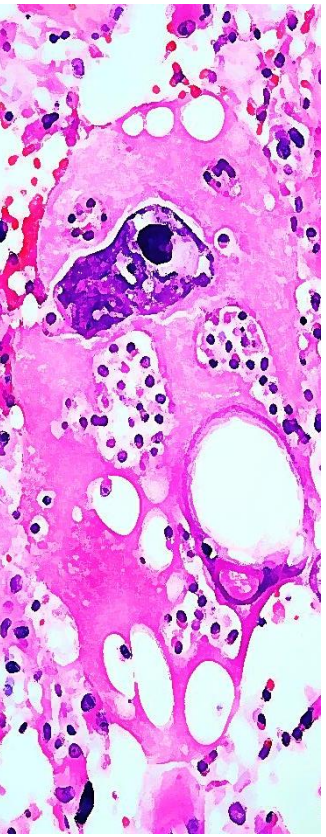
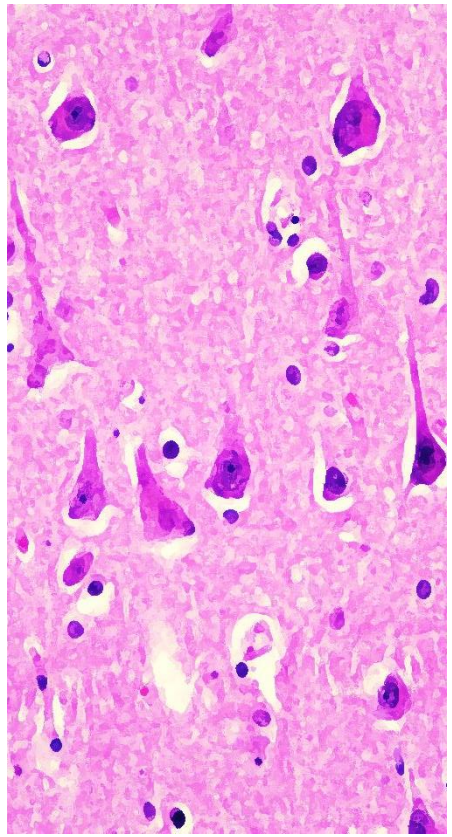
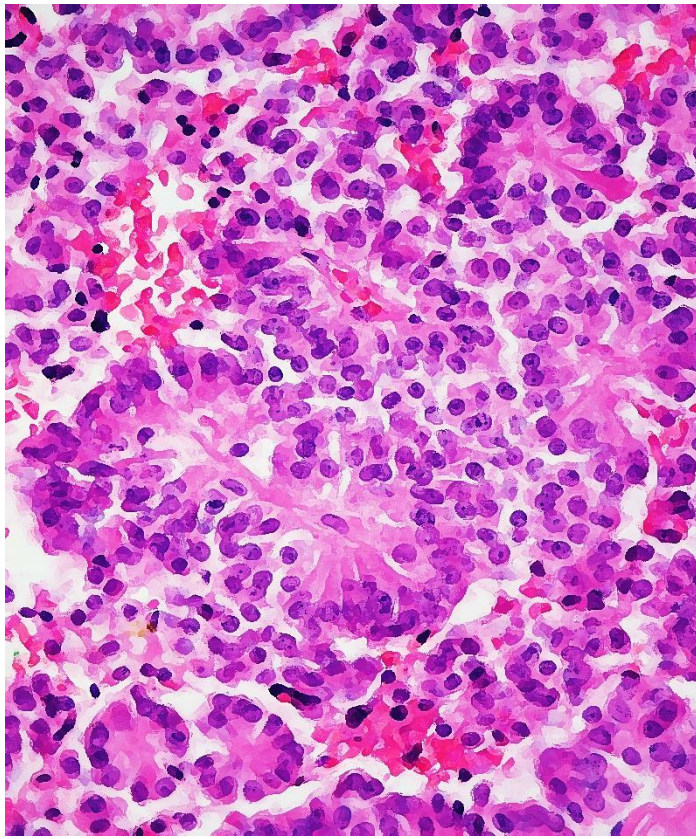


Academia Mexicana de Neuropatología, A.C.

Sesión Mensual
Neuropatología quirúrgica
Caso 3

14 de agosto de 2025





Dra. Dafne Thamara Ayala Dávila

dafneayaladavila@gmail.com

Hombre, 40 años.

- **Ingreso, octubre 2020.**
  - Referencia institucional para continuar tratamiento quimio-radioterapia.
- **Antecedentes:**
  - ← **2 años**, HAS controlada.

Padecimiento actual

- ← **8 meses** (Feb, 2020).
  - Hifema izquierdo y posterior proptosis.
  - → **1 mes**, tumor intracerebral (TAC).
- ← **5 meses** (May, 2020).
  - Resección de lesión con neoplasia remanente macroscópica.
  - **Dx. Neuroblastoma olfatorio.**
- ← **3 meses** (Jul, 2020).
  - Radioterapia fraccionada estereotáxica (Jul-Ago).
- ← **1 mes** (Sep, 2020).
  - HIC/signos meníngeos/deterioro neurológico.
  - **RM Invasión paquimeníngea.**

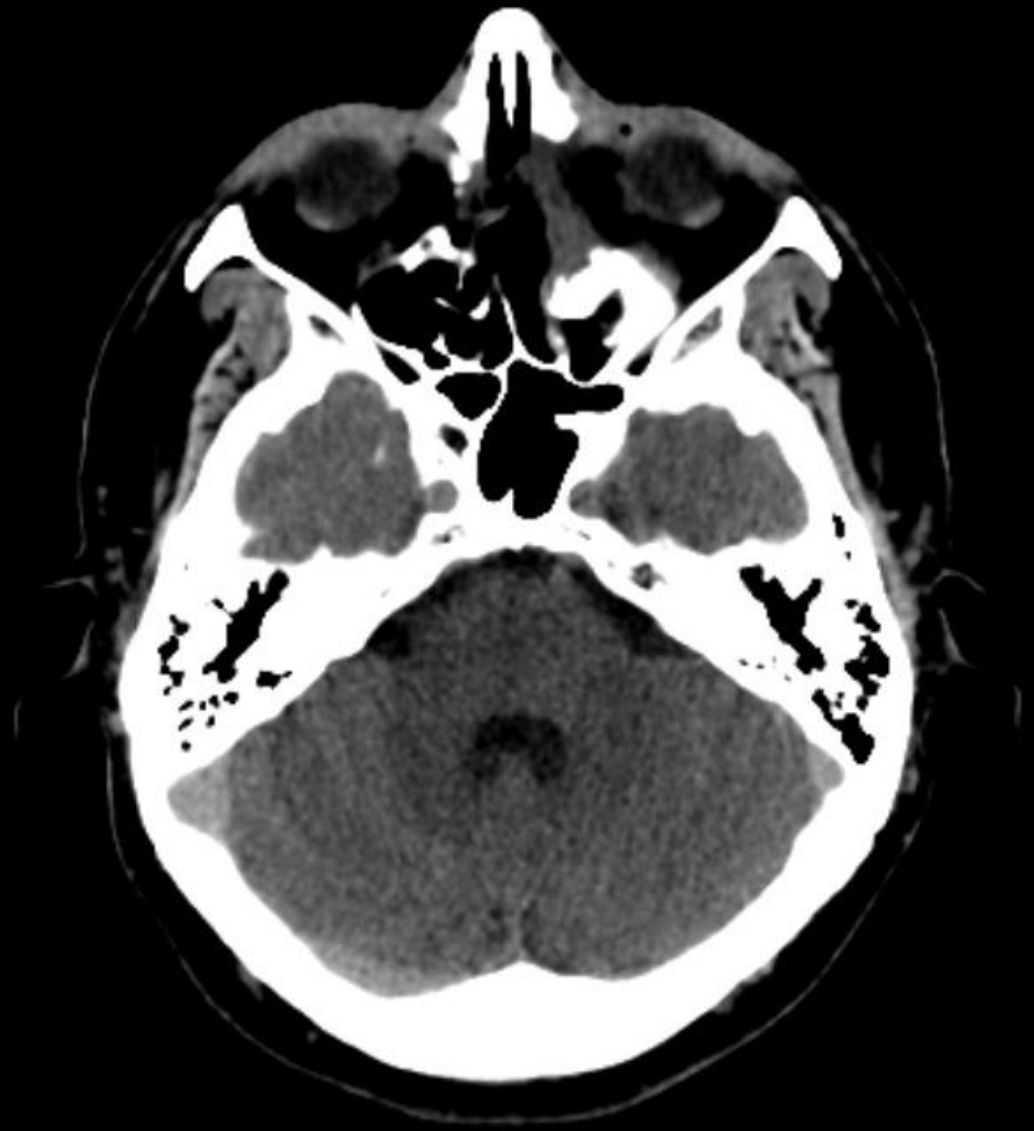
Padecimiento actual

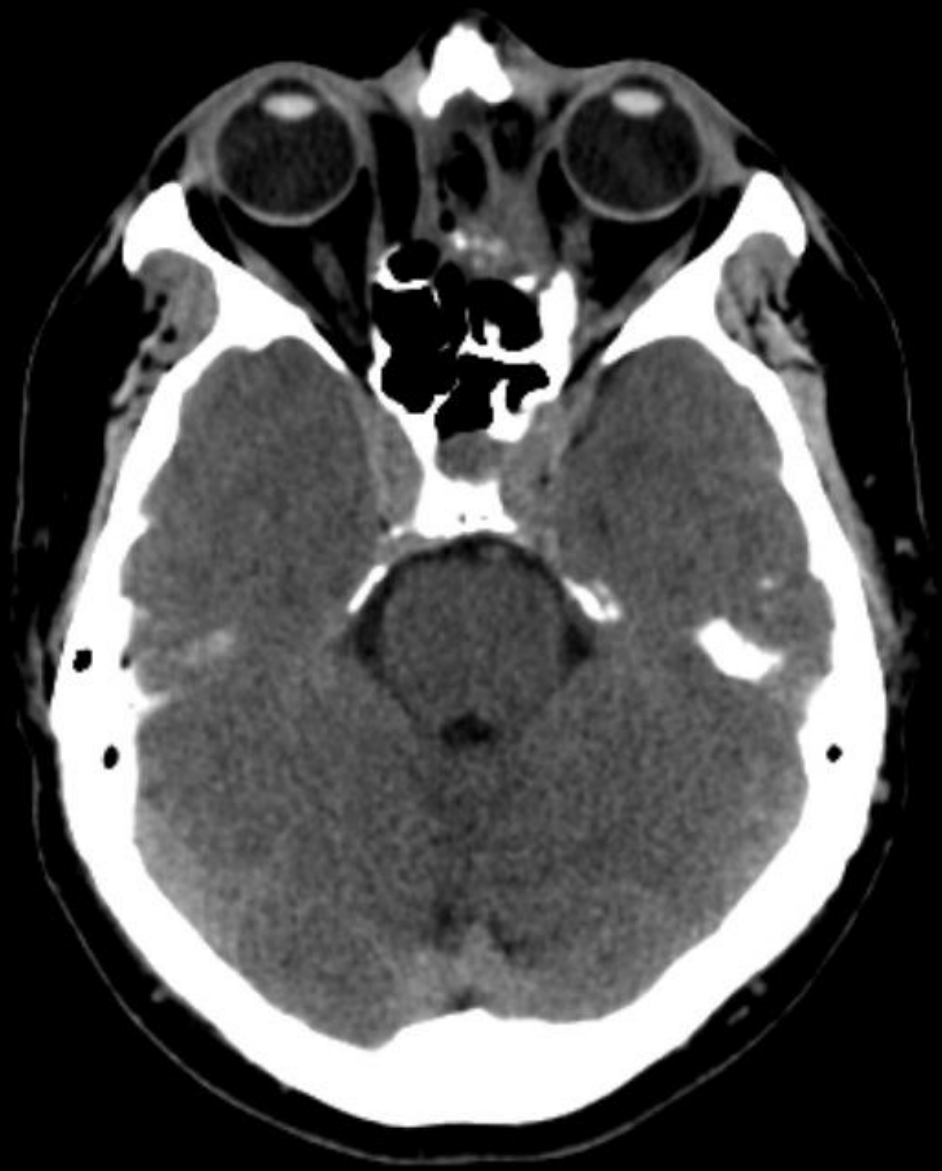
- **Ingreso (Oct, 2020)**
  - ECOG 2 / KPS 70%
  - Debilidad generalizada, alerta, alteraciones del lenguaje, desorientado en tiempo, paresia del m. recto interno ojo izquierdo y ataxia.
  - Dx. Neuroblastoma olfatorio localmente avanzado con afectación paquimeníngea.
  - **Plan:** radioterapia holocraneana y quimioterapia sistémica posterior.

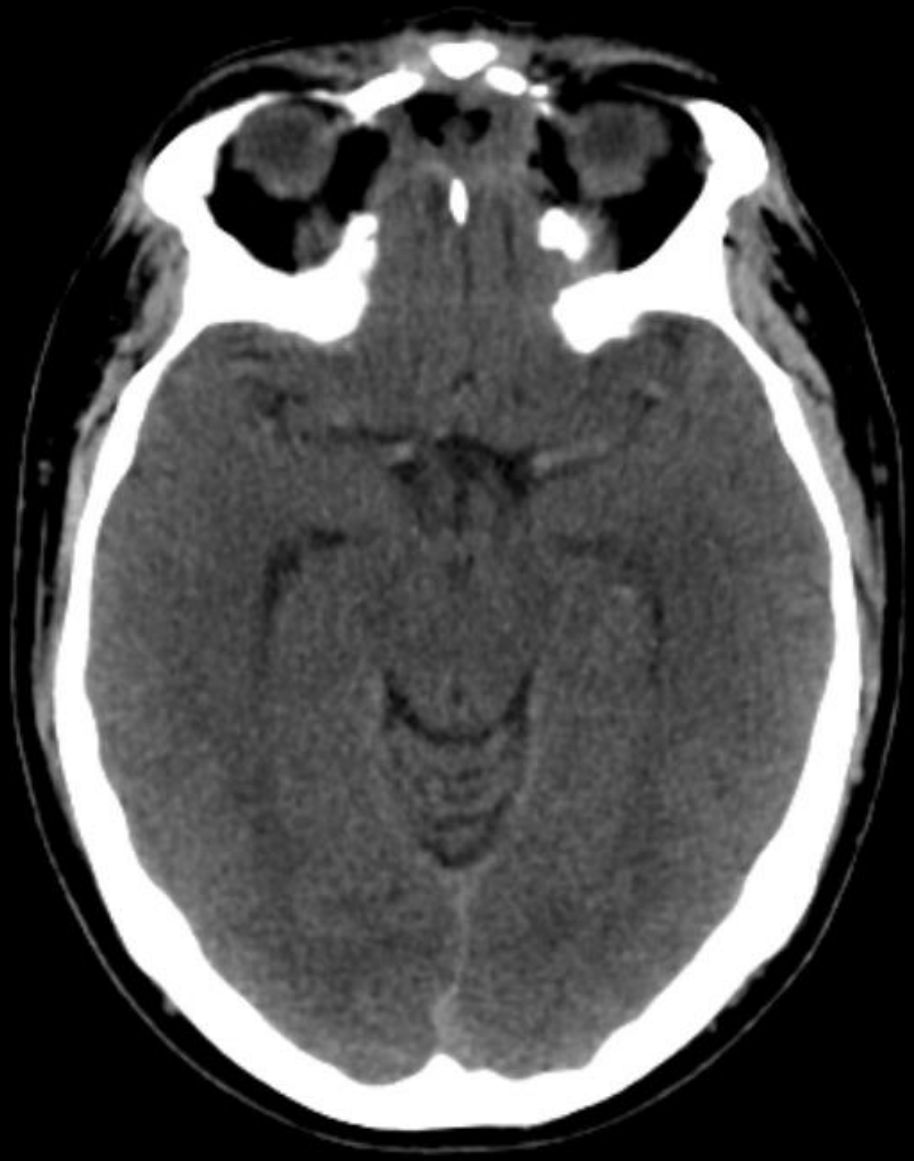
TAC contrastada, ingreso

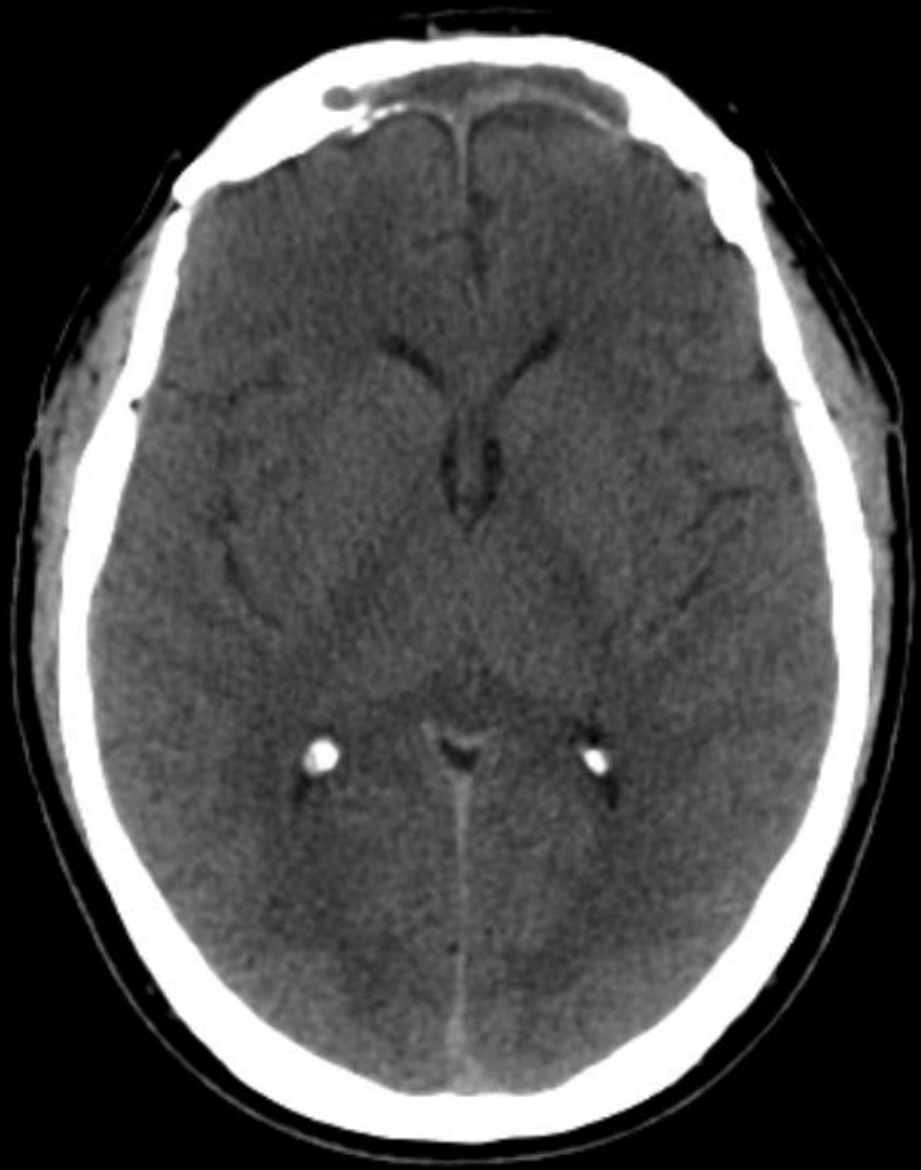
- Cambios post quirúrgicos.
- Ausencia quirúrgica:
  - Seno frontal, pared posterior
  - Celdillas etmoidales anteriores
  - Lámina papirácea bilateral
  - Lámina cribosa
  - Techo orbitario
- Malacia frontal.

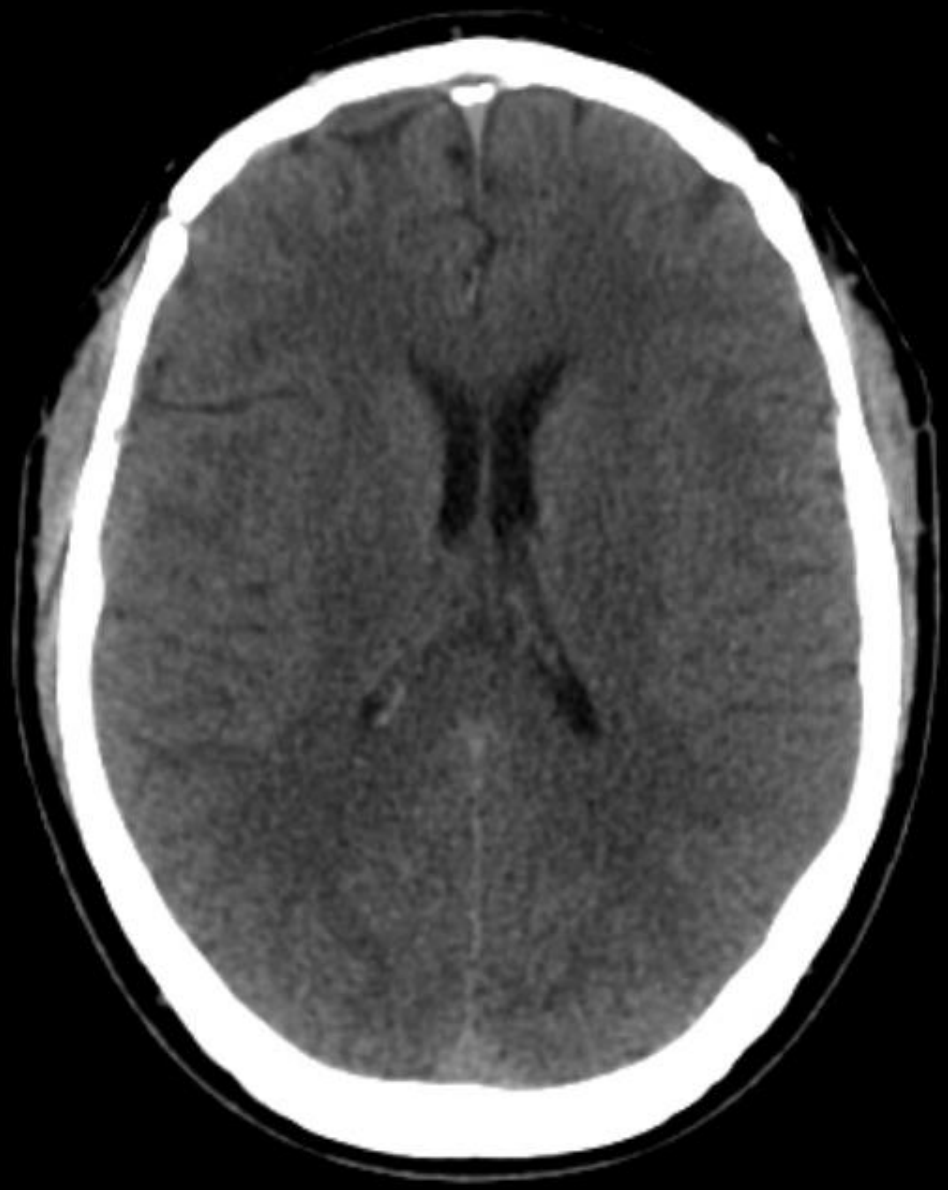
- Hiperdensidad y captación de contraste paquimeníngea frontal y hoz cerebral rostral (nodular), además del músculo recto interno.

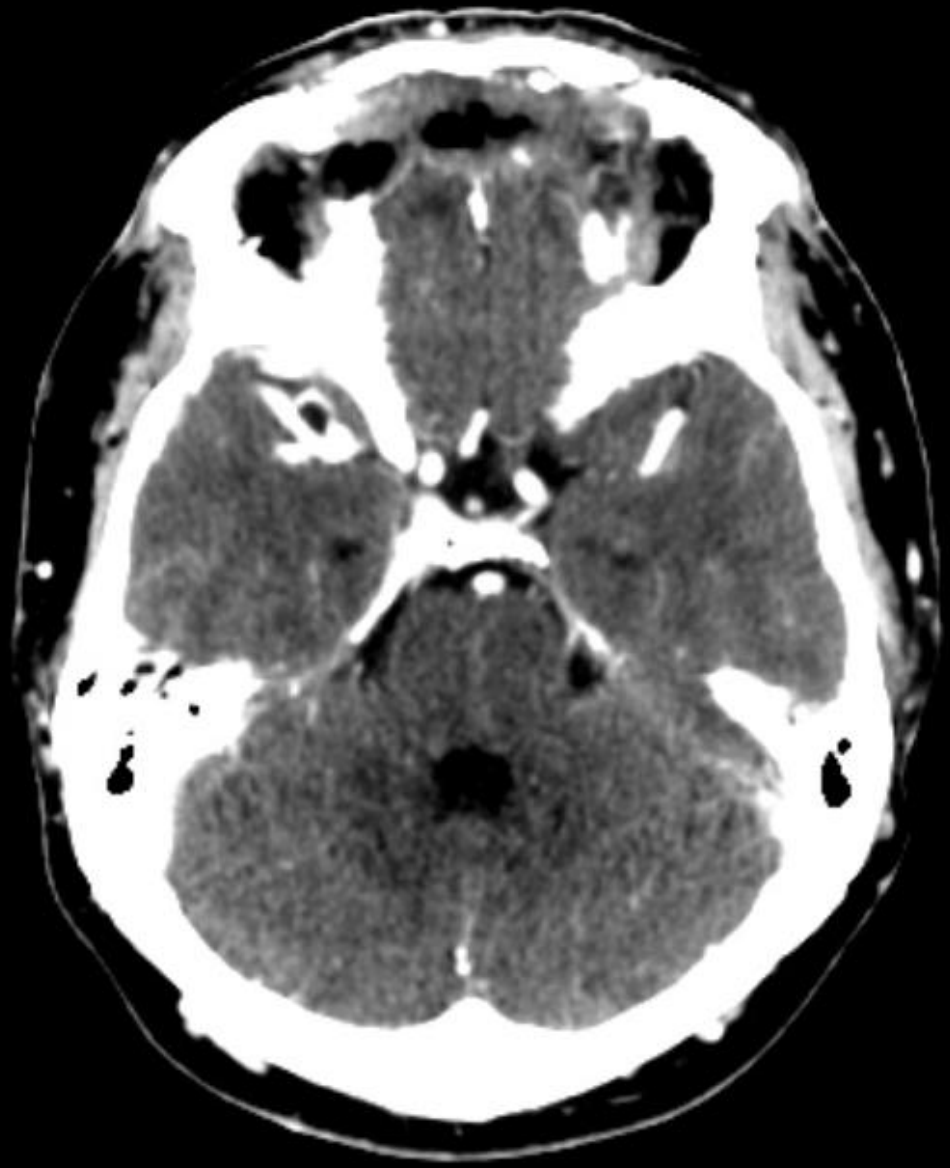


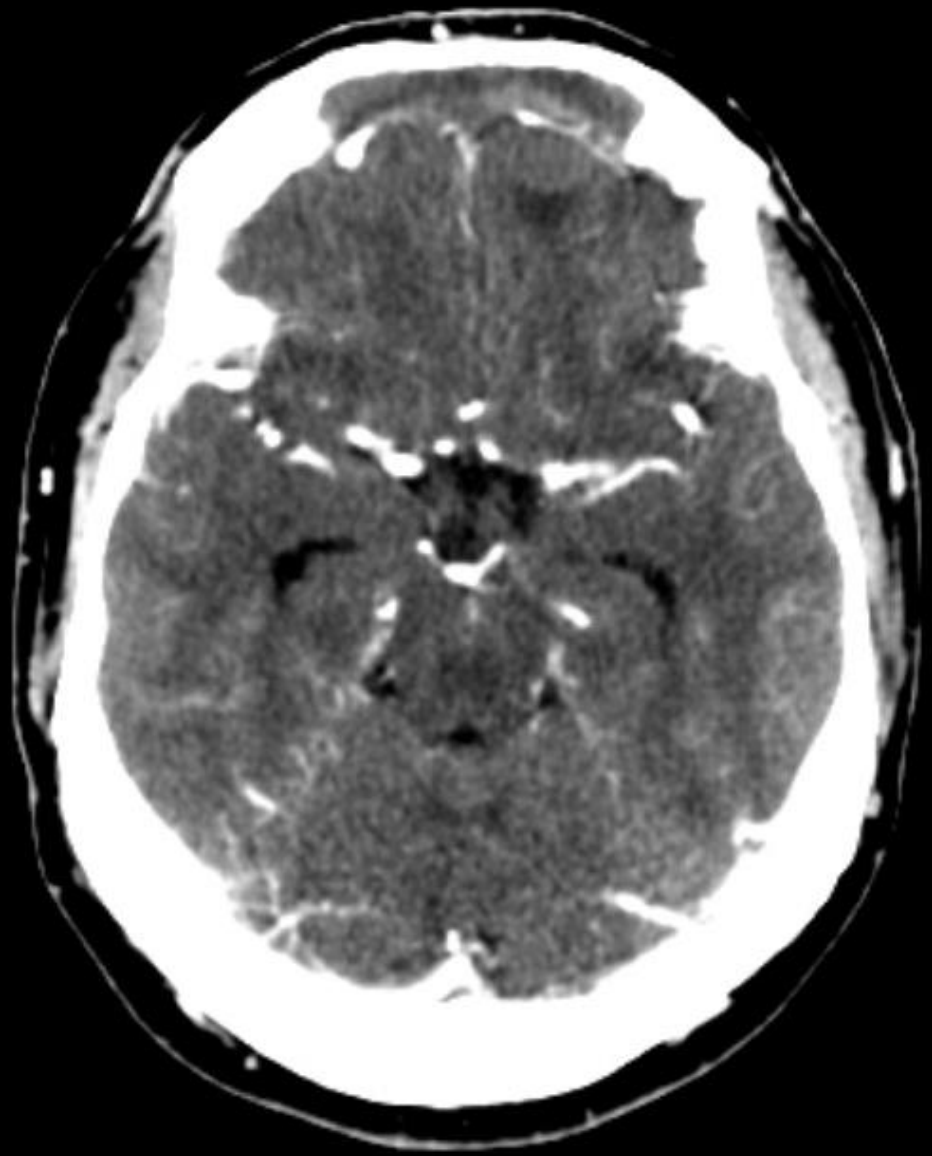


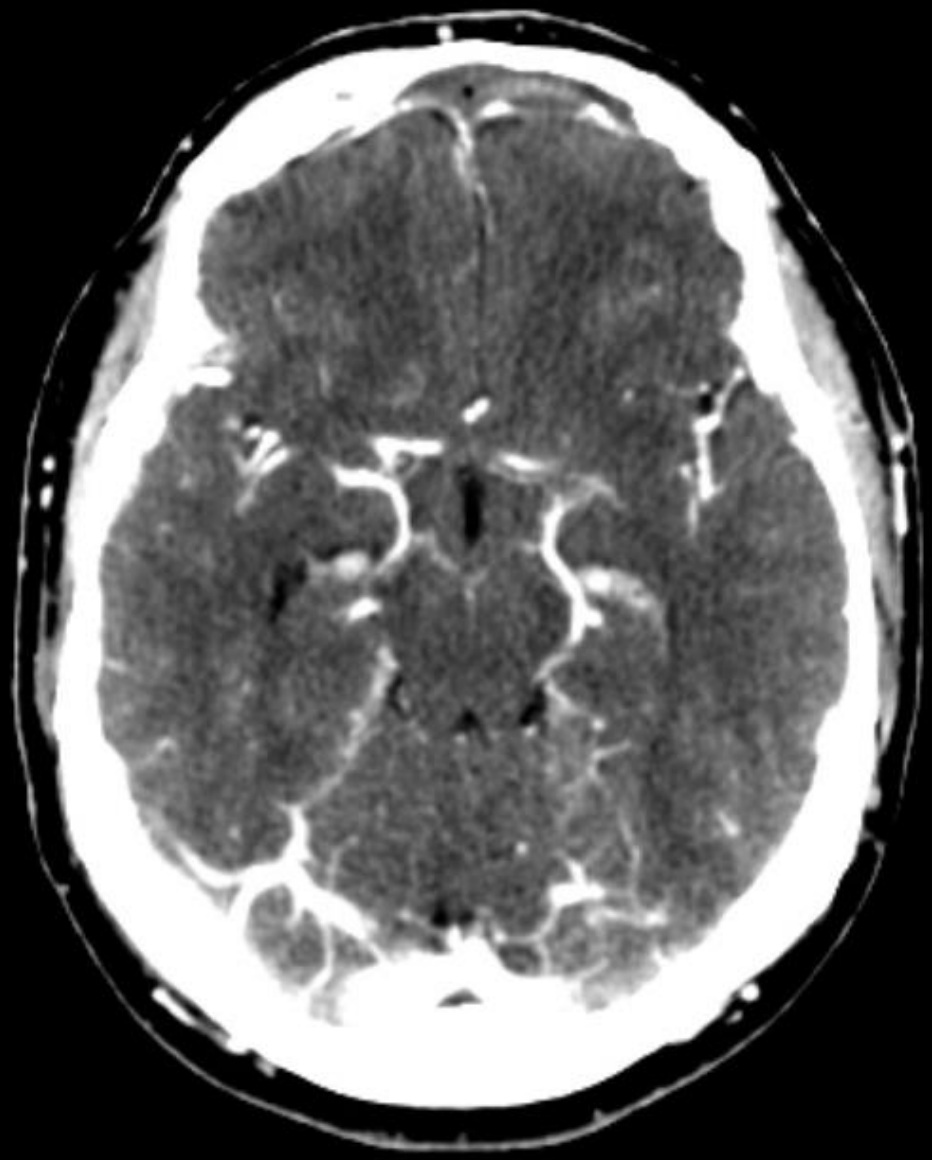


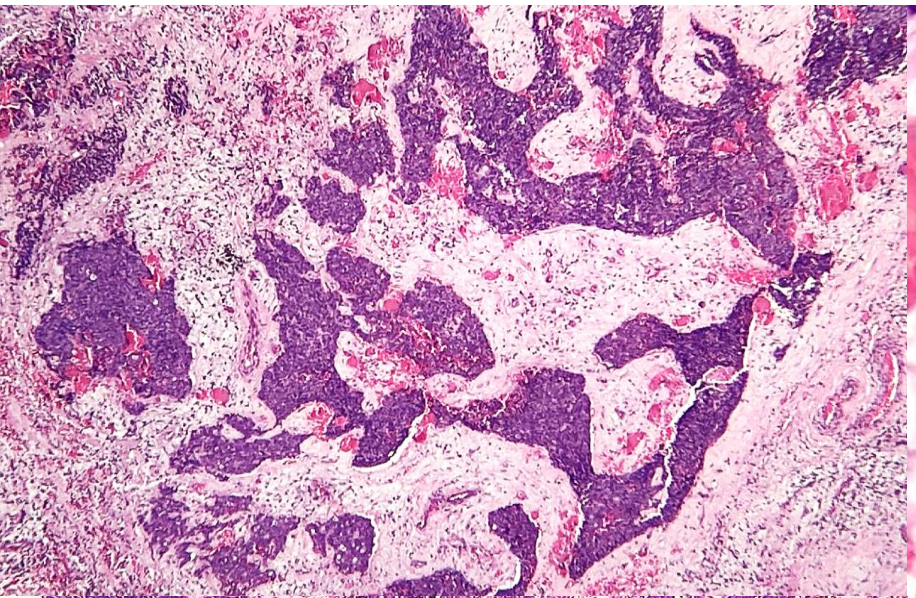


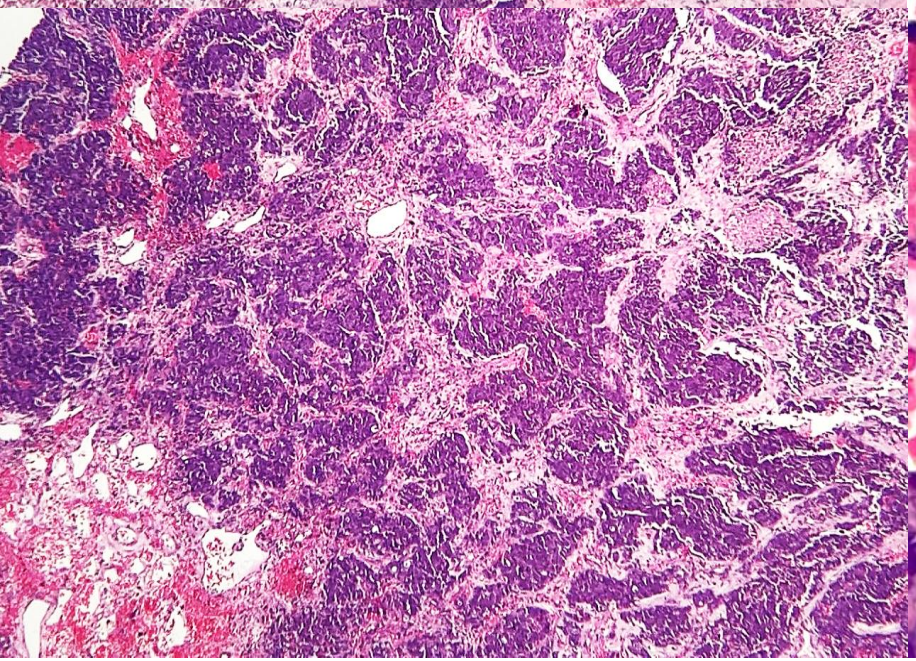


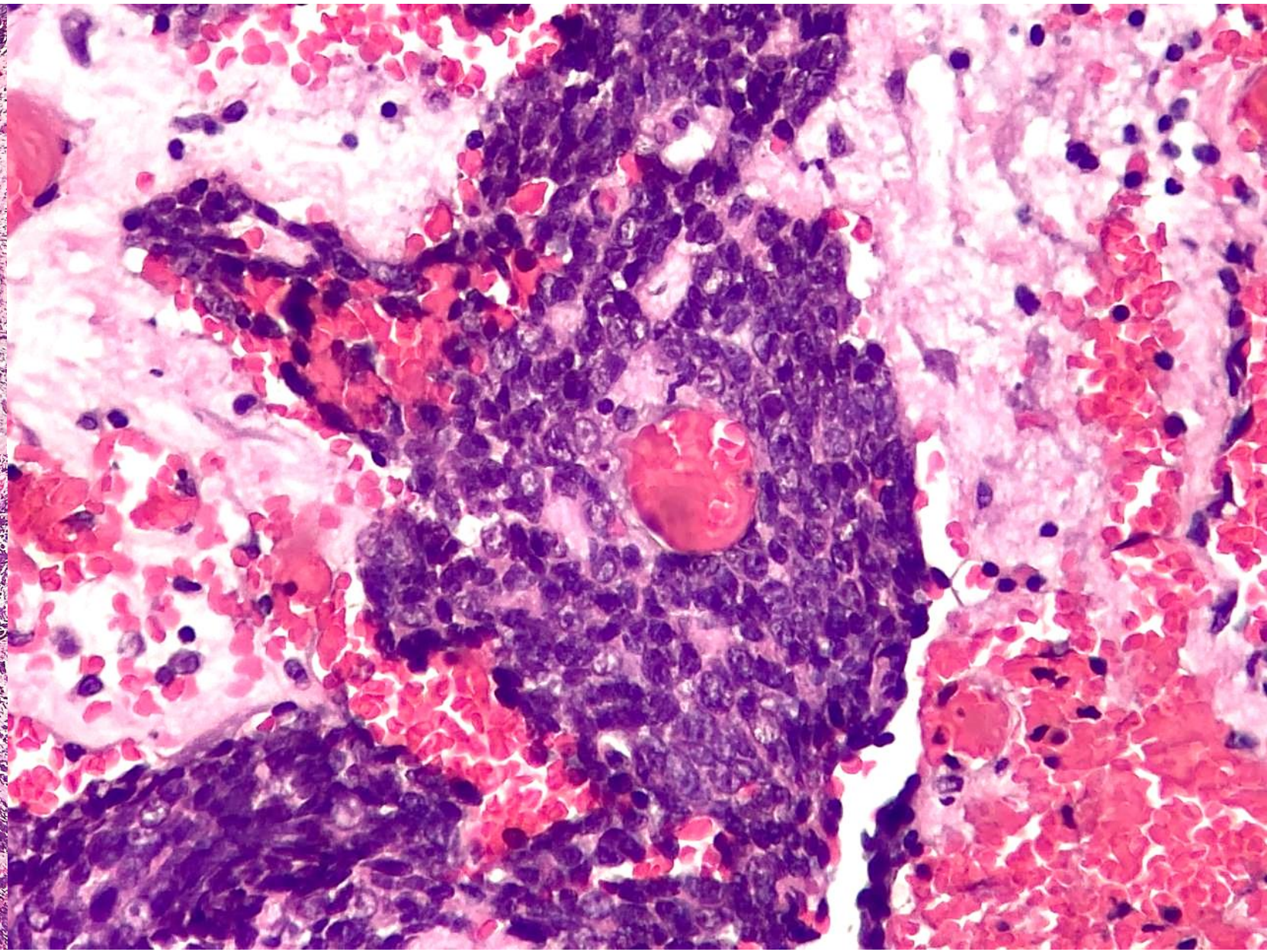


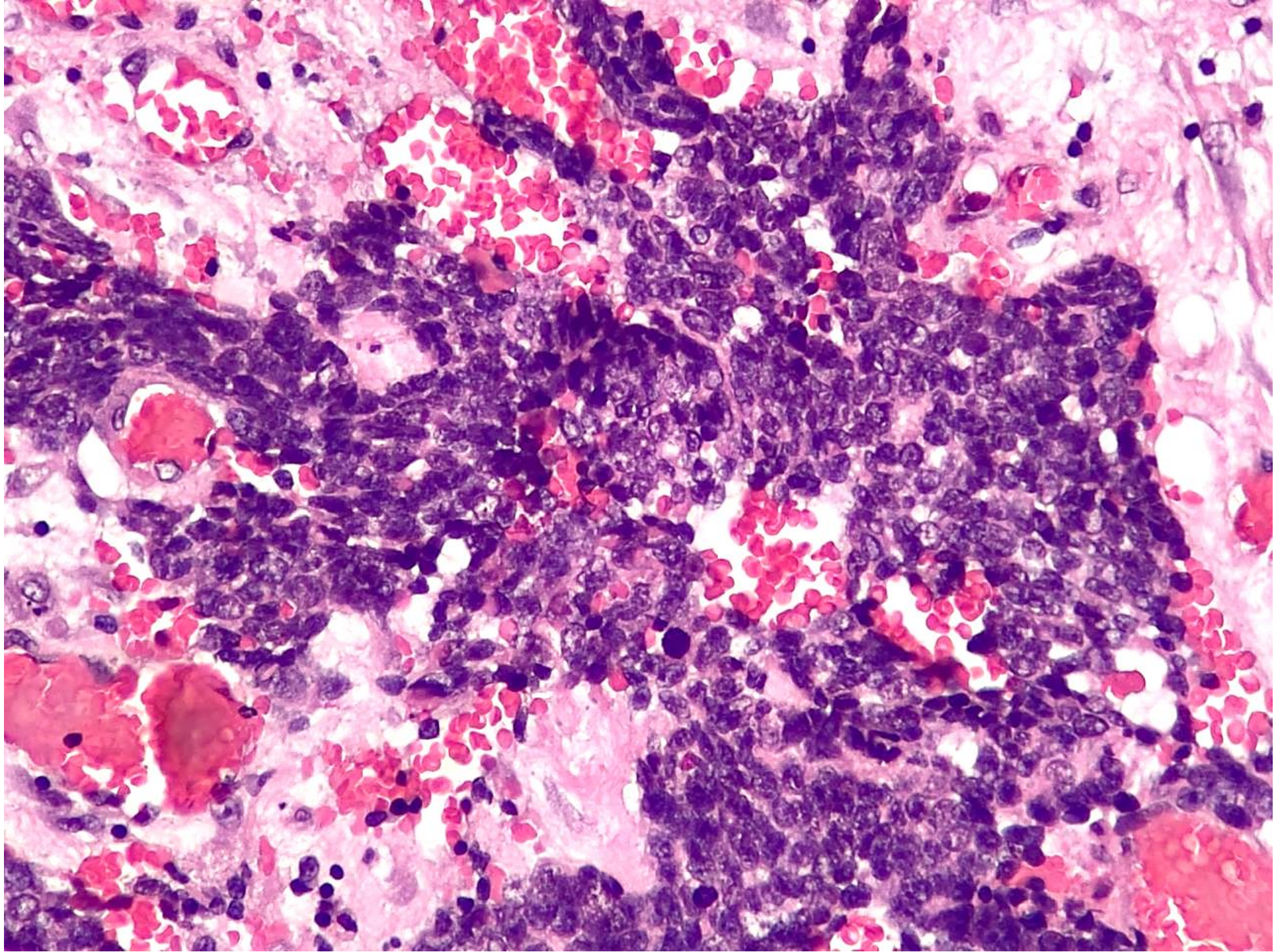


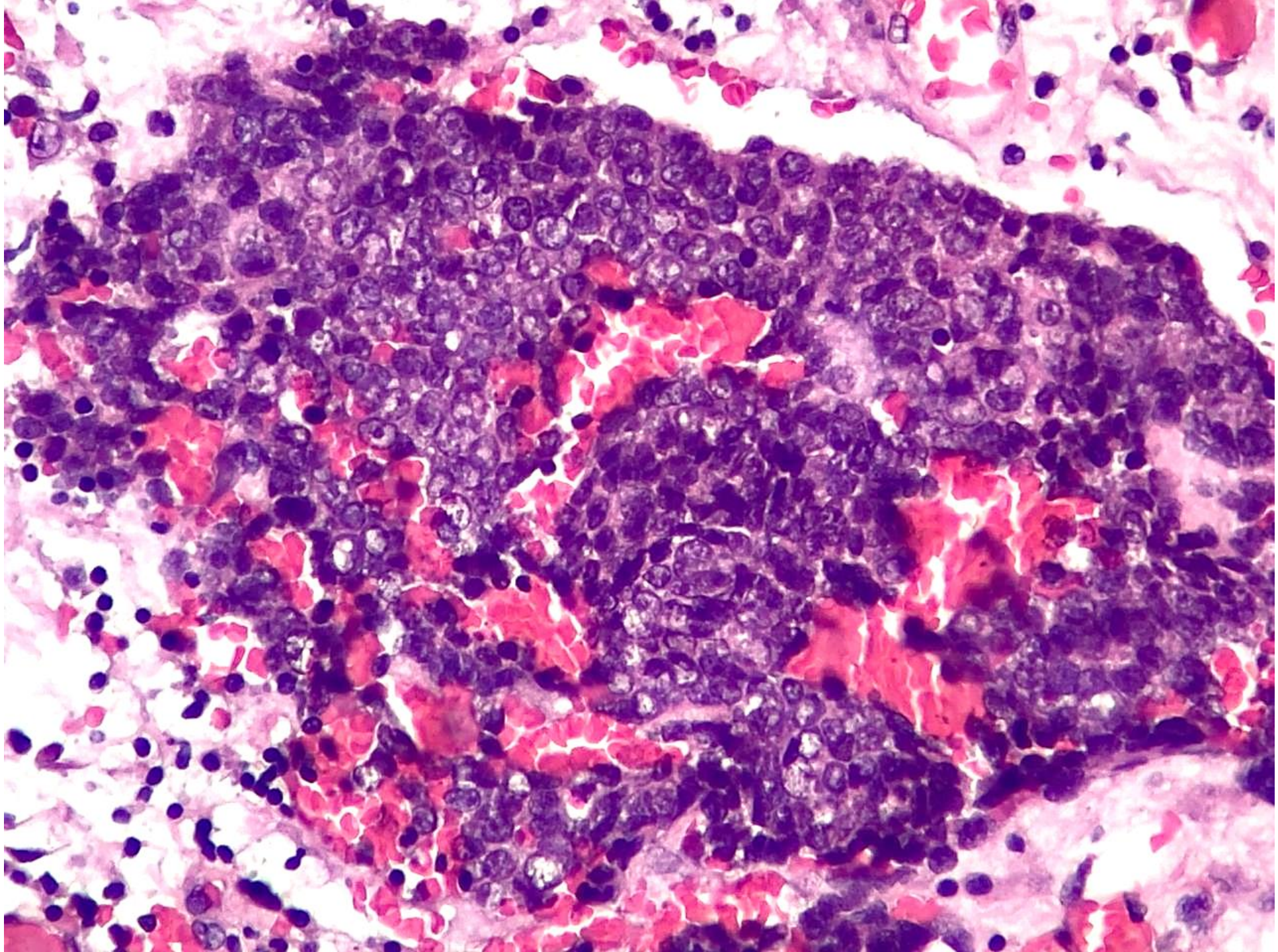


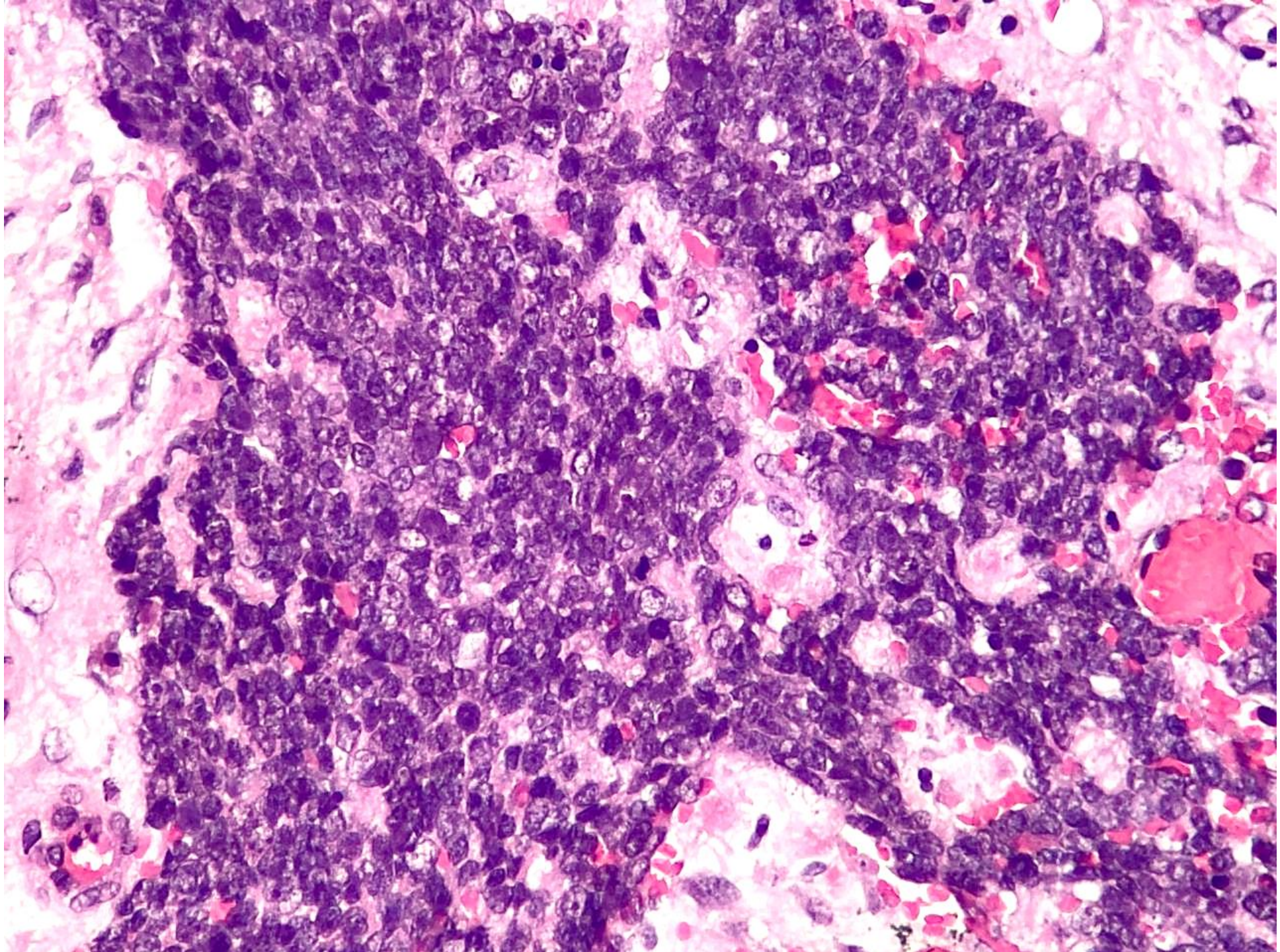


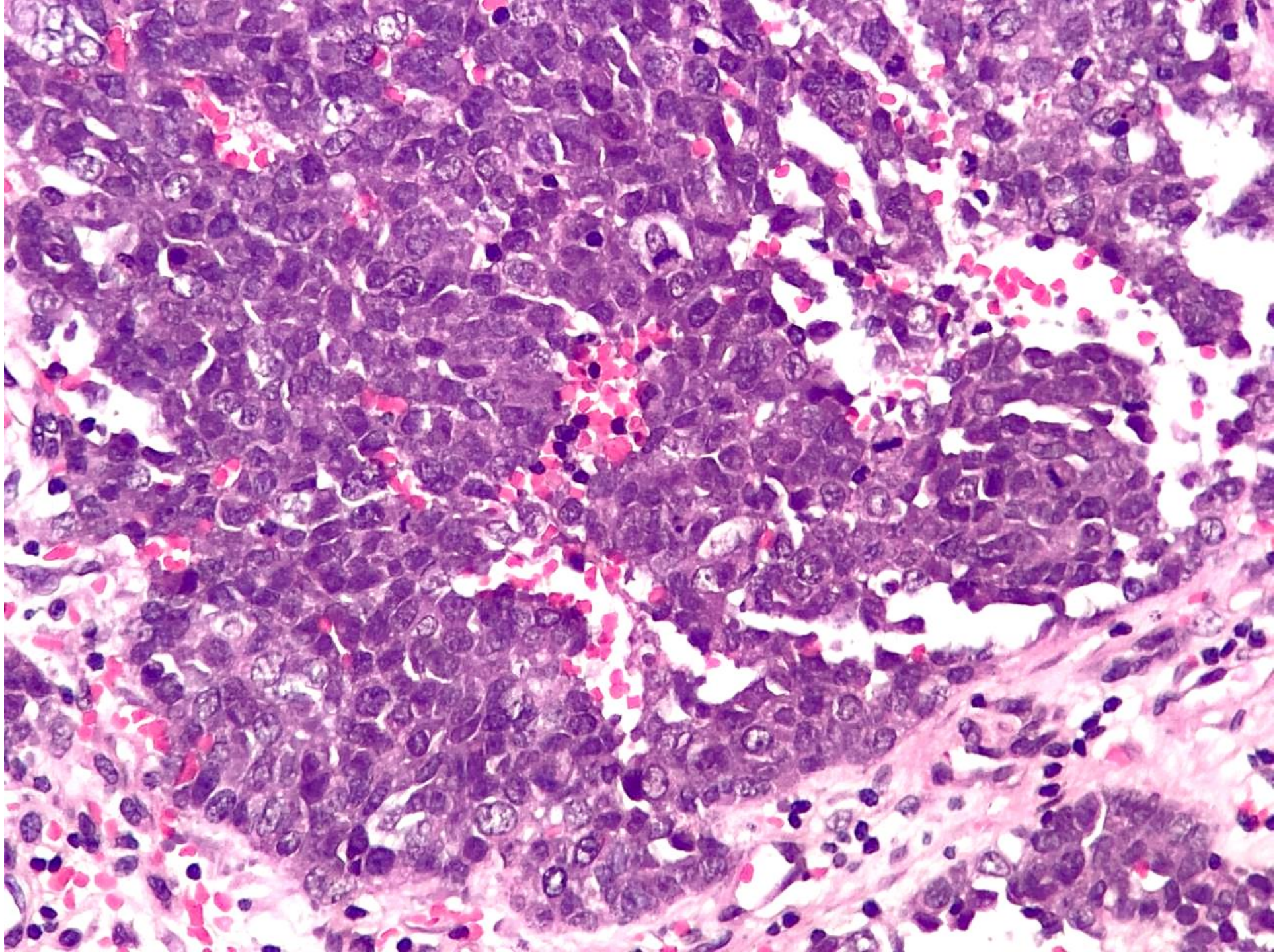


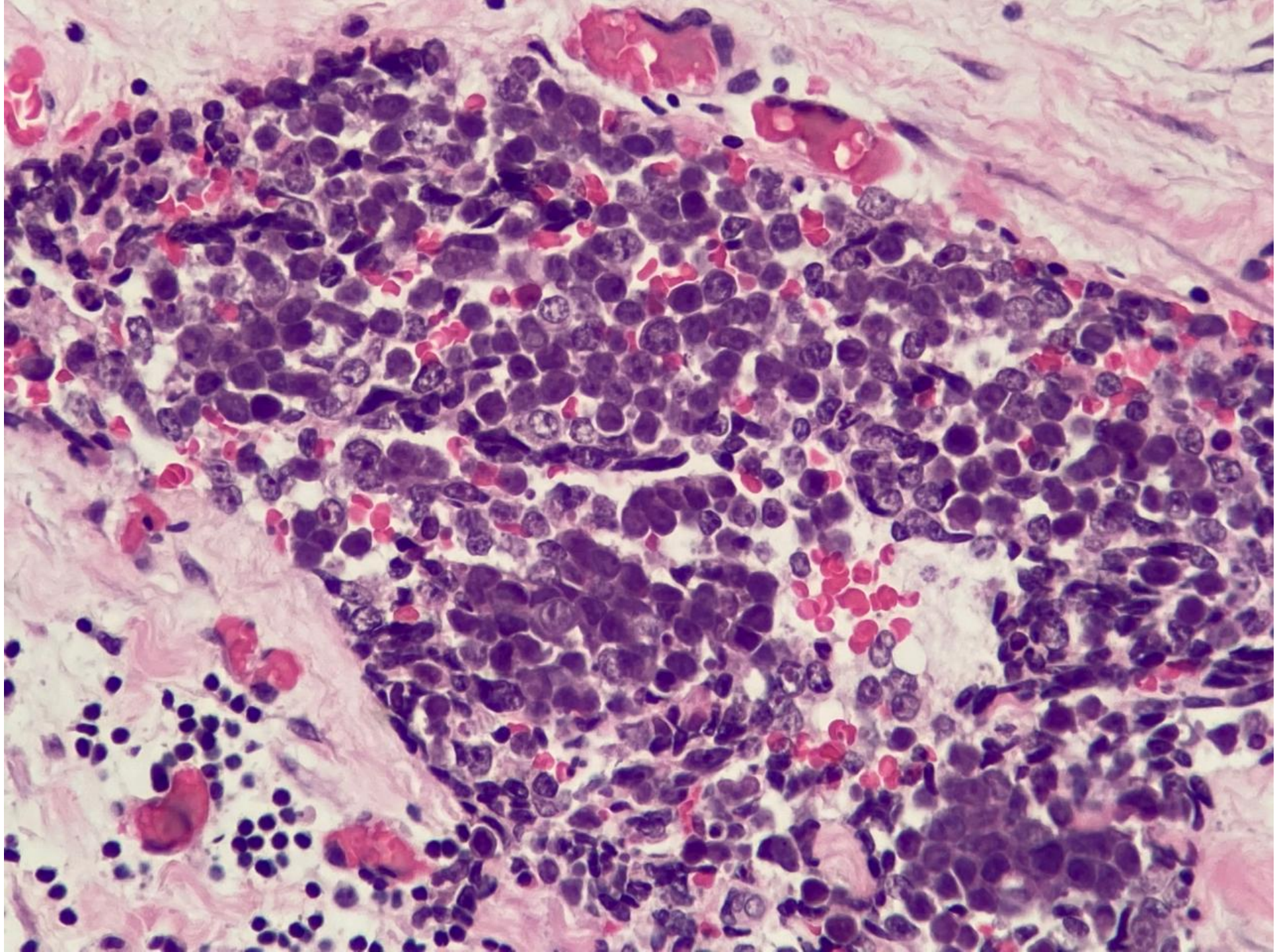


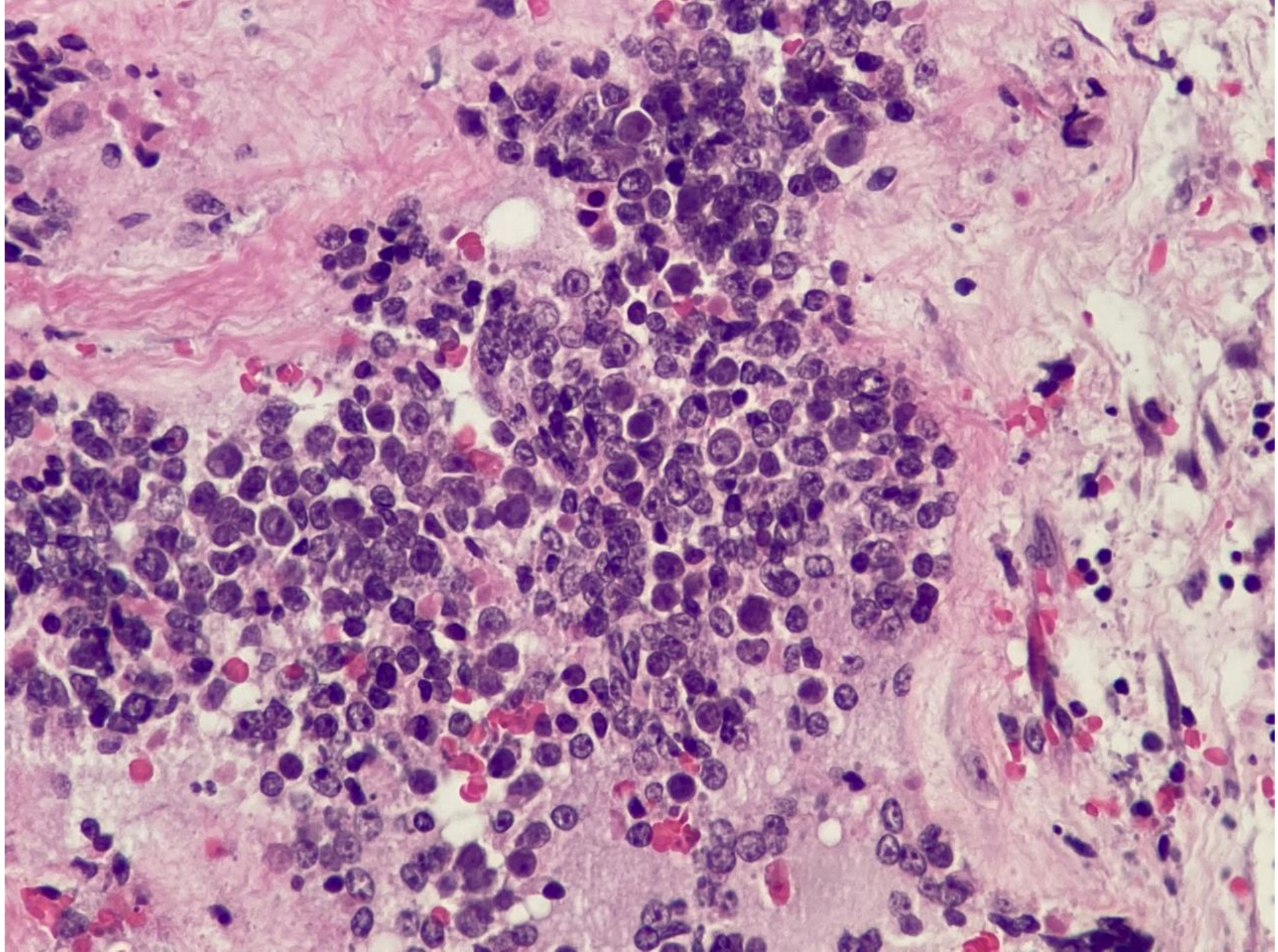


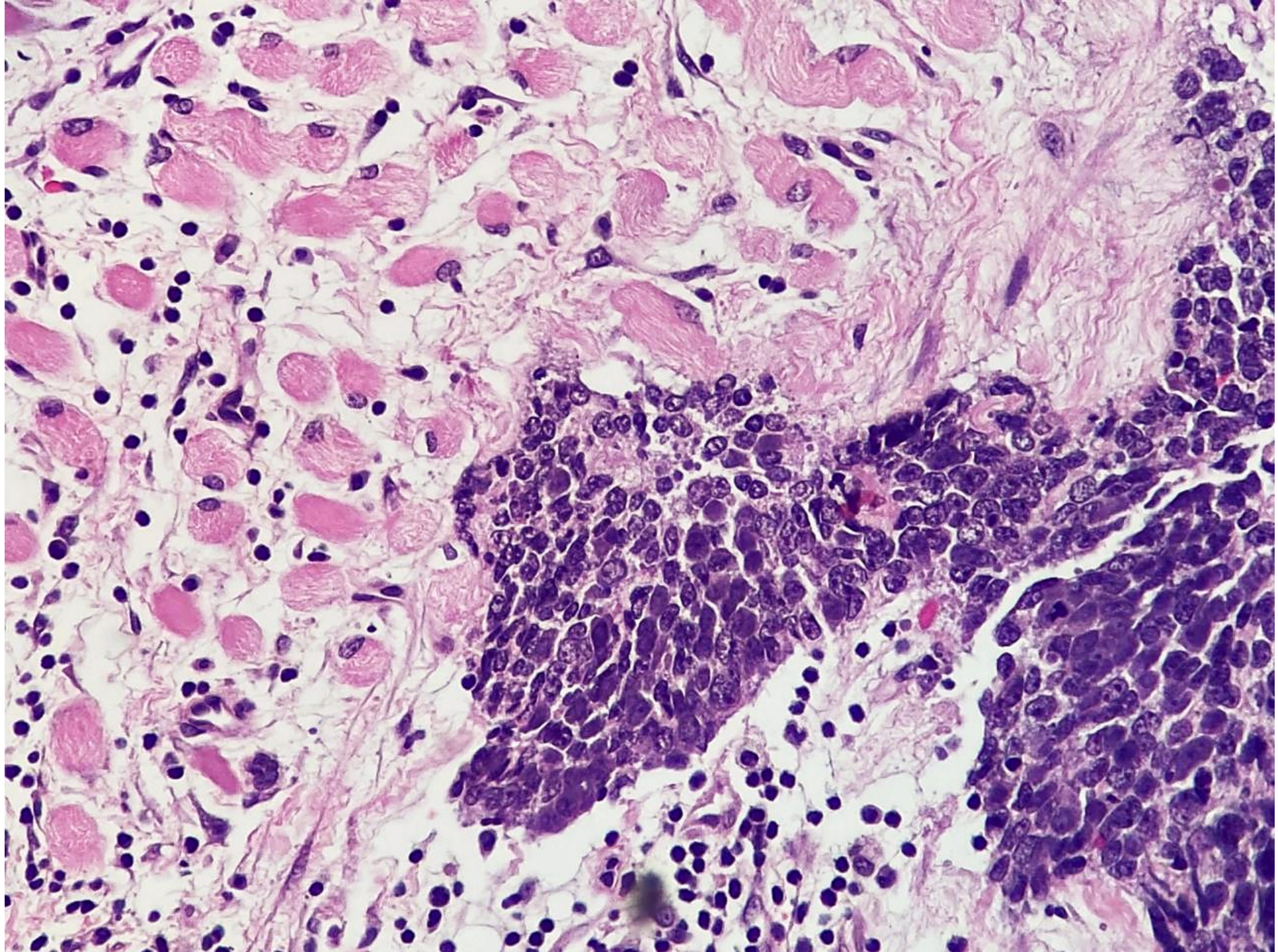




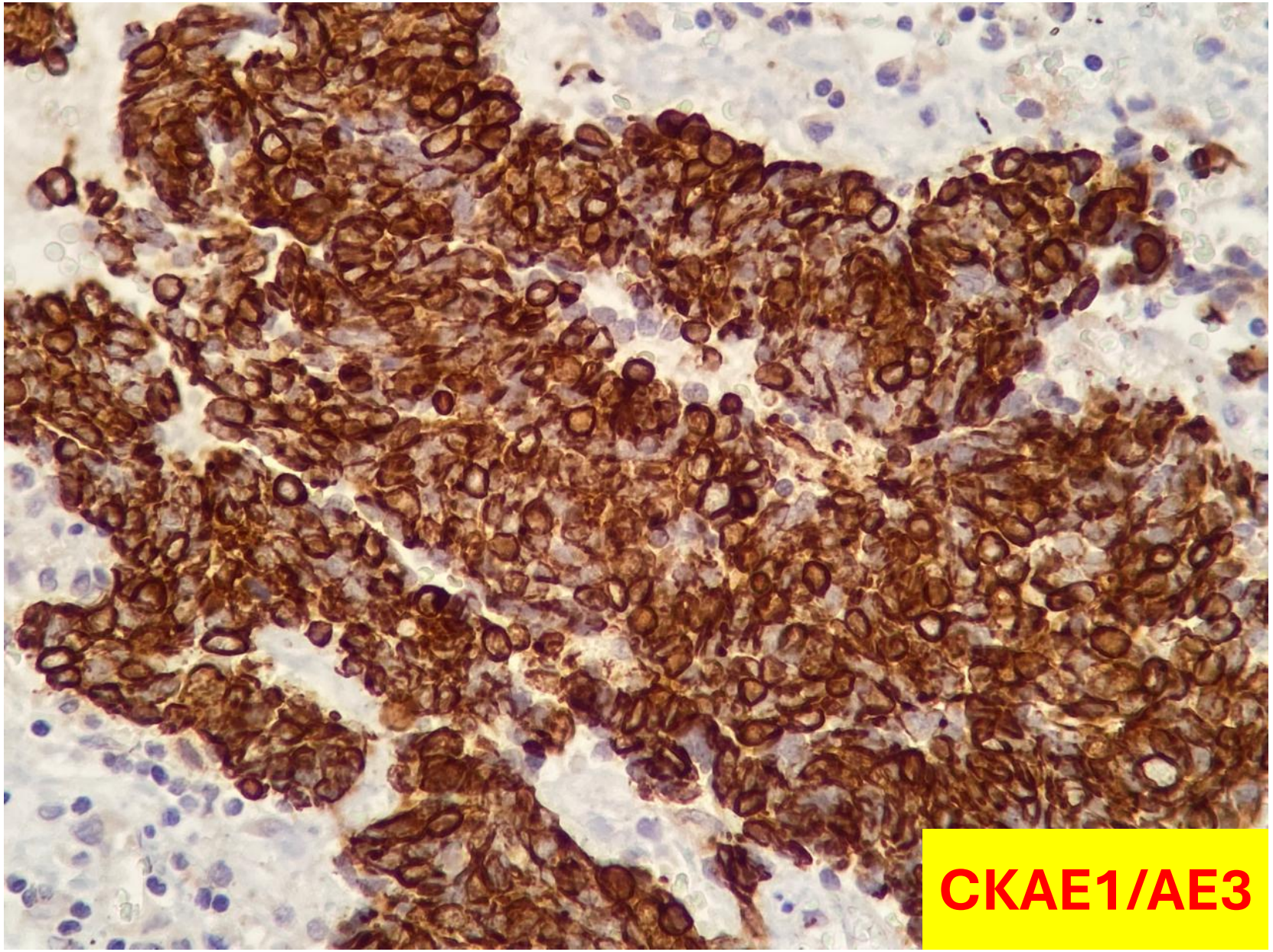


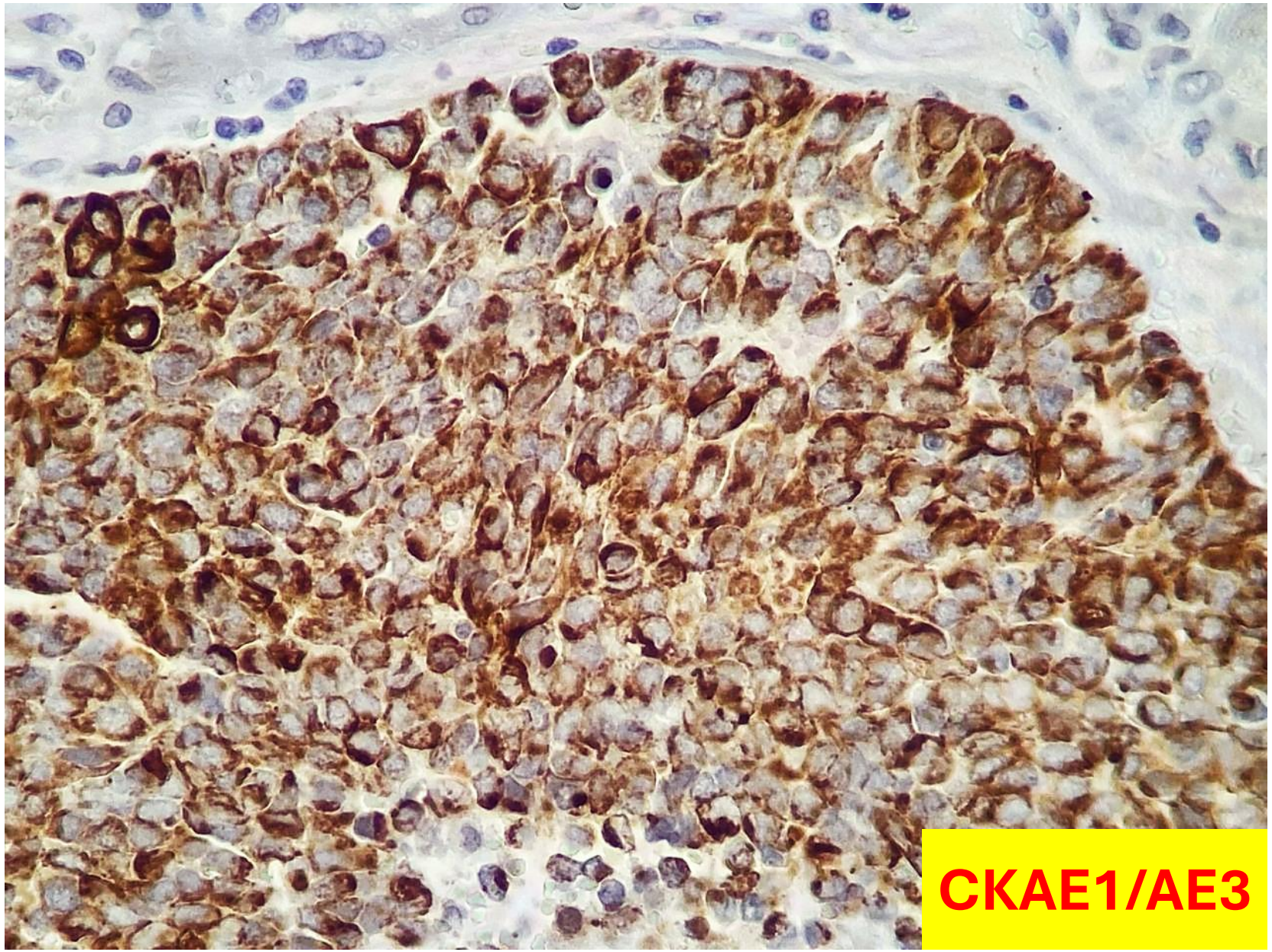






Neoplasia maligna poco diferenciada compatible con carcinoma


CKAE1/AE3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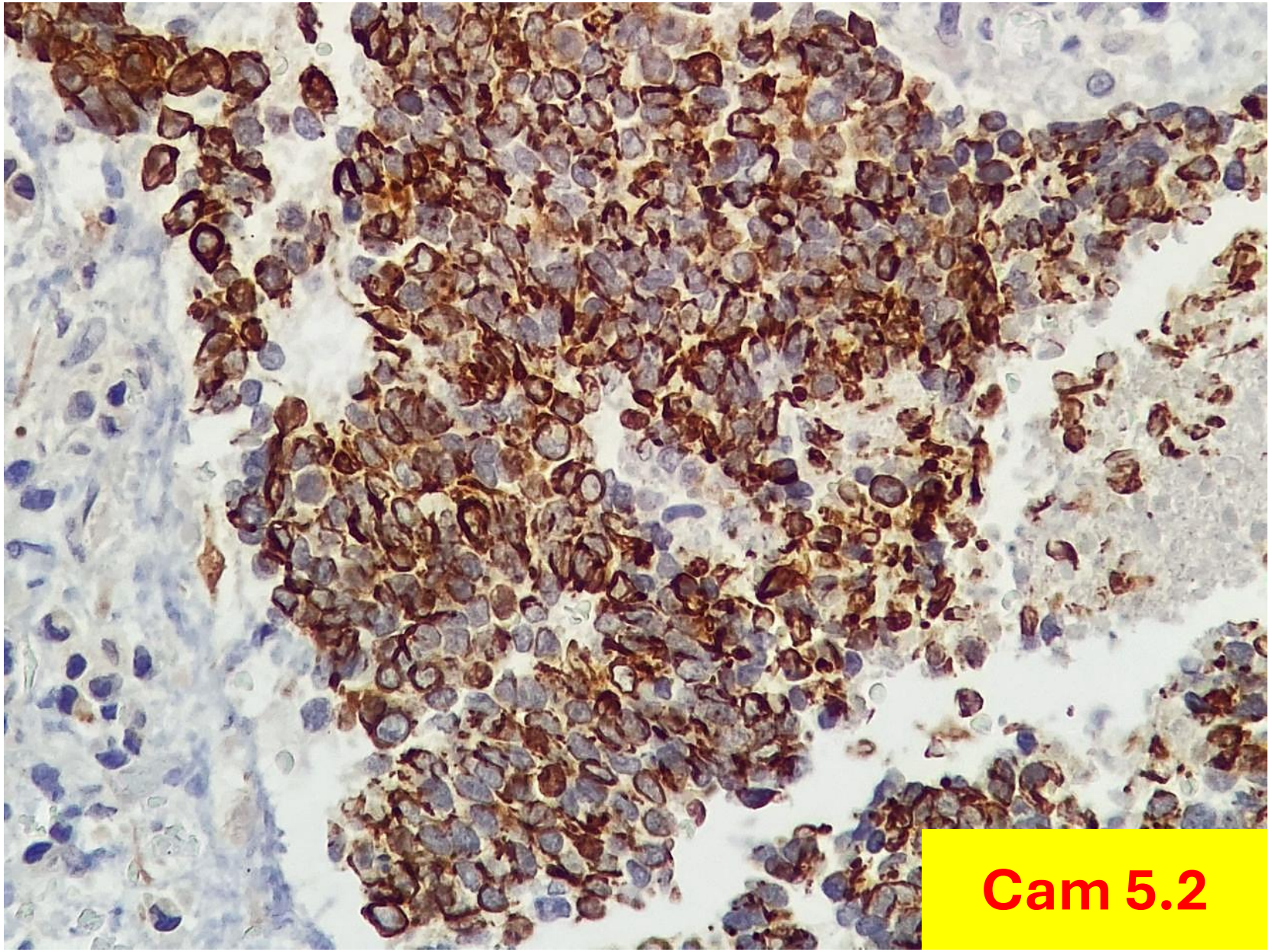
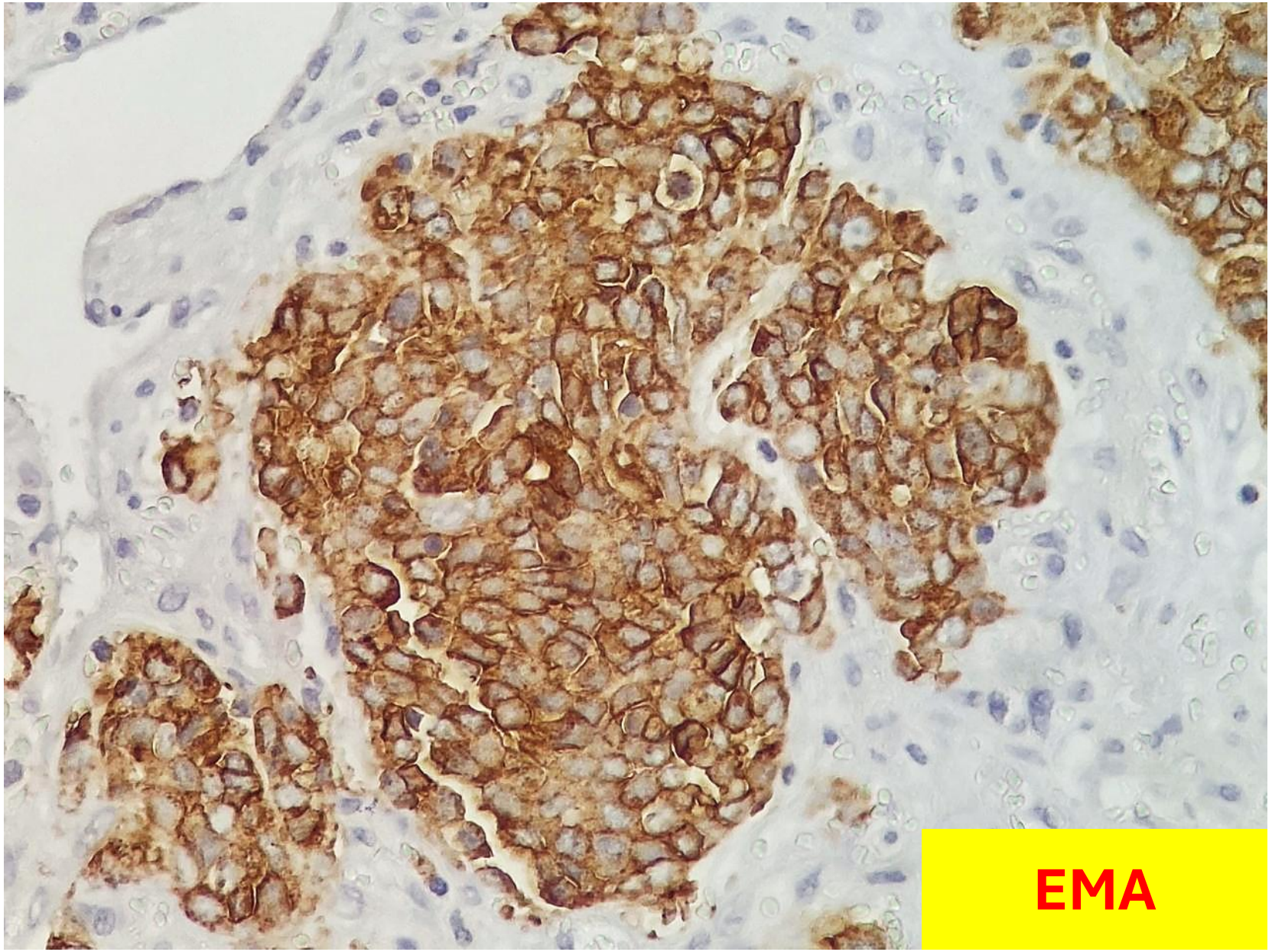
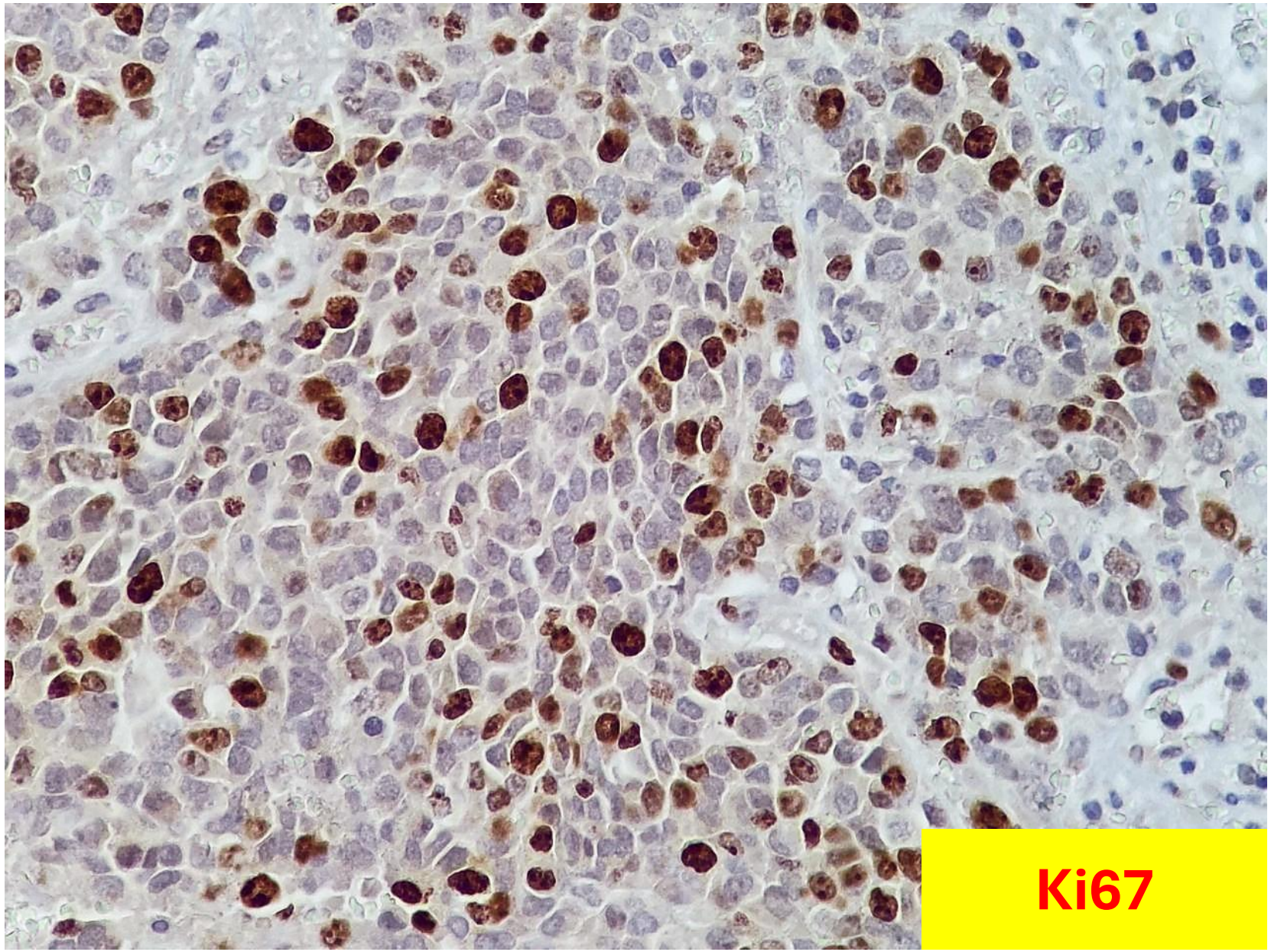
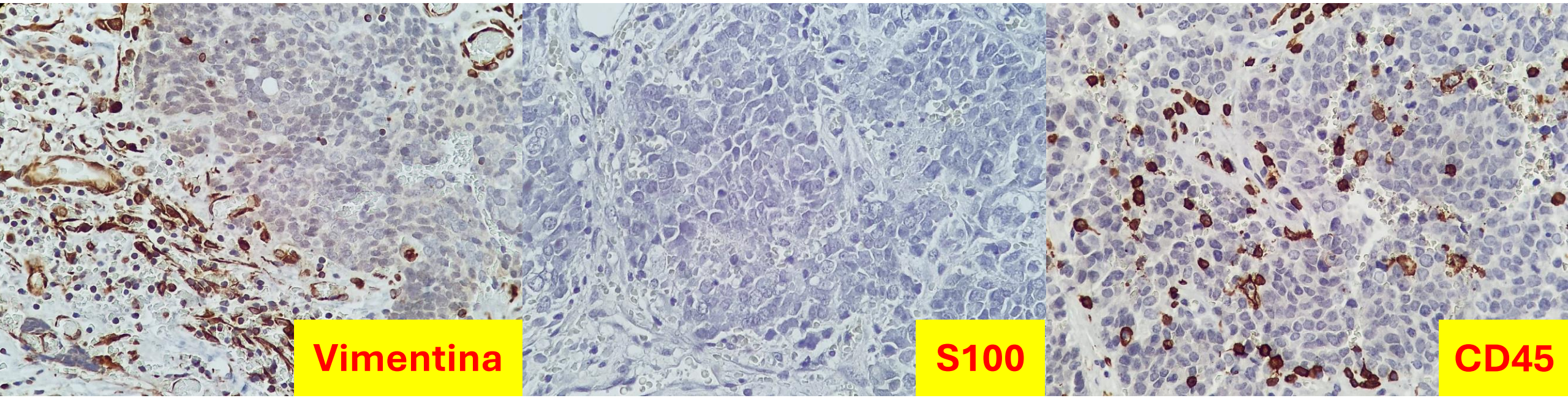

Cam 5.2


EMA


Ki67


Vimentina
S100
CD45

Carcinoma poco diferenciado

Carcinomas sinonasales

Poco frecuentes

(0.5-1 / 100,000 / año / mundial)

Mal pronóstico:

- Difícil resección (órbita / encéfalo)
- Resistencia a Radio y Quimiotx.
- Tipo histológico

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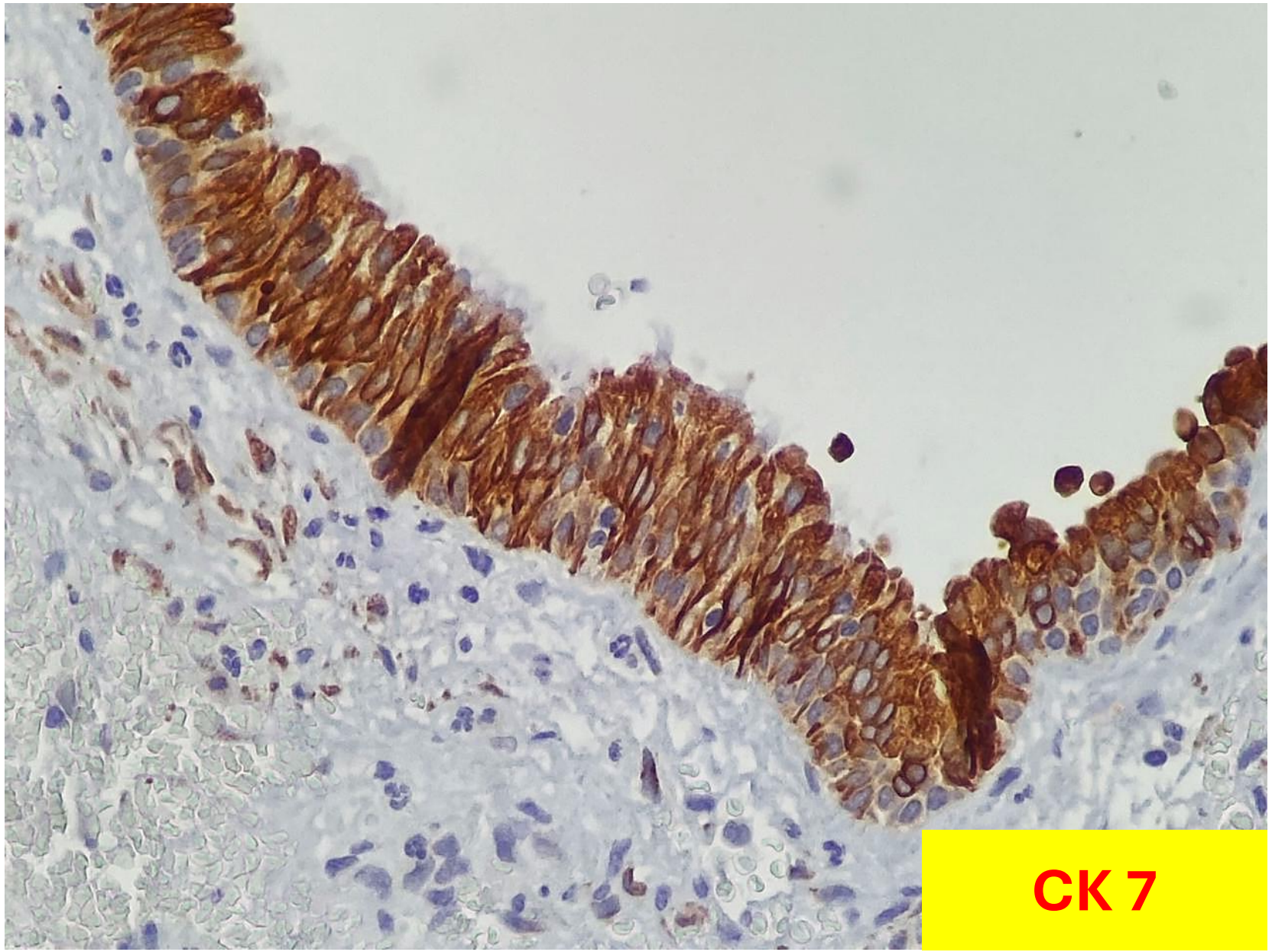
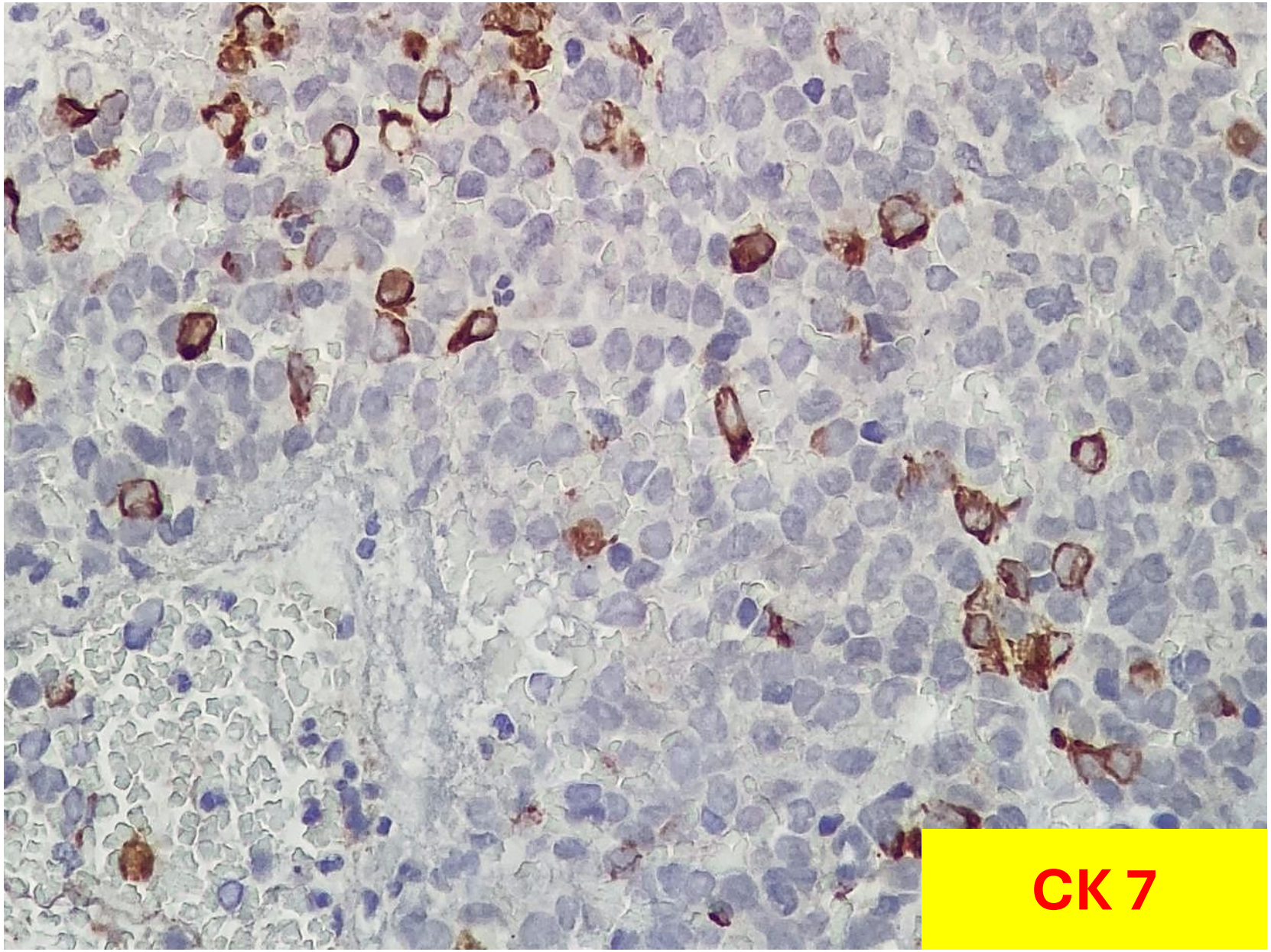
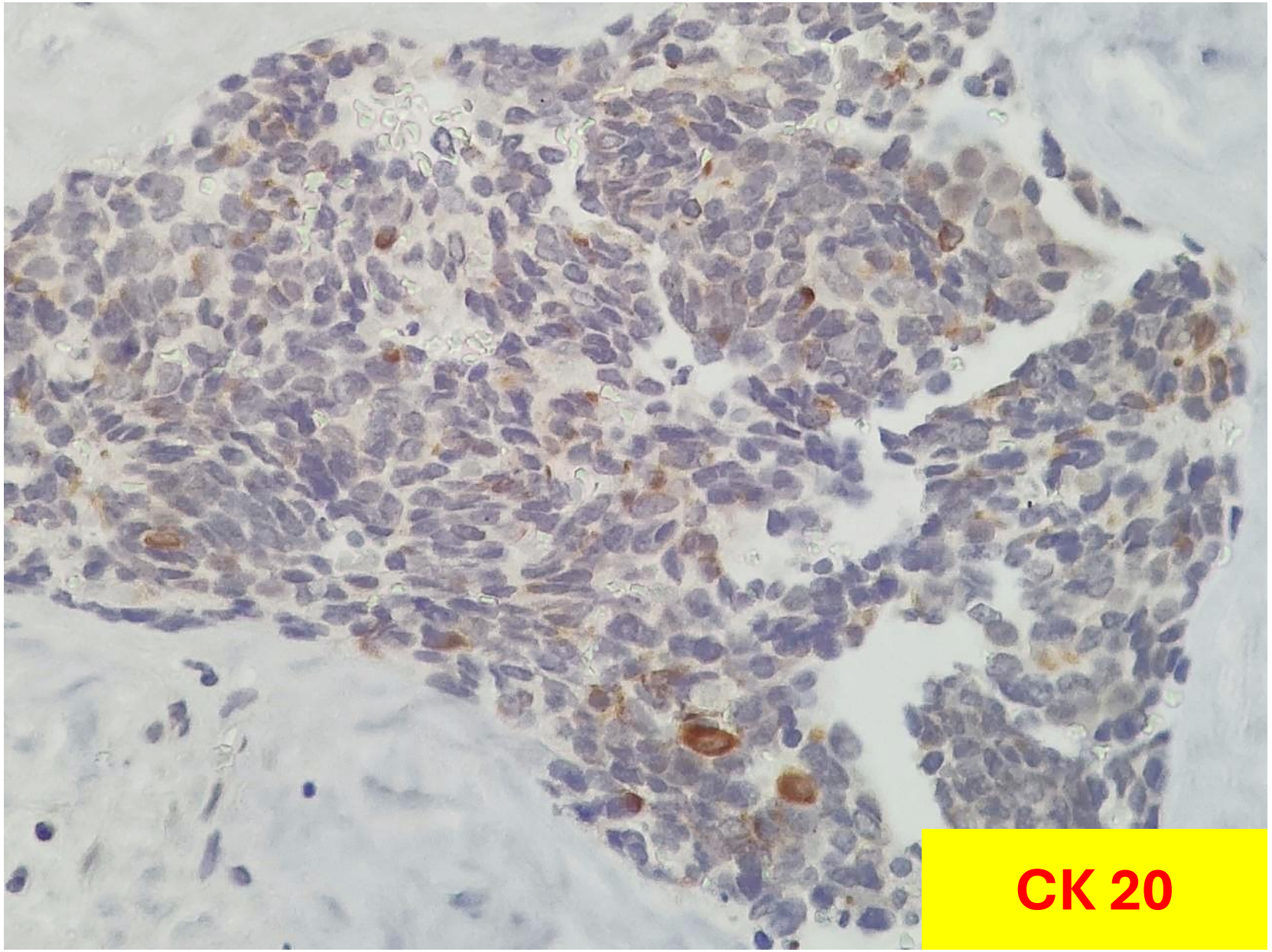
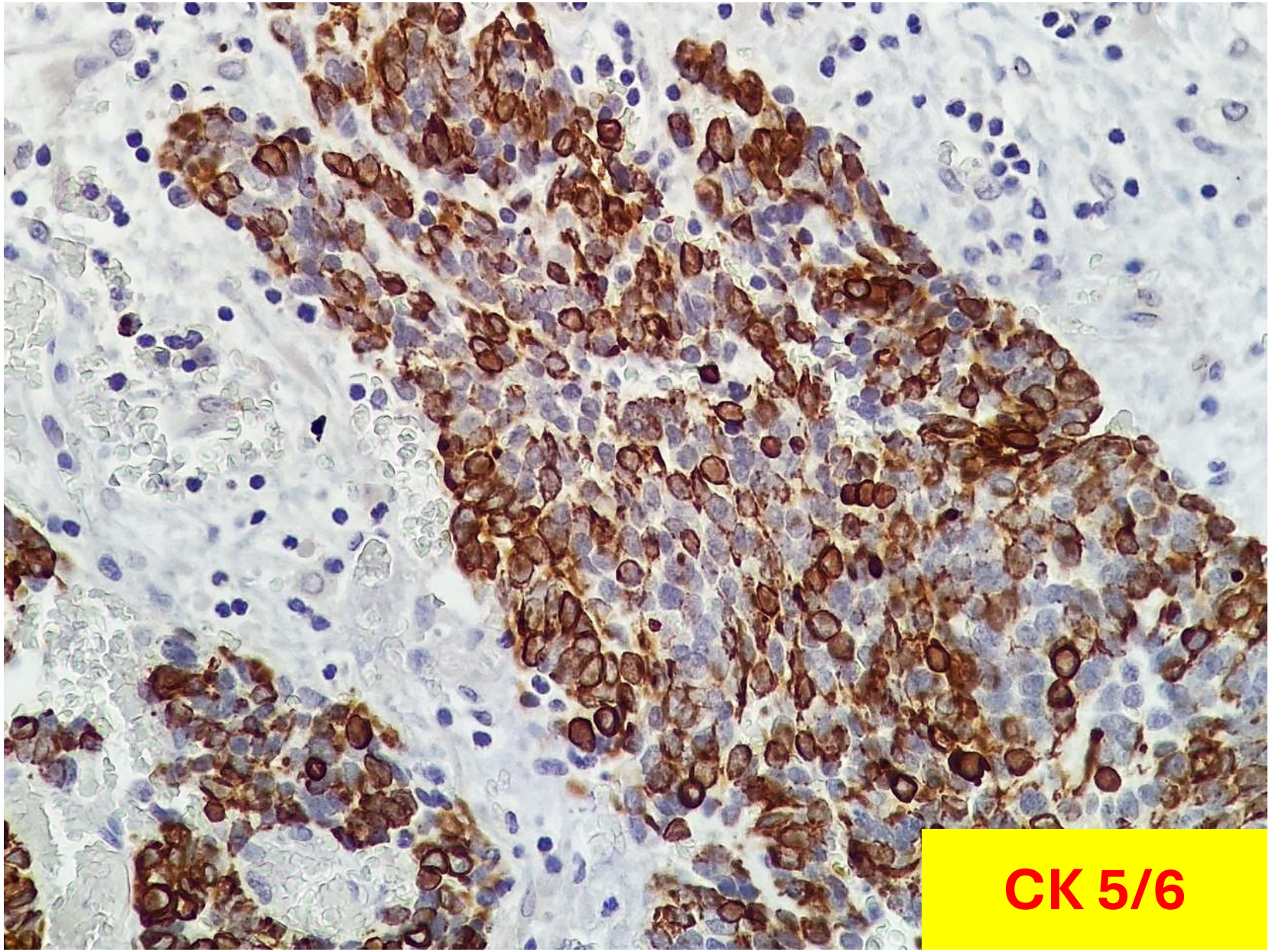
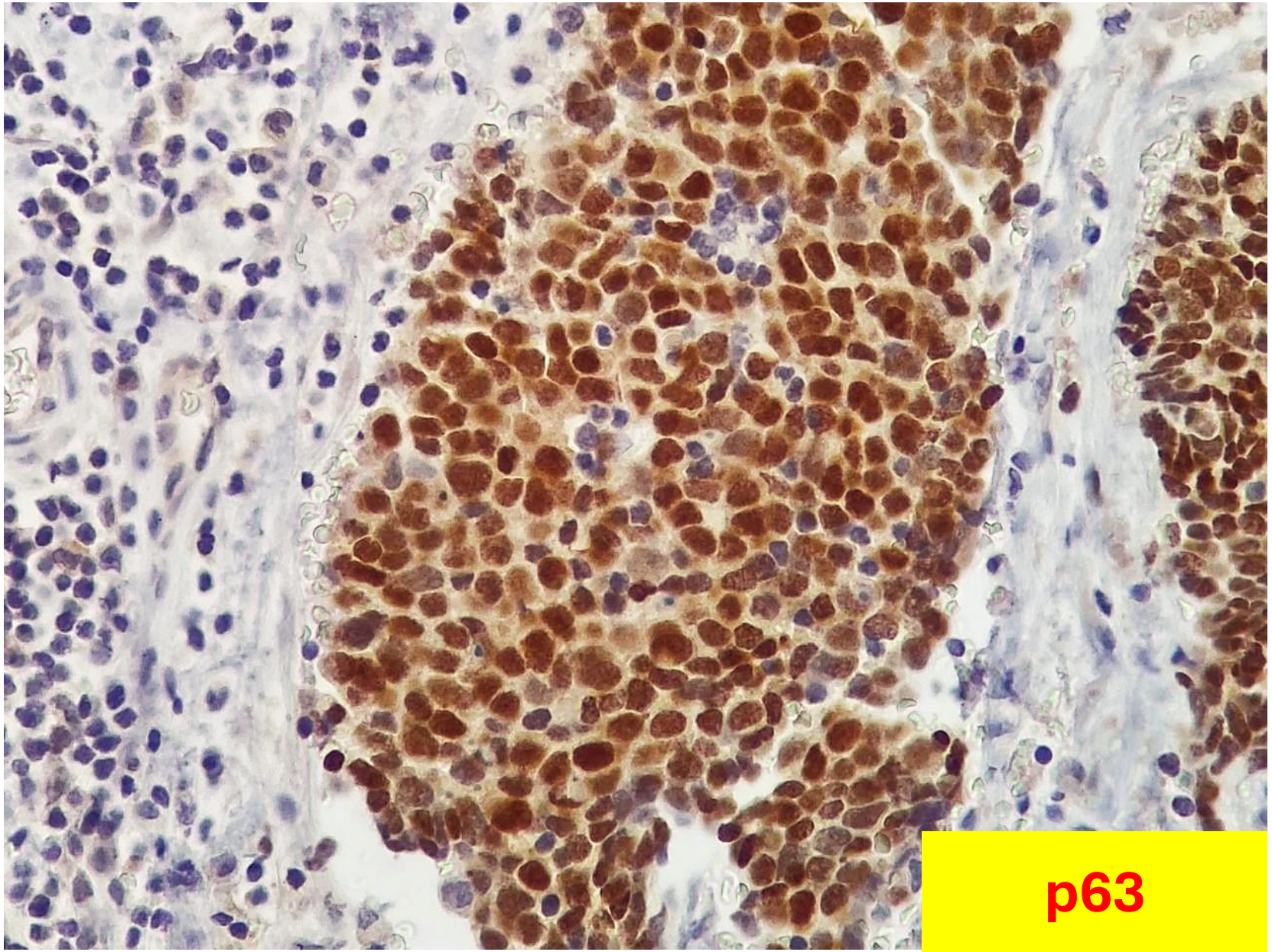
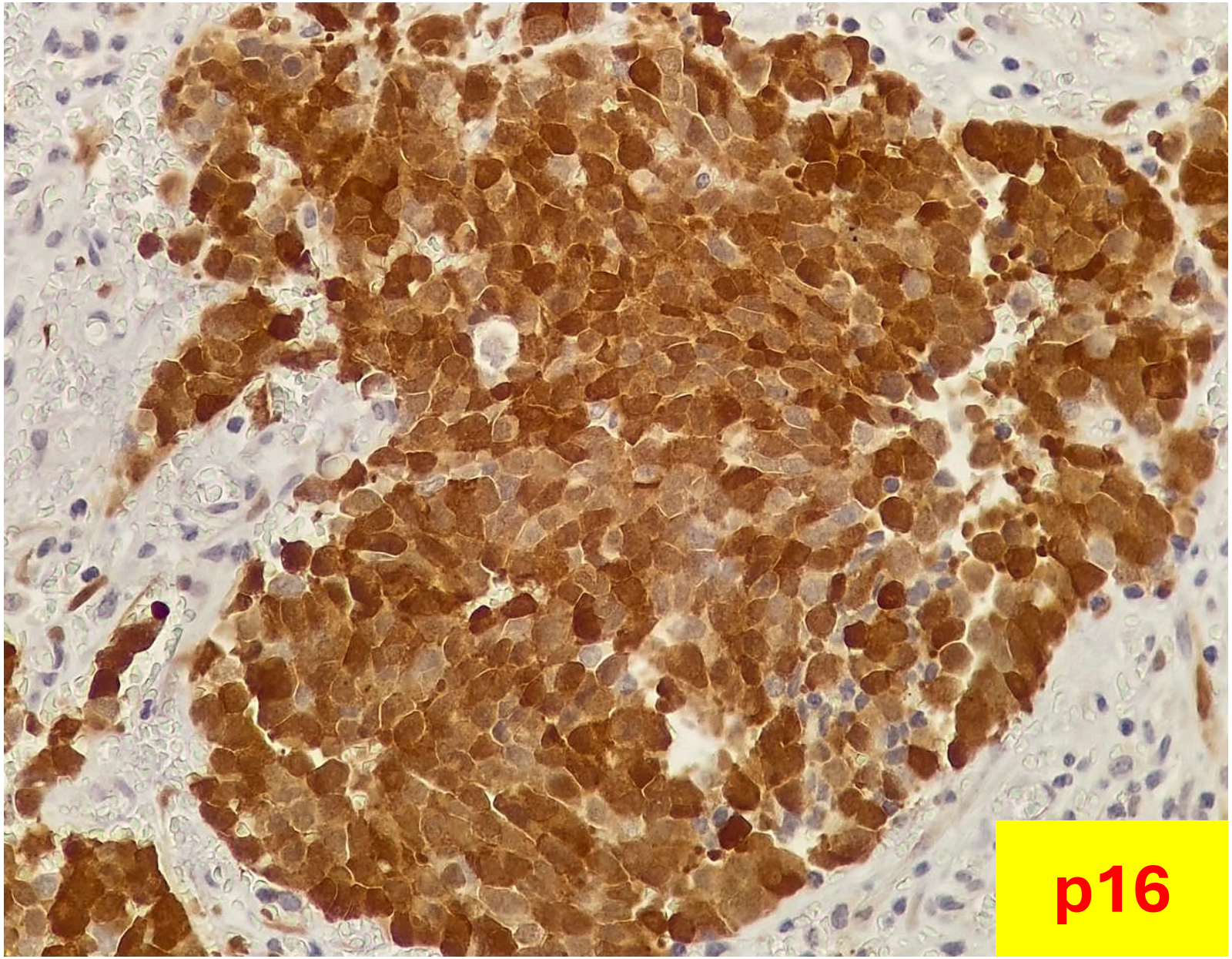

CK 7

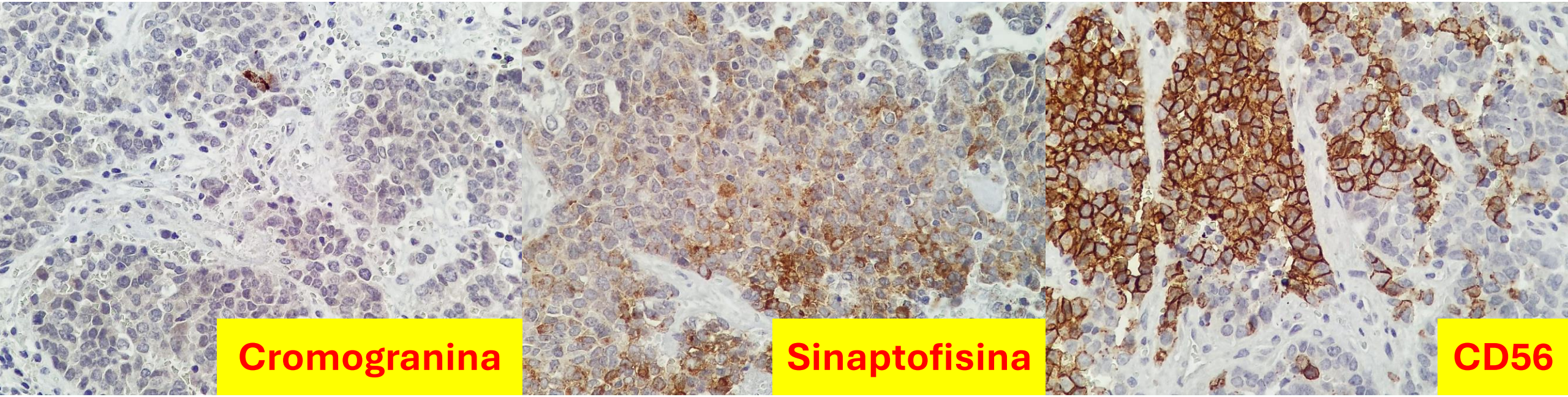

CK 7


CK 20


CK 5/6


p63


p16


Cromogranina
Sinaptofisina
CD56

Neoplasias nasales, paranasales y de la base del cráneo (OMS, 2023)

- **Carcinomas**
  - ✓ Epidermoide (Q / NoQ)
  - ✓ NUT
  - ✓ Sinonasal complejo SWI/SNF deficiente
  - ✓ Linfoepitelial sinonasal
  - ✓ Sinonasal indiferenciado *(incluido IDH-mutado)*
  - ✓ Teratocarcinosarcoma
  - ✓ Sinonasal multifenotípico relacionado con VPH
- **Adenocarcinomas**
  - ✓ Sinonasal de tipo intestinal
  - ✓ Sinonasal de tipo no intestinal
- **Otros**
  - ✓ Ameloblastoma sinonasal
  - ✓ Craneofaringioma adamantinimatoso
  - ✓ Meningioma del tracto sinonasal, oído y hueso temporal
  - ✓ Neuroblastoma olfatorio

https://tumourclassification.iarc.who.int/chapters/52 (Head and neck tumours, 2023).

Neoplasias nasales, paranasales y de la base del cráneo

- **Otros (2)**

  - ✓Neoplasias neuroendocrinas
  - ✓Carcinoma olfatorio
  - ✓Carcinoma adenoideo quístico sólido
  - ✓Sarcoma de Ewing tipo adamantinoma

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Table 2
Differential diagnostic features of sinonasal undifferentiated and poorly differentiated carcinomas

Tumor	Histologic Features	Immunohistochemistry	Molecular Alterations
NUT carcinoma	Small to large basaloid cells; abrupt squamous differentiation +/–; interspersed granulocytes	PanCK, p63/p40 +; speckled nuclear staining with NUT1; retained INI1 and BRG1	*NUTM1* fusions with *BRD4* (most common), *BRD3*, *NSD3*, ZNFs
SMARCB1-deficient sinonasal carcinoma	Basaloid cells with variable number of plasmacytoid/ rhabdoid cells; relatively uniform nuclei; no true keratinization	PanCK +; p63, p40 +/–, CD34, NE markers +/-; loss of INI1; retained BRG1	*SMARCB1* inactivating mutations
SMARCB1-deficient sinonasal adenocarcinoma	Basaloid and rhabdoid morphology in glandular pattern	CK7 +; CK20/CDX2 focal +; Loss of INI1	*SMARCB1* inactivating mutations
SMARCA4-deficient carcinoma	Trabeculae and nests of pleomorphic epithelioid cells with a NE appearance; rarely, basaloid/rhabdoid	PanCK+; p63/p40 +/–; NE markers viz. SYN, CG +/- but INSM1 negative/faint +; loss of BRG1; retained INI1	Loss-of-function/ truncating mutations in *SMARCA4*
Teratocarcinosarcoma	Triphasic growth of neuroepithelial, carcinomatous, and sarcomatous elements	p63/p40 in squamous, CK7 in glandular epithelial components; NE markers in neuroepithelial component; desmin, myogenin, SMA in mesenchymal elements; nuclear β-catenin +, loss of BRG1 in a subset	Inactivating *SMARCA4* and activating *CTTNB1* mutations may be present
Small cell neuroendocrine carcinoma	NE architecture; cells with high N:C ratio, nuclear molding; abundant mitoses, necrosis, apoptosis	NE markers diffuse +; panCK dot +; retained INI1 and BRG1; loss of Rb, aberrant p53 staining	*RB1*, *TP53* mutations
Large cell neuroendocrine carcinoma	NE architecture; large cells with stippled nuclear chromatin; prominent nucleoli +/–	NE markers diffuse +; panCK +; retained INI1 and BRG1; loss of Rb, aberrant p53 staining	*RB1*, *TP53* mutations
Sinonasal undifferentiated carcinoma	Monomorphic large undifferentiated cells; absence of squamous or glandular differentiation; frequent mitoses, necrosis, apoptosis	PanCK +; p63 -, p40 –/+; NE markers -/focal +; retained INI1 and BRG1; NUT -; IDH1/2 +/–; p16 often +	*IDH1/2* mutations may be present; HR-HPV negative
Solid adenoid cystic carcinoma	Biphasic tumor; basaloid cells with angulated hyperchromatic nuclei in solid sheets, islands; cribriform/tubular pattern +/–; basement membrane material +/–	CK7, EMA, CD117 + in luminal cells; p40, p63, S100, SMA, SOX10, calponin + in abluminal cells; MYB +; retained INI1 and BRG1; NUT -; p16 often +	*MYB/MYBL1::NFIB* fusions; HR-HPV negative

(*continued on next page*)

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Table 2
(continued)

Tumor	Histologic Features	Immunohistochemistry	Molecular Alterations
Lymphoepithelial carcinoma	Large cells with vesicular nuclei, prominent nucleoli, admixed lymphoplasmacytes	PanCK, HMWCK +; p63/p40 +/–; EBV-LMP1 +/–, p53 diffuse positive	EBER ISH positive
Adamantinoma-like Ewing sarcoma	Small monotonous basaloid cells; peripheral palisading, rosette formation +/–; overt squamous differentiation +/–;	Ewing sarcoma markers CD99, NKX2.2, FLI1 and squamous markers panCK, p40/p63 +; retained INI1 and BRG1	*EWSR1* gene fusions; rarely *FUS* fusions
High grade olfactory neuroblastoma	Undifferentiated neurectodermal cells in lobular or diffuse architecture, with intervening vasculature; fibrillary matrix +/–; true rosettes, pseudorosettes +/–; necrosis, calcification +/–	NE markers +; S100, SOX10 + in sustentacular cells; panCK –/+, EMA -	Nil
Mucosal melanoma	Pleomorphic epithelioid, plasmacytoid or spindled cells; peritheliomatous pattern; cytoplasmic melanin +/–	S100, SOX10, HMB-45, Melan-A, PRAME +; SYN, panCK, desmin –/+	*KIT, NRAS, BRAF, NF1, SF3B1, SPRED*, WNT-pathway mutations
Basaloid SCC	Primitive cells in nests, lobules; high N:C ratio; peripheral palisading; myxoid/hyaline stroma	PanCK, HMWCK, p40, p63 +; SOX10, CD117 +/-	Nil
Undifferentiated nasopharyngeal carcinoma	Large cells with vesicular nuclei, prominent nucleoli in a syncytium	PanCK, HMWCK +; p40, p63, EBV-LMP1 +/–	EBER ISH positive
Solid alveolar rhabdomyosarcoma	Primitive round to ovoid cells in sheets; rhabdomyoblastic differentiation –/+; multinucleated tumor cells	Desmin, myogenin, MyoD1 +	*PAX3/PAX7::FOXO1* fusions
Non-Hodgkin lymphoma	Discohesive cells; angiocentric angioinvasive destruction in ENKTL; abundant necrosis	LCA, lineage specific markers (CD3, CD56, CD20) +; EBV+	EBER ISH positive
Germ cell tumor: teratomas	Mature/immature tissues from all 3 germ cell layers	Lineage specific markers; SALL4	Isochromosome 12p
Germ cell tumor: Yolk sac tumor	Reticular/microcystic, macrocystic architecture; cells with pale cytoplasm, vesicular nuclei, prominent nucleoli Schiller–Duval bodies; other GCT components +/–	SALL4, AFP, glypican-3, Hep-par1, panCK +	Nil

Abbreviations: -, negative; –/+, infrequently positive; +, positive; +/–, frequently positive; CG, chromogranin; ENKTL: extranodal NK/T-cell lymphoma; ISH, in situ hybridization; LCA, leukocyte common antigen; NE, neuroendocrine; panCK, pancytokeratin; SMA, smooth muscle actin; SYN, synaptophysin.

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Diagnósticos diferenciales de carcinomas sinonasales poco diferenciados / indiferenciados

- **Neuroblastoma olfatorio de alto grado**
- **Melanoma**
- **Rabdomiosarcoma alveolar**
- **Linfoma No Hodgkin**
- **Tumores germinales**

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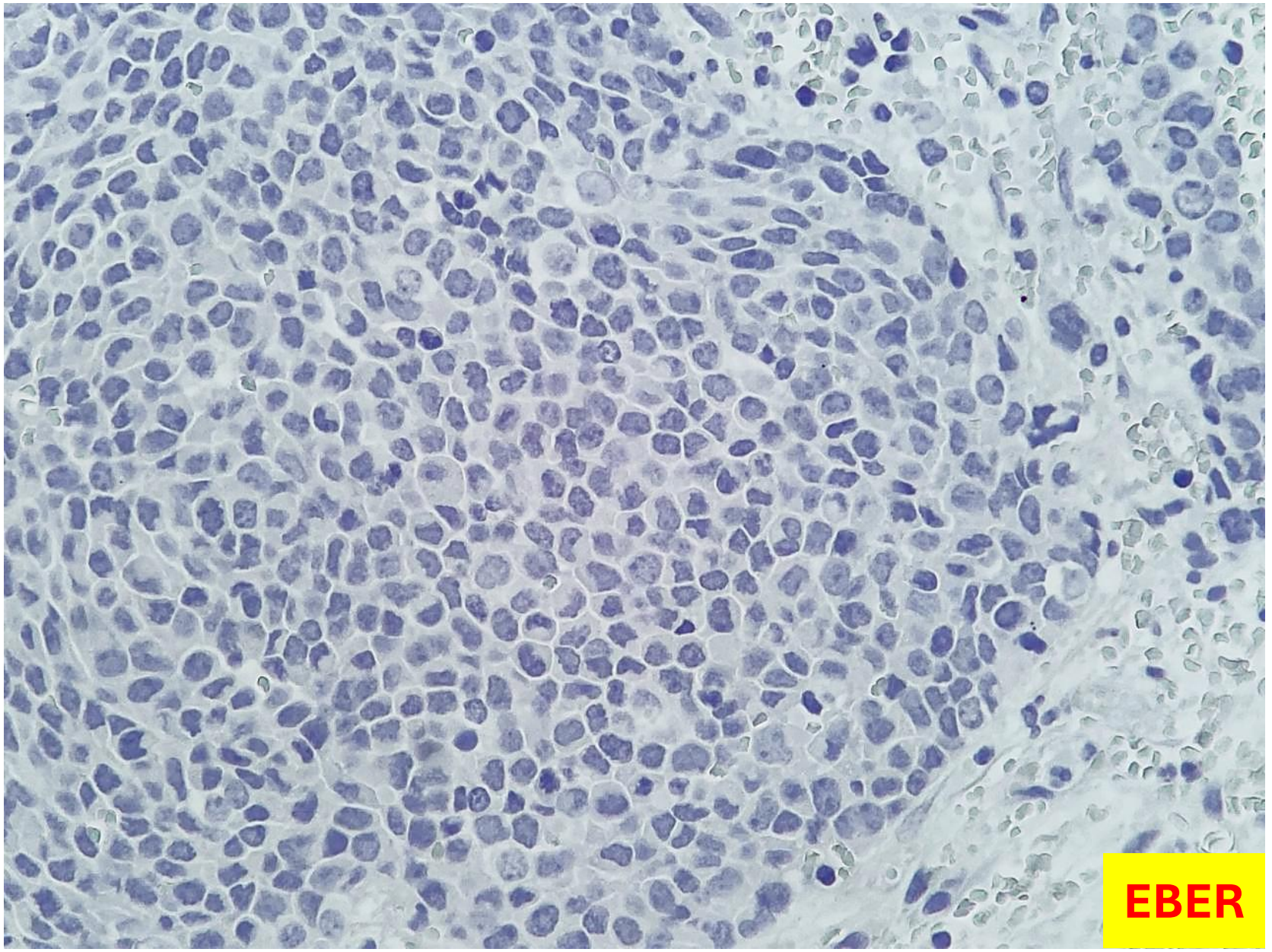
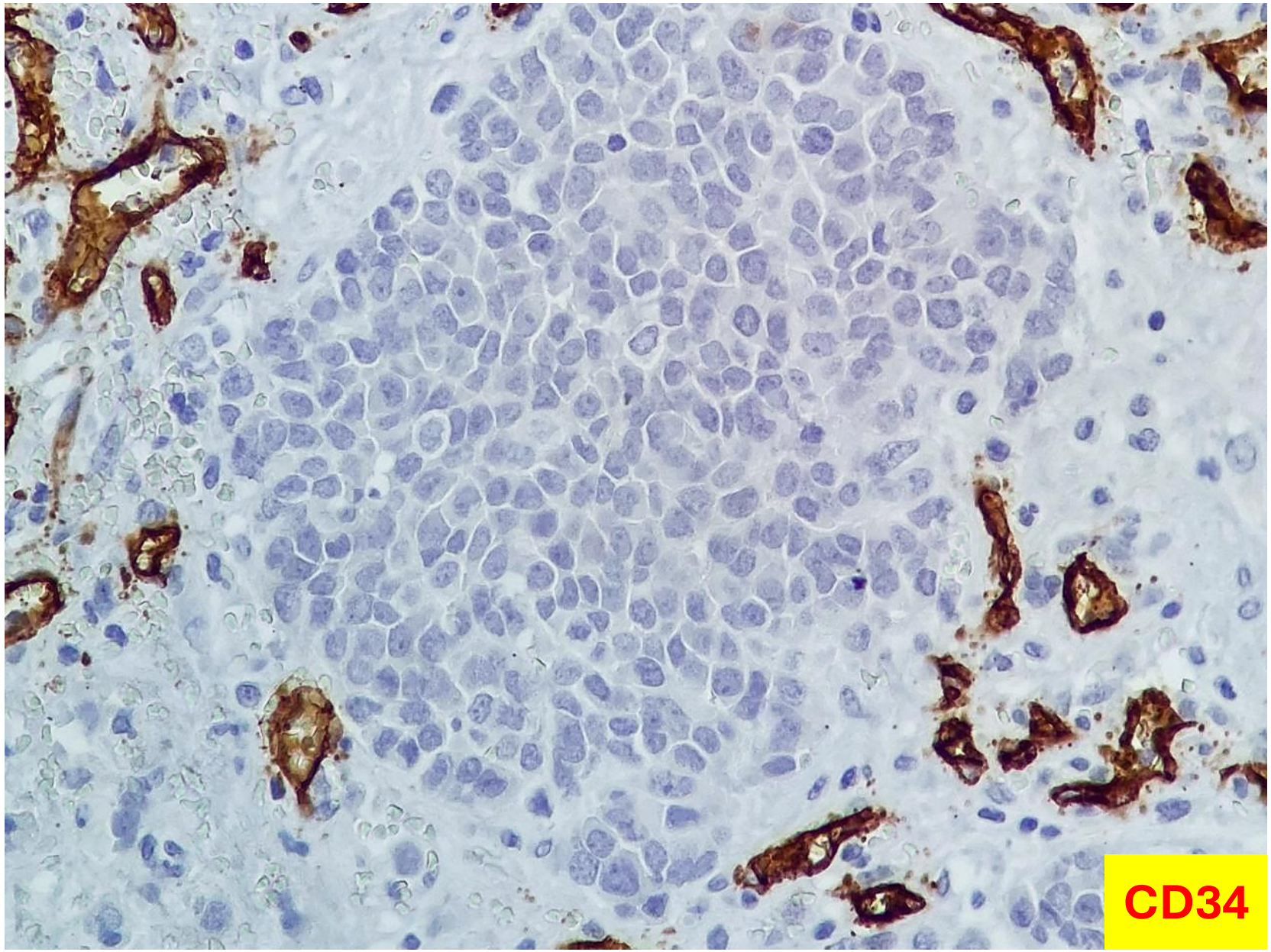

EBER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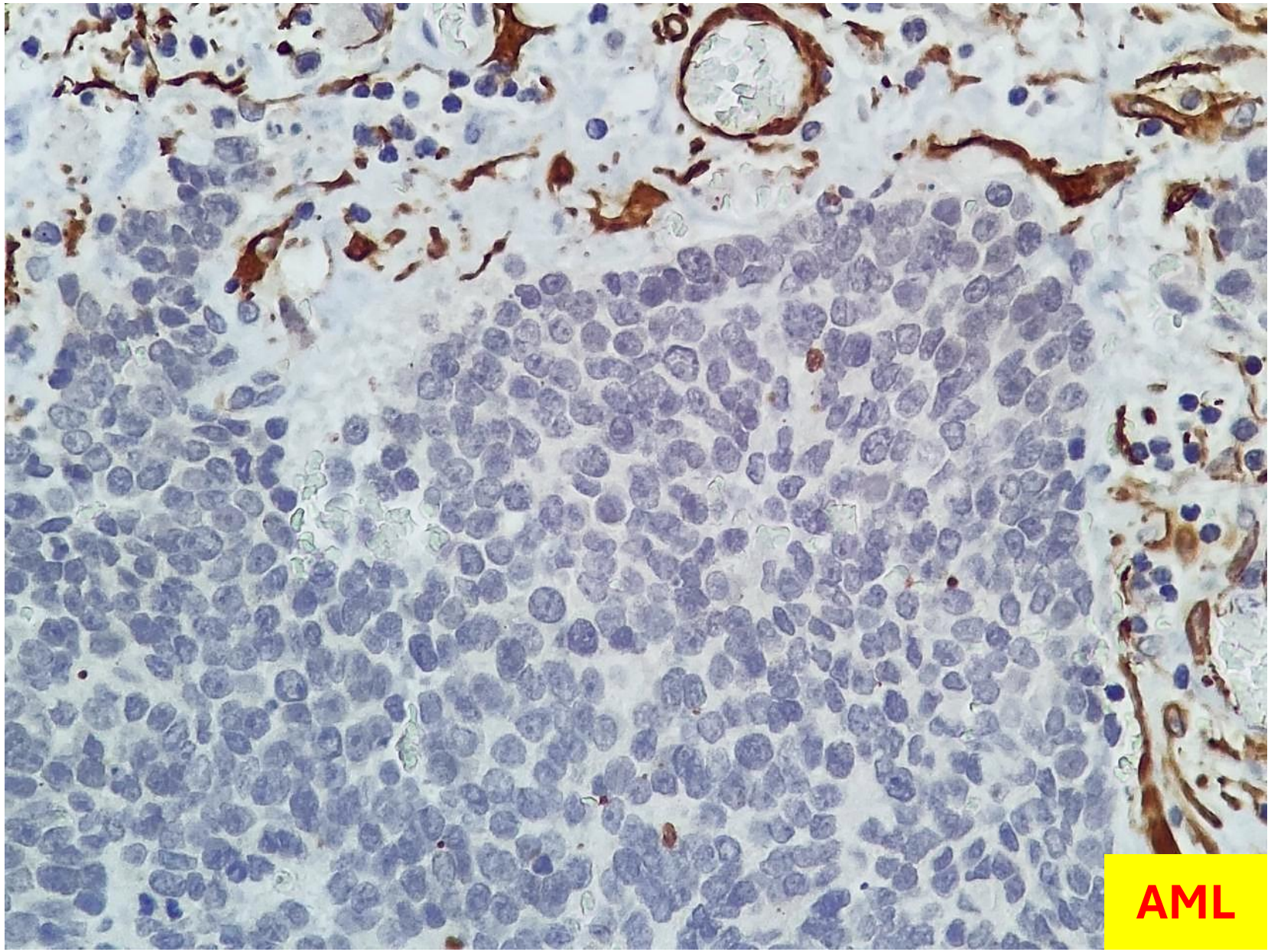
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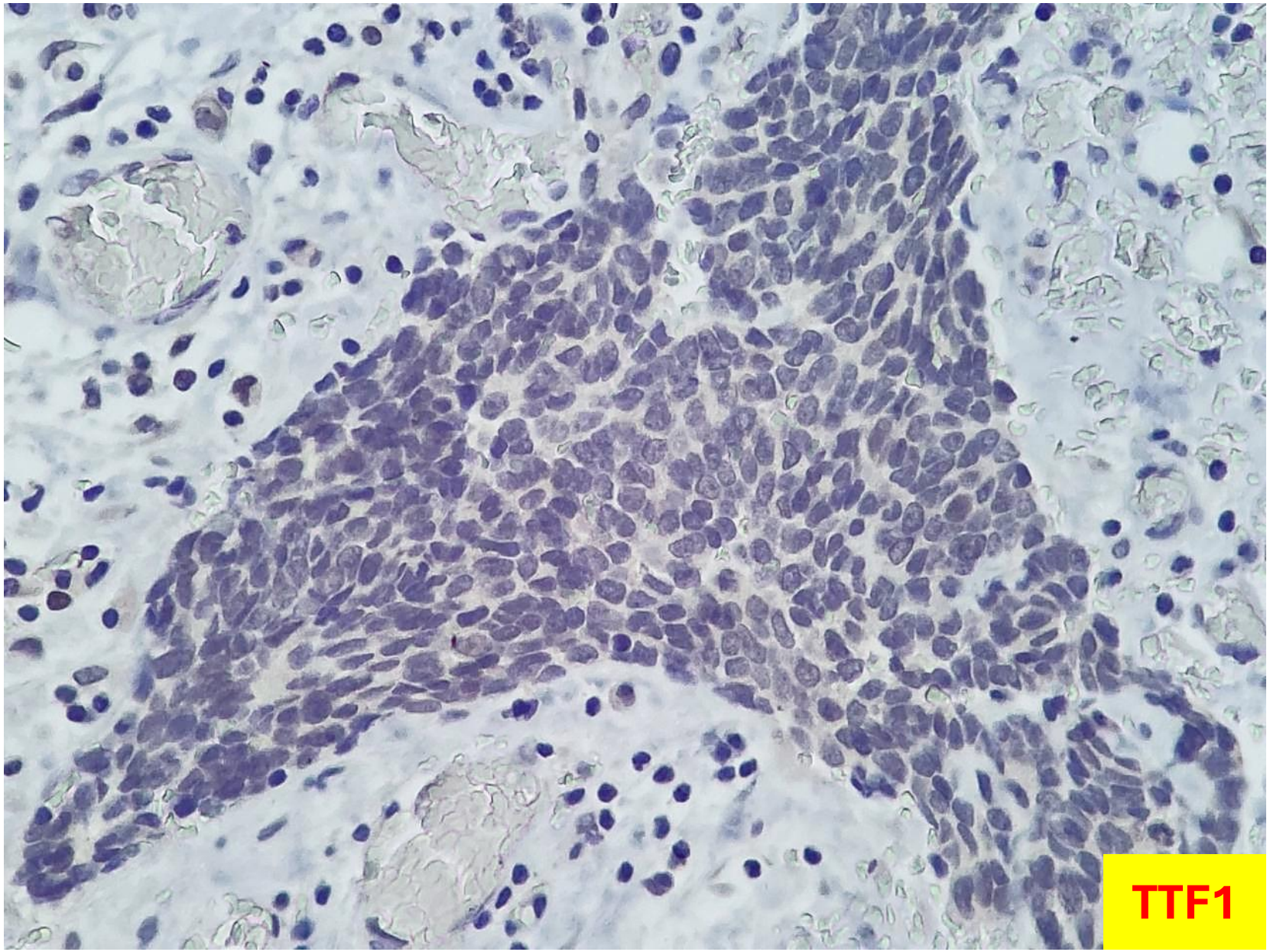
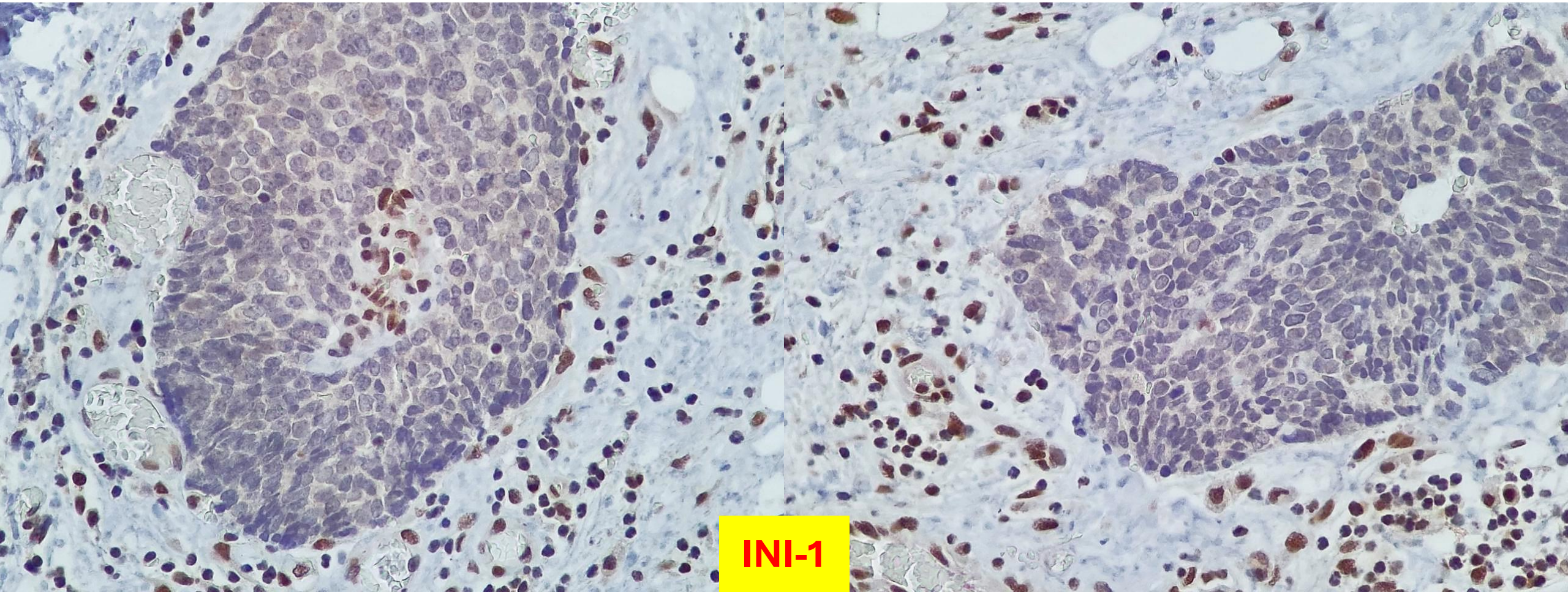
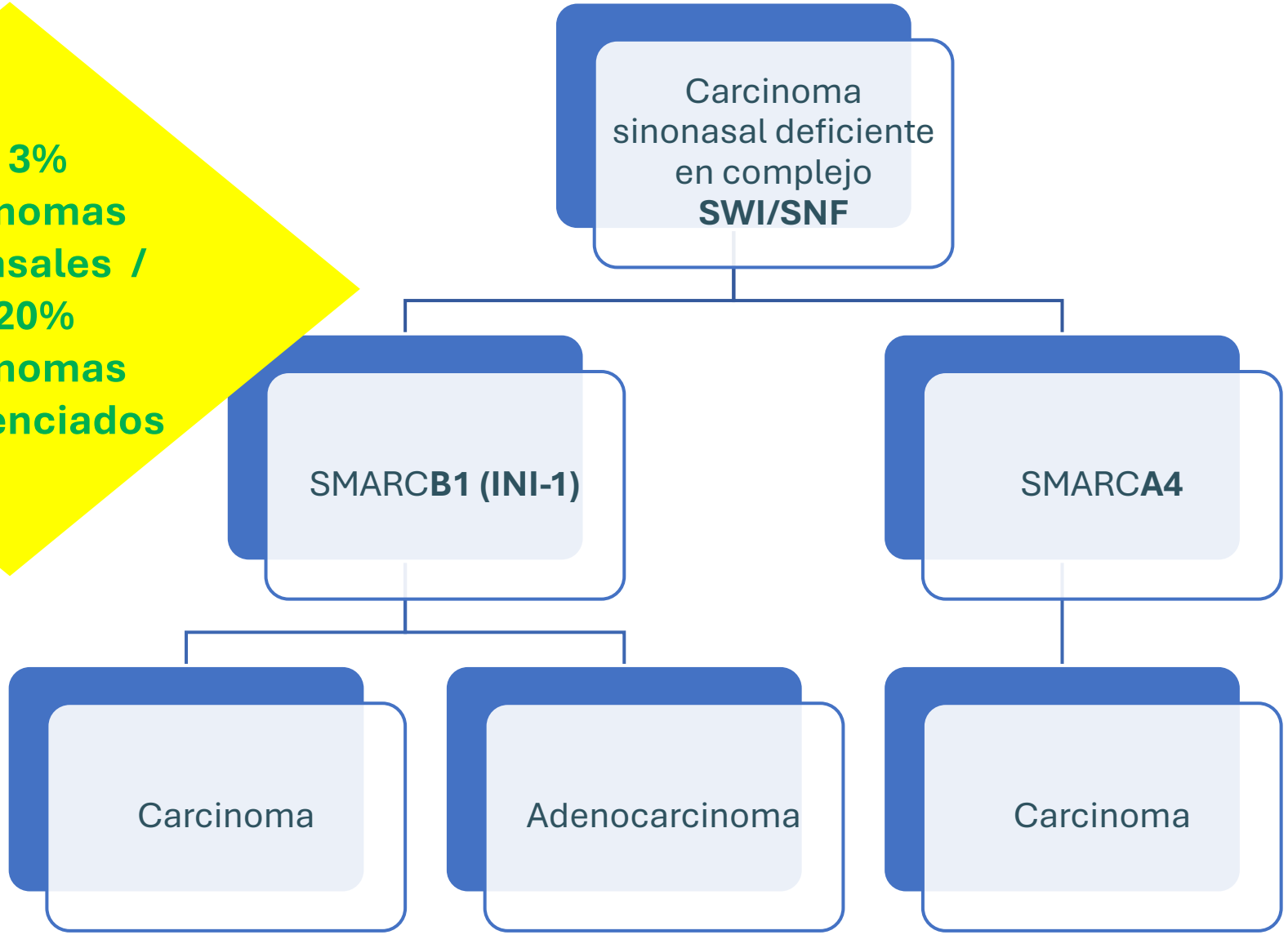

TTF1


INI-1

Carcinoma sinonasal SMARCB1 (INI-1) deficiente

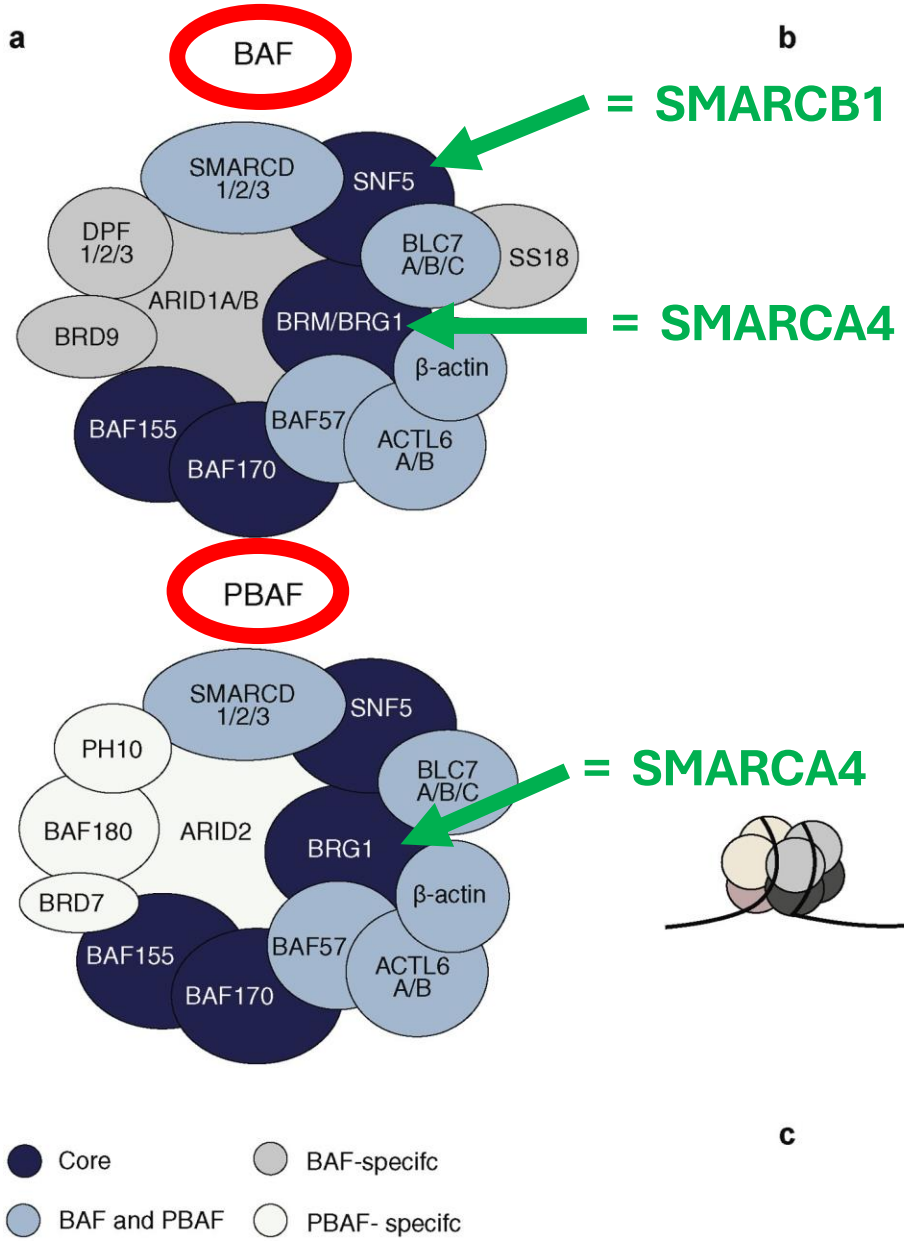
1 - 3%
carcinomas sinonasales /
3 -20%
carcinomas indiferenciados

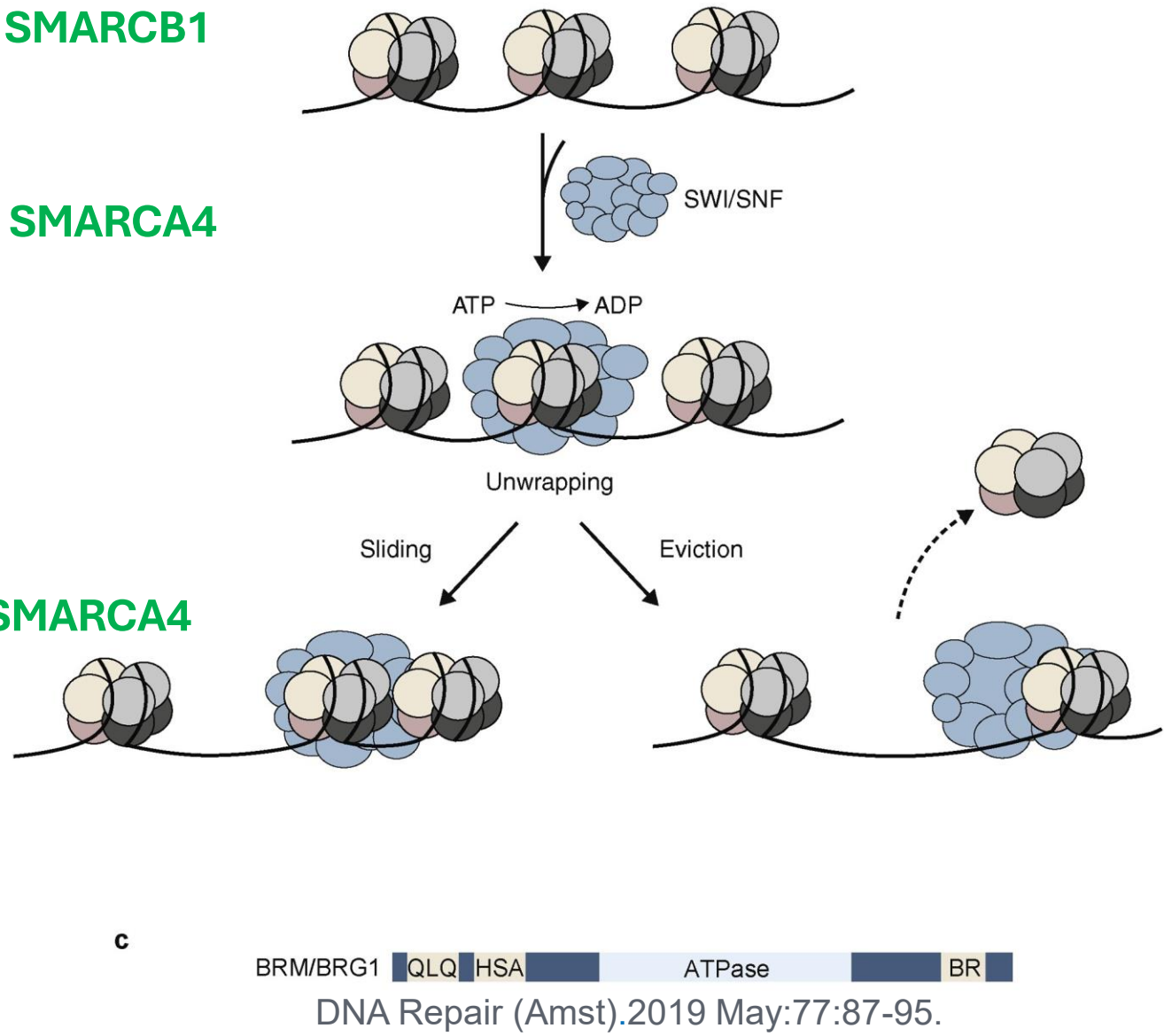


https://tumourclassification.iarc.who.int/chapters/52 (Head and neck tumours, 2023).

Familia de complejo SWI/SNF

(switching defective/sucrose non-fermenting)





DNA Repair (Amst).2019 May:77:87-95.

Carcinogénesis

SWI/SNF subunits, domains and frequency of alteration in cancer.

Subunit	HUGO name	Synonyms	Domains	% Alteration in cancer
BRG1	SMARCA4	–	Bromo, ATPase, HAS, QLQ	Ovarian cancer (> 10%), medulloblastoma (5-10%), melanoma (5-10%), small cell cancer of the ovary (100%)
BRM	SMARCA2	–	Bromo, ATPase	Rhabdoid tumor (60%); lung (4.8-10%), breast (15%), gastric (15%) and bladder (15%) cancers
SNF5	SMARCB1	INI1, BAF47	COIL	Rhabdoid tumor (> 98%), epithelioid sarcomas (> 55%), familial schwannomatosis (30-45%)
BAF155	SMARCC1	–	CHROMO, SANT, COIL	Prostate cancer (30-31%)
BAF170	SMARCC2	–	CHROMO, SANT, COIL	Rarely mutated
ARID1A	ARID1A	BAF250A	ARID	Clear cell ovarian (50%), endometrioid ovarian (21-48%), breast (2.5%), liver (15%), bladder (17%), gastric (14-18%), lung (9.8%) cancer
ARID1B	ARID1B	BAF250B	ARID	Childhood neuroblastoma (7%), clear cell ovarian (> 10%), gastric, colorectal and liver cancer (5-10%)
ARID2	ARID2	BAF200	ARID, Zinc finger	Melanoma (5-15%), lung and colorectal (5-10%) and liver (5-14%) cancer
BAF180	PBRM1	–	Bromo, HMG	Renal cancer (41%), epithelioid sarcoma (83%)
BRD7	BRD7	–	Bromo	Breast cancer
BRD9	BRD9	–	Bromo	Rarely mutated
PH10	PH10	BAF45A	PHD finger	Rarely mutated
DPF1/2/3	DPF1/2/3	BAF45B/C/D	PHD finger	Rarely mutated
BAF57	SMARCE1	–	HMG, COIL	Familial spinal meningiomas (45%)
SMARCD1/2/3	SMARCD1/2/3	BAF60 A/B/C	SWIB	Rarely mutated
BCL7A/B/C	BCL7A/B/C	–	–	Non-Hodgkin's lymphoma (19.7%)
ACTL6A/B	ACTL6A/B	BAF53 A/B	Actin	Rarely mutated
SS18	SS18	SSXT	–	Synovial sarcoma (100%)

DNA Repair (Amst).2019 May:77:87-95.

Descripción en 2014, a la fecha alrededor de 200 casos reportados.

SMARCB1 (INI-1) Deficient Carcinomas of the Sinonasal Tract

Justin A. Bishop, M.D.[1,2,*], **Cristina R. Antonescu, M.D.**[3], and **William H. Westra, M.D.**[1,2,4]

[1]Department of Pathology, The Johns Hopkins Medical Institutions, Baltimore, Maryland [2]Department of Otolaryngology/Head and Neck Surgery, The Johns Hopkins Medical Institutions, Baltimore, Maryland [3]Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, New York [4]Department of Oncology, The Johns Hopkins Medical Institutions, Baltimore, Maryland

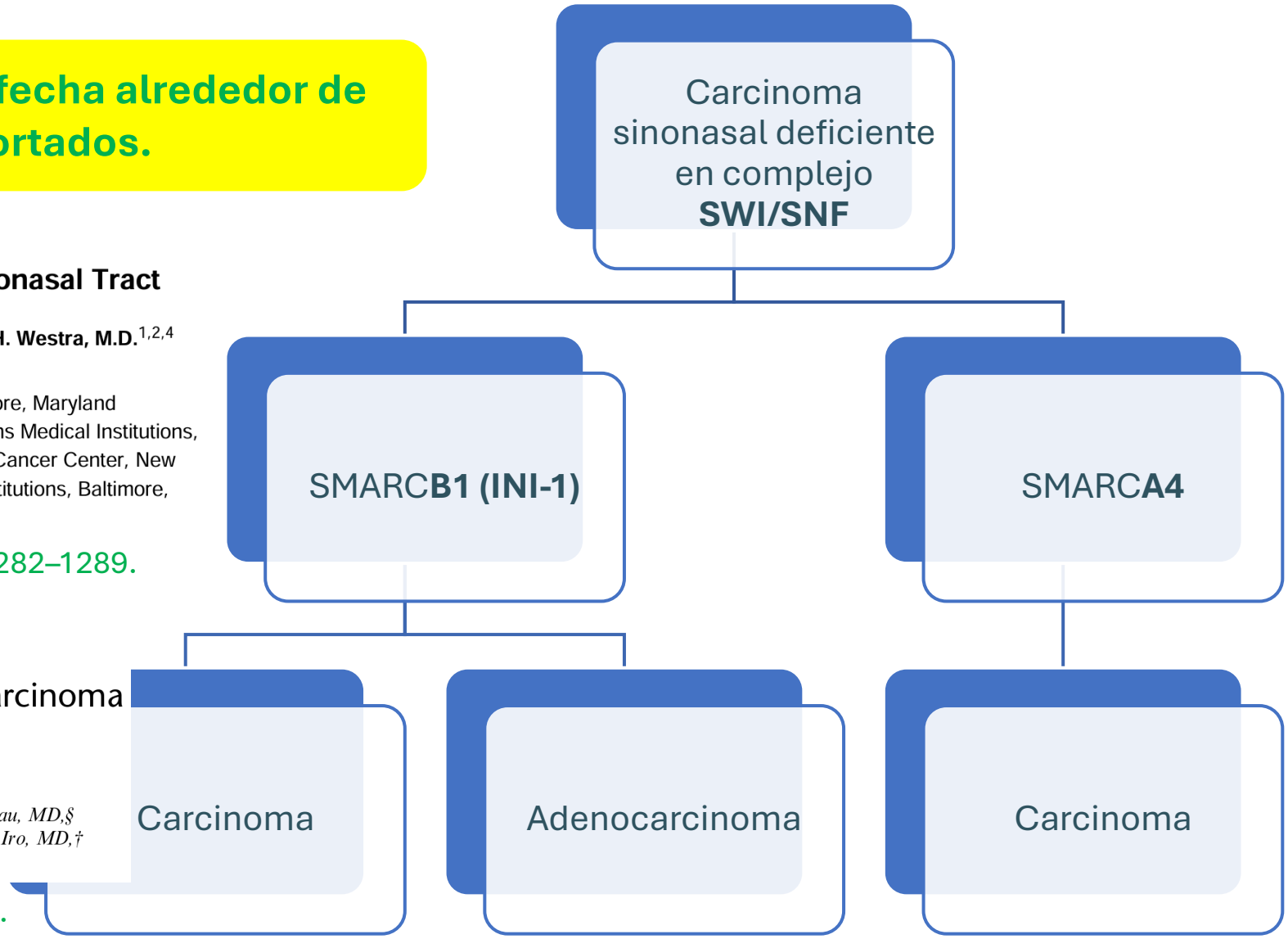
Am J Surg Pathol. 2014 September ; 38(9): 1282–1289.

SMARCB1(INI1)-deficient Sinonasal Basaloid Carcinoma

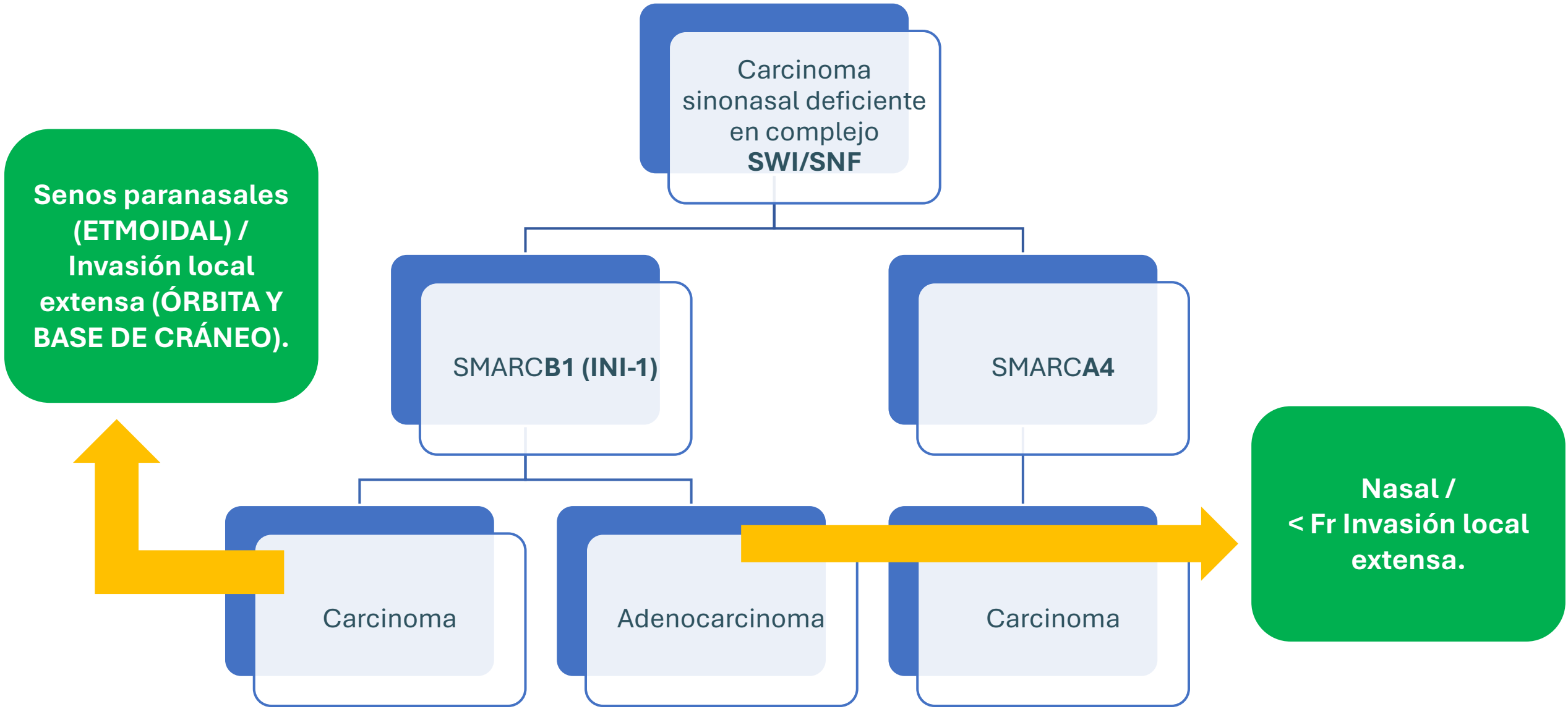
A Novel Member of the Expanding Family of SMARCB1-deficient Neoplasms

Abbas Agaimy, MD, Michael Koch, MD,† Michael Lell, MD,‡ Sabine Semrau, MD,§ Wojciech Dudek, MD,‖ David L. Wachter, MD,* Antje Knöll, MD,¶ Heinrich Iro, MD,† Florian Haller, MD,* and Arndt Hartmann, MD**

Am J Surg Pathol . 2014 Sep;38(9):1274-81.



Am J Surg Pathol . 2025 Apr 1;49(4):381-393.



https://tumourclassification.iarc.who.int/chapters/52 (Head and neck tumours, 2023).

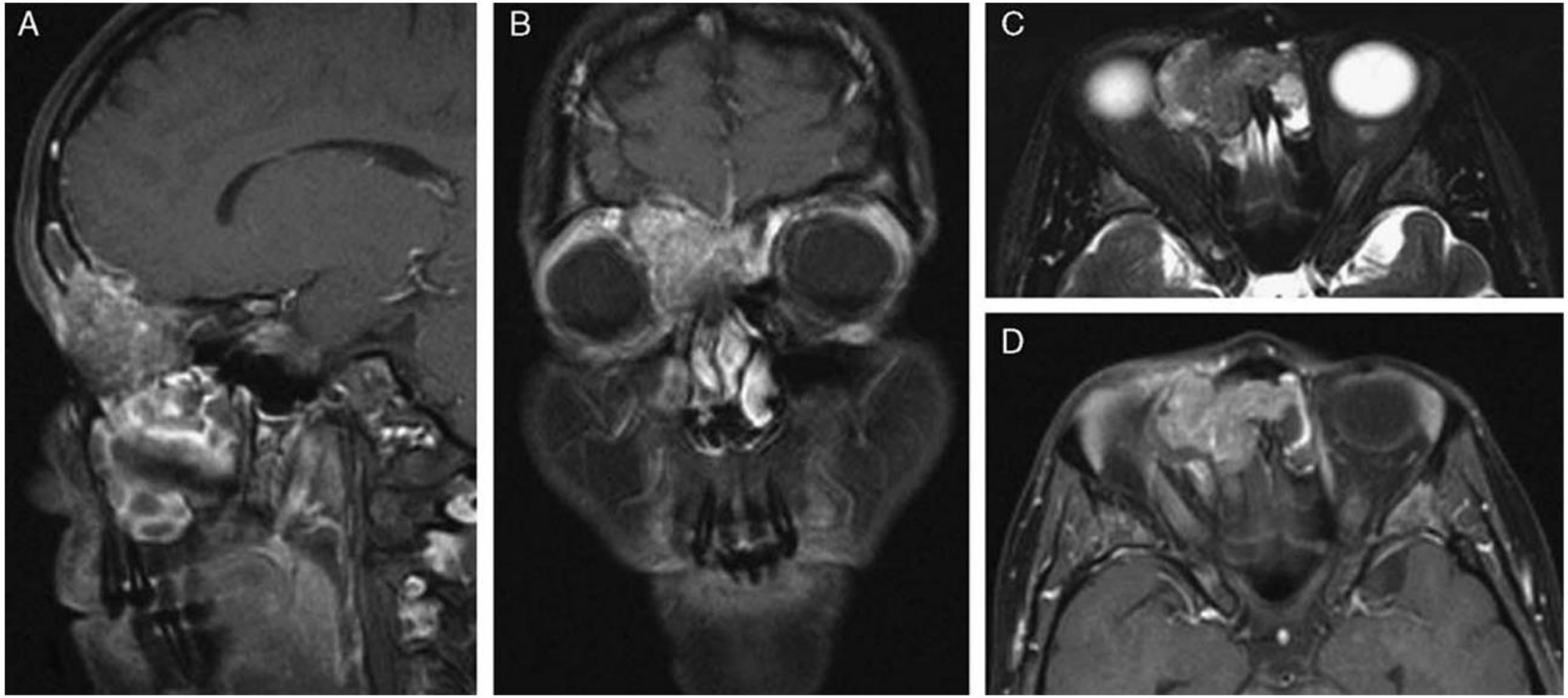
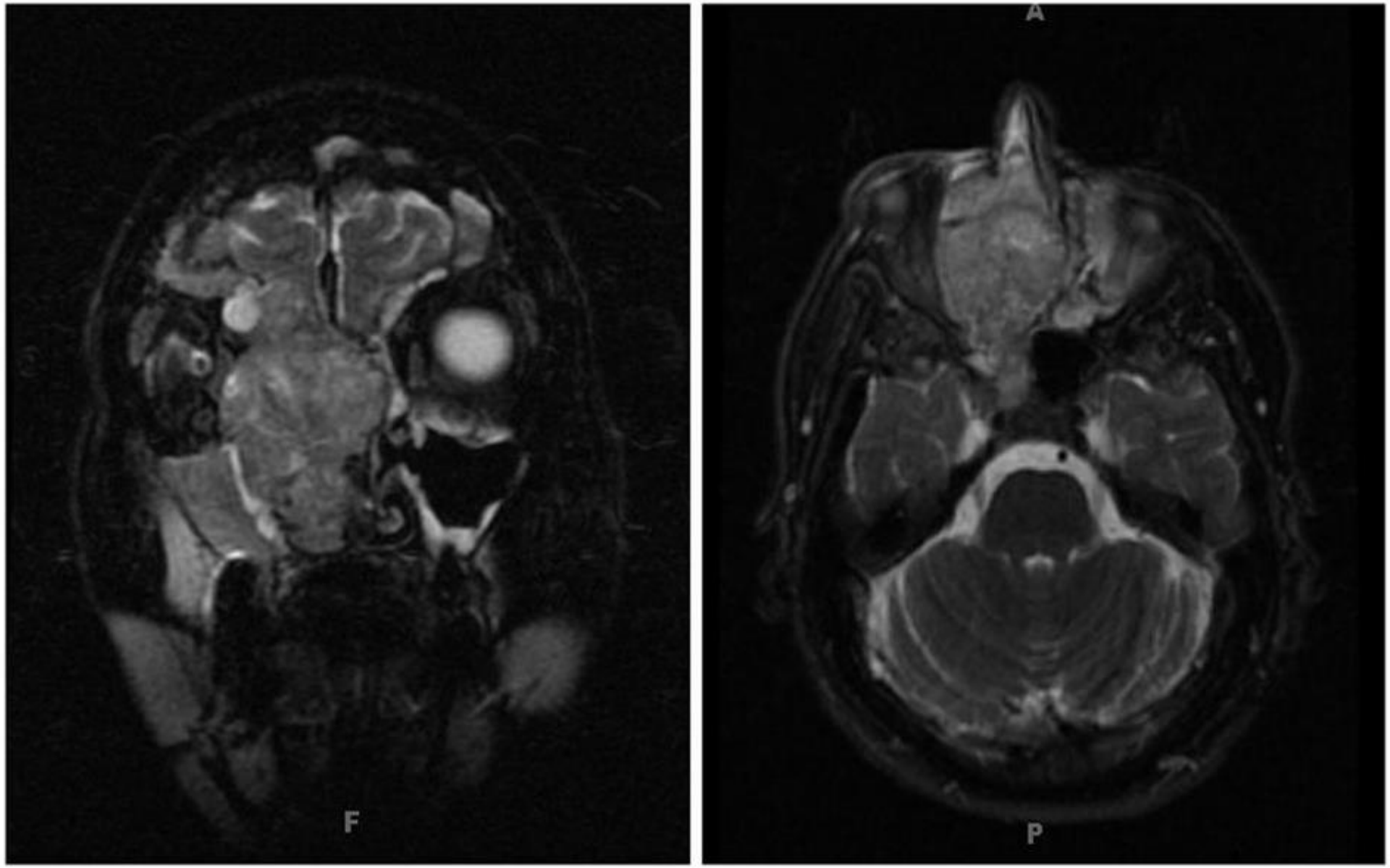


FIGURE 1. Representative magnetic resonance tomography of case 1 showed a mass in the right anterior ethmoid cells extending into both frontal sinuses with destruction of the frontal bone and the right medial orbital wall. The lesion has a salt and pepper–like appearance on both postcontrast T1w images (A, B, D) and T2w images (C). Infiltration of the extraconal space and displacement of the right eye ball were noted.

Am J Surg Pathol . 2014 Sep;38(9):1274-81.

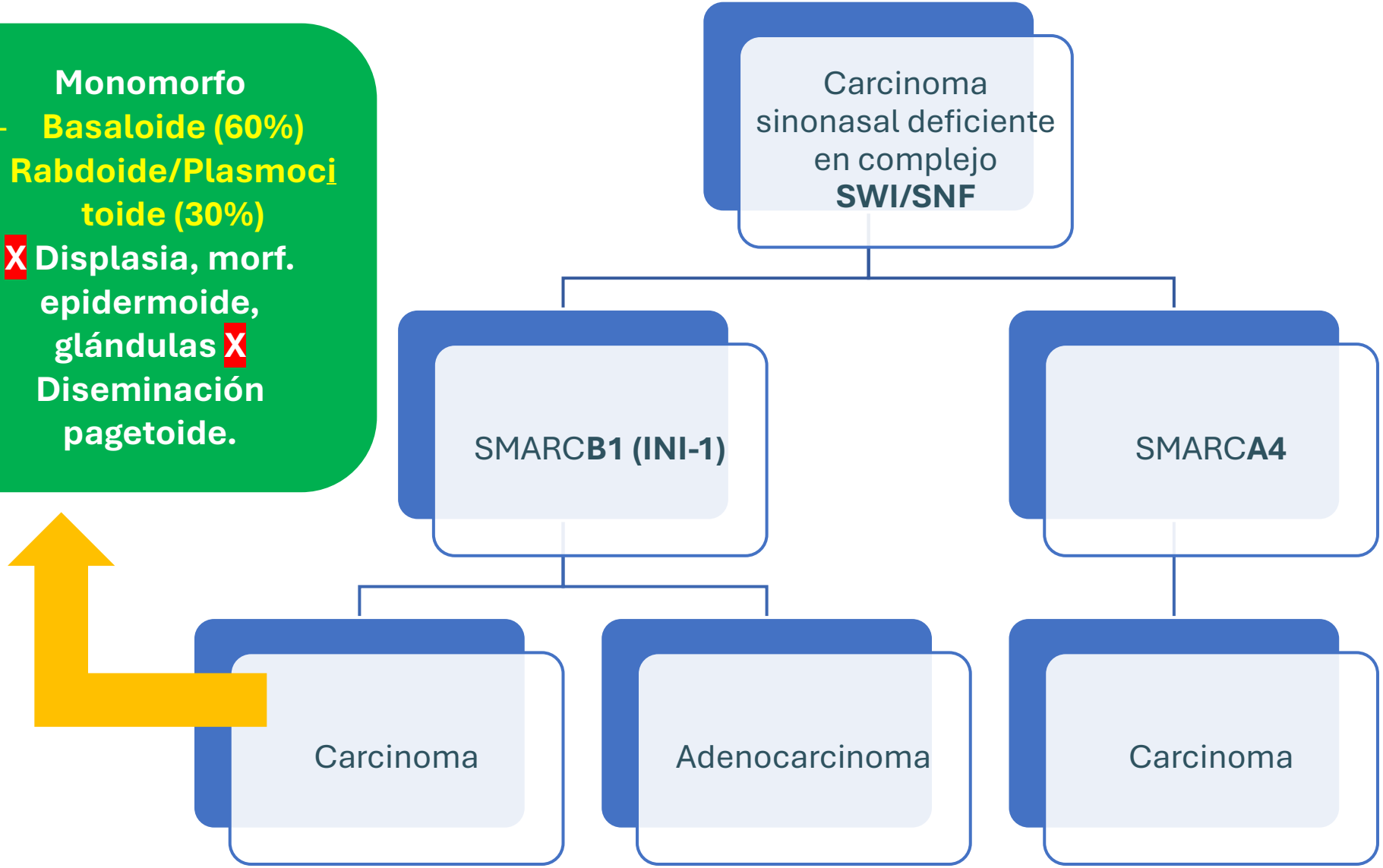
Figure 5. Most of the SMARCB1 deficient sinonasal carcinomas exhibited aggressive clinical behavior. This tumor extended from the right sinonasal tract to involve the orbit and brain (T2-weighted magnetic resonance imaging).



Am J Surg Pathol. 2014 Sep ; 38(9): 1282–1289.

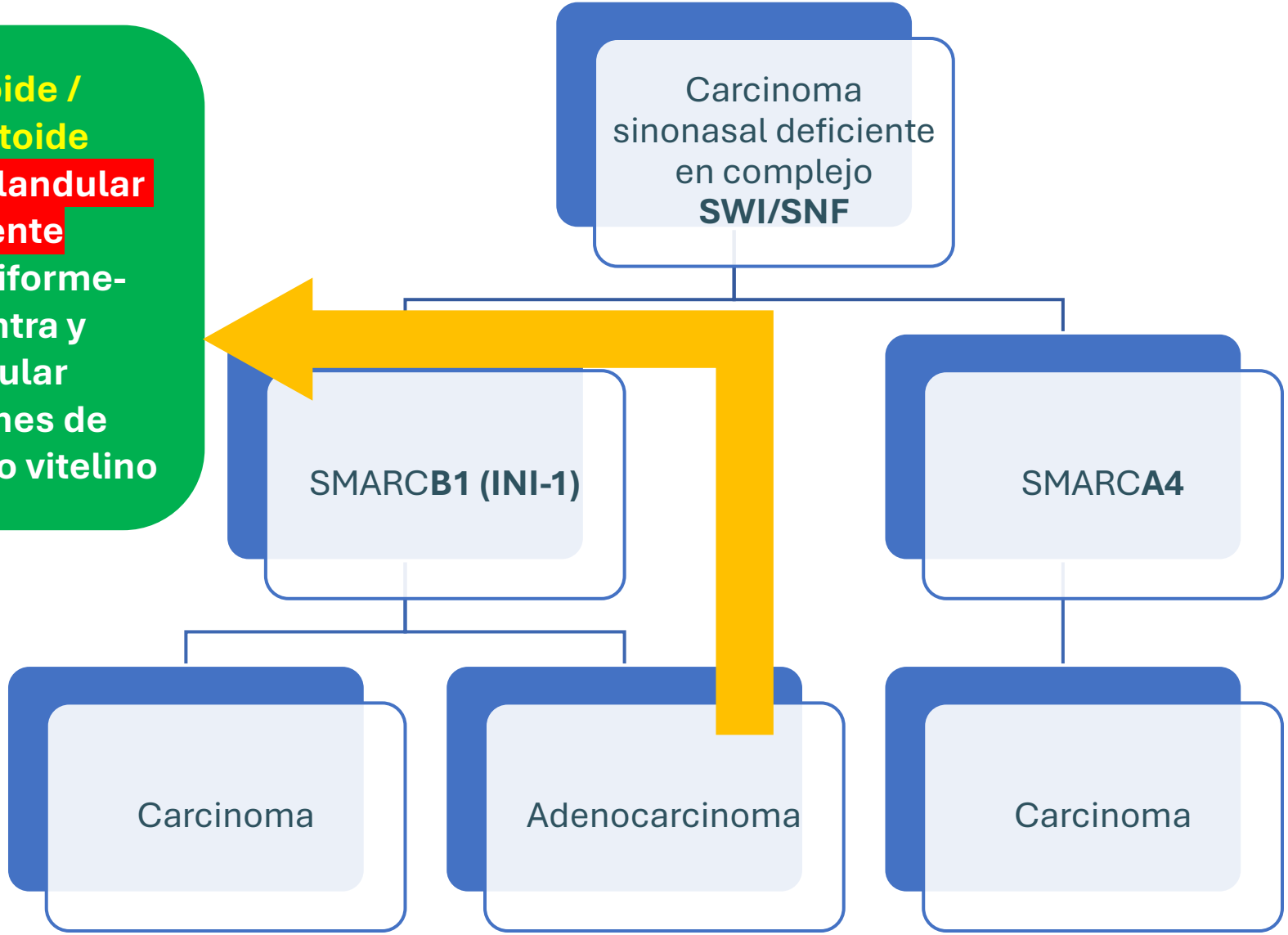
Monomorfo
- **Basaloide (60%)**
- **Rabdoide/Plasmocitoide (30%)**

X Displasia, morf. epidermoide, glándulas X Diseminación pagetoide.



https://tumourclassification.iarc.who.int/chapters/52 (Head and neck tumours, 2023).

Oncocitoide / Plasmocitoide
Formación glandular prominente
Ductal-cribiforme-mucina intra y extracelular
25% Patrones de tumor de saco vitelino



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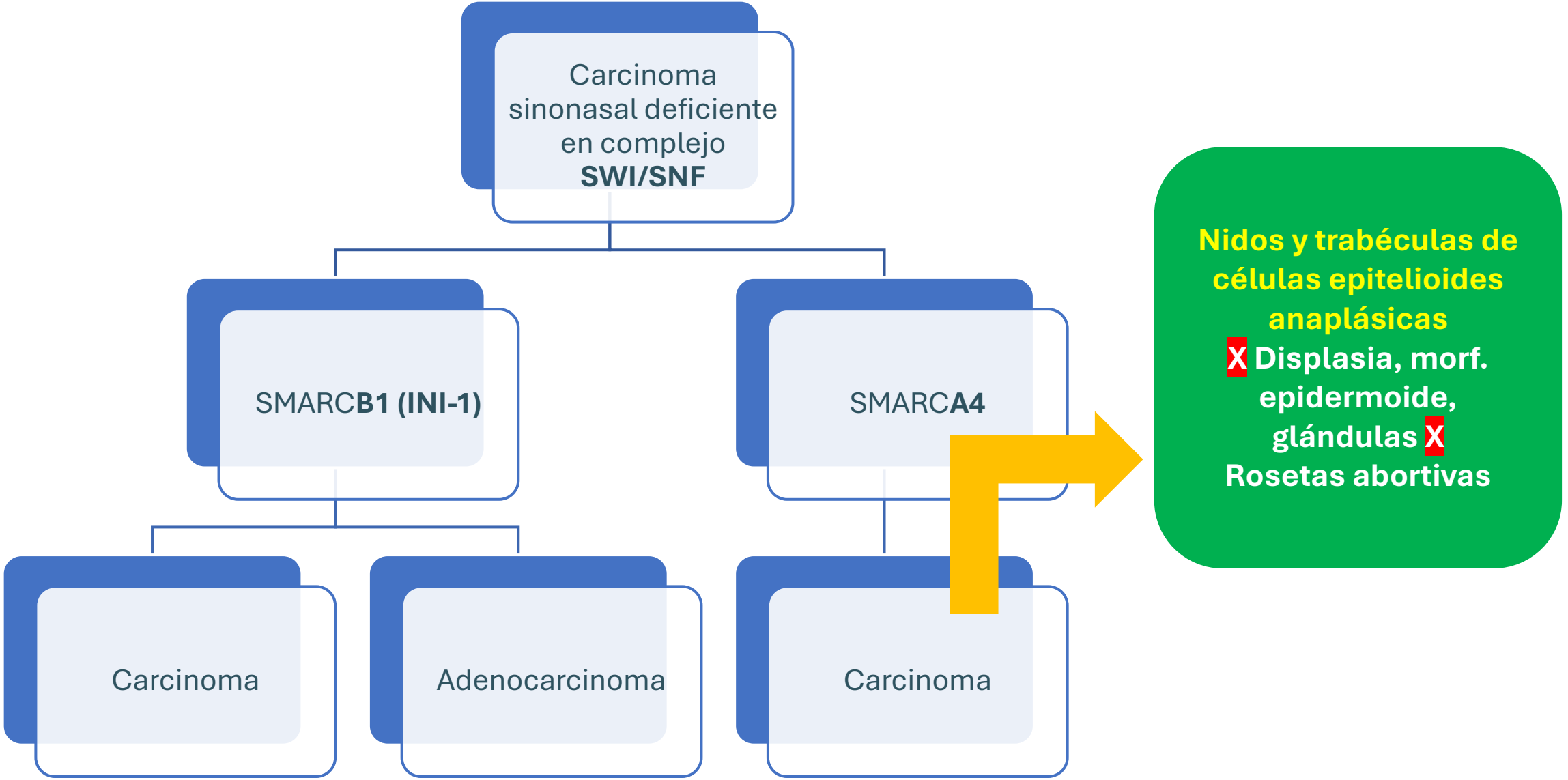


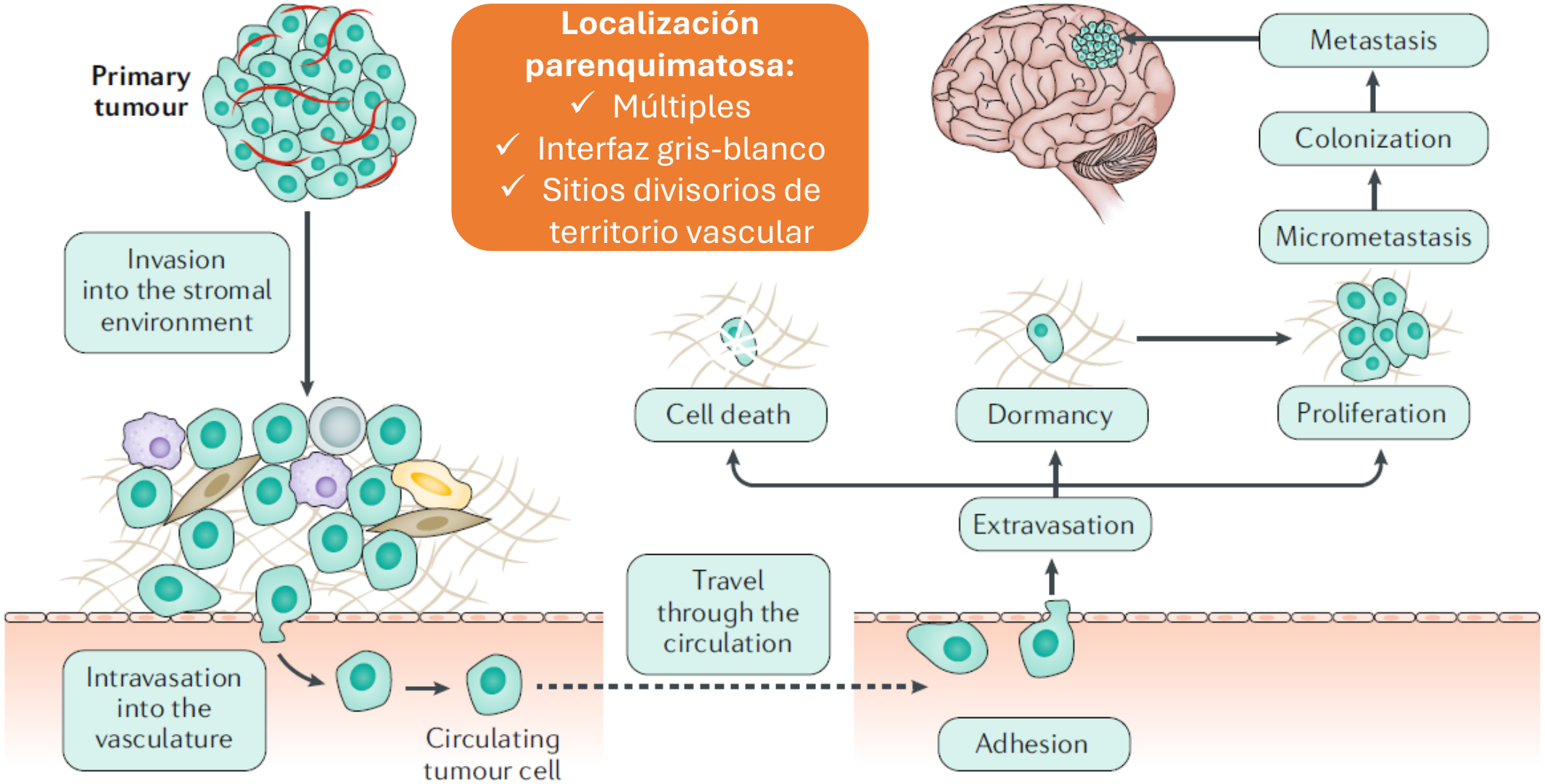
https://tumourclassification.iarc.who.int/chapters/52 (Head and neck tumours, 2023).

Metástasis cerebrales

- Neoplasia intracraneana más frecuente en adultos
  - ≠ 0-14 a /15-19 a → Neoplasias primarias SNC: 1ª / 2ª causas más frecuentes de cáncer
- 10 veces más frecuentes que neoplasias primarias del SNC
- Causa de morbilidad / mortalidad en ≈ 20% de personas con cáncer
  - 40% en estudio de autopsia
- 70,000 – 300,000 casos / año
- 10 / 100, 000 personas
- Supervivencia 4-8 meses
- Falta de registros

En el contexto de progreso:
Tamizaje / Imagenología / Tratamiento
Localización y frecuencia:
Parenquimatosa / Leptomeninges / Duramadre / Ósea

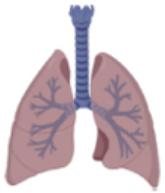
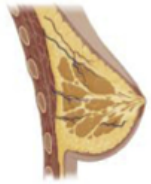
Neurosurg Clin N Am . 2020 Oct;31(4):481-488.
Nat Rev Dis Primers 5, 5 (2019).
Curr Neurol Neurosci Rep. 2021.



Nat Rev Dis Primers 5, 5 (2019).

Neoplasia primaria infrecuente:
Linfoma Hodgkin
Carcinoma de poróstata, ovario, esófago, orofaringe, piel.

Table 1
Risk of brain metastasis based on cancer type

Primary Tumor	Nussbaum et al,[29] 1996	Stark et al,[34] 2011	Fabi et al,[28] 2011
	39%	50%	—
	17%	15%	30%
	11%	7%	6%
	5%	—	—

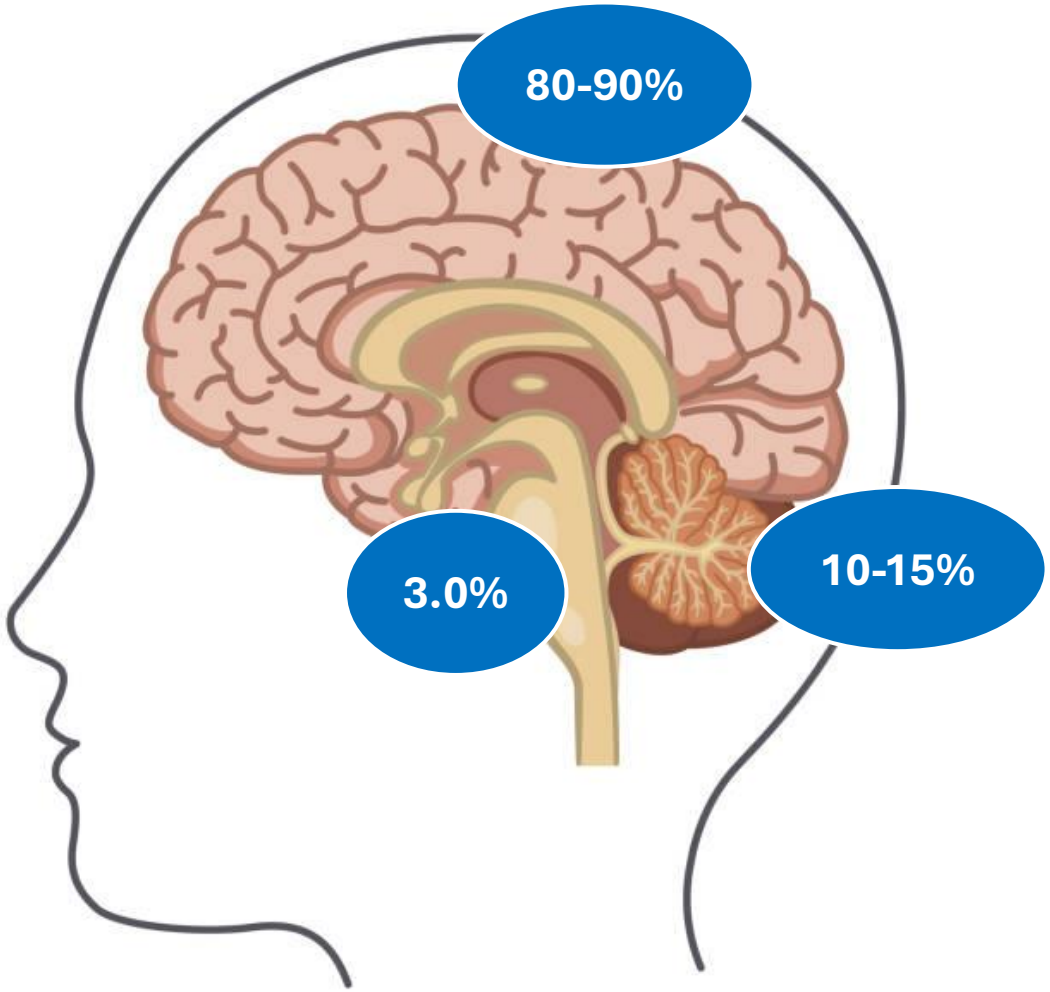
80-85% carcinoma de células no pequeñas

Factores de riesgo:
<35a, > 2.0cm, > 2 sitios, ↑ Grado > Fr, HER2+

Incluso posterior a estudio exhaustivo (PET-CT) / autopsia.

90% autopsia
Factores de riesgo:
H, ulceración, nodular-acral lentiginoso, cabeza-cuello.
Corteza / 40% hemorragia.

Neurosurg Clin N Am.
2020 Oct;31(4):481-488.



Neurosurg Clin N Am.
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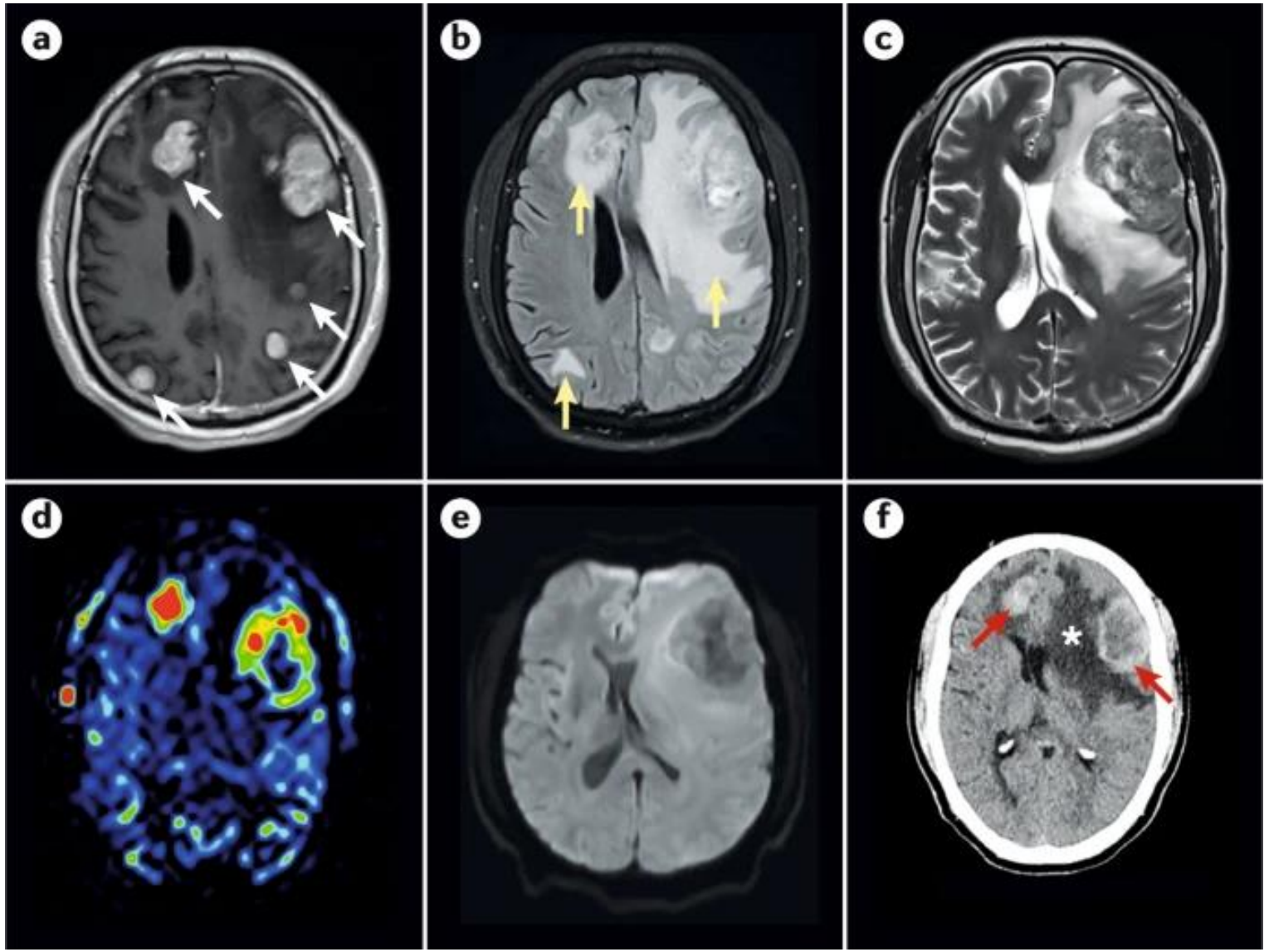

39% únicas
Mama / Colon / Riñón

Neurosurg Clin N Am . 2020 Oct;31(4):481-488.
Nat Rev Dis Primers 5, 5 (2019).

Metástasis cerebrales en neuropatología quirúrgica

- **Resección**
  - Paliativa
  - Contención

- **Biopsia estereotáxica**
  - Neoplasia 1ª *vs* 2ª
  - Lesión inflamatoria *vs* neoplásica
  - Pb. linfoma

ETO

Clínica-Imagen

Neurosurg Clin N Am . 2020 Oct;31(4):515-526.

¡Gracias!