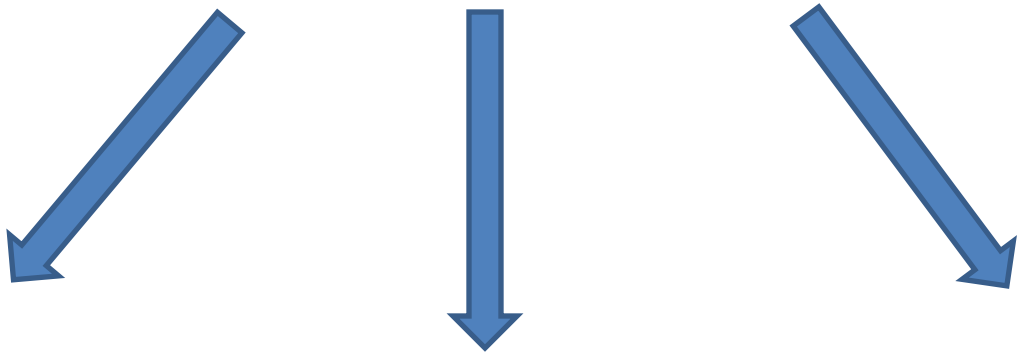
HHV-8



Diagnosis?
Kaposi’s Sarcoma

Human Herpes Virus 8

γ-herpesvirus was first identified as the etiological agent of Kaposi sarcoma in 1994



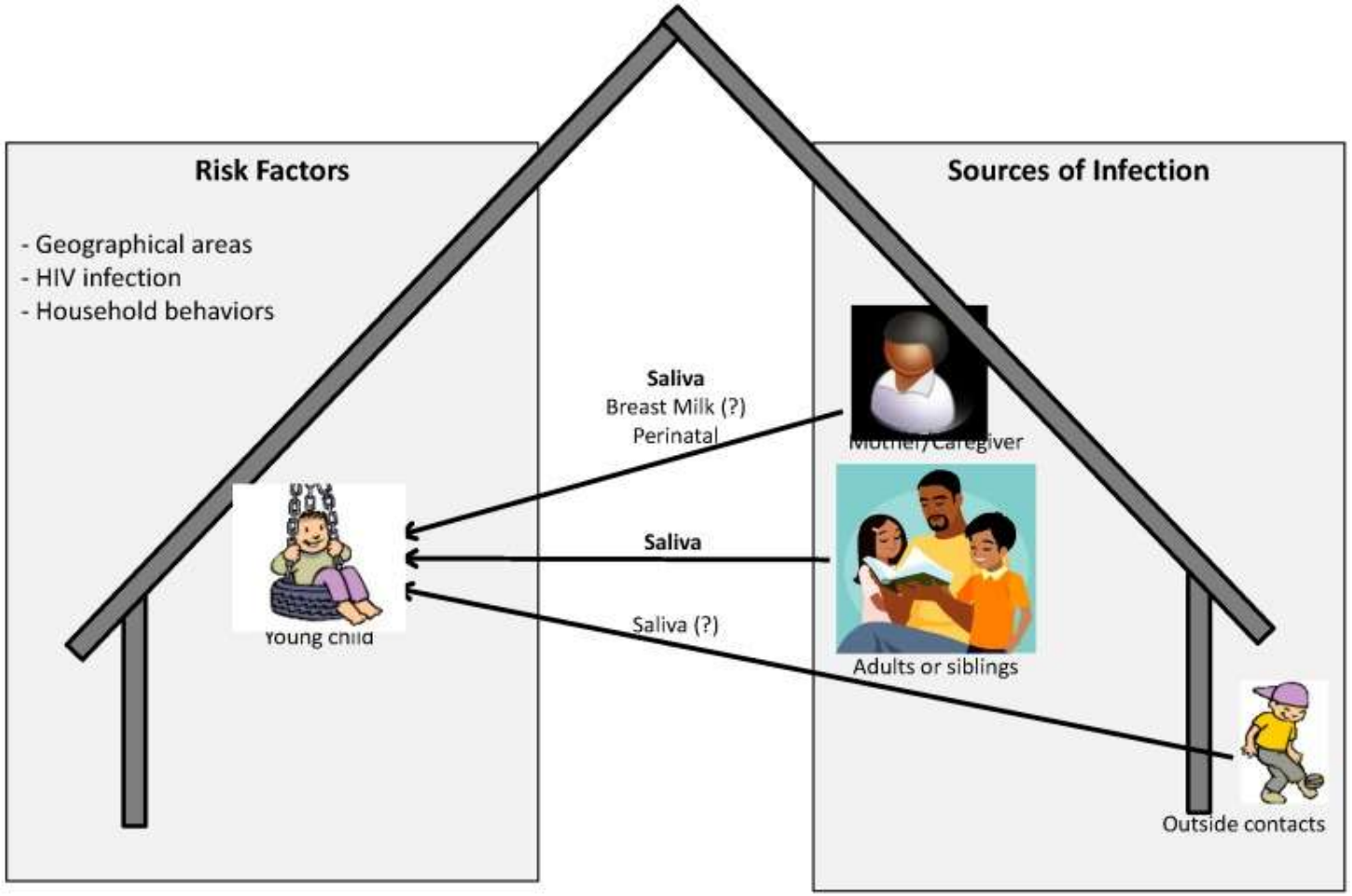
Kaposi's Sarcoma

Multi-centric Castleman's

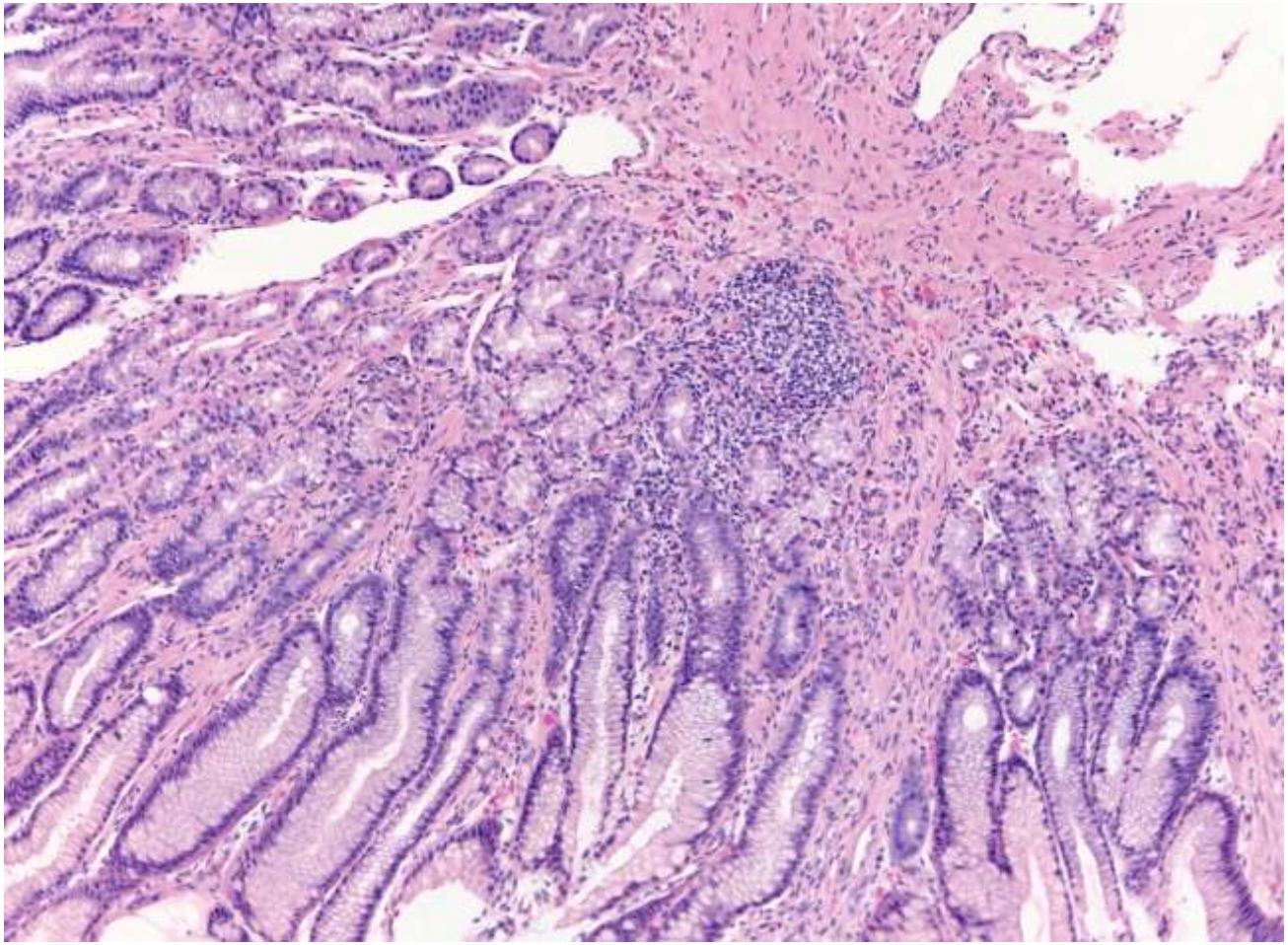
HHV8 associated Lymphoma

Primary effusion lymphoma
HHV8+ diffuse large B cell lymphoma

Epidemiology



Minhas, V., & Wood, C. (2014). Epidemiology and transmission of kaposi's sarcoma-associated herpesvirus. *Viruses*, *6*(11), 4178–4194.



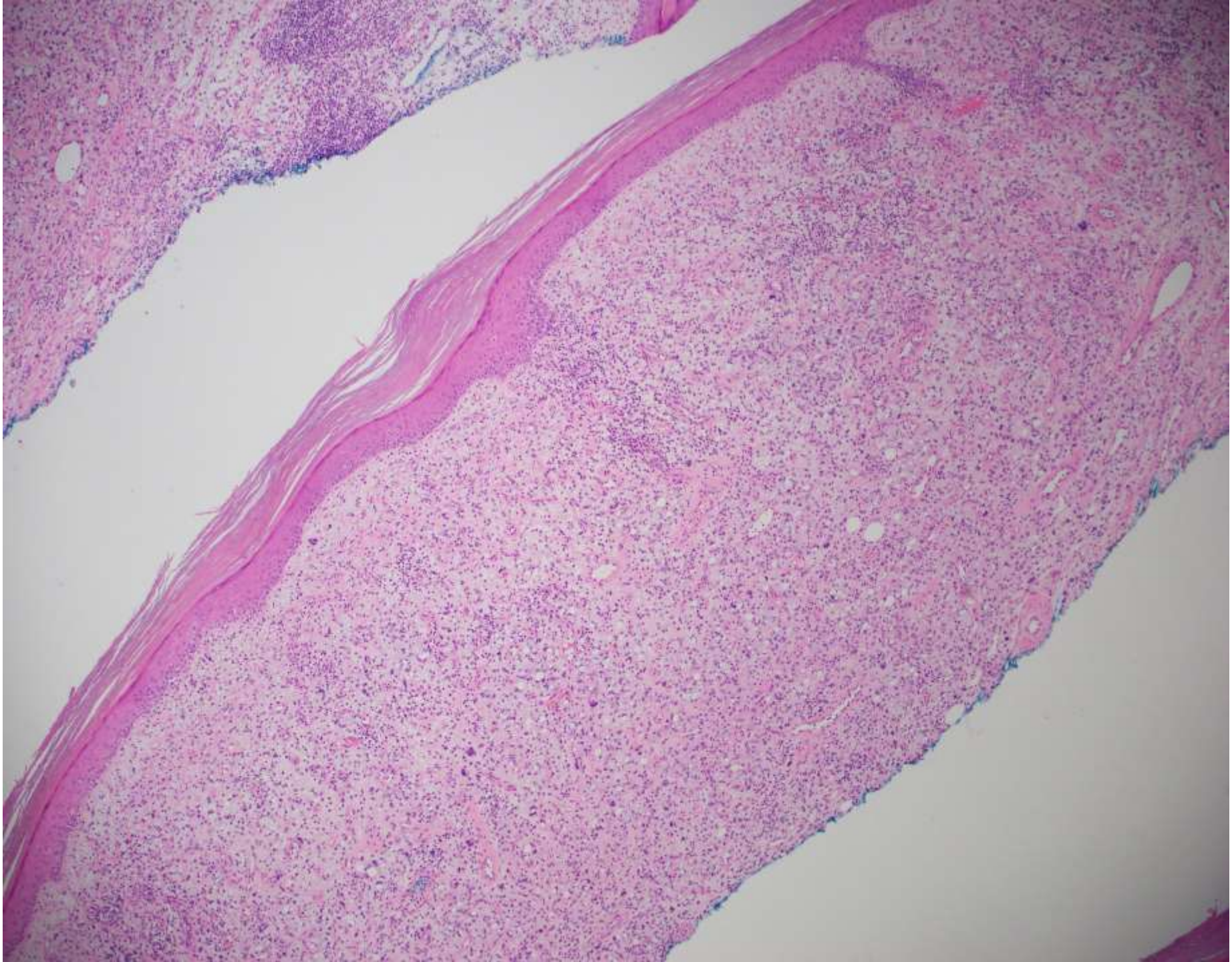
Bibliography

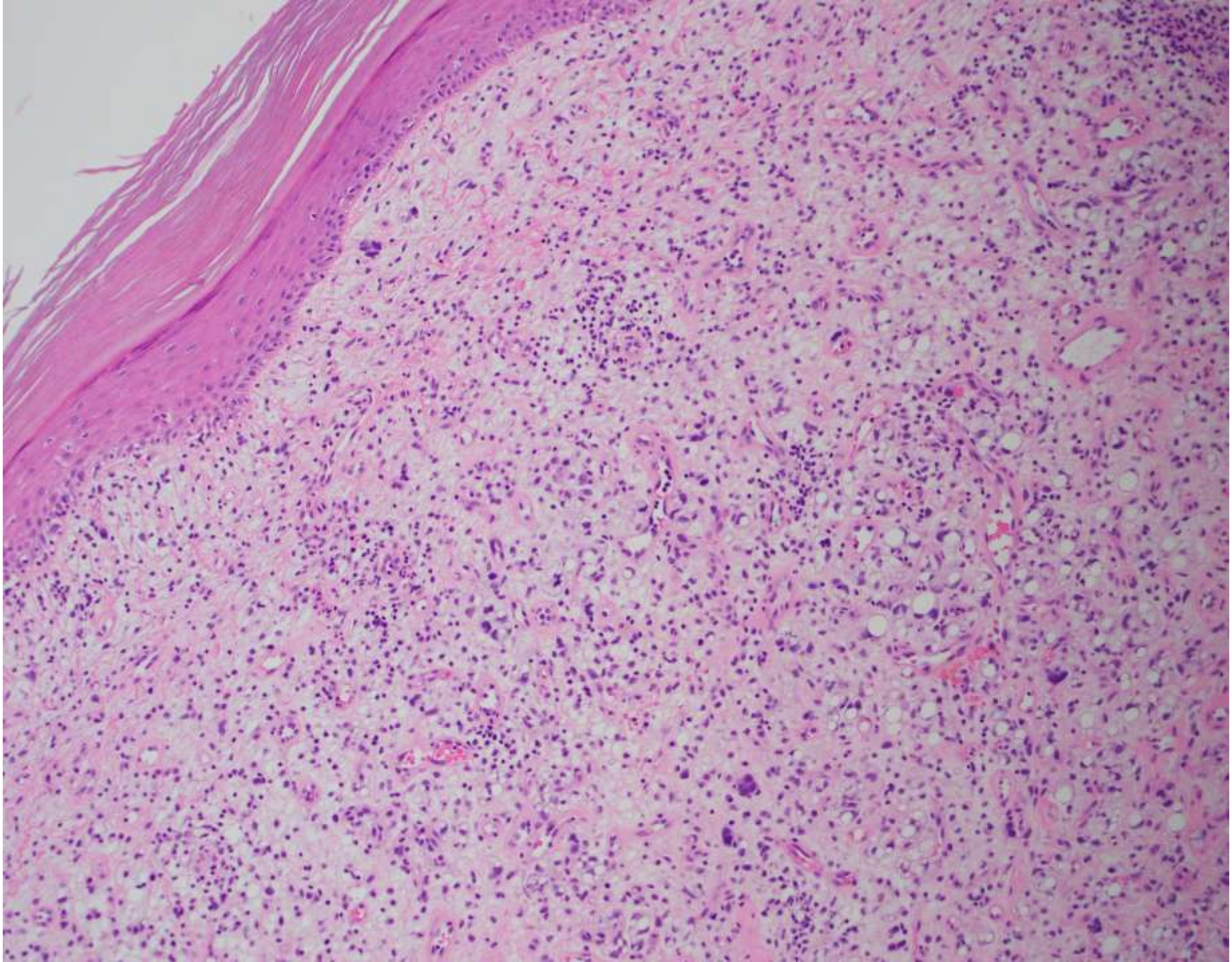
- Minhas, V., & Wood, C. (2014). Epidemiology and transmission of kaposi's sarcoma-associated herpesvirus. *Viruses*, *6*(11), 4178–4194. https://doi.org/10.3390/v6114178
- Gonzalez-Farre, B., Martinez, D., Lopez-Guerra, M., Xipell, M., Monclus, E., Rovira, J., … Martinez, A. (2017). HHV8-related lymphoid proliferations: A broad spectrum of lesions from reactive lymphoid hyperplasia to overt lymphoma. *Modern Pathology*, *30*(5), 745–760. https://doi.org/10.1038/modpathol.2016.233
- Voltaggio, L., & Montgomery, E. A. (2015). Gastrointestinal tract spindle cell lesions-just like real estate, it's all about location. *Modern Pathology*, *28*(s1), S47–S66. https://doi.org/10.1038/modpathol.2014.126

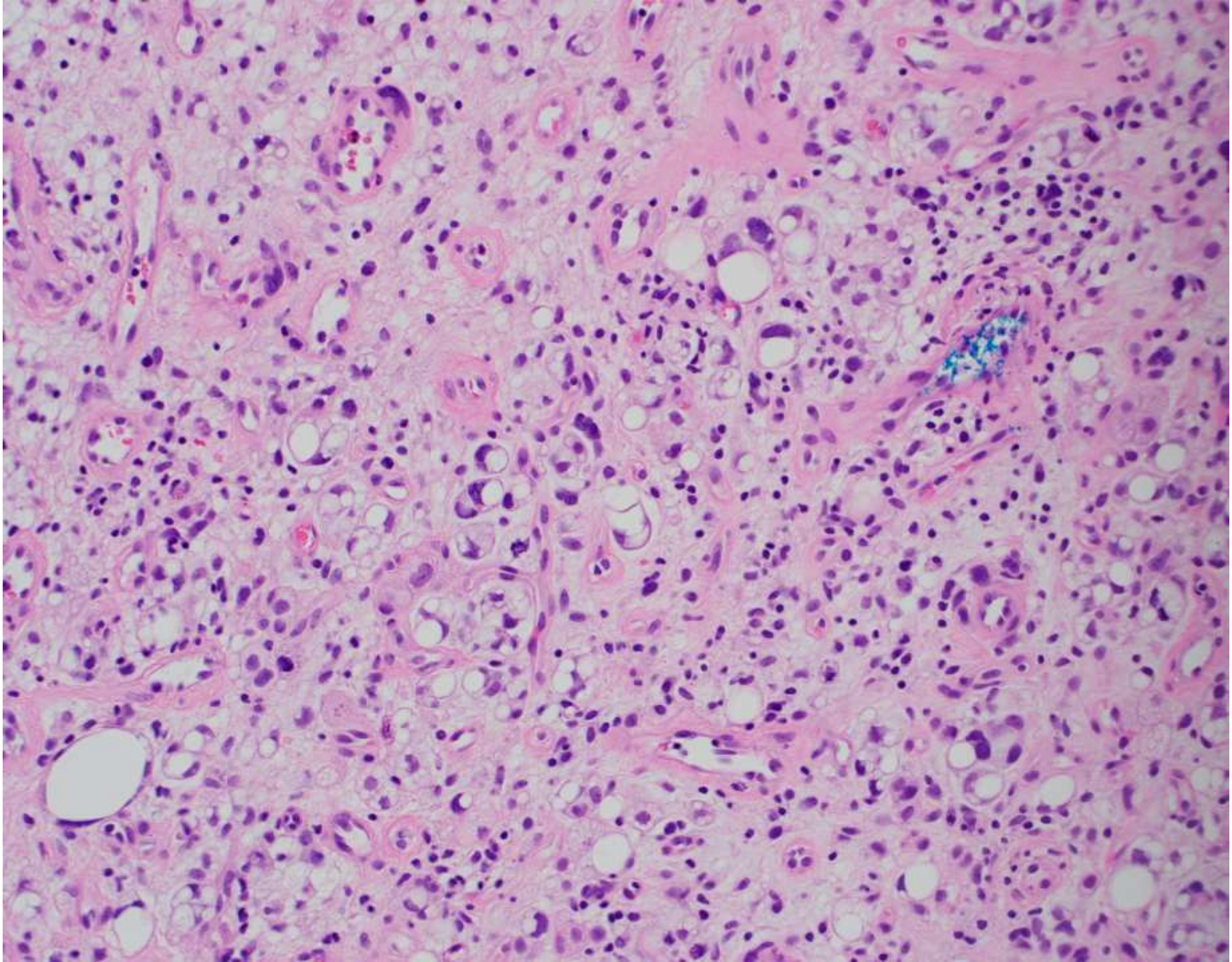
19-0603

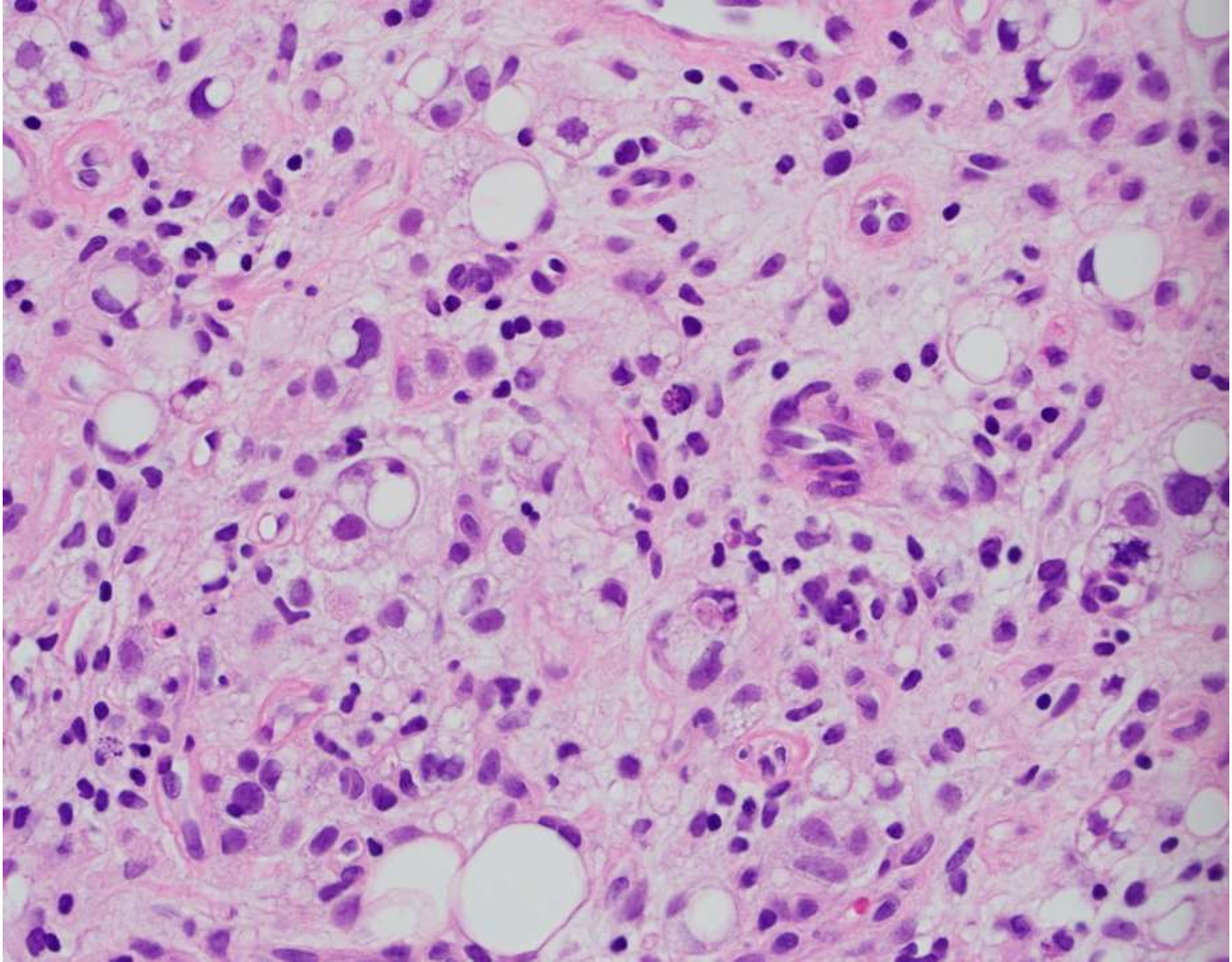
Sarah Cherny; Kaiser San Francisco

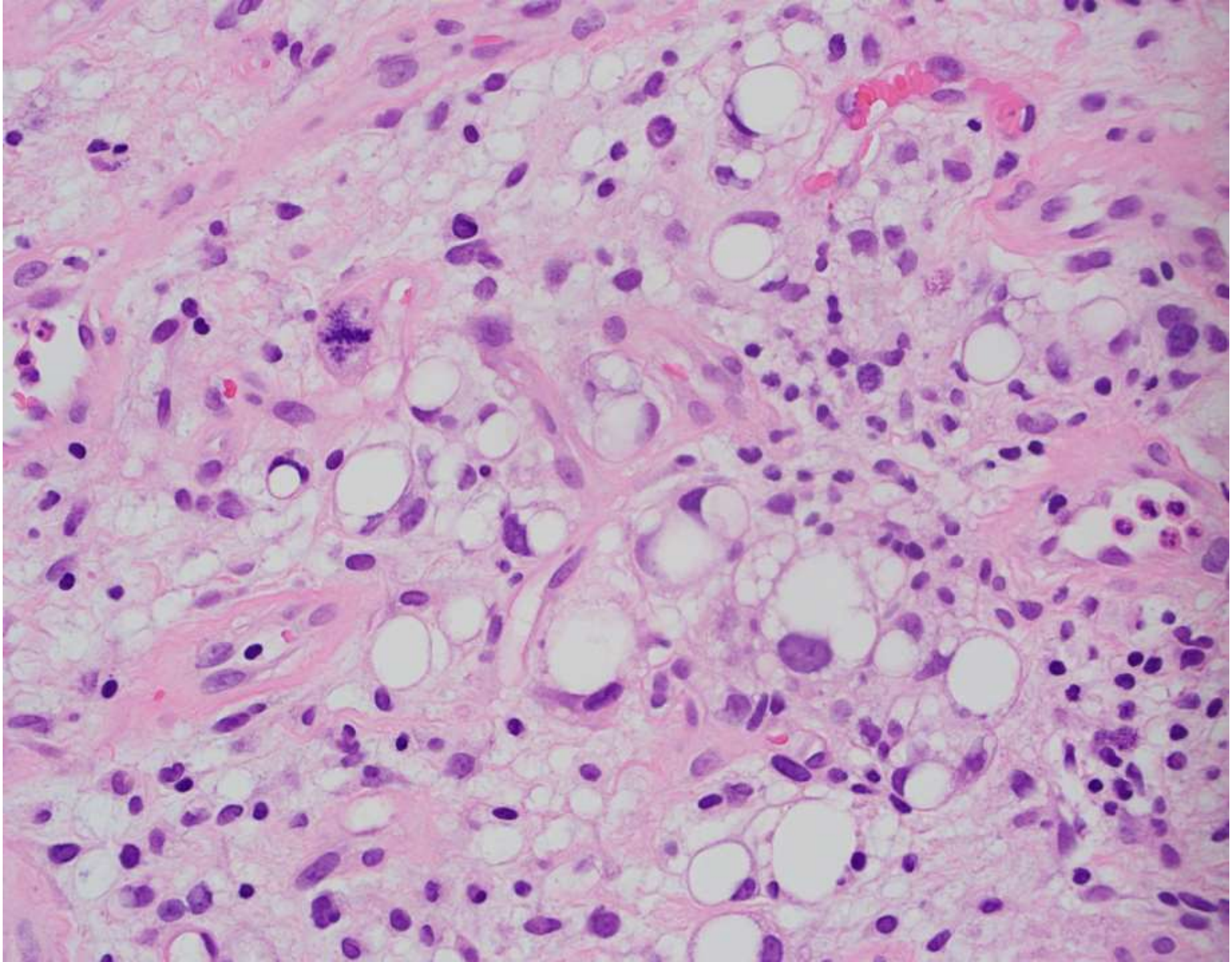
45-year-old female reports sudden appearance and subsequent growth of a 6mm red papule on her left shin over prior 2 months. Dermatologist performed shave biopsy.

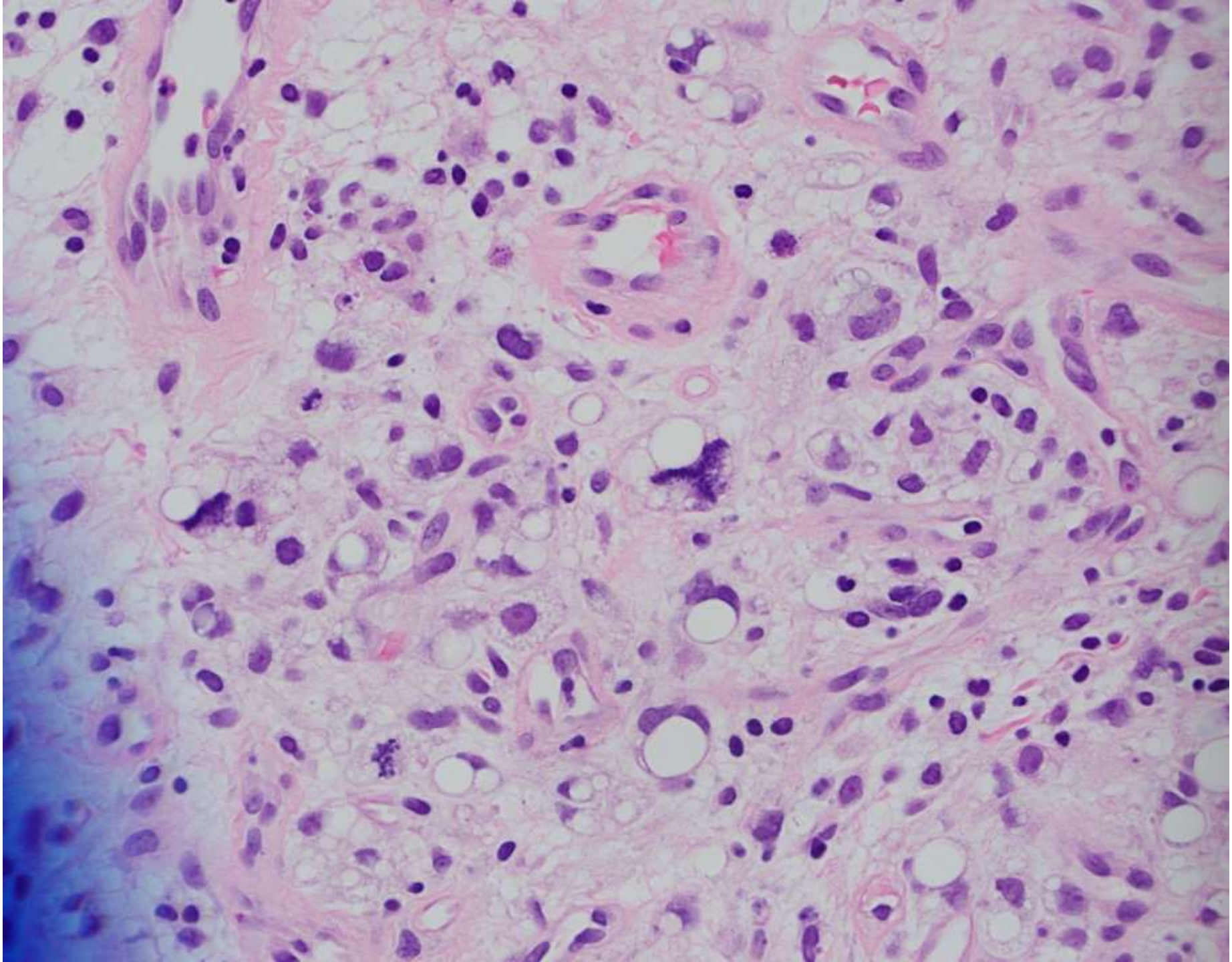


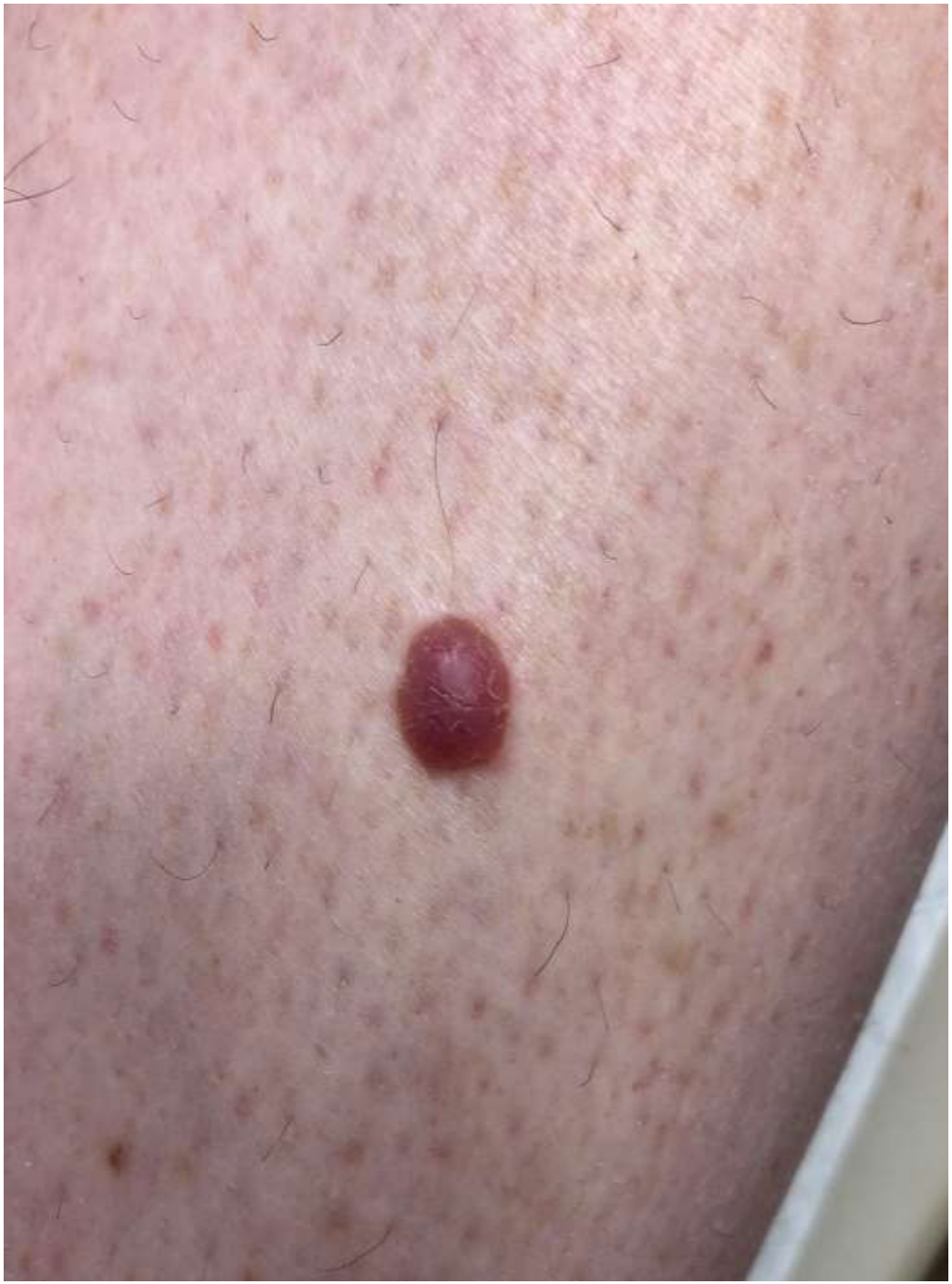


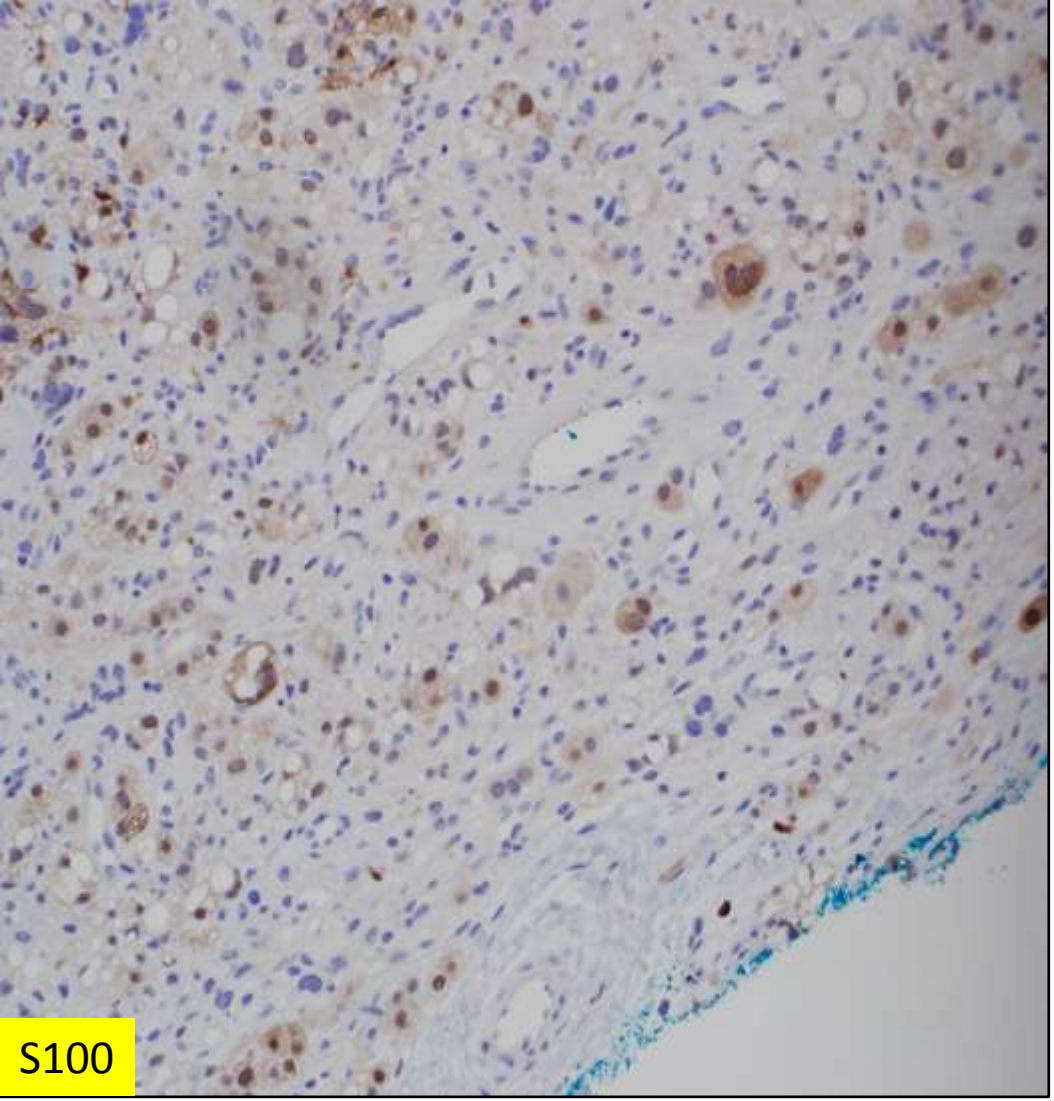








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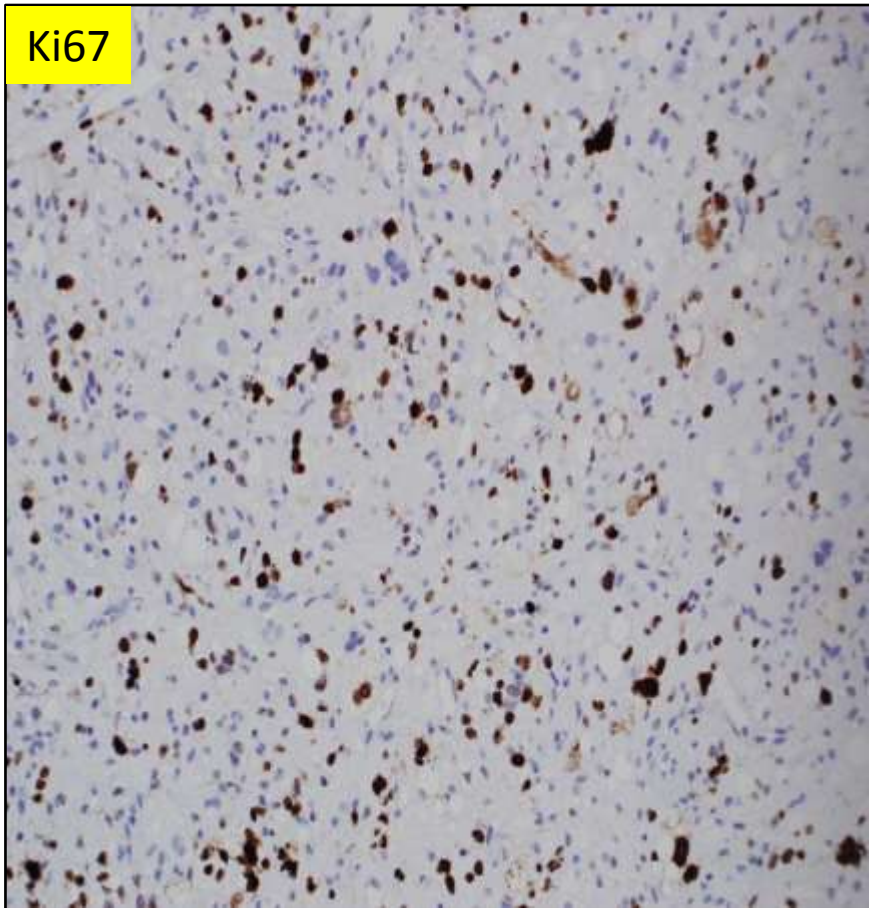

Ki67

NEGATIVE STAINS:

- Melan A
- SOX10
- MiTF
- HMB45
- Desmin
- CD34
- ERG
- CD68
- Pancytokeratin
- EMA
- CK7
- CK20
- CDX2

My Ddx

- Rare variant of melanoma??
  - “Primary cutaneous malignant melanoma with lipoblast-like cells” (Arch Path Lab Med, 2003 Mar; 127 (3): 370-1)
  - Signet-ring cell melanoma?
  - Balloon cell melanoma?
- Liposarcoma??
  - Met?
  - Primary?

- Superficial pleomorphic liposarcoma

Cutaneous and Subcutaneous Pleomorphic Liposarcoma

A Clinicopathologic Study of 29 Cases With Evaluation of MDM2 Gene Amplification in 26

Jerad M. Gardner, MD, Monisha Dandekar, MD,† Dafydd Thomas, MD, PhD,† John R. Goldblum, MD,‡ Sharon W. Weiss, MD,* Steven D. Billings, MD,‡§ David R. Lucas, MD,† Jonathan B. McHugh, MD,† and Rajiv M. Patel, MD†‖*

Abstract: Pleomorphic liposarcoma (PL) is an uncommon form of liposarcoma that rarely occurs in the skin and subcutis. As its behavior in this setting is incompletely characterized, we undertook a study of a series of superficial PLs, defined as those arising or based primarily in the dermis and/or subcutis without involvement of deep structures. In addition, *MDM2* gene amplification, a diagnostic signature of well-differentiated/dedifferentiated liposarcoma (WDL/DL), was evaluated to address favorable outcome compared with their deep-seated counterparts, most likely attributed to their small size and superficial location. The low incidence of *MDM2* gene amplification in our series indicates that most superficial PLs are unrelated to WDL/DL. PL likely evolves by way of more than 1 molecular pathway.

Key Words: liposarcoma, pleomorphic liposarcoma, *MDM2* gene amplification, dedifferentiated liposarcoma, cutaneous sarcoma

Epidemiology: Series of 29 Patients

- Age: 5 – 93 years, median = 55 years
- M:F = 1.4:1
- 50% on extremity, 25% trunk, 25% head and neck
- May involve dermis, dermis and subcutis, or just subcutis
  - Those confined to dermis tend to be more circumscribed; subcutaneous component tends to be more infiltrative
- Size ranged from 0.8 cm to 15 cm (median = 2 cm)
- All were mitotically active, FNCLCC grade 2 or 3, with either pleomorphic spindled or epithelioid pattern
- MDM2 gene amplification present in only 3 of 26 cases

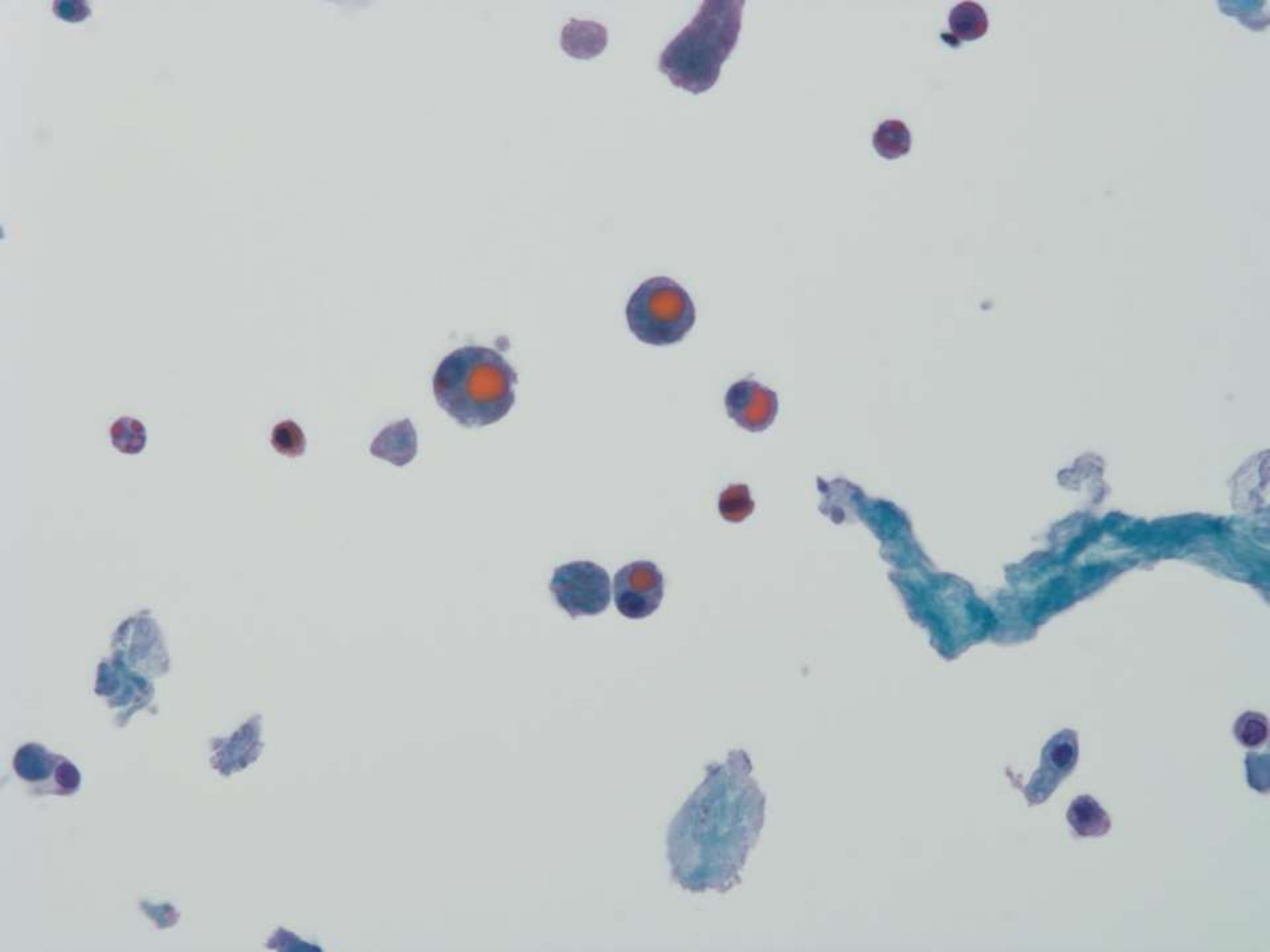
Prognosis: Series of 29 Patients

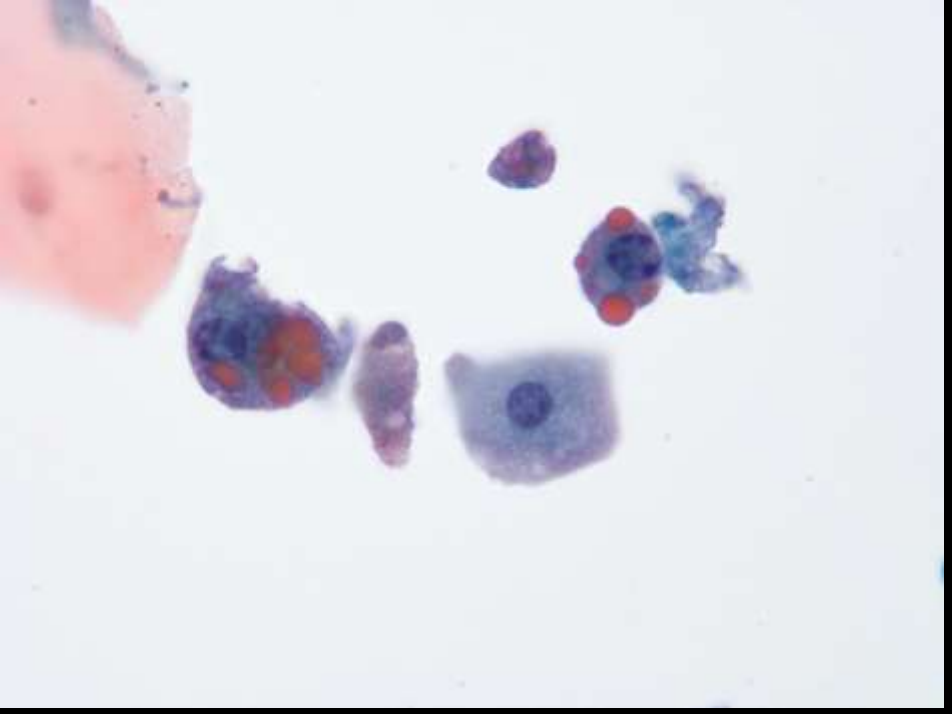
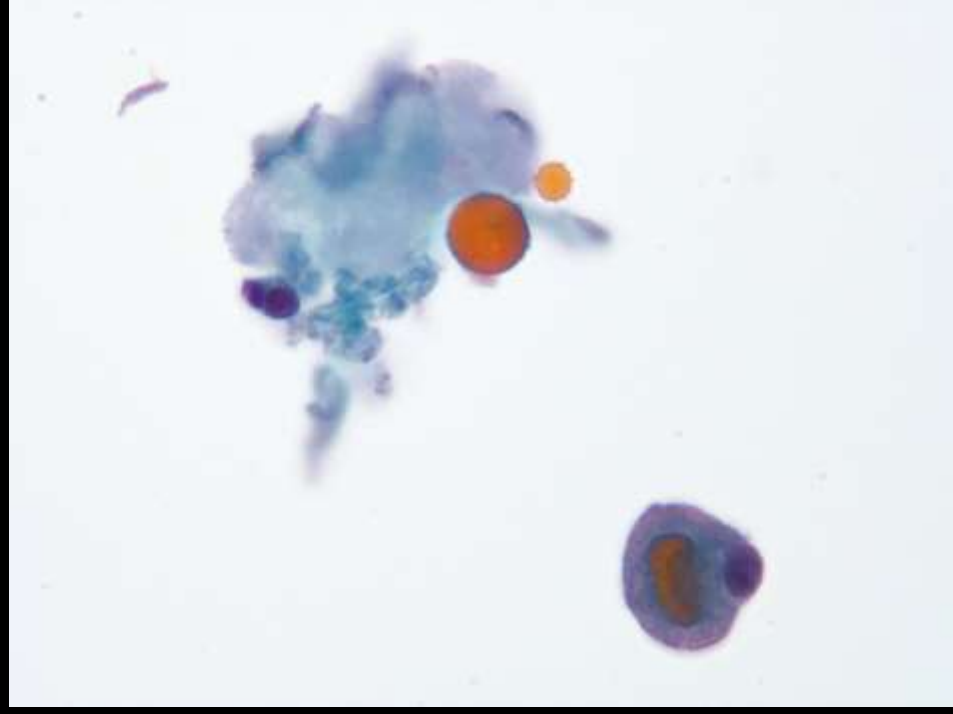
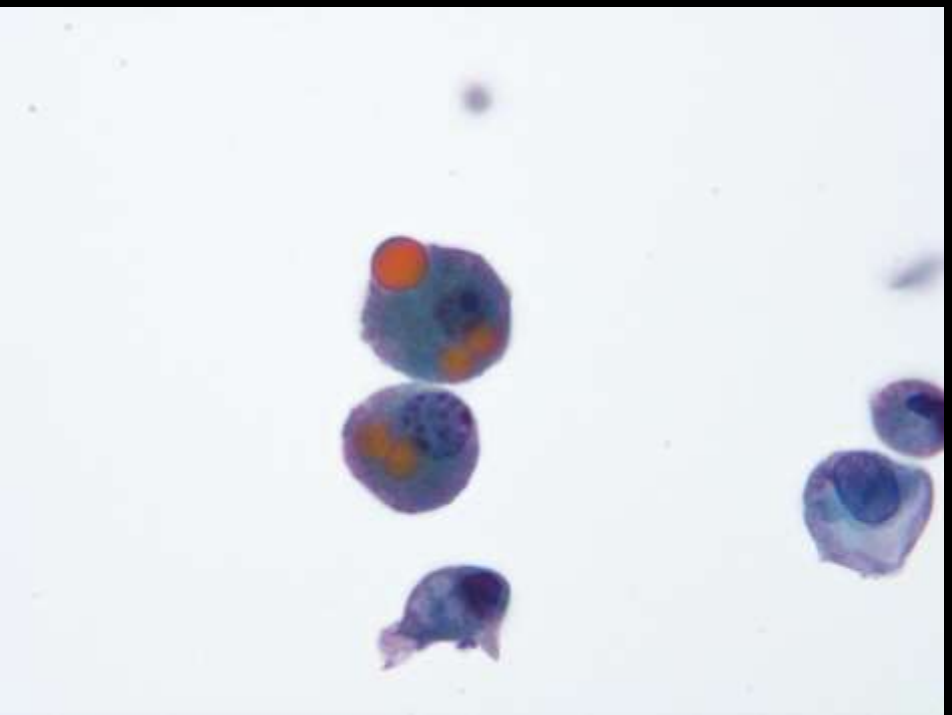
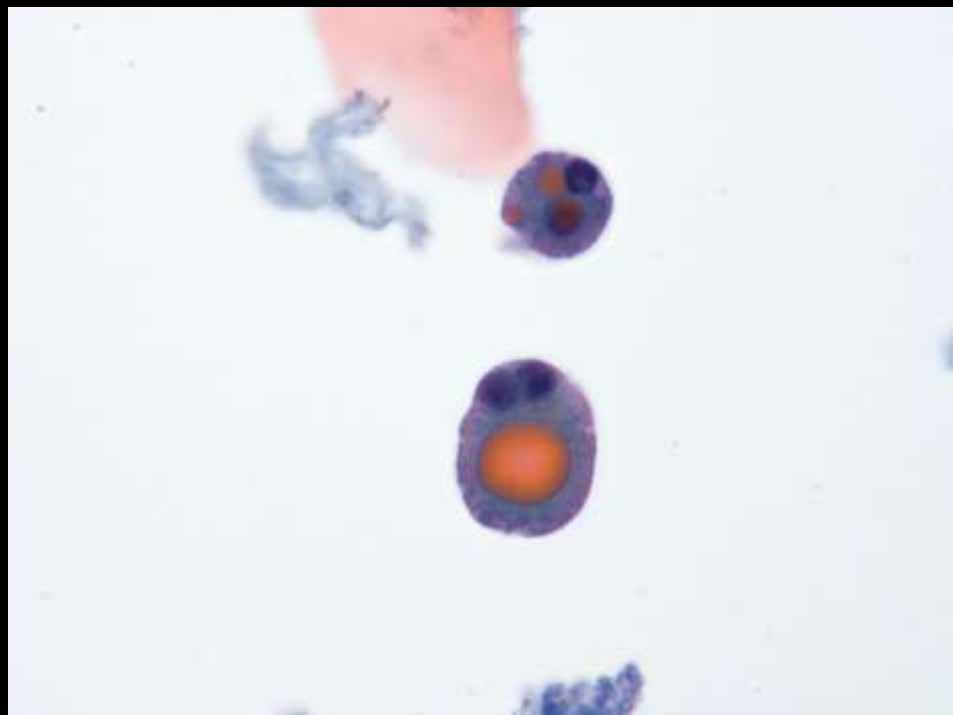
- Local recurrence in 4 (of 24) cases
  - 1 had positive margin, 2 had narrowly clear margins, and 1 had unknown margin status
  - 3 of those 4 had multiple local recurrences, with one requiring amputation
  - Time to first recurrence ranged from 4 months to 6.7 years
- No metastases or death in this series
  - Follow up ranged from 1 month to 16 years, median = 4 years
  - Rare metastases have been reported from other series / case reports
- Favorable prognosis attributed to smaller size and superficial resection → complete wide excision more feasible than deeply seated counterparts

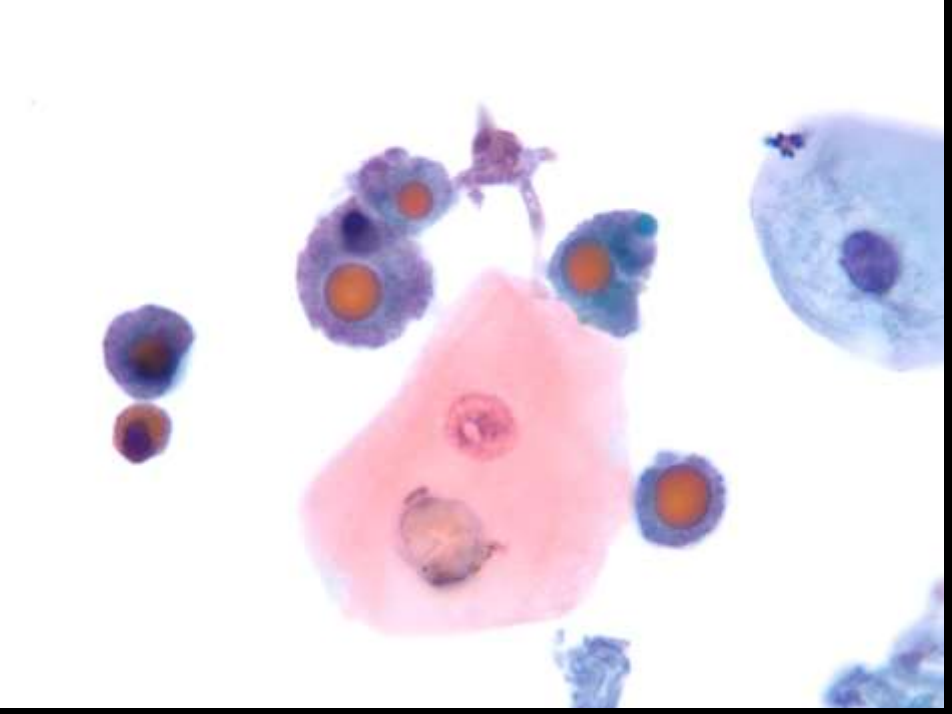
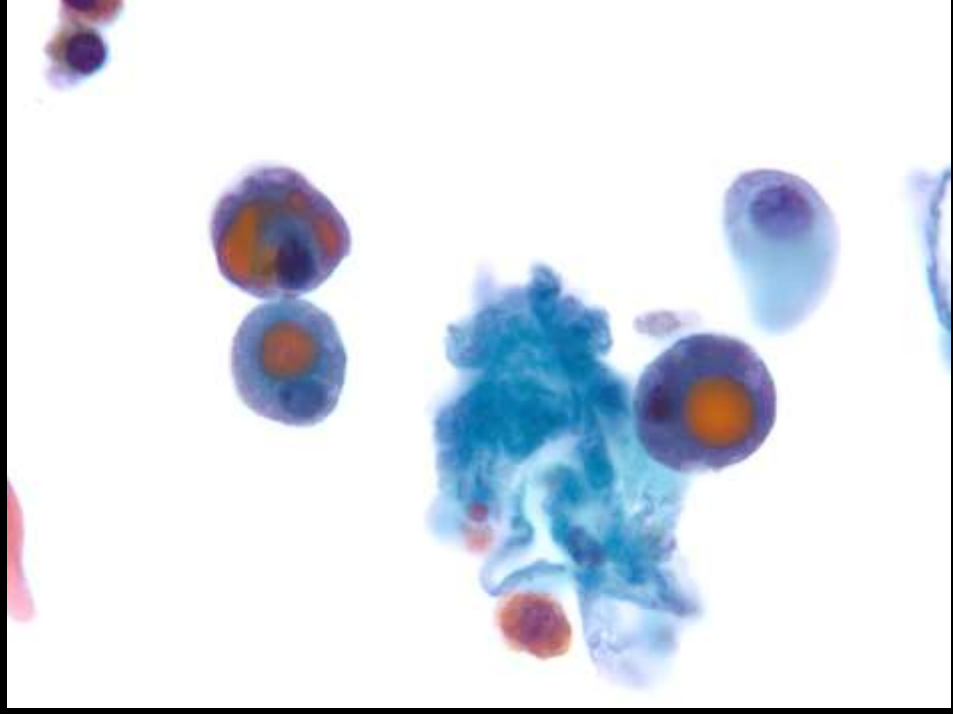
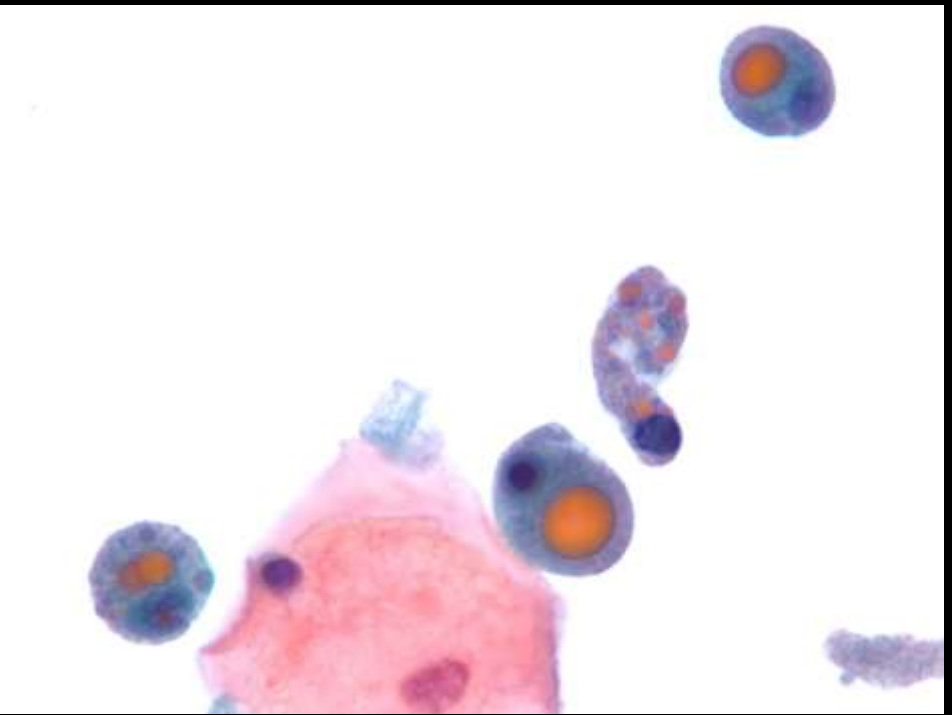
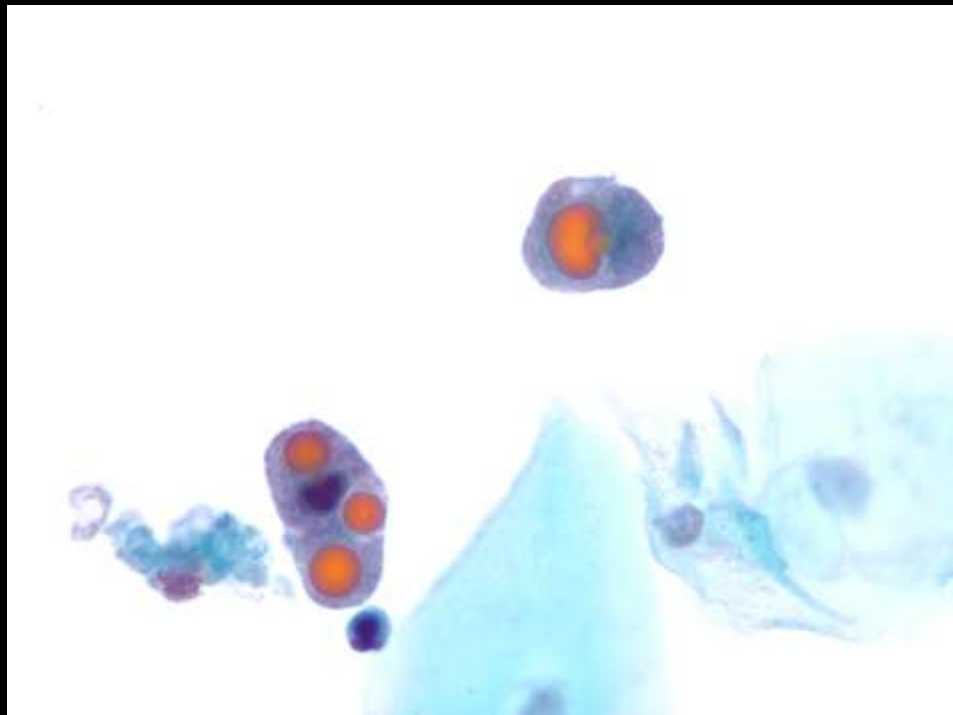
19-0604

Ankur Sangoi; El Camino Hospital

80-year-old male with h/o pT1 bladder urothelial carcinoma and urothelial carcinoma in situ. Urine submitted for cytology.



DDx

- **Malignant cells**
  - prostate vs urothelial ca?
- **Viral inclusions**
- **Degenerative benign urothelial cells**
- **Macrophages with bacteria**
- **Macrophages with RBCs**

Melamed-Wolinska bodies

- **Globular inclusions of degnerated urothelial cells**
  - Usually cytoplasmic, rarely nuclear
- **Nonspecific**
  - Probably giant lysosomes
- **Voided>cath urine specimens**
- **Specific for “urothelial” origin???**

Intracytoplasmic Eosinophilic Inclusions (Melamed-Wolinska Bodies)

Association with Metastatic Transitional Cell Carcinoma in Pleural Fluid

Andrew A. Renshaw, M.D., **Rebecca Madge,** C.T.(ASCP), and **Scott R. Granter,** M.D.

OBJECTIVE: To determine if eosinophilic cytoplasmic inclusions (Melamed-Wolinska bodies) (ECIs) can help to distinguish metastatic transitional cell carcinoma (TCC) from pulmonary carcinoma (PC) in pleural effusions.

STUDY DESIGN: The presence of ECIs was evaluated in malignant pleural effusions from 8 cases (5 patients) of TCC and 38 cases of pulmonary carcinoma (PC). ECIs were categorized as absent, rare (< 2 per case), occasional (2 per case to < 1 per high-power field), frequent (1–2 per high-power field) or numerous (> 2 per high-power field).

RESULTS: In pleural fluids with TCC, ECIs were numerous in 1 case, frequent in 2 cases, occasional in 3 cases and absent in 2 cases. In contrast, in pleural fluids with PC, ECIs were occasional in 1 case, rare in 5 cases and absent in 32 cases.

CONCLUSION: While not present in every case, frequent ECIs in a malignant pleural effusion are suggestive of TCC rather than PC. (Acta Cytol 1997; 41:995–998)

Keywords: pleural effusion; carcinoma, transitional cell; lung neoplasms; diagnosis, differential.

Frequent ECIs in a malignant pleural effusion suggest a carcinoma of transitional cell, rather than pulmonary, origin.

Metastatic transitional cell carcinoma (TCC) in an effusion is rare and is among the most difficult neoplasms to correctly identify. TCC was correctly diagnosed in only two of seven cases in the largest series to date.[4] Specific features that may aid in distinguishing TCC from other carcinomas are few. In the two cases correctly identified by Spieler and Gloor,[4] they noted large, monolayered sheets that they thought were typical of TCC. Recently,

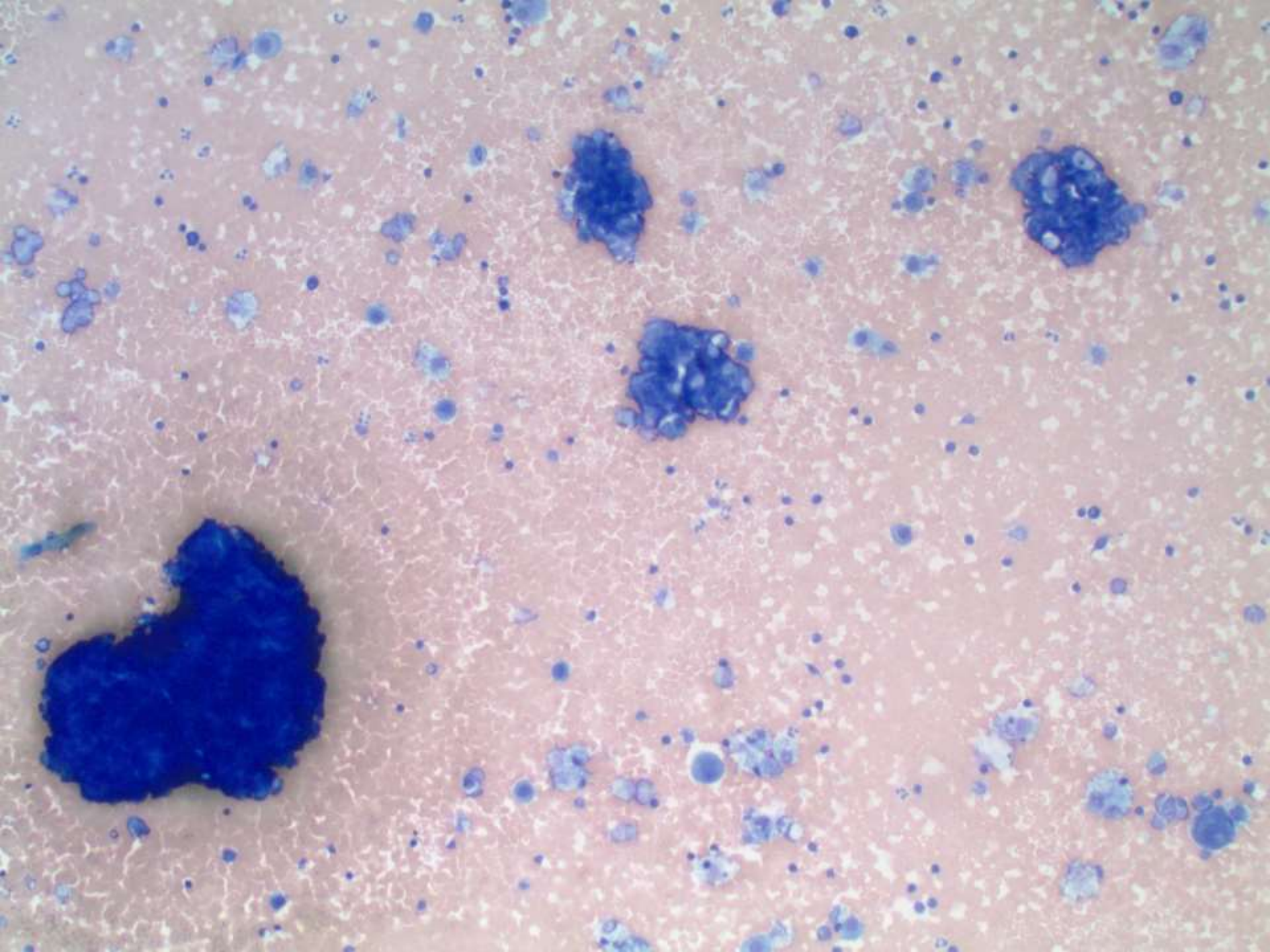
Acta Cytologica

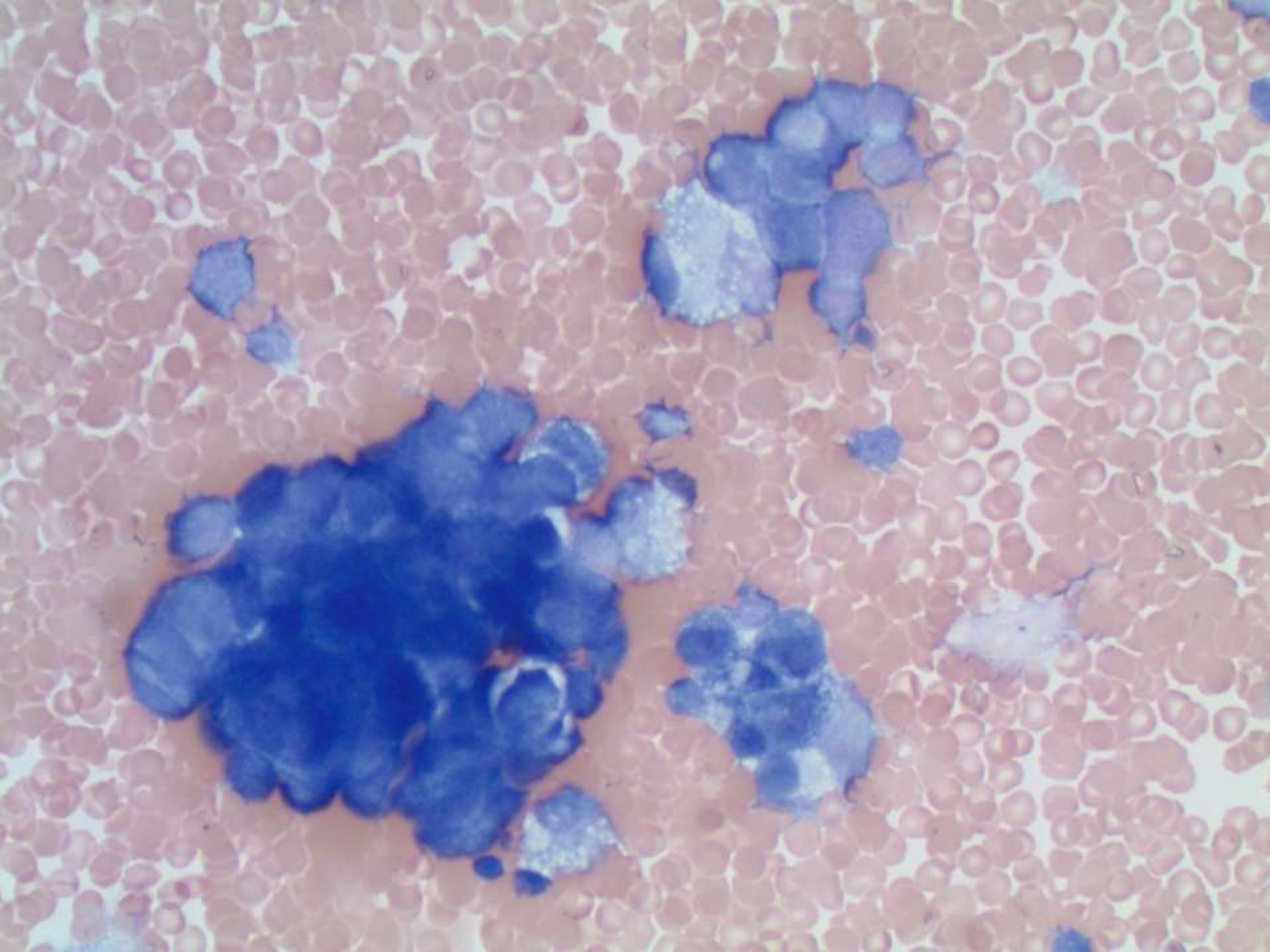
Volume 41, Number 4/July–August 1997

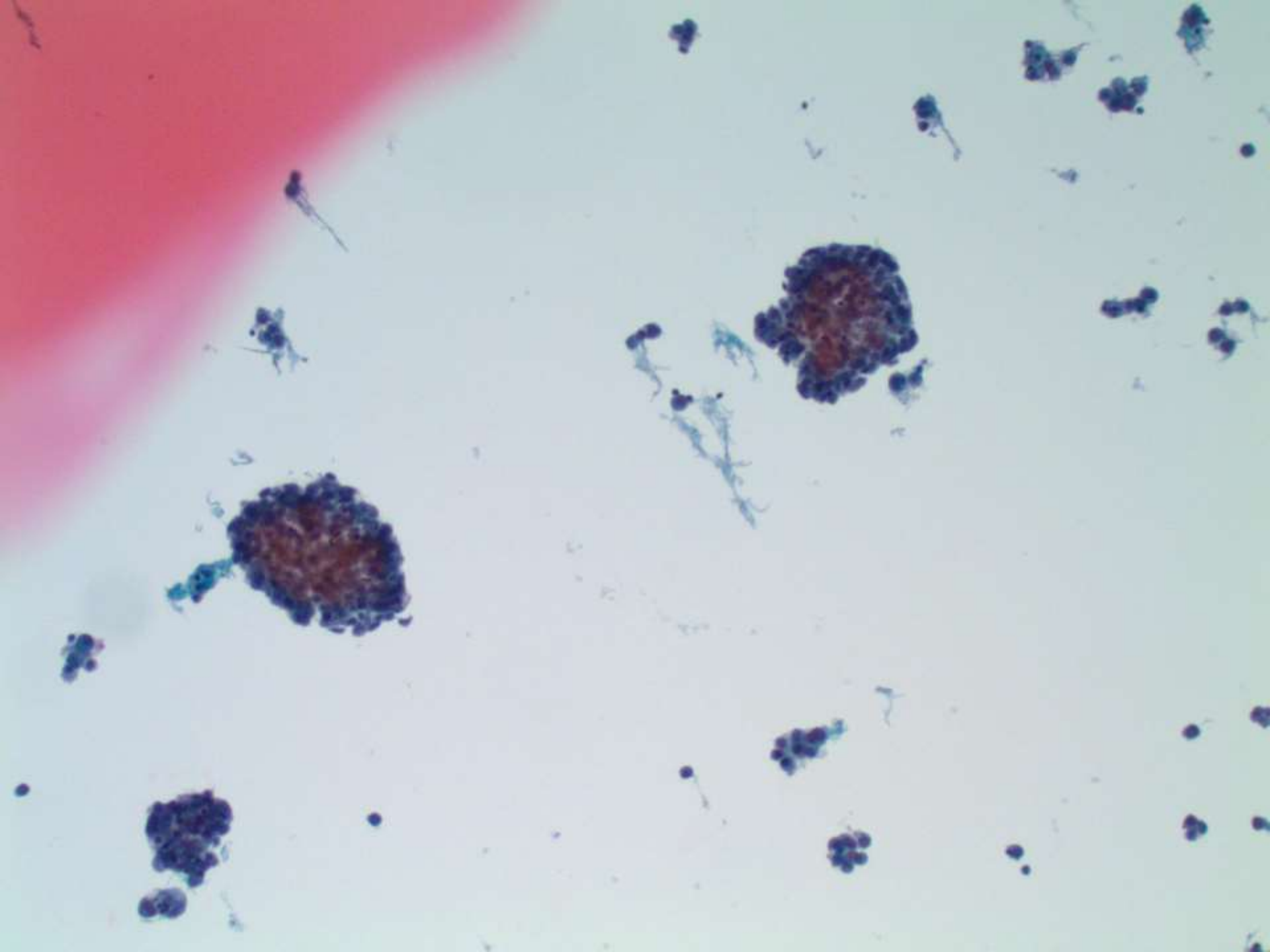
19-0605

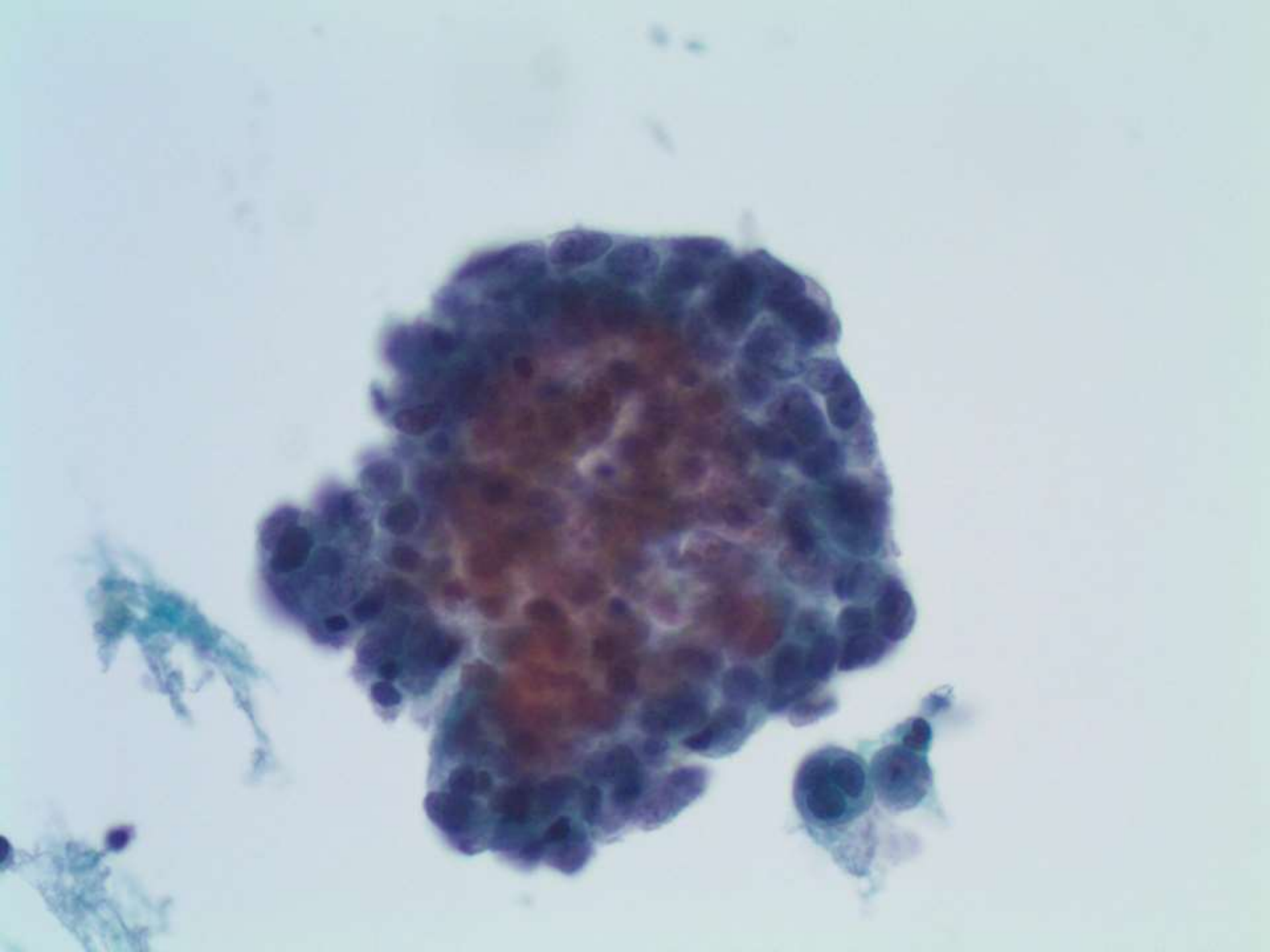
Ankur Sangoi; El Camino Hospital

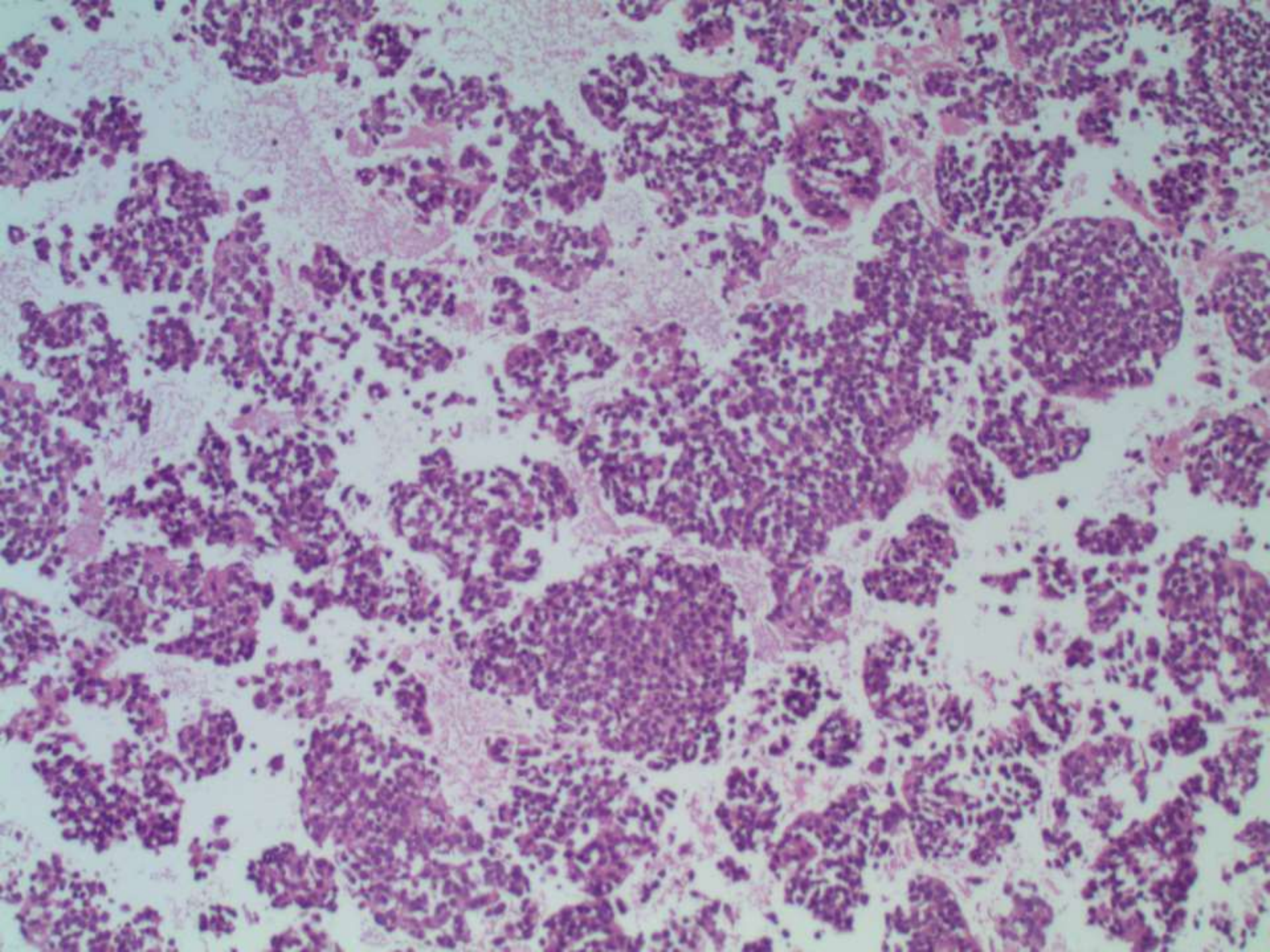
73-year-old male with h/o Gleason 4+5 prostate cancer now presents with pleural nodules. Pleural effusion submitted for cytology.

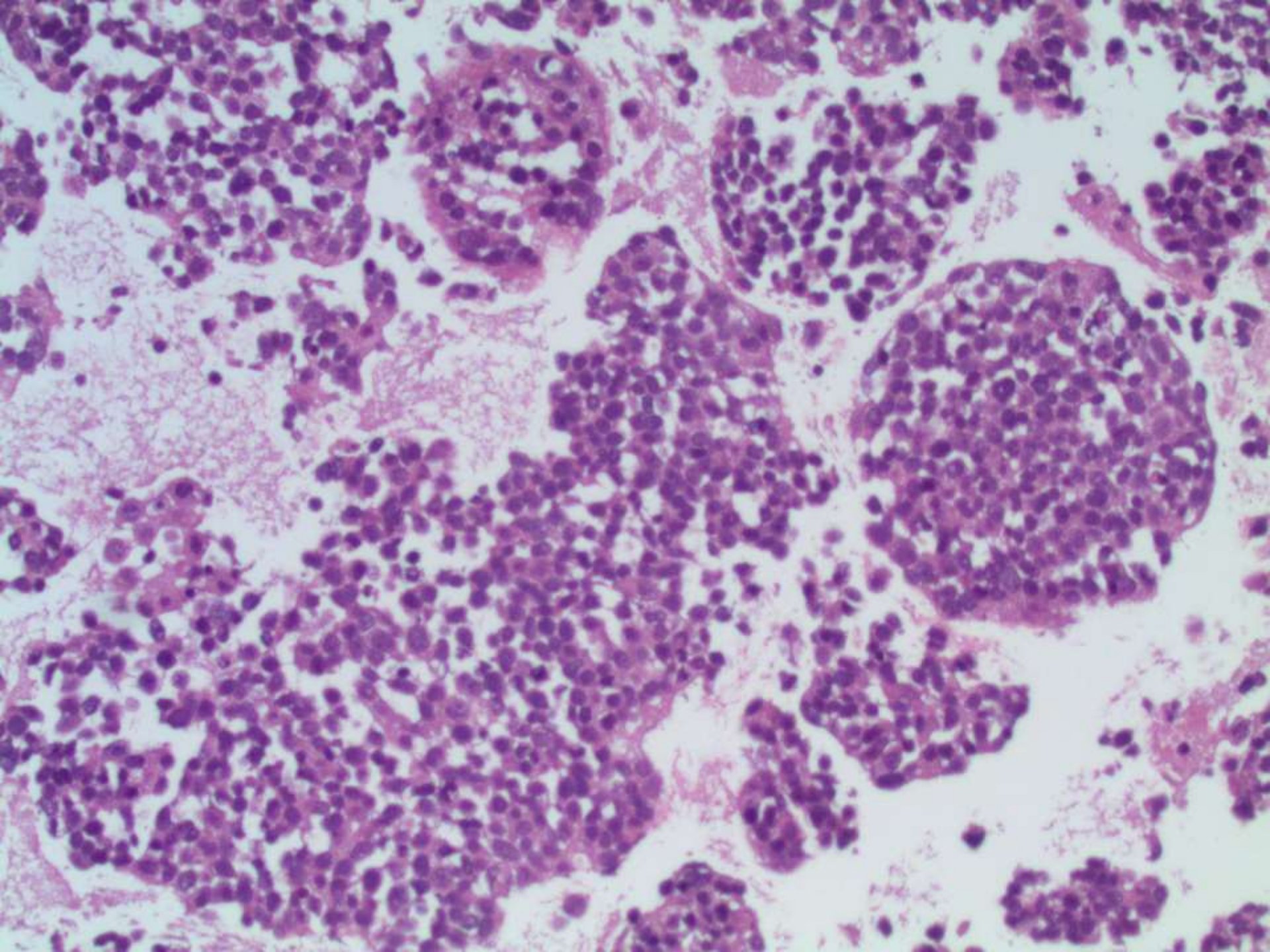


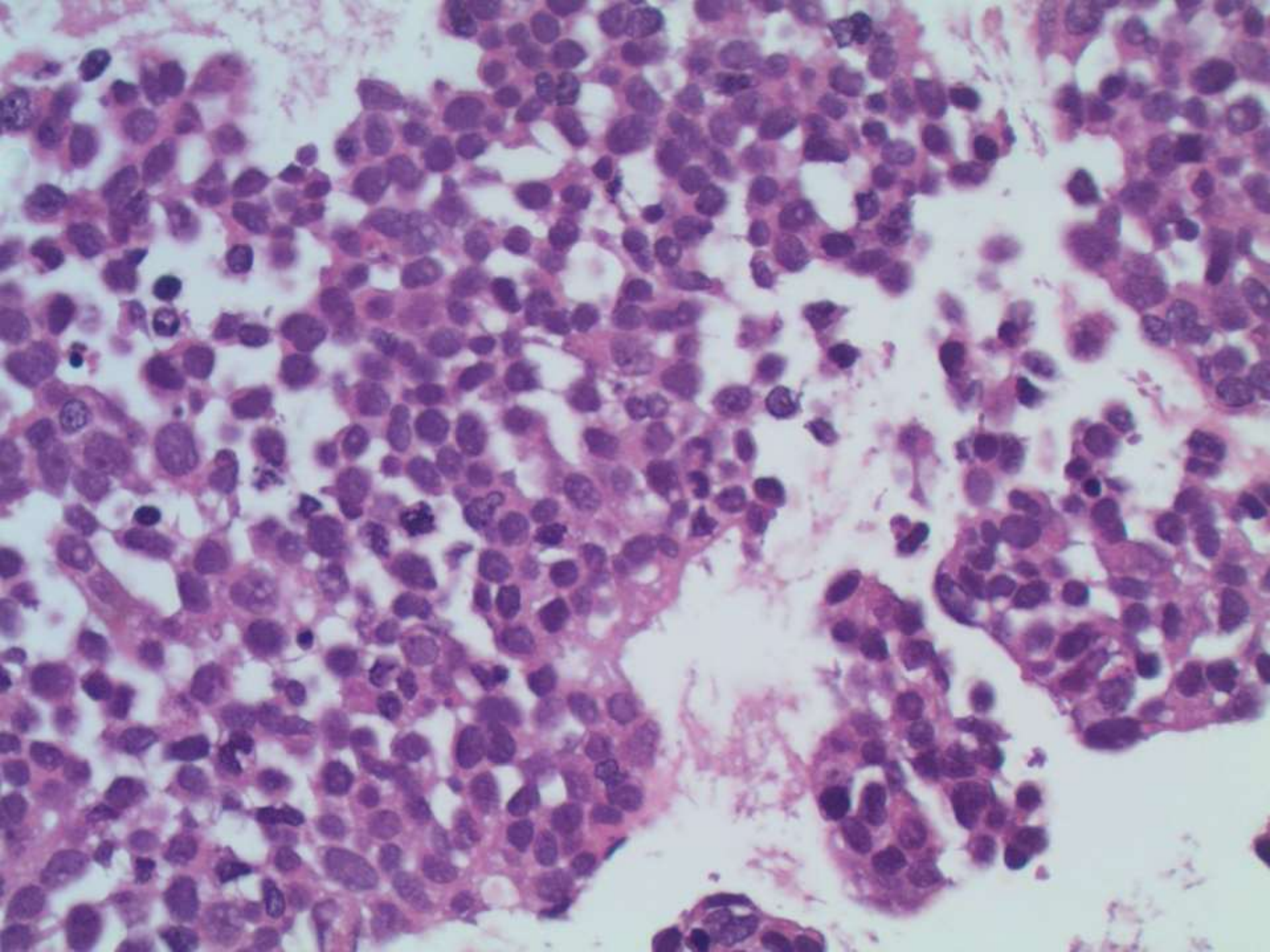


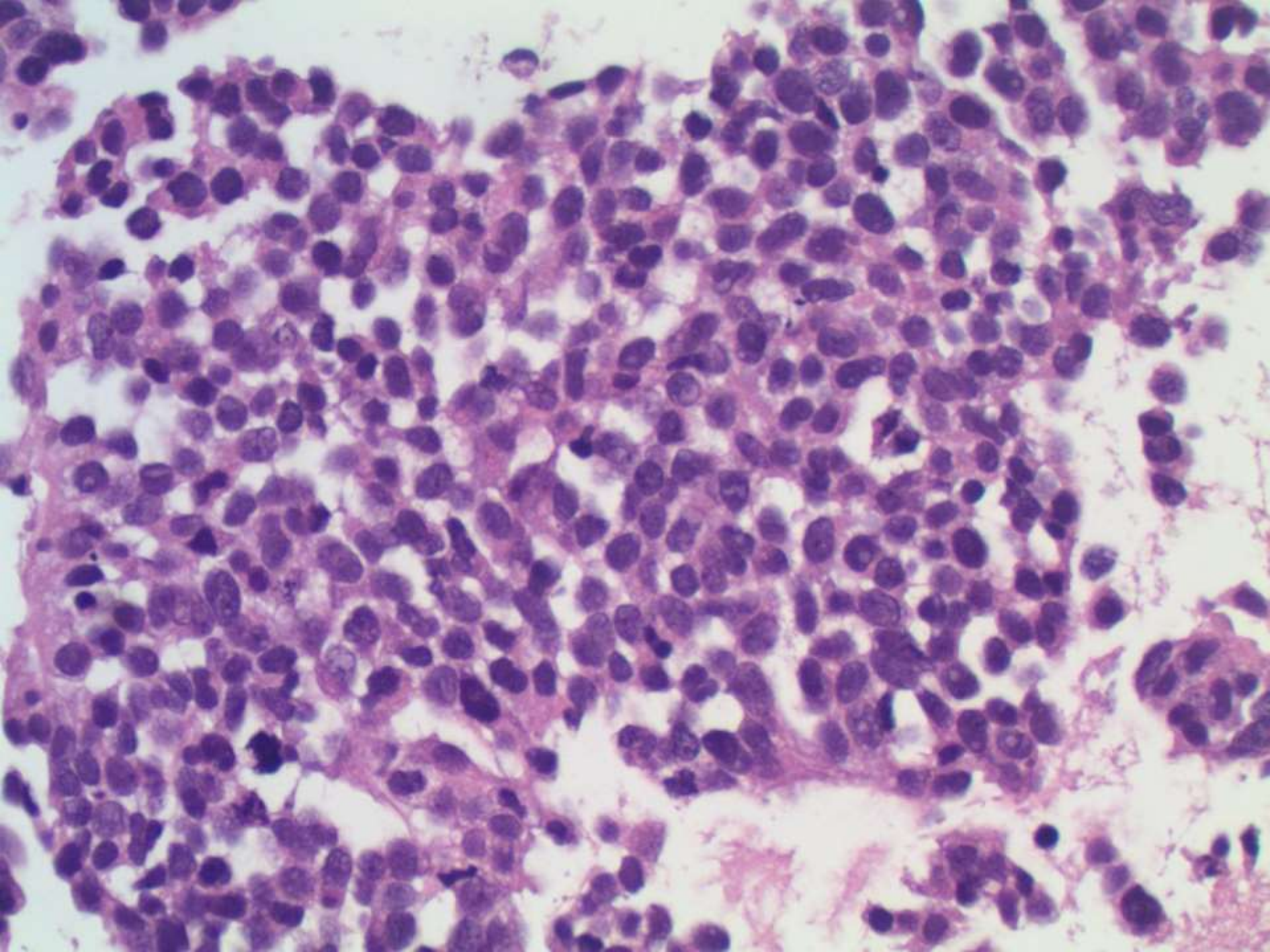






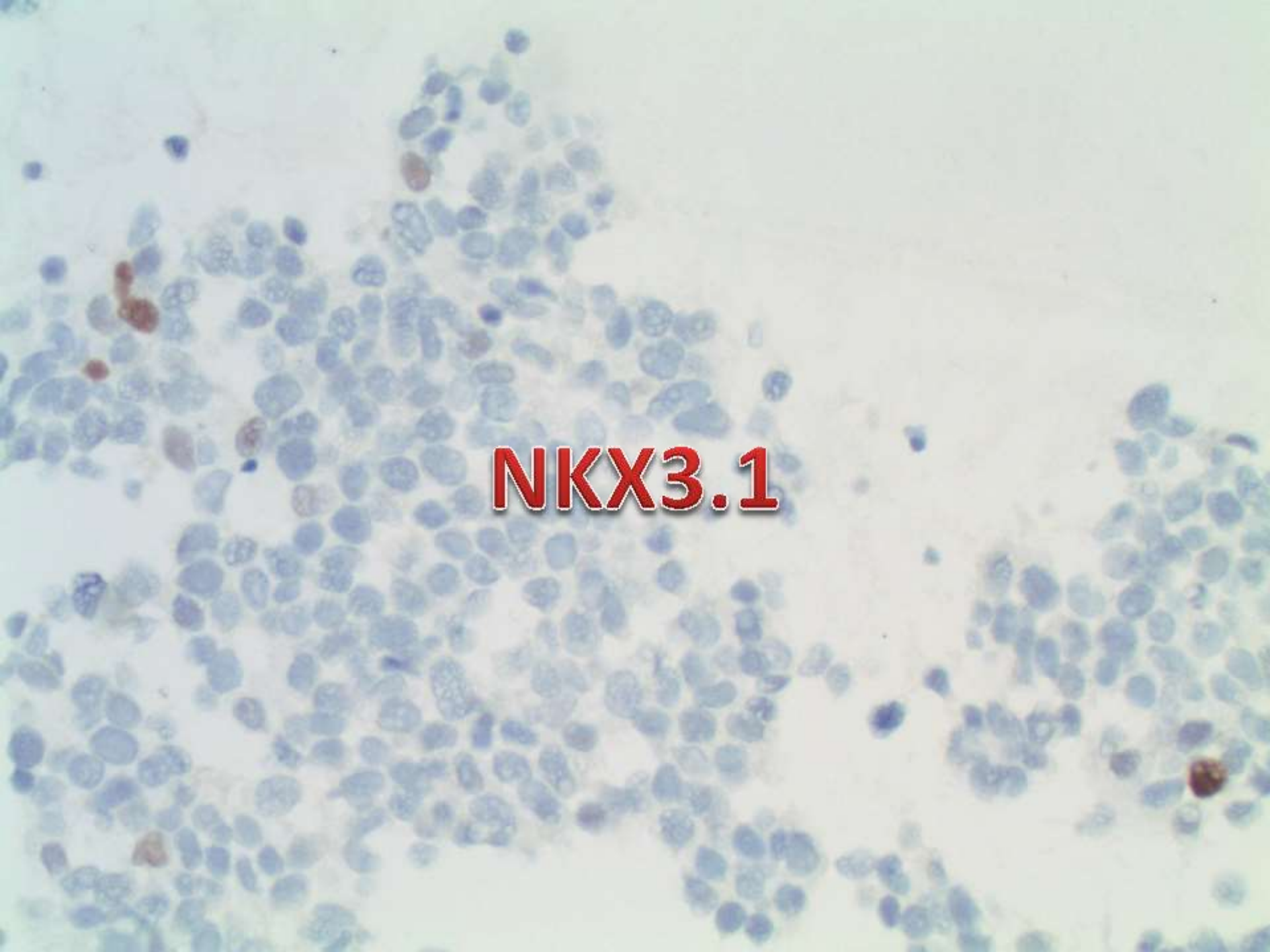


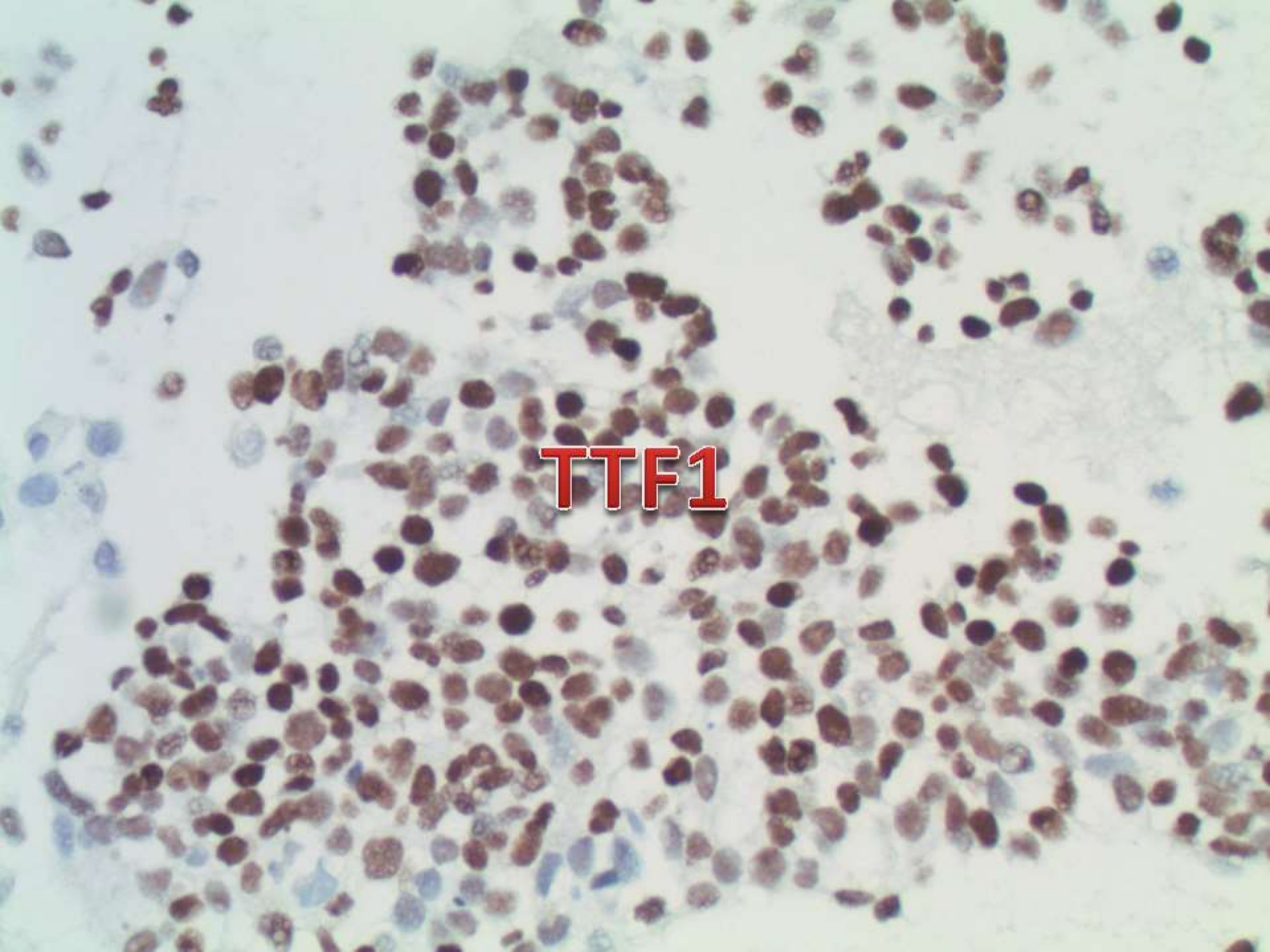


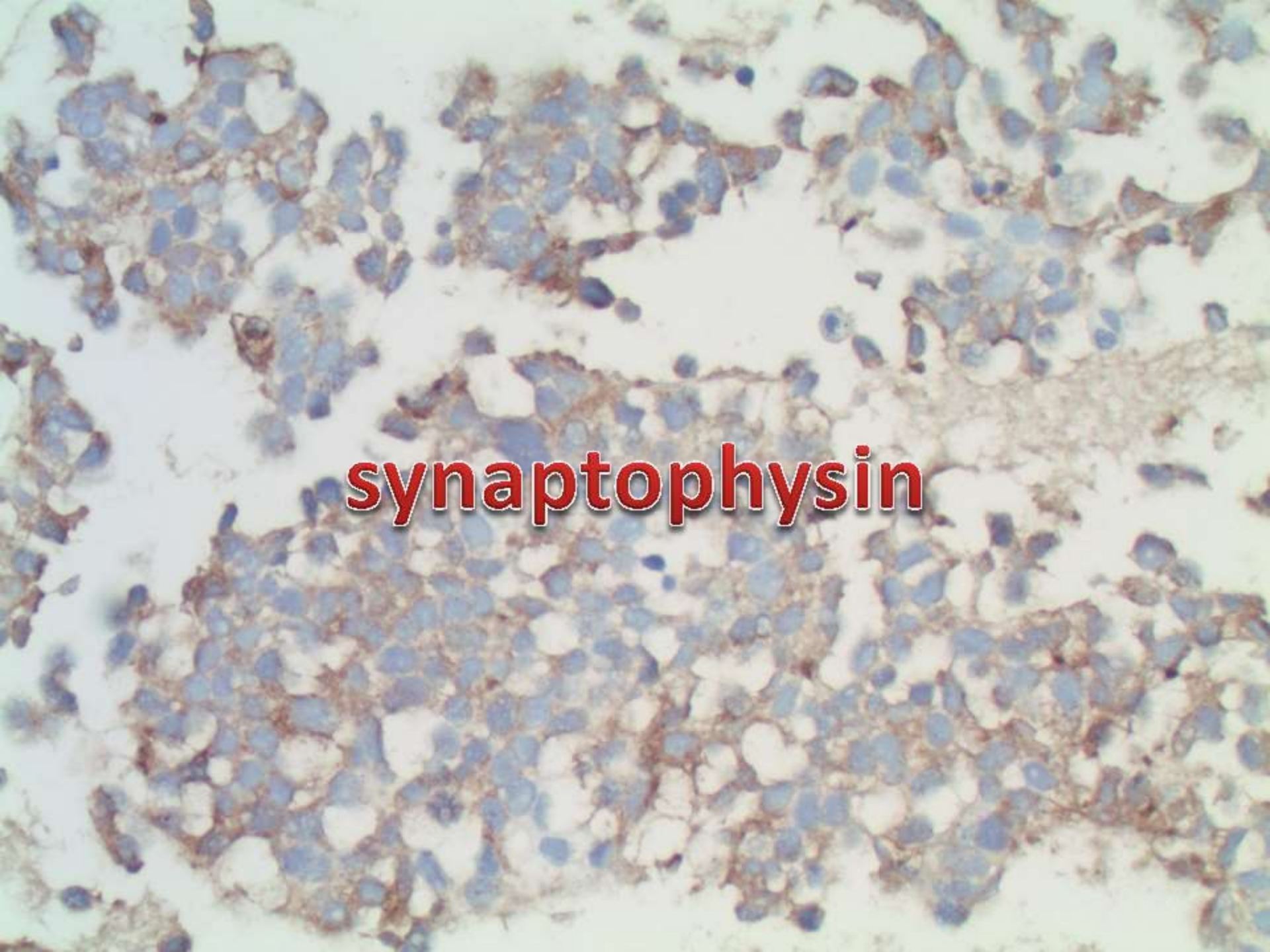


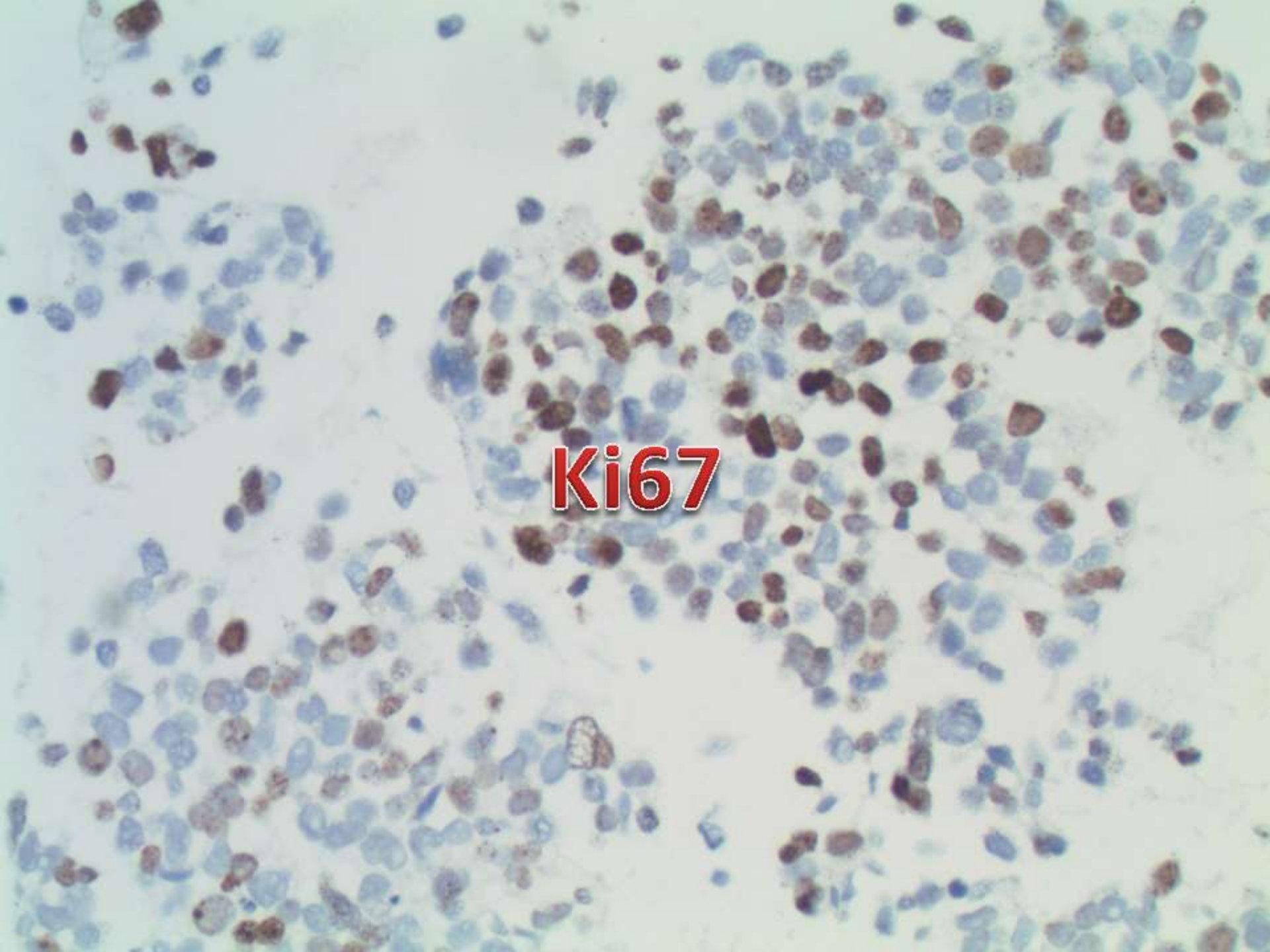
DDx

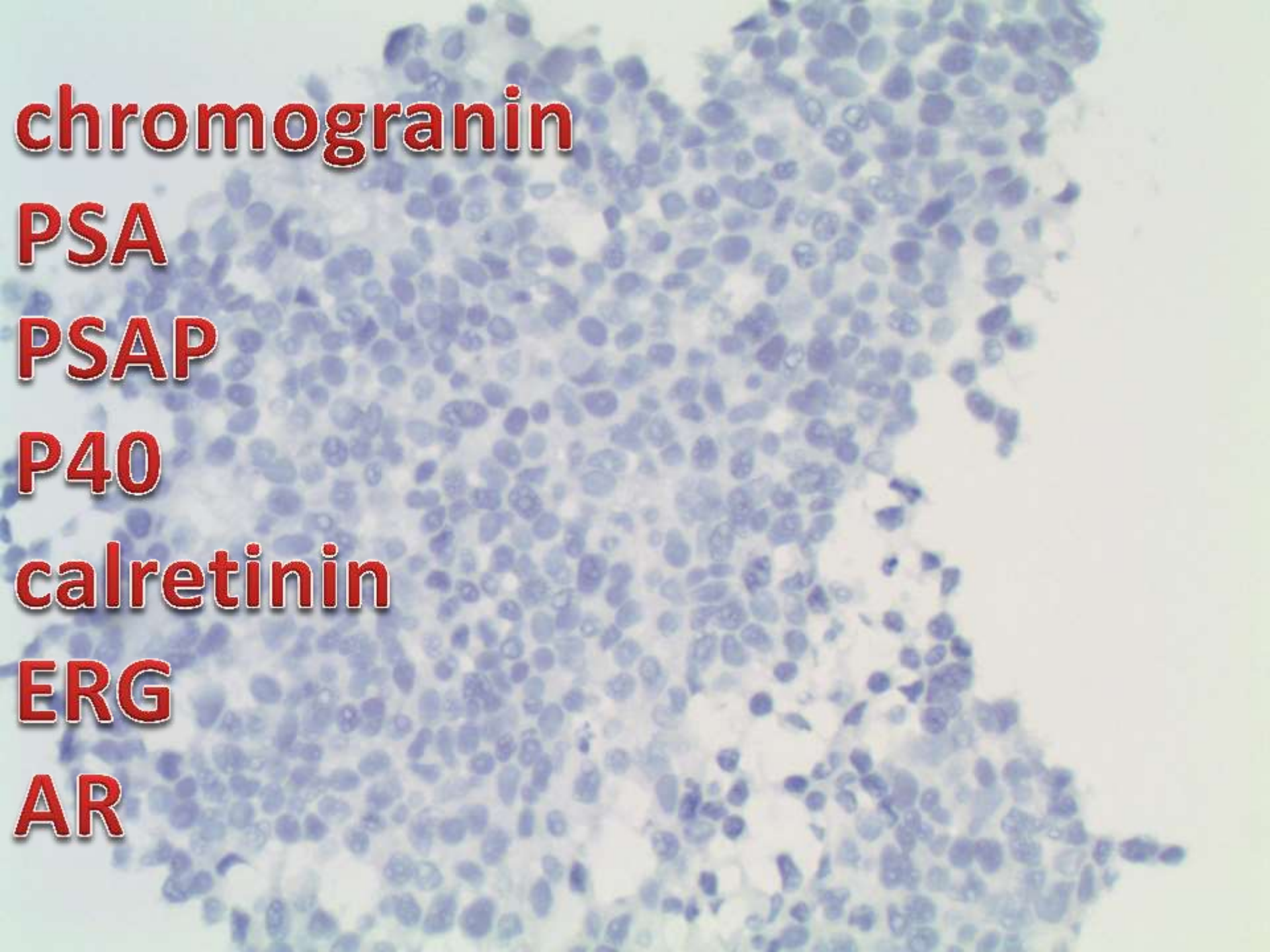
- **Metastatic carcinoma**
  - prostate vs urothelial vs lung?
- **Epithelioid mesothelioma**
- **Neuroendocrine tumor**
- **Leukemia/lymphoma**
- **Reactive**


NKX3.1

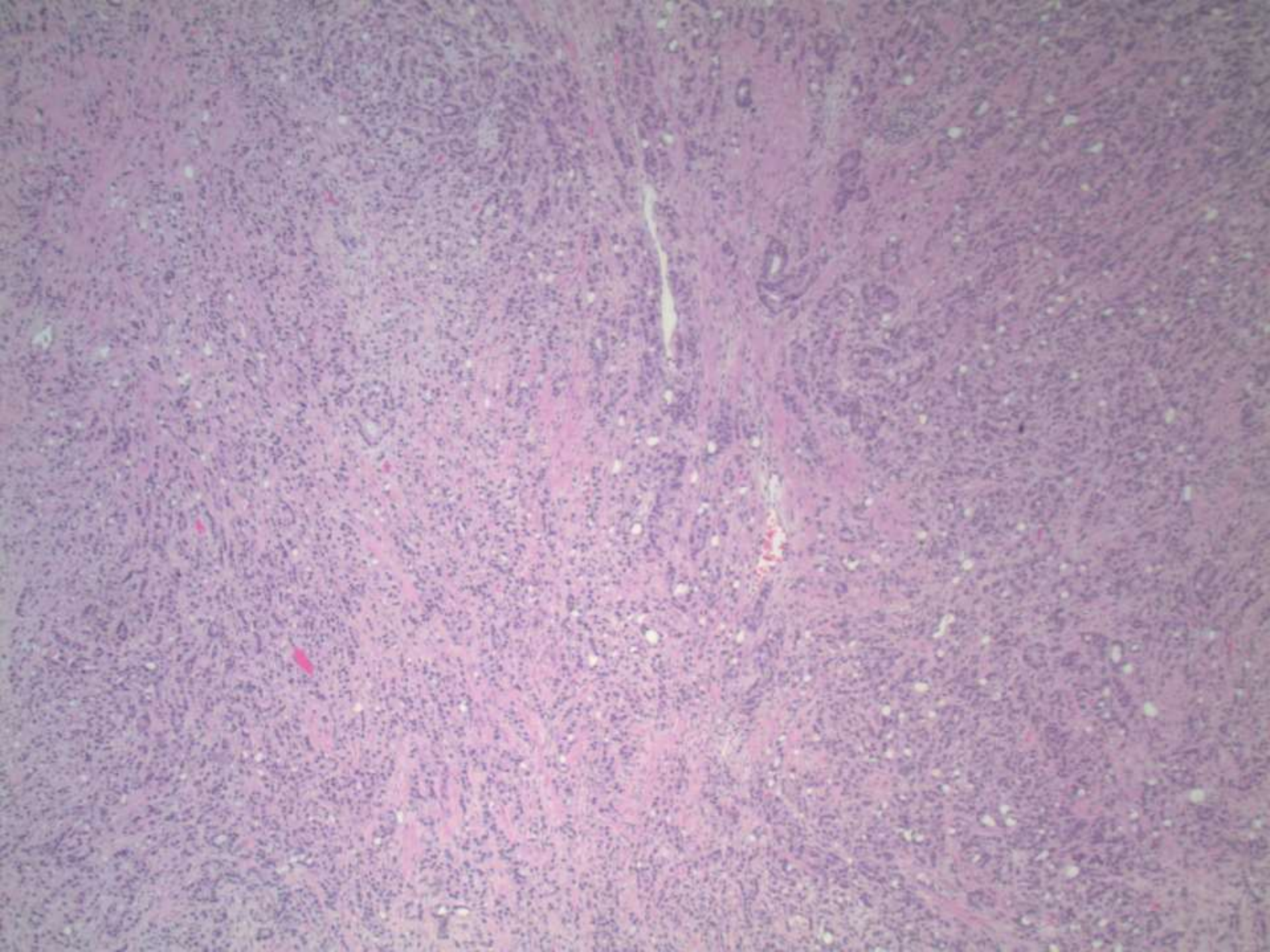

TTF1

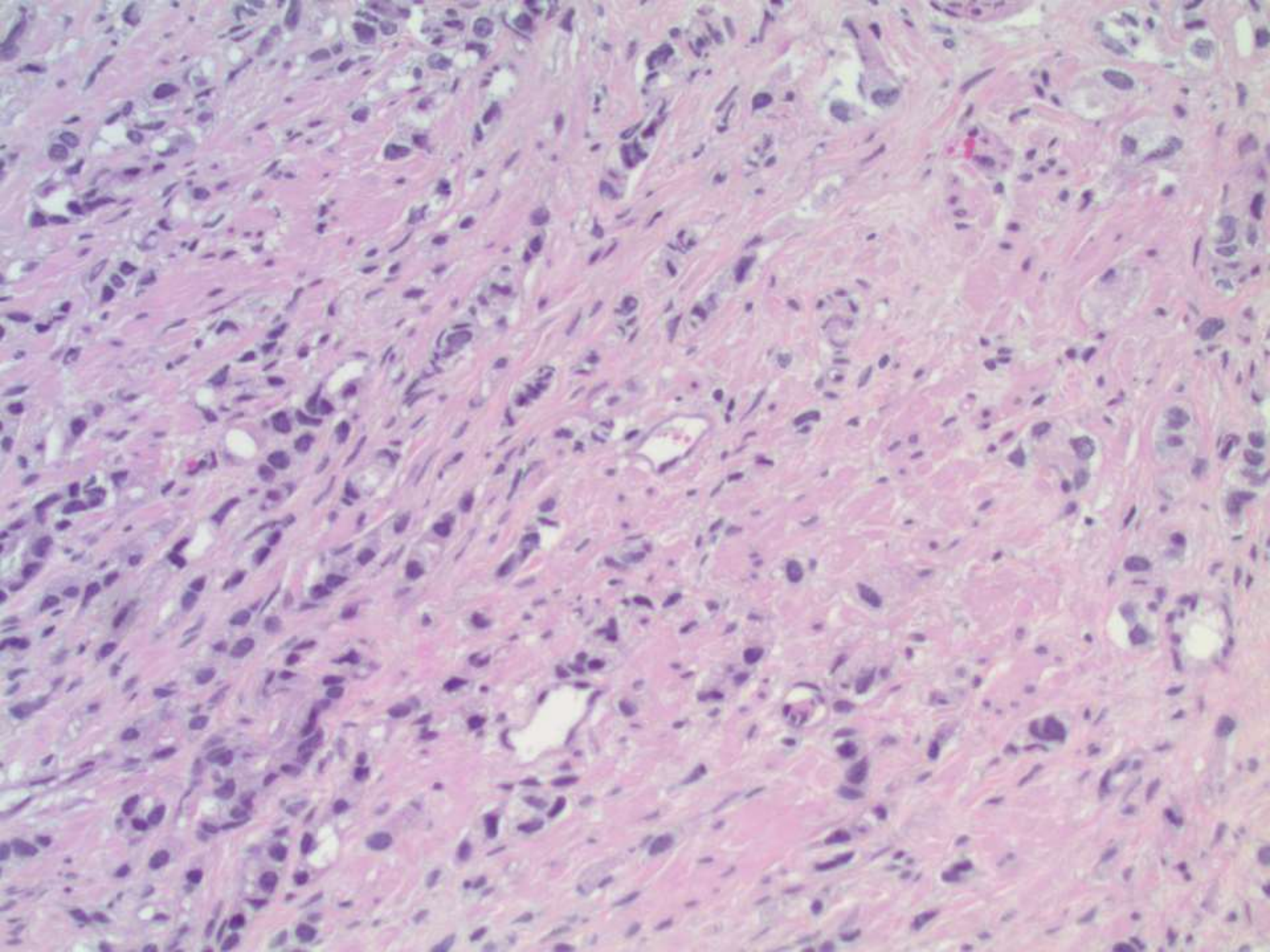

synaptophysin


Ki67


chromogranin
PSA
PSAP
P40
calretinin
ERG
AR

Let’s dig up prior TURP to re-review



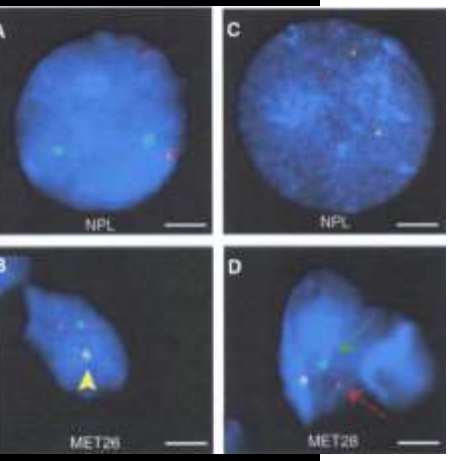


2012 specimen

- **Prostate, transurethral resection:**
  - Extensive involvement by prostatic adenocarcinoma, Gleason grade 4+5
  - No neuroendocrine features

current cytology specimen

- **Right pleural fluid, cytology:**
  - Neuroendocrine neoplasm, possibly prostatic origin
    - Pending FISH for TMPRSS2-ERG rearrangement



RESEARCH ARTICLE

Recurrent Fusion of *TMPRSS2* and ETS Transcription Factor Genes in Prostate Cancer

Scott A. Tomlins,[1] Daniel R. Rhodes,[1,2] Sven Perner,[7,9] Saravana M. Dhanasekaran,[1] Rohit Mehra,[1] Xiao-Wei Sun,[7] Sooryanarayana Varambally,[1,6] Xuhong Cao,[1] Joelle Tchinda,[7] Rainer Kuefer,[10] Charles Lee,[7] James E. Montie,[3,5,6] Rajal B. Shah,[1,3,5,6] Kenneth J. Pienta,[3,4,5,6] Mark A. Rubin,[7,8] Arul M. Chinnaiyan[1,2,3,5,6]*

Recurrent chromosomal rearrangements have not been well characterized in common carcinomas. We used a bioinformatics approach to discover candidate oncogenic chromosomal aberrations on the basis of outlier gene expression. Two ETS transcription factors, *ERG* and *ETV1*, were identified as outliers in prostate cancer. We identified recurrent gene fusions of the 5′ untranslated region of *TMPRSS2* to *ERG* or *ETV1* in prostate cancer tissues with outlier expression. By using fluorescence in situ hybridization, we demonstrated that 23 of 29 prostate cancer samples harbor rearrangements in *ERG* or *ETV1*. Cell line experiments suggest that the androgen-responsive promoter elements of *TMPRSS2* mediate the overexpression of ETS family members in prostate cancer. These results have implications in the development of carcinomas and the molecular diagnosis and treatment of prostate cancer.

28 OCTOBER 2005 VOL 310 SCIENCE www.sciencemag.org

Prevalence of *TMPRSS2-ERG* Fusion Prostate Cancer among Men Undergoing Prostate Biopsy in the United States

Juan-Miguel Mosquera,[1,2] Rohit Mehra,[3] Meredith M. Regan,[2,12] Sven Perner,[1,2,10] Elizabeth M. Genega,[2,5] Gerri Bueti,[6] Rajal B. Shah,[3,4,8,9] Sandra Gaston,[2,7] Scott A. Tomlins,[3] John T. Wei,[3,4,9] Michael C. Kearney,[2,6] Laura A. Johnson,[1] Jeffrey M. Tang,[1] Arul M. Chinnaiyan,[3,4,8,9] Mark A. Rubin,[1,2,11,12] and Martin G. Sanda[2,6]

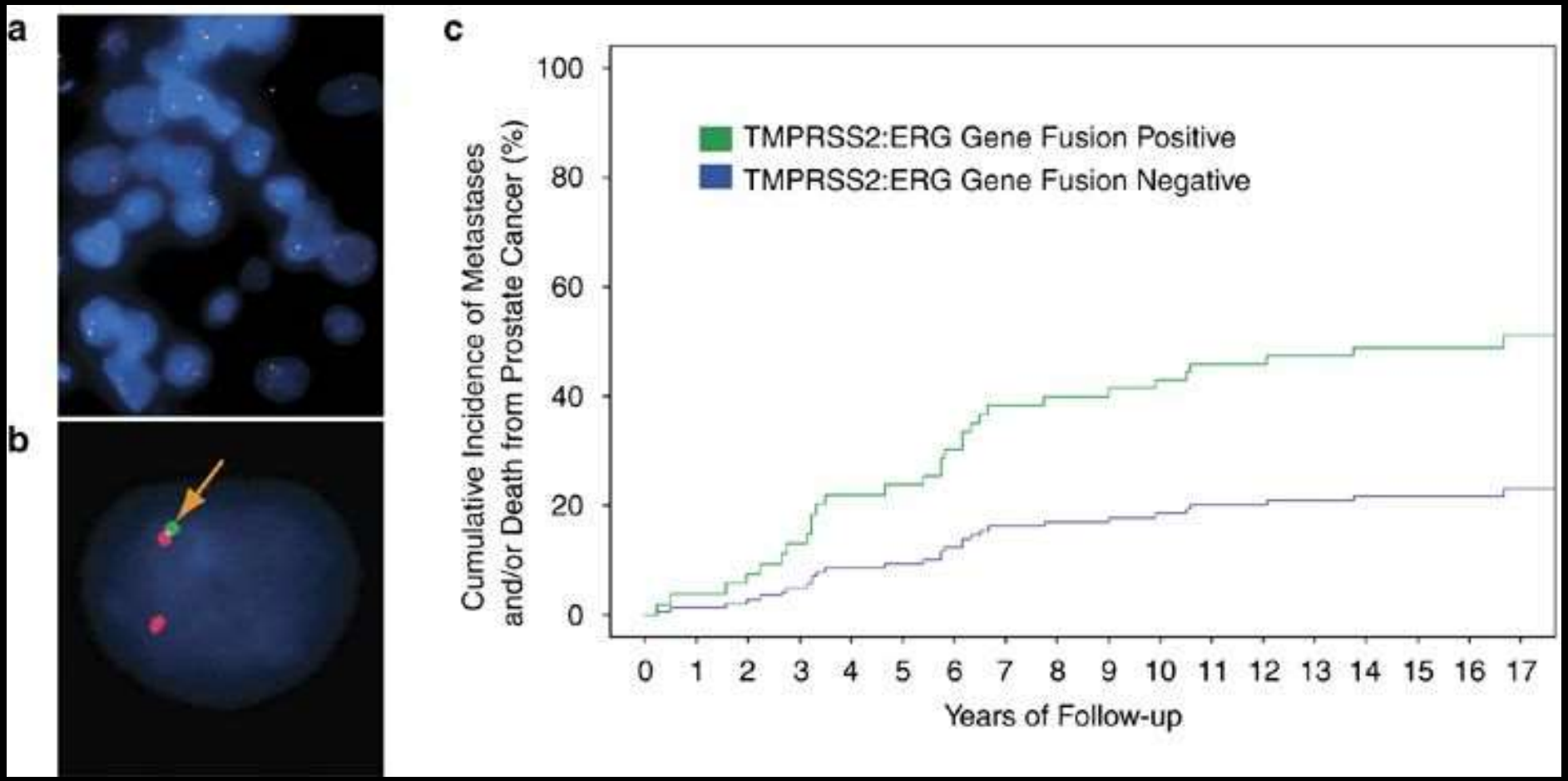
Abstract

Purpose: Fusion of the *TMPRSS2* prostate-specific gene with the *ERG* transcription factor is a putatively oncogenic gene rearrangement that is commonly found in prostate cancer tissue from men undergoing prostatectomy. However, the prevalence of the fusion was less common in samples of transurethral resection of the prostate from a Swedish cohort of patients with incidental prostate cancer followed by watchful waiting, raising the question as to whether the high prevalence in prostatectomy specimens reflects selection bias. We sought to determine the prevalence of *TMPRSS2-ERG* gene fusion among prostate-specific antigen–screened men undergoing prostate biopsy in the United States.

Experimental Design: We studied 140 prostate biopsies from the same number of patients for *TMPRSS2-ERG* fusion status with a fluorescent *in situ* hybridization assay. One hundred and thirty-four samples (100 cancer and 34 benign) were assessable.

Results: *ERG* gene rearrangement was detected in 46% of prostate biopsies that were found to have prostate cancer and in 0% of benign prostate biopsies ($P < 0.0001$). Evaluation of morphologic features showed that cribriform growth, blue-tinged mucin, macronucleoli, and collagenous micronodules were significantly more frequent in *TMPRSS2-ERG* fusion–positive prostate cancer biopsies than gene fusion–negative prostate cancer biopsies ($P \leq 0.04$). No significant association with Gleason score was detected. In addition, non-Caucasian patients were less likely to have positive fusion status ($P = 0.02$).

Conclusions: This is the first prospective North American multicenter study to characterize *TMPRSS2-ERG* prostate cancer prevalence in a cohort of patients undergoing needle biopsy irrespective of whether or not they subsequently undergo prostatectomy. Our results show that this gene rearrangement is common among North American men who have prostate cancer on biopsy, is absent in benign prostate biopsy, and is associated with specific morphologic features. These findings indicate a need for prospective studies to evaluate the relationship of *TMPRSS2-ERG* rearrangement with clinical course of screening-detected prostate cancer in North American men, and a need for the development of noninvasive screening tests to detect *TMPRSS2-ERG* rearrangement.


a
b
c
100
80
60
40
20
0
Cumulative Incidence of Metastases and/or Death from Prostate Cancer (%)
TMPRSS2:ERG Gene Fusion Positive
TMPRSS2:ERG Gene Fusion Negative
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17
Years of Follow-up

Human Pathology (2013) 44, 2227–2233

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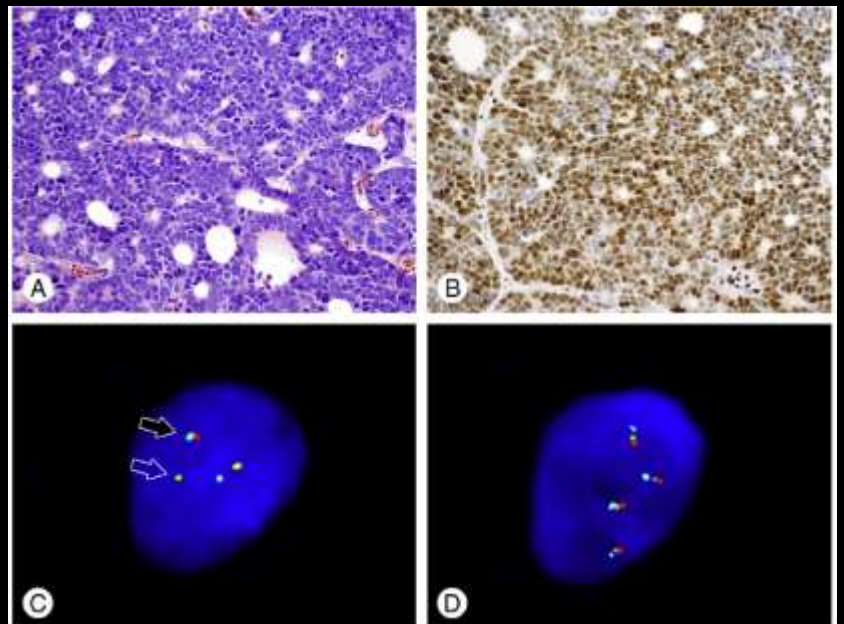
Original contribution

Frequent *TMPRSS2-ERG* rearrangement in prostatic small cell carcinoma detected by fluorescence in situ hybridization: the superiority of fluorescence in situ hybridization over ERG immunohistochemistry

Lindsay A. Schelling MD[a,1], Sean R. Williamson MD[a,1], Shaobo Zhang MD[a], Jorge L. Yao MD[b], Mingsheng Wang MD[a], Jiaoti Huang MD[c], Rodolfo Montironi MD[d], Antonio Lopez-Beltran MD[e], Robert E. Emerson MD[a], Muhammad T. Idrees MD[a], Adeboye O. Osunkoya MD[f], Yan-Gao Man MD[g], Gregory T. MacLennan MD[h], Lee Ann Baldridge BA, HT(AJCP)[a], Eva Compérat MD[i], Liang Cheng MD[a,j,*]



Clinical and Genomic Characterization of Treatment-Emergent Small-Cell Neuroendocrine Prostate Cancer: A Multi-institutional Prospective Study

Purpose

The prevalence and features of treatment-emergent small-cell neuroendocrine prostate cancer (t-SCNC) are not well characterized in the era of modern androgen receptor (AR)–targeting therapy. We sought to characterize the clinical and genomic features of t-SCNC in a multi-institutional prospective study.

Methods

Patients with progressive, metastatic castration-resistant prostate cancer (mCRPC) underwent metastatic tumor biopsy and were followed for survival. Metastatic biopsy specimens underwent independent, blinded pathology review along with RNA/DNA sequencing.

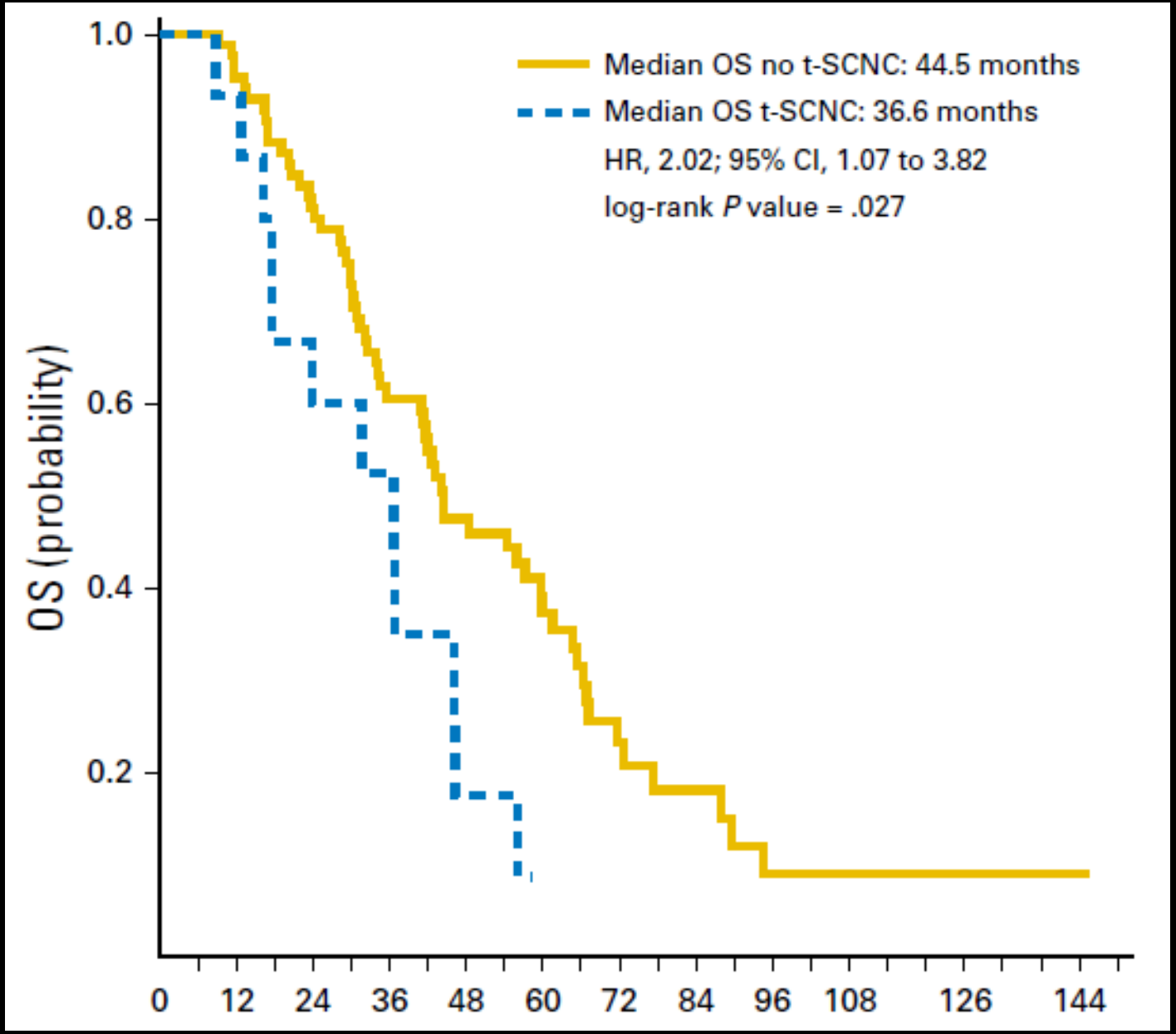
Results

A total of 202 consecutive patients were enrolled. One hundred forty-eight (73%) had prior disease progression on abiraterone and/or enzalutamide. The biopsy evaluable rate was 79%. The overall incidence of t-SCNC detection was 17%. AR amplification and protein expression were present in 67% and 75%, respectively, of t-SCNC biopsy specimens. t-SCNC was detected at similar proportions in bone, node, and visceral organ biopsy specimens. Genomic alterations in the DNA repair pathway were nearly mutually exclusive with t-SCNC differentiation ($P = .035$). Detection of t-SCNC was associated with shortened overall survival among patients with prior AR-targeting therapy for mCRPC (hazard ratio, 2.02; 95% CI, 1.07 to 3.82). Unsupervised hierarchical clustering of the transcriptome identified a small-cell–like cluster that further enriched for adverse survival outcomes (hazard ratio, 3.00; 95% CI, 1.25 to 7.19). A t-SCNC transcriptional signature was developed and validated in multiple external data sets with $> 90\%$ accuracy. Multiple transcriptional regulators of t-SCNC were identified, including the pancreatic neuroendocrine marker *PDX1*.

Conclusion

t-SCNC is present in nearly one fifth of patients with mCRPC and is associated with shortened survival. The near-mutual exclusivity with DNA repair alterations suggests t-SCNC may be a distinct subset of mCRPC. Transcriptional profiling facilitates the identification of t-SCNC and novel therapeutic targets.

J Clin Oncol 36:2492-2503.


Median OS no t-SCNC: 44.5 months
Median OS t-SCNC: 36.6 months
HR, 2.02; 95% CI, 1.07 to 3.82
log-rank P value = .027
OS (probability)
1.0
0.8
0.6
0.4
0.2
0
12
24
36
48
60
72
84
96
108
126
144

Final diagnosis

- **Right pleural fluid, cytology:**
  - ERG FISH POSITIVE

  → consistent with metastatic prostatic adenocarcinoma with neuroendocrine differentiation

    - “treatment emergent NE prostate cancer”

TAKE HOME POINTS

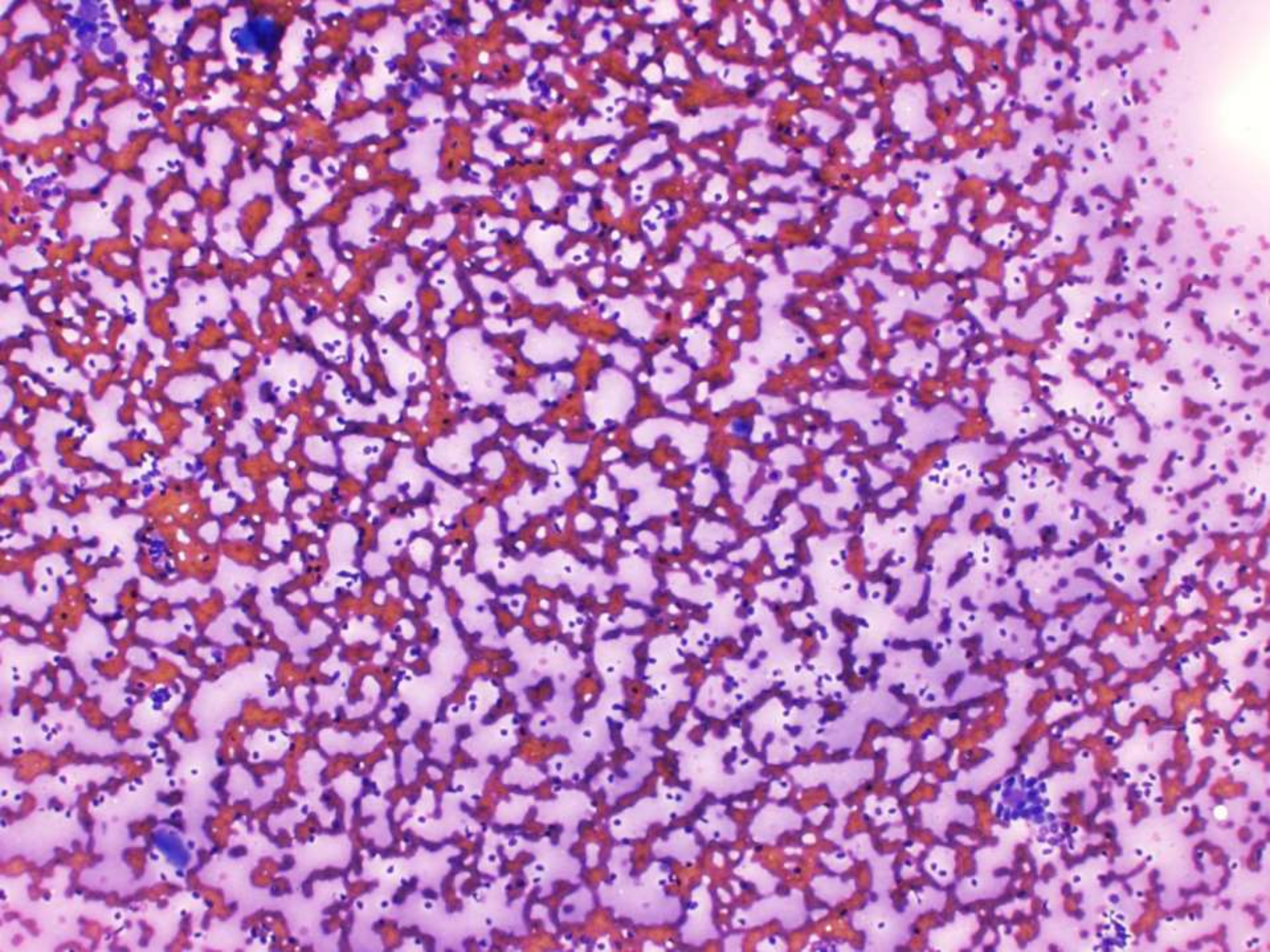
- **PROSTATE WITH SMALL CEL CA:**
  - Use ERG FISH, not ERG IHC

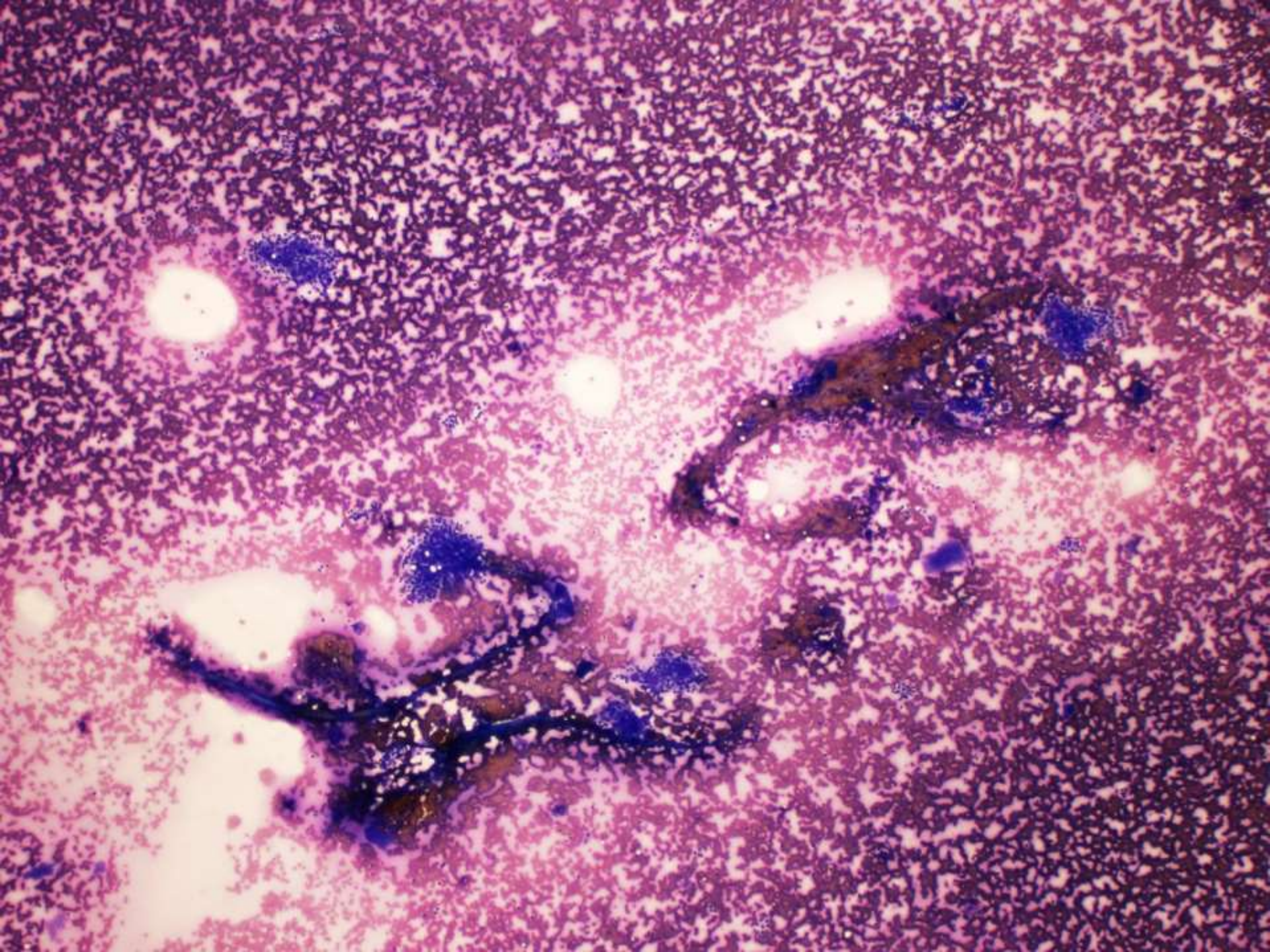
- **METASTATIC SMALL CELL CA (in patient with prior prostate ca)**
  - ERG FISH can be useful to confirm prostatic origin

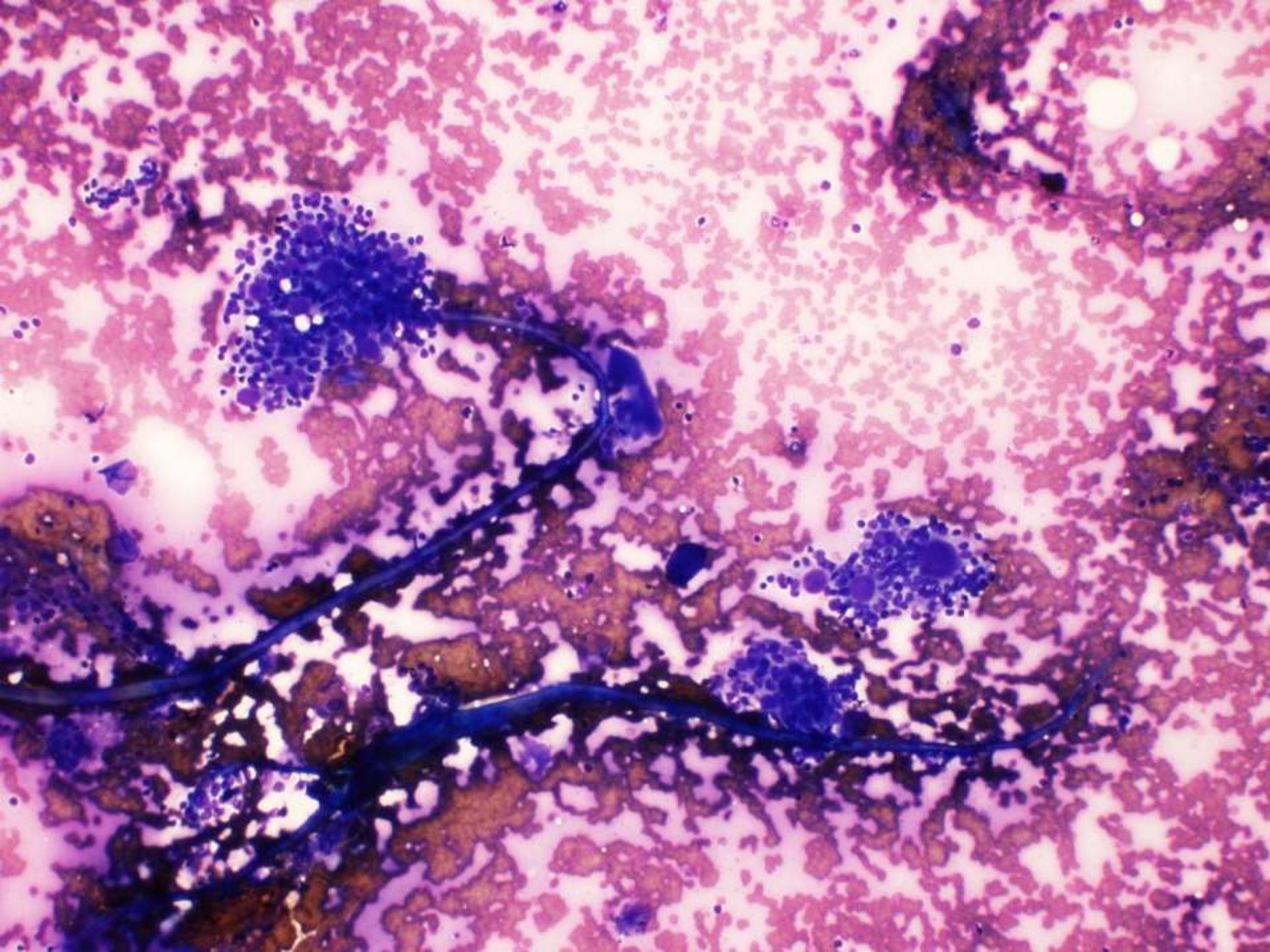
19-0606

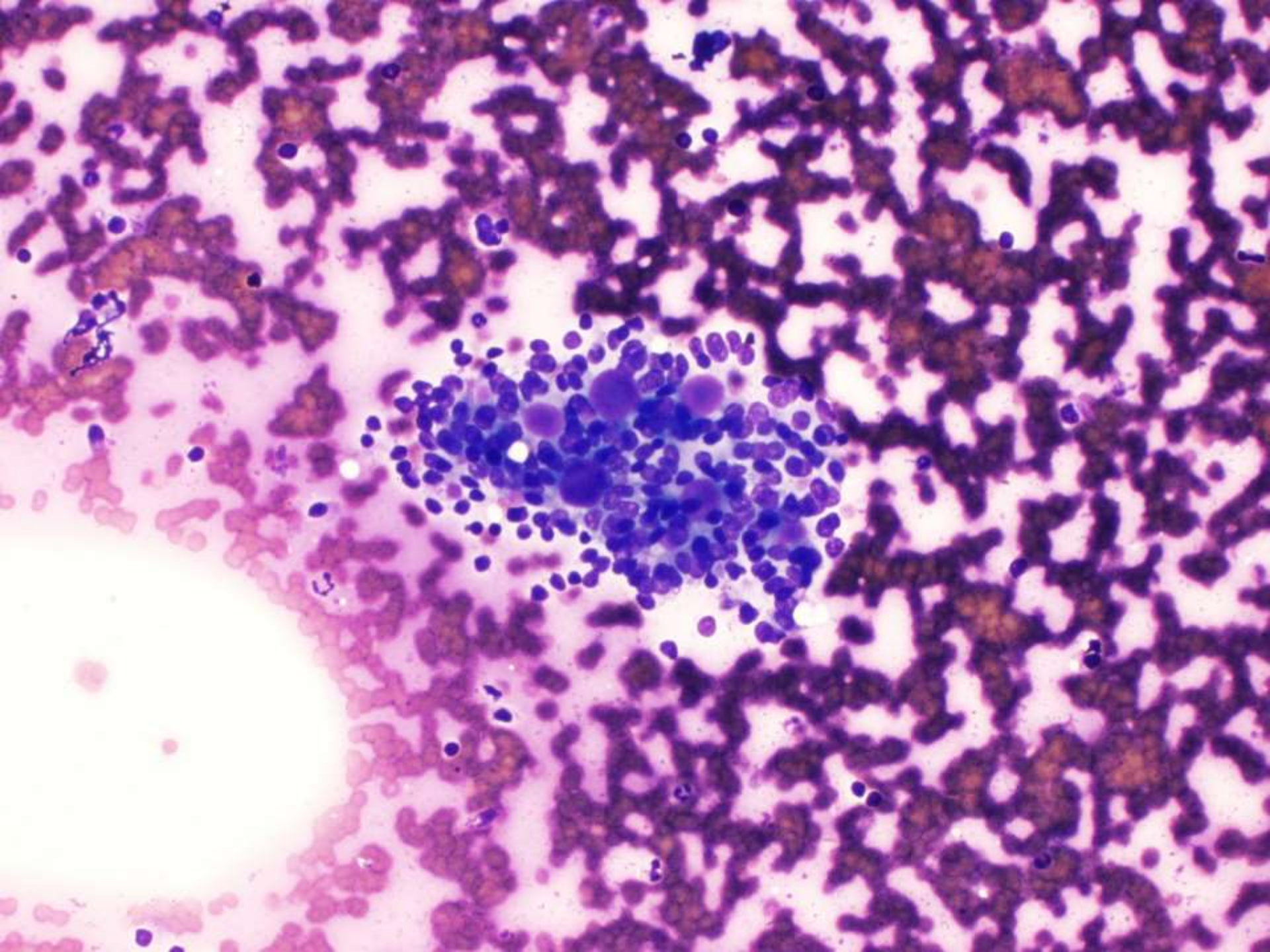
Angel Li/Brock Martin; Stanford

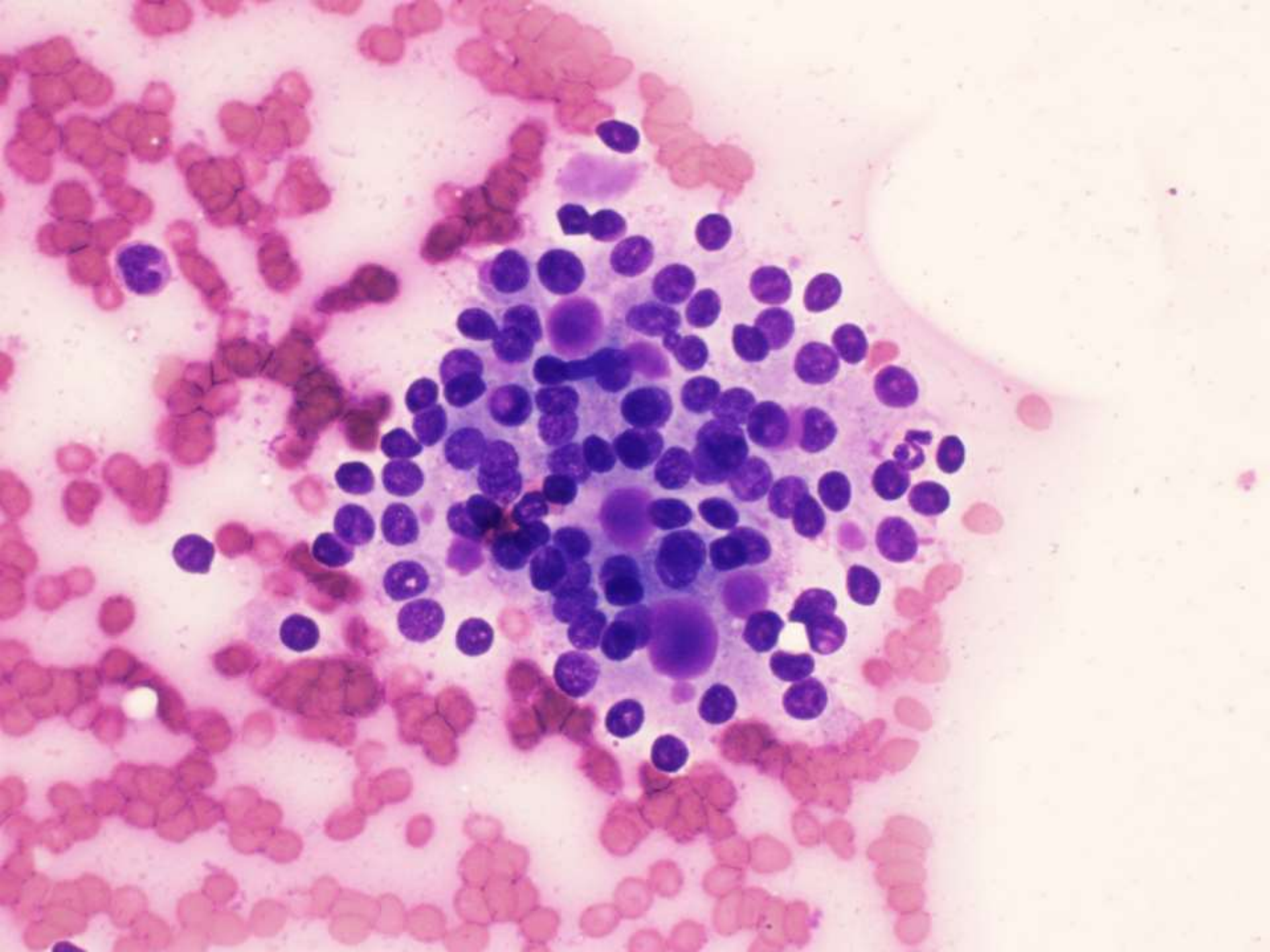
80-year-old female with 5.6cm large complex thyroid nodule, predominantly solid with calcifications, replacing majority of left thyroid lobe.

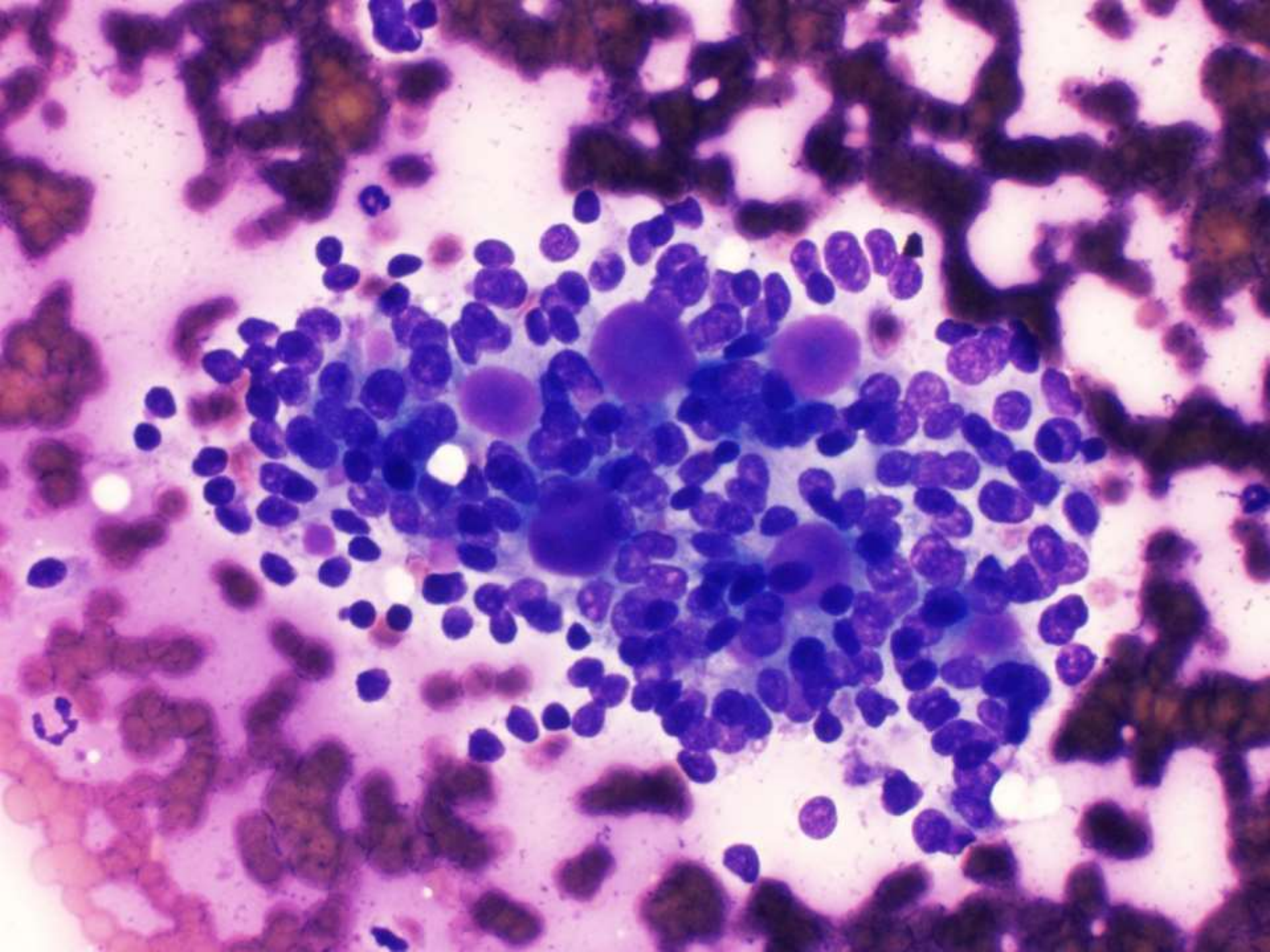


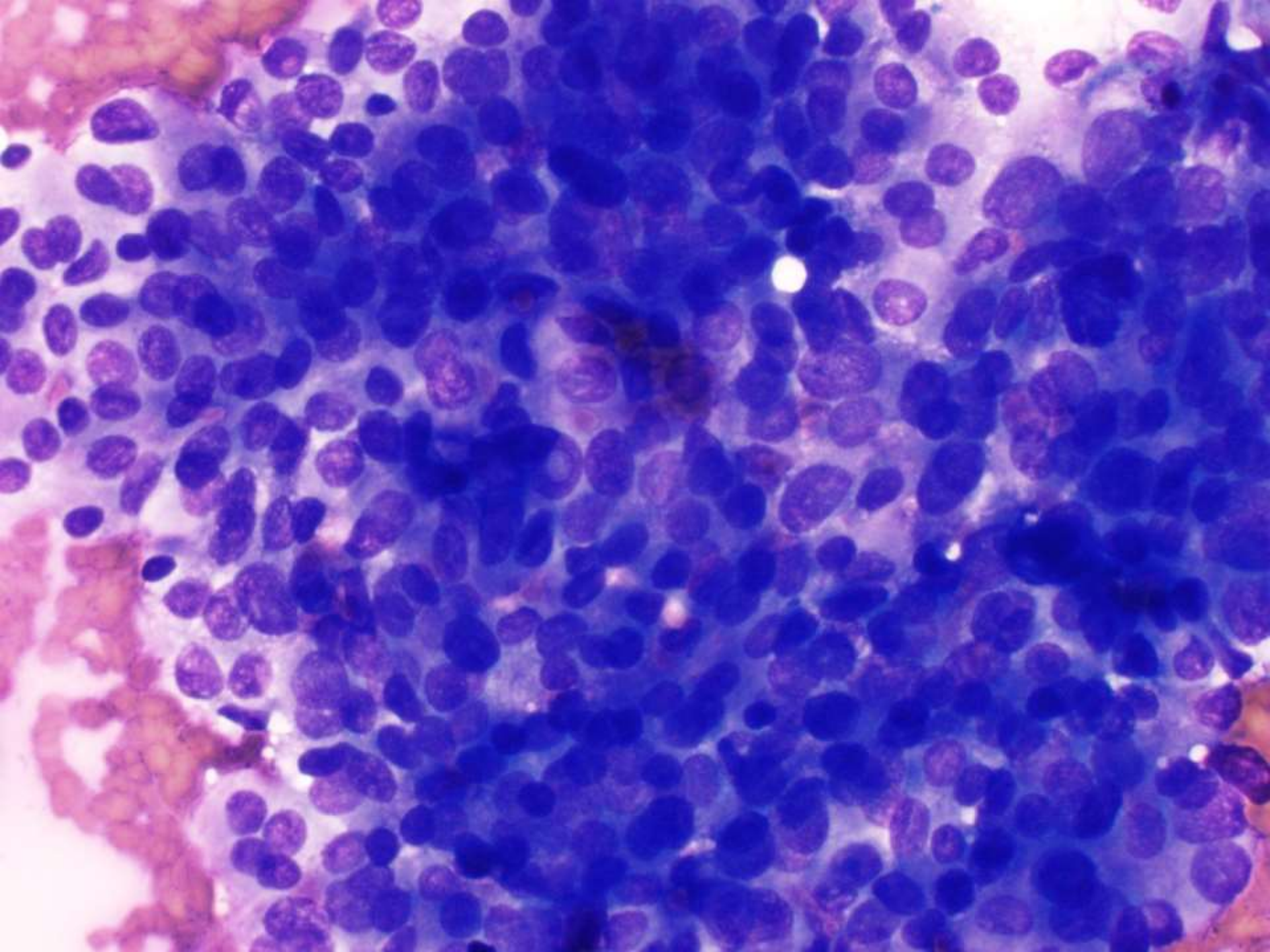


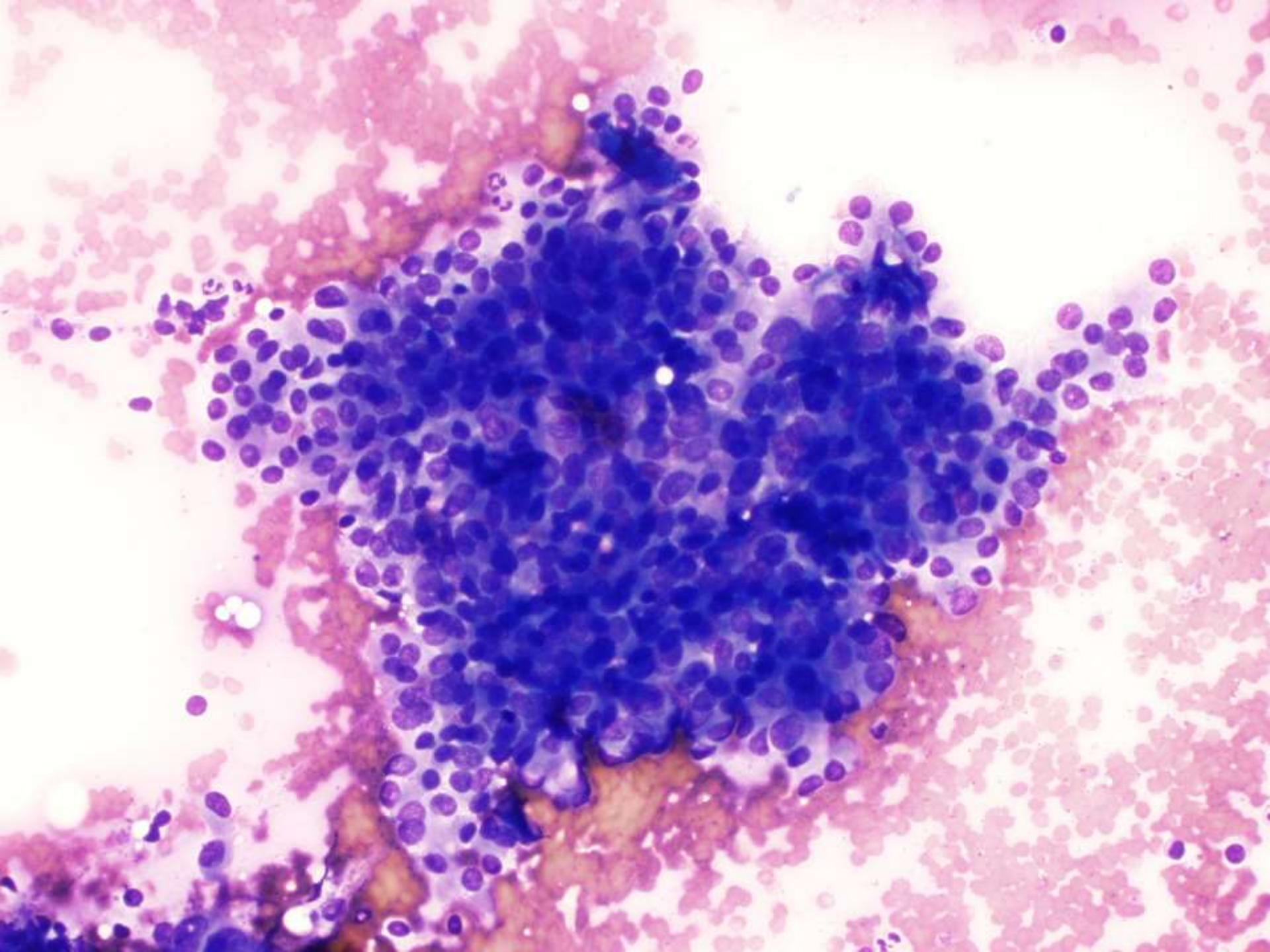


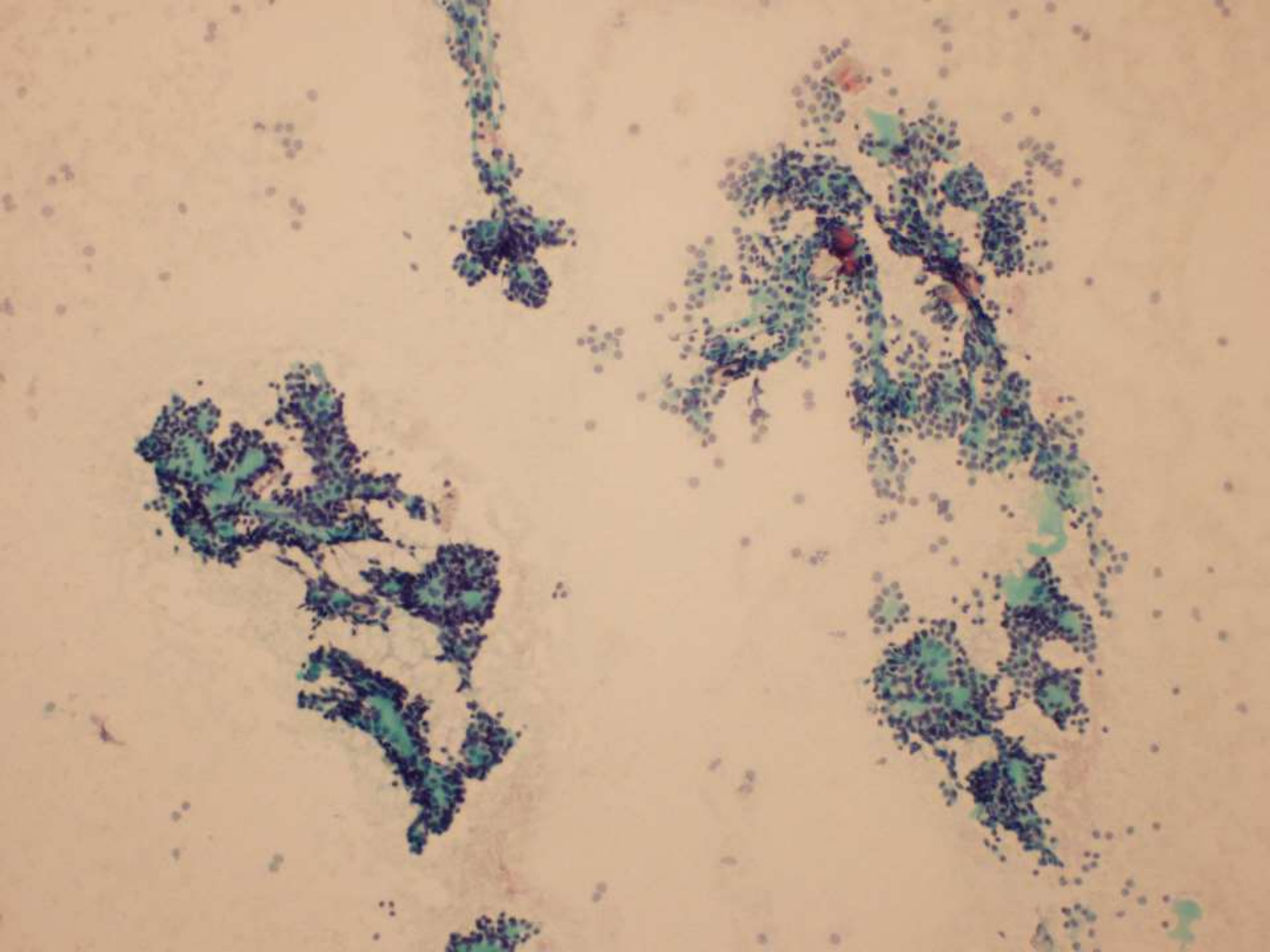


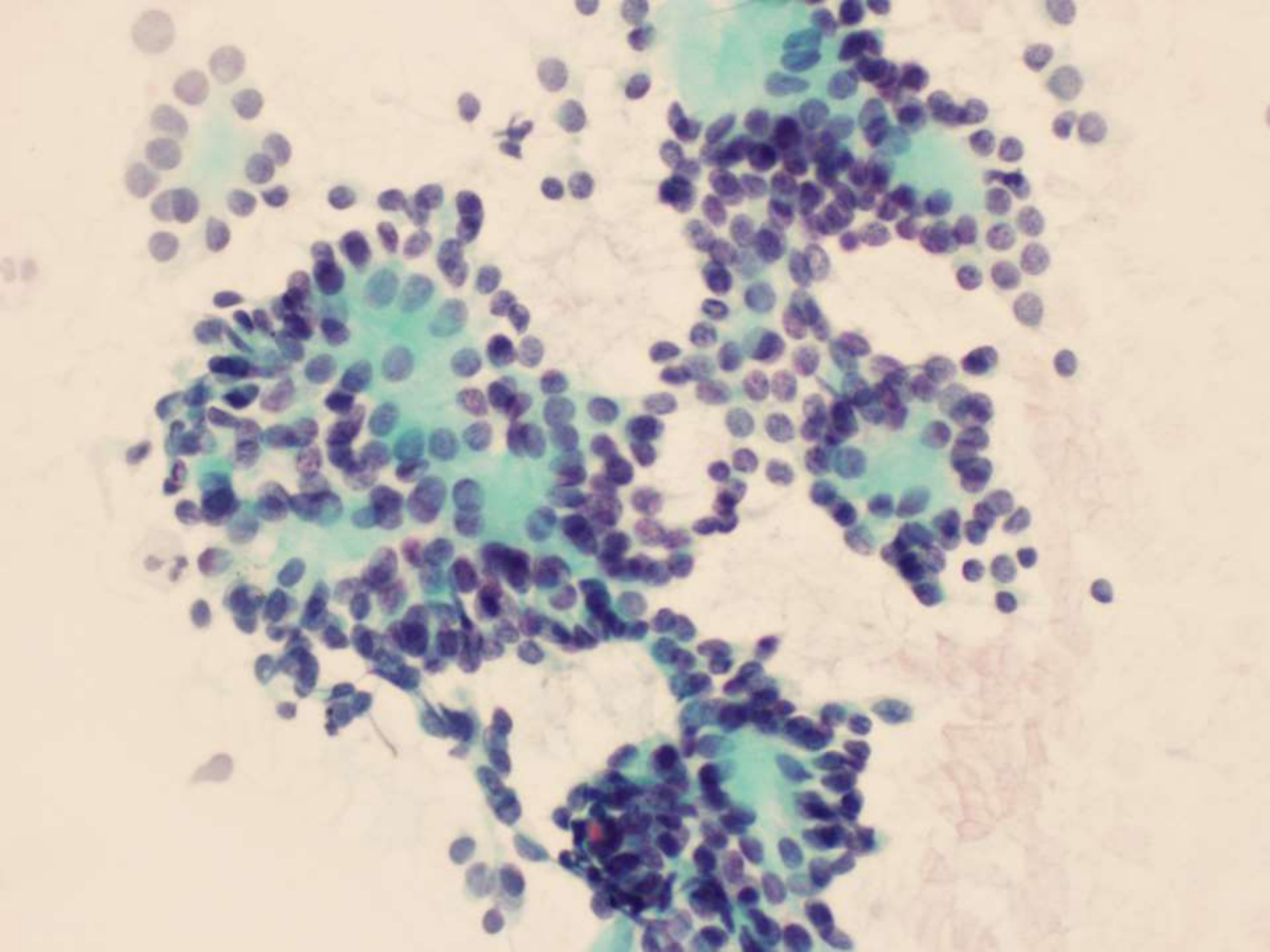












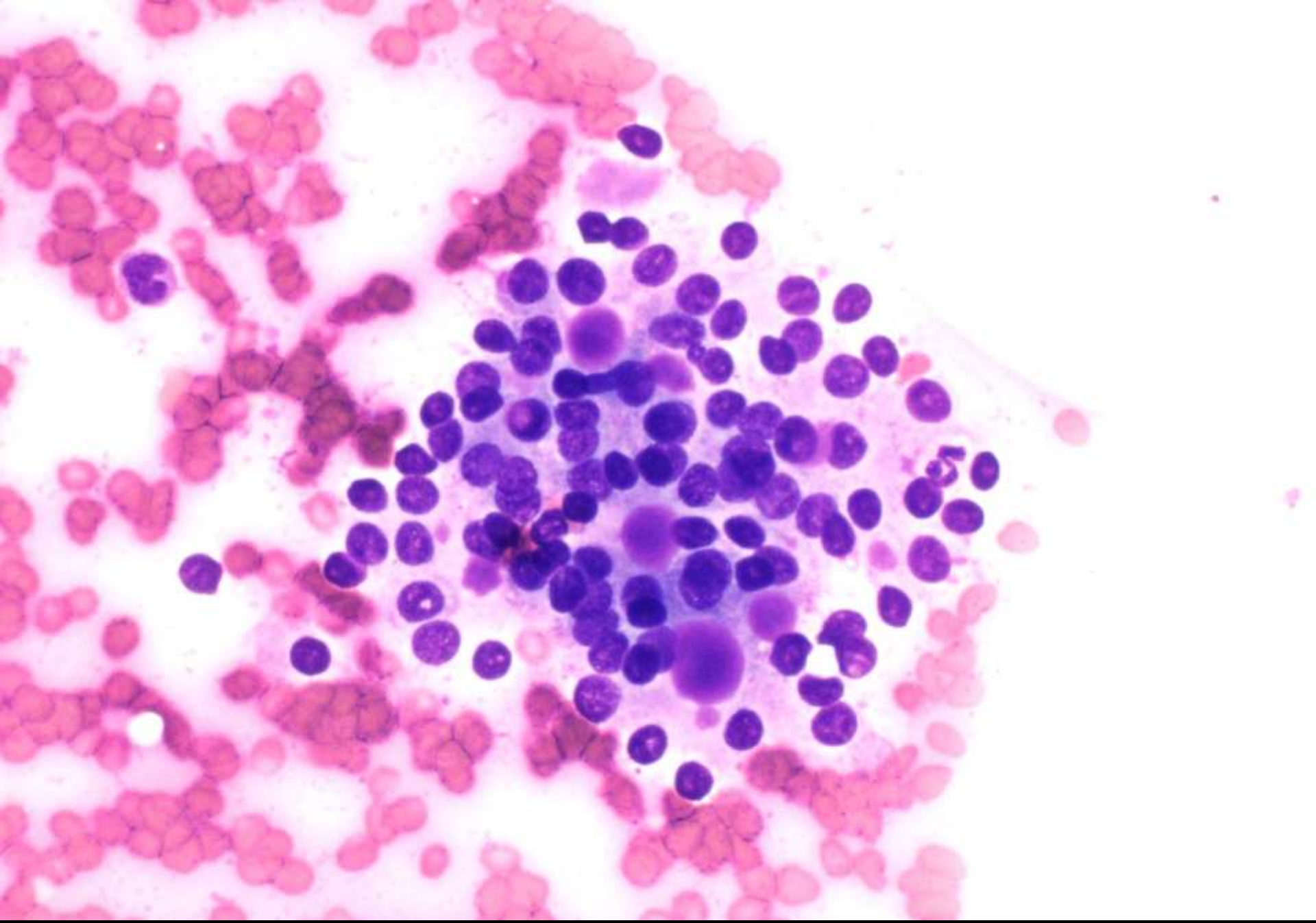
19-0606
80-year-old female with large complex thyroid nodule

Angel Li, Brock Martin

Stanford

Differential Diagnosis

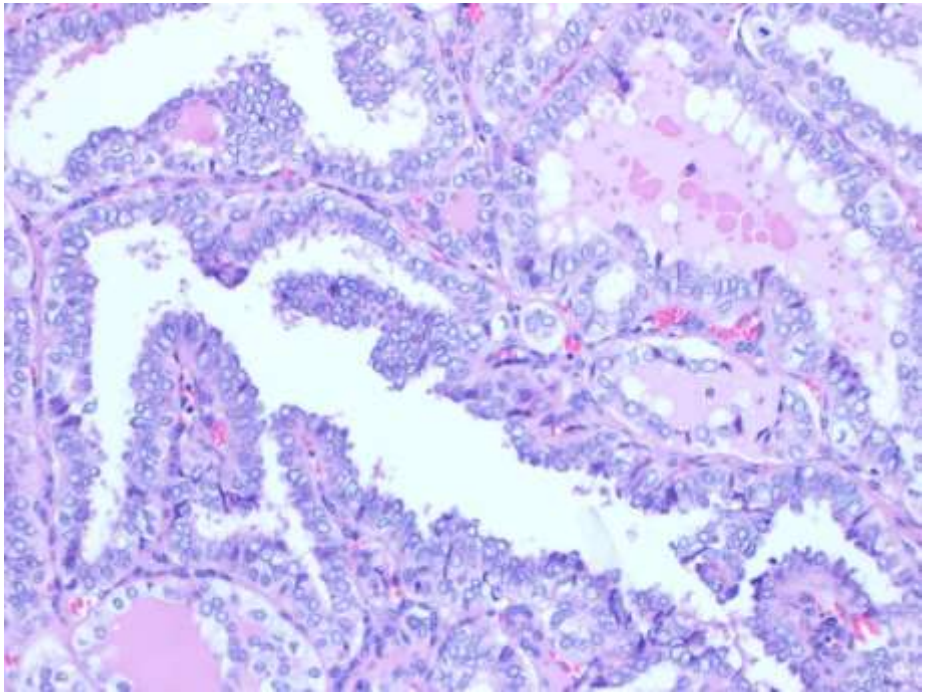
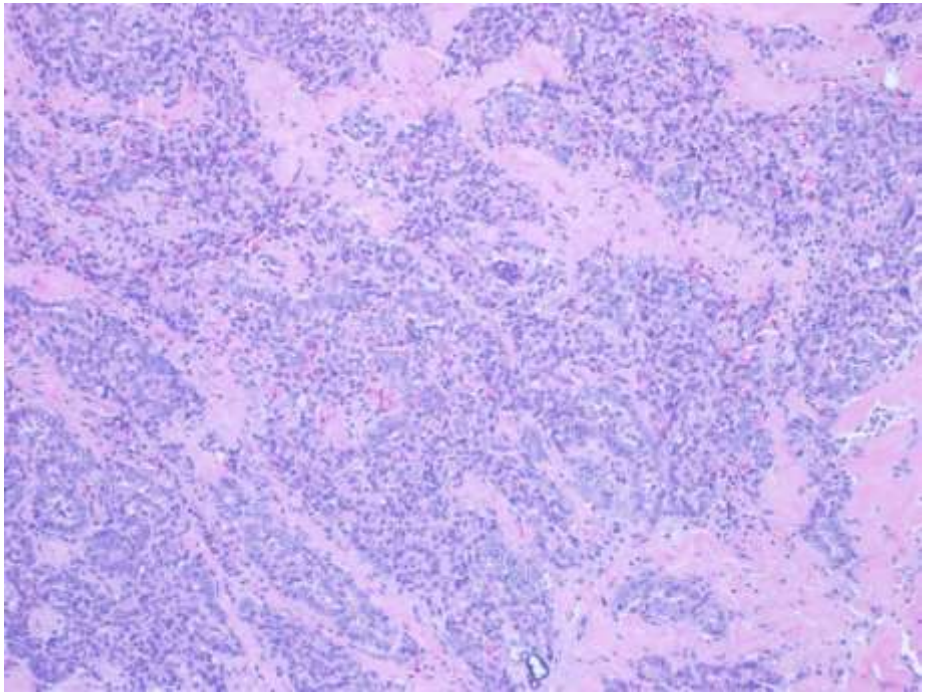
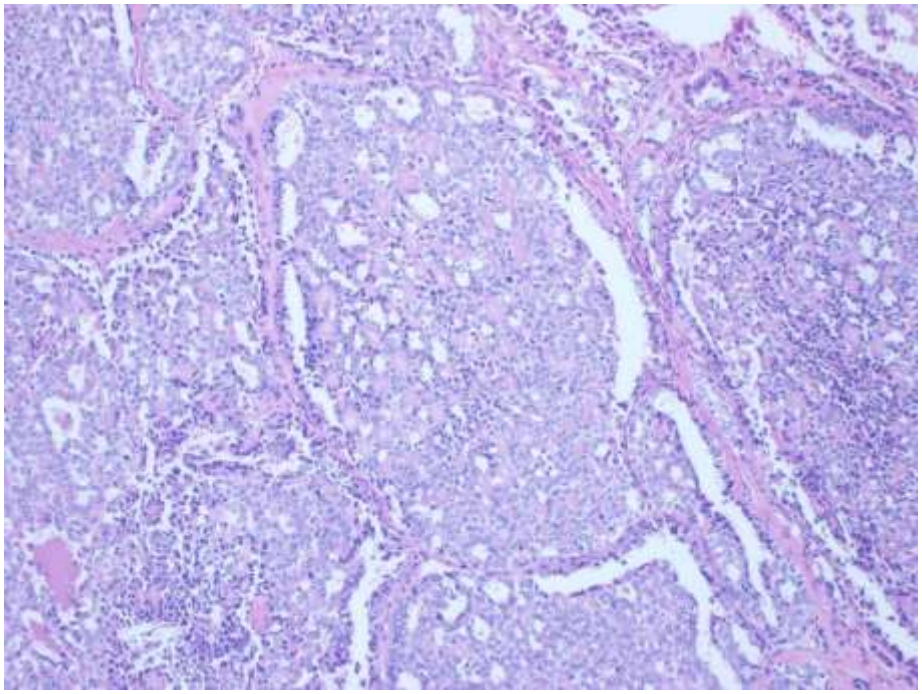
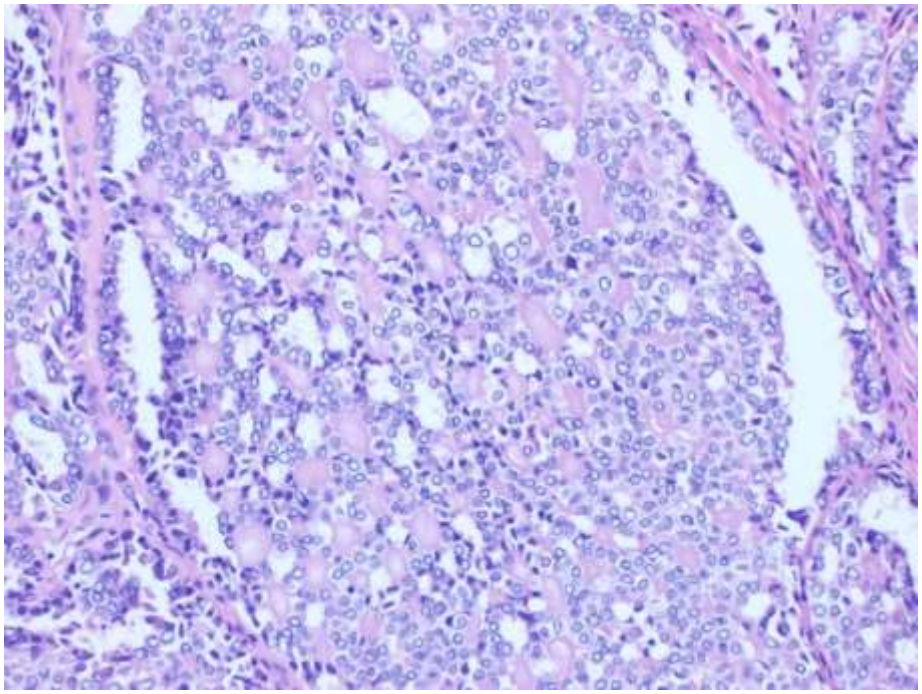
- Follicular neoplasm
- Medullary carcinoma
- Hyalinizing trabecular tumor
- Papillary thyroid carcinoma
- Metastatic adenoid cystic carcinoma



Papillary thyroid carcinoma with an adenoid cystic-like pattern

Clinical Course and Outcome

- 2010-2017: Asymptomatic but visible enlargement of thyroid
- 4/2017: Large 5.6 cm complex nodule replacing the left thyroid lobe
- 8/2017: Outside FNA diagnosis of AUS, AFIRMA suspicious
- 1/2019: Patient developed dyspnea and dysphagia
  - Outside FNA diagnosis of suspicious for papillary thyroid carcinoma
- 2/2019: FNA of left level 3 lymph node showed metastatic PTC
  - Outside pathology reviewed and confirmed as
    - PTC (2019)
    - Atypical follicular cells, retrospectively consistent with papillary thyroid carcinoma with an adenoid cystic-like pattern (2017)
  - Total thyroidectomy with tracheal resection: poorly differentiated thyroid carcinoma with invasion of trachea and mediastinal vessels (pT4bN1b)
- 5/2019: Plan to start RAI in June

Papillary Thyroid Carcinoma with Adenoid Cystic-like Pattern

- Rare and unusual growth pattern seen in thyroid carcinomas
  - Columnar cell and cribriform morular variants of PTC (Baloch et al. 2011)
  - Poorly differentiated carcinoma (Malhotra et al. 2009)
  - Angioinvasive follicular carcinoma (Yamazaki. 2003)
- Fine needle aspiration cytology
  - Atypical follicular cells arranged around spherical hyaline globules resembling adenoid cystic carcinoma
  - Architectural and nuclear features of PTC may not be present
- Awareness of this rare and unusual growth pattern will help to prevent misdiagnosis

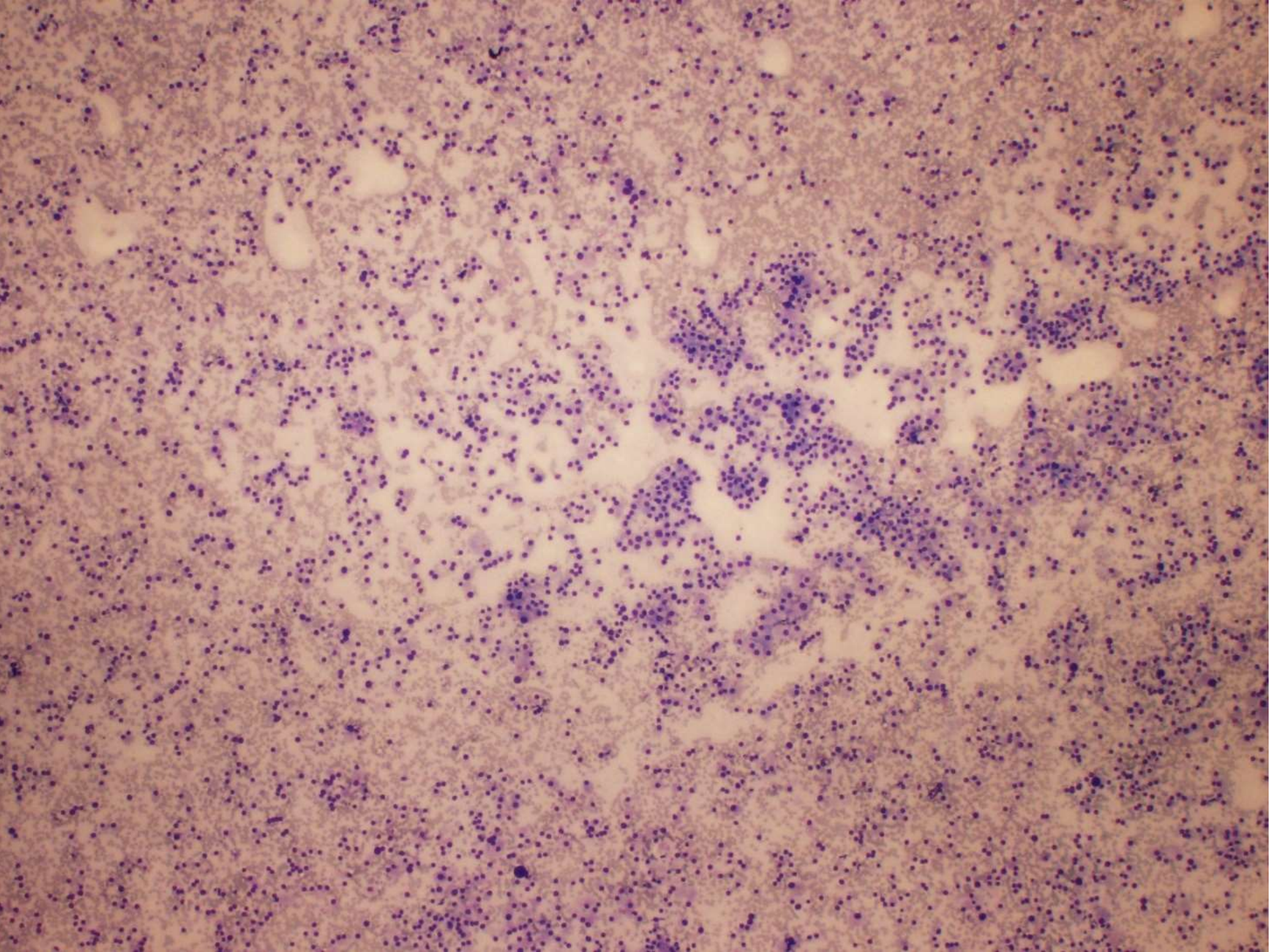
Reference

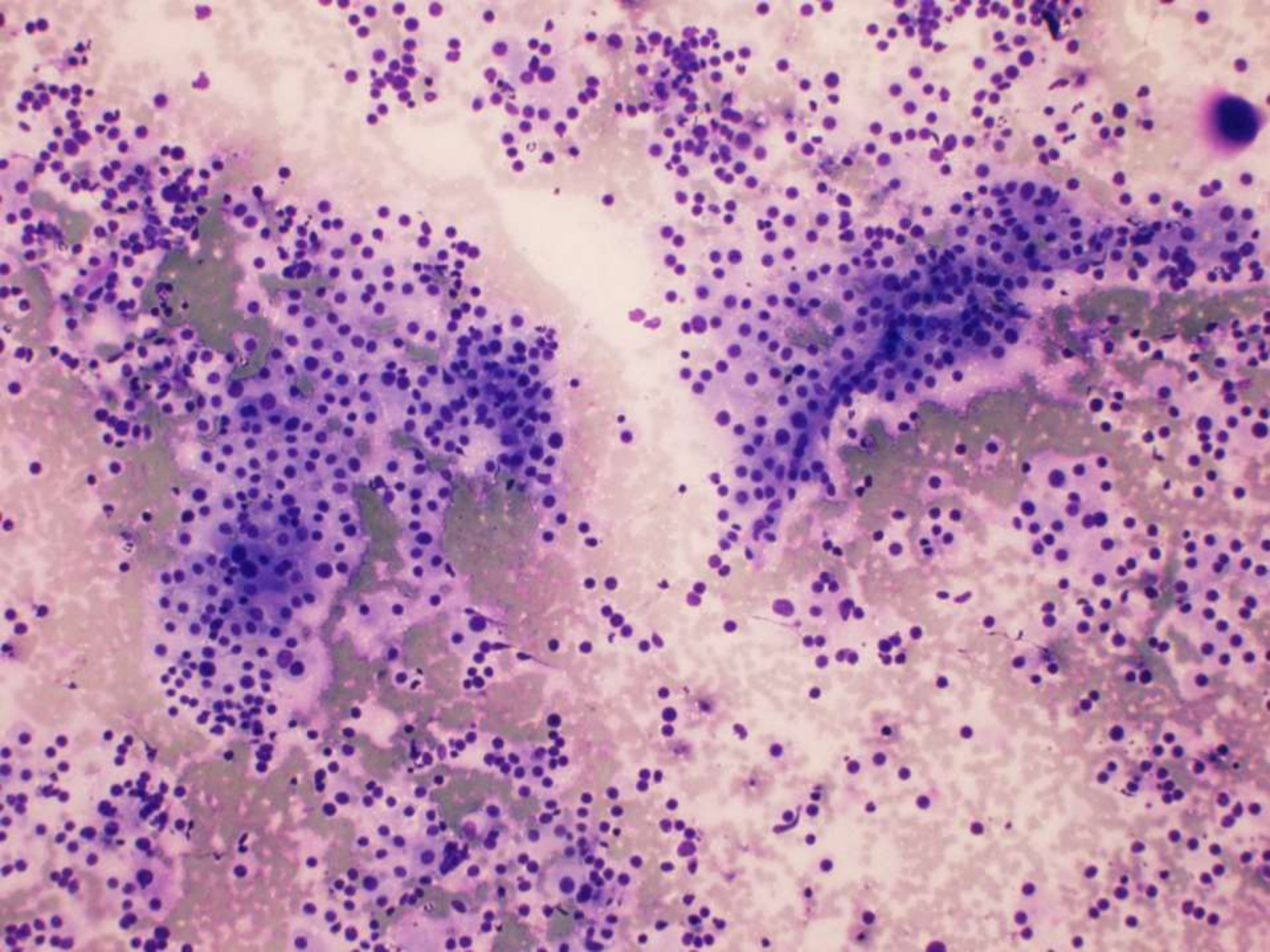
- Baloch ZW, Segal JP, Livolsi VA. Unique growth pattern in papillary carcinoma of the thyroid gland mimicking adenoid cystic carcinoma. *Endocr Pathol*. 2011;22(4):200-205.
- Malhotra P, Deewan U, and Krishnani N. Poorly differentiated thyroid carcinoma mimicking adenoid cystic carcinoma on aspiration cytology: a case report. *Acta Cytol*. 2009;53(5):591–3.
- Yamazaki, K. Unique follicular carcinoma of the thyroid gland with extracellular deposition of amorphous globular structures mimicking an adenoid cystic pattern. *Virchows Arch*. 2003;443(5):690–2.

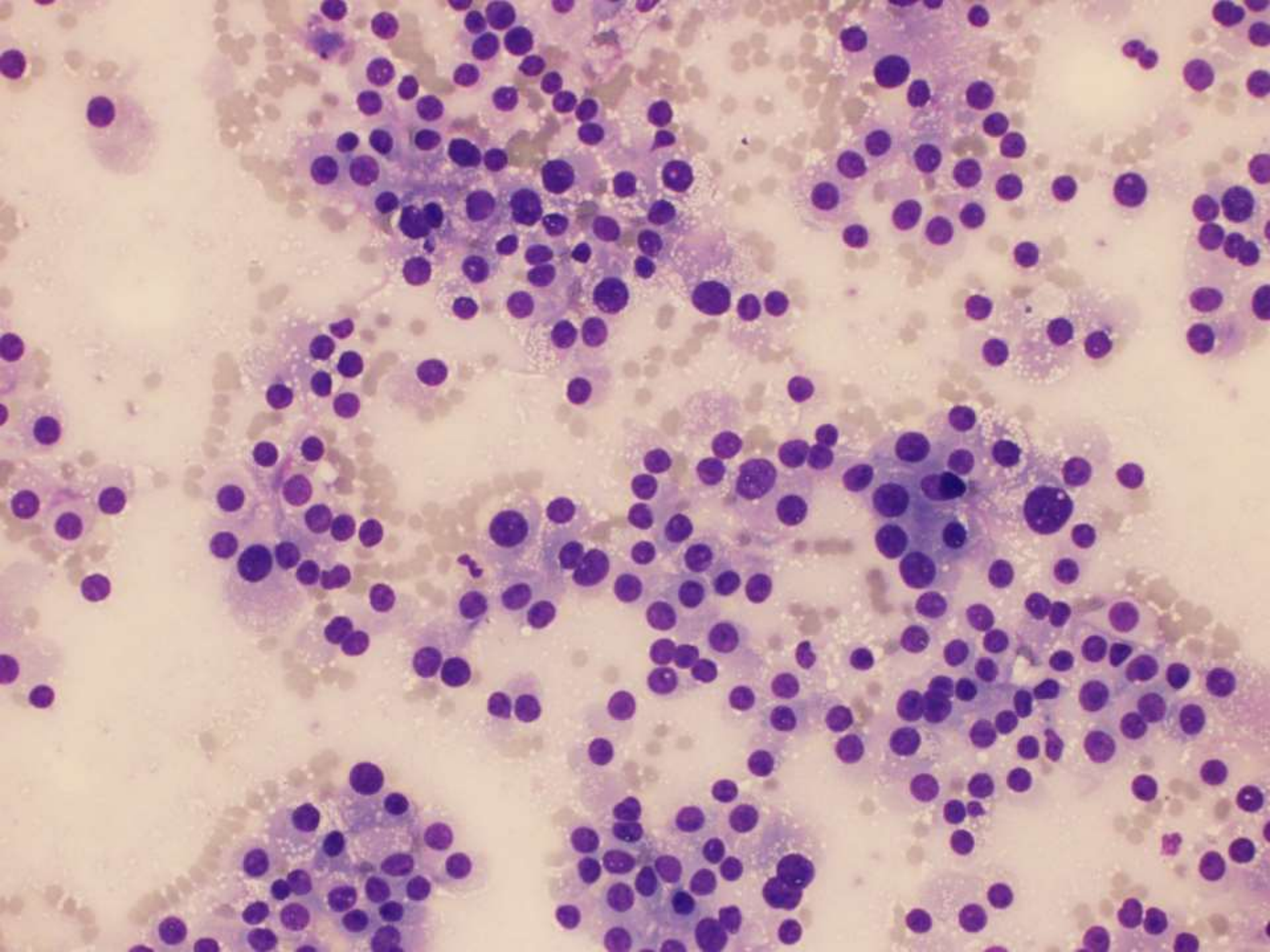
19-0607

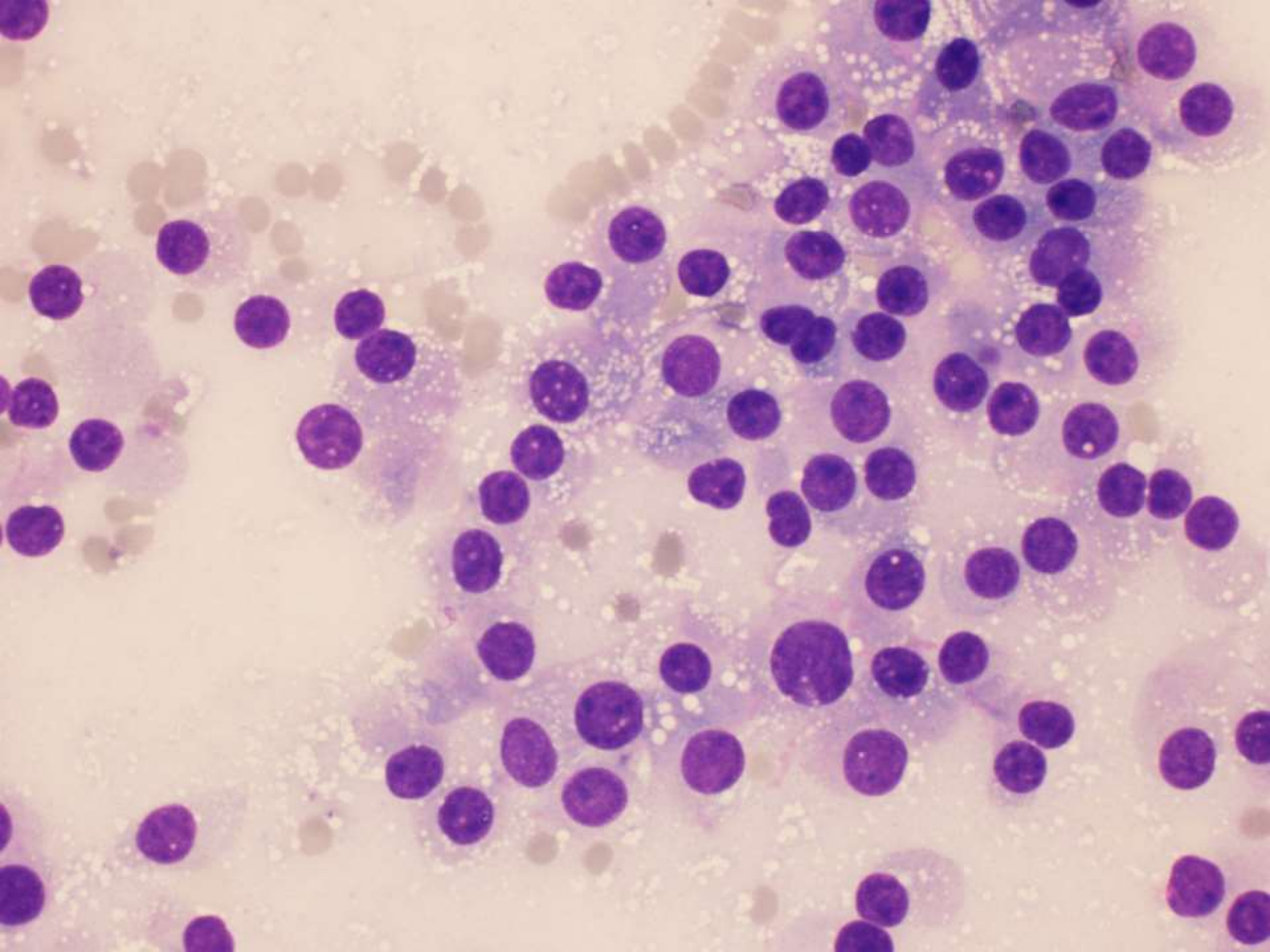
Angel Li/Sunny Kao; Stanford

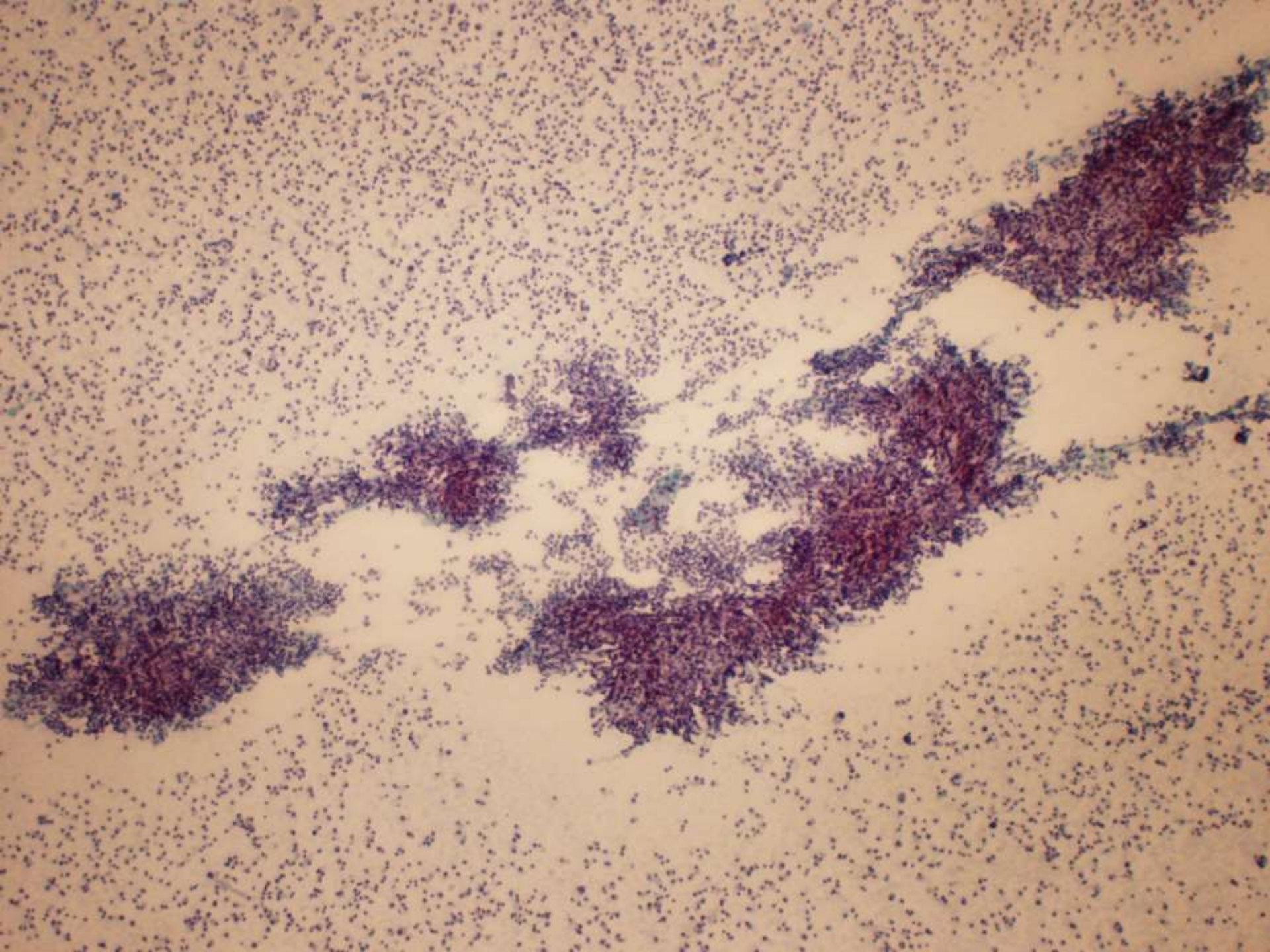
44-year-old male with h/o testicular cancer and inguinal lymphadenopathy.

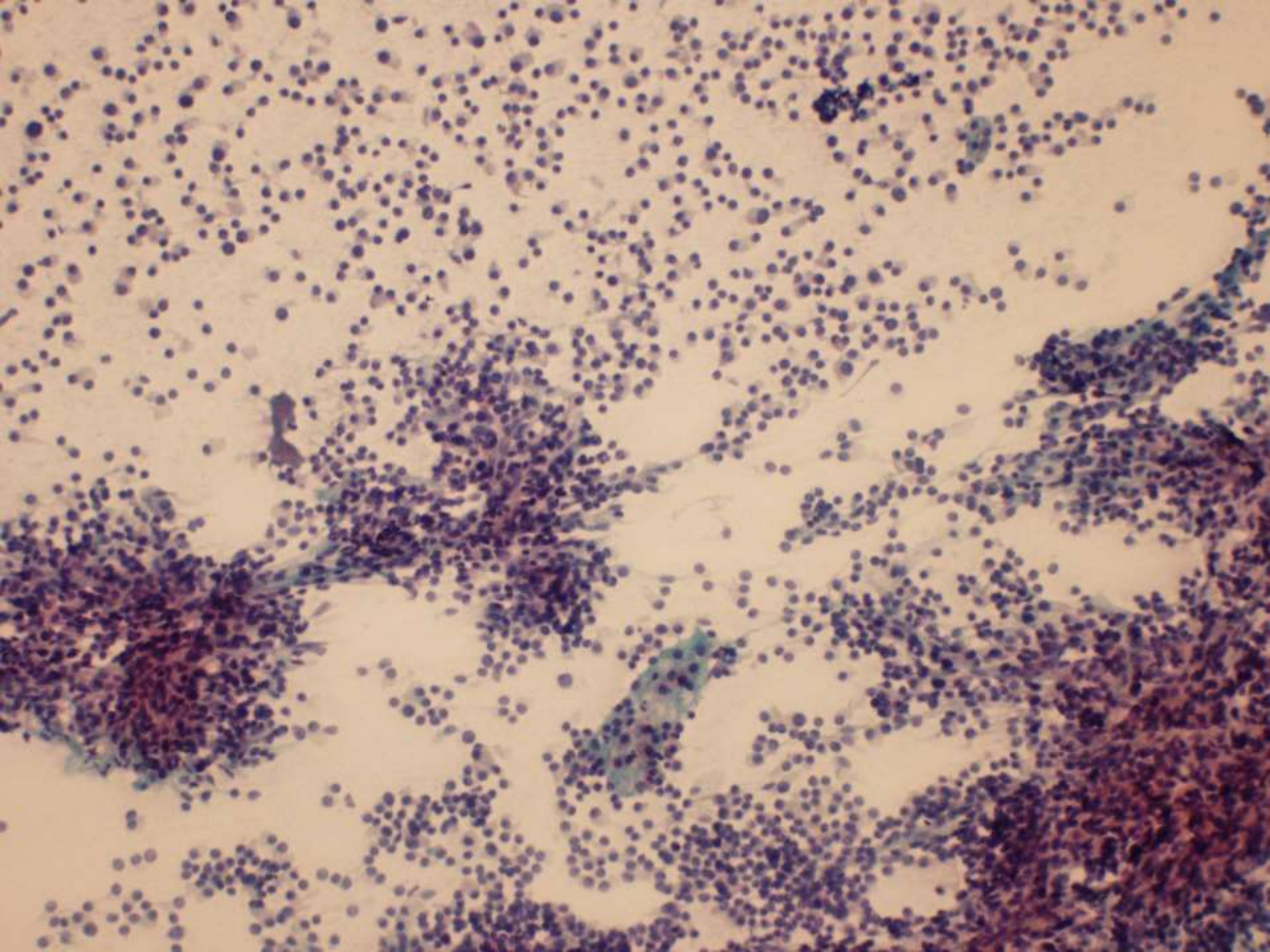


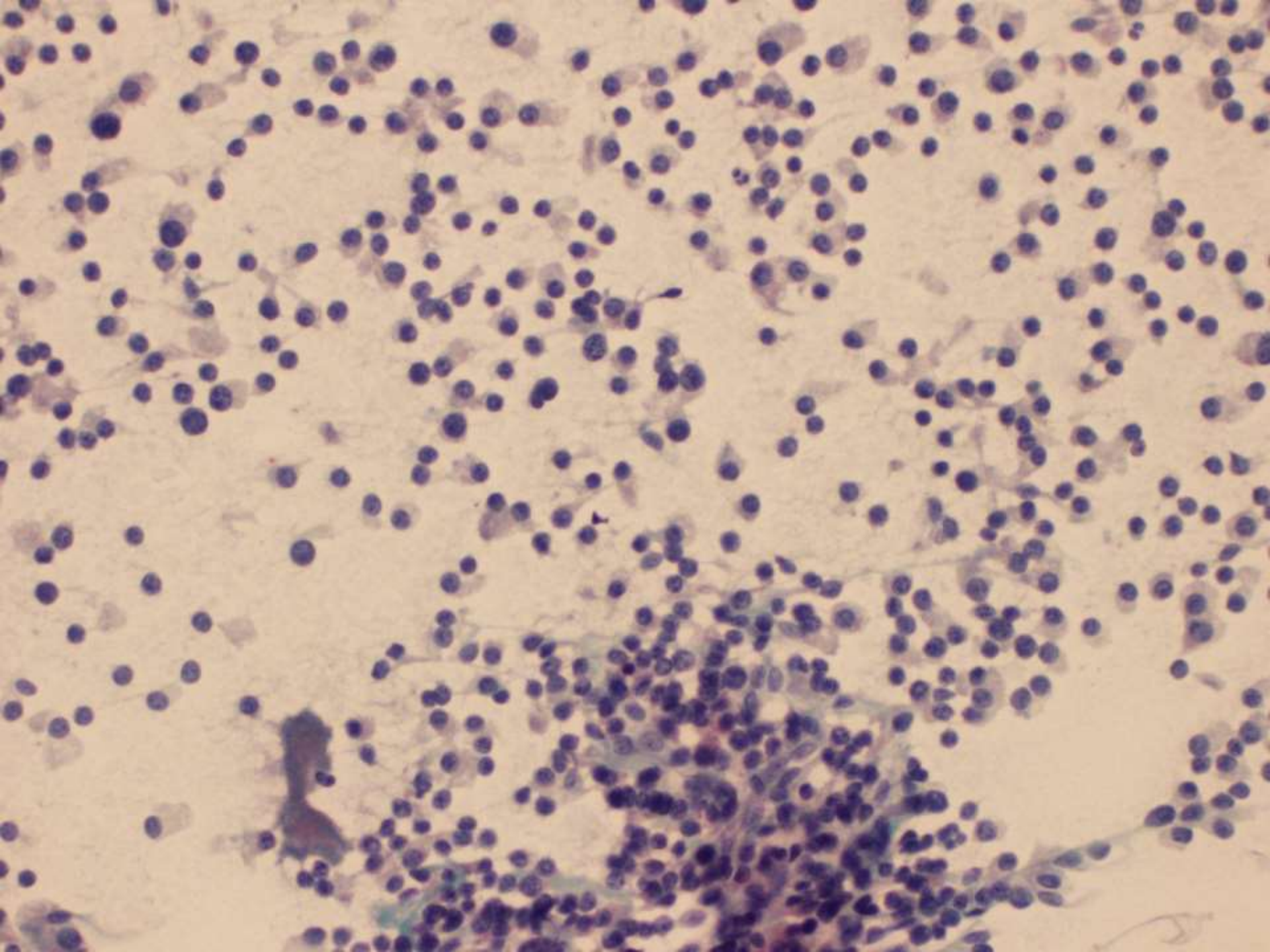


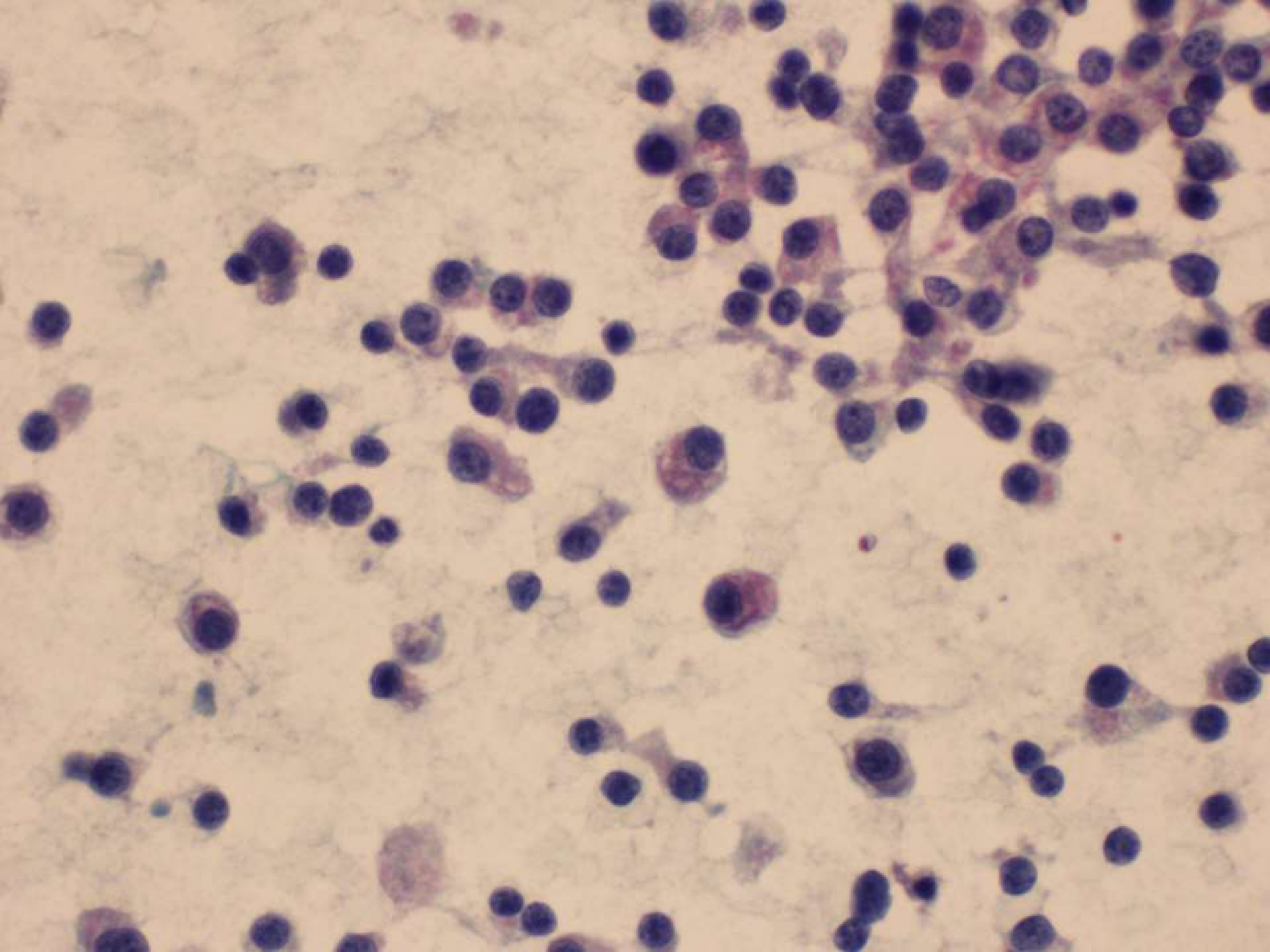


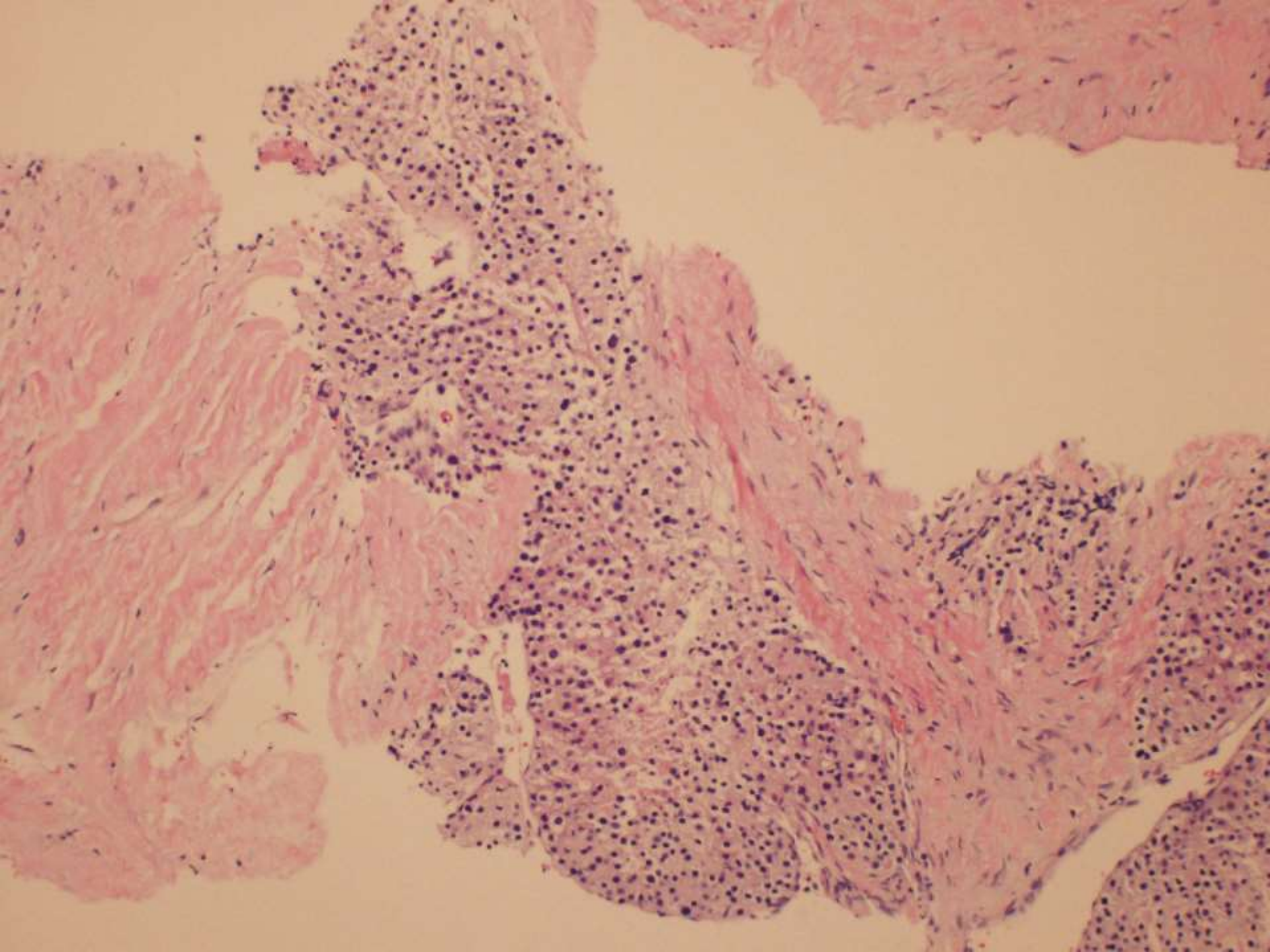


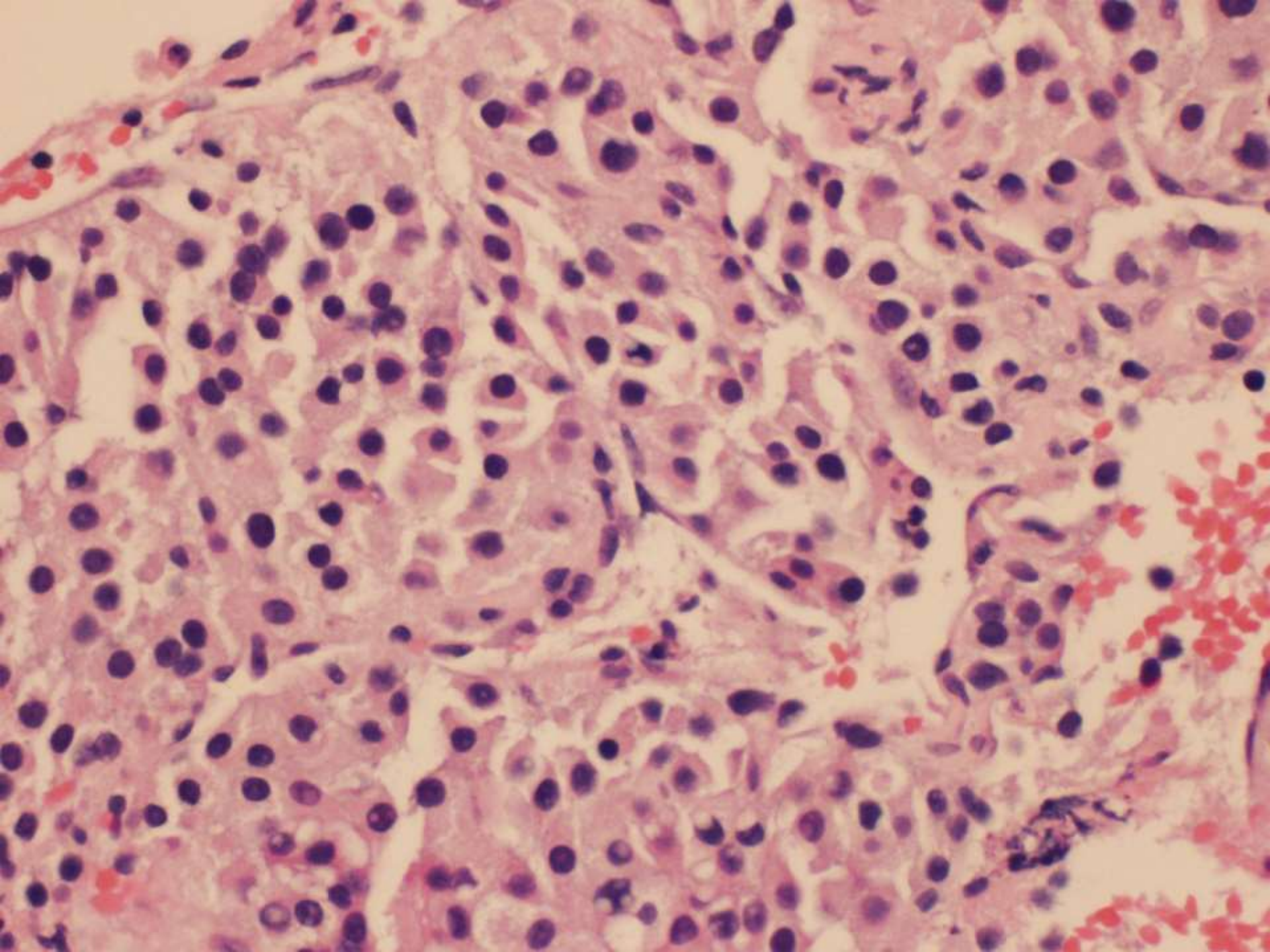












19-0607

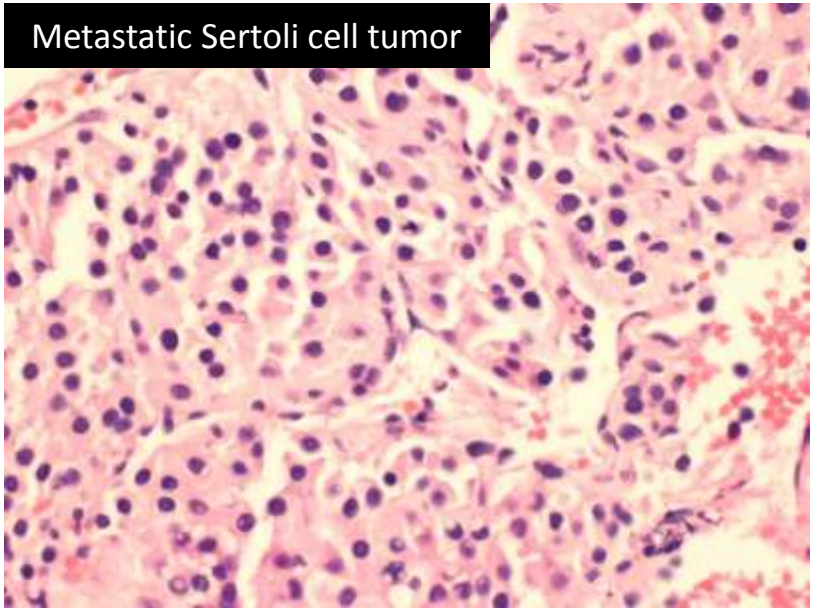
44-year-old male with history of testicular cancer and inguinal lymphadenopathy

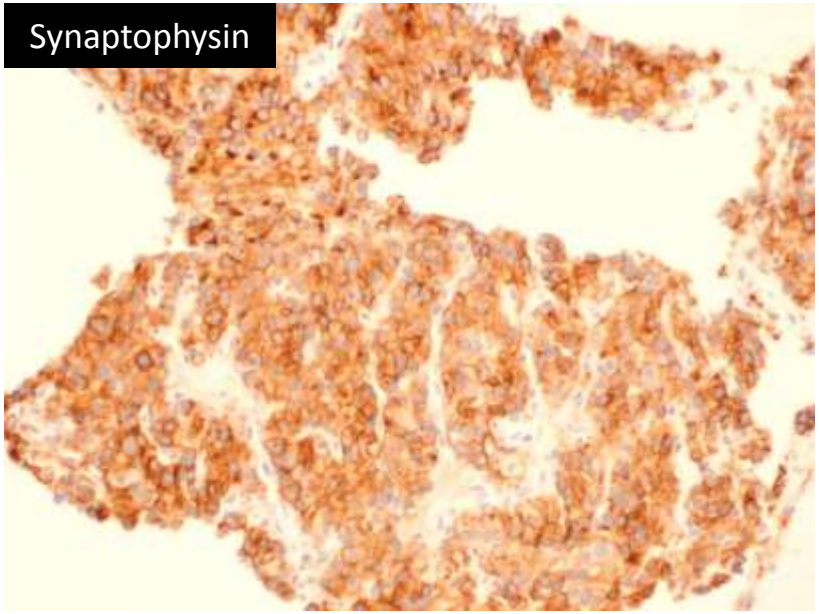
Angel Li, Sunny Kao

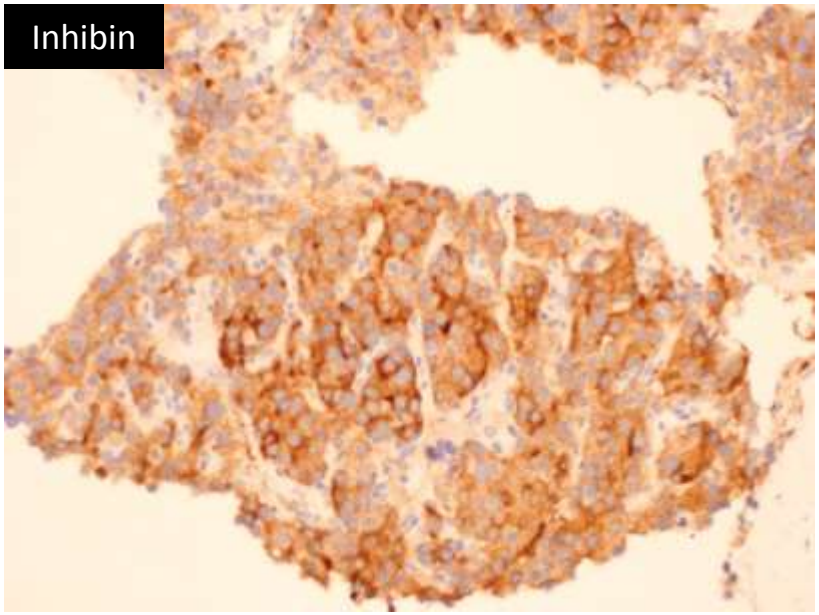
Stanford

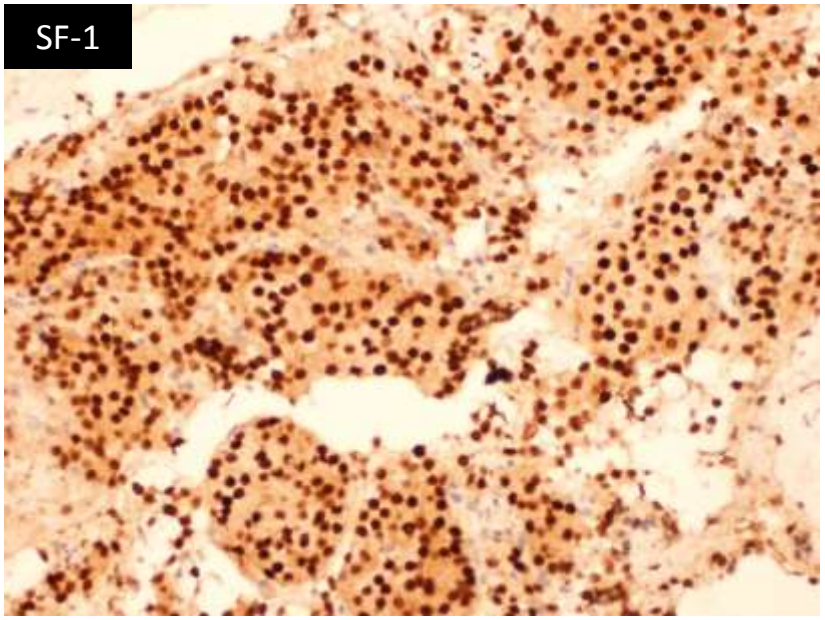
Differential Diagnosis

- Metastatic sex cord stromal tumor (Hx of Sertoli cell tumor)
- Metastatic germ cell tumor
- Carcinoid tumor
- Paraganglioma


Metastatic Sertoli cell tumor


Synaptophysin


Inhibin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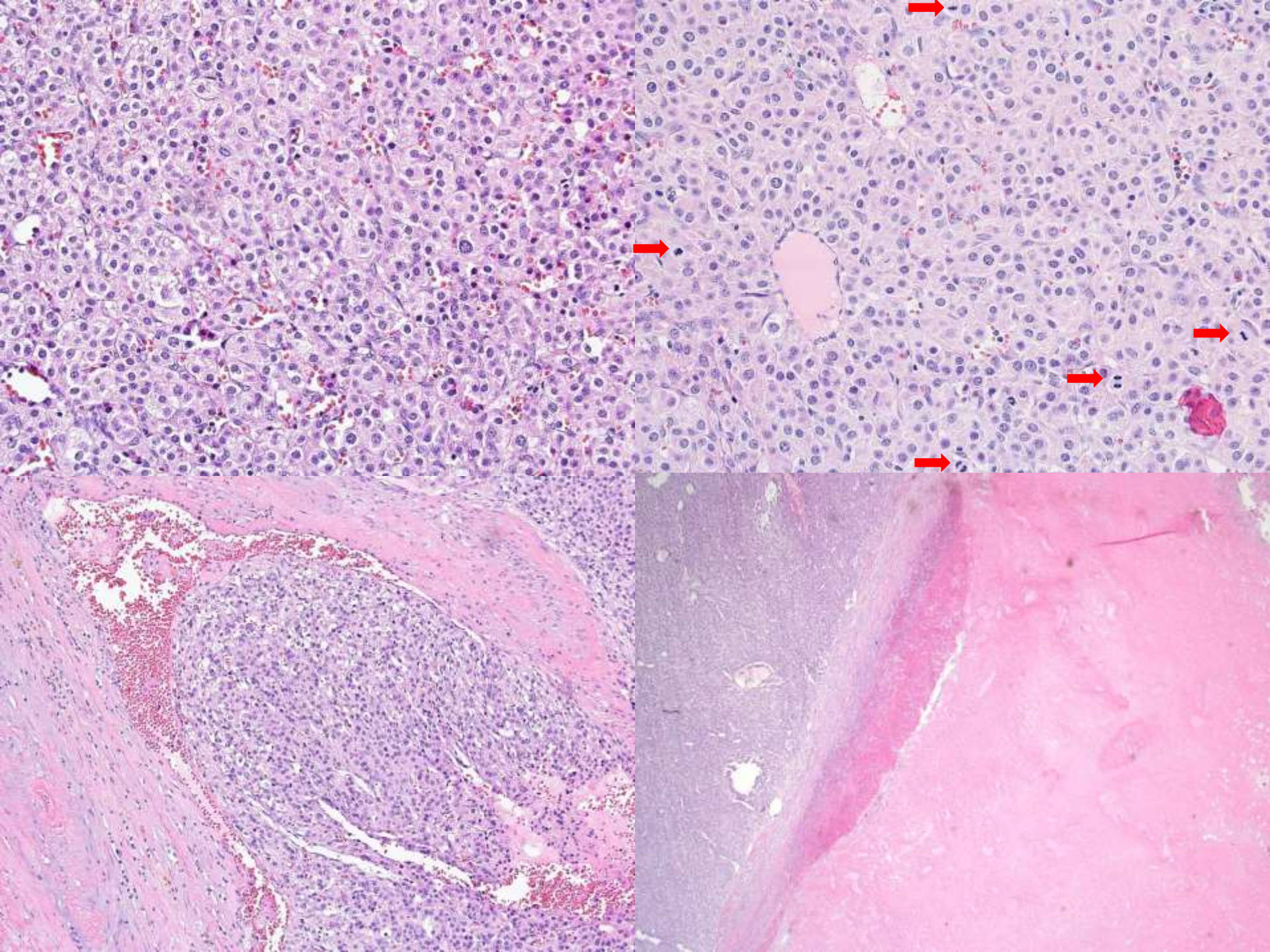


Clinical Course and Outcome

- 2/2016: Sertoli cell tumor of right testis with malignant features and lymphovascular invasion
- 12/2018: PET/CT shows inguinal mass and lung nodules
- 1/2019: FNA confirms metastatic Sertoli cell tumor
- 2/2019: Resection and RPLND
- 3/2019: Growing lung nodules, plan to start chemotherapy

Testicular Sex Cord Stromal Tumor

- Features associated with malignancy
  - Large size (Sertoli >5 cm)
  - Infiltrative growth pattern (into surrounding parenchyma or extratesticular soft tissue)
  - Moderate to severe nuclear atypia
  - Increased mitotic activity (Sertoli >5/10HPFs)
  - Necrosis
  - Lymphovascular invasion

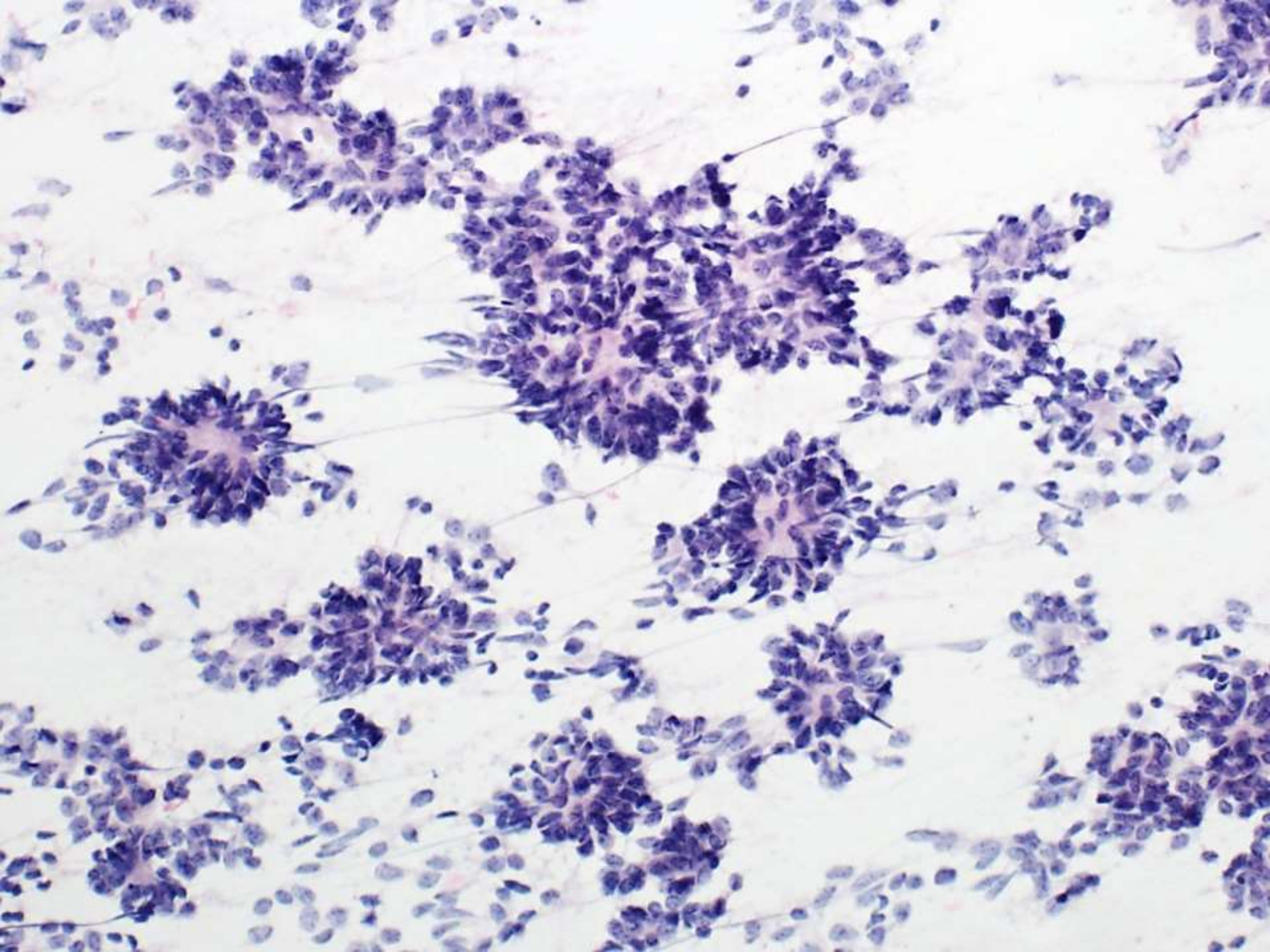
References

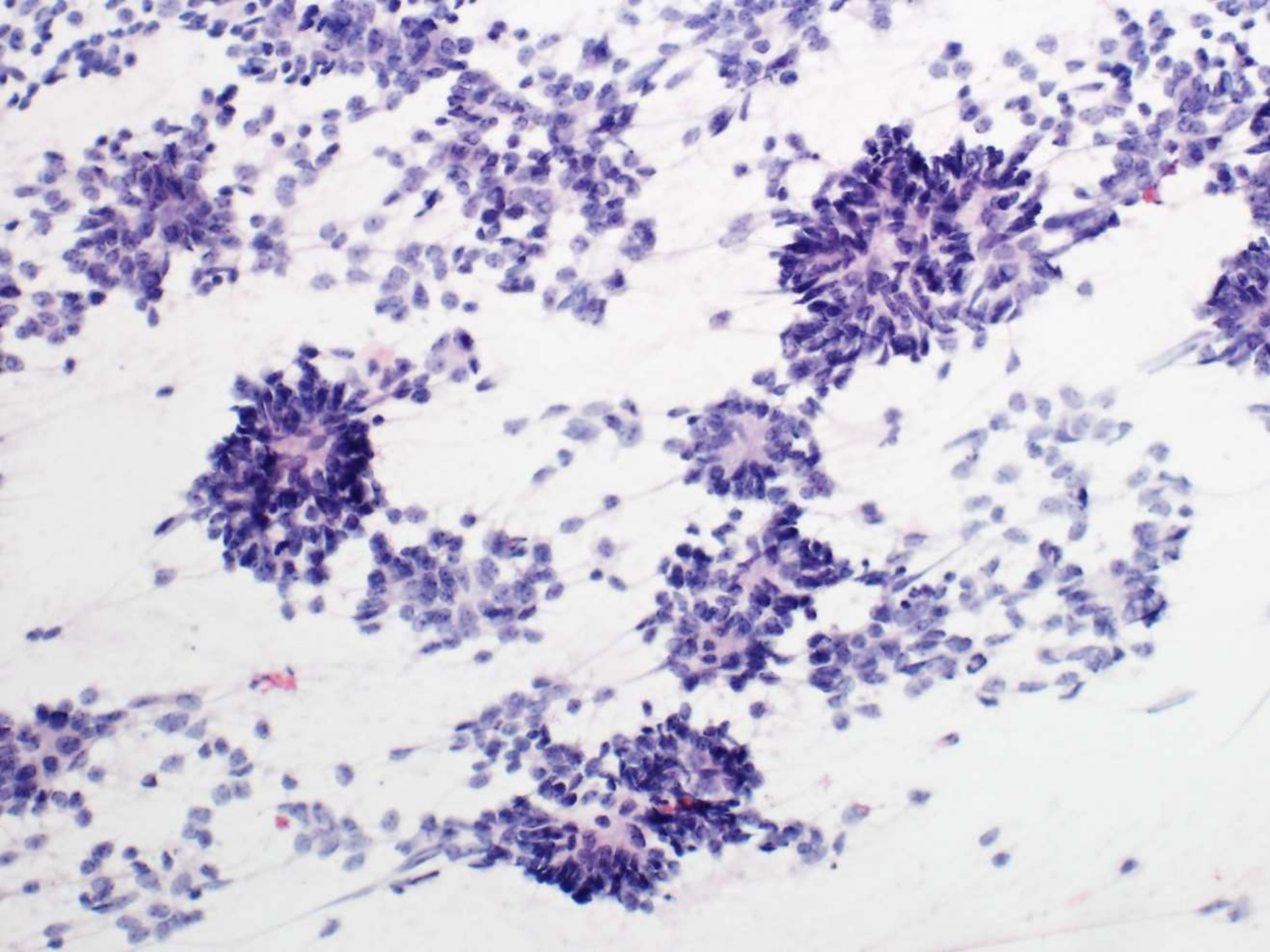
- Kronz JD, Nicol TL, Rosenthal DL, Ali SZ. Metastatic testicular Sertoli-cell tumor: cytopathology findings on fine-needle aspiration. Diagn Cytopathol 1998;19(2):127-30.
- Young RH, Koelliker DD, Scully RE. Sertoli cell tumors of the testis, not otherwise specified: a clinicopathologic analysis of 60 cases. Am J Surg Pathol 1998;22:709-21.

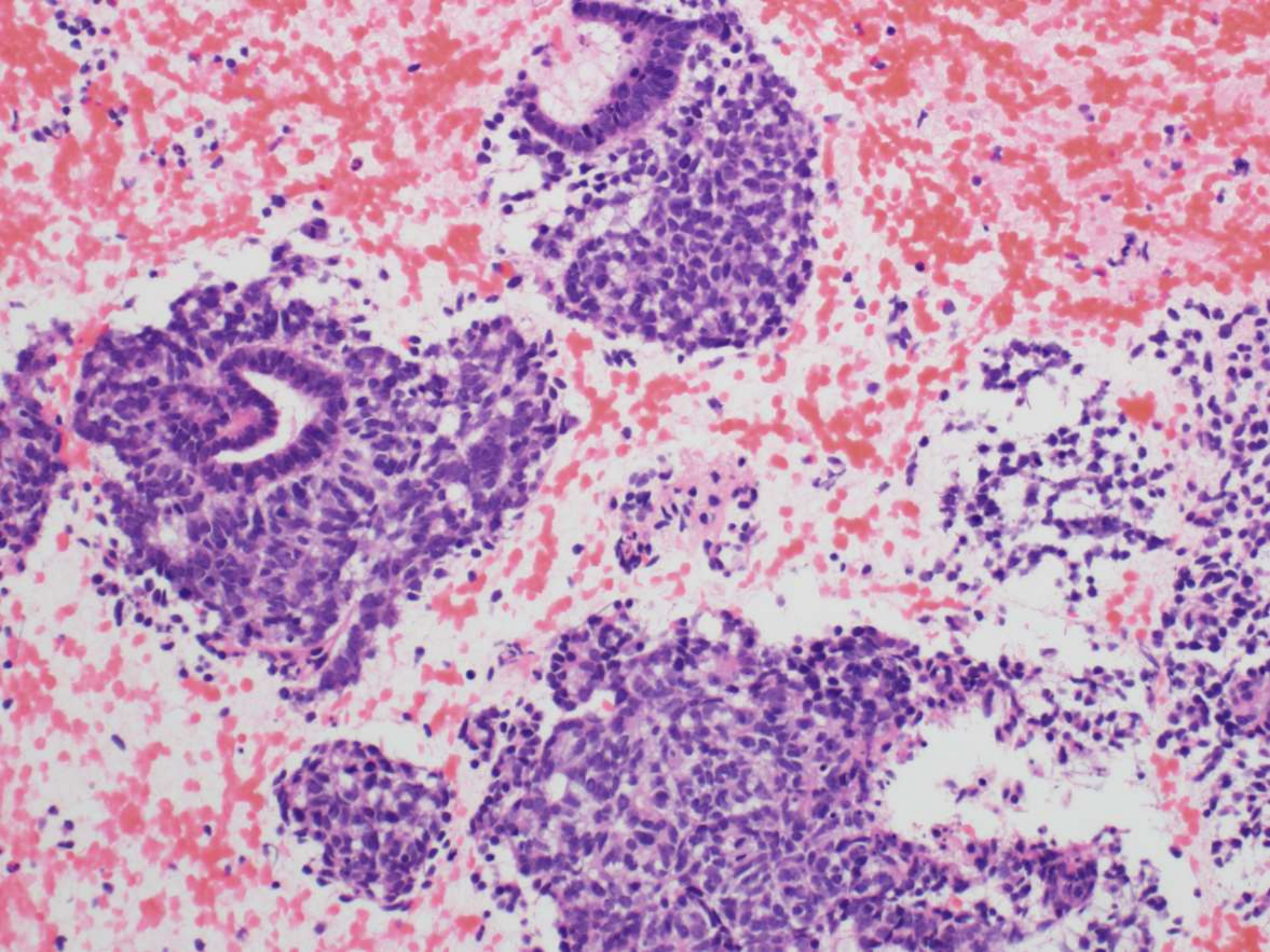
19-0608

Lucy Han/Emily Chan/Ron Balassanian/Jeff Simko; UCSF

44-year-old female with 8.7cm left renal mass. She also has a recently diagnosed papillary thyroid carcinoma.







44-year-old woman with a left renal mass.

South Bay Meeting

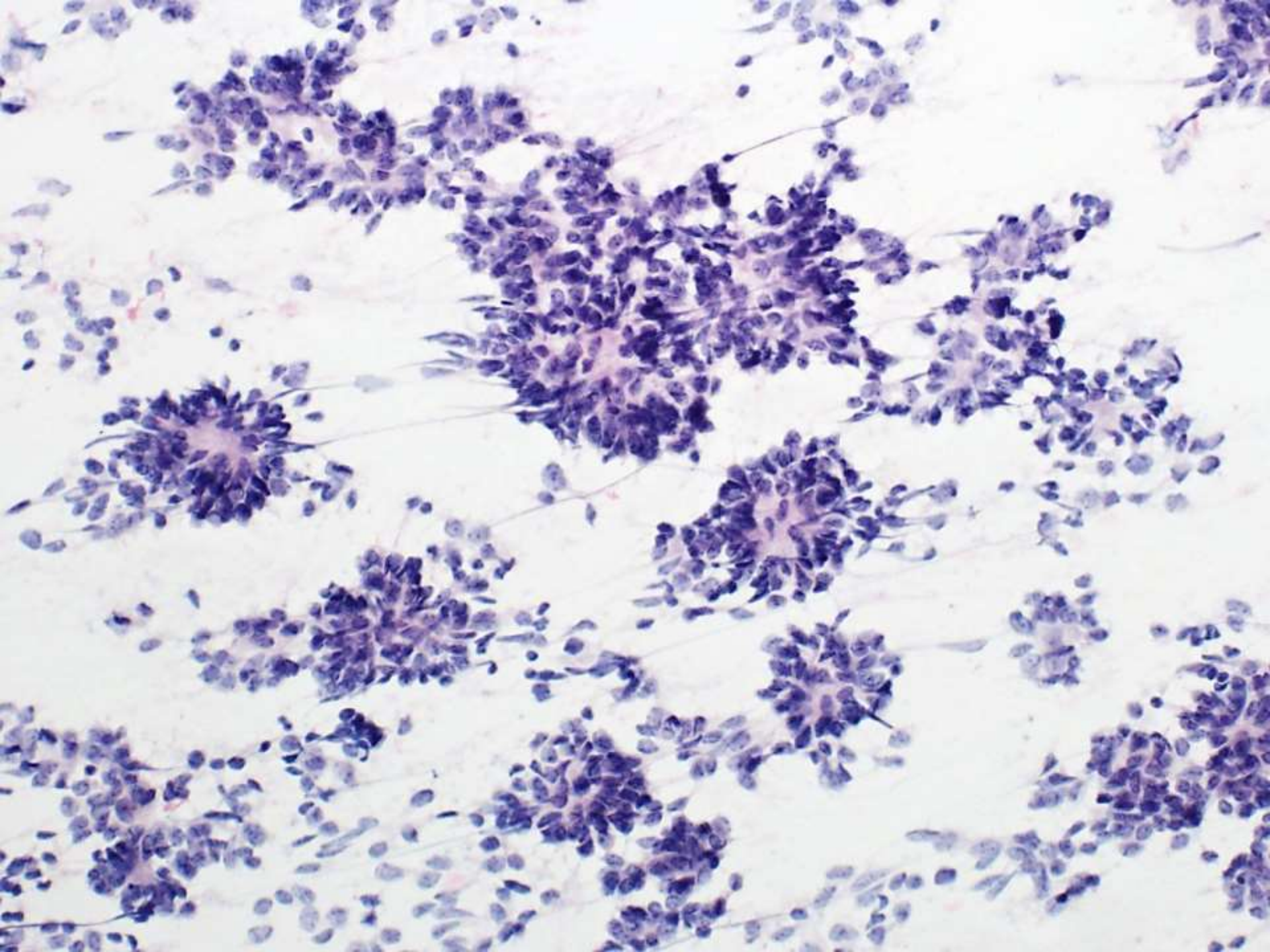
Lucy Han, PGY3

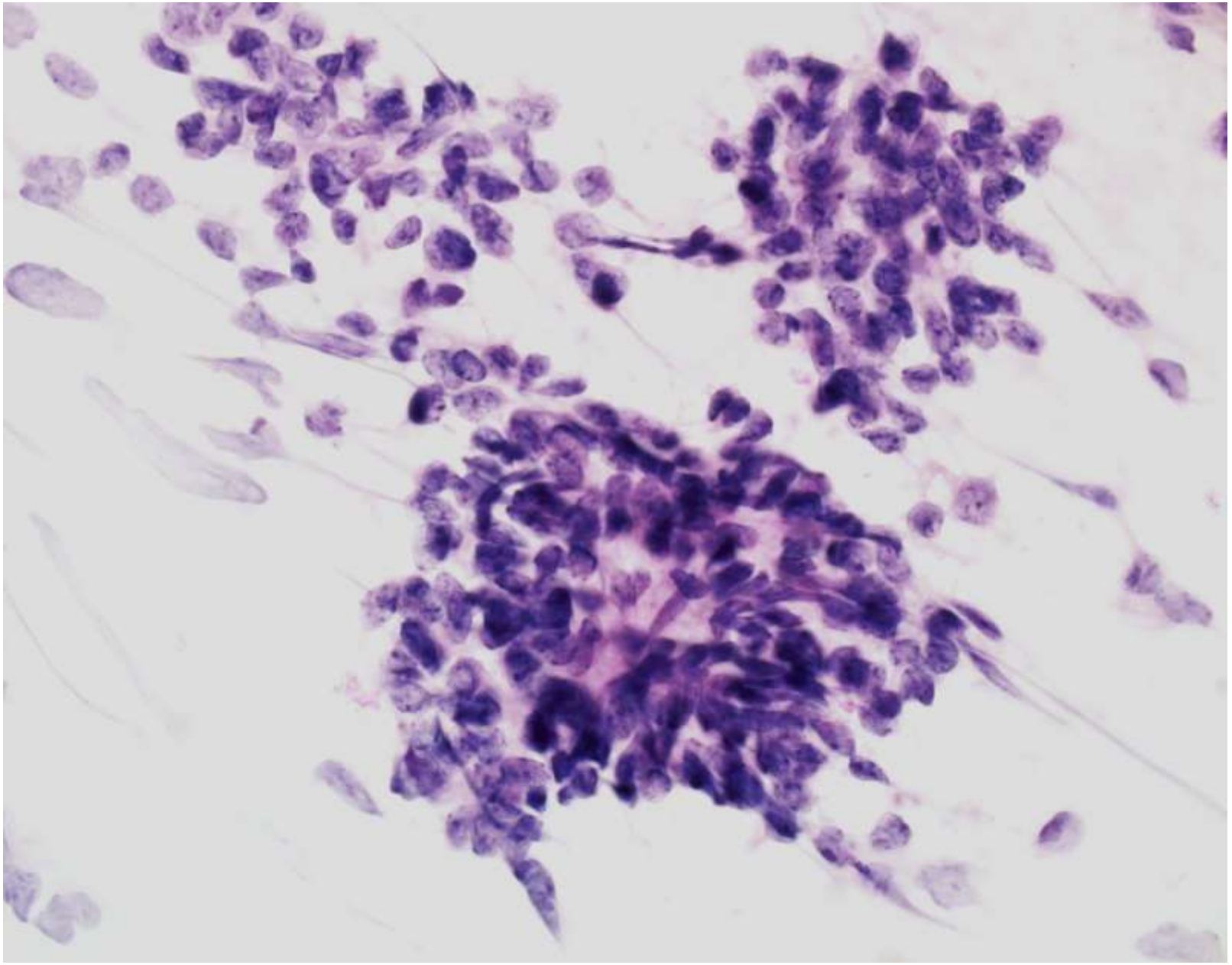
Drs. Emily Chan, Jeffry Simko, Brad Stohr,
Ron Balassanian, Soo-Jin Cho

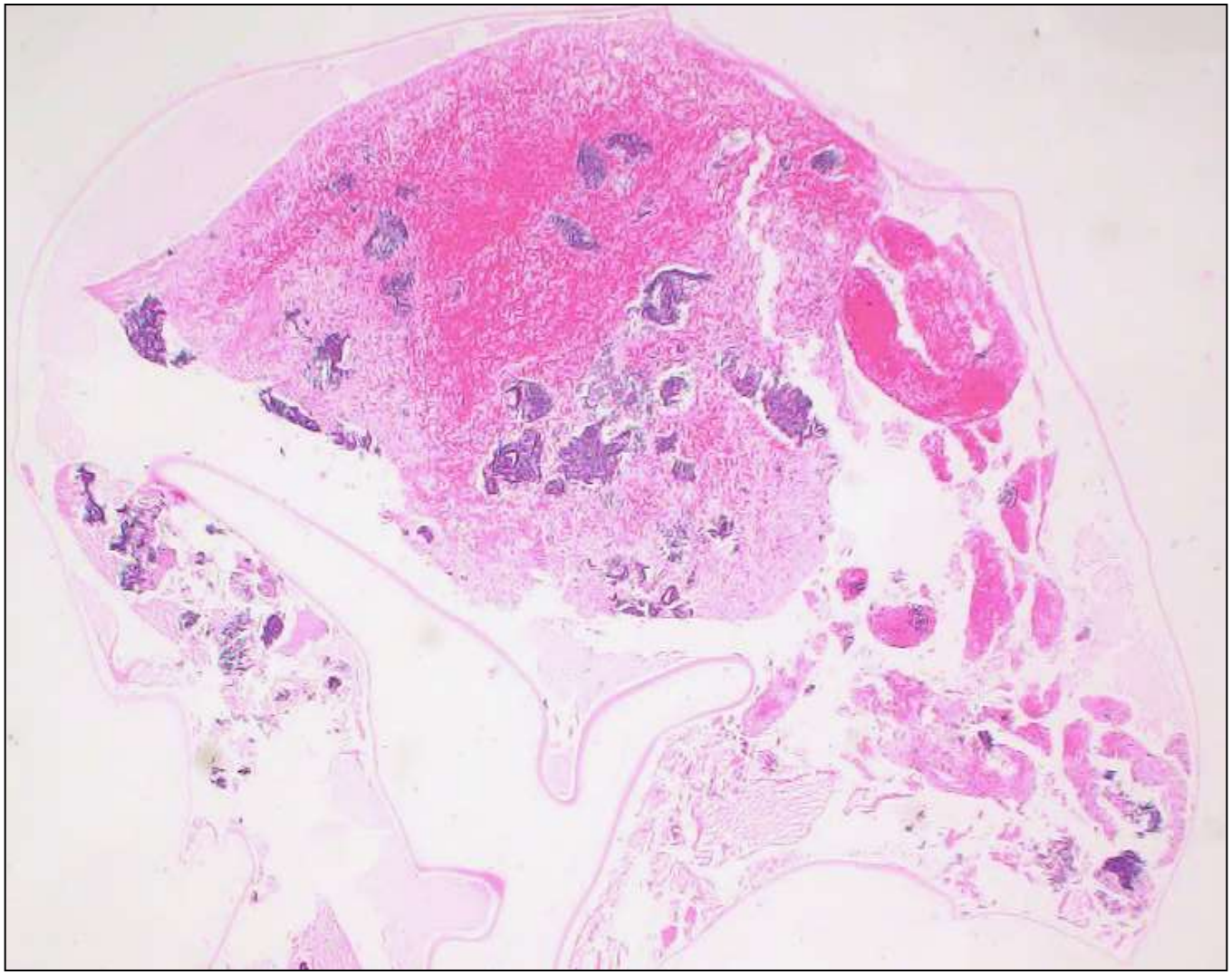
UCSF

Clinical History

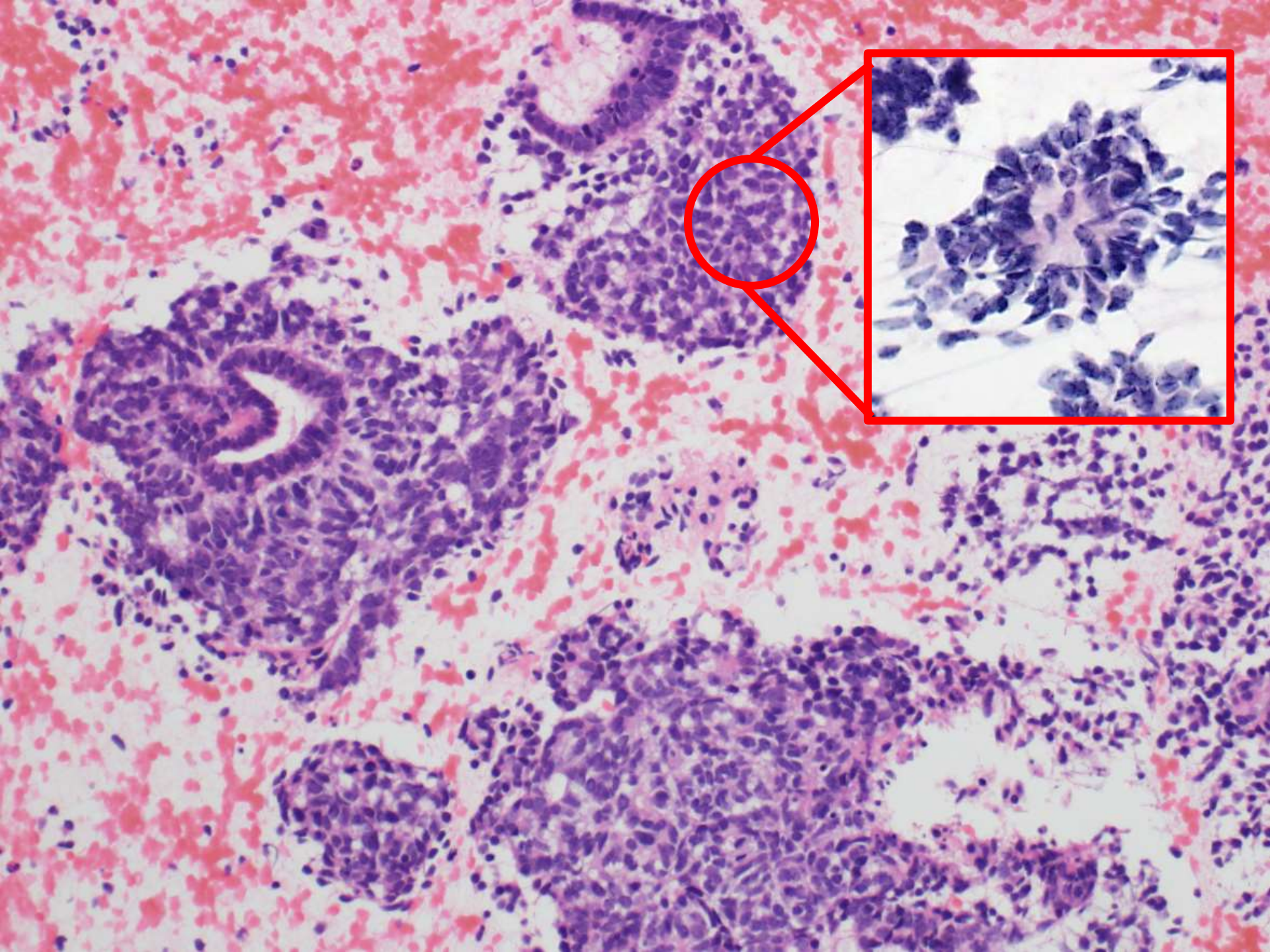
- CT Imaging: Large left renal mass.
  - Para-aortic lymphadenopathy (up to 4.1 cm)
  - Numerous small liver nodules
- Recently diagnosed with papillary thyroid carcinoma, not yet treated.

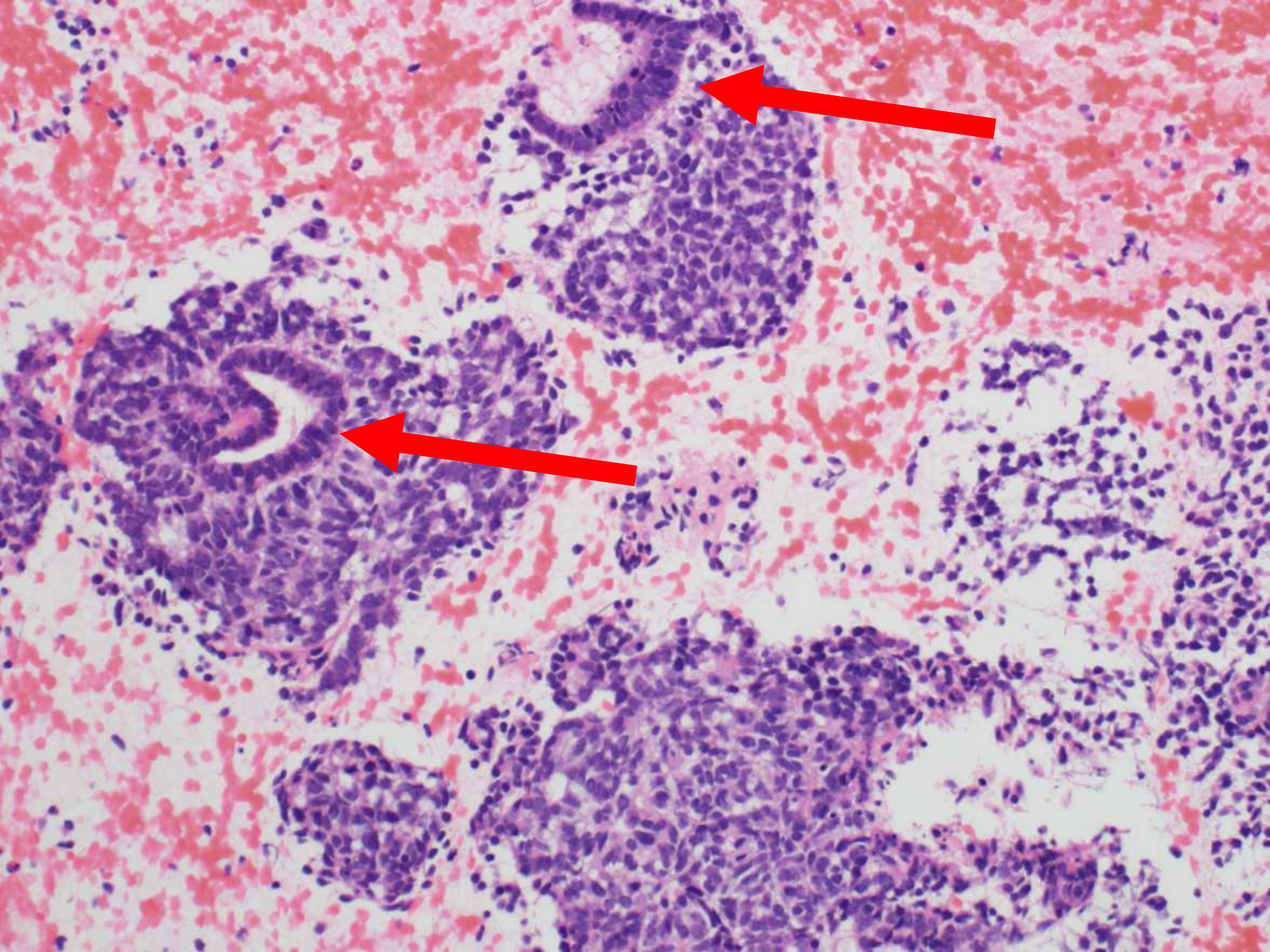


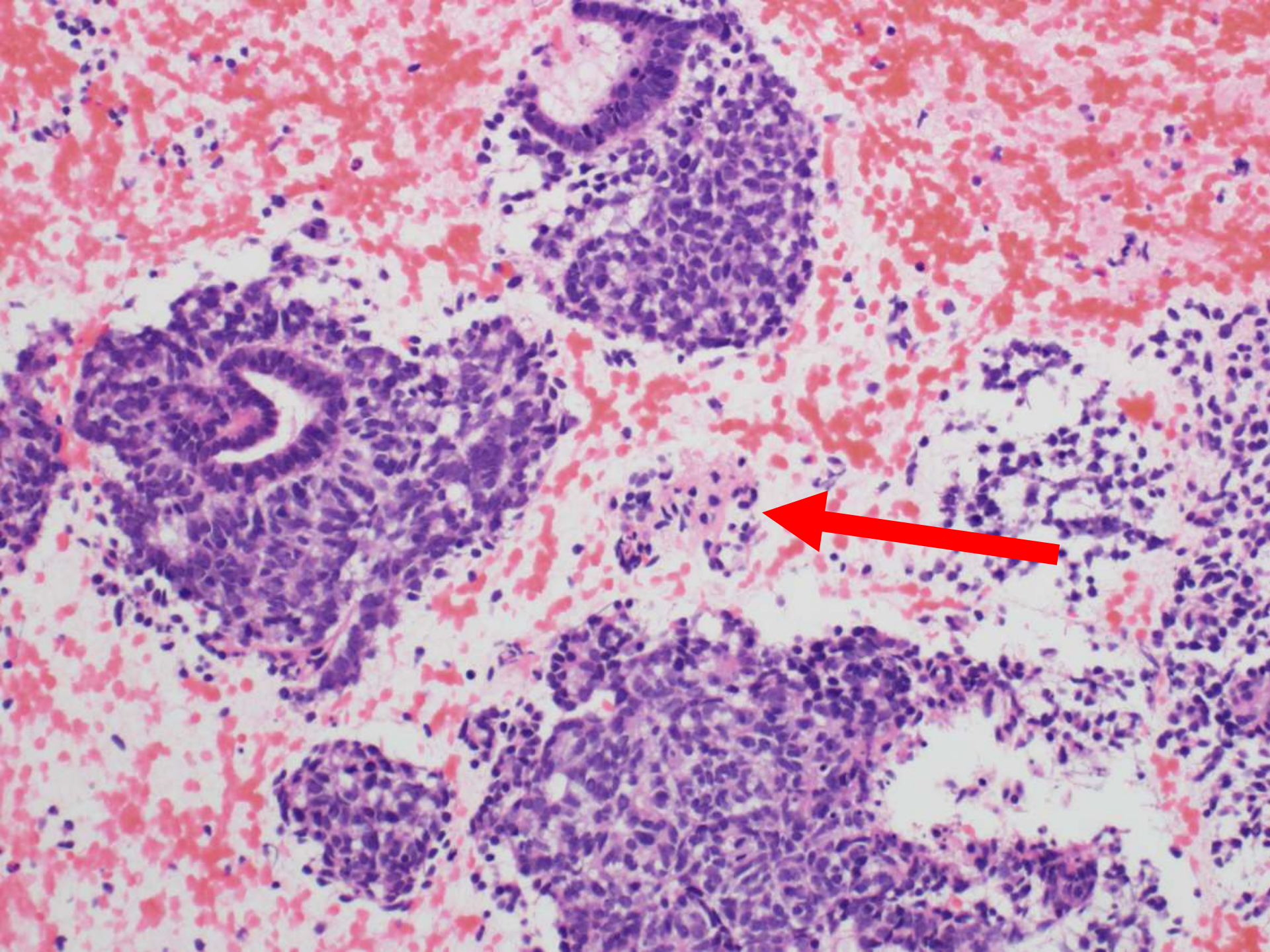




“Core-lets”





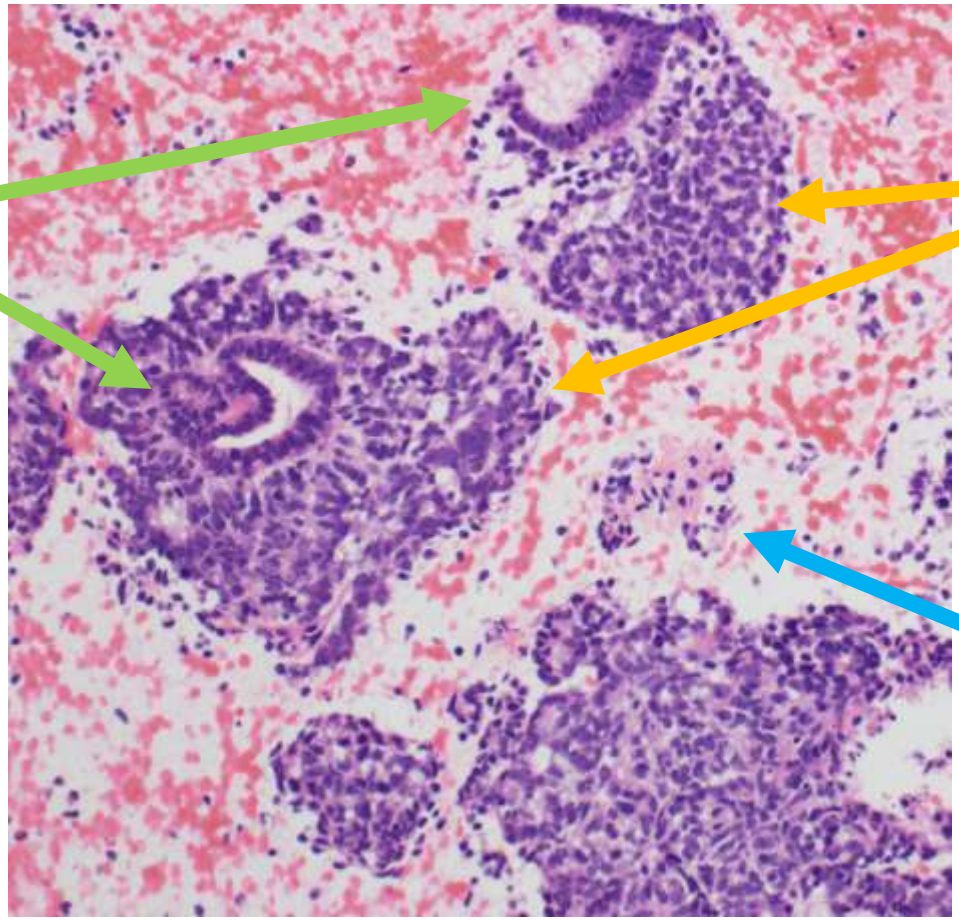


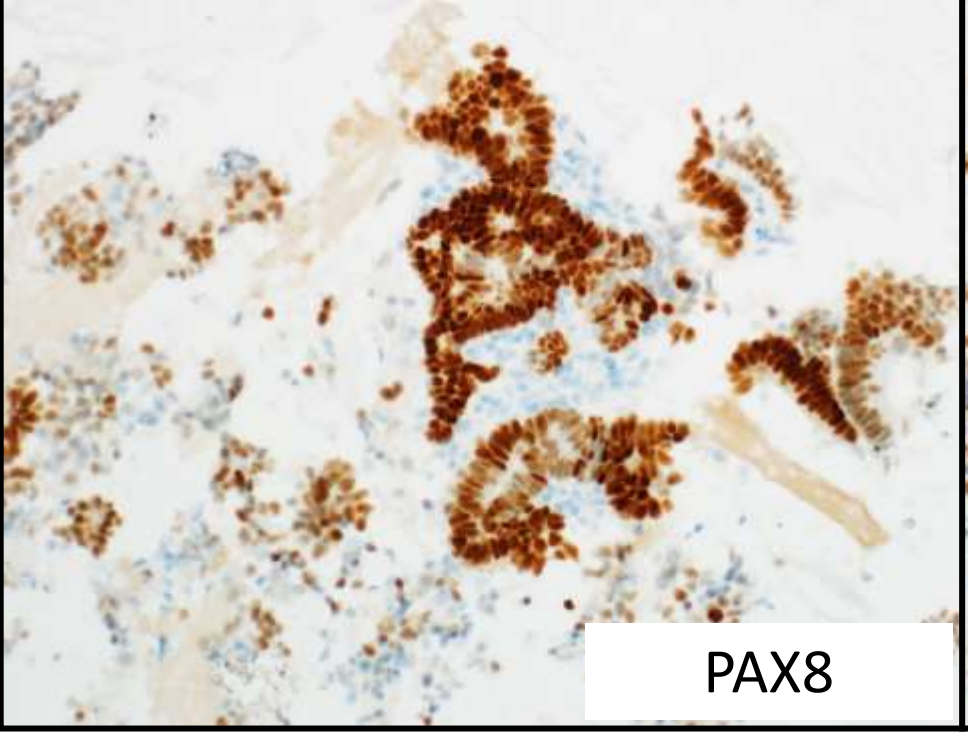
Differential diagnosis

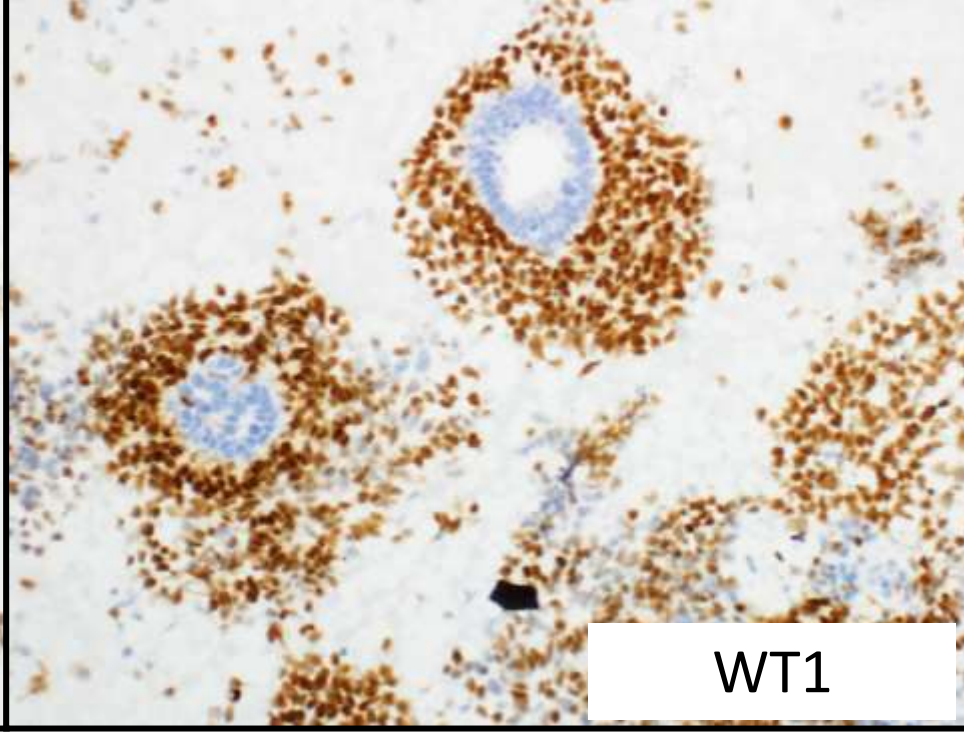
- Small round blue cell tumors
  - Nephroblastoma/Wilms tumor
  - Ewing sarcoma
  - Rhabdomyosarcoma
  - Neuroblastoma
  - Neuroendocrine carcinoma
- Unusual RCC with sarcomatous or poorly differentiated component
- Metastasis (PTC, germ cell tumor, others…)

Diagnosis

Nephroblastoma (Wilms Tumor)







Negative Stains

- Synaptophysin
- Chromogranin
- Neurofilament
- CD99
- Myogenin
- SALL4

Wilms Tumor: Pediatric versus Adult

	Pediatric	Adult
Incidence (of renal tumors)	85% (peak 2-3 yo)	Less than 1%
Genetics	10% genetic/syndromic (e.g. WAGR, Denys-Drash, Beckwith-Wiedemann) 90% sporadic: multiple tumor loci (including WT1, WT2, p53, others)	Sporadic Genetics largely unknown
Treatment	Research protocols (largely based on initial stage and histology) (some also incorporate molecular studies)	
Survival/ prognosis	Overall 70-90% 5 year survival	

Detailed histologic parameters required for further management

Mahmoud F et al. *Perm J*. 2016 ;20(2):e119-21.
Segers H. Expert Rev Anticancer Ther. 2011 Review

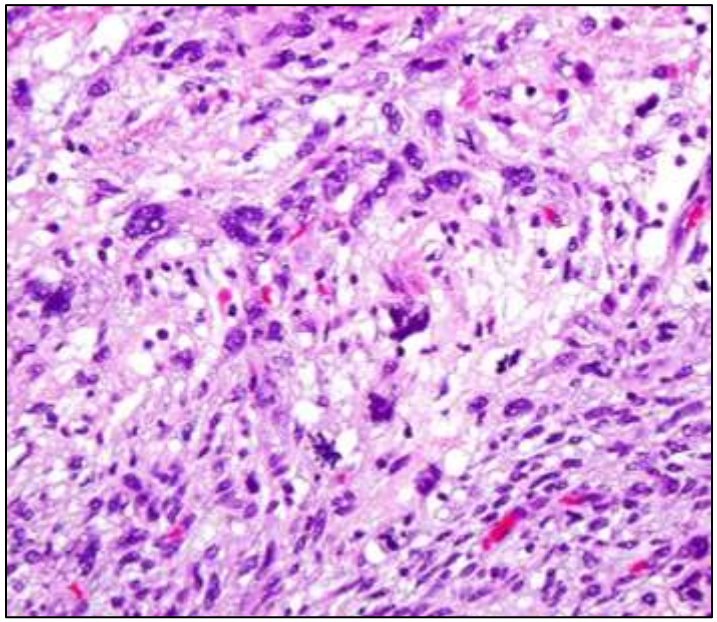
COLLEGE of AMERICAN PATHOLOGISTS

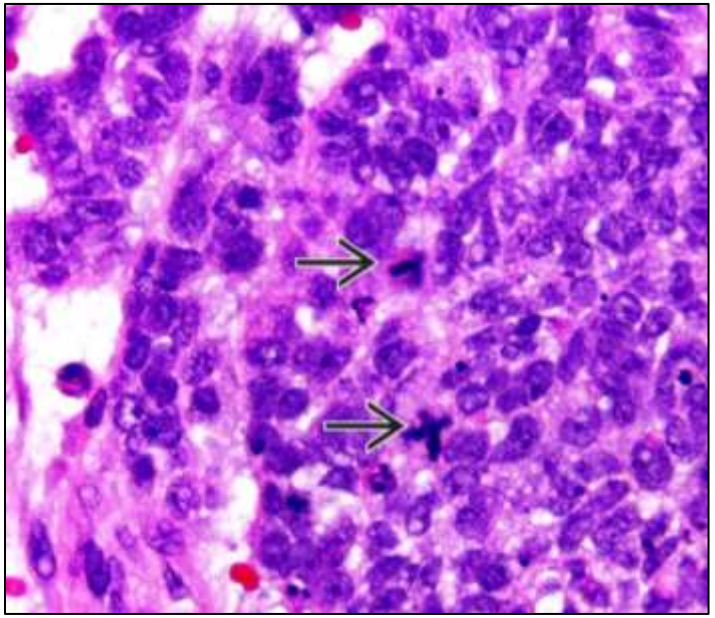
https://www.cap.org/protocols-and-guidelines/cancer-reporting-tools/cancer-protocol-templates

Protocol for the Examination of Resection Specimens From Patients With Wilms and Other Pediatric Renal Tumors

Anaplasia:

- Markedly enlarged nuclei (3x normal) with hyperchromasia
- Atypical mitotic figures
- Report as diffuse vs. focal





Tickoo et al. Nephroblastoma (Wilms Tumor). ExpertPath. 2019 Elsevier.

Important Elements to Include Post-Treatment WT Path report

- % Viable tumor
- % of tumor that is blastemal
- Histology risk groups:
  - Low risk: Completely necrotic tumor
  - Intermediate risk: Viable tumor (<33%) OR viable (>33%) + blastemal histology <66% of viable tumor
  - High risk: Viable tumor (>33%) + blastemal >66%

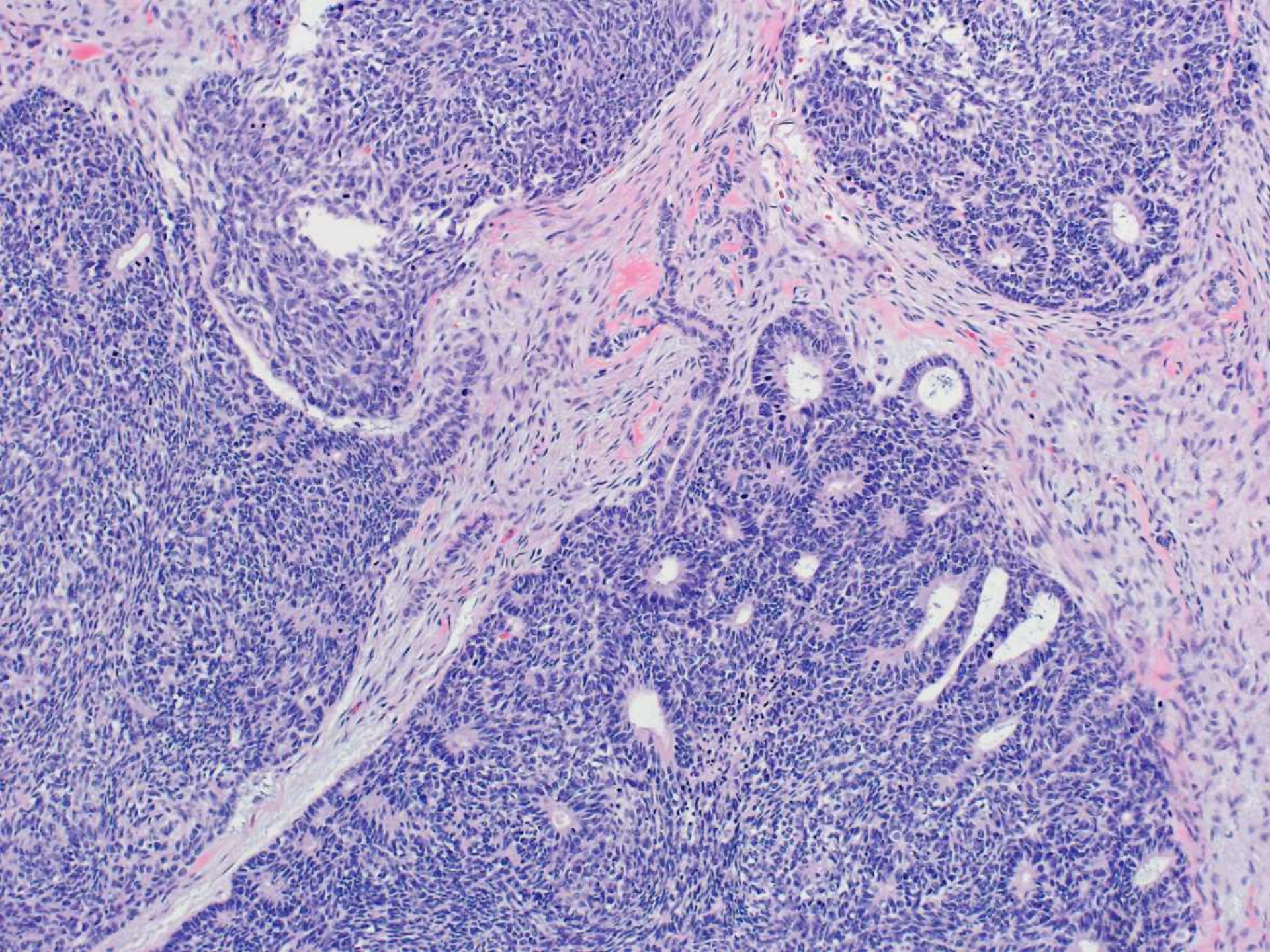
Wilms Tumor: Pediatric versus Adult

	Pediatric	Adult
Incidence (of renal tumors)	85% (peak 2-3 yo)	Less than 1%
Genetics	10% genetic/syndromic (e.g. WAGR, Denys-Drash, Beckwith-Wiedemann) 90% sporadic: multiple tumor loci (including WT1, WT2, p53, others)	Sporadic Genetics largely unknown
Treatment	Research protocols (largely based on initial stage and histology) (some also incorporate molecular studies)	**According to pediatric protocols?**
Survival/ prognosis	Overall 70-90% 5 year survival	**Higher stage and poorer prognosis?**

Mahmoud F et al. *Perm J*. 2016 ;20(2):e119-21.
Segers H. Expert Rev Anticancer Ther. 2011 Review

Patient Follow-up

- Treated per AREN0533 protocol (COG peds protocol)
  - 12 weeks neoadjuvant chemotherapy: vincristine/dactinomycin/doxorubicin
  - Decrease in size of primary tumor and liver lesions by imaging
- Left radical nephrectomy



Our Patient: Follow up

- Liver radiation and additional chemotherapy (37 weeks total)
- Currently no recurrence or metastatic disease on imaging at 20 months post resection
- Total thyroidectomy – PTC
  - Radioactive iodine

Summary

- Adult Wilms tumors occurs, but rarely.
- Recognize triphasic morphology and think about Wilms tumor, even in adults!
- Refer to CAP synoptic guidelines for reporting WT and don’t forget anaplasia.
- In treated WT cases, report % viable, % blastemal.

19-0609

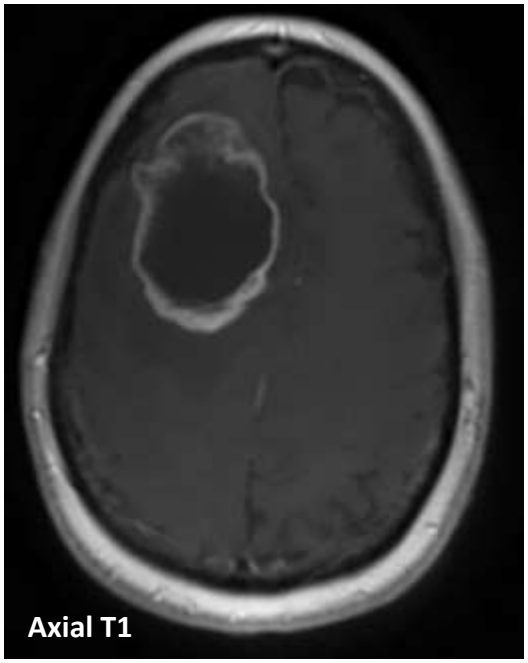
Romain Cayrol/Hannes Vogel; Stanford

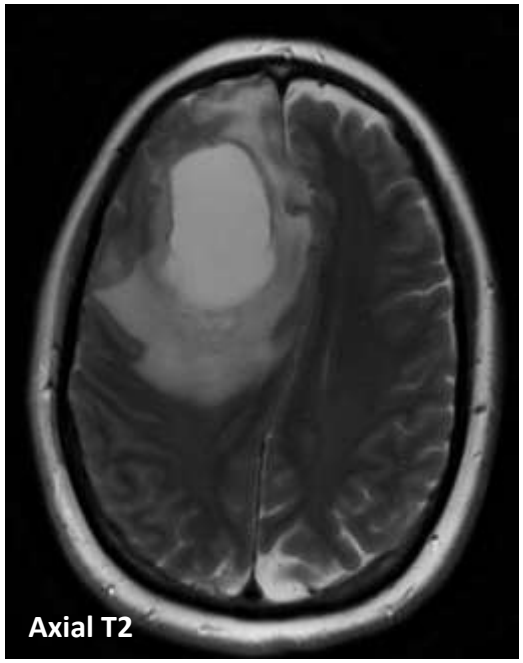
63-year-old female who presented with 3 weeks of weakness and decreased dexterity of left upper extremity and increased tendency to fall towards the left. Patient has history of hypertension, melanoma, and basal cell carcinoma of nose. Imaging: cystic/necrotic 5.4cm mass in right frontal lobe.

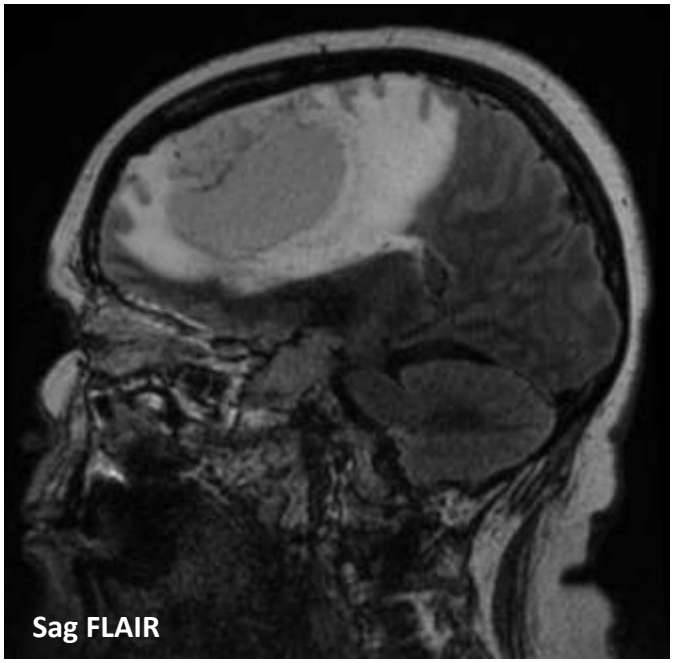
Clinical history

- 63-year-old female who presented with 3 weeks of weakness and decreased dexterity of the left upper extremity and increased tendency to fall towards the left
- The patient has a history of hypertension, melanoma and basal cell carcinoma of the nose

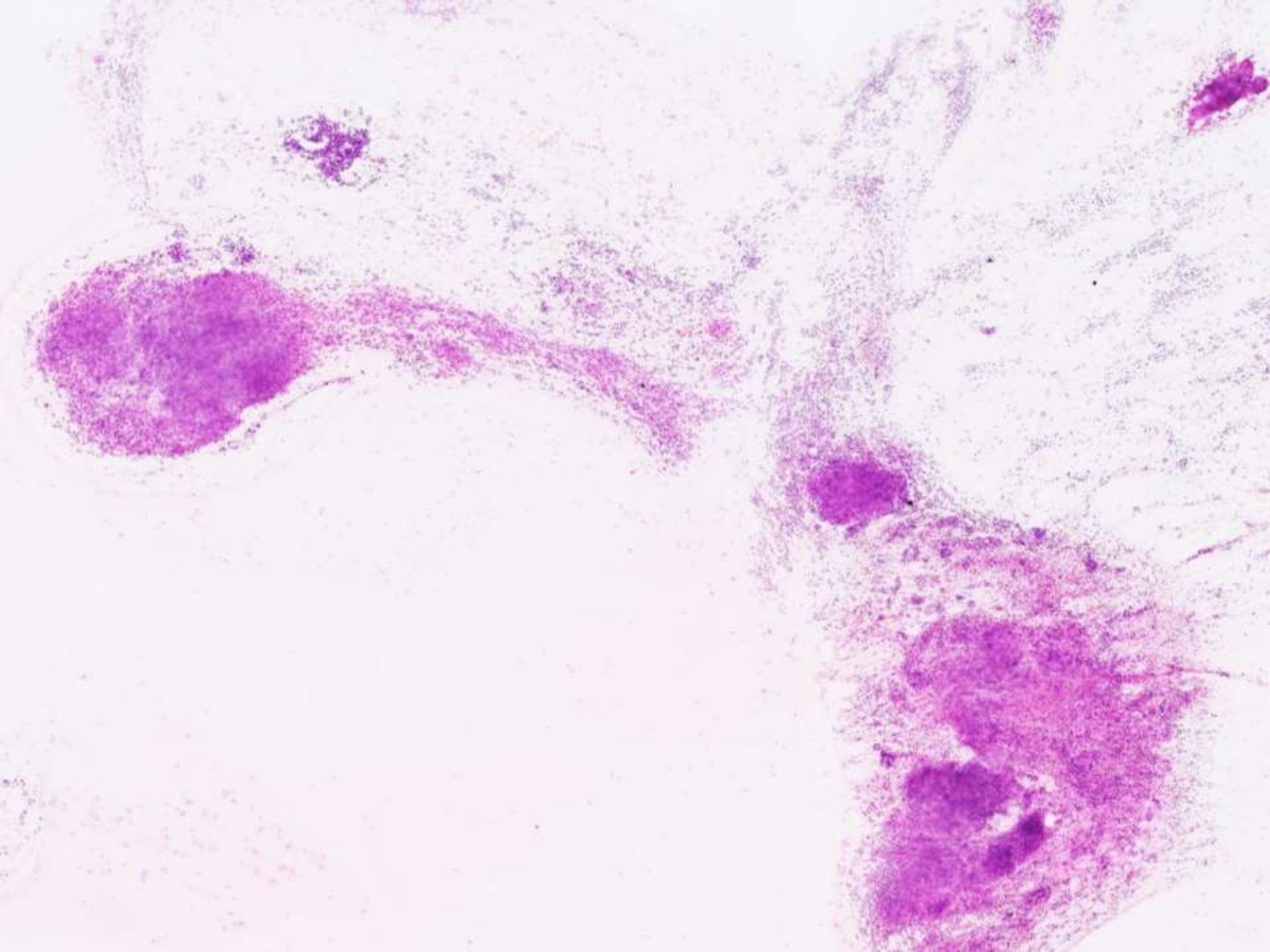
Imaging

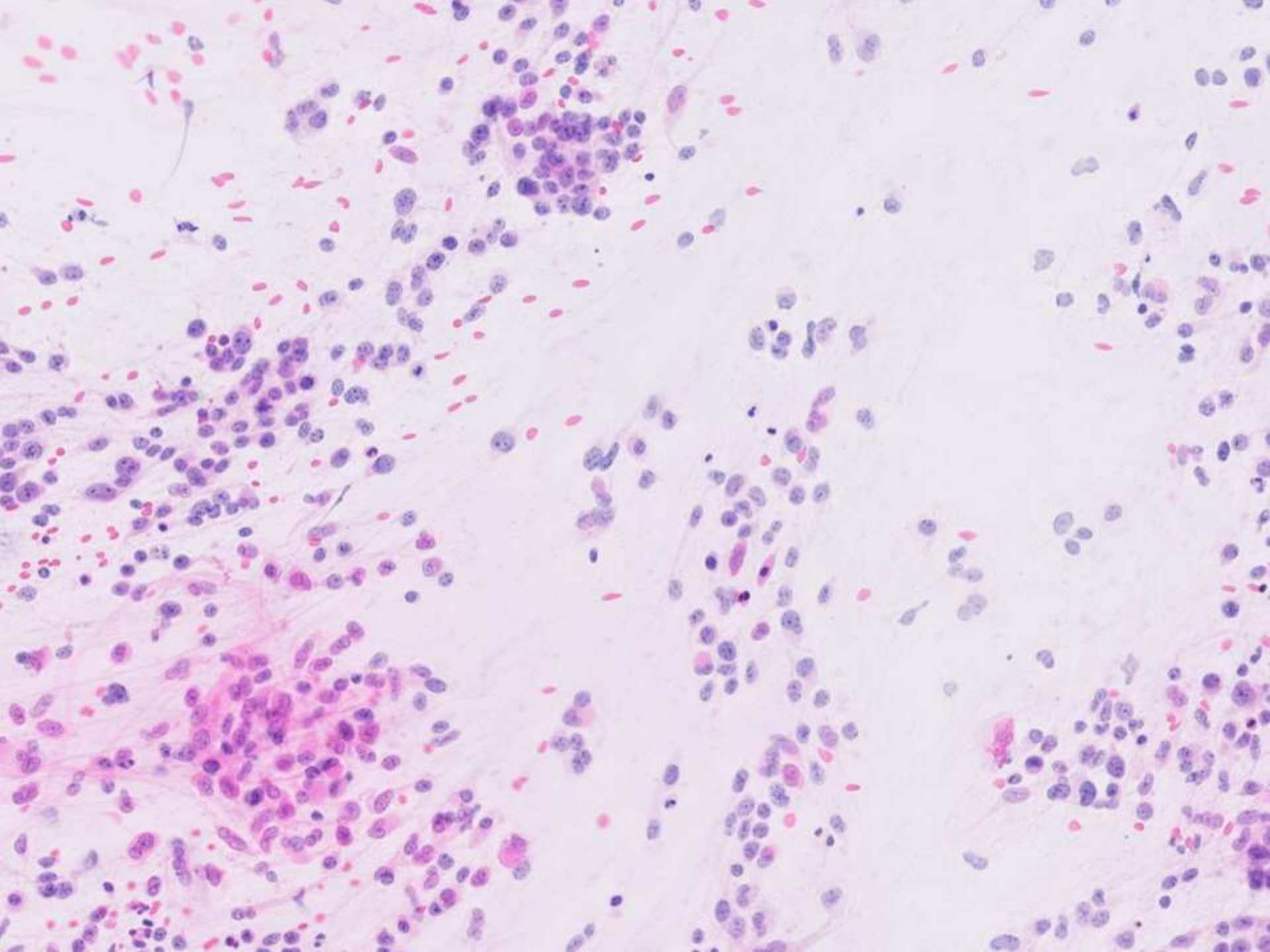


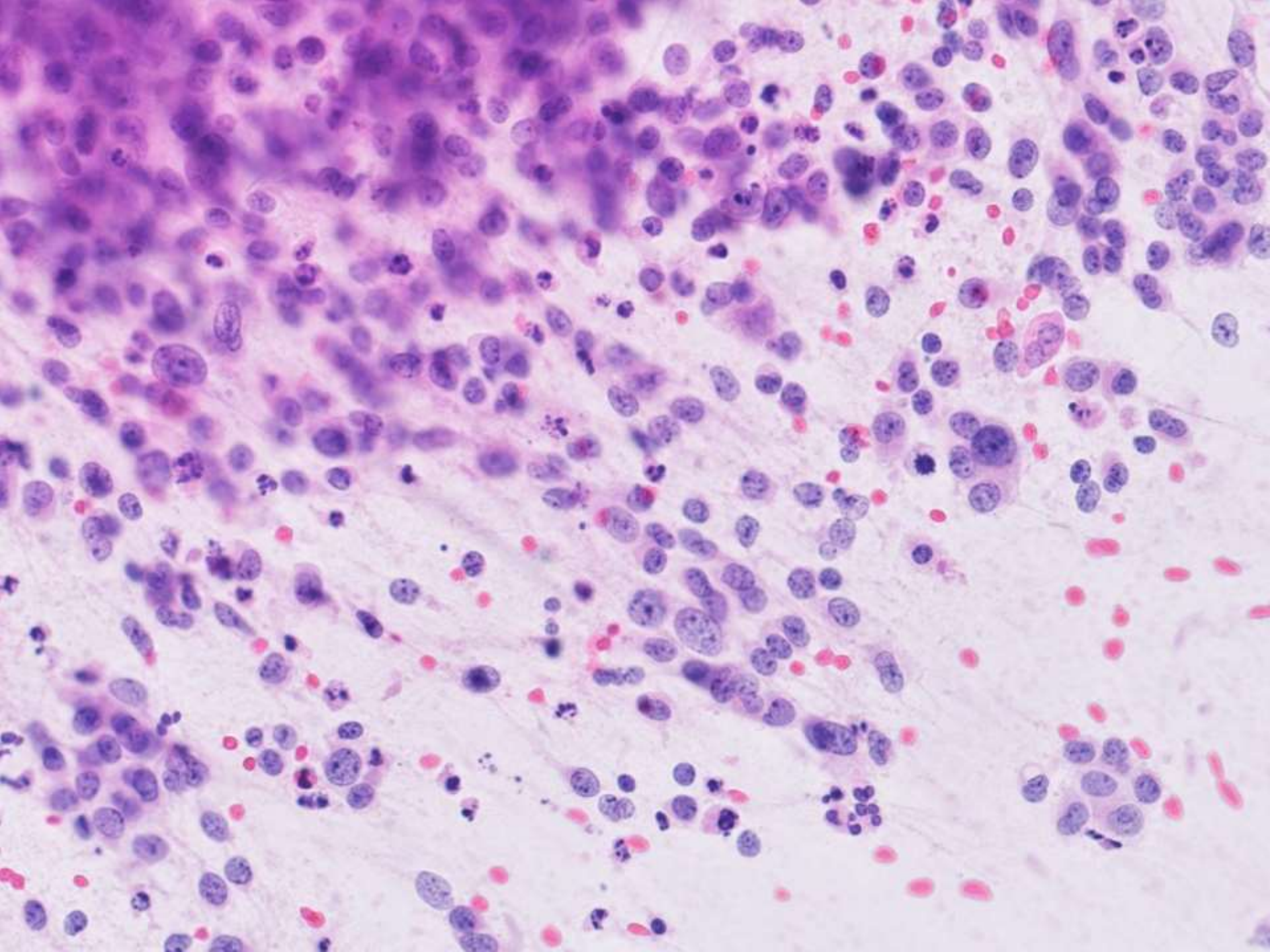


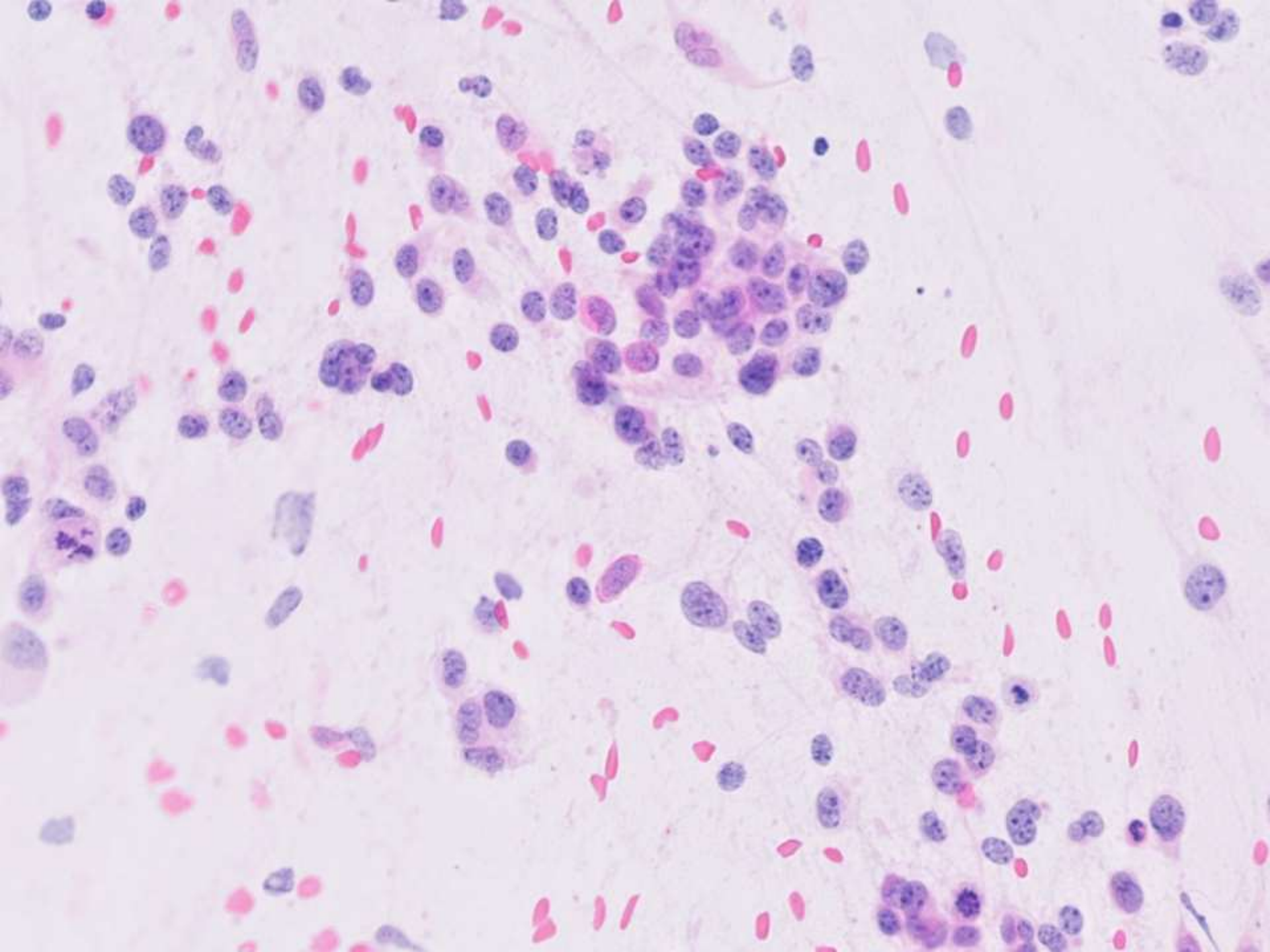


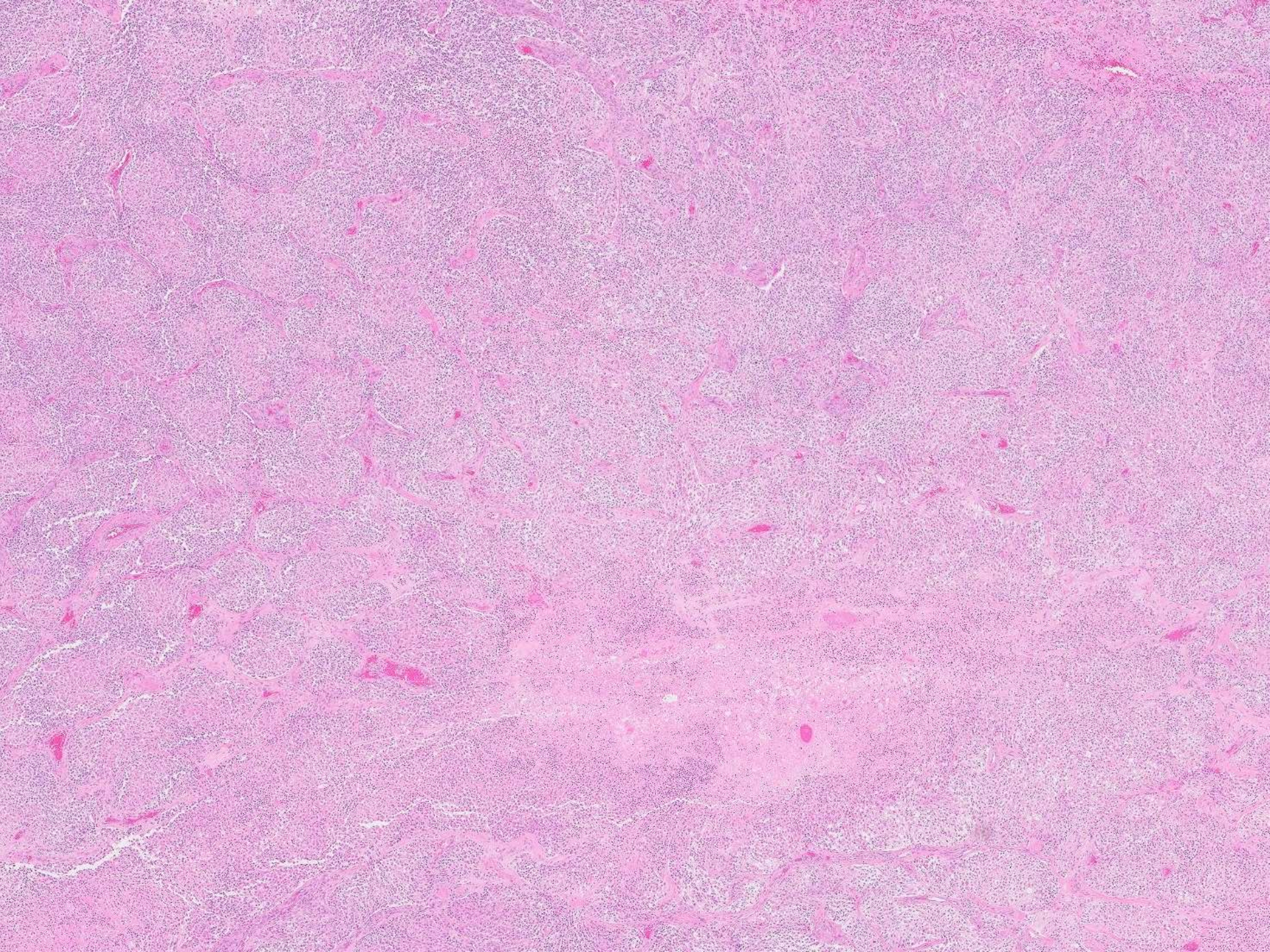
- Irregular cystic/necrotic mass, 5.4 x 4.1 x 3.2 cm, right frontal lobe
- Irregular and nodular rim enhancement with vasogenic edema and mass effect

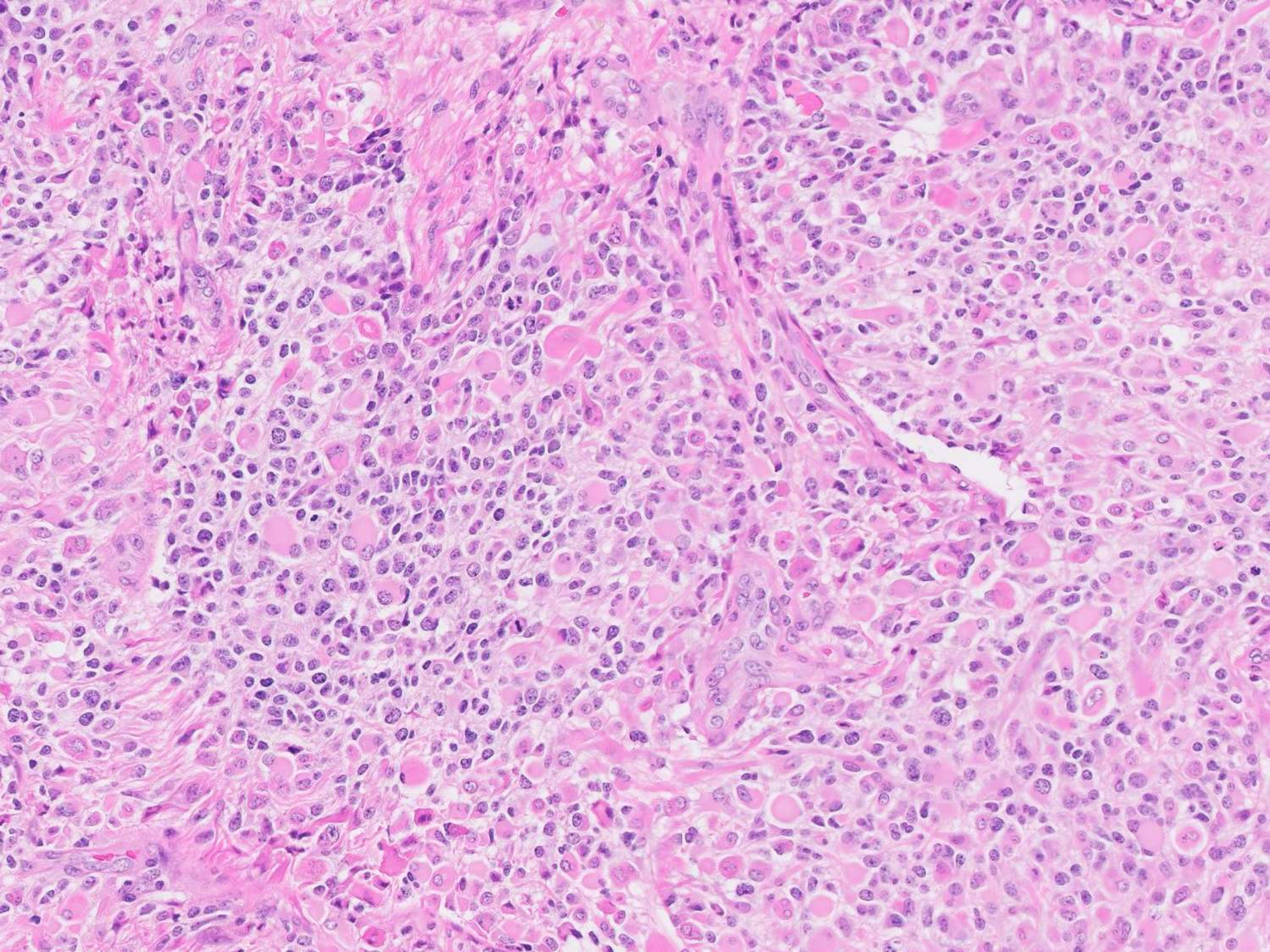


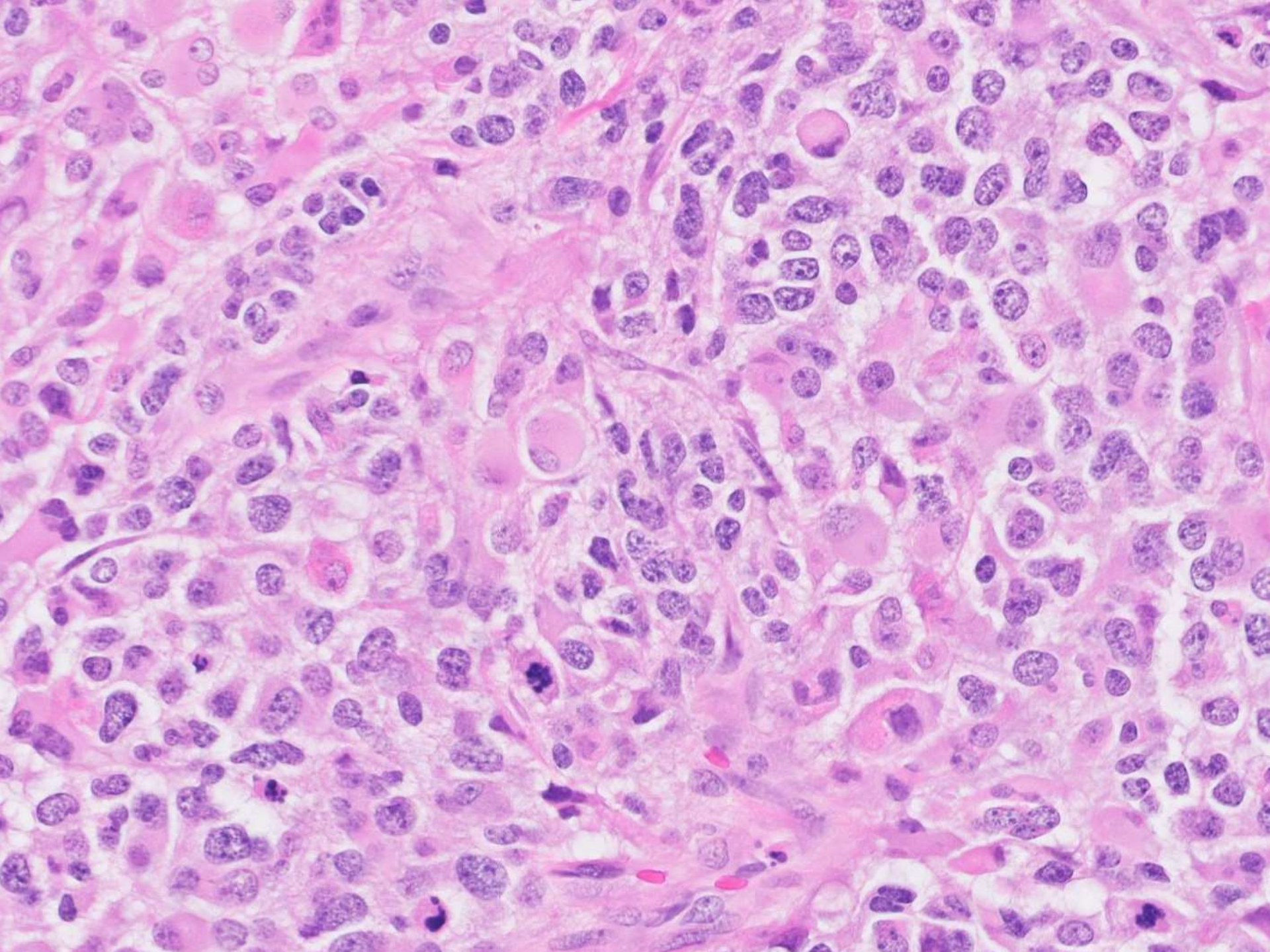


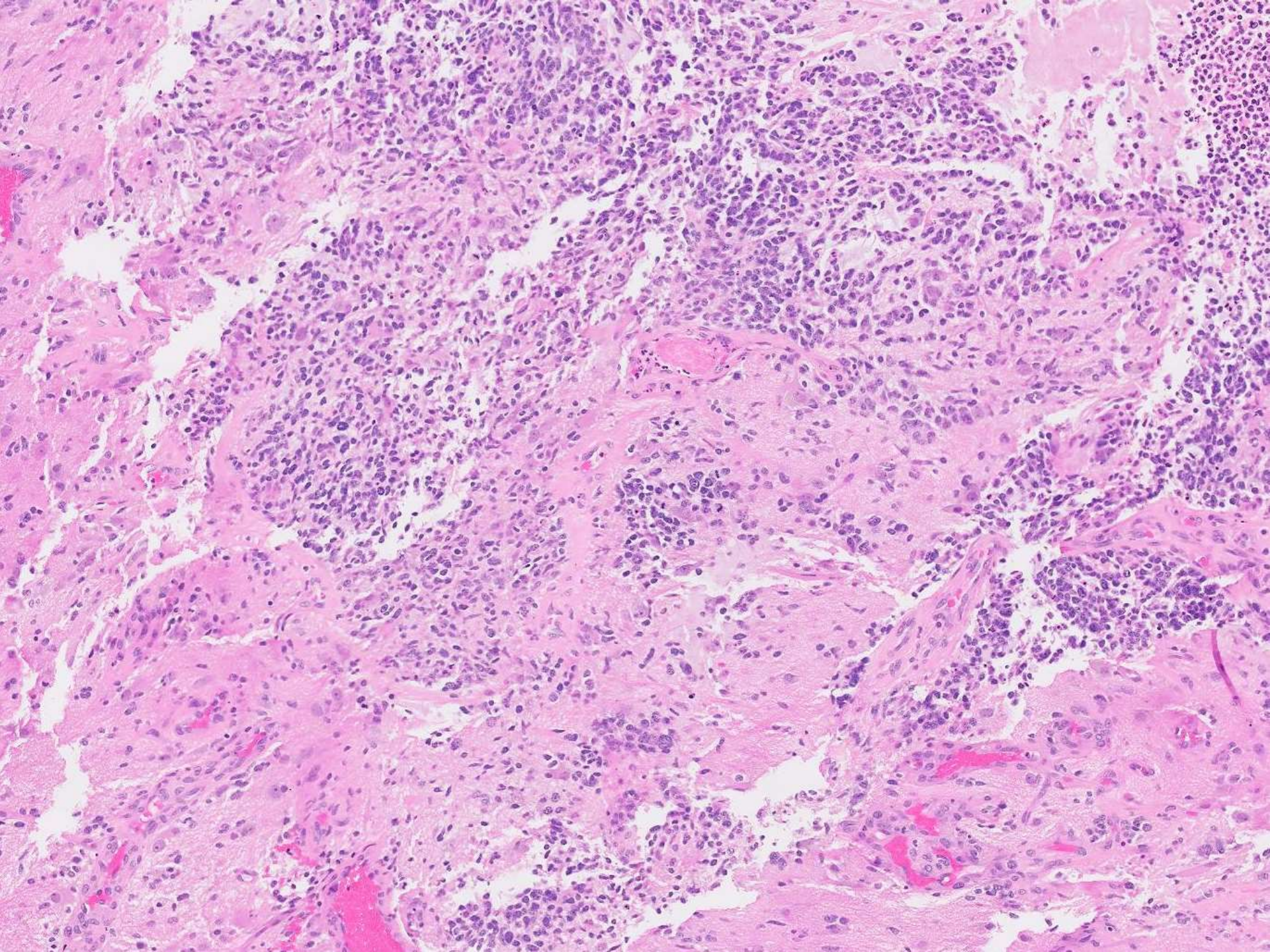


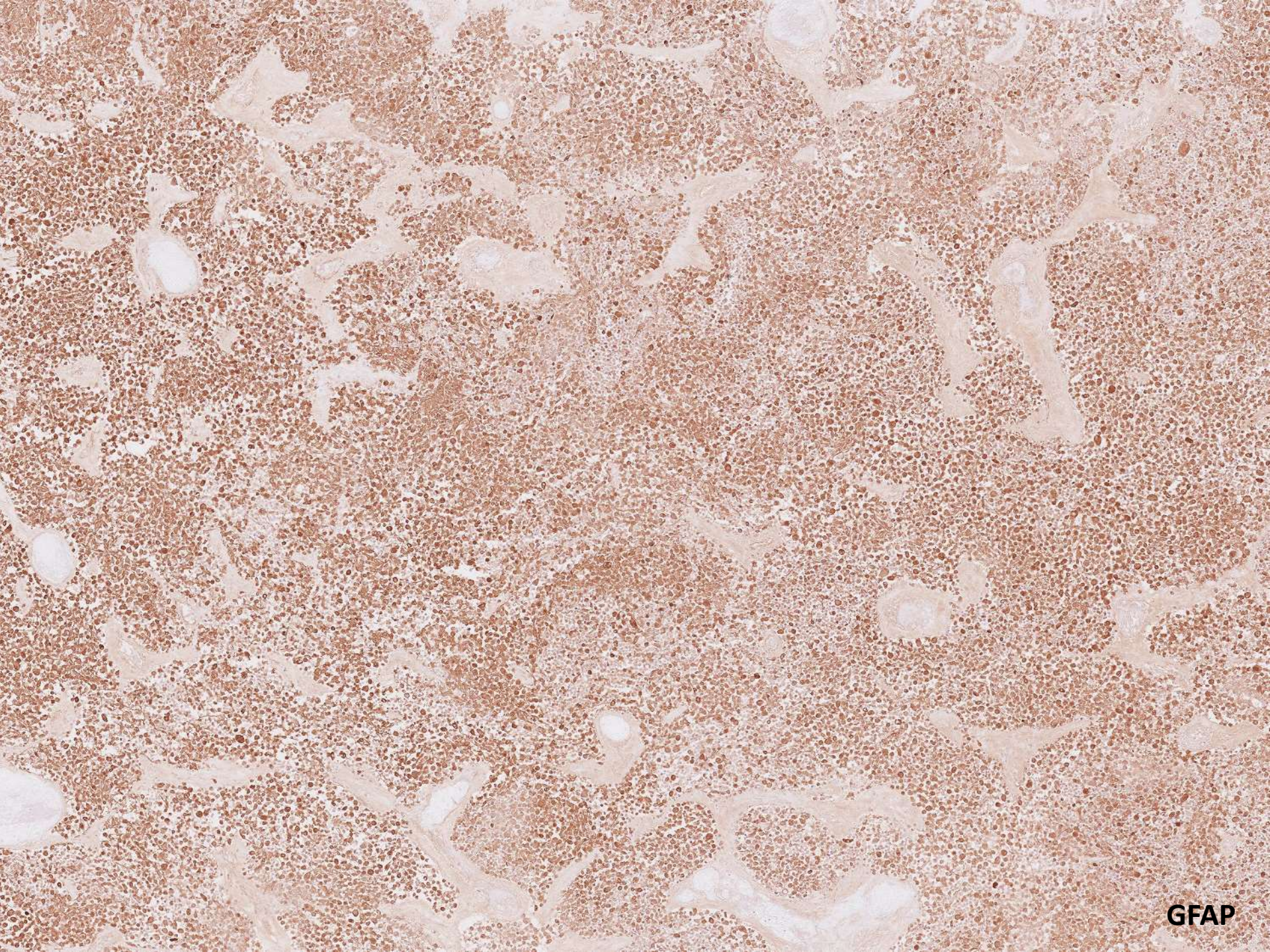


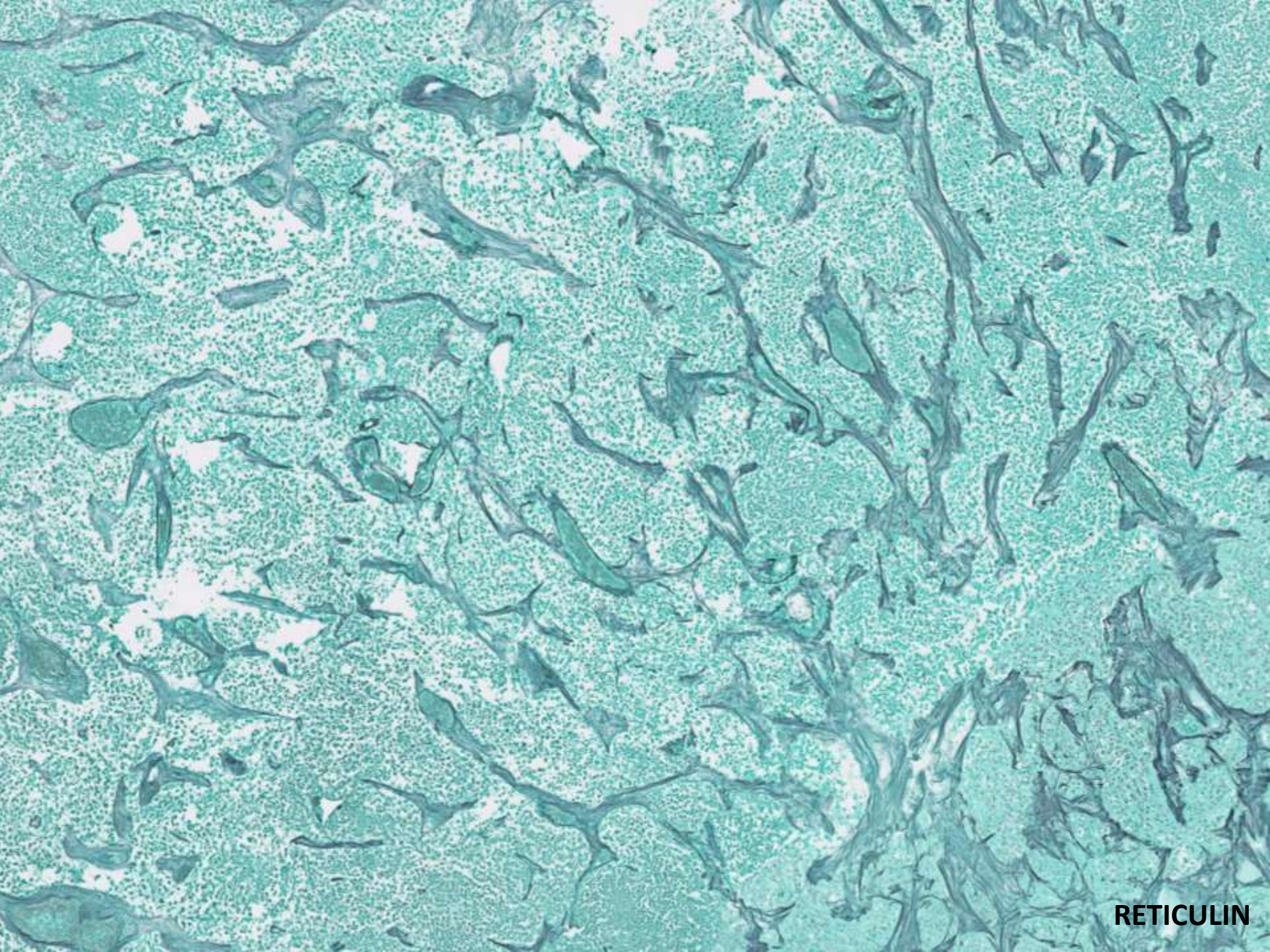


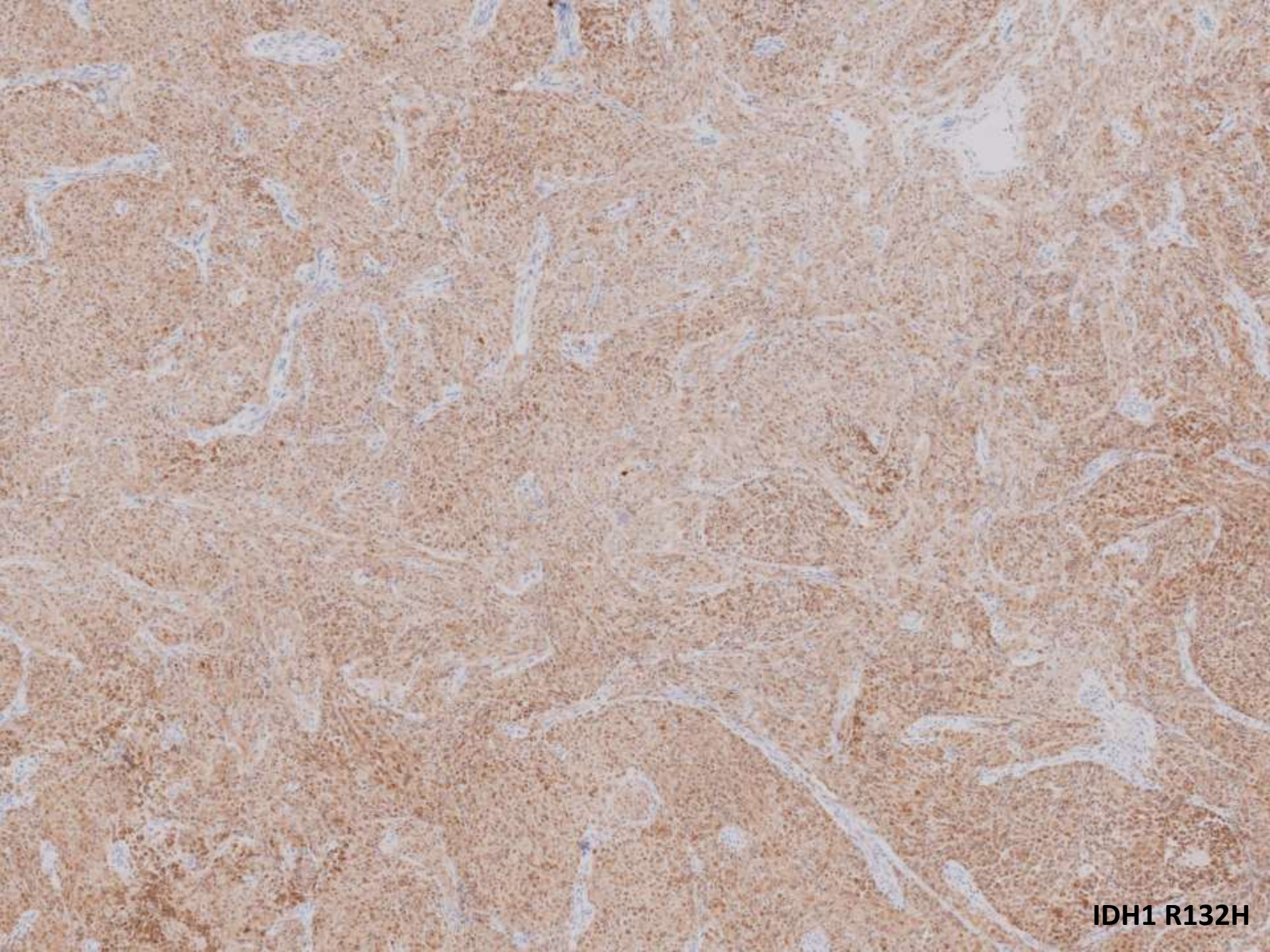




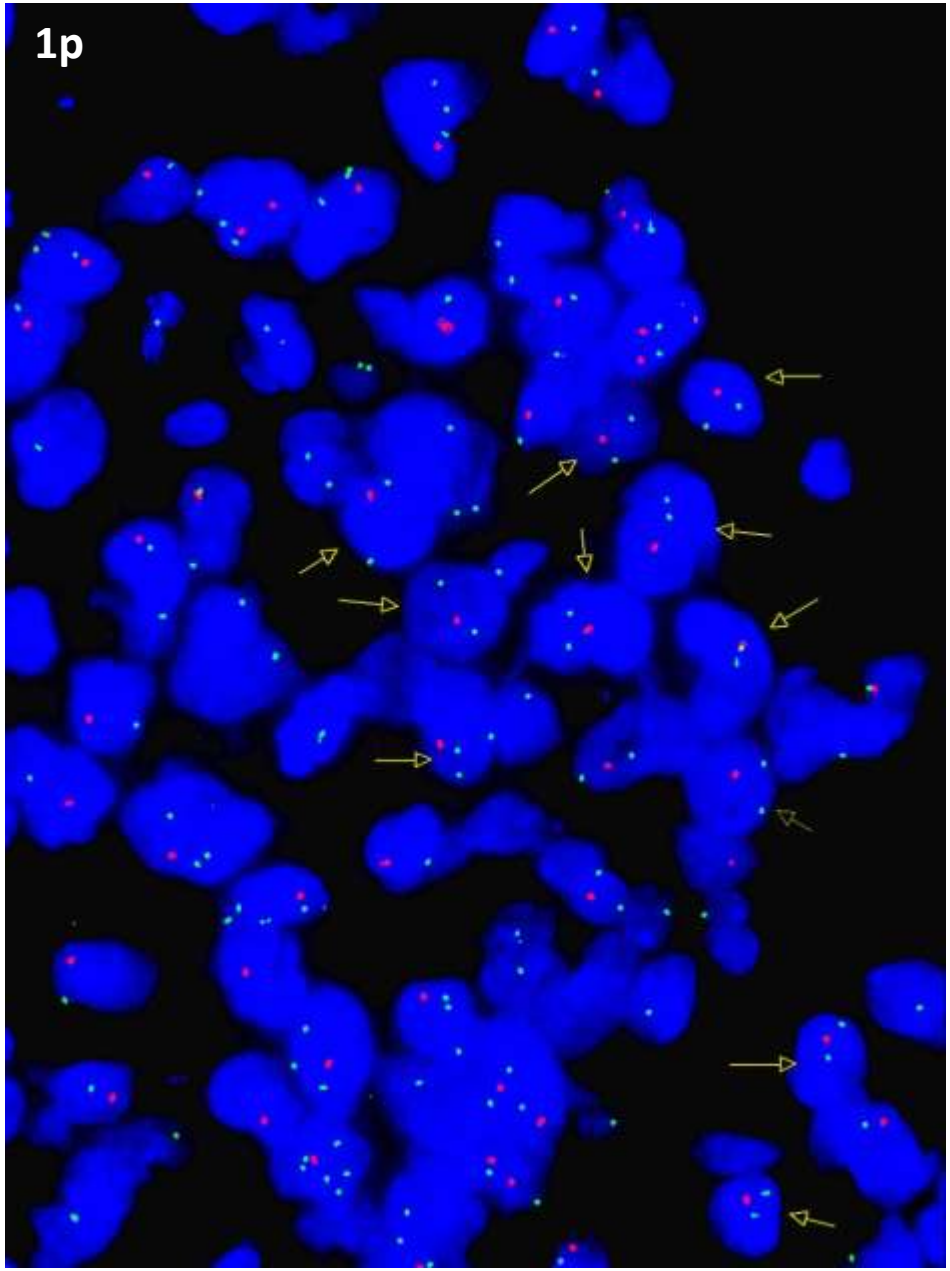


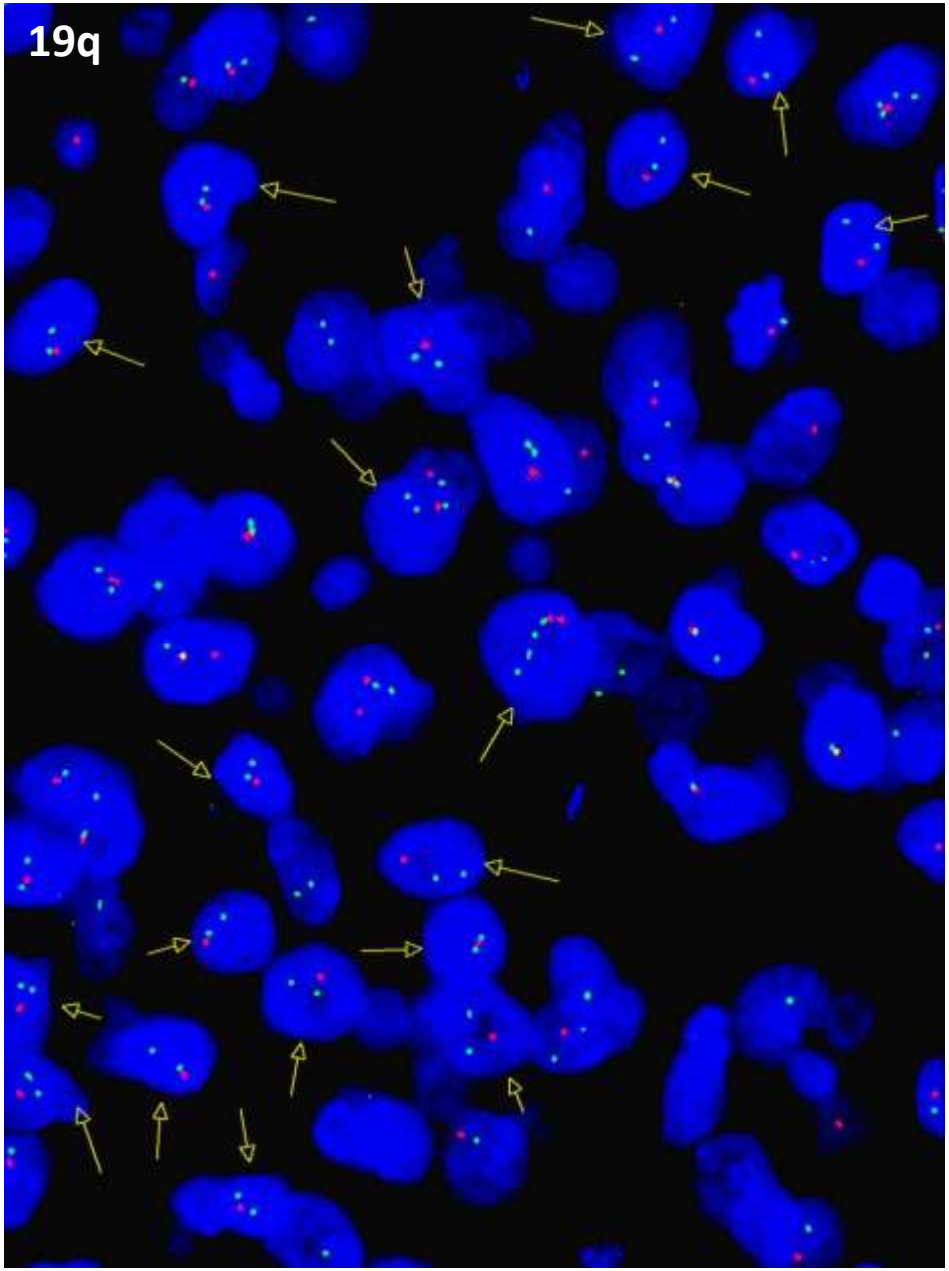

GFAP


RETICULIN


IDH1 R132H

ATRX is conserved, p53 is non mutated



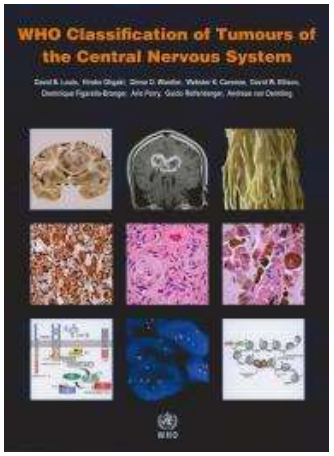


Diagnosis

- **BRAIN TUMOR, RESECTION**

-- **ANAPLASTIC OLIGODENDROGLIOMA, IDH1 R132H MUTANT, 1p/19q CO-DELETED, WHO GRADE III**

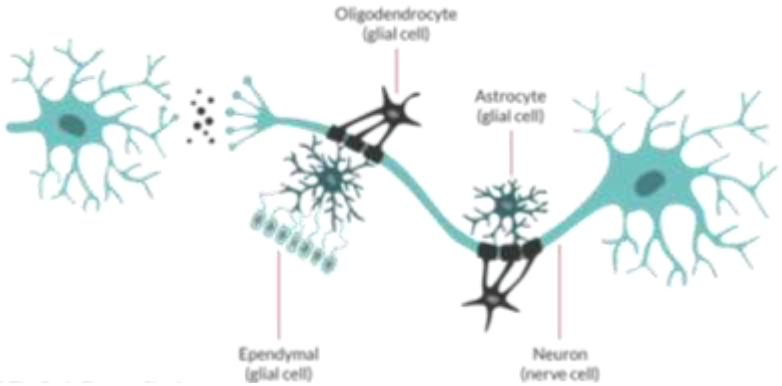
Oligodendroglioma



- Diffuse glioma with IDH1/2 mutation and 1p/19q co-deletion
  - 0.26 cases per 100 000 population, 1.7% of all primary brain tumors
  - Mostly seen in adults (35-45 years old), rare in the pediatric population
  - Preferentially in the white matter and cortex of the cerebral hemispheres (often involves the frontal lobe)

- Clinical presentation: seizures, headache, intracranial pressure increase

- Imaging: T1 hypointense and T2 hyperintense, well demarcated lesion, calcifications are common, +/- cystic degeneration, gadolinium enhancement is rare (20%)

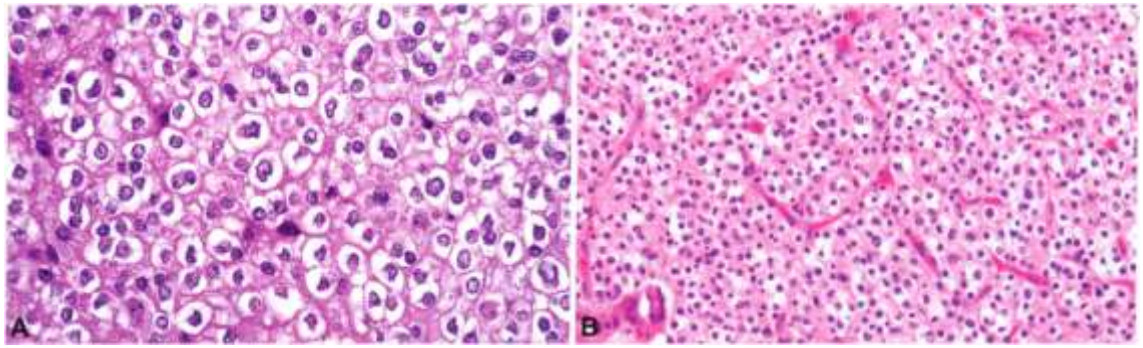


Oligodendroglioma

- Histology: Oligodendroglial like cells with round nuclei, swollen clear cytoplasm on FFPE, microcalcification, small branching vessels (chicken wire), +/- nodular growth
  - MAP2, S100, GFAP, Olig2, Sox10, Ki67 <5%, H3K27me3 loss
  - ATRX conserved and p53 wildtype

- Defined molecularly by IDH1/2 mutation and 1p/19q co-deletion
  - CIC gene chromosome 19 (?) and FUBP1 gene chromosome 1 (?)
  - TERT mutation, hypermethylation, POT1 gene (familial oligodendroglioma)
  - Pediatric cases lack IDH mutations and 1p/19q co-deletion

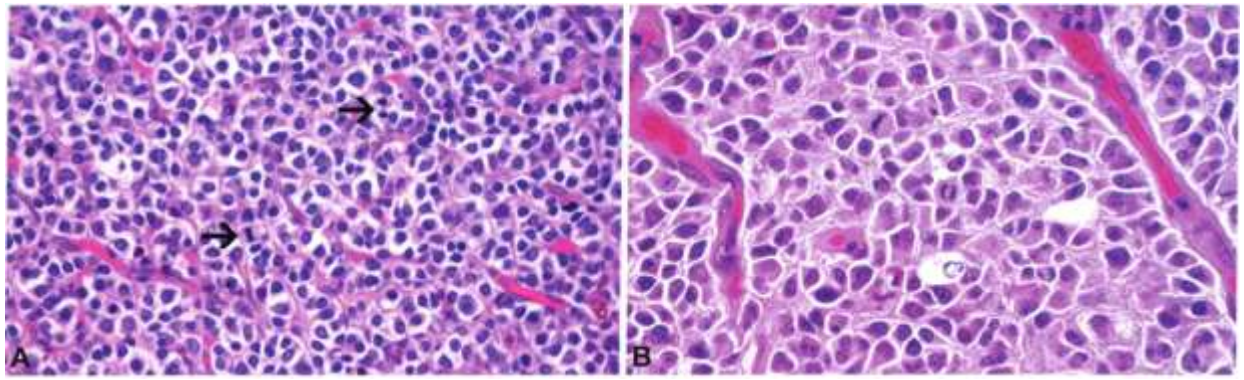
- Prognosis: slow growing tumor with risk of local recurrence, 11 to 15 years median survival
  - Younger patient, frontal tumor, seizures, lack of contrast enhancement, high Karnofsky, gross total resection



Louis D et al, WHO Classification of Tumours of the CNS, 2016

Anaplastic Oligodendroglioma (OA)

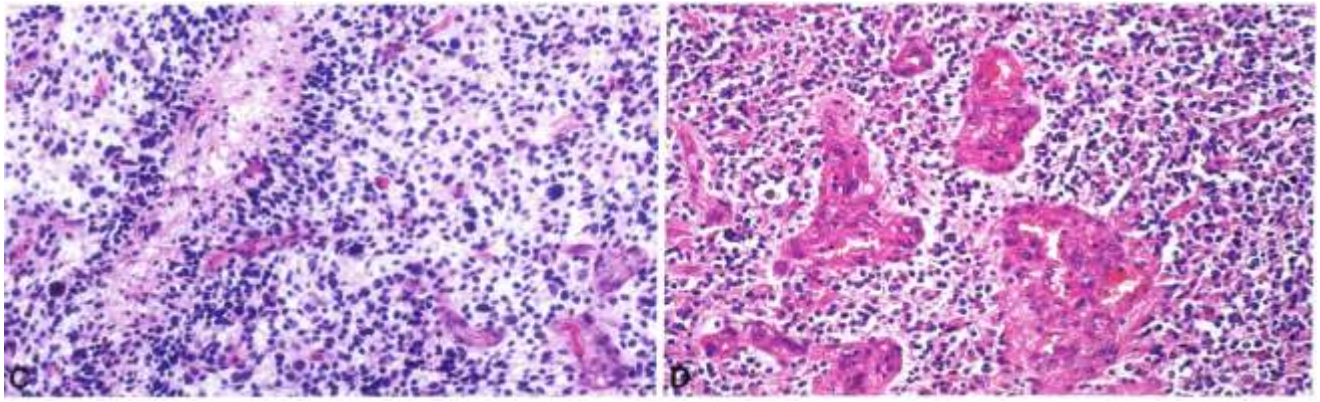
- Diffuse glioma with IDH1/2 mutation and 1p/19q co-deletion and anaplastic features
  - 1/3 to 1/4th of all ologidendrogliomas, seen in adults (median 49 years old), never described before 14 years of age
- Clinical presentation: focal neurologic or cognitive deficits, intracranial pressure increase
- Imaging: Contrast enhancement is common (70%, ring enhancement is uncommon)



Louis D et al, WHO Classification of Tumors of the CNS, 2016

Anaplastic Oligodendroglioma (OA)

- Histology: hypercellular, infiltrating glioma with oligodendroglial like cells and focal or diffuse anaplastic features
  - Mitoses (>5 per 10 HPF), microvascular proliferation, +/- necrosis
  - Ki67 >5%, p53 can be positive (mutated)
- Defined molecularly by IDH mutation and 1p/19q co-deletion
  - Pediatric cases lack IDH mutations and 1p/19q co-deletion
- Prognosis: slow growing tumor with risk of local recurrence, 3-8 years median survival and 10-12 years in some studies
  - Younger patient, high Karnofsky, gross total resection

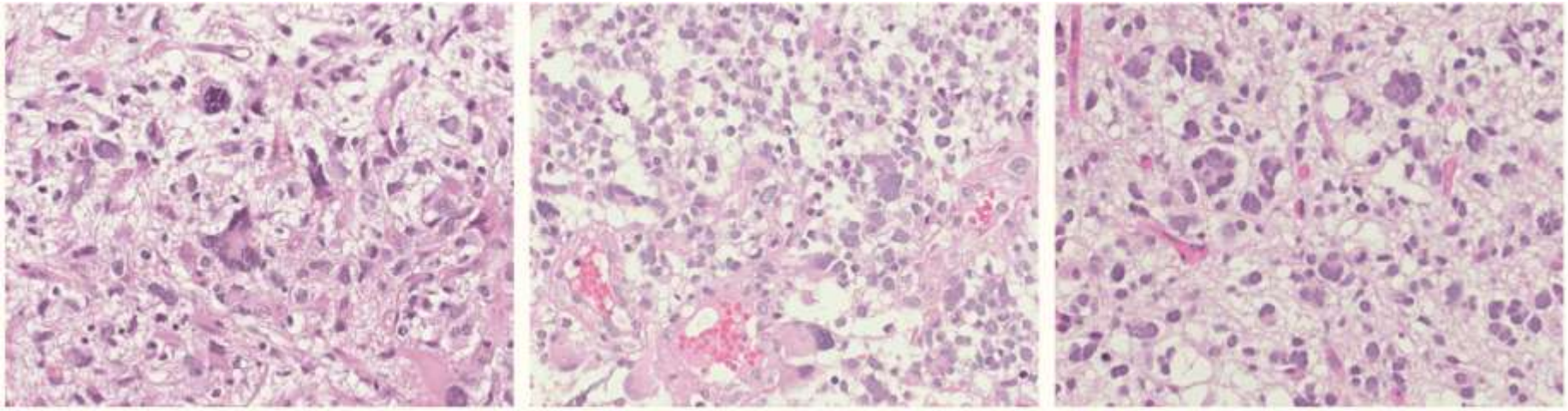


Louis D et al, WHO Classification of Tumors of the CNS, 2016

Gene	Change	% of cases	References
IDH1/IDH2	Mutation	100%	[3462464]
1p/19q	Codeletion	100%	[3462464]
TERT	Promoter mutation	> 95%	[3462464]
MGMT	Promoter methylation	> 90%	[17332731]
CIC	Mutation	~60%	[3462464]
CDKN2A/p14ARF	LOH	~40%	[454]
CDKN2A/p14ARF	Promoter methylation	15–30%	[27102A,2775]
FUBP1	Mutation	~30%	[3462464]
NOTCH1	Mutation	20–30%	[3462464]
PIK3CA	Mutation	10–20%	[3462464]
PIK3R1	Mutation	~9%	[3462464]
TCF12	Mutation	7.5%	[1467]
ARID1A	Mutation	~7%	[3462464]
CDKN2C	Homozygous deletion or mutation	< 5%	[1069,1863, 2464]

Polymorphic variant of Zulch

- Rare morphological variant of oligodendroglioma described by Dr. Zülch in 1960's
  - Polymorphic variant with marked nuclear pleomorphism, giant multi-nucleated cells, anaplastic features
    - Series of 9 cases only 3 had 1p/19q co-deletion
  - Other historical variants include minigemistocytic, sarcomatous, neurocytic, gangliocytic, etc.



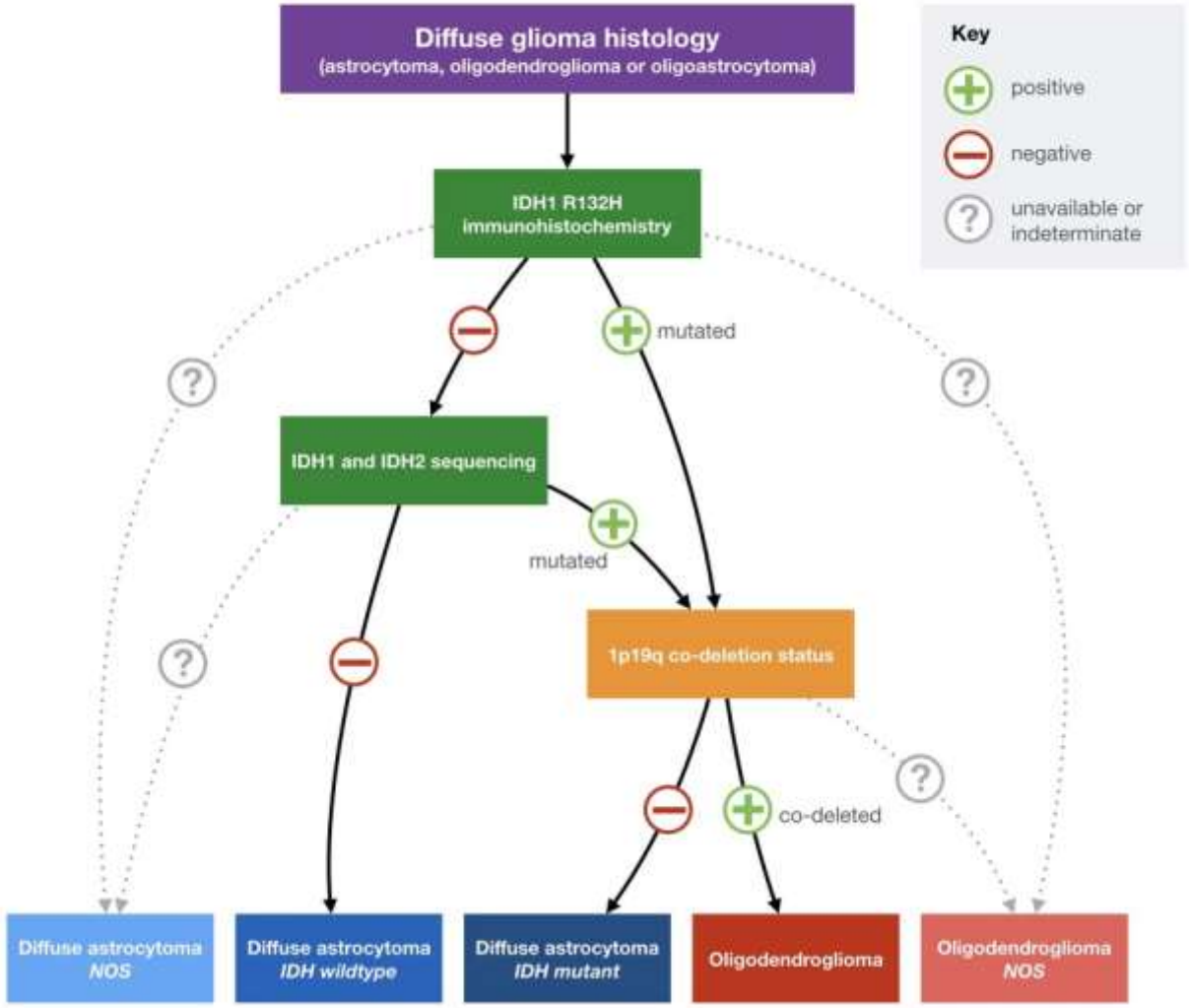
Hewer E et al, Polymorphous oligodendroglioma of Zülch, Neuropathology (2014) 34: 323-332

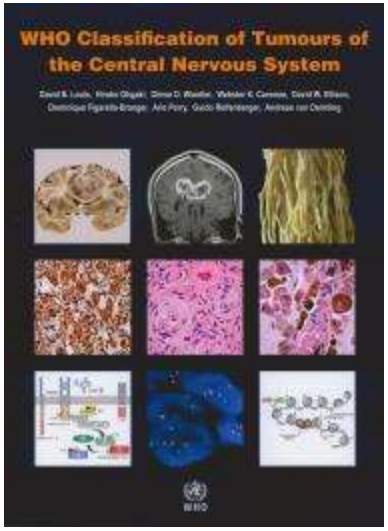
1p/19q co-deletion

“Recently, evidence has amassed that FISH is insufficient to fully distinguish oligodendrogliomas from other brain tumors (usually glioblastoma) that harbor focal deletions of 1p and 19q and thus give false positive results on FISH analysis. For this reason, the WHO 2016 recommends molecular testing by a method that assess whole-arm chromosomal loss, such as molecular inversion probe array, single nucleotide polymorphism chromosomal microarrays, or next-generation sequencing with copy number analysis”.

Wood M et al, Diagnostic Pathology (2019) 14:29-39

Diffuse glioma classification





References

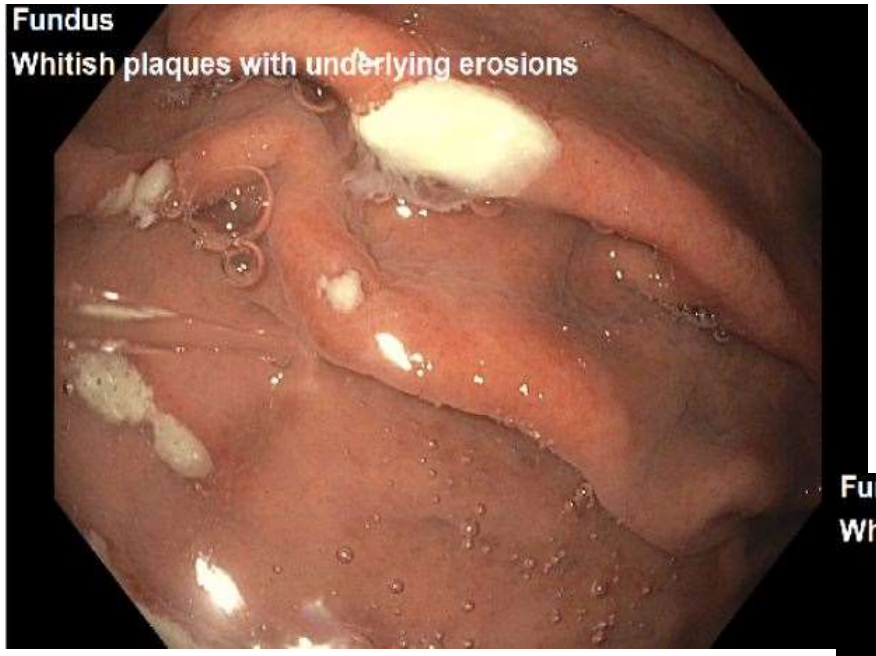
- Wood M et al, Diagnostic Pathology (2019) 14:29-39
- Louis D et al, WHO Classification of Tumors of the CNS, 2016
- Hewer E et al, Polymorphous oligodendroglioma of Zülch, Neuropathology (2014) 34: 323-332

19-0610

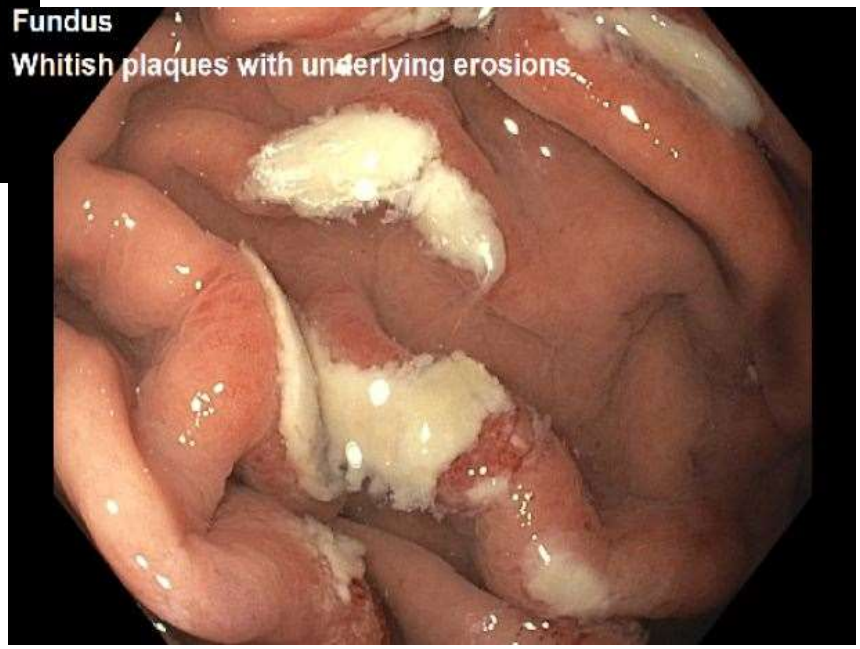
Lisa Wong/Christine Louie; Palo Alto VA

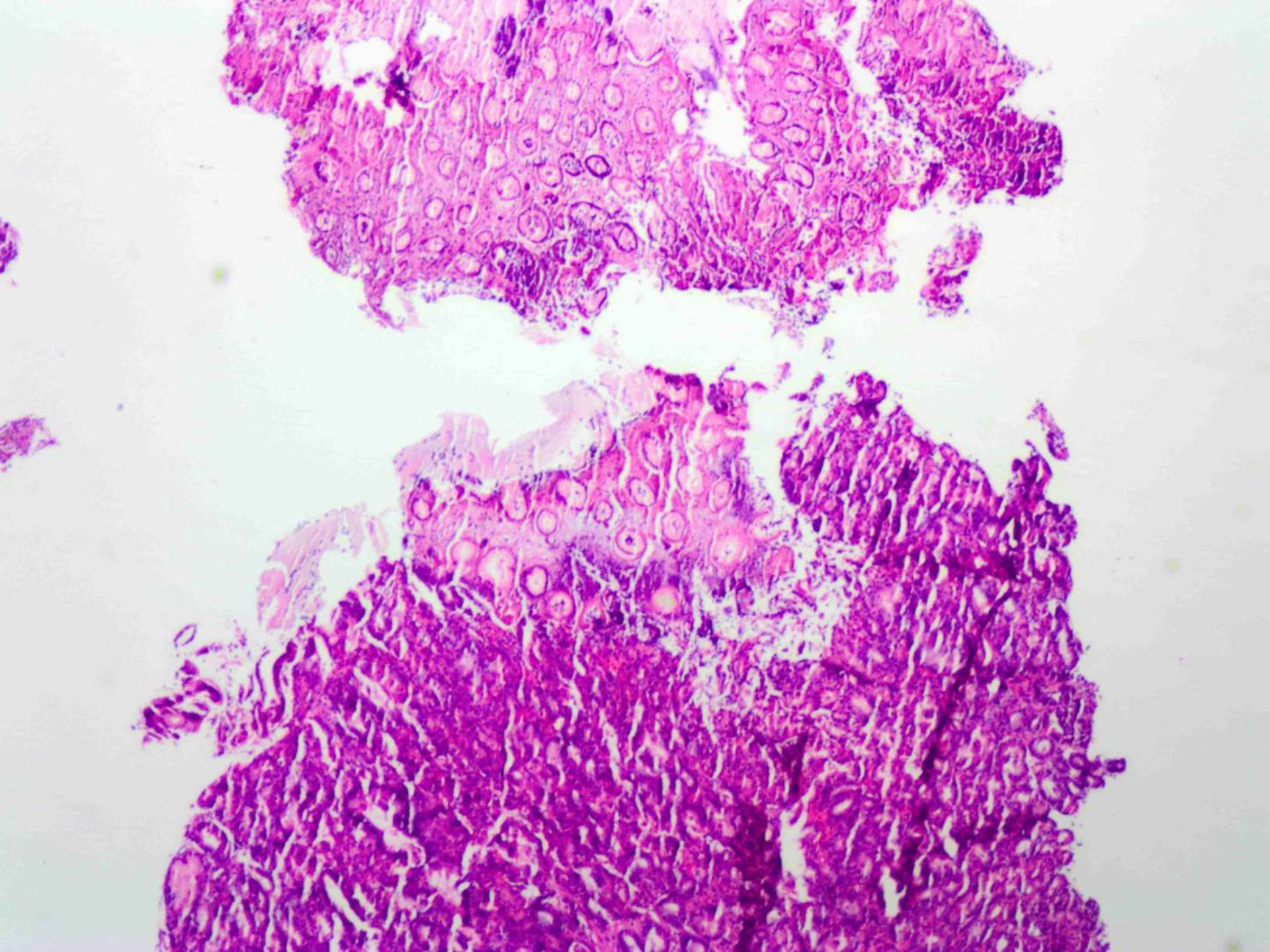
77-year-old male with h/o emphysema, recent bronchitis, dysphagia, and heartburn.

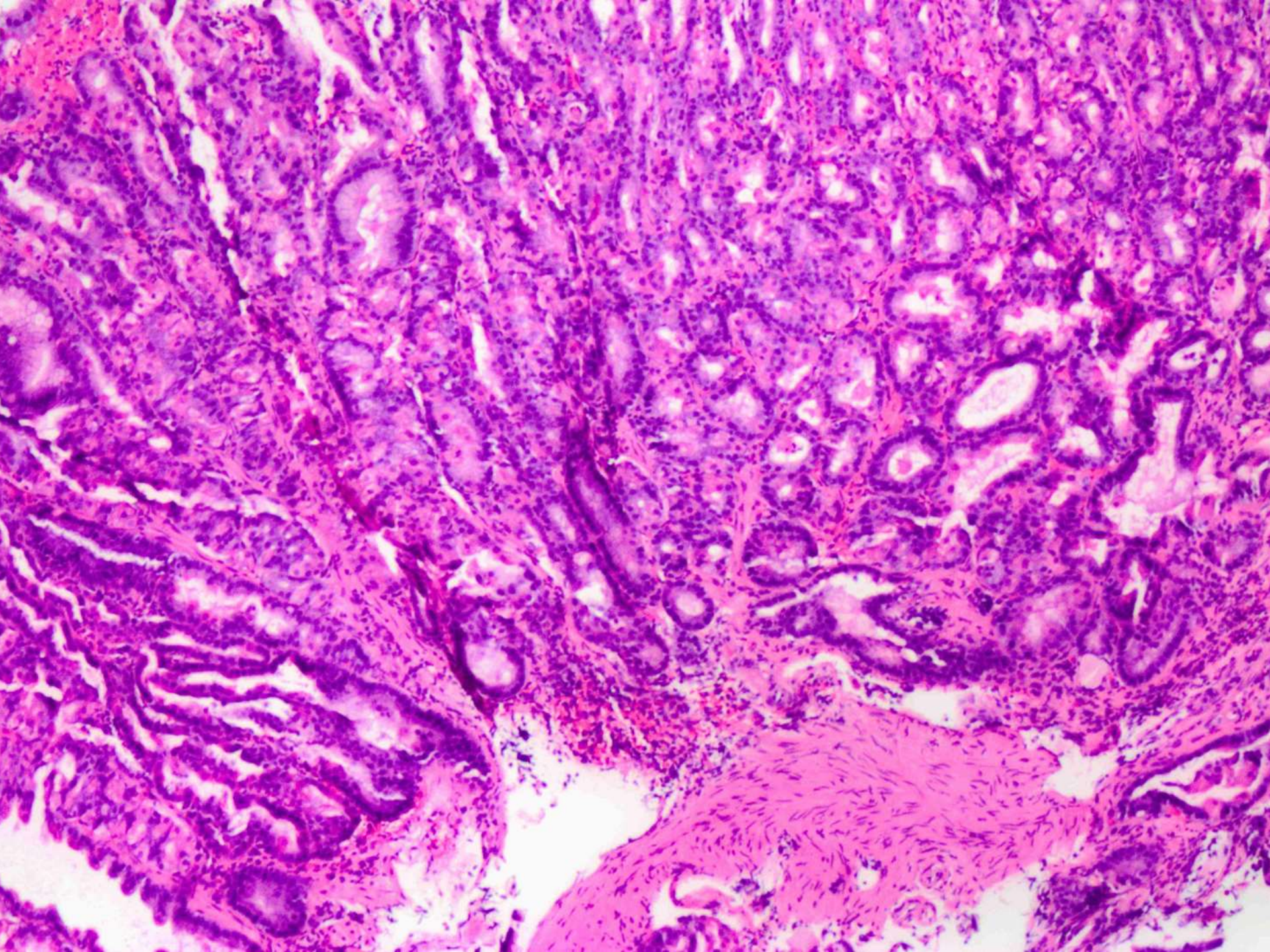
Endoscopy of the stomach fundus

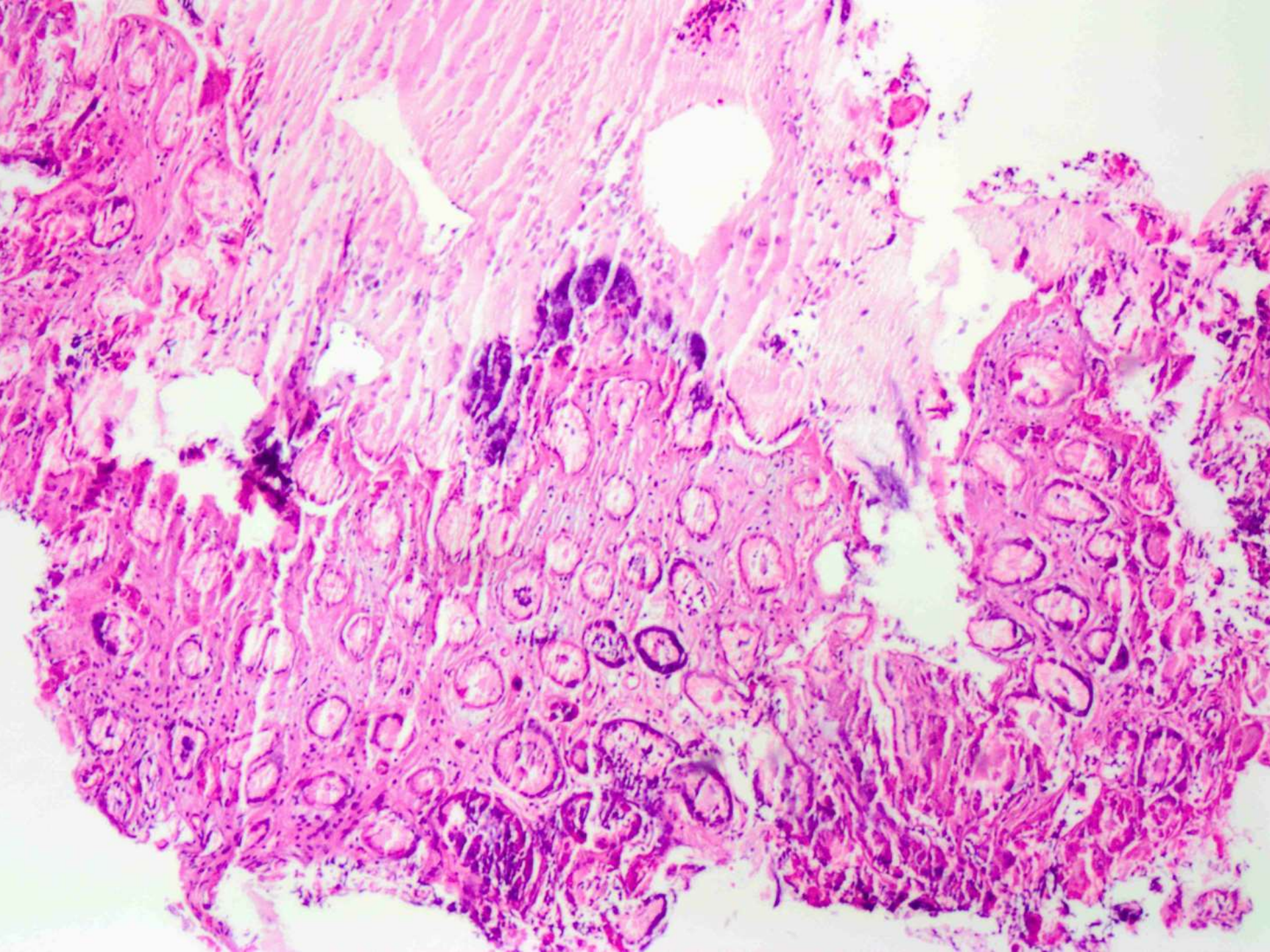


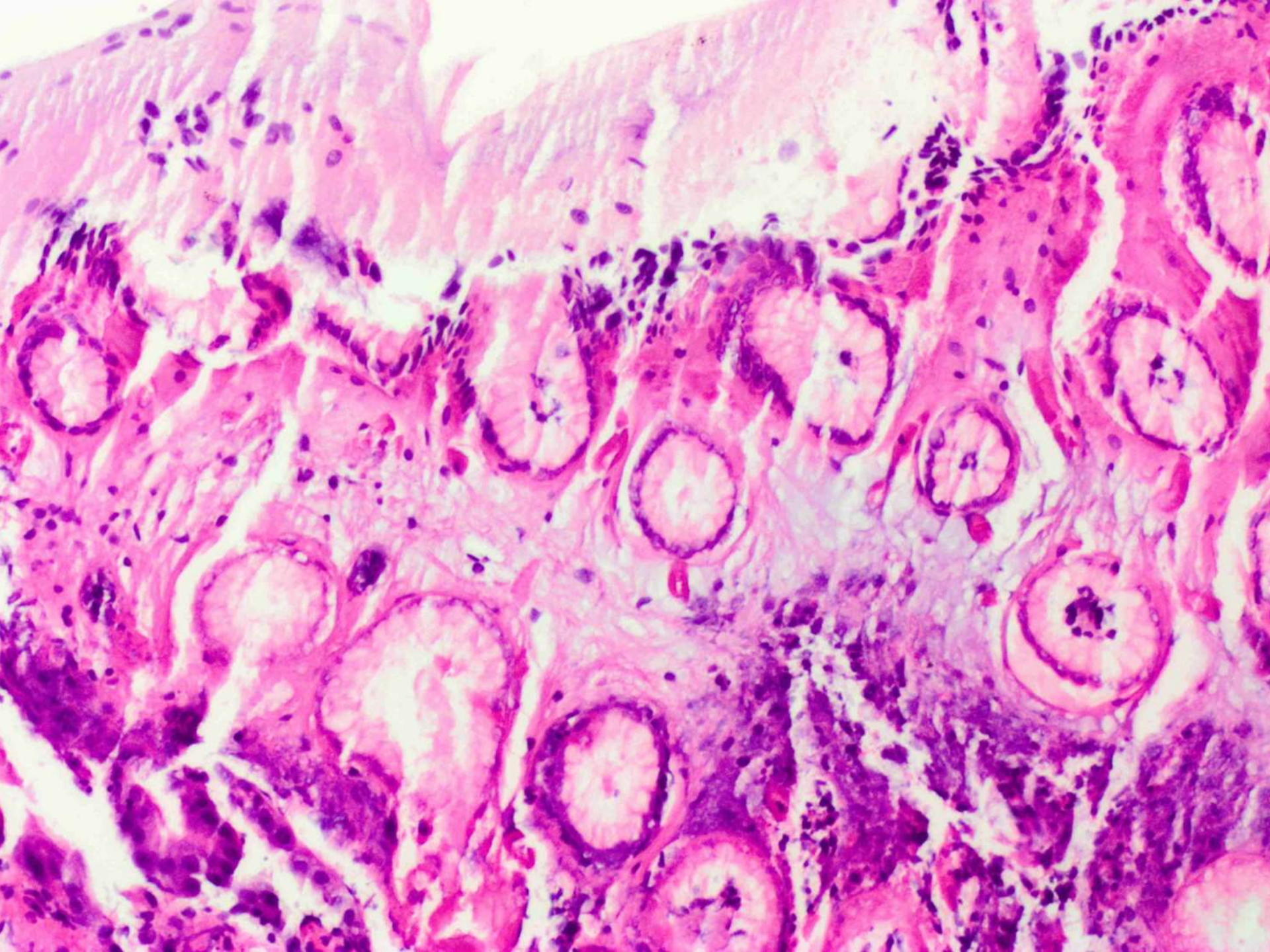
EGD performed for patient's symptoms of recurrent dysphagia and moderate heartburn

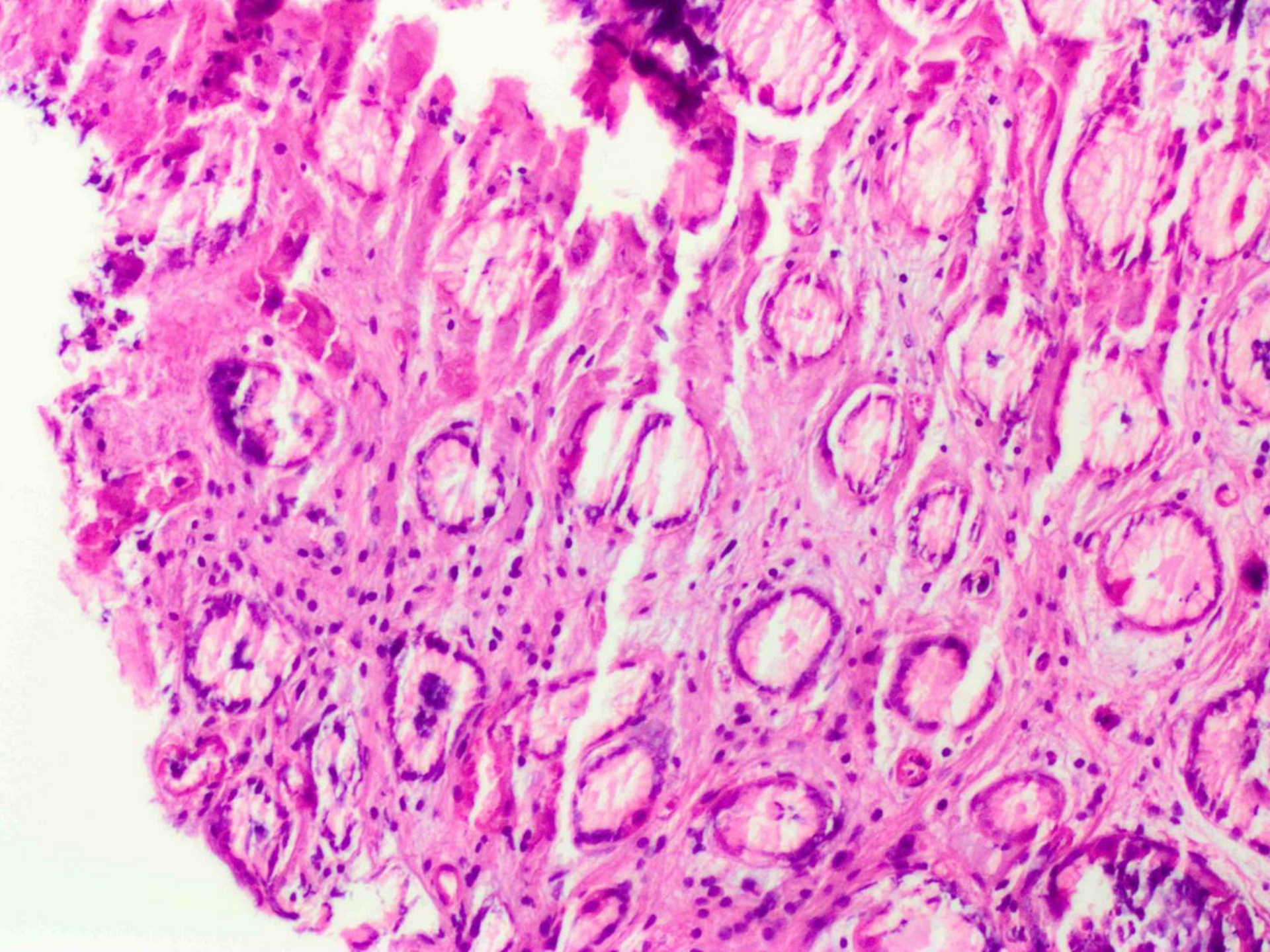












Doxycycline-induced upper GI tract mucosal injury

Lisa Wong/Christine Louie

Palo Alto VA

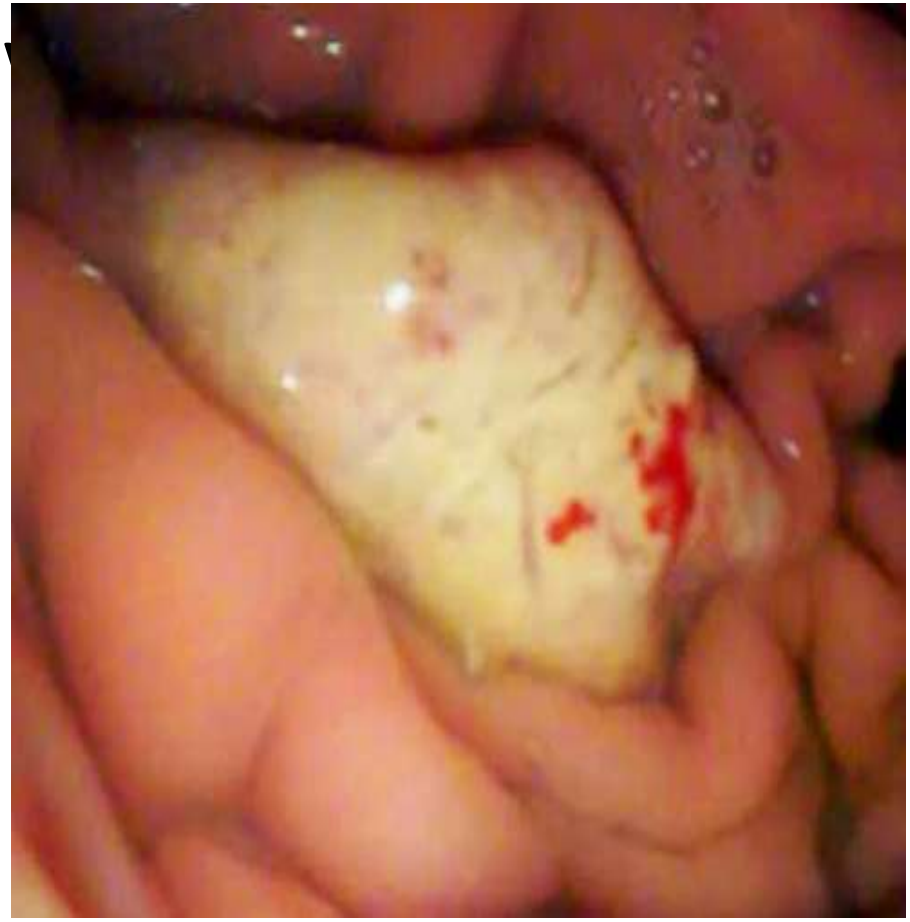
Medication induced GI Injury

- Presents with non-specific symptoms (odynophagia/dysphagia and/or chest pain) prompting endoscopy/biopsy
- Known list of medications associated with GI injury
  - Antibiotics (clinda, tetracycline)
  - NSAIDS
  - Bisphosphonates
  - Iron

  Injury is usually nonspecific (ulceration, reactive gastropathy)

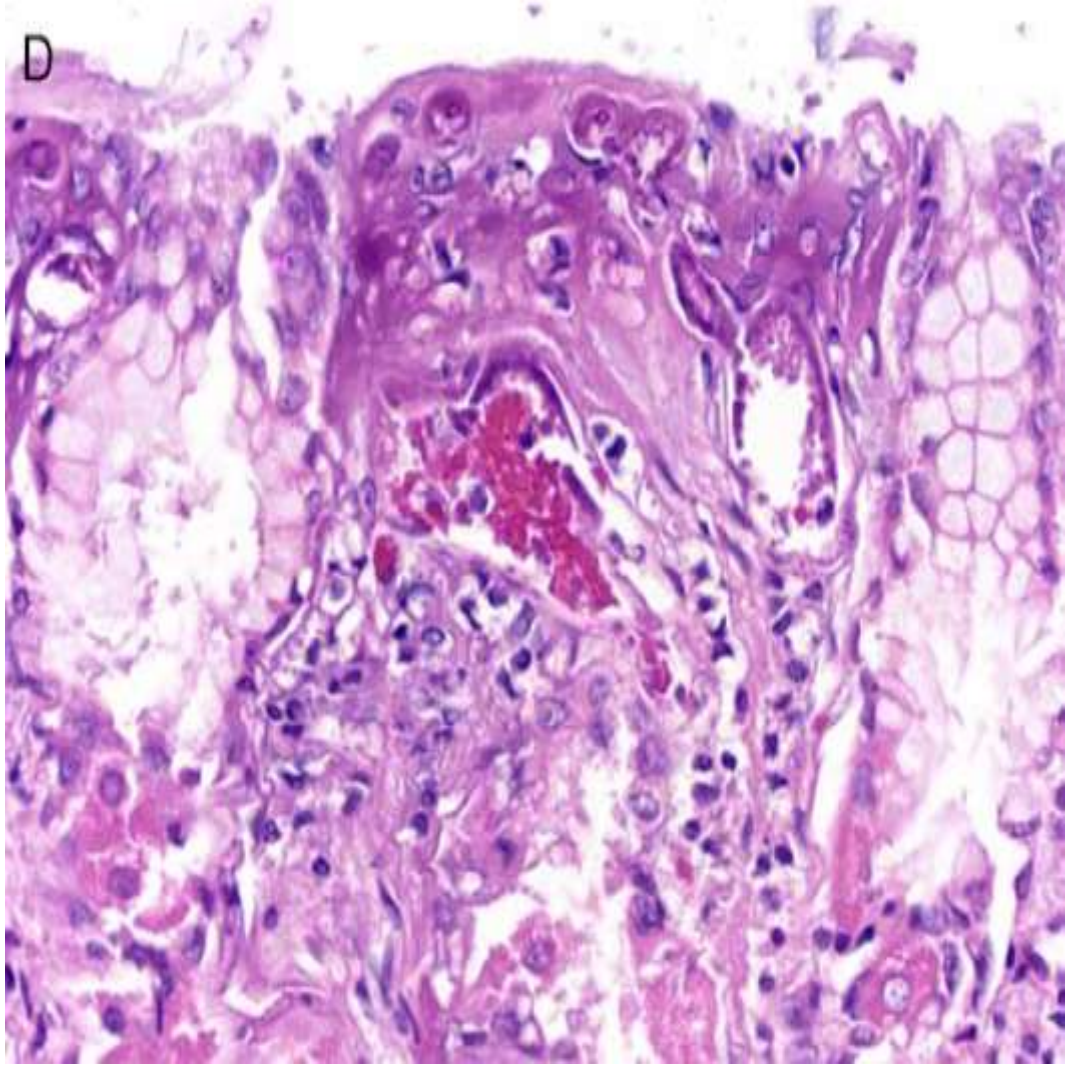
Endoscopic vie

- Doxycycline-induced gastric injury appears white plaque-like or ulcer-like
  - Lesions in the gastric fundus or body
    - Can be mistaken for PUD or reactive gastropathy



Doxycycline

- Oral tetracycline antibiotic
  - Well-known cause of esophageal ulcers
- Recent literature findings of gastric injury (superficial mucosal necrosis) with vascular degeneration
  - One study found all patients with gastric doxycycline-induced injury had characteristic superficial mucosal necrosis and eosinophilic capillary degeneration with or without fibrin thrombi
  - Mechanism not well understood
    - Likely related to corrosive nature of drug itself causing direct injury, as necrosis is usually superficial
  - Esophageal injury related to doxycycline was ulcerative
    - Stomach showed superficial necrosis and erosion but not full-thickness ulceration



Eosinophilic necrosis of superficial capillaries with fibrin thrombi

Take home points

- Drug injury should be included in the differential diagnosis of gastritis
- Consider doxycycline in cases showing ulceration/plaque formation
- Look for mucosal necrosis with eosinophilic degeneration of capillaries and fibrin thrombi

References

- Shih AR et al. Vascular Injury Characterizes Doxycycline-induced Upper Gastrointestinal Tract Mucosal Injury. Am J Surg Pathol 2017;41:374-381.
- Xiao SY et al. Doxycycline-induced gastric and esophageal mucosal injuries with vascular degeneration. Am J Surg Pathol. 2013;37:1115–1116.