Seminar of Young Pathologists
Litomysl, Czech Republic
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# Slide seminar on controversial issues in thyroid pathology

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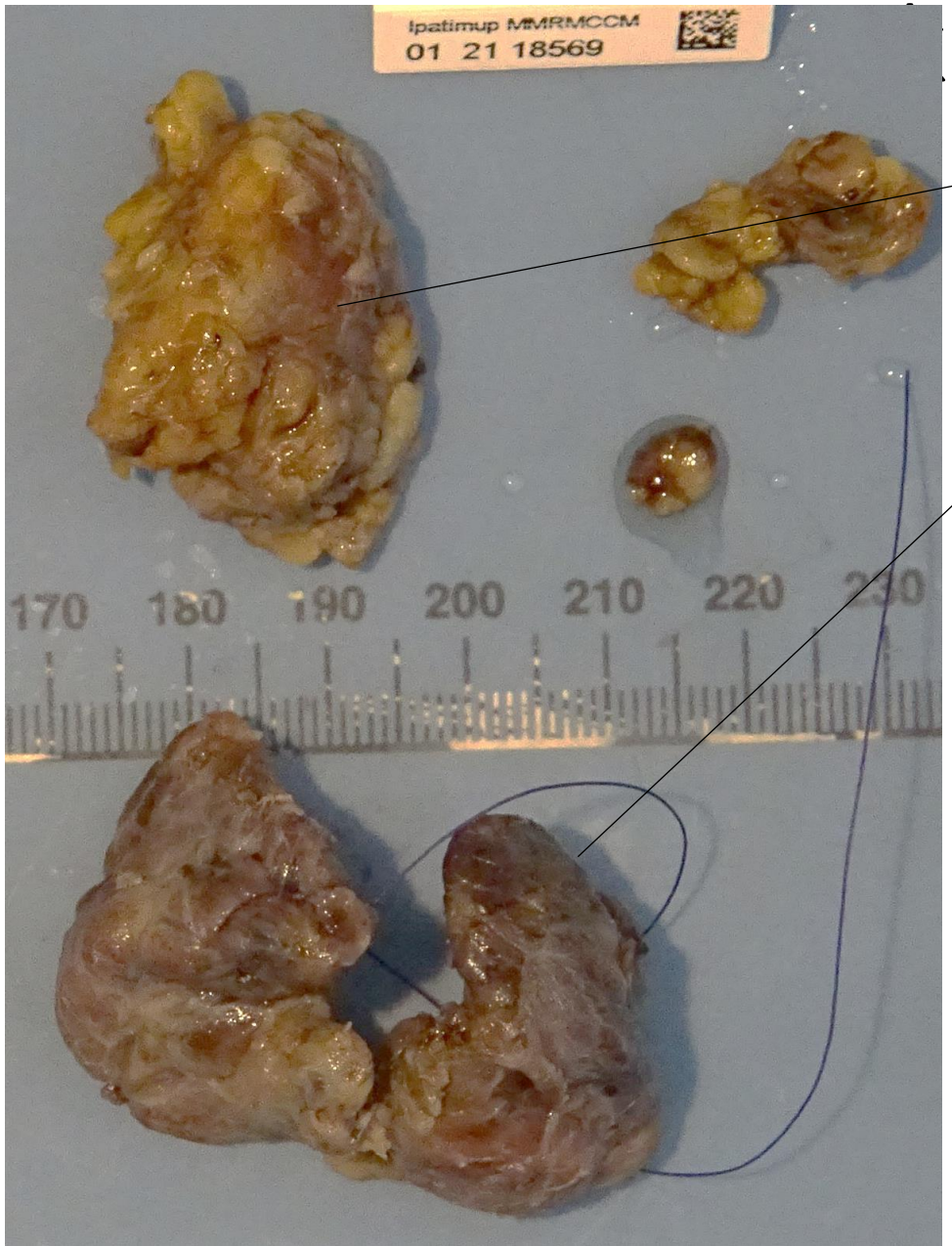
# CASE 1

- 48-year-old female
- Thyroid nodule in the left lobe

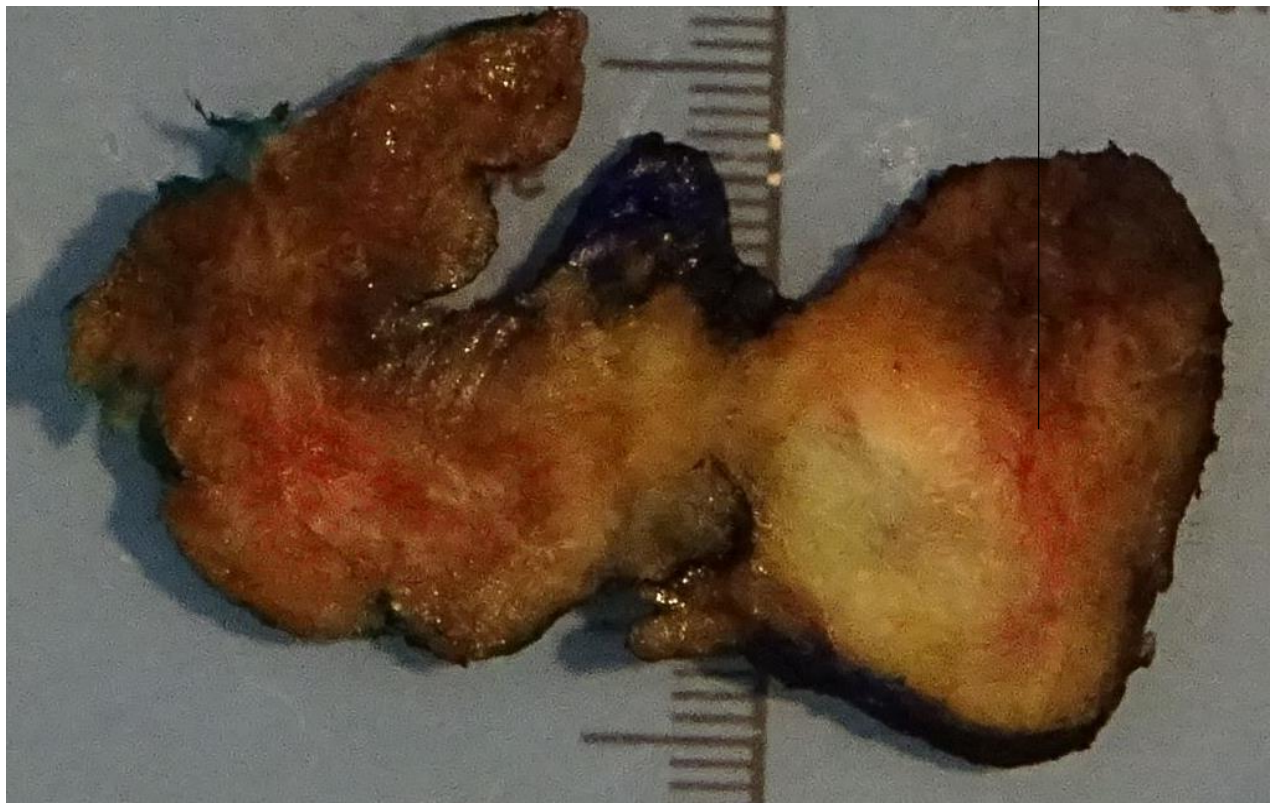
  - FNAB: papillary thyroid carcinoma
  - Surgery: total thyroidectomy with lymph node dissection of the central compartment (VI and VII)



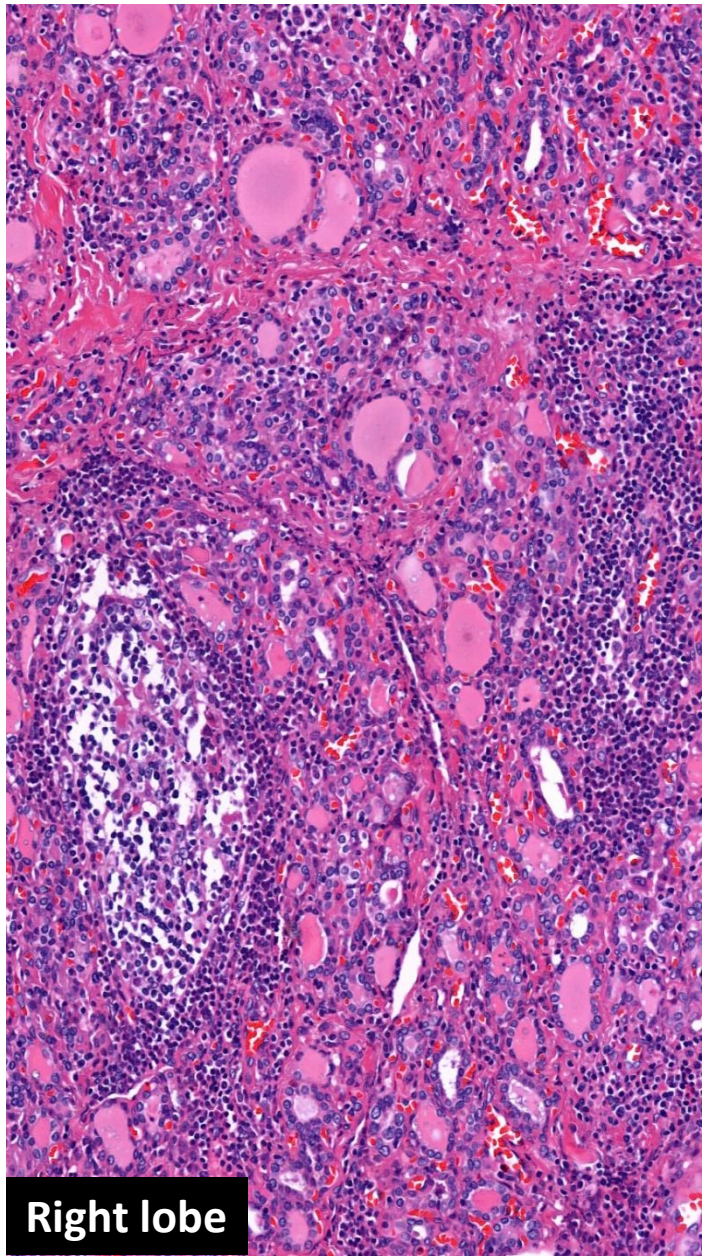

Lymph node dissection – 18g; 12 lymph nodes

Total thyroidectomy – 11g (reference in the right lobe)
Right lobe: 3cm; Isthmus:2.8cm; Left lobe: 3cm and a nodule

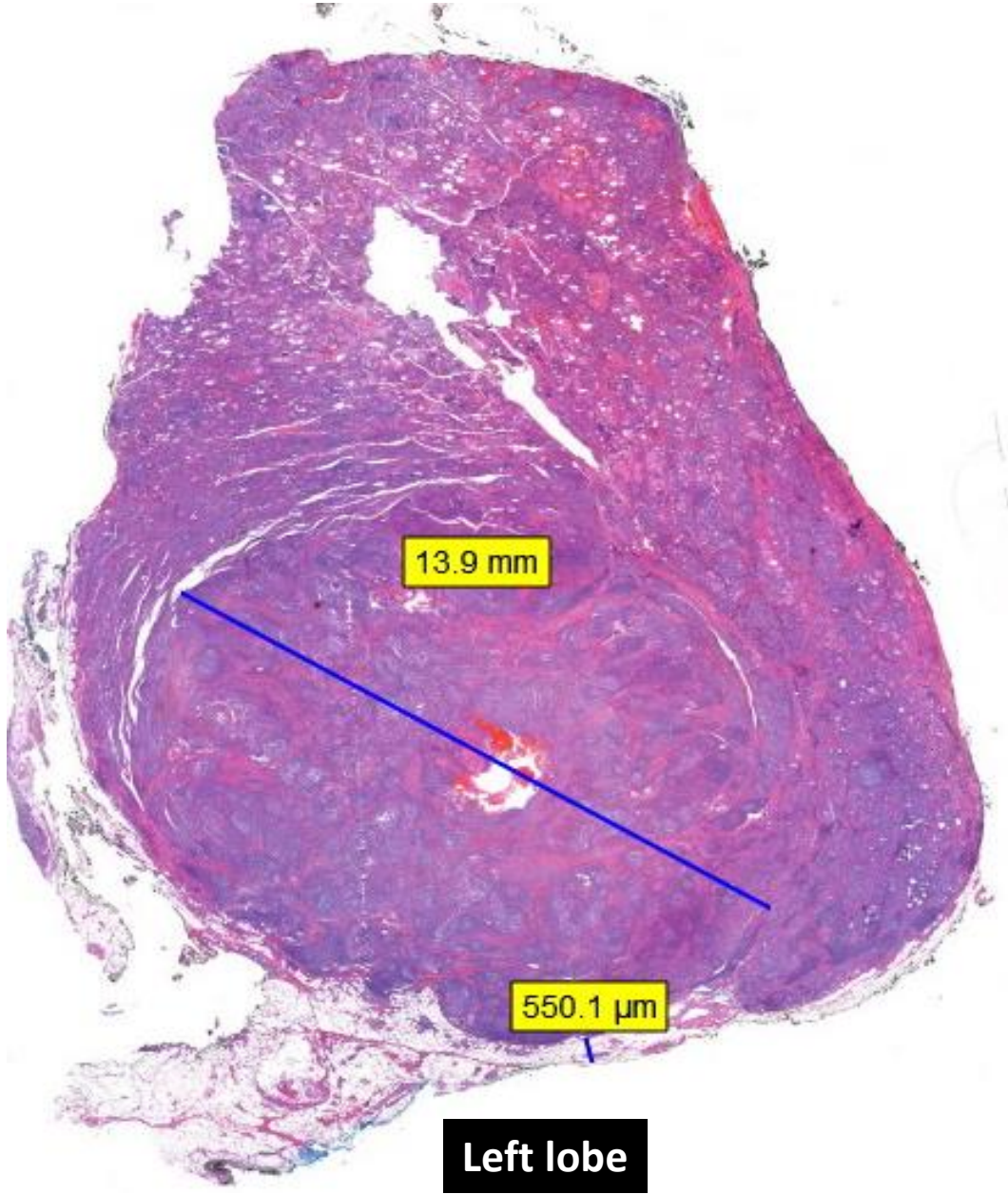
FNAB hemorrhage



# Microscopy

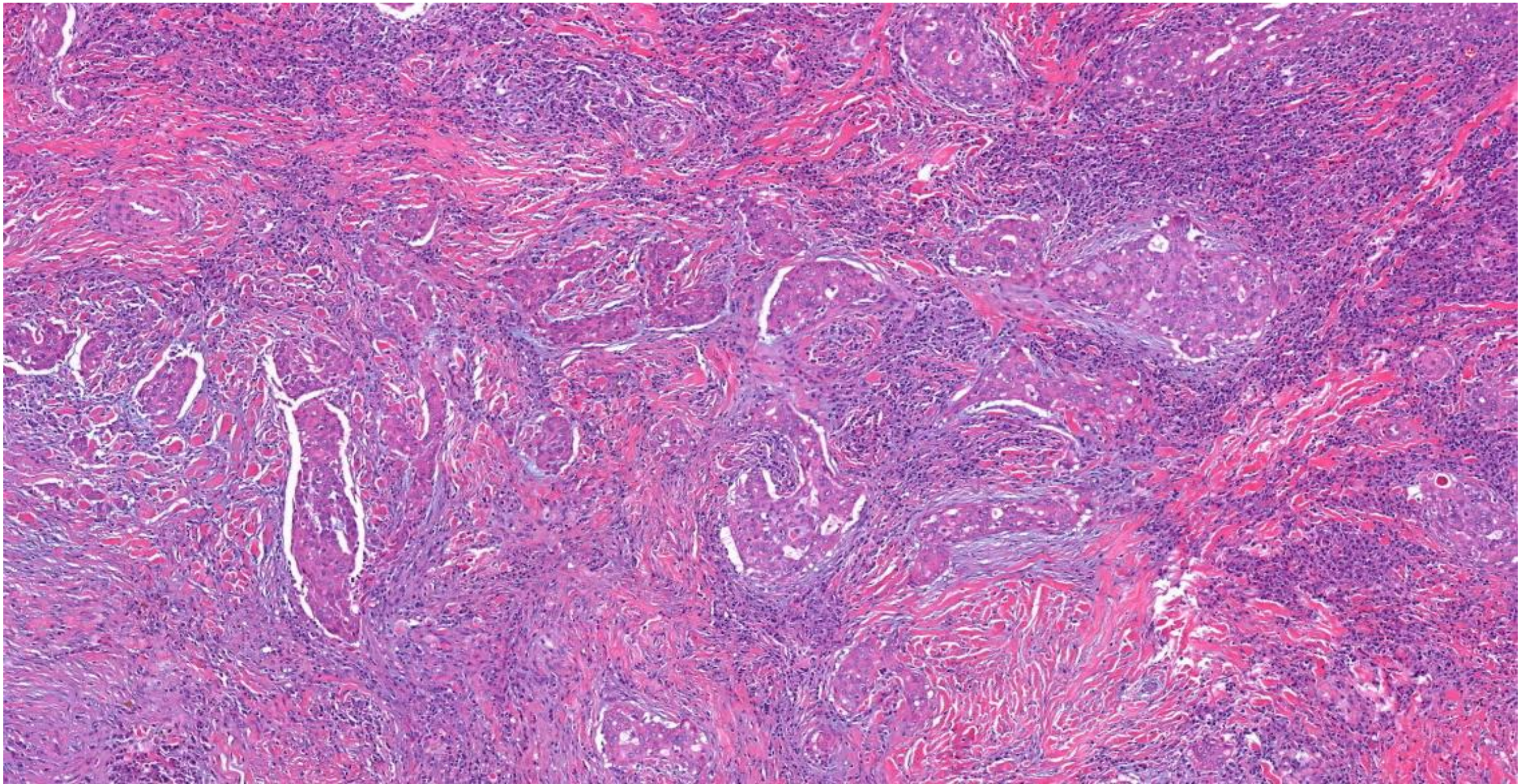


Right lobe

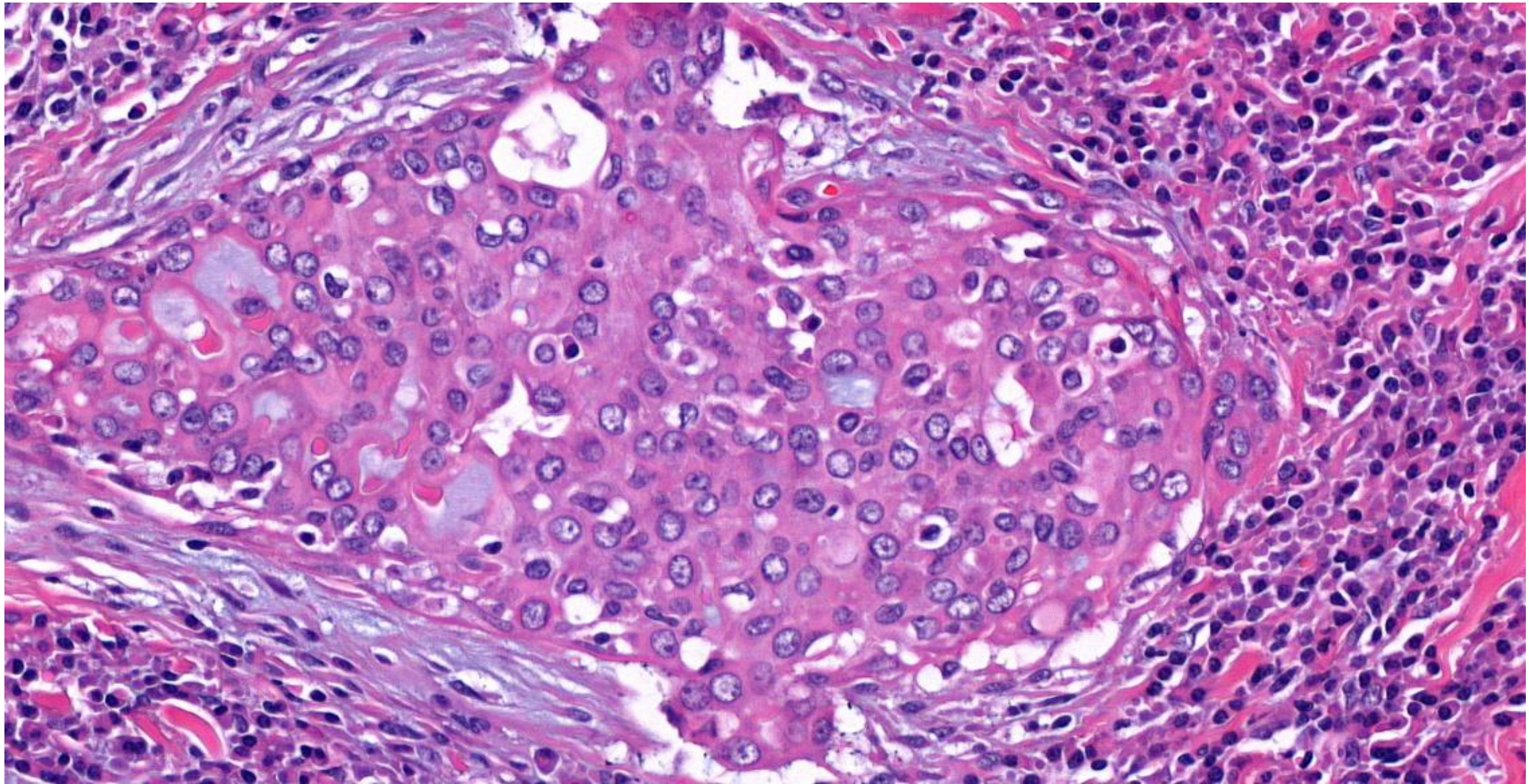



Left lobe

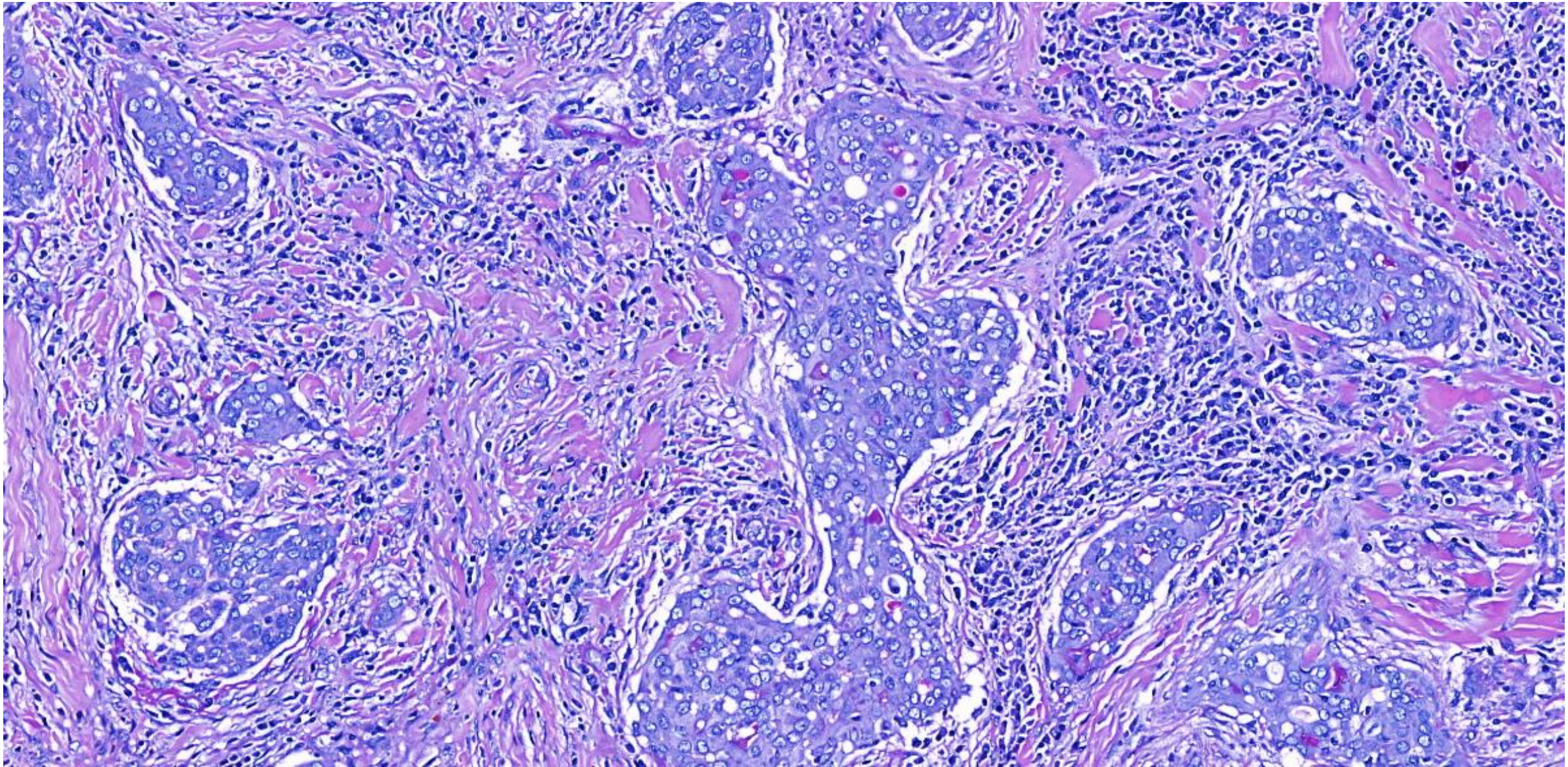
# Microscopy: nodule (H&E, 7x)



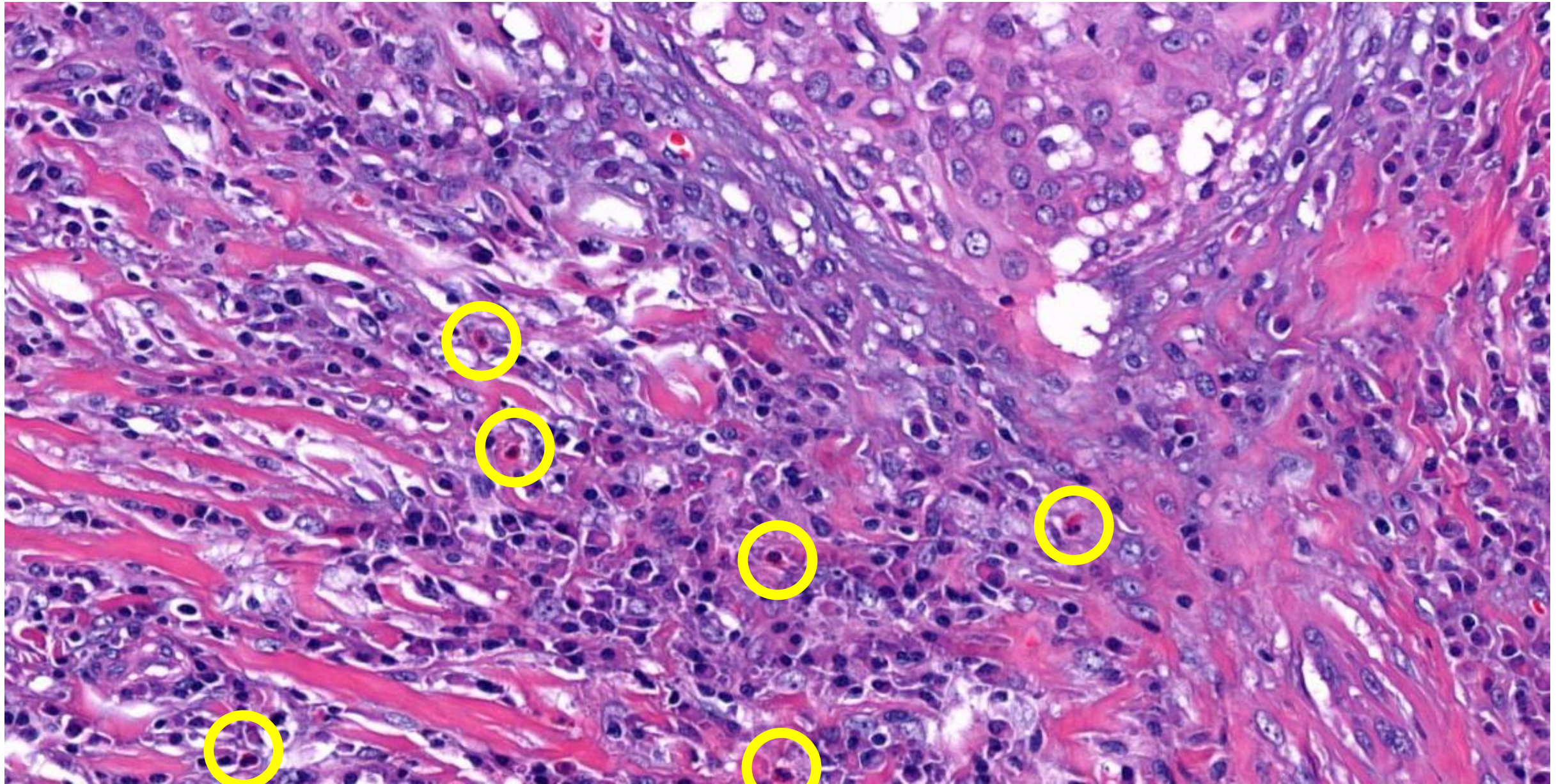
# Microscopy: nodule (H&E, 40x)



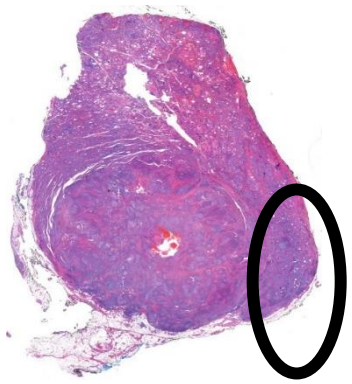
# Microscopy: nodule (PAS-D, 16x)

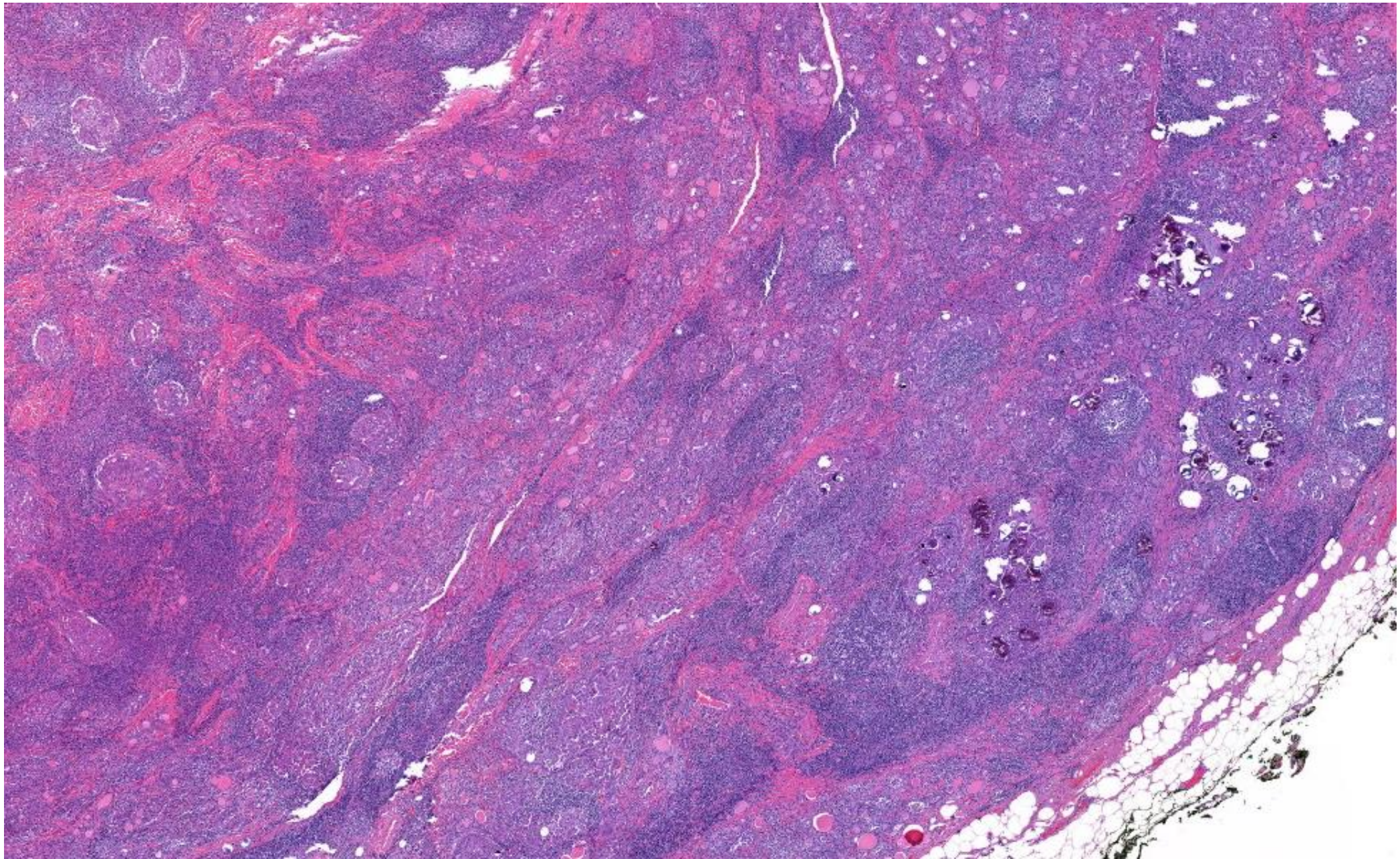


# Microscopy: eosinophils (H&E, 33x)

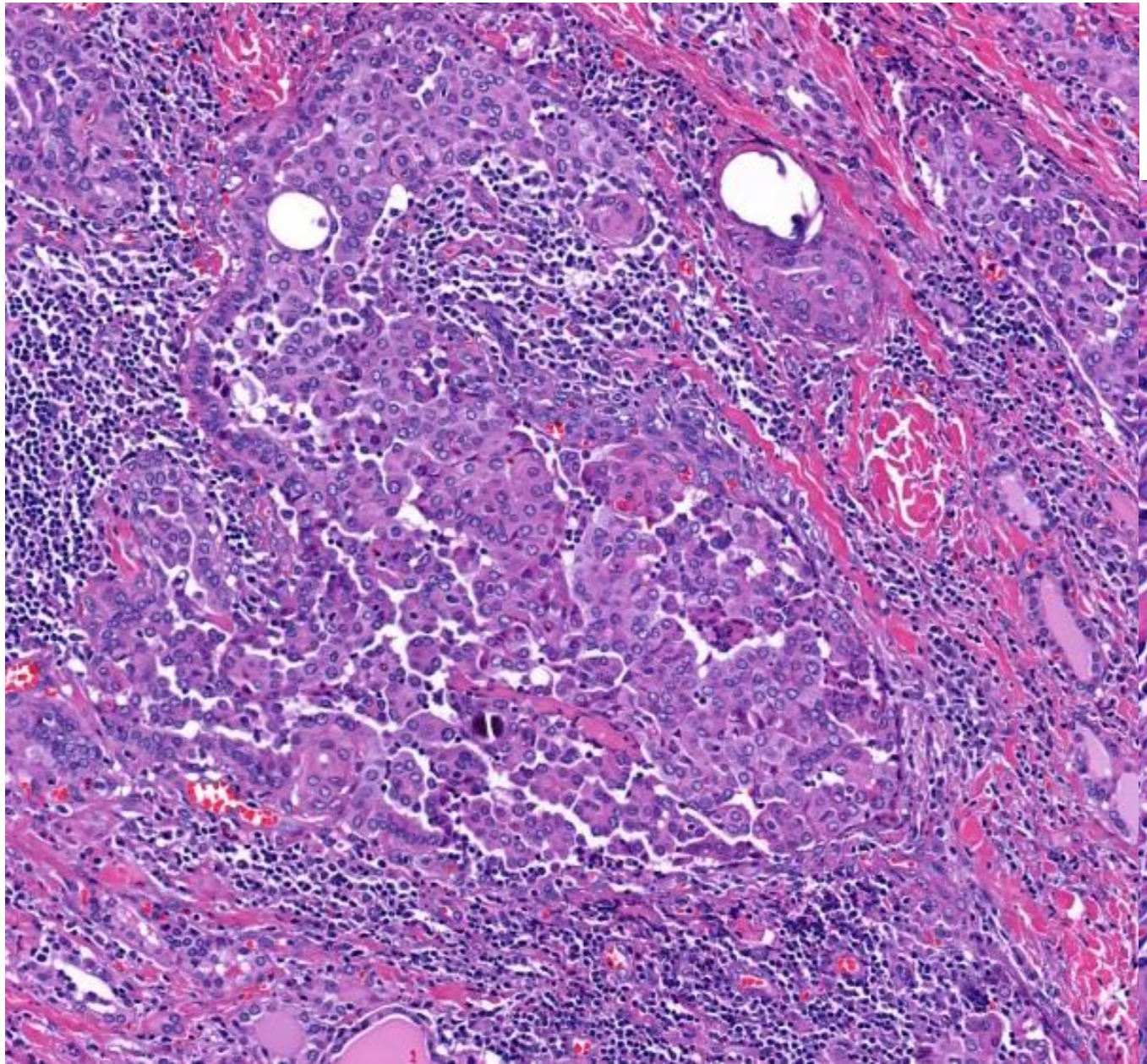


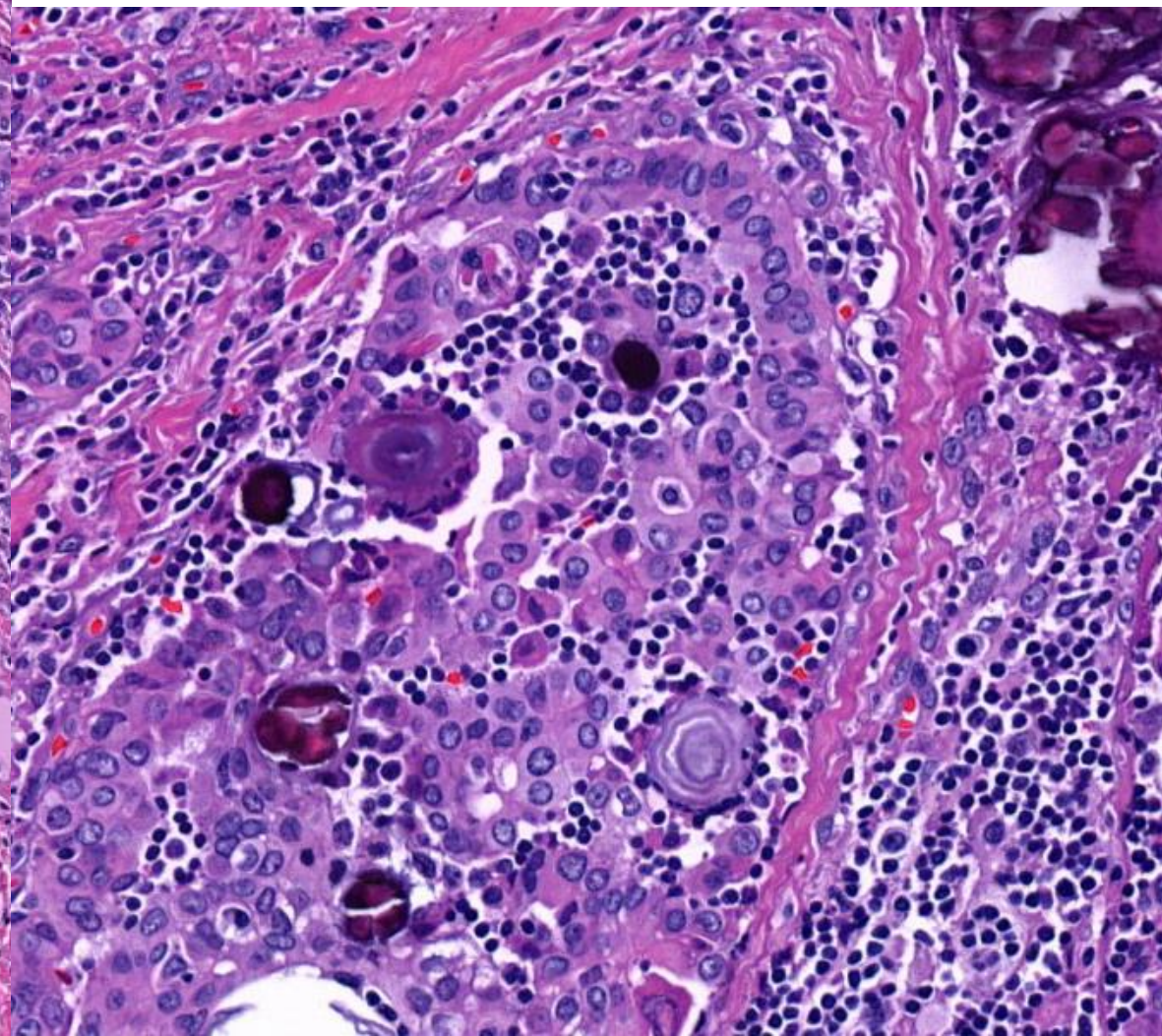
# Microscopy: periphery (H&E, 5x)





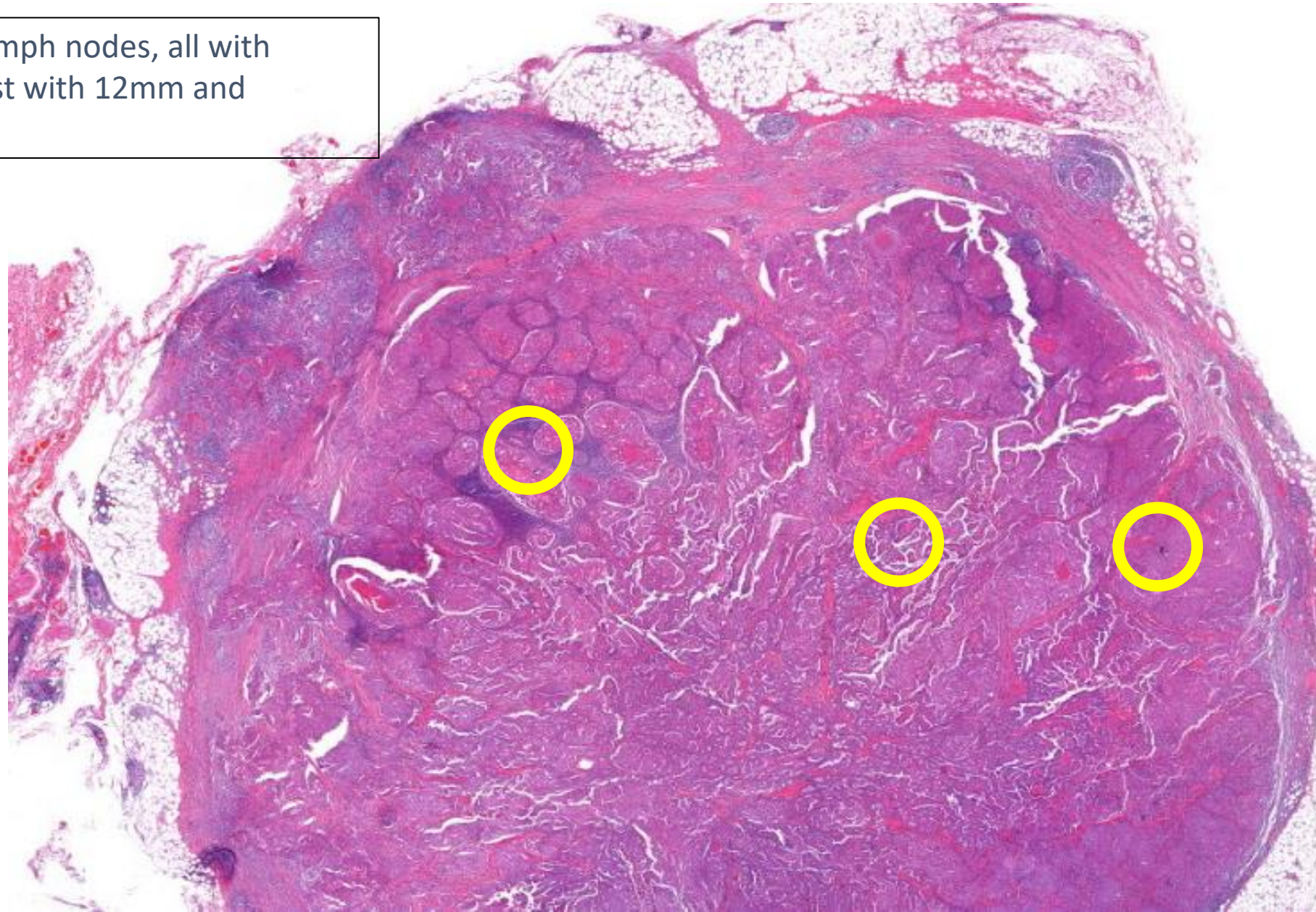
# Microscopy: periphery (H&E, 3x, 32x)



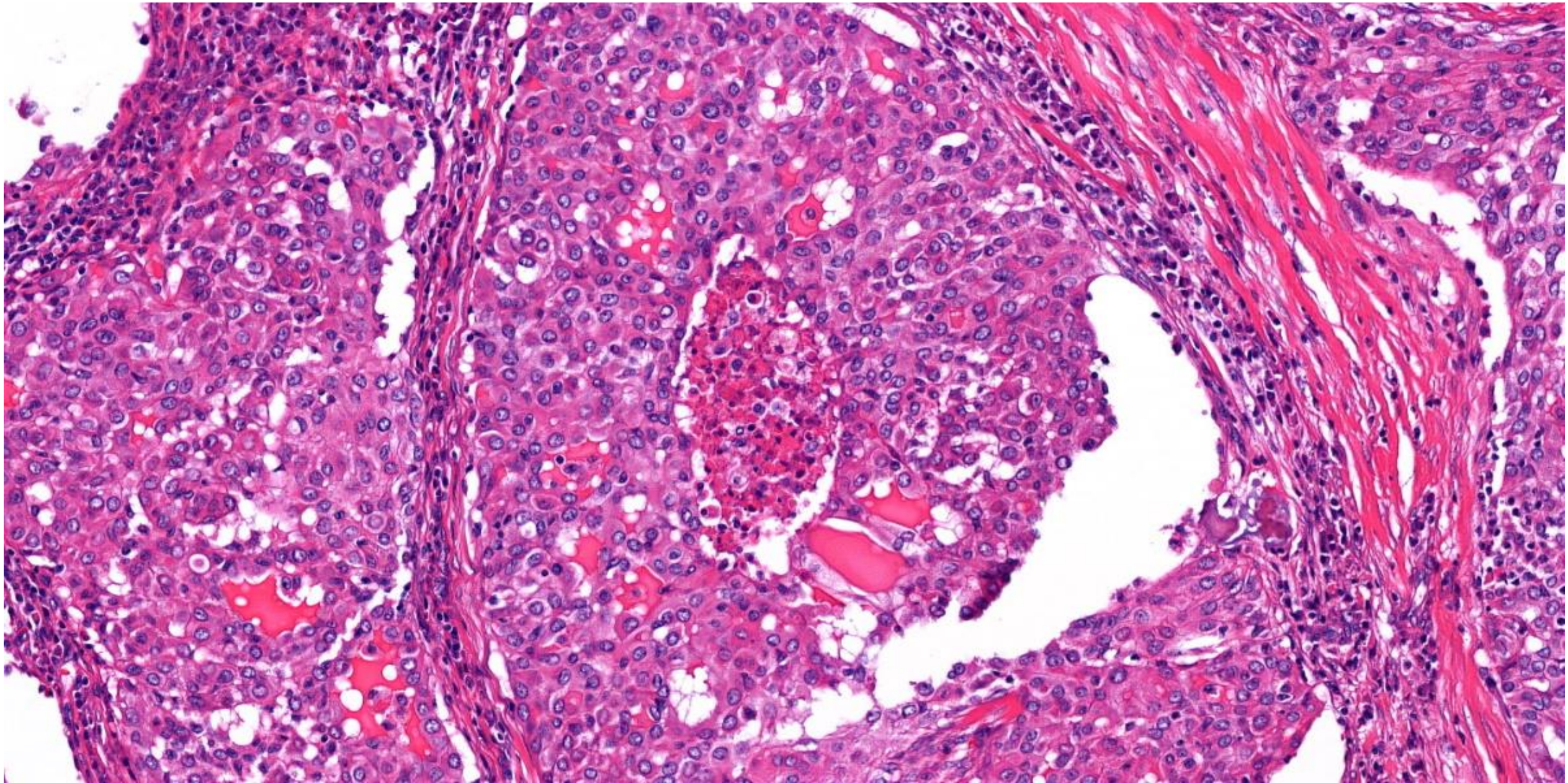


# Microscopy: lymph nodes (H&E, 1x)

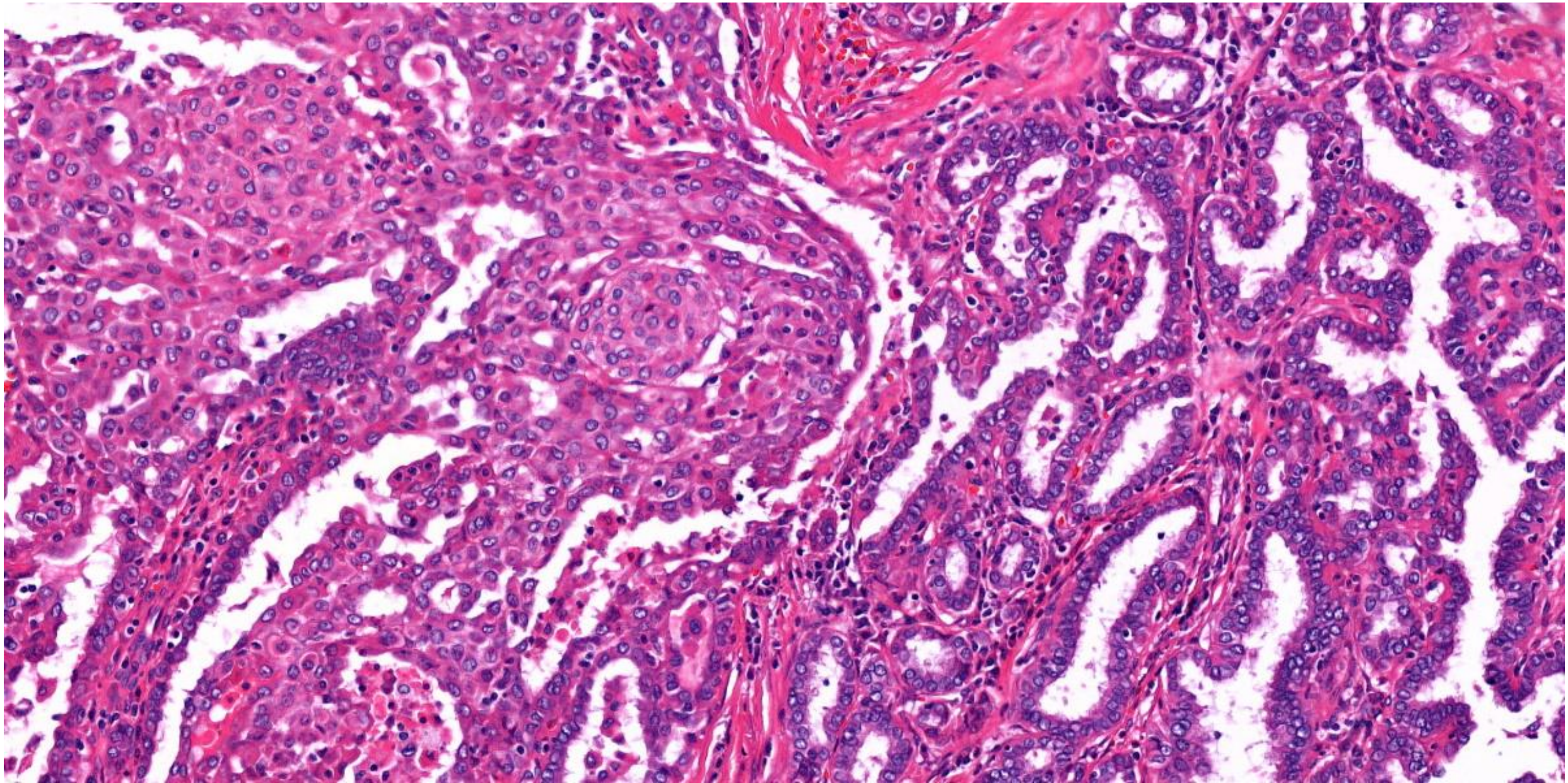
Lymph node dissection – 18g; 12 lymph nodes, all with metastases of carcinoma, the largest with 12mm and invasion of soft tissues



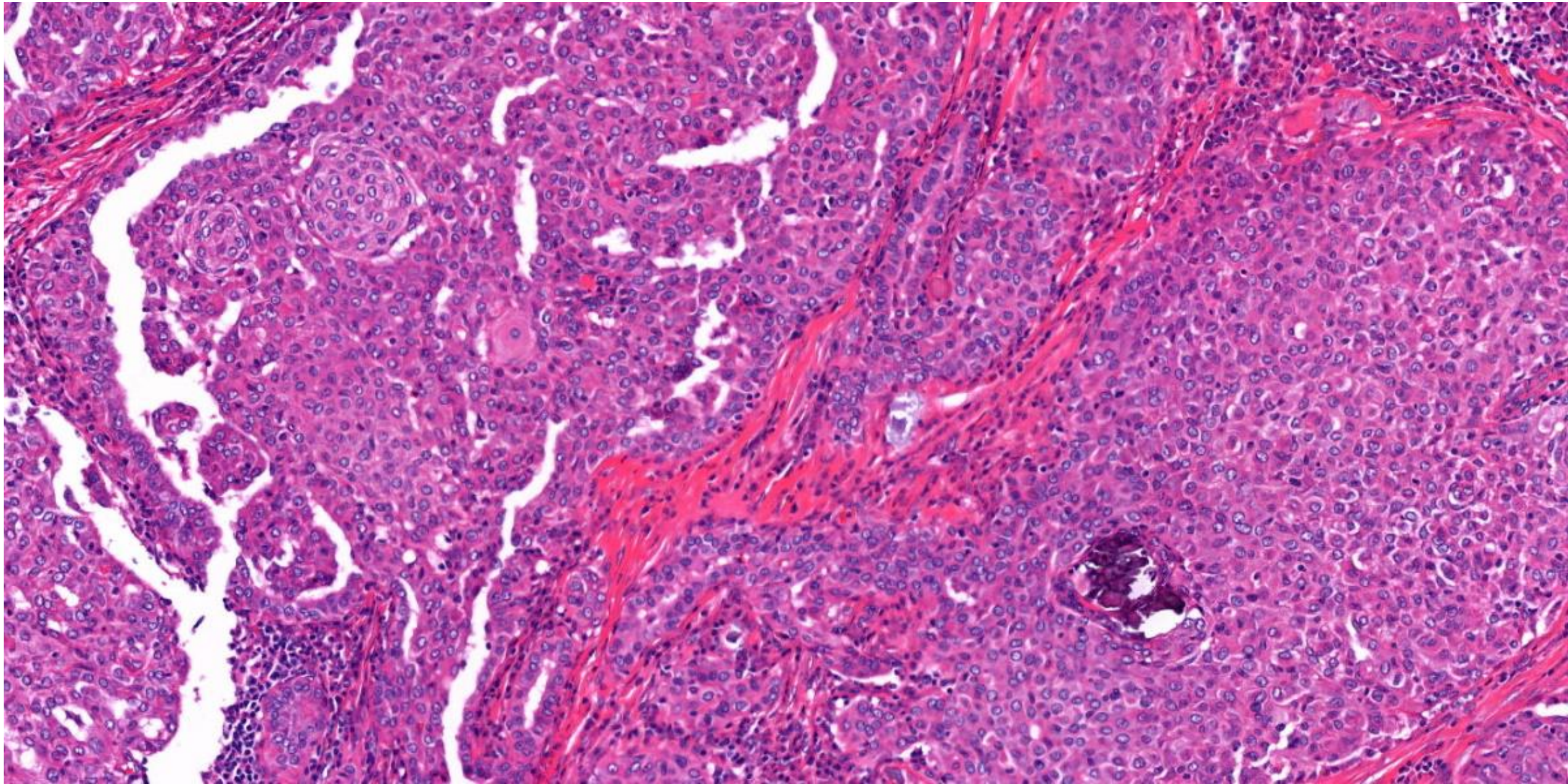
# Microscopy: lymph nodes (H&E, 20x)



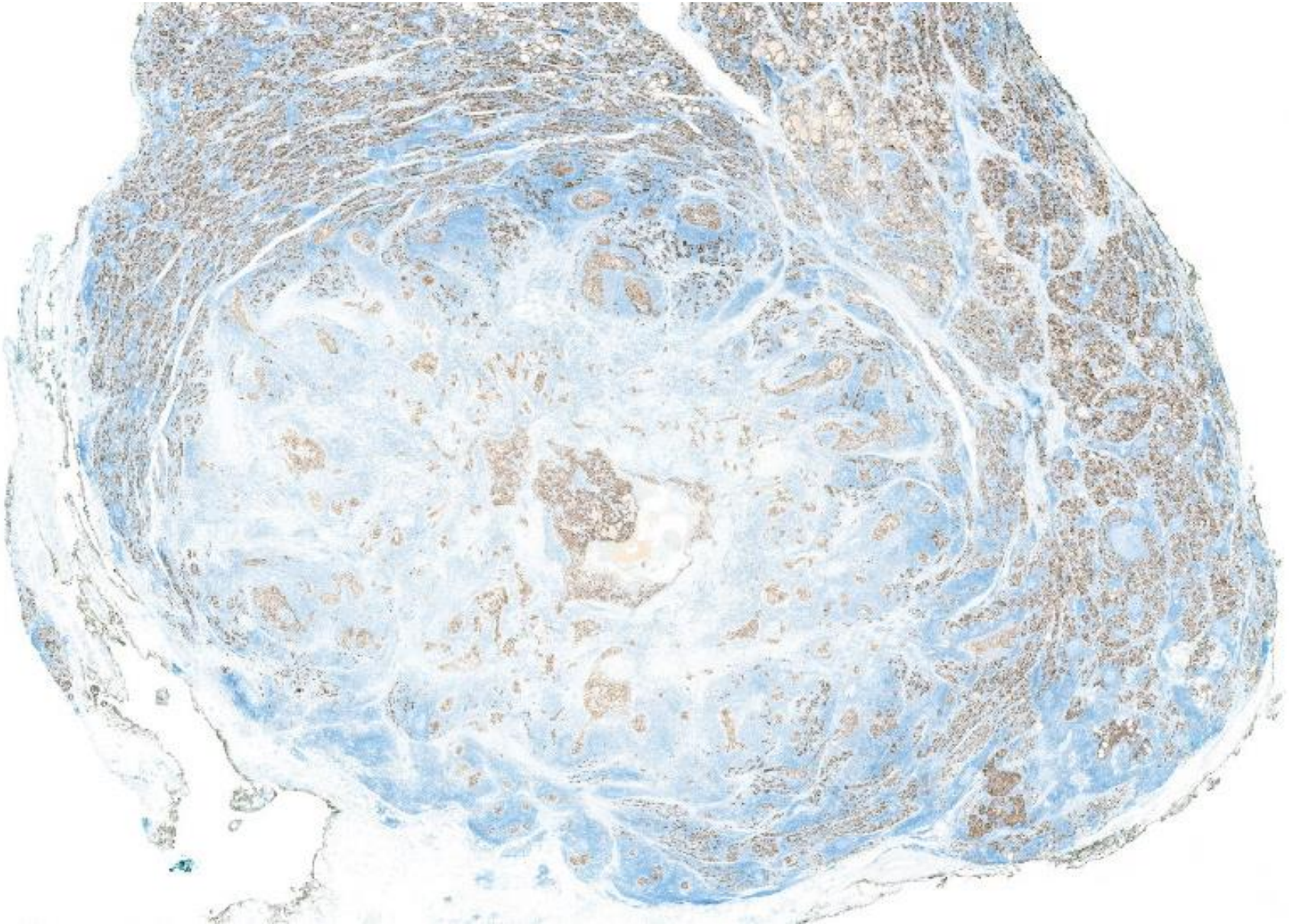
# Microscopy: lymph nodes (H&E, 20x)

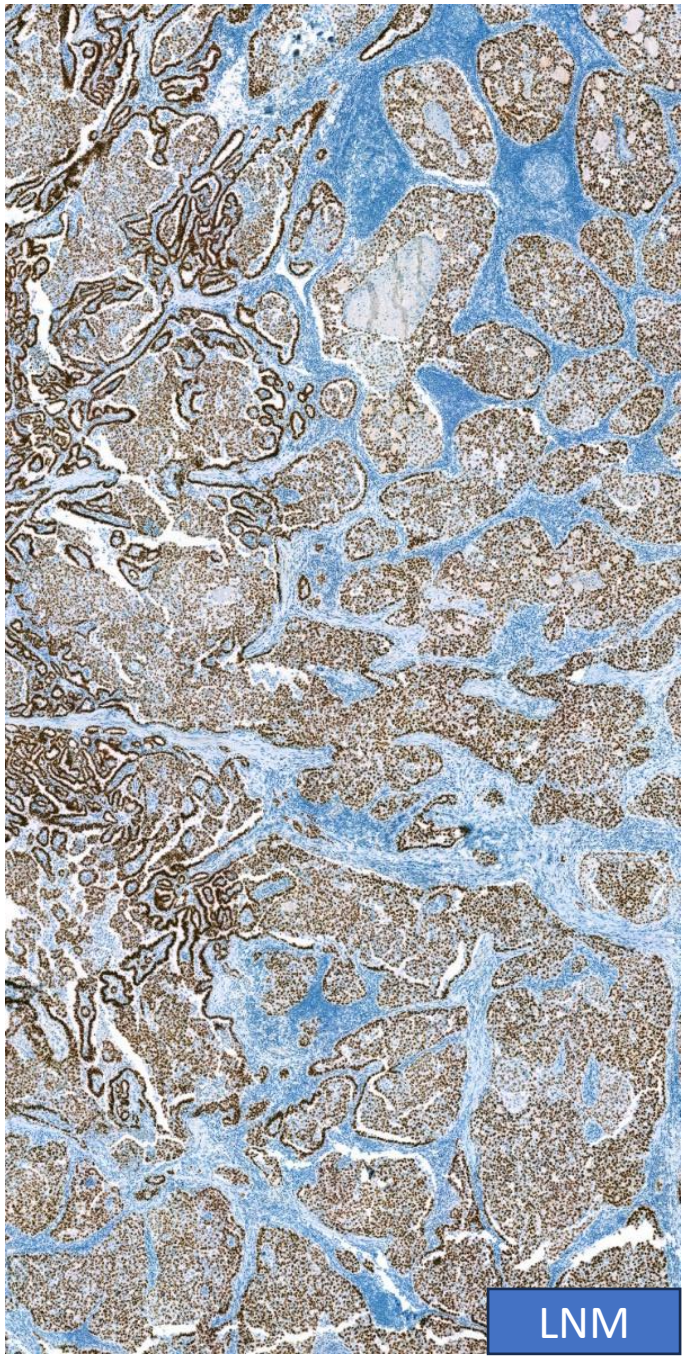


# Microscopy: lymph nodes (H&E, 20x)

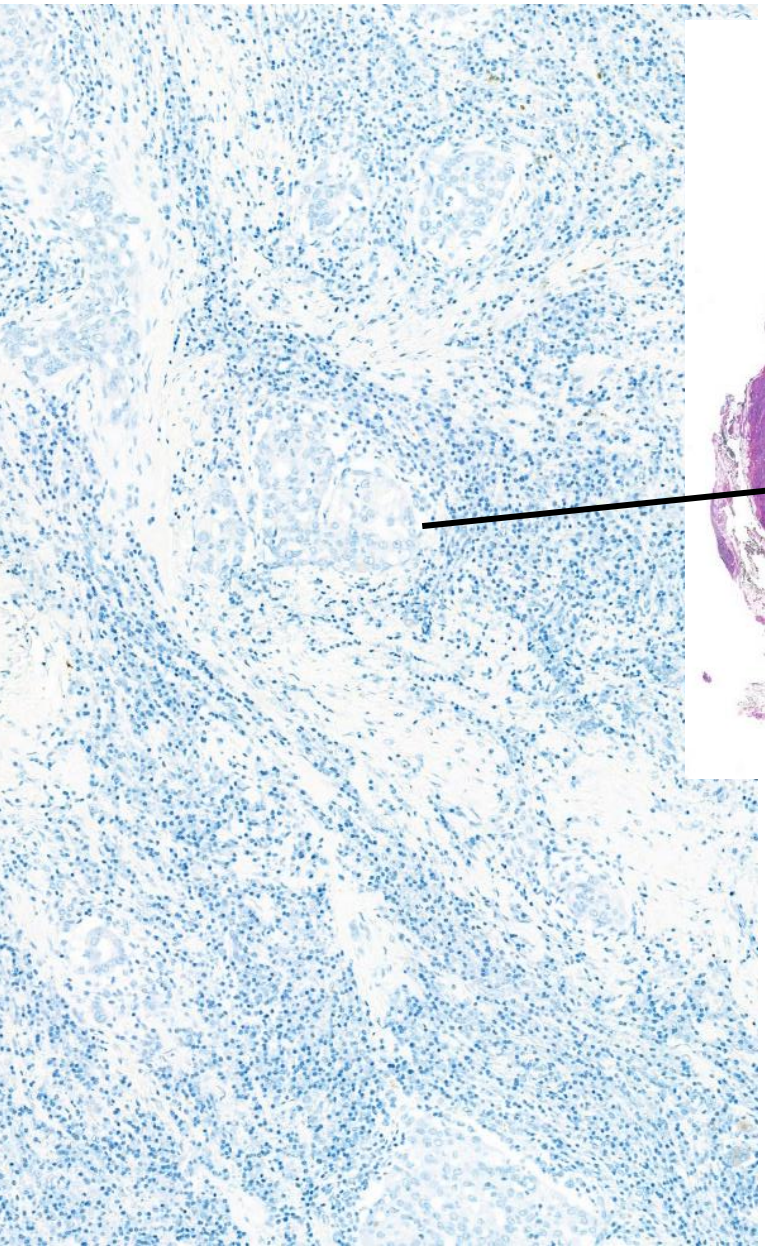


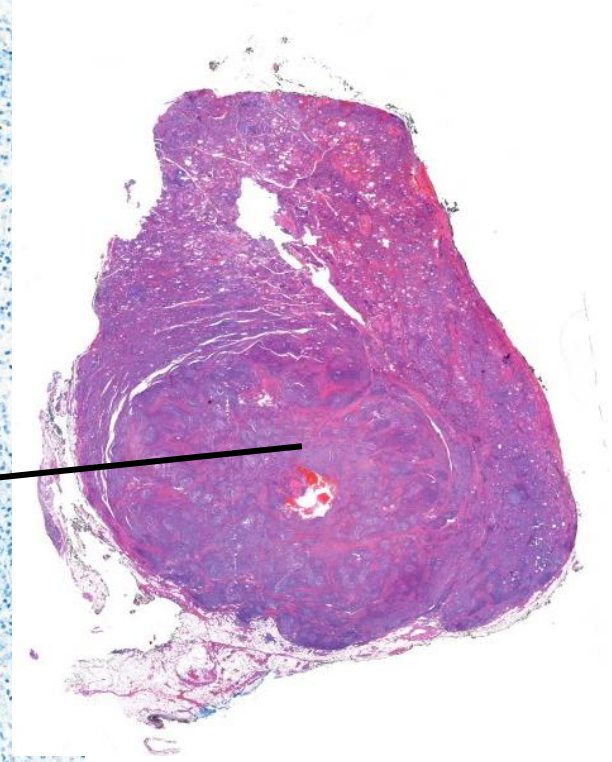
# Immunohistochemistry (TTF1)

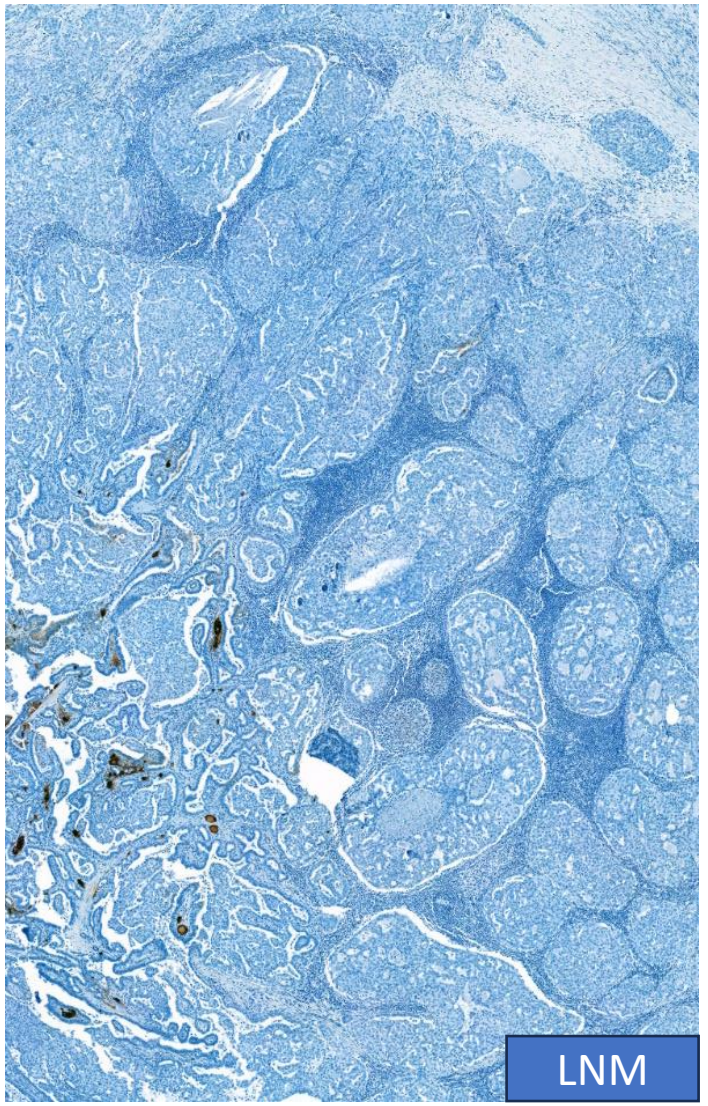




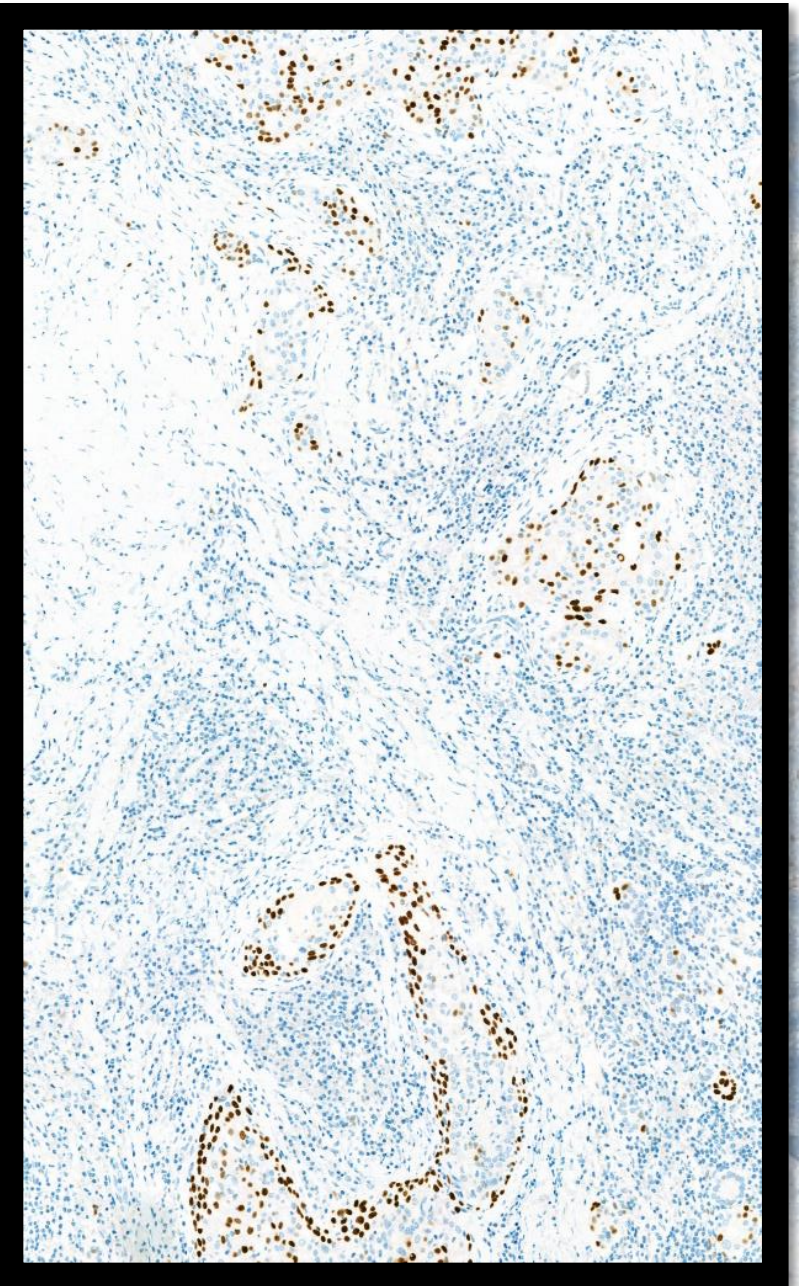
# Immunohistochemistry (Thyroglobulin)

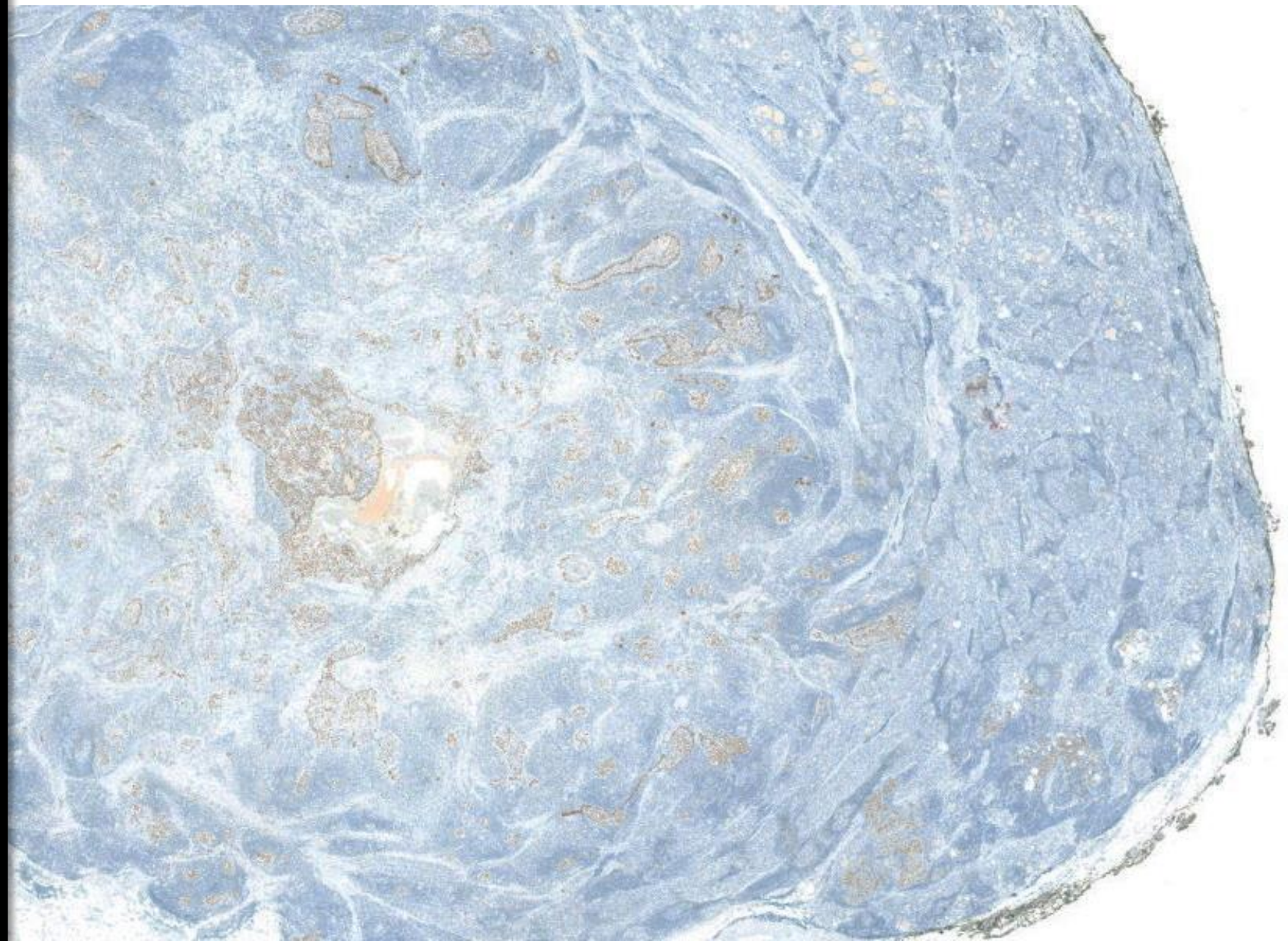




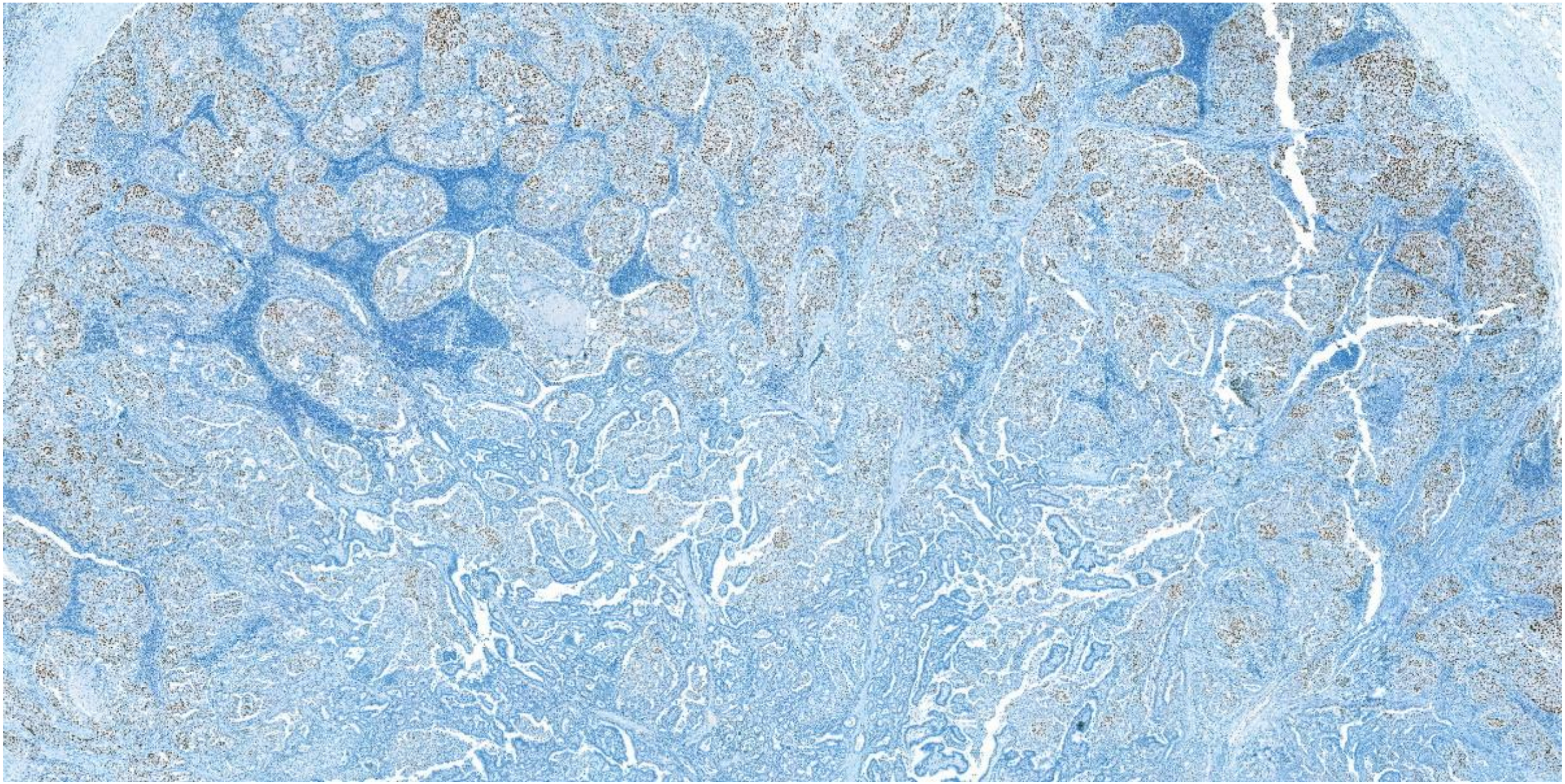


# Immunohistochemistry (p63, 1x, 10.x)

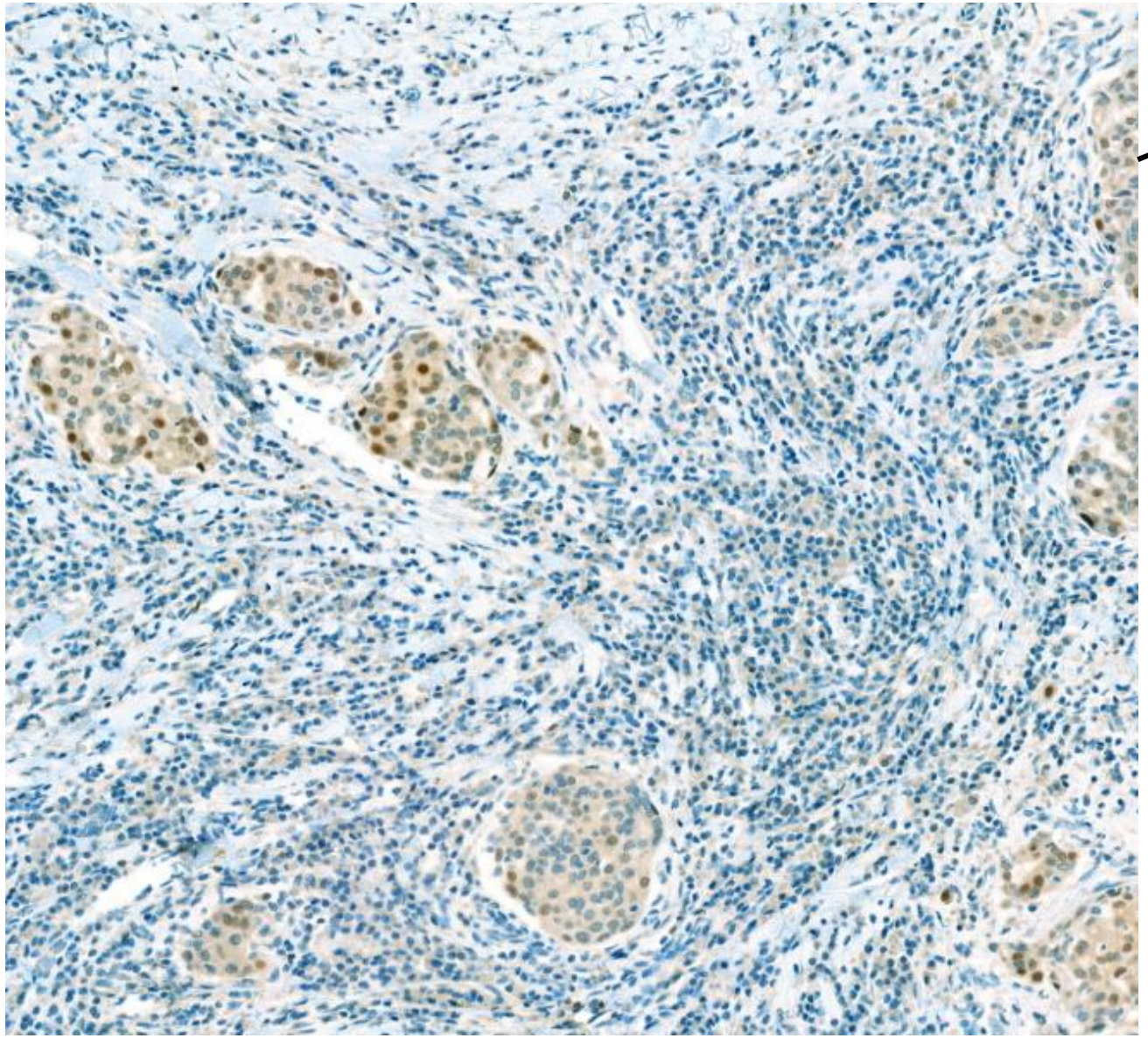


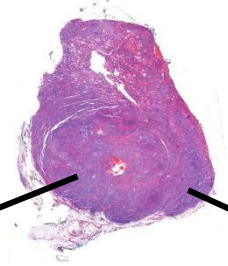


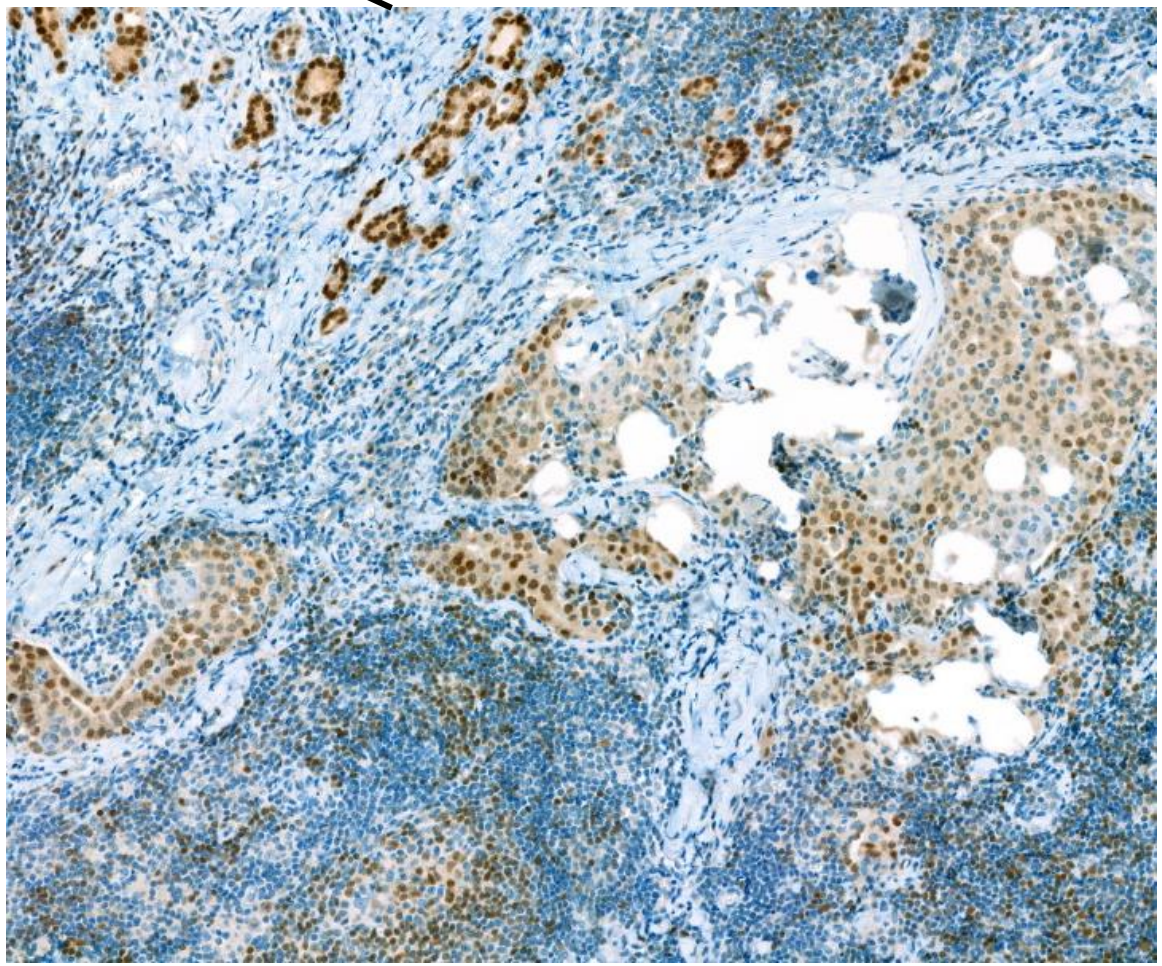
# Immunohistochemistry (LN; p63, 5x)



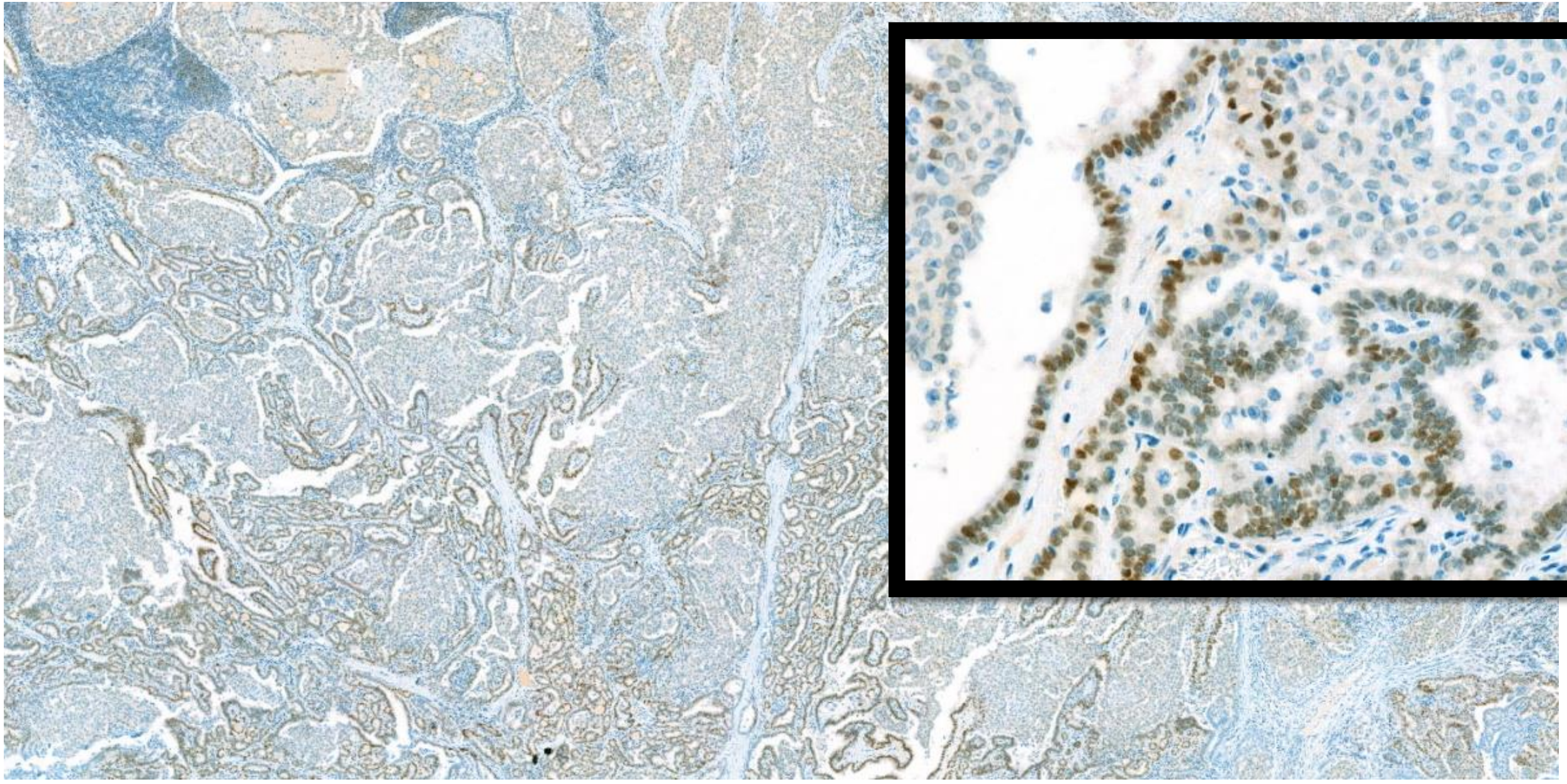
# Immunohistochemistry (PAX8, 23x)



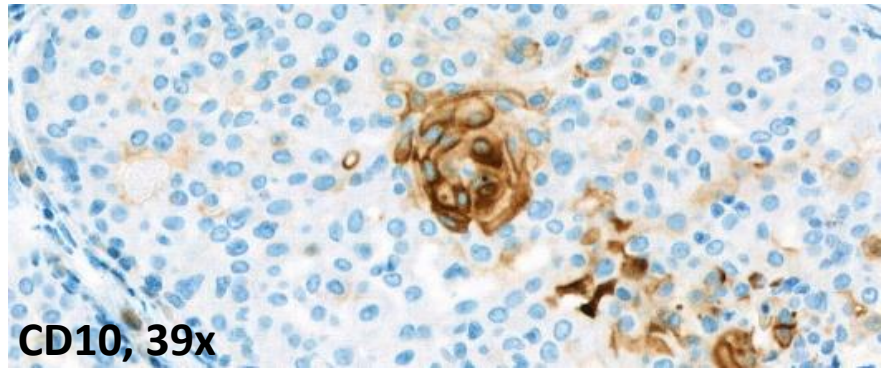




# Immunohistochemistry (LN; PAX8, 5x, 41x)



# Immunohistochemistry: summary




| Test | Primary | Periphery/satelite | Lymph node metastases |
|---|---|---|---|
| TTF1 | Positive | Positive | Positive |
| Thyroglobulin | Negative | Negative | Focal (papillary area) |
| PAX8 | Focal | Focal | Positive (papillary area) |
| p63 | Positive | Positive (focal) | Positive (solid area) |
| CD10 | - | - | Squamous morula - positive |
| Beta-catenin | Cytoplasmatic staining | Cytoplasmatic staining | Cytoplasmatic staining |
| Calcitonin | Negative | Negative | NA |
| p53 | Normal | Normal | NA |
| CD5 | Negative | Negative | NA |
| NUT | Negative | Negative | NA |

# Diagnosis

- Sclerosing mucoepidermoid carcinoma with eosinofilia(SMEC) and papillary thyroid carcinoma in the setting of Hashimoto thyroiditis
  - pT1N1aR0 (8th ed. AJCC)
  - BRAF and TERTp negative

## Primary Mucoepidermoid Carcinoma and Sclerosing Mucoepidermoid Carcinoma with Eosinophilia of the Thyroid Gland: A Report of Nine Cases

Zubair W. Baloch, M.D., Ph.D., Alyson C. Solomon, B.S., Virginia A. LiVolsi, M.D.
*Department of Pathology and Laboratory Medicine, University of Pennsylvania Medical Center, Philadelphia, Pennsylvania*

Non-RAS, non BRAF-like tumors

Table 2.11 Clinical and pathological features of mucoepidermoid carcinoma (MEC) and sclerosing mucoepidermoid carcinoma with eosinophilia (SMECE)

| | MEC | SMECE |
|---|---|---|
| Median patient age (range) | 47 years (10–91 years) | 55 years (32–89 years) |
| Female-to-male ratio | 2:1 | 7:1 |
| Extrathyroidal extension | ~25% | ~40% |
| Cervical lymph node metastasis | ~40% | ~35% |
| Distant metastasis | < 10% | ~22% |
| Perineural invasion | Rare | Common |
| Chronic lymphocytic thyroiditis (Hashimoto thyroiditis) | ~40% | Common |
| Association with papillary thyroid carcinoma | ~50% | Rare |
| Thyroglobulin | Usually positive | Usually negative |
| TTF1 | Usually positive | ~50% |

WHO, 2007

Table 1 WHO classification scheme of thyroid neoplasms, 5th edition

**Developmental abnormalities**
1. Thyroglossal duct cyst
2. Other congenital thyroid abnormalities

**Follicular cell–derived neoplasms**
1. Benign tumors
   a. Thyroid follicular nodular disease
   b. Follicular adenoma
   c. Follicular adenoma with papillary architecture
   d. Oncocytic adenoma of the thyroid
2. Low-risk neoplasms
   a. Non-invasive follicular thyroid neoplasm with papillary-like nuclear features
   b. Thyroid tumors of uncertain malignant potential
   c. Hyalinizing trabecular tumor
3. Malignant neoplasms
   a. Follicular thyroid carcinoma
   b. Invasive encapsulated follicular variant papillary carcinoma
   c. Papillary thyroid carcinoma
   d. Oncocytic carcinoma of the thyroid
   e. Follicular-derived carcinomas, high-grade
      i. Differentiated high-grade thyroid carcinoma
      ii. Poorly differentiated thyroid carcinoma
   f. Anaplastic follicular cell–derived thyroid carcinoma

**Thyroid C-cell–derived carcinoma**
1. Medullary thyroid carcinoma

**Mixed medullary and follicular cell–derived carcinomas**

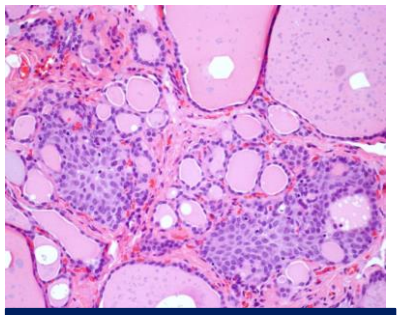
**Salivary gland–type carcinomas of the thyroid**
1. Mucoepidermoid carcinoma of the thyroid
2. Secretory carcinoma of salivary gland type

**Thyroid tumors of uncertain histogenesis**
1. Sclerosing mucoepidermoid carcinoma with eosinophilia
2. Cribriform morular thyroid carcinoma

**Thymic tumors within the thyroid**
1. Thymoma family
2. Spindle epithelial tumor with thymus-like elements
3. Thymic carcinoma family

**Embryonal thyroid neoplasms**
1. Thyroblastoma

Non-RAS, non BRAF-like tumor
*ETV6-NTRK3* fusion gene



Solid cell nests

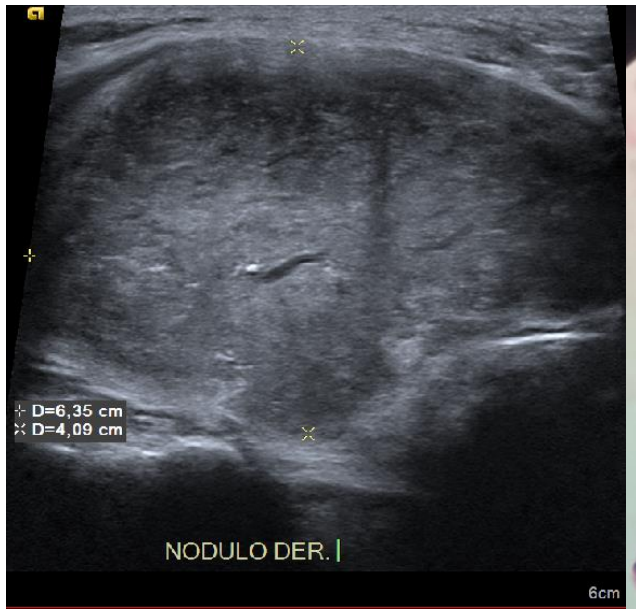
# Conclusions - SMEC

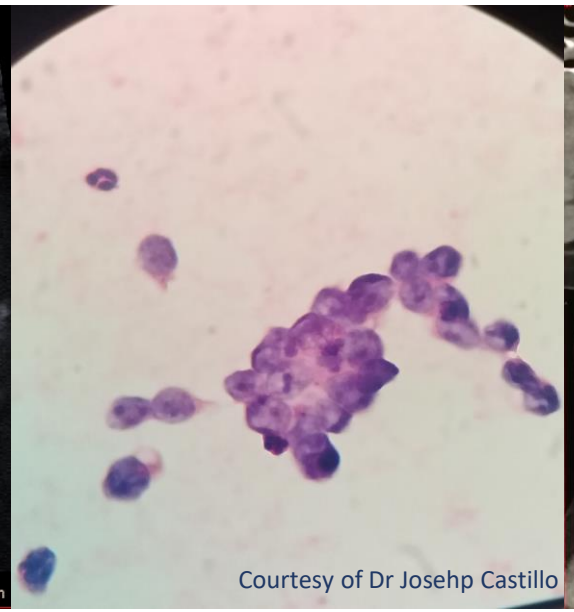
- Differential diagnosis
  - Cytology: PTC is a known mimicker
  - Histology: may be difficult to separate from MEC, PTC with squamous metaplasia/diffuse sclerosing variant-PTC, squamous cell carcinoma/anaplastic carcinoma, exuberant squamous metaplasia and thymus carcinoma
- Unusual findings: coexistence with PTC (psammoma bodies), squamous morula and necrosis
- Not so unusual findings: scant eosinophils despite abundant lymphocytes and plasma cells

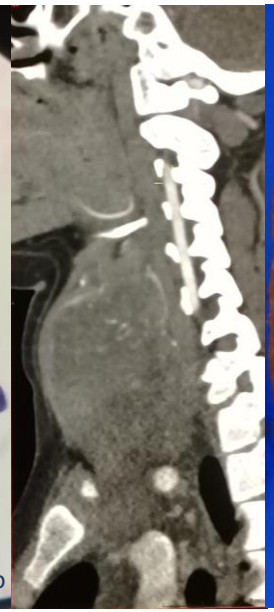
# CASE 2

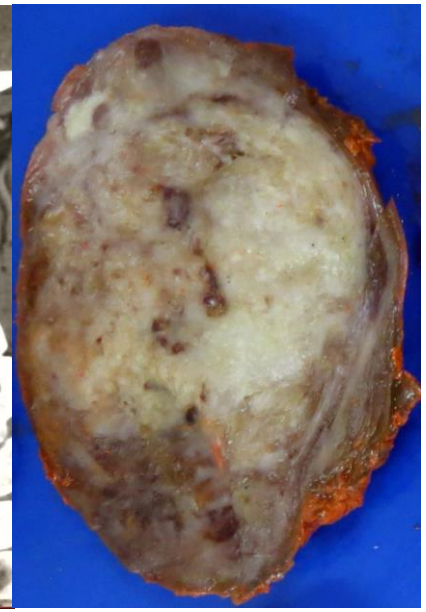
**17-year-old female patient with a rapidly growing, large mass in the neck**

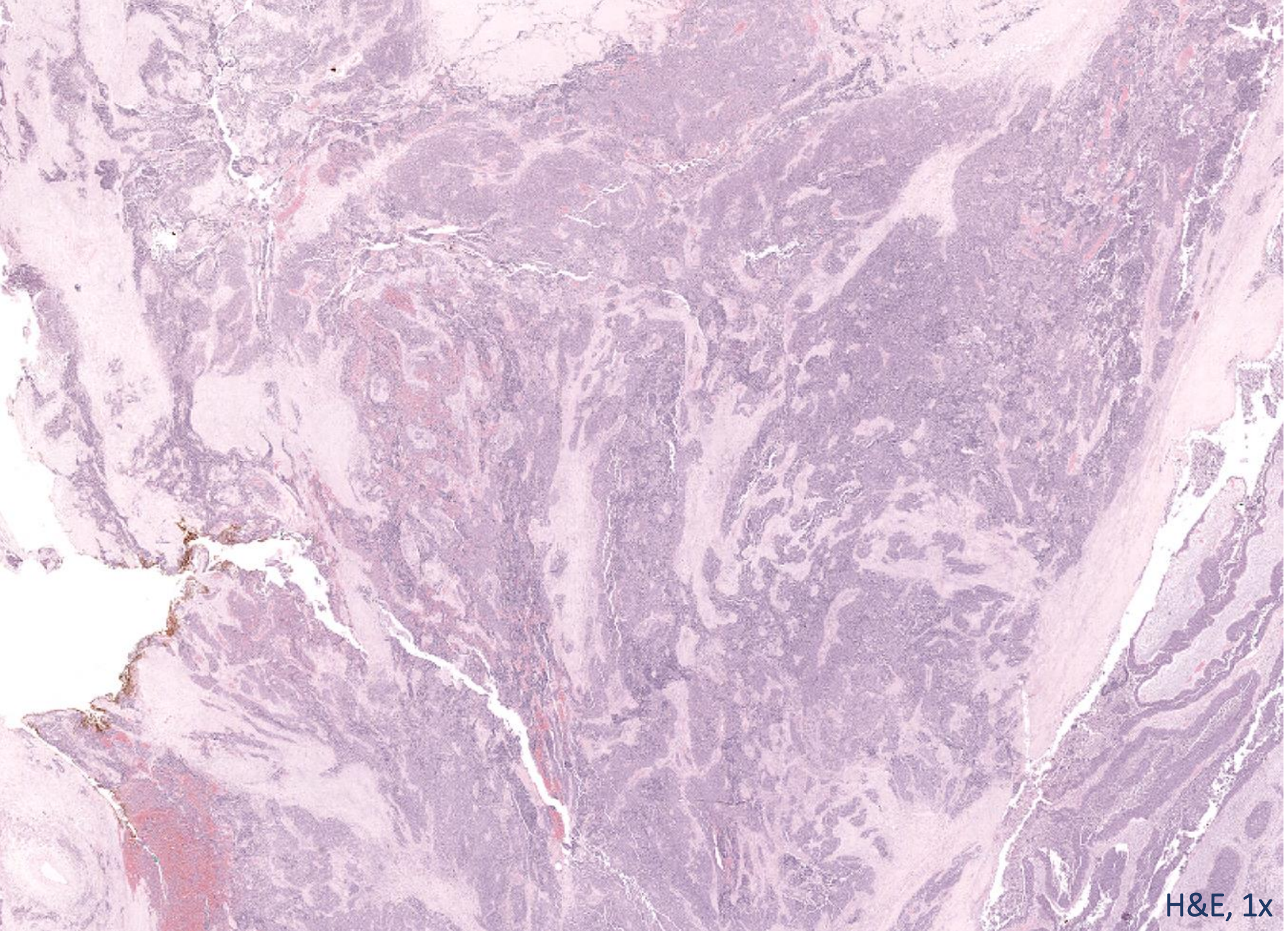
Euthyroid
Cytology was “suspicious for medullary carcinoma”
Total thyroidectomy was performed
Rapid progression of the disease into the mediastinum after surgery
Clinical diagnosis was Ewing sarcoma and the patient was treated according to this diagnosis

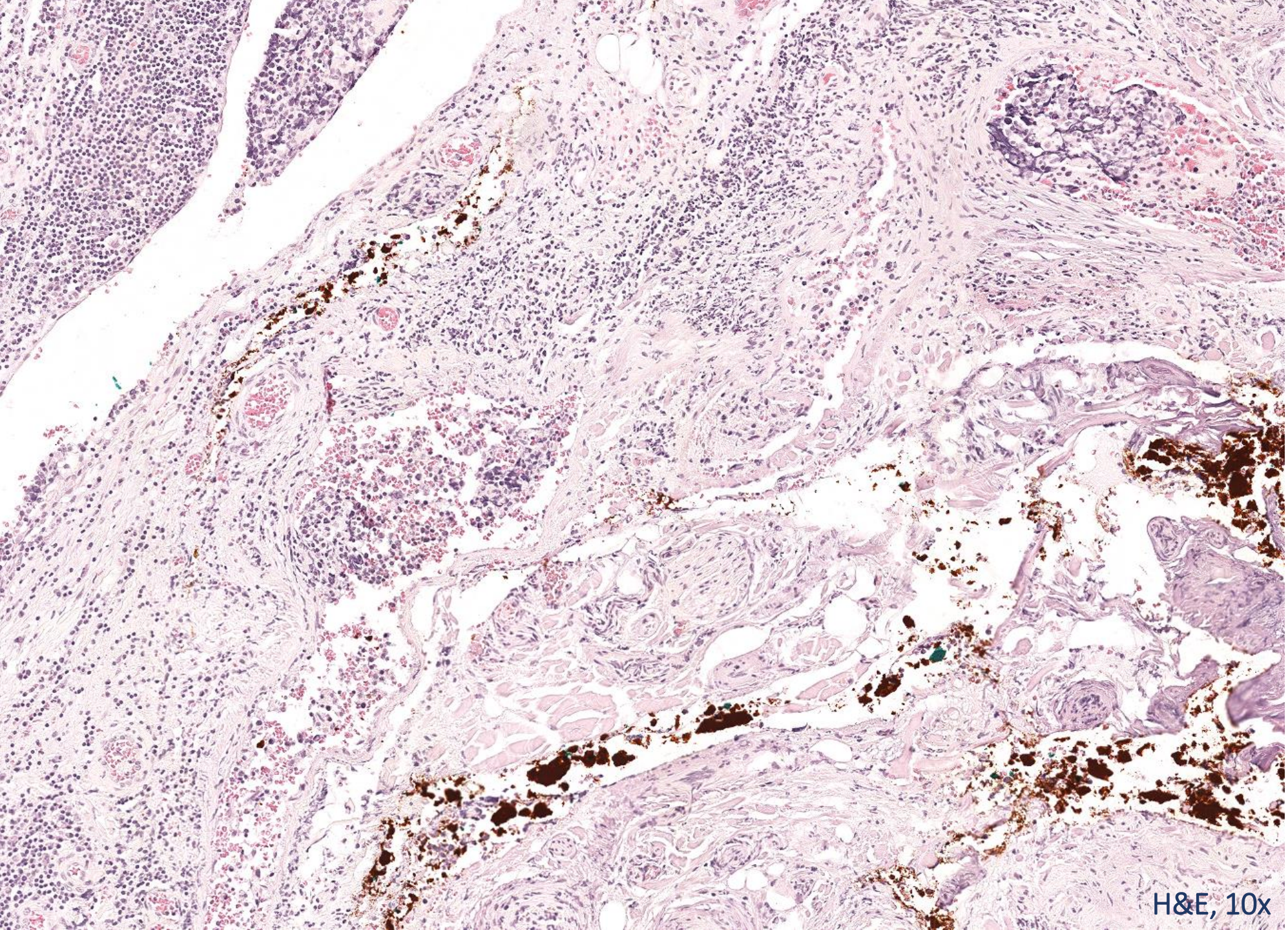


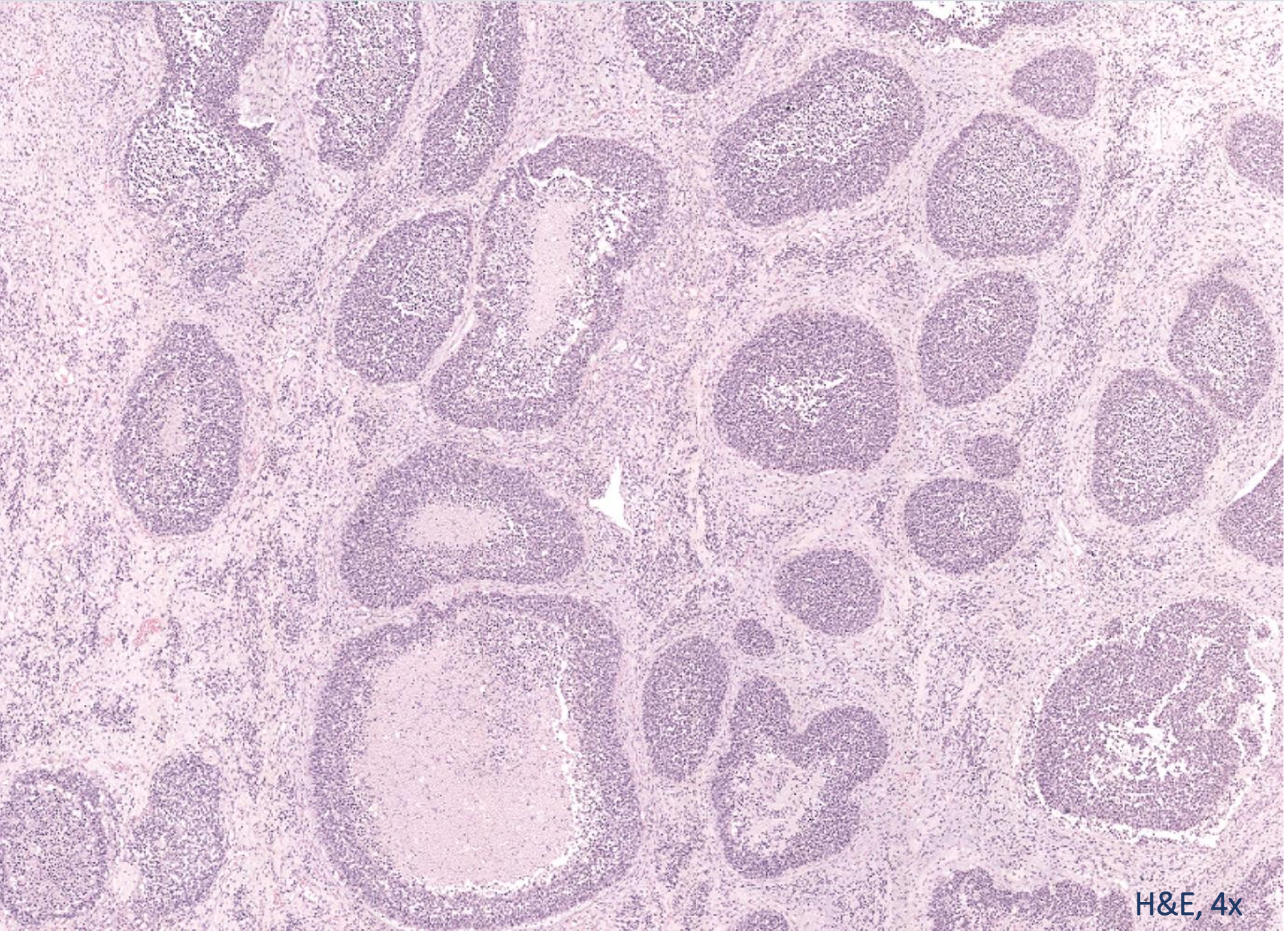



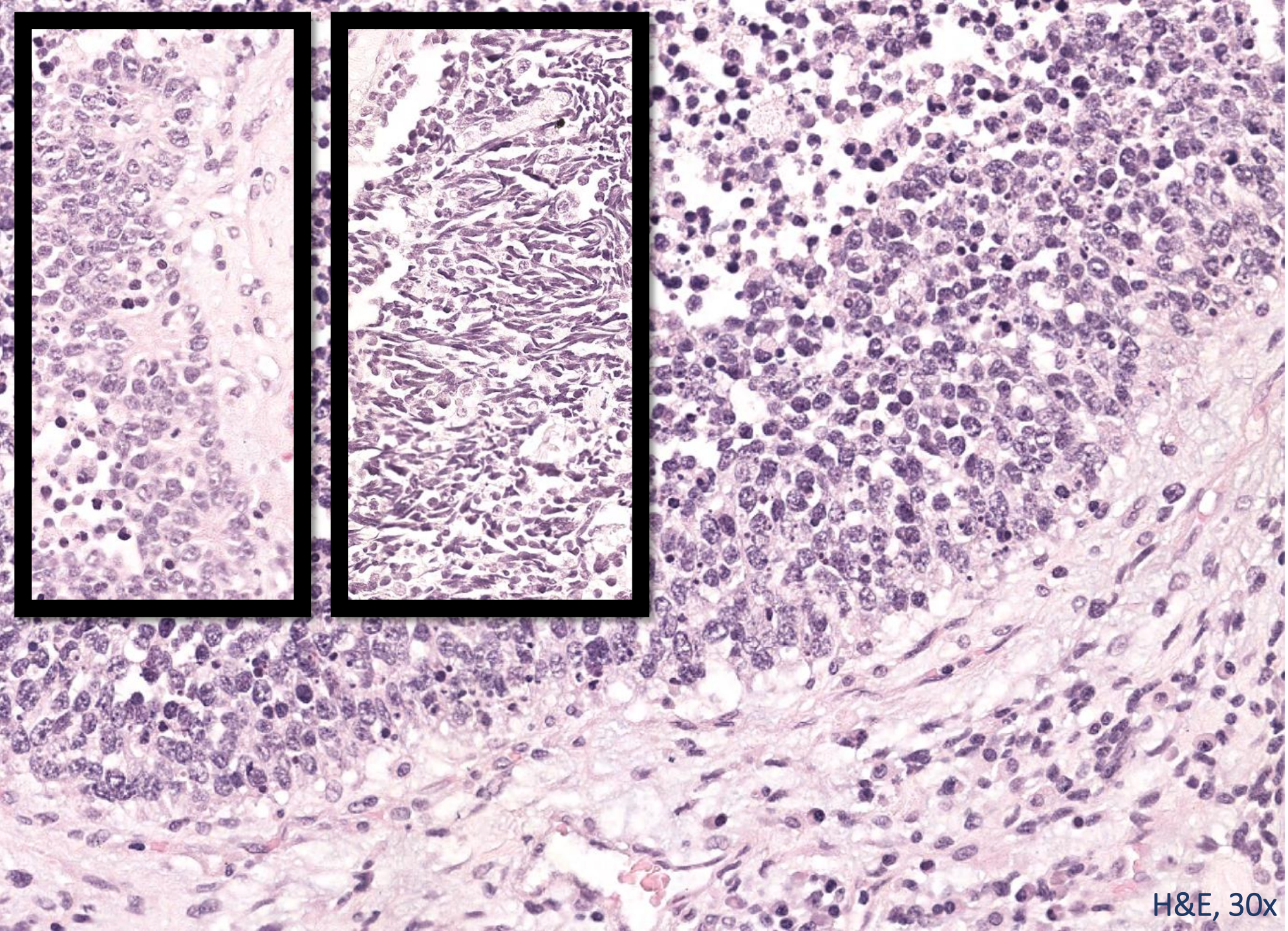


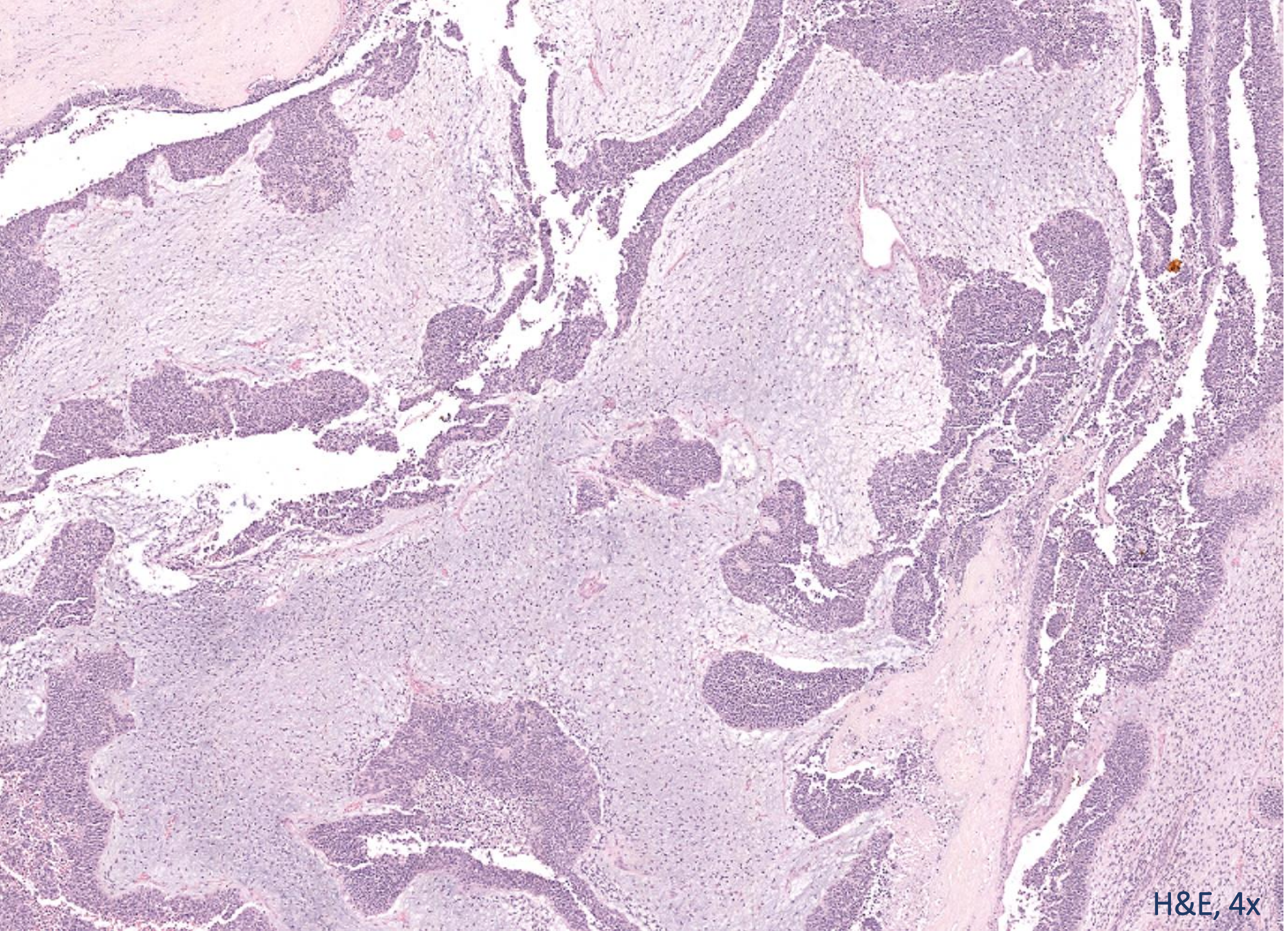

H&E, 1x

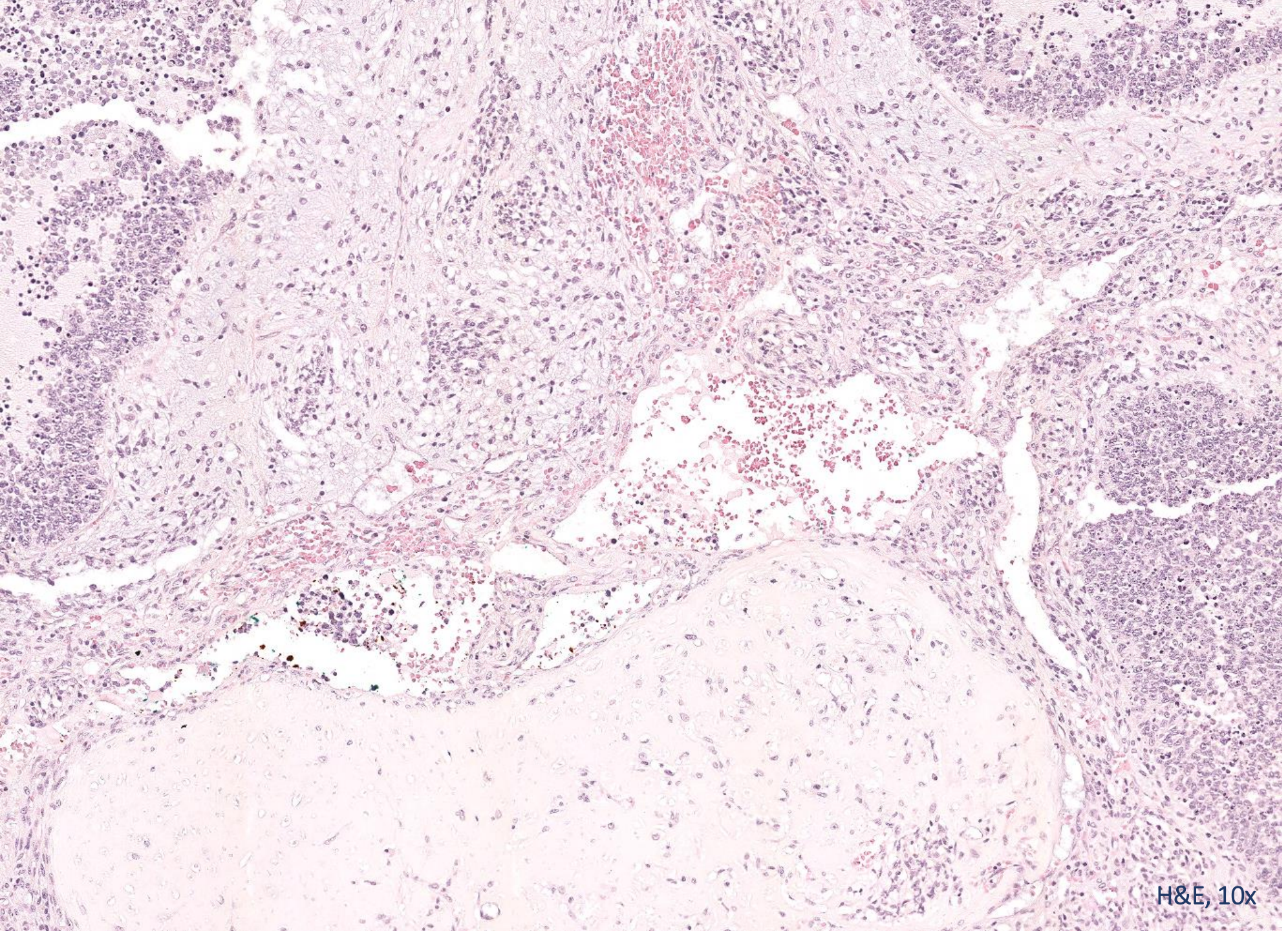


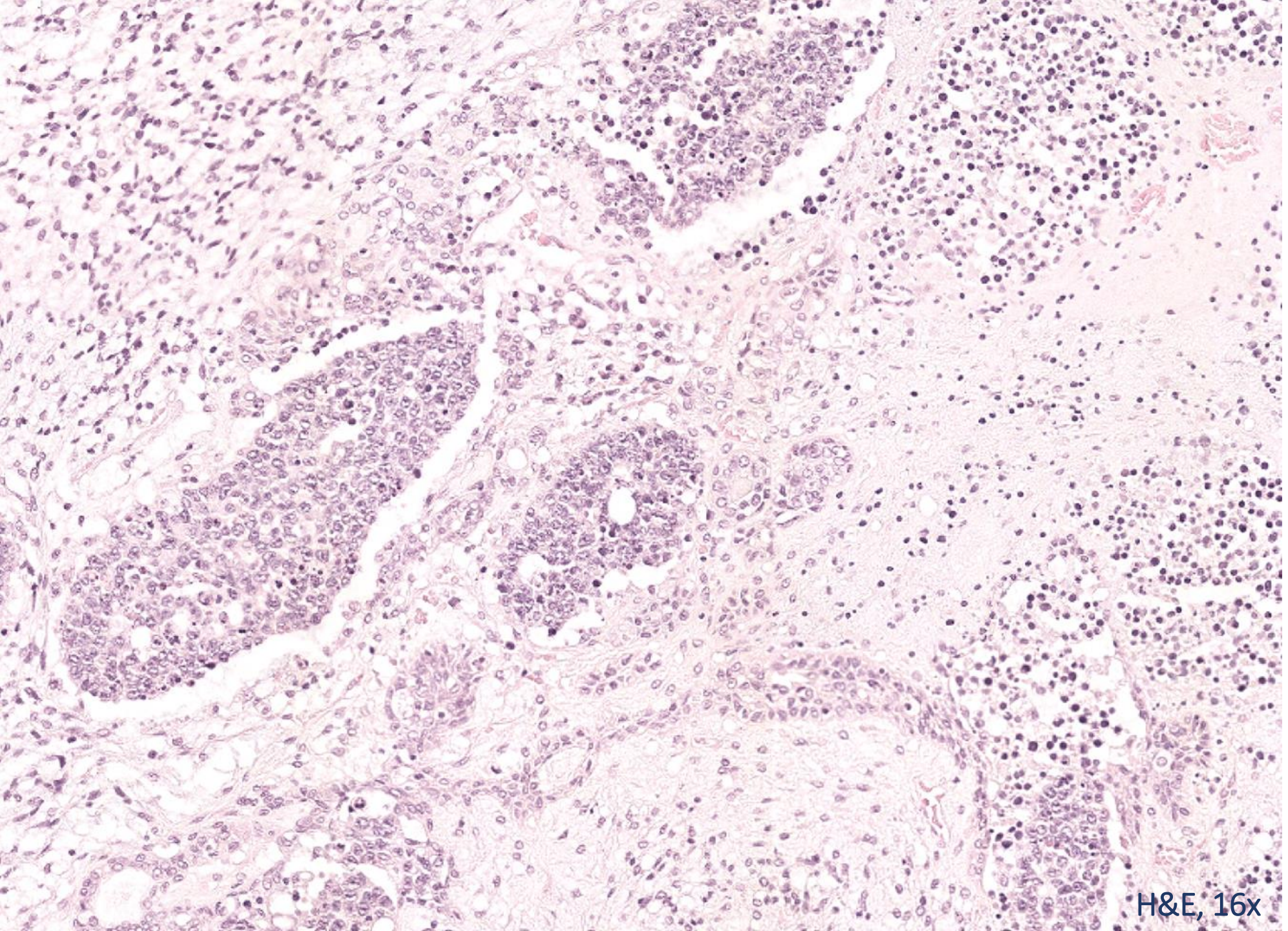
H&E, 10x


H&E, 4x

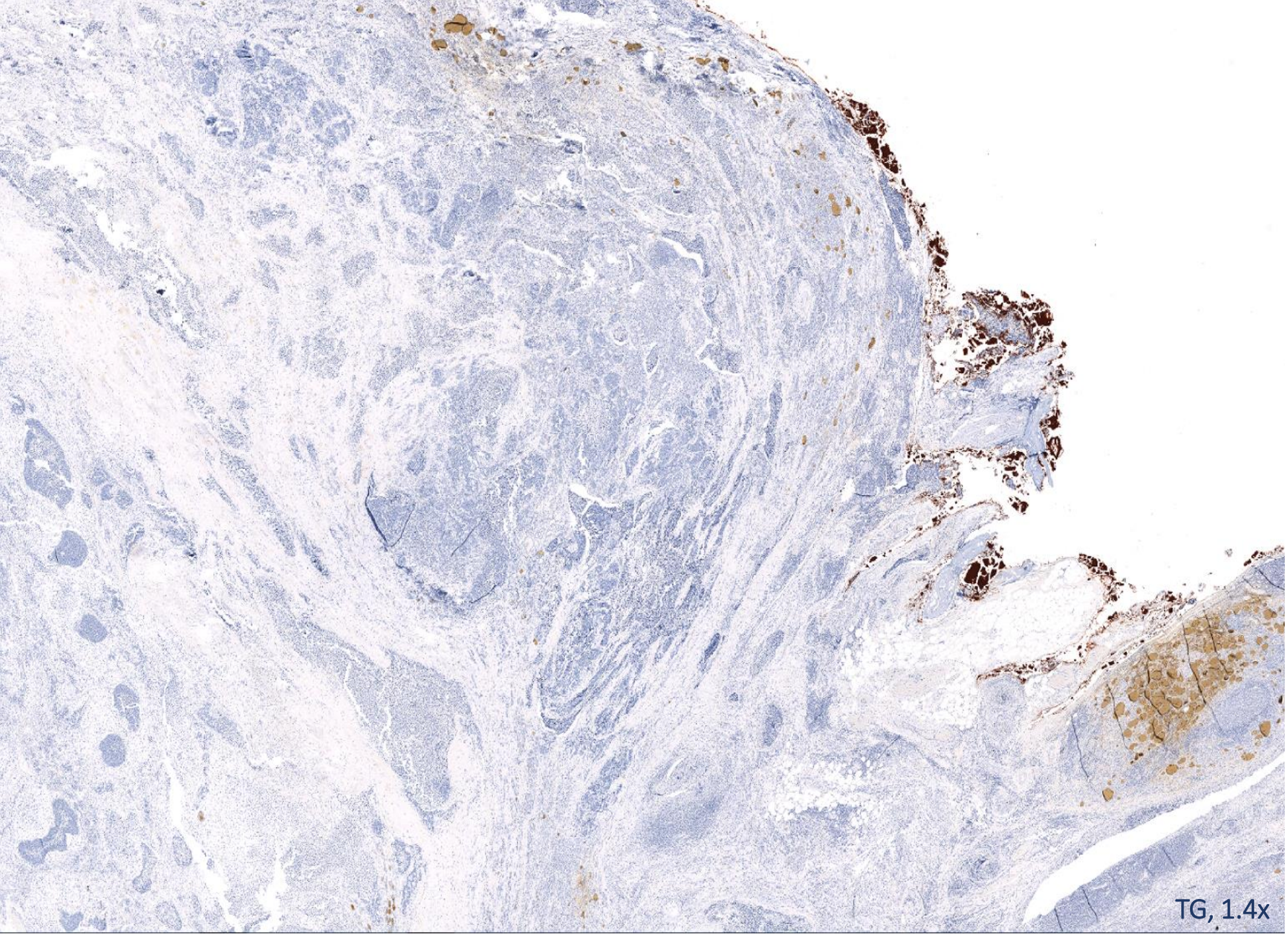

H&E, 30x


H&E, 4x


H&E, 10x

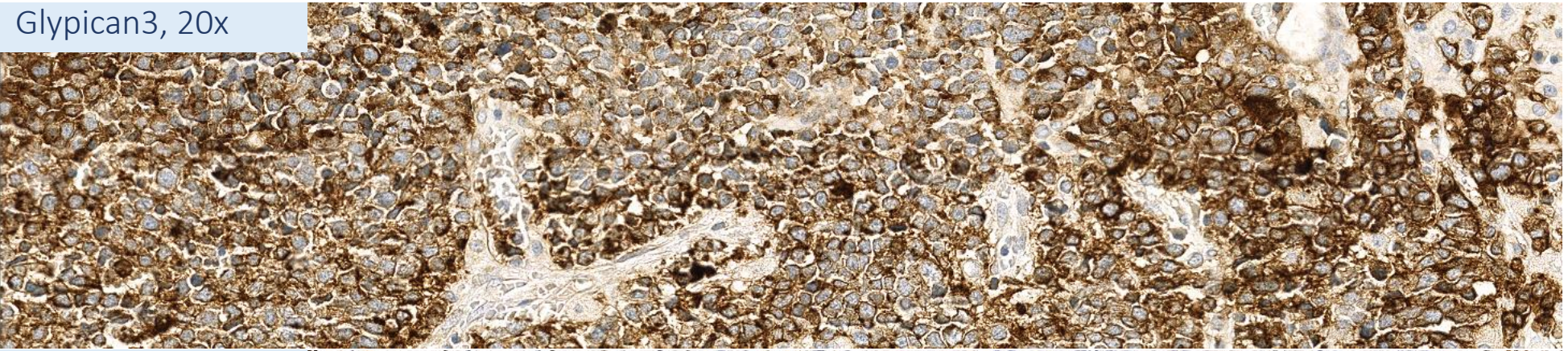


H&E, 16x

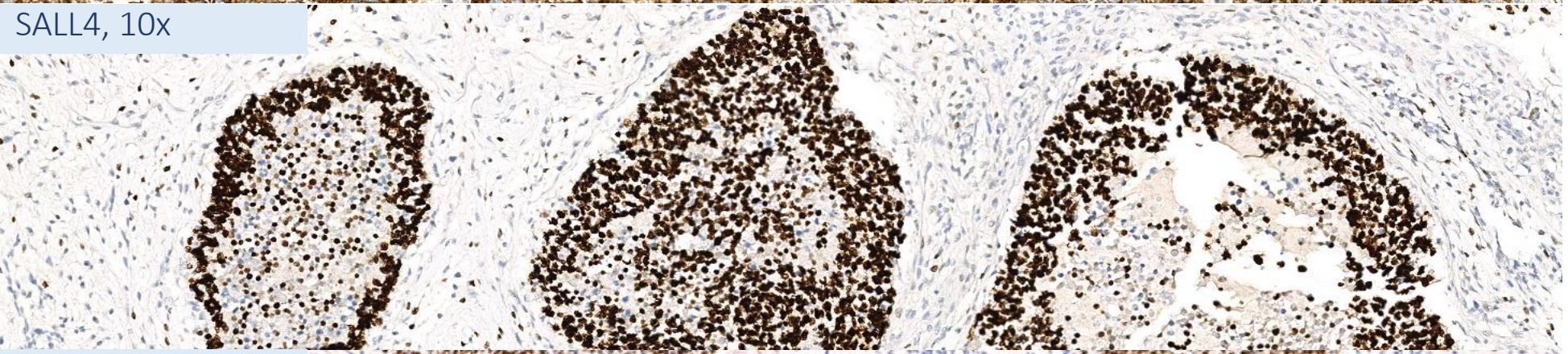

TG, 1.4x

# Immunohistochemical profile – small cells

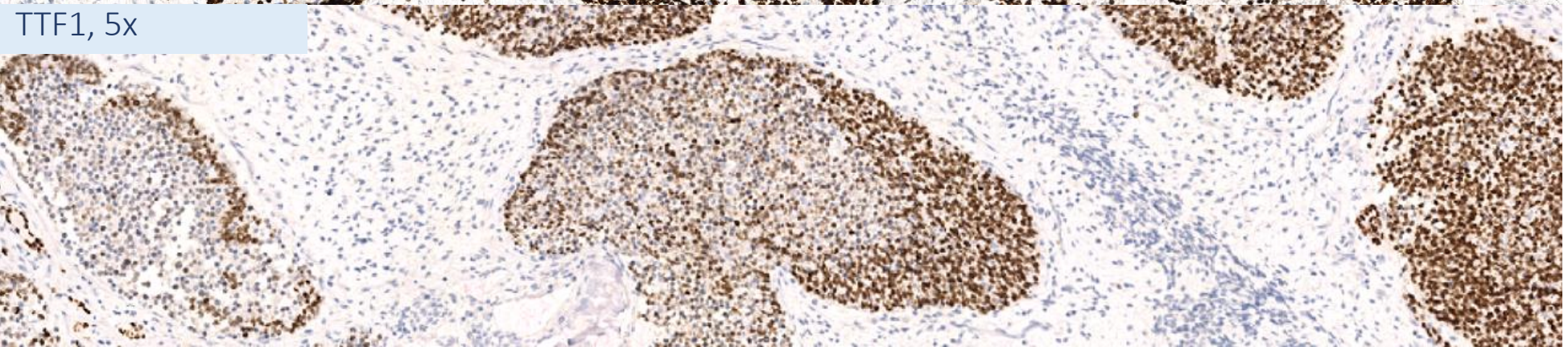
Glypican3, 20x



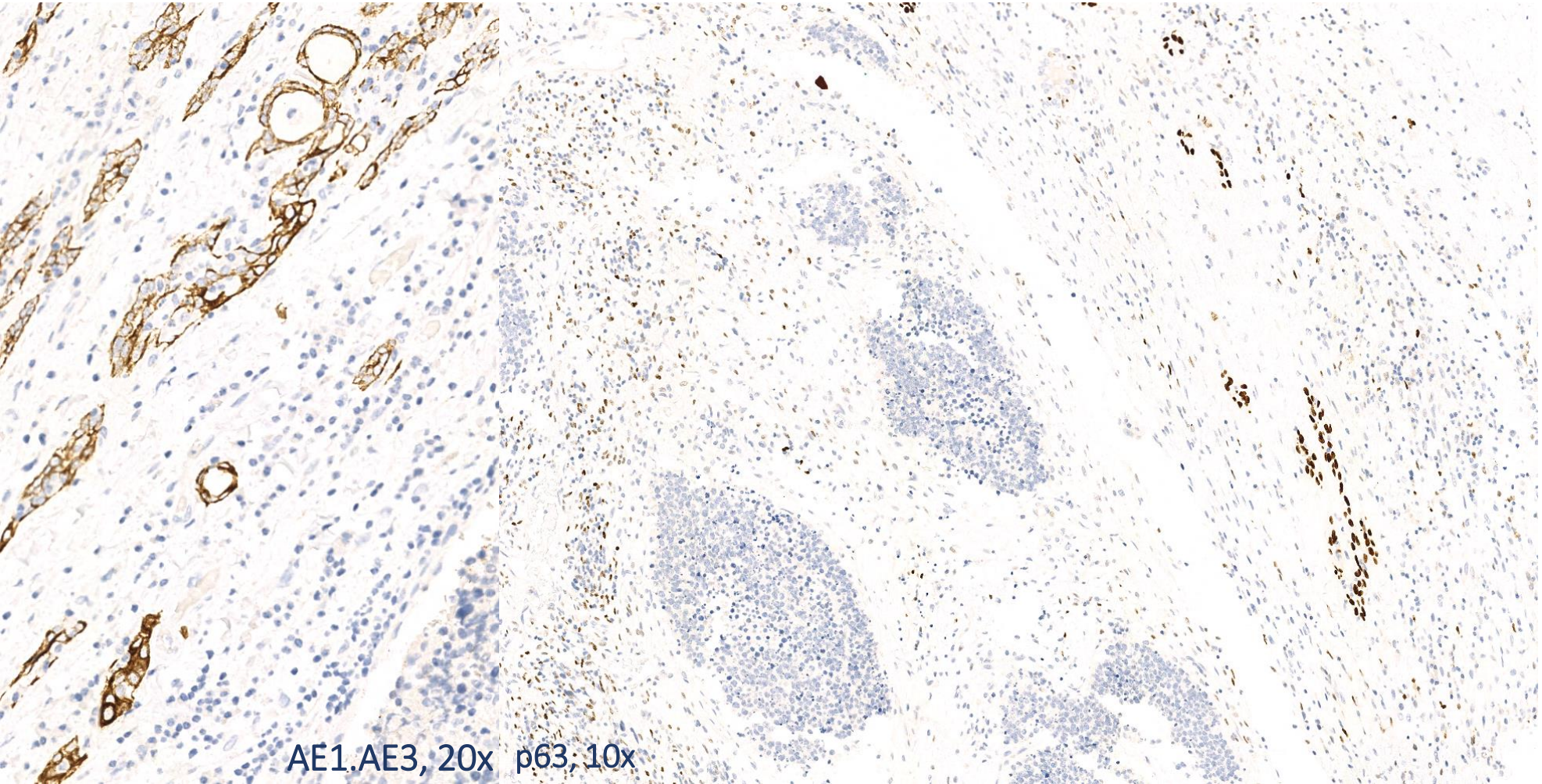
SALL4, 10x



TTF1, 5x

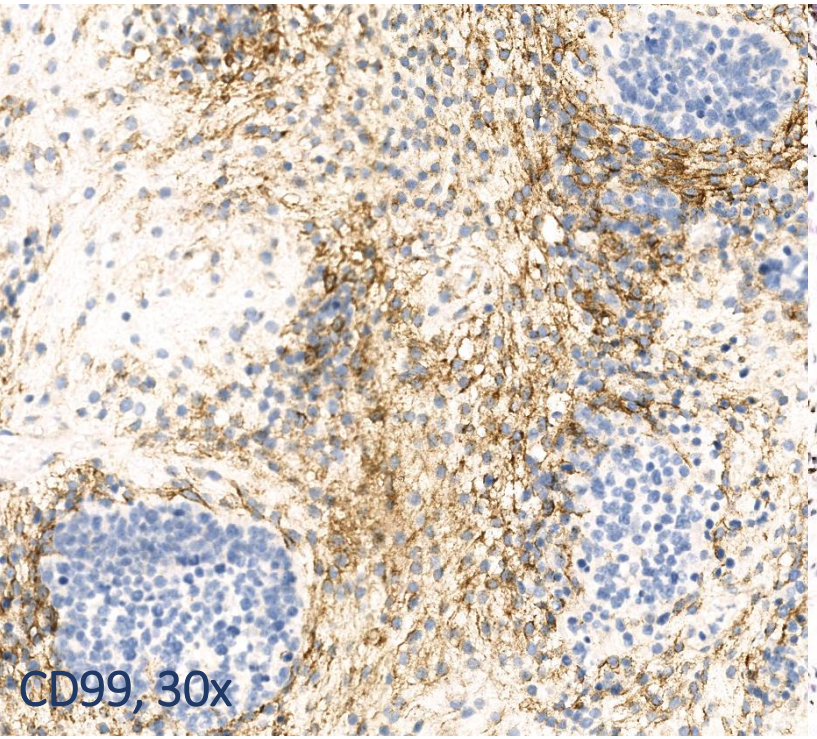


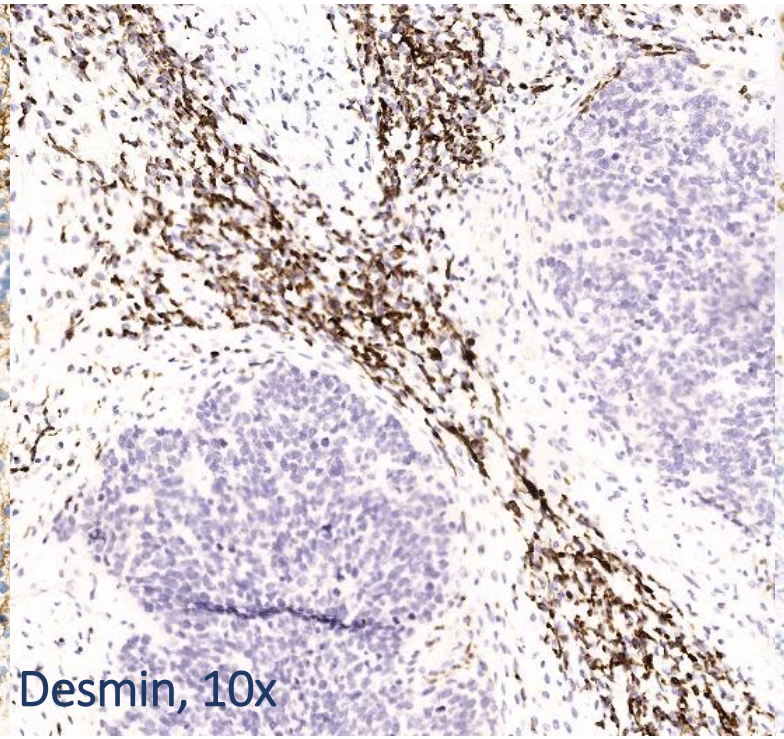
# Immunohistochemical profile – tubules

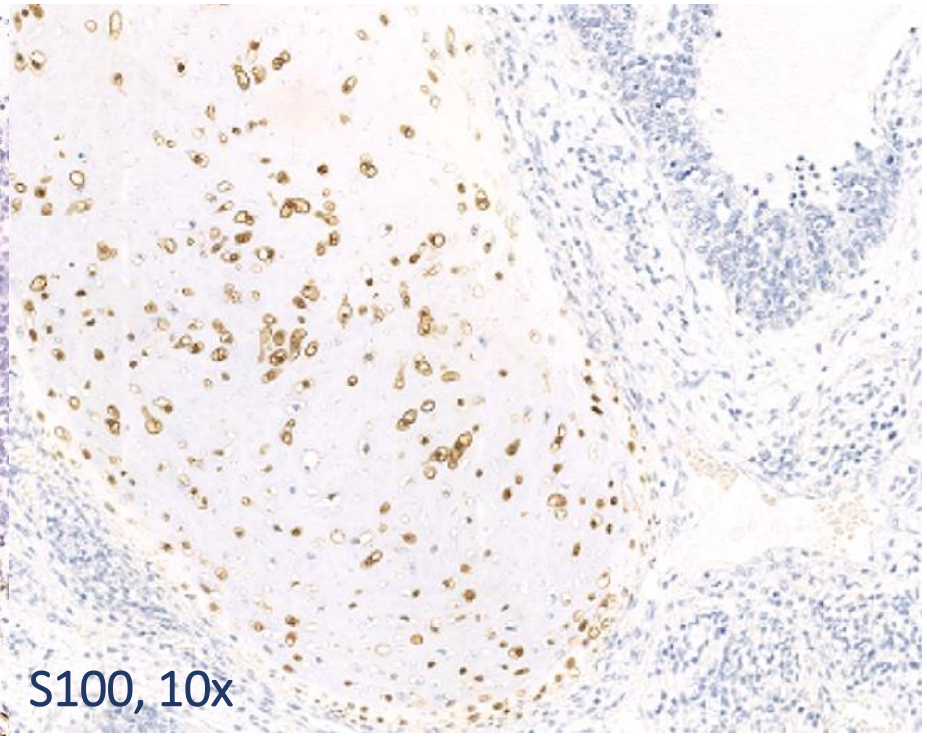


AE1.AE3, 20x p63, 10x

# Immunohistochemical profile – stromal cells


CD99, 30x


Desmin, 10x


S100, 10x

# Summary of ancillary tests

| Antibody | Expression |
|---|---|
| Thyroglobulin & Calcitonin | - |
| Chromogranin A & Synaptophysin | - |
| TTF1 | + |
| PAX8 & Napsin A | - |
| Pan-cytokeratins (AE1.AE3 & CK8/18) | - (+ in the tubules) |
| Cytokeratin 20 &CEA | - |
| p63 | - (+ in the stroma) |
| CD99 | - (+ in the stroma) |
| NUT | - |
| Glypican 3 | + |
| SALL 4 | + |
| INI 1 | + |
| HMB45 | - |
| Desmin & myogenin | - (+ in the stroma) |
| S100 | - (+ in the stroma) |
| NSE | + |
| GFAP & Neurofilaments | - |
| CD30 & α-Fetoprotein | - |
| CD45 & Cyclin D1 | - |
| Ki-67 | >90% |
| EWSR1/FLI1 rearrangement | - |

# Malignant teratoma (of the thyroid)

malignant. Benign tumors contained only mature elements (Grade 0). Immaturity, identified as immature tissues that resemble those of the embryo (usually immature neuroectodermal tissues arranged in primitive neuroepithelial rosettes and tubules), was divided into three grades to separate immature from malignant tumors, by a modification of the grading of ovarian and sacrococcygeal teratomas[16–18] as follows: Grade 1: a limited degree of immaturity, with embryonal-type tissue in only 1 low-power magnification field (×4 objective with a ×10 ocular, using an Olympus BX40 microscope; Olympus, Melville, NY); Grade 2: > than 1 but < 4 low-power fields of immature foci; Grade 3: > 4 low-power fields of immature tissue, along with mitoses and cellular atypia. By these definitions, tumors that we graded as Grade 0 were called benign, Grade 1 or Grade 2 tumors were categorized as immature, and Grade 3 immature tumors were considered malignant. The presence of embryonal carcinoma or yolk sac tumor also would have placed a teratoma into a malignant category, but none of the cases in the current study had these components.

Thompson et al, 2000

Virchows Archiv (2020) 477:787–798
https://doi.org/10.1007/s00428-020-02853-1

ORIGINAL ARTICLE

# Malignant teratoid tumor of the thyroid gland: an aggressive primitive multiphenotypic malignancy showing organotypical elements and frequent *DICER1* alterations—is the term "thyroblastoma" more appropriate?

Abbas Agaimy[1] · Leora Witkowski[2] · Robert Stoehr[1] · Joseph Christopher Castillo Cuenca[3] · Carlos Alberto González-Muller[3] · Alfred Brütting[4] · Markus Bährle[4] · Konstantinos Mantsopoulos[5] · Randa M. S. Amin[6] · Arndt Hartmann[1] · Markus Metzler[7] · Samir S. Amr[6] · William D. Foulkes[2,8,9] · Manuel Sobrinho-Simões[10,11,12,13] · Catarina Eloy[10,11,12]

Received: 24 April 2020 / Revised: 15 May 2020 / Accepted: 21 May 2020 / Published online: 7 June 2020


**Abstract**

Primary thyroid teratomas are exceedingly rare. Mature and immature variants recapitulate their gonadal counterparts (predilection for infants/children, triphasic germ layer differentiation, and favorable outcome). On the other hand, the so-called malignant teratomas affect predominantly adults and elderly, are highly aggressive, and, according to a few published cases, harbor *DICER1* mutations. We describe three highly aggressive sporadic malignant teratoid thyroid tumors in 2 females (17 and 45 years) and one male (17 years). Histology showed triphasic neoplasms composed of solid nests of small primitive monomorphic cells embedded in a cellular stroma with primitive immature rhabdomyosarcoma-like (2) or pleomorphic sarcoma-like (1) phenotype. The third component was represented by TTF1+/PAX8+ primitive teratoid epithelial tubules reminiscent of primitive thyroid follicles and/or Wilms tumor, admixed with scattered respiratory- or enteric-type tubules, neuroepithelial rosettes, and fetal-type squamoid nests. Foci of cartilage were seen in two cases, but none contained mature organoid adult-type tissue or skin adnexa. SALL4 was expressed in the small cell (2) and stromal (1) component. Other germ cell markers were negative. Molecular testing revealed a known "hotspot" pathogenic *DICER1* mutation in two cases. In addition, case 1 had a missense *TP53* variant. This type of thyroid malignancy is distinct from genuine teratomas. The immunoprofile suggests primitive thyroid- or branchial cleft-like differentiation. Given that "blastoma" is a well-accepted terminology in the spectrum of DICER1-associated malignancies, the term "thyroblastoma" might be more convenient for these malignant teratoid tumors of the thyroid gland. Relationship of thyroblastoma to the DICER1 syndrome remains to be addressed.

DICER1 mutational study

known somatic pathogenic missense mutation in DICER1 p.Gly1809Arg

the variant allele frequency was consistent with these variants being present in the heterozygous state

# Recurrent *DICER1* Hotspot Mutations in Malignant Thyroid Gland Teratomas

## *Molecular Characterization and Proposal for a Separate Classification*

*Lisa M. Rooper, MD,* Jennifer P. Bynum, MD,* Karin P. Miller, MD,* Ming T. Lin, MD, PhD,* Jeffrey Gagan, MD, PhD,† Lester D.R. Thompson, MD,‡ and Justin A. Bishop, MD†*

**Abstract:** Thyroid gland teratomas are rare tumors that span a wide clinicopathologic spectrum. Although benign and immature teratomas arise in infants and young children and generally have good outcomes, malignant teratomas affect adults and follow an aggressive course. This divergent behavior raises the possibility that benign/immature and malignant teratomas are separate entities rather than different grades of a single tumor. However, the histogenesis and molecular underpinnings of thyroid gland teratomas are poorly understood regardless of grade. In this study, we performed next-generation sequencing on 8 thyroid gland teratomas, including 4 malignant, 3 benign, and 1 immature. We identified *DICER1* hotspot mutations in all 4 malignant cases (100%) but not in any benign/immature cases (0%). No clinically significant mutations in other genes were found in either group. We also performed immunohistochemistry to characterize the primitive components of malignant teratomas. Not only did all cases consistently contain immature neural elements (synaptophysin and INSM1 positive), but also spindled cells with rhabdomyoblastic differentiation (desmin and myogenin positive) and bland epithelial proliferations of thyroid follicular origin (TTF-1 and PAX8 positive). Although *DICER1* mutations have previously been implicated in multinodular hyperplasia and well-differentiated thyroid carcinomas, these findings demonstrate the first recurrent role for *DICER1* in primitive thyroid tumors. The combined neural, rhabdomyoblastic, and homologous epithelial elements highlighted in this series of malignant thyroid gland teratomas parallel the components of *DICER1*-mutated tumors in other organs. Overall, these molecular findings further expand the differences between benign/immature teratomas and malignant teratomas, supporting the classification of these tumors as separate entities.

**Key Words:** thyroid neoplasms, teratomas, malignant teratoma, DICER1 protein, human, immunohistochemistry, molecular diagnostics

(*Am J Surg Pathol* 2020;44:826–833)

## BACKGROUND

In the thyroid gland, teratomas are extremely rare tumors that span a wide clinical and pathologic spectrum. As in other anatomic sites, diagnosis of thyroid gland teratoma is broadly defined by the presence of tissues derived from all 3 embryonal layers, that is, ectoderm, mesoderm, and endoderm. Within this category, these tumors are graded as benign, immature, and malignant based on the histologic fraction of immature neuroectodermal components they contain,[1] a distinction that separates them into 2 divergent demographic and prognostic groups. Benign and immature thyroid teratomas almost exclusively arise in infants and young children, including a significant subset of tumors that occurs congenitally.[2] While they can cause morbidity and even mortality due to compression of vital structures, this subset of tumors has an excellent prognosis when completely excised.[2–4] In contrast, malignant thyroid gland teratomas generally occur in older children and adults. These are aggressive tumors that can give rise to locally infiltrative growth, widespread metastasis, and death from disease, although good outcomes can be achieved through intensive multimodality therapy.[2,5]

Given the vast differences in clinical presentation and outcomes between benign/immature and malignant thyroid gland teratomas, it is not clear whether these

Case Reports > Thyroid. 2017 Jan;27(1):125-128. doi: 10.1089/thy.2016.0201. Epub 2016 Nov 28.

# Successful Management of a Patient with Malignant Thyroid Teratoma

Guilherme Rabinowits [1], Justine Barletta [2], Lynette M Sholl [2], Encarnacion Reche [3], Jochen Lorch [1], Laura Goguen [4]

Affiliations + expand

PMID: 27784193 DOI: 10.1089/thy.2016.0201

## Abstract

**Background:** Malignant thyroid teratomas are rare tumors with a poor prognosis. Little is known about their pathogenesis or treatment. Here, the case is reported of an adult woman with an aggressive thyroid teratoma with primitive neuroectodermal tumor (PNET) malignant transformation, successfully managed with neoadjuvant chemotherapy and surgery.

**Patient findings:** Sequencing of paired tumor and normal tissues revealed a DICER1 c.5438A>G (p.E1813G) somatic mutation in 56% of sequencing reads consistent with a driver event.

**Summary and conclusions:** To the authors' knowledge, DICER1 mutations have not been previously reported in teratomas but have been described in PNETs, suggesting a role in the malignant transformation of this case.

BJC

FULL PAPER

British Journal of Cancer (2013) 109, 2744–2750 | doi: 10.1038/bjc.2013.637

Keywords: DICER1; germ cell tumours; sex cord-stromal tumours; ovarian; testicular; microRNA

# *DICER1* hotspot mutations in non-epithelial gonadal tumours

L Witkowski[1,2,3], J Mattina[2], S Schönberger[4], M J Murray[5,6], D G Huntsman[7], J S Reis-Filho[8], W G McCluggage[9], J C Nicholson[5], N Coleman[6], G Calaminus[10], D T Schneider[11], J Arseneau[12], C J R Stewart[13] and W D Foulkes*[,1,2,3,14]

Table 3. Summary of all mutations found

| Codon change | Tumour types | Age of patient in years (gender) | Protein change | Previously reported (tumour types) |
|---|---|---|---|---|
| c.5113G→A | Unclassified SCST | 54 (F) | p.E1705K | Yes (ERMS, SLCT) (Heravi-Moussavi *et al*, 2012) |
| c.5125G→A | SLCT | 21 (F) | p.D1709N | Yes (SLCT,TGCT,YST) (Heravi-Moussavi *et al*, 2012) |
| c.5428G→T | Mixed GCT (YST/IT) | 27 (F) | p.D1810Y | Yes (SLCT, ERMS, MT) (Heravi-Moussavi *et al*, 2012, Wu *et al*, 2013) |
| c.5429A→G[a] | Mixed gonadoblastoma/dysgerminoma | 15 (F) | p.E1788fs*41 | No |
| c.5429A→T | SLCT with components of JGCT | 16 (F) | p.D1810V | No |
| c.5437G→A | SLCT | 32 (F) | p.E1813K | Yes (SLCT) (Heravi-Moussavi *et al*, 2012) |
| c.5437G→C | SLCT<br>SLCT | 13 (F)<br>20 (F) | p.E1813Q | Yes (SLCT) (Heravi-Moussavi *et al*, 2012) |
| c.5438A→G[b] | Mixed GCT (dysgerminoma/YST)<br>Mixed GCT (embryonal carcinoma/IT/choriocarcinoma)<br>YST<br>SLCT | 9 (F)<br>12 (M)<br>1 (M)<br>24 (F) | p.E1788fs*41 | Yes (SLCT, WT) (Heravi-Moussavi *et al*, 2012; Wu *et al*, 2013) |
| c.5439G→C | SLCT<br>SLCT | 16 (F)<br>30 (F) | p.E1813D | No |

Abbreviations: ERMS = embryonal rhabdomyosarcoma; F = female; IT = immature teratoma; JGCT = juvenile granulosa cell tumour; M = male; MT = mature teratoma; SCST = sex cord-stromal tumour; SLCT = Sertoli–Leydig cell tumour; WT = Wilms tumour; YST = yolk sac tumour.

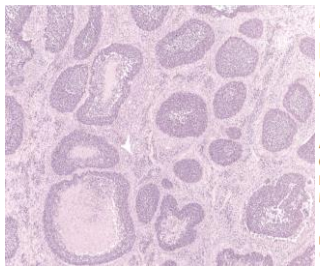
[a]Codon change is at D1810 but causes an A to G substitution causes a skip of exon 25 (unpublished data, Foulkes lab).

[b]Codon change is at E1813 but causes an A to G substitution causes a skip of exon 25.

# Diagnosis

- Thyroblastoma

The patient died of the disease, less than one year after the diagnosis



**Malignant teratoid tumor of the thyroid gland: an aggressive primitive multiphenotypic malignancy showing organotypical elements and frequent *DICER1* alterations—is the term "thyroblastoma" more appropriate?**

Abbas Agaimy[1] · Leora Witkowski[2] · Robert Stoehr[1] · Joseph Christopher Castillo Cuenca[3] · Carlos Alberto González-Muller[3] · Alfred Brütting[4] · Markus Bähnle[4] · Konstantinos Mantsopoulos[5] · Randa M. S. Amin[6] · Arndt Hartmann[1] · Markus Metzler[7] · Samir S. Amr[6] · William D. Foulkes[2,8,9] · Manuel Sobrinho-Simões[10,11,12,13] · Catarina Eloy[10,11,12]

Received: 24 April 2020 / Revised: 15 May 2020 / Accepted: 21 May 2020 / Published online: 7 June 2020


Non-RAS, non BRAF-like tumor

**Table 1** WHO classification scheme of thyroid neoplasms, 5th edition

**Developmental abnormalities**
1. Thyroglossal duct cyst
2. Other congenital thyroid abnormalities

**Follicular cell–derived neoplasms**
1. Benign tumors
   a. Thyroid follicular nodular disease
   b. Follicular adenoma
   c. Follicular adenoma with papillary architecture
   d. Oncocytic adenoma of the thyroid
2. Low-risk neoplasms
   a. Non-invasive follicular thyroid neoplasm with papillary-like nuclear features
   b. Thyroid tumors of uncertain malignant potential
   c. Hyalinizing trabecular tumor
3. Malignant neoplasms
   a. Follicular thyroid carcinoma
   b. Invasive encapsulated follicular variant papillary carcinoma
   c. Papillary thyroid carcinoma
   d. Oncocytic carcinoma of the thyroid
   e. Follicular-derived carcinomas, high-grade
      i. Differentiated high-grade thyroid carcinoma
      ii. Poorly differentiated thyroid carcinoma
   f. Anaplastic follicular cell–derived thyroid carcinoma

**Thyroid C-cell–derived carcinoma**
1. Medullary thyroid carcinoma

**Mixed medullary and follicular cell–derived carcinomas**

**Salivary gland–type carcinomas of the thyroid**
1. Mucoepidermoid carcinoma of the thyroid
2. Secretory carcinoma of salivary gland type

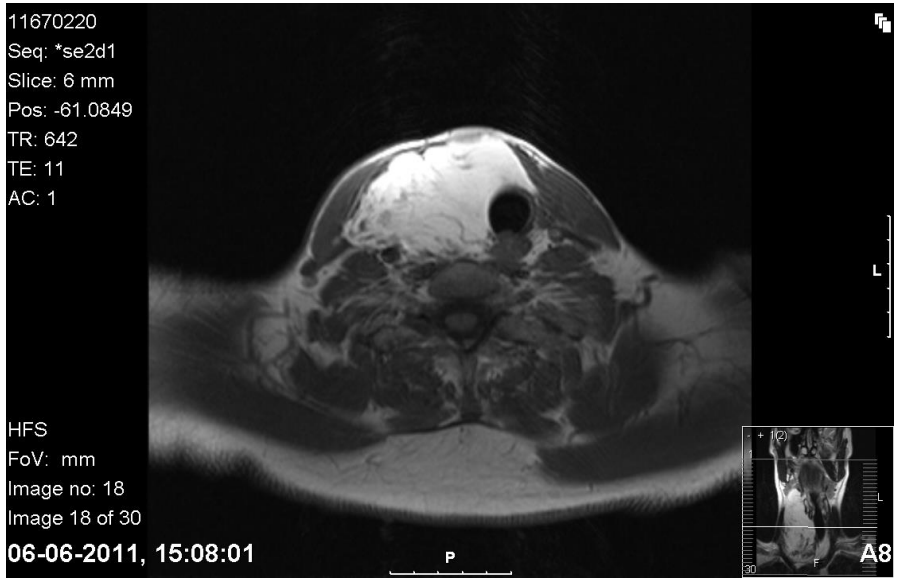
**Thyroid tumors of uncertain histogenesis**
1. Sclerosing mucoepidermoid carcinoma with eosinophilia
2. Cribriform morular thyroid carcinoma

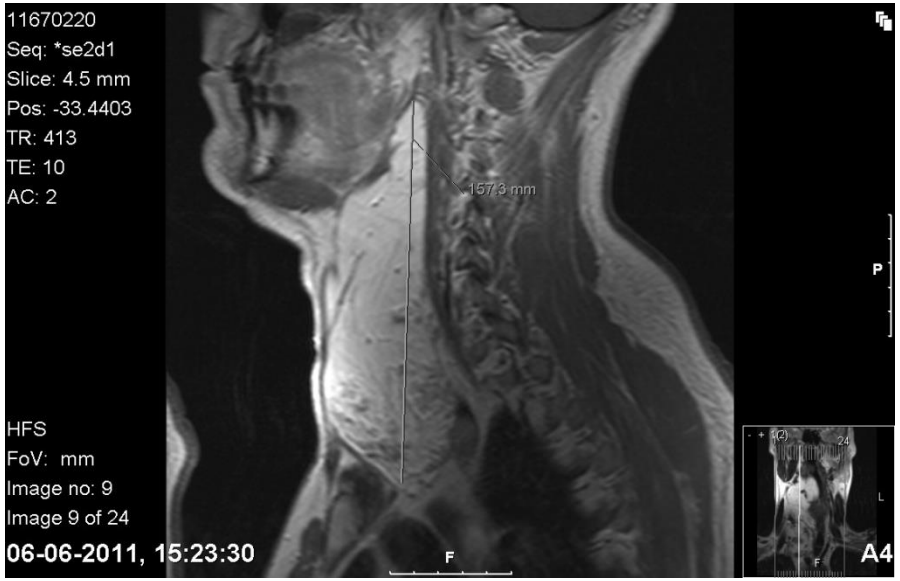
**Thymic tumors within the thyroid**
1. Thymoma family
2. Spindle epithelial tumor with thymus-like elements
3. Thymic carcinoma family

**Embryonal thyroid neoplasms**
1. Thyroblastoma

# Case 3

- 47-year old male followed by hypothyroidism
- Presented with a painless, slow growing, right cervical mass (for 10 years) located in the thyroid region and retropharyngeal space



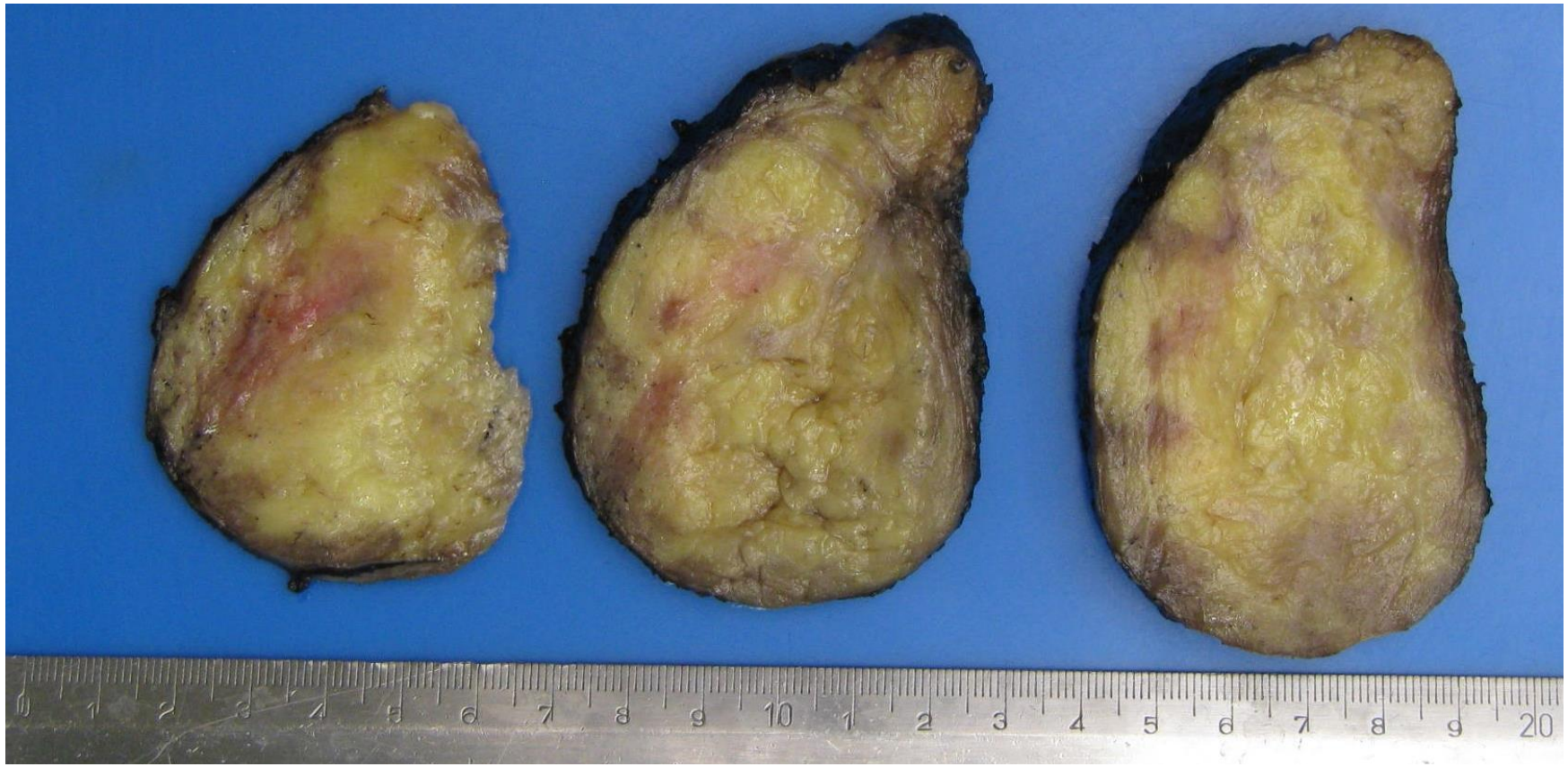



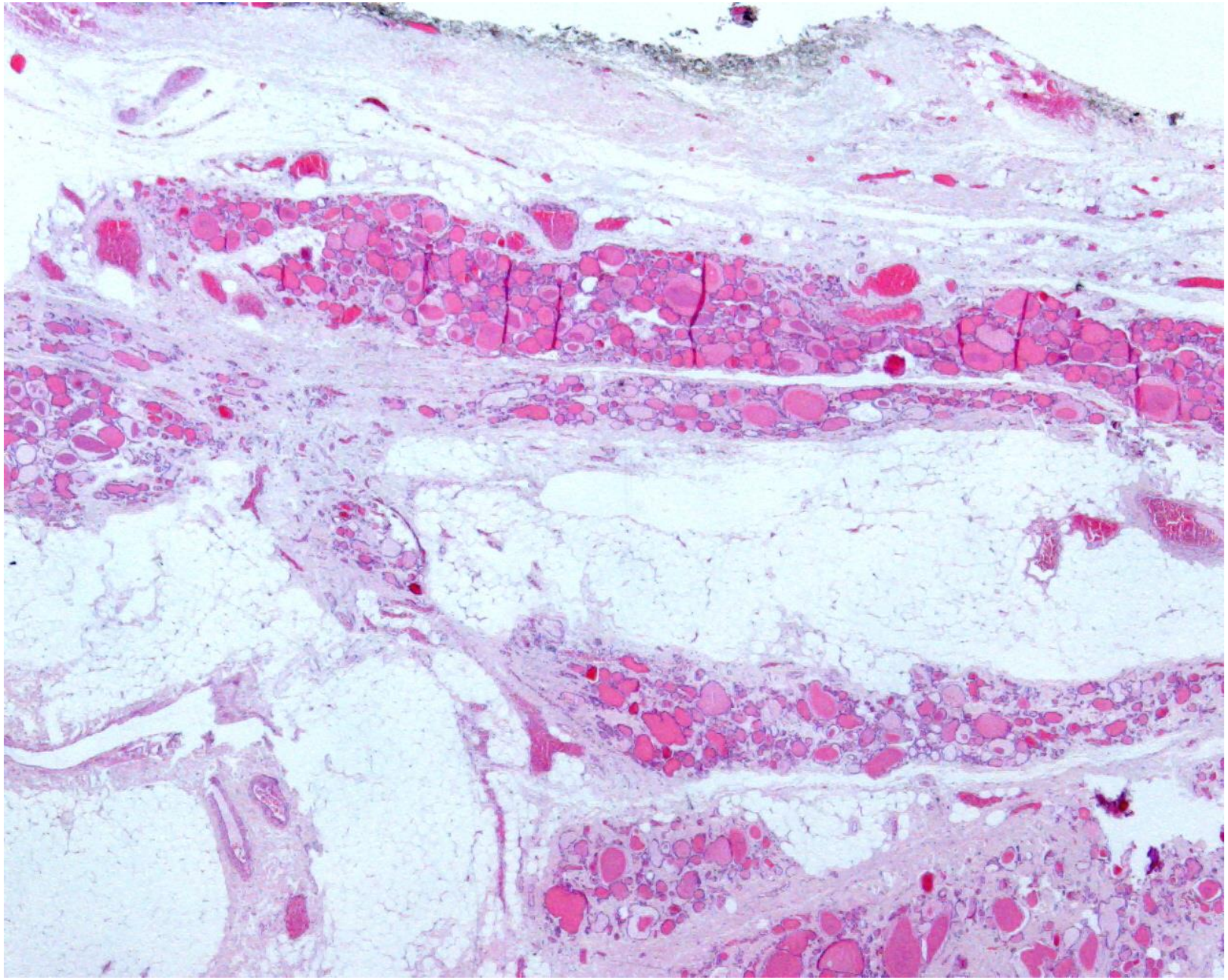

- FNA cytology was repeatedly inconclusive
- Core needle biopsy was representative of mature adipose tissue

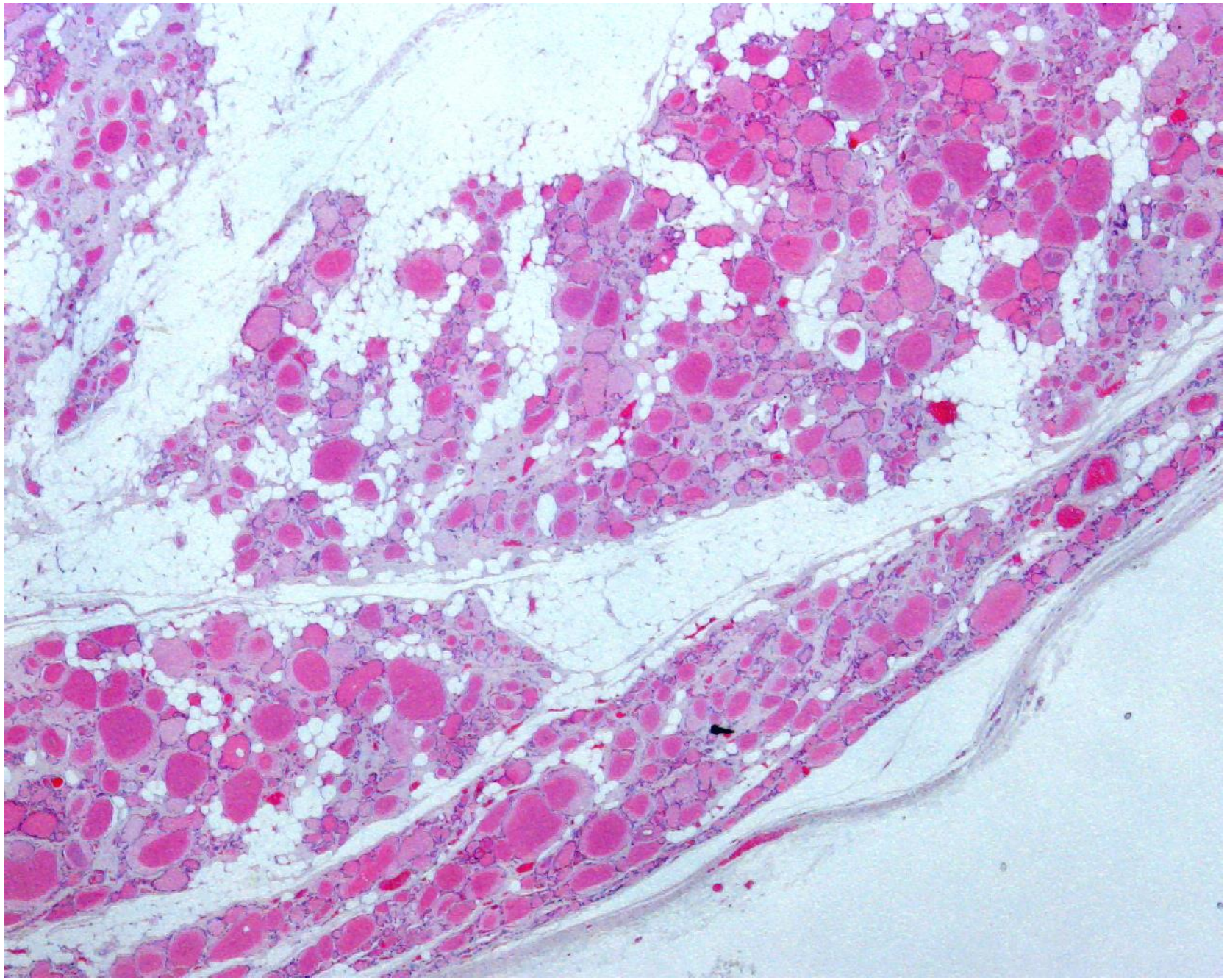
# Excision specimen

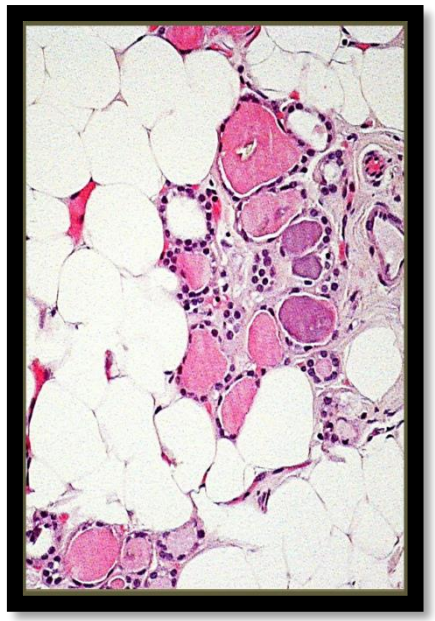
240g

16,5x8,0x5,5cm









# Differential diagnosis

- Lesion of the thyroid or lesion of the neck?
  - Well-differentiated lipomatous tumor of the neck infiltrating the thyroid
  - Lipomatous lesion of the thyroid

| Lesions of the thyroid with adipose tissue content |
| --- |
| Adipose metaplasia/infiltration of the interfollicular stroma |
| Adenolipoma |
| Diffuse lipomatosis |
| Amyloid goiter |
| Papillary carcinoma |
| Soft tissue sarcoma |
| Intraparenchymatous parathyroid with adipose stroma |

# Complementary studies

- Congo Red was negative
- Calcitonin was negative
- TTF1 and thyroglobulin were positive in the follicular cells

# Diagnosis

- Diffuse lipomatosis of the thyroid

ELSEVIER

Available online at www.sciencedirect.com
ScienceDirect
Annals of Diagnostic Pathology 13 (2009) 384–389

Annals of DIAGNOSTIC PATHOLOGY

## Thyrolipoma and thyrolipomatosis: 5 case reports and historical review of the literature

Yimin Ge, MD[a], Mario A. Luna, MD[b,*], Daniel F. Cowan, MD[c], Luan D. Truong, MD[a], Alberto G. Ayala, MD[a,*]

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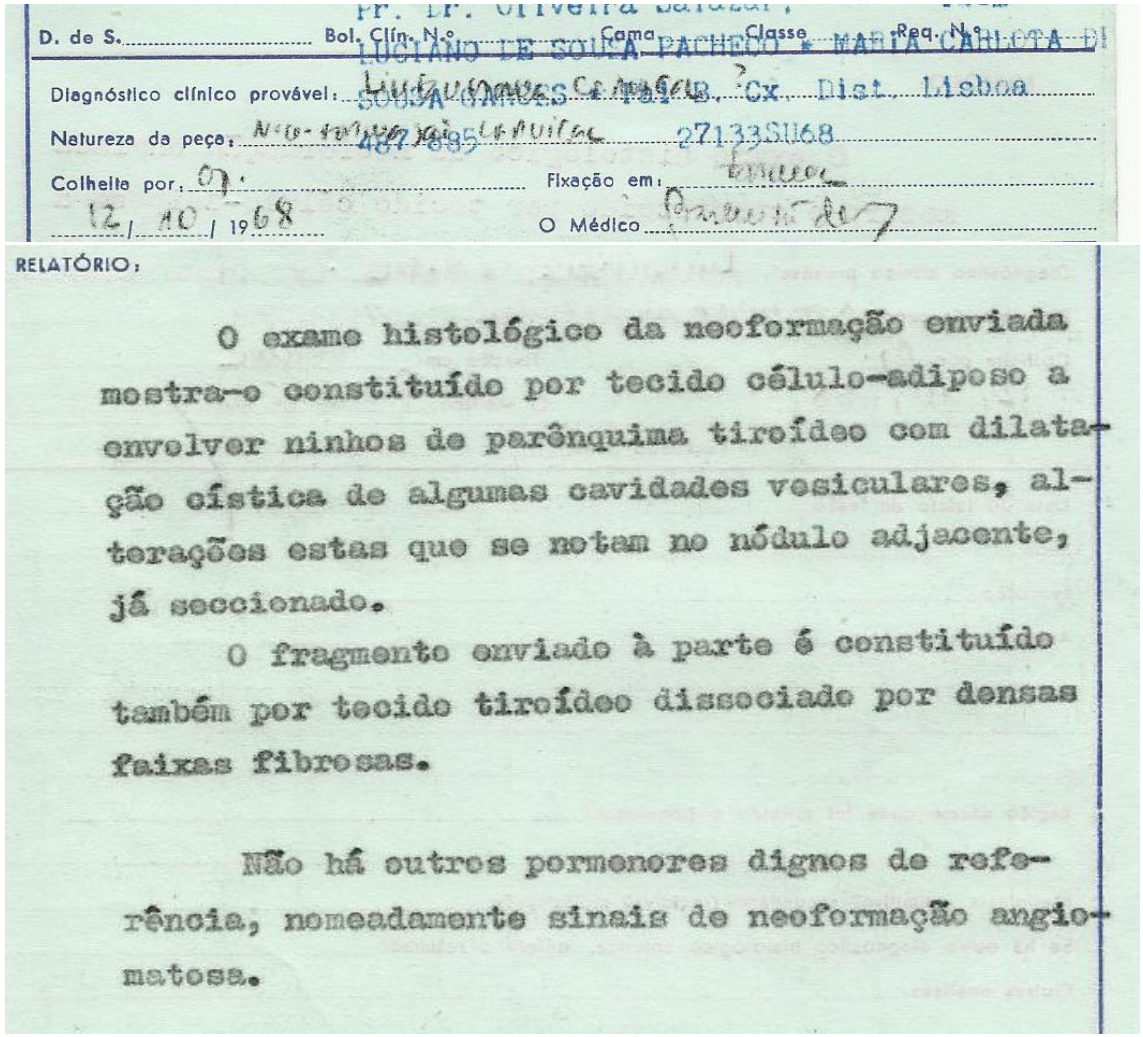
[b]*Department of Pathology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, USA*
[c]*Department of Pathology, University of Texas Medical Branch, Galveston, TX, USA*

Table 1
Clinicopathologic features of reported cases with diffuse lipomatosis of thyroid

| Author | Age (y) | Sex | Clinical features | Thyroid function | Weight /size | Gross features | Microscopic features |
|---|---|---|---|---|---|---|---|
| Dhayagude (1942) | 32 | M | Diffuse goiter × 3.5 y, local compression | NS | 500 g/ Rt 10 × 8 × 5.5 cm and 8 × 6 × 5.5 cm | Nodular, soft, yellow-white, with amber-colored colloid | Diffuse infiltration of fibrofatty tissue, irregular follicles, focal fibrosis |
| Simard (1945) | 11 | F | Diffuse goiter since birth, multiple lipomas | BMR +3% | "five times normal size of the thyroid" | Bosselated, soft, pale yellow | Lobules with fibrous septa, diffuse fat infiltration, small thyroid follicles |
| Chesky (1953) | 15 | M | Diffuse goiter since birth | Normal | 253 g/Rt 12 × 7 × 4 cm; Lt 8 × 5 × 2.5 cm | Bosselated, soft, yellow-brown to light yellow, fat/thyroid 4:1 | Diffuse fat infiltration, small to medium follicles, stromal edema, lymphocytes |
| Bielicki (1968) | 58 | M | Diffuse goiter × 5 years, local compression, tuberculosis | Hyper-thyroidism | NS | Irregular surfaces, brittle tissue | Diffuse fat infiltration, normal follicles, fibrosis, lymphocytic aggregates |
| Dalforna (1969) | 51 | NS | Diffuse goiter × 3 years | Normal | NS | Diffusely enlarged, pale brown | Diffuse fat infiltration, normal follicles, fibrosis |
| Asirwatham (1979) | 73 | F | Diffuse goiter × 4 y, colon cancer | Normal | 120 g/NS | Enlarge, nodular, firm | Diffuse fat infiltration, uniform follicles, lymphocytes |
| Simha (1983) | 12 | M | Right neck mass × 8 y | Normal | 415 g/Rt 13 × 8 × 6.5 cm | Yellow, soft, scattered irregular pinkish areas and small cystic spaces | Diffuse fat infiltration, normal follicles, mild fibrosis, lymphocytic aggregates |
| Arslan (1999) | 38 | M | Diffuse goiter × 7 y | Normal | 465 g/Rt 13 × 7 × 3 cm; Lt 15 × 9 × 5 cm; isthmus: 4 × 3 × 2 cm | Yellow, soft, fragile | Diffuse infiltration of mature fat between normal follicles |
| Current case 4 | 67 | F | Nodular goiter × 5 years, morbid obesity | Normal | 41 g/Lt 7 × 3.5 × 2 cm | Yellow-brown-red, soft, nodules, focally cystic | Diffuse infiltration of mature fat, adenomatous nodules, fibrosis |
| Current case 5 | 59 | F | Nodular goiter × 6 y, renal transplantation | Mild hypo-thyroidism | 56 g/Rt with isthmus 7 × 4 × 1.2 cm, Lt 6 × 3 × 1.2 cm | Yellow-brown, soft, focally cystic | Diffuse fat infiltration of thyroid including follicular adenomas, papillary thyroid carcinoma |

Rt indicates right lobe; Lt, left lobe; NS, not specified.

# Previous history



D. de S. ..... Bol. Clín. N.º ..... Cama ..... Classe ..... Req. N.º .....

Diagnóstico clínico provável: ..... Cx. Dist. Lisboa

Natureza da peça: ..... 27133SU68

Colhelte por: ..... Fixação em: .....

12 / 10 / 1968 O Médico .....

RELATÓRIO:

O exame histológico da neoformação enviada mostra-o constituído por tecido célulo-adiposo a envolver ninhos de parênquima tiroídeo com dilatação cística de algumas cavidades vesiculares, alterações estas que se notam no nódulo adjacente, já seccionado.

O fragmento enviado à parte é constituído também por tecido tiroídeo dissociado por densas faixas fibrosas.

Não há outros pormenores dignos de referência, nomeadamente sinais de neoformação angiomatosa.

At 3 years of age…

Neck mass (left side)

Suspicious for lipoma

Similar histological features

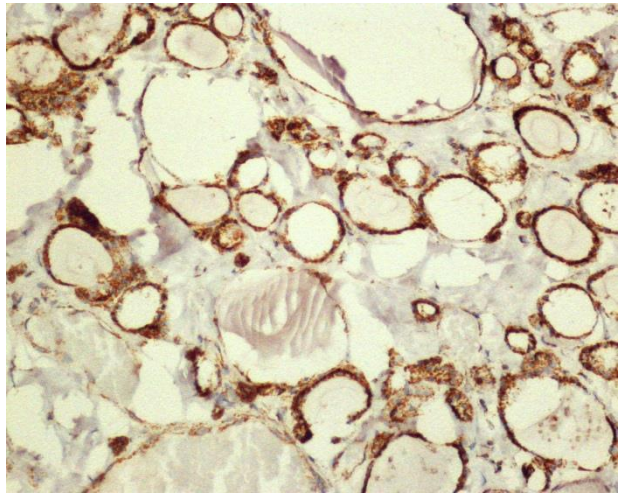
The infiltration of the neck by adipose tissue can occur in other well-known conditions such as multiple symmetric lipomatosis that can be associated with mitochondrial DNA mutations

*Molecular and Cellular Biochemistry* **174:** 271–275, 1997.

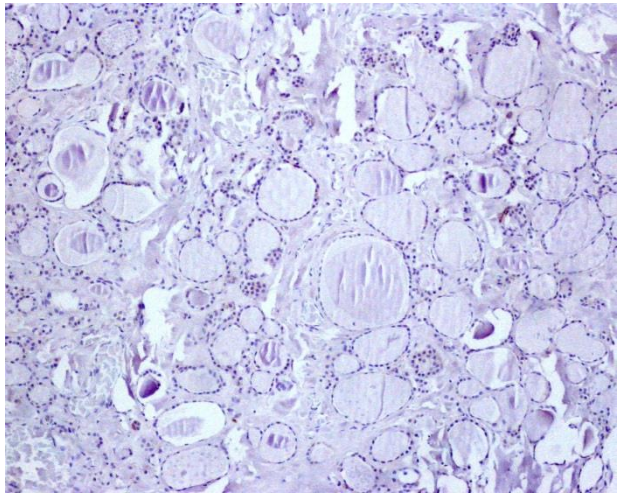

**Mitochondrial DNA mutations in multiple symmetric lipomatosis**

Thomas Klopstock,[1,2] Markus Naumann,[1] Peter Seibel,[1]
Bertold Shalke,[1] Karlheinz Reiners[1] and Heinz Reichmann[1,3]
[1]*Department of Neurology, University of Würzburg, Würzburg;* [2]*Department of Neurology, University of München, Klinikum Grosshadern, München;* [3]*Department of Neurology, Technical University of Dresden, Dresden, Germany*

Mitochondrial SDHA and SDHB expression in the present case



SDHA



SDHB

SDHB gene large deletion involving exon 1

## The pathophysiology of adipose tissue infiltration in the thyroid gland remains unknown

- The deregulation of mitochondrial respiratory chain, demonstrated by reduced expression and large deletion of SDHB, may play a role on fat accumulation in cases of diffuse lipomatosis of the thyroid.

  - Oxidative phosphorylation plays a role in mature adipocytes differentiation, by regulation of fatty acid synthesis, fatty acid oxidation and lipolysis.
  - It has already been demonstrated that, in preadipocytes, mithocondrial respiration impairment, through a decrease in fatty acid oxidation and an increase in lipogenesis, triggering fat accumulation.

De Pauw , 2009

Horm Metab Res. 2015 Mar;47(3):165-7. doi: 10.1055/s-0034-1398559. Epub 2015 Feb 13.

**Loss of Mitochondrial SDHB Expression: What is its Role in Diffuse Thyroid Lipomatosis?**

Lau E[1], Freitas P[1], Costa J[2], Batista R[3], Máximo V[3], Coelho R[3], Matos-Lima L[4], Eloy C[2], Carvalho D[1].

⊕ **Author information**

**Abstract**

Diffuse lipomatosis of the thyroid gland is a very rare disease, characterized by extensive infiltration of thyroid parenchyma by mature adipose tissue, usually not accompanied by amyloid fibrils deposition. The pathophysiology of adipose tissue infiltration in the thyroid gland remains unknown. We report a clinical case of a diffuse thyroid lipomatosis, whose immunohistochemical study of succinate dehydrogenase - subunit B (SDHB) revealed loss of expression of this protein in the follicular or adipose cells. We detected the presence of a recently described SDHB gene large deletion. Loss of mitochondrial SDHB expression may have a key role in understanding the pathophysiology of thyrolipomatosis, by regulating status of lipid metabolism.

Seminar of Young Pathologists
Litomysl, Czech Republic
April 12-13, 2024

# Slide seminar on controversial issues in thyroid pathology

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