Prípad č. 1

- 68 ročný muž
- Klinická diagnóza: tumor ossis sacri

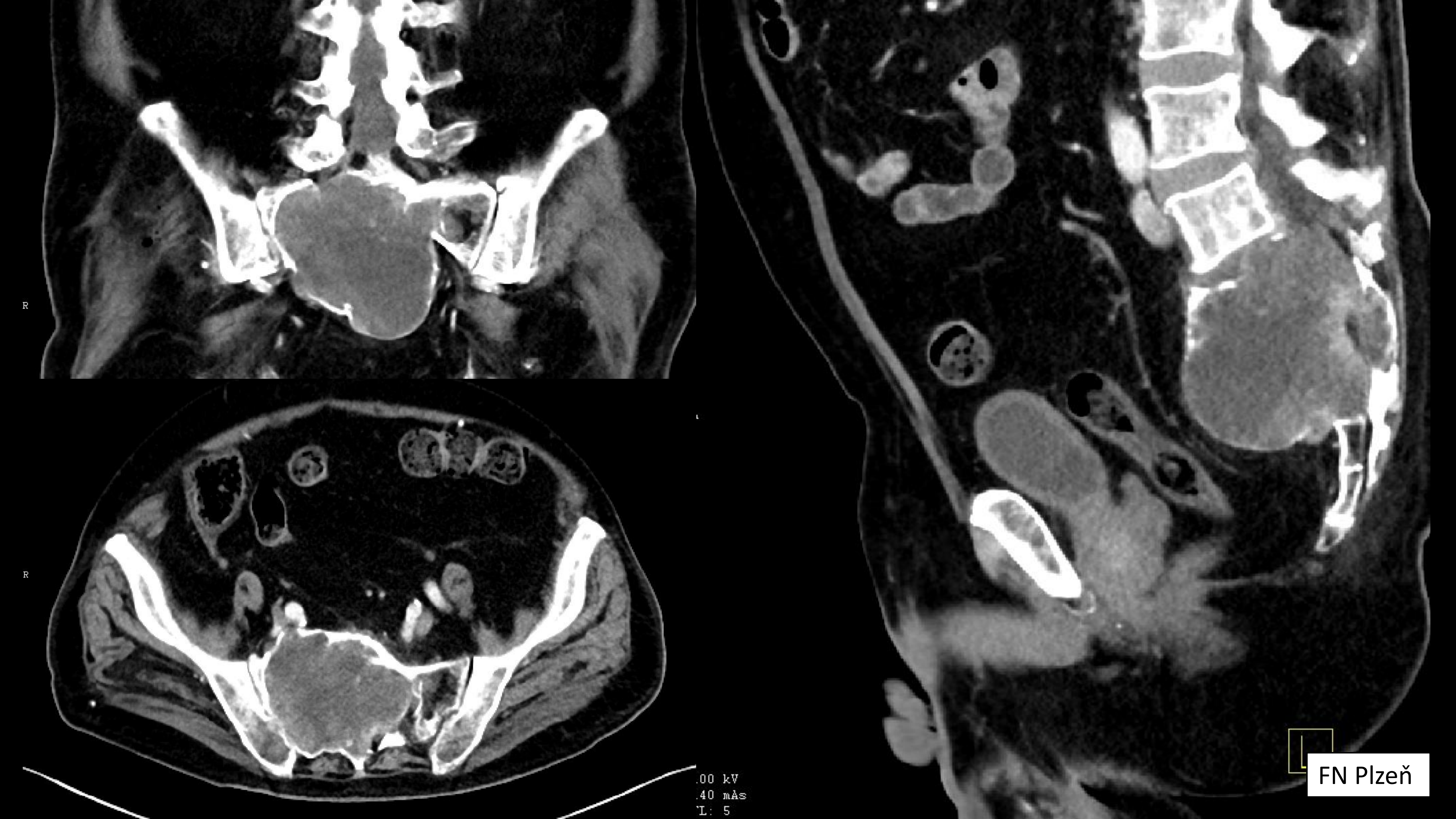
- Biopsia z oblasti S1
- Zaslané 2 väzivové častice rozmerov 23x10x6 mm a 6x3x3 mm

- MUDr. Šašková, FN Plzeň

- CT pánve a kyčleních kloubů:
- *Postkontrastně*

- **Solidní expanze sakra (ve výši S1 až S3)** s nehomogenním sycením při nekrotických okrscích tumorózních hmot. Proti PET/CT vyšetření 10.3.2010 je **nález v progresi**, při dnešní kontrole léze měří **108 x 80 x 63 mm** (na PET/CT v axiálním řezu 72 x 58 mm). Ušetřena je část massa lateralis sakra a kaudální část kosti (S4 a S5). Tumor má osteolytickou aktivitu, ventrální kortikalis kosti je místy zcela vymizelá, dorsálně slupkovitě zeslabená, nepravidelně rozrušená. Tumor dosahuje k oběma SI kloubům (více vpravo) a nově způsobuje i osteolýzu těla obratle **L5 dorsolaterálně** vpravo. Tumor stenozuje až okluduje i canalis sacralis.
- Jiné patologické změny nezjištěny.

- Závěr: Progrese velikosti objemné solidní osteolytické expanze sakra. Tumor zasahuje k oběma SI kloubům a nově infiltruje i tělo obratle L5. Stenóza až okluze canalis sacralis tumorem. Patologický proces je omezen na popisovanou lokalitu, neprokazuji známky generalizace v rozsahu vyšetření.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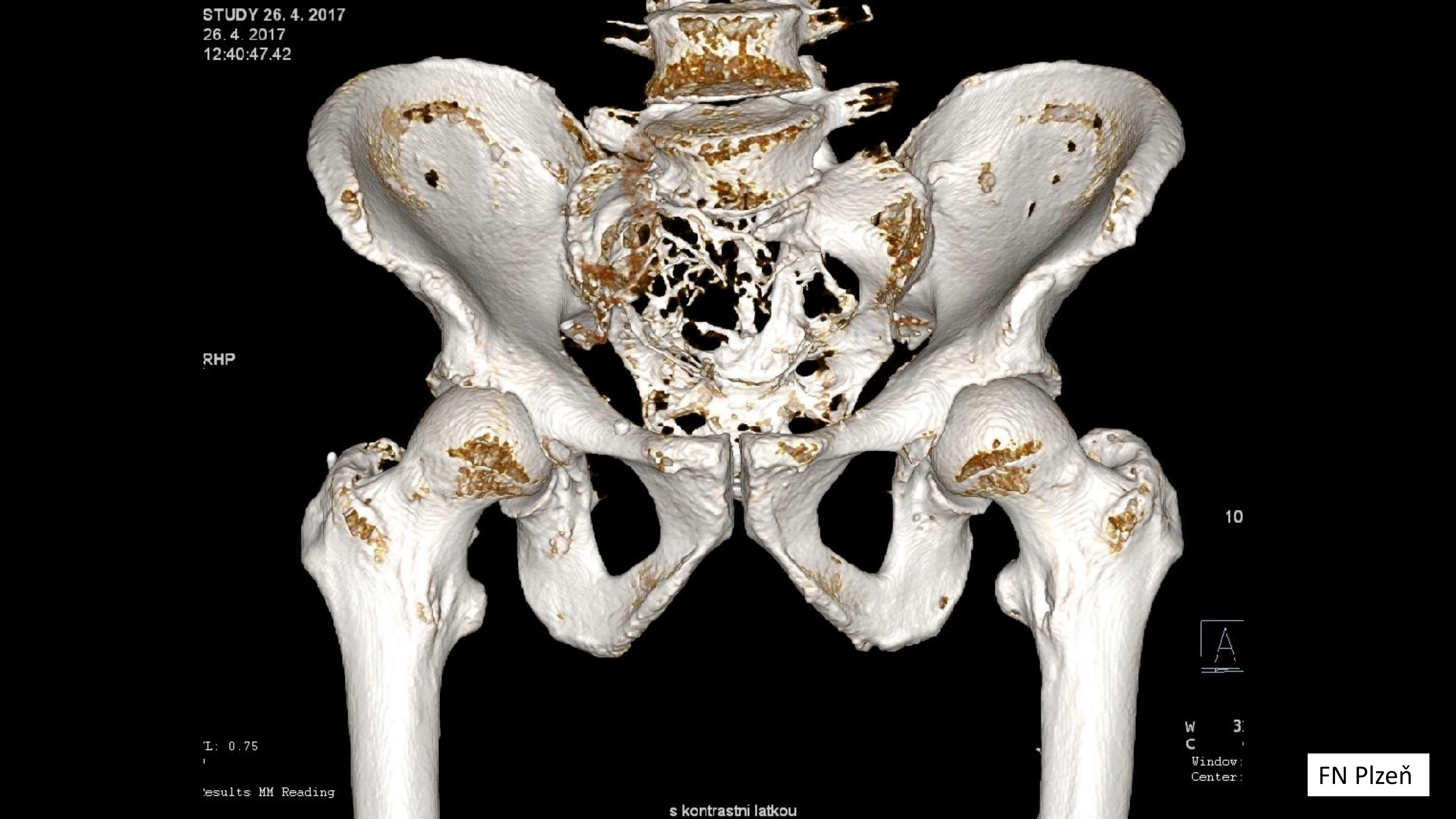
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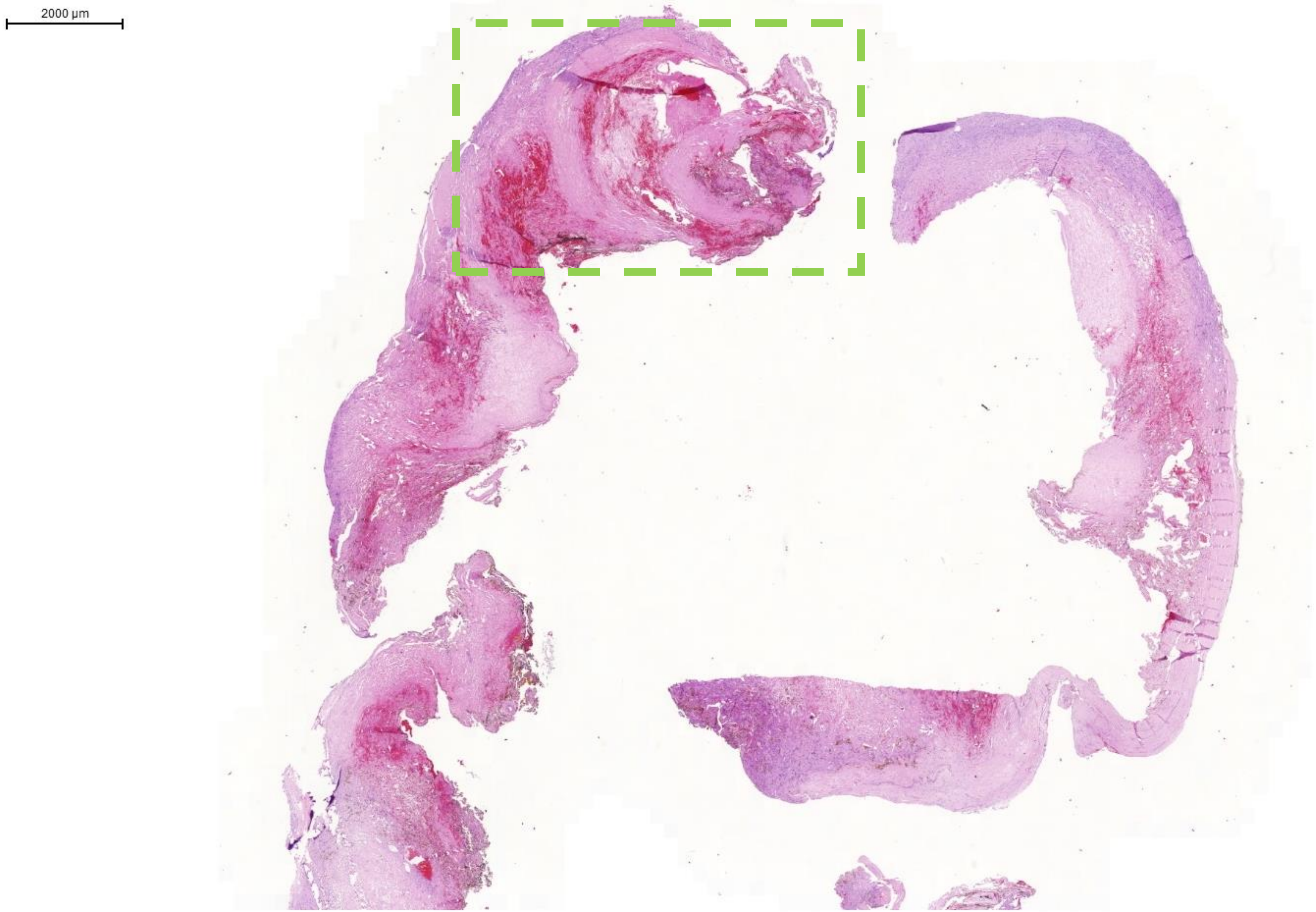
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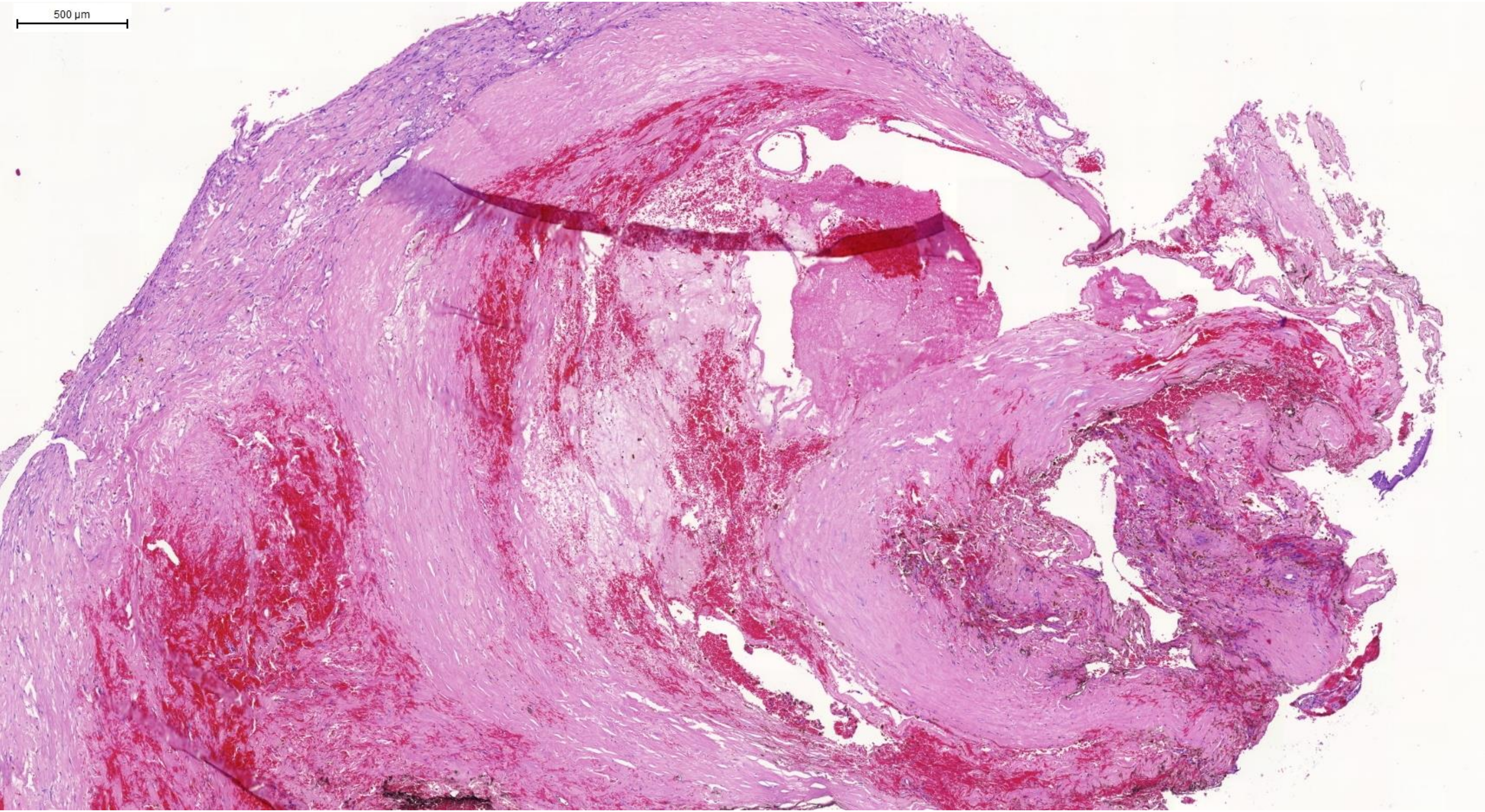
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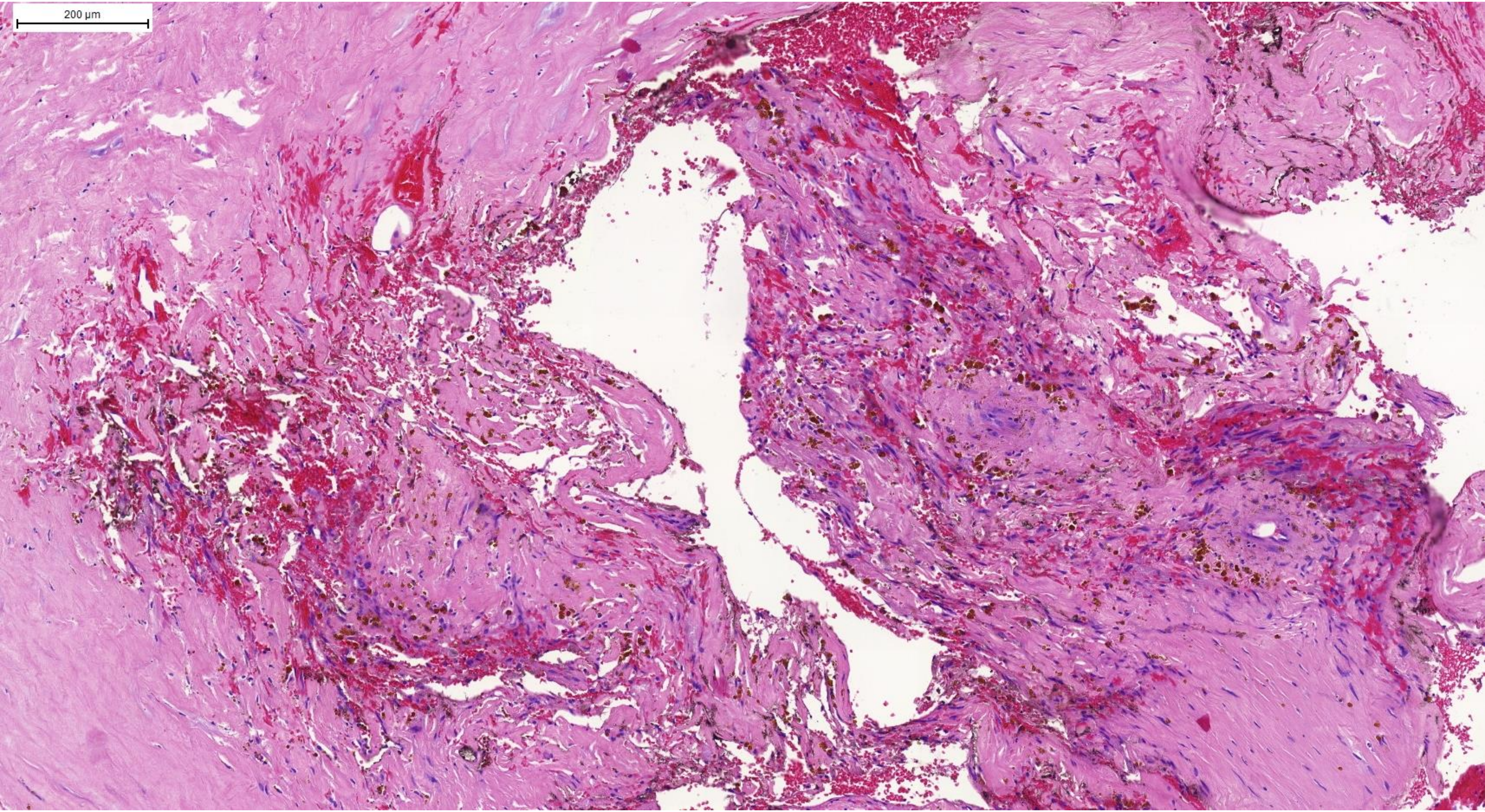
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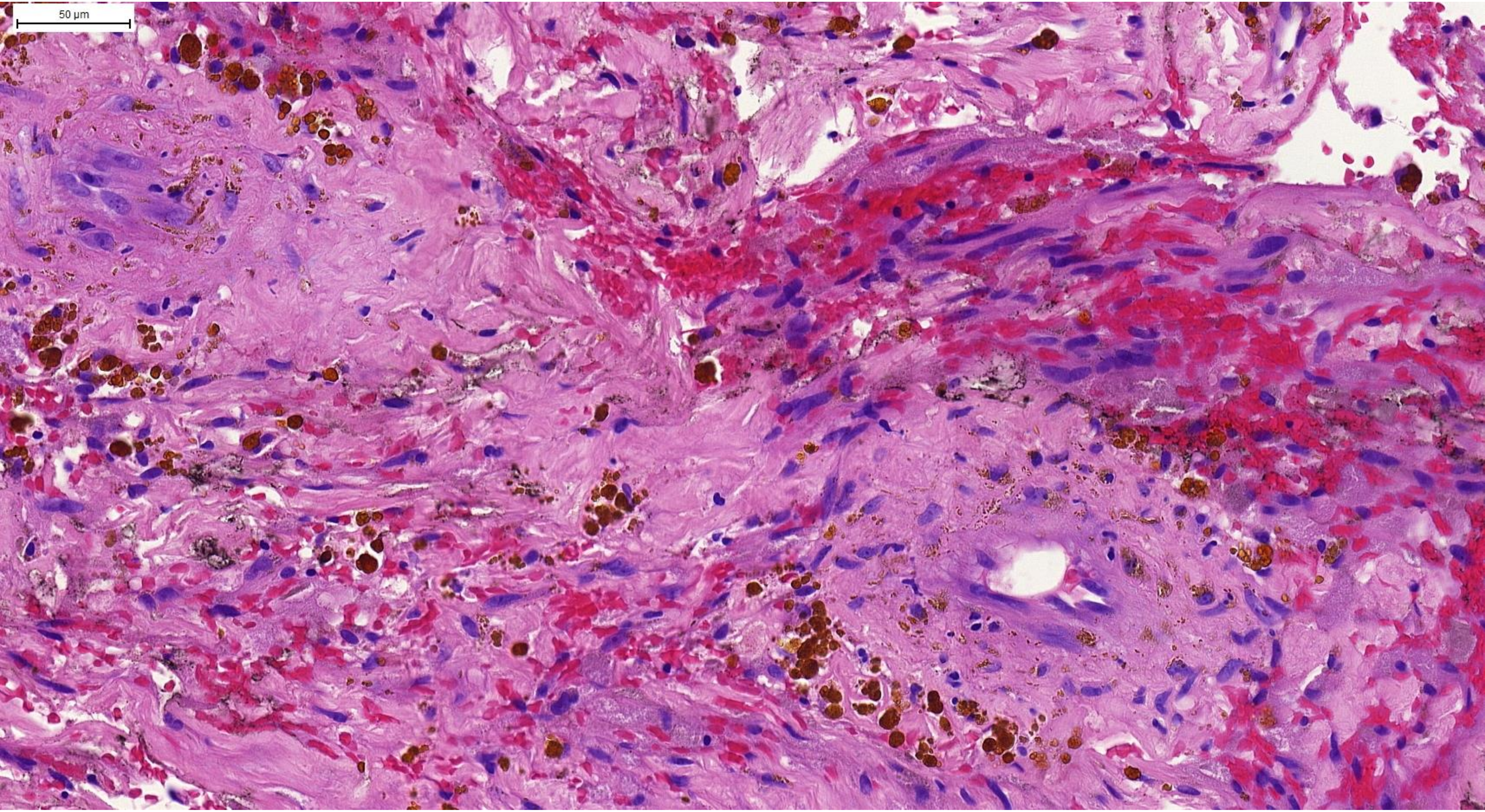
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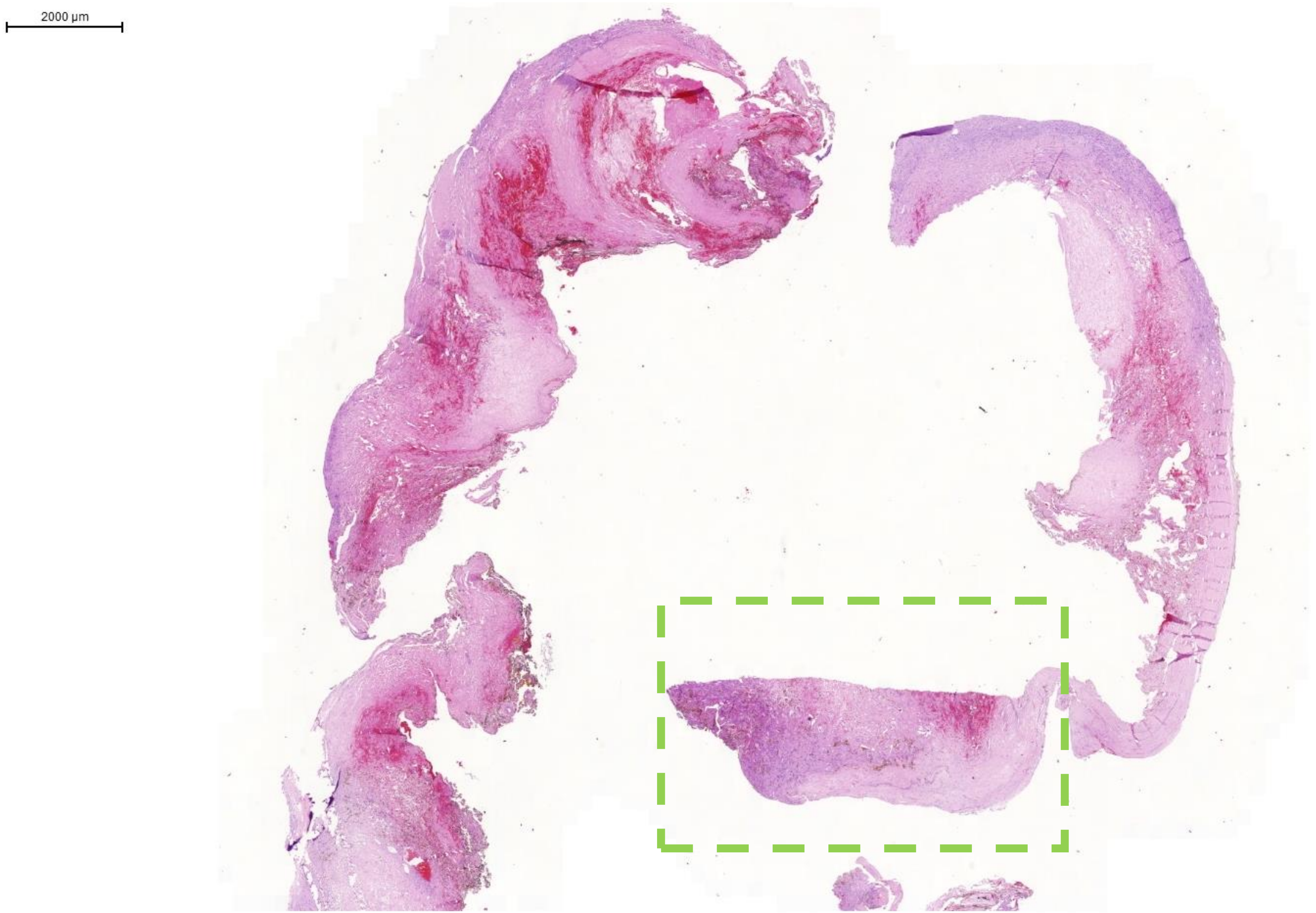
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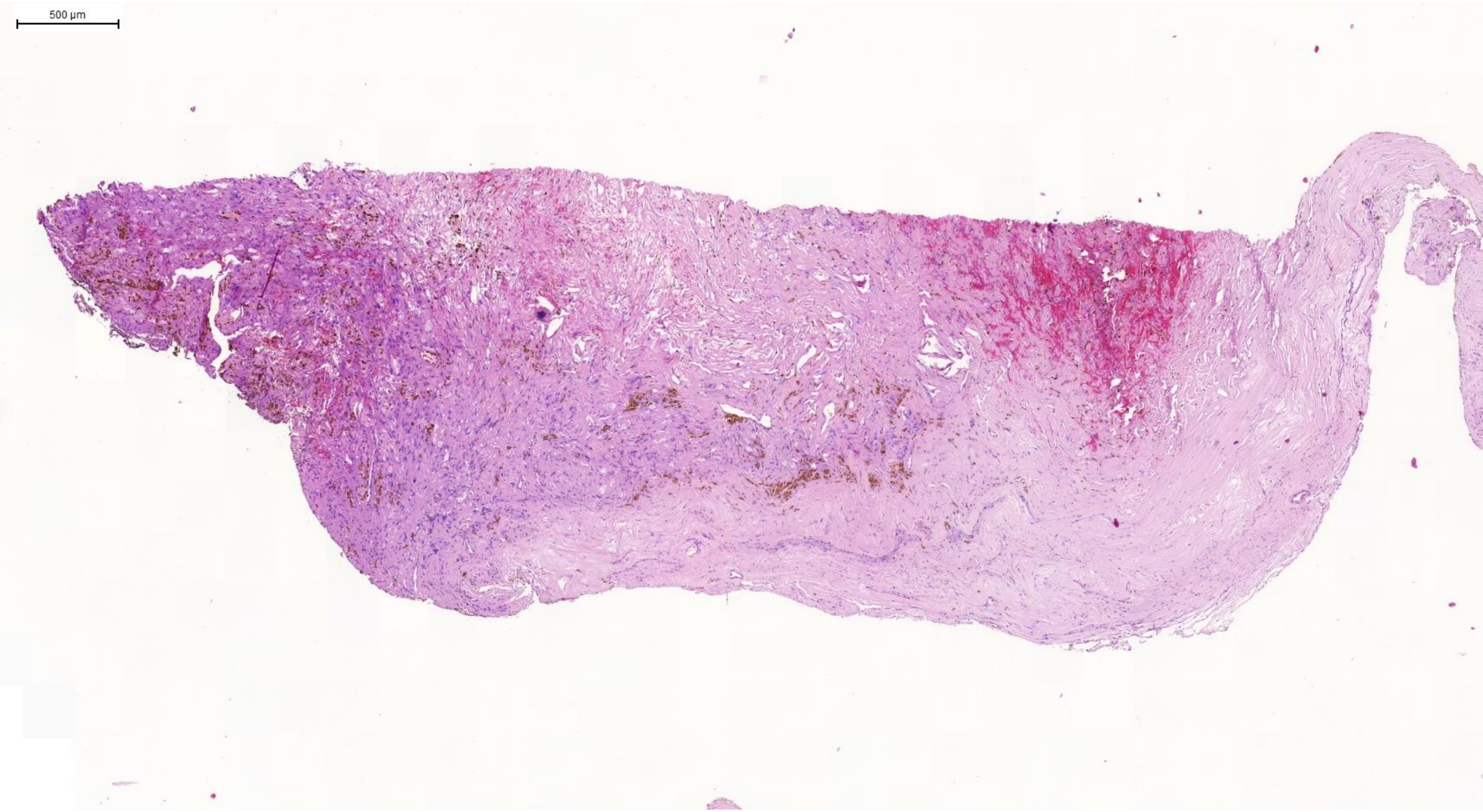
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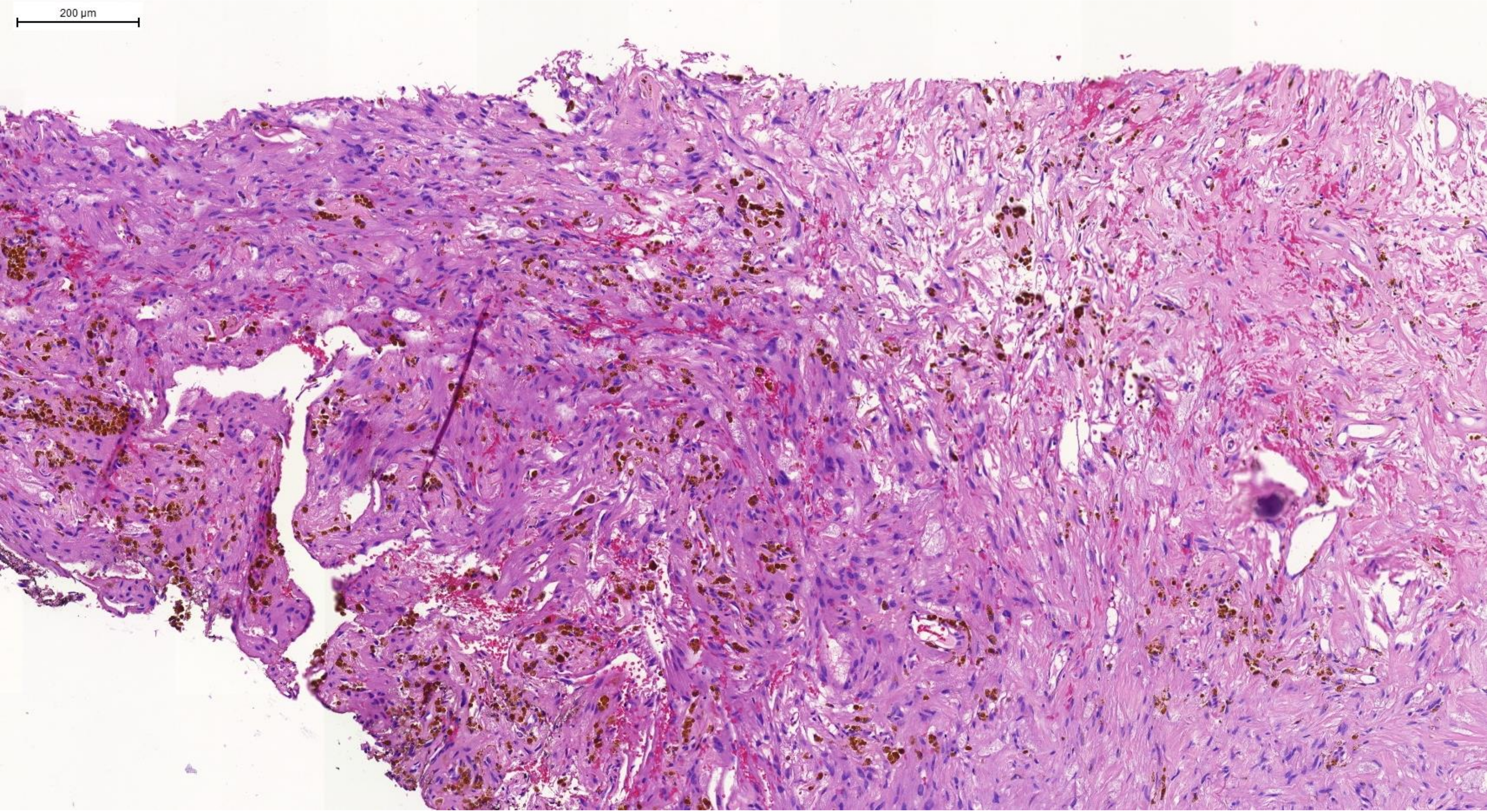
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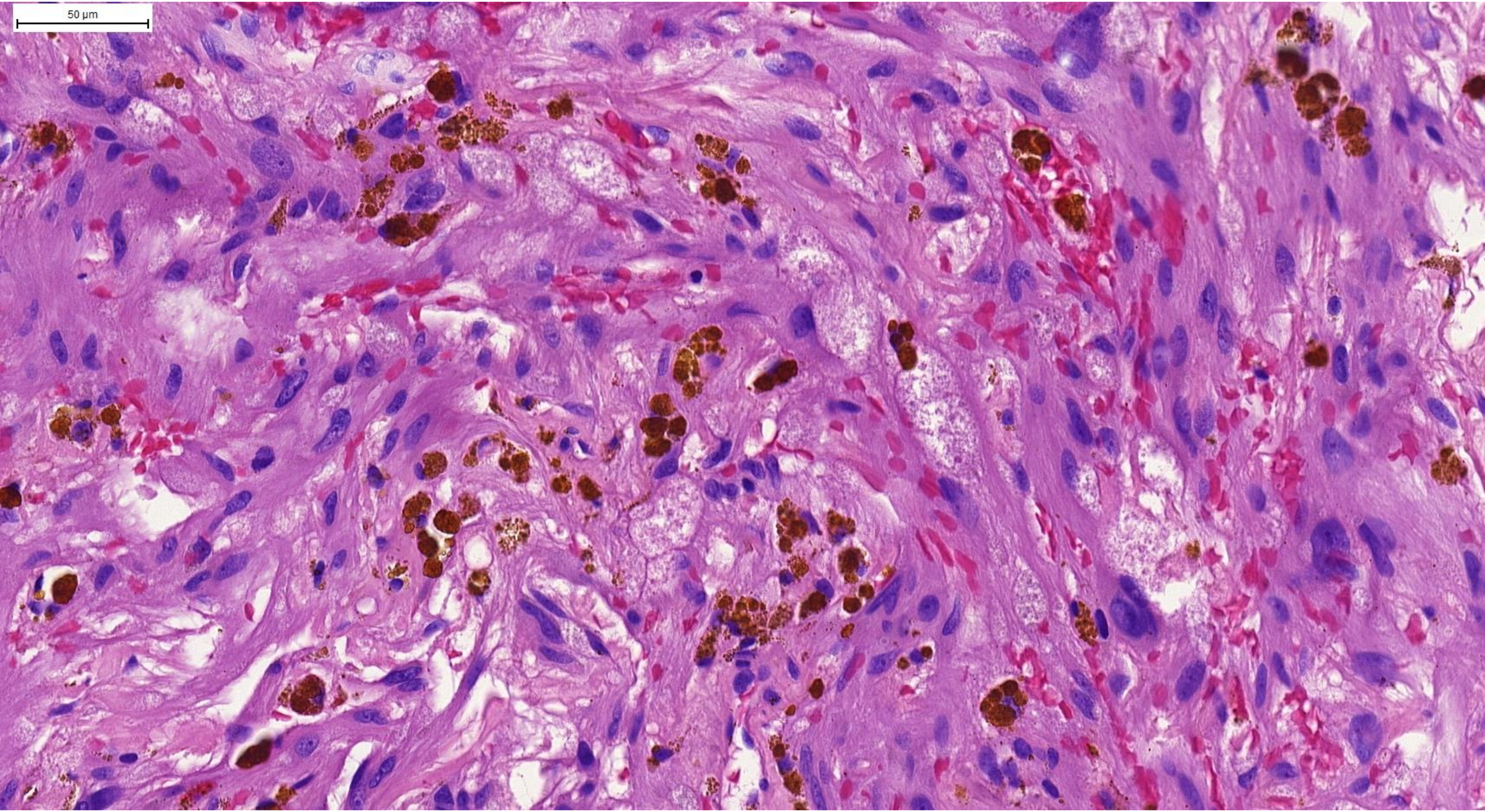
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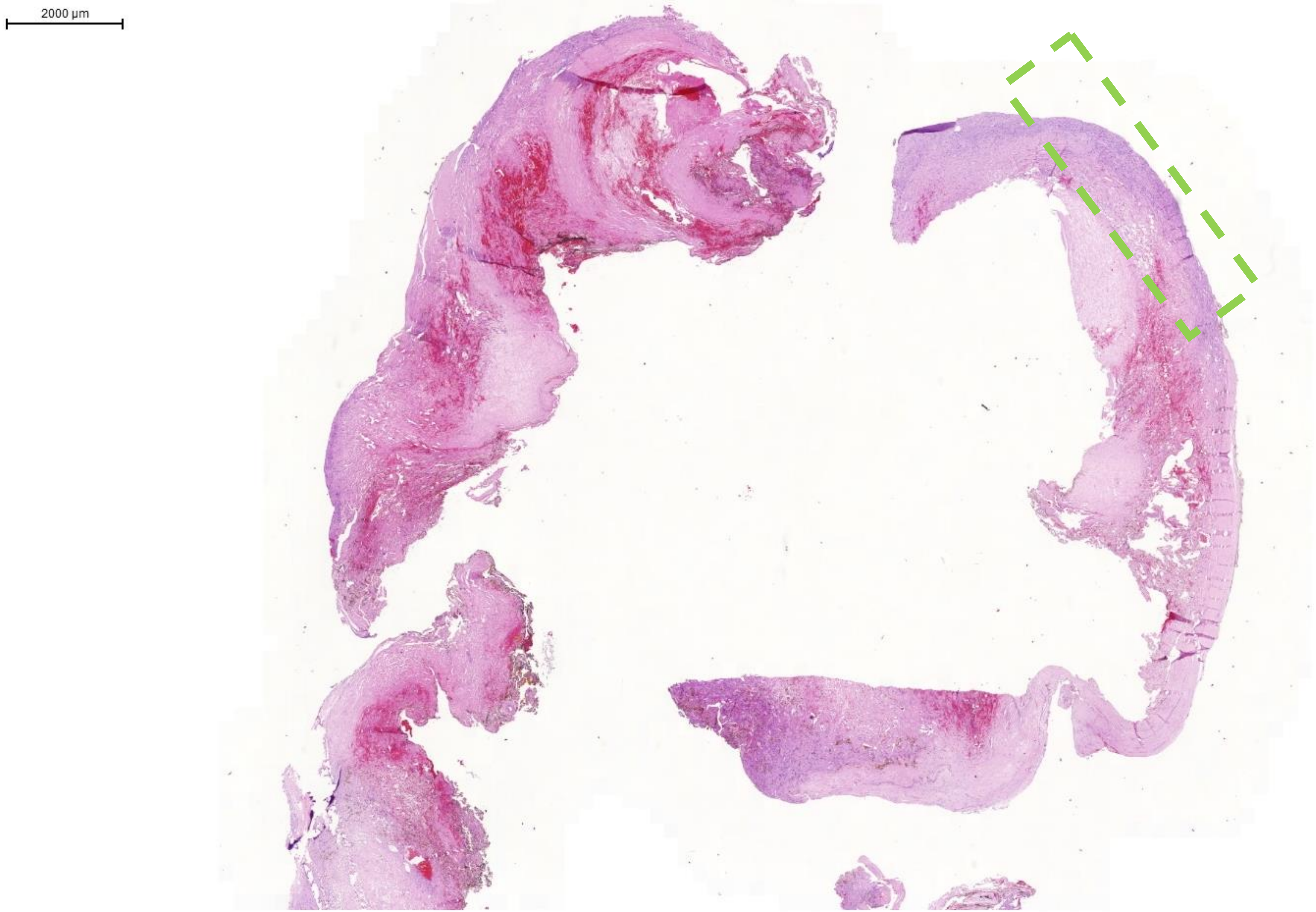

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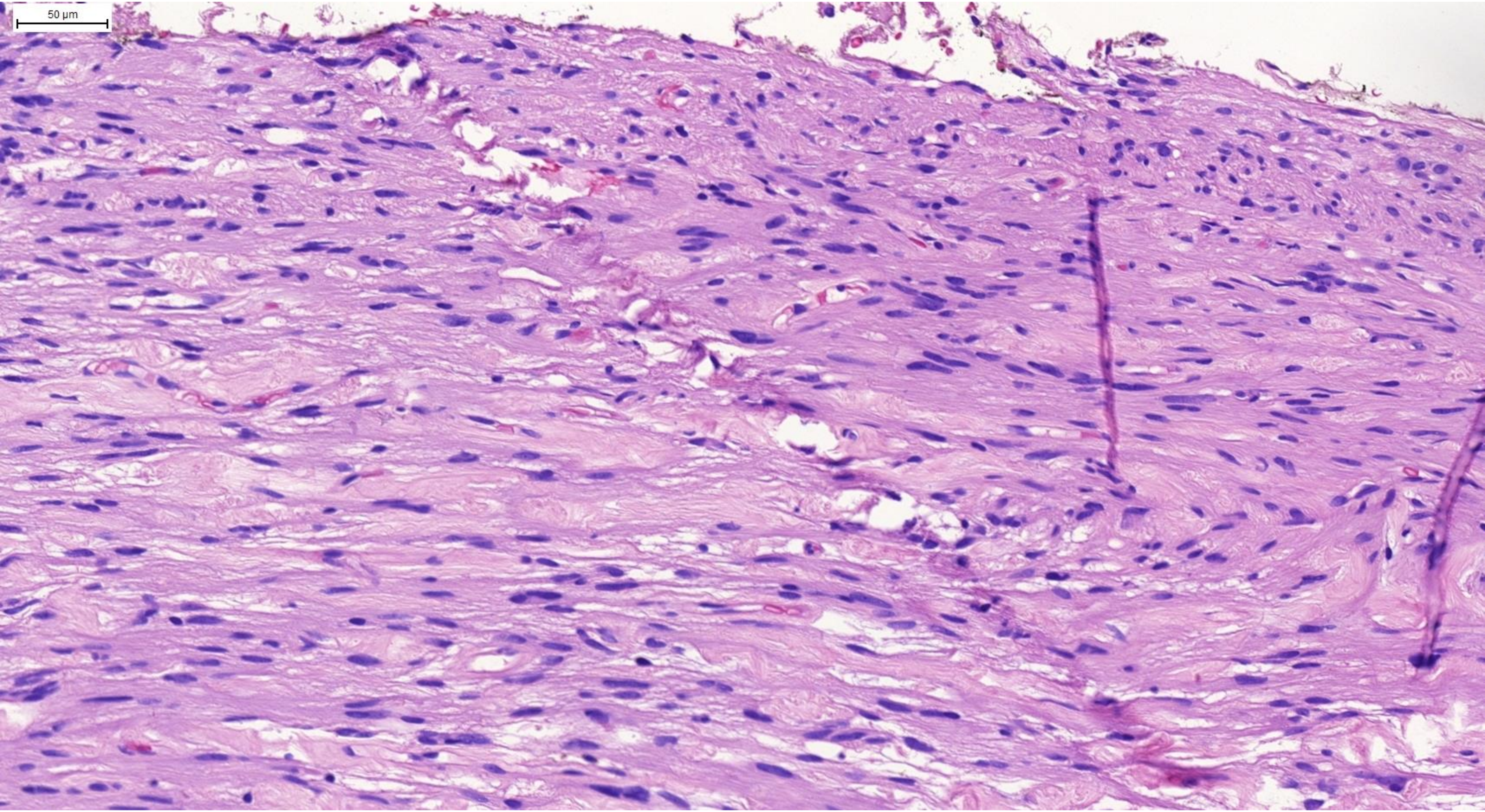
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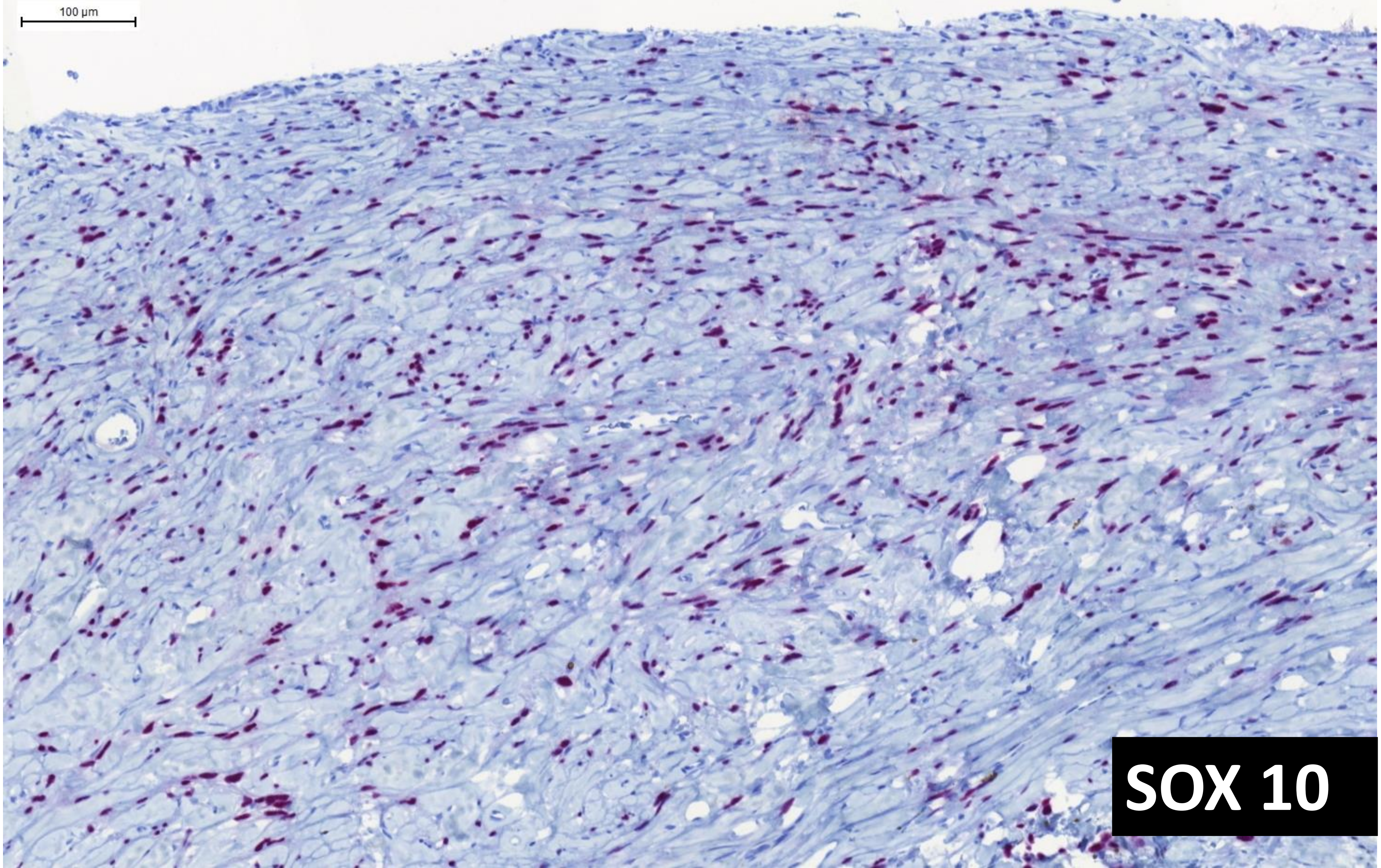
DIAGNÓZA?

Tip na 1 imuno?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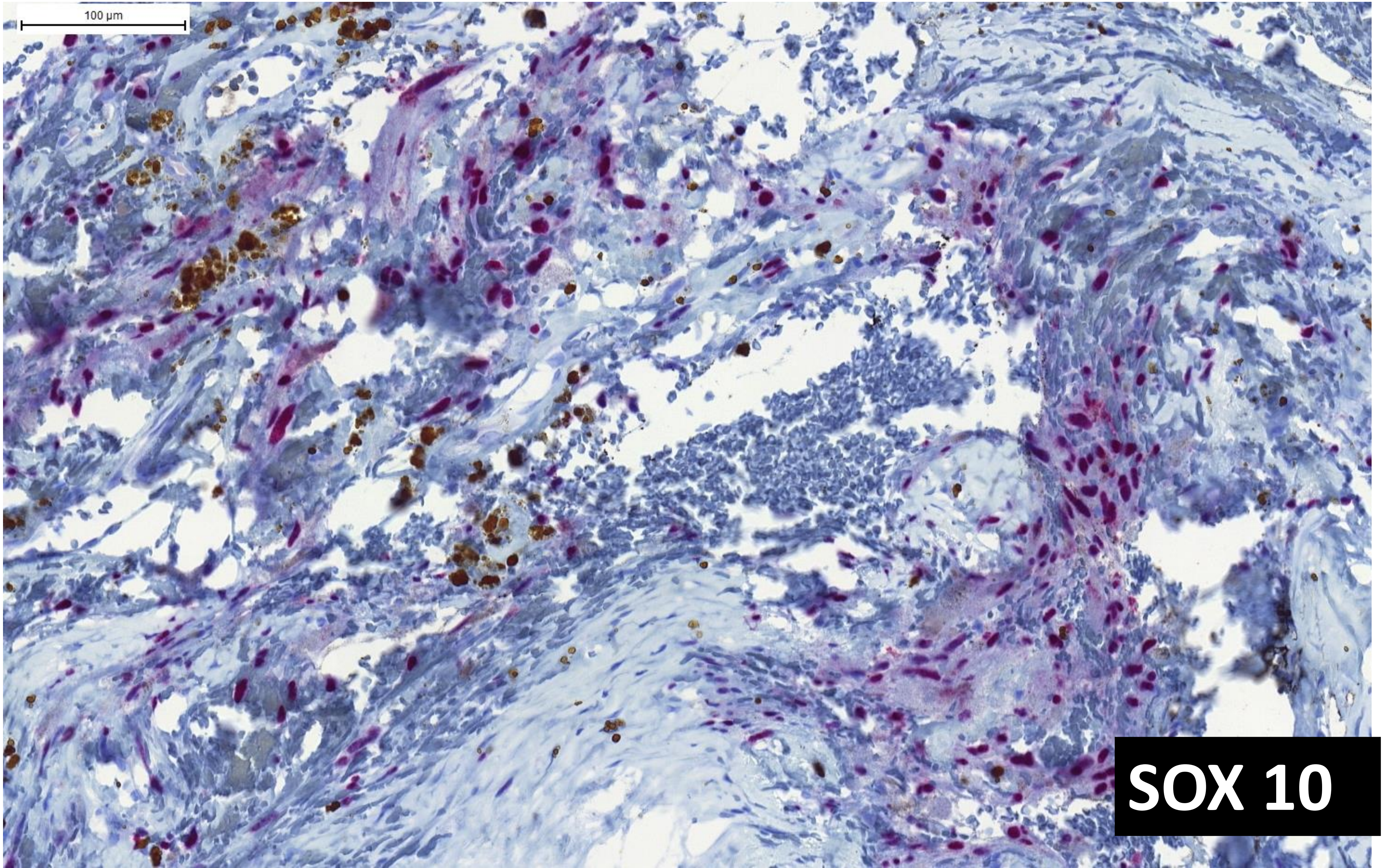
SOX 10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SOX 10

Imunofenotyp

- S100 a SOX10 +
- SMA, ERG, CD34, EMA, PgR, AE1/AE3 –
- Mib-1 ~ 1%

Sakrálny schwannóm

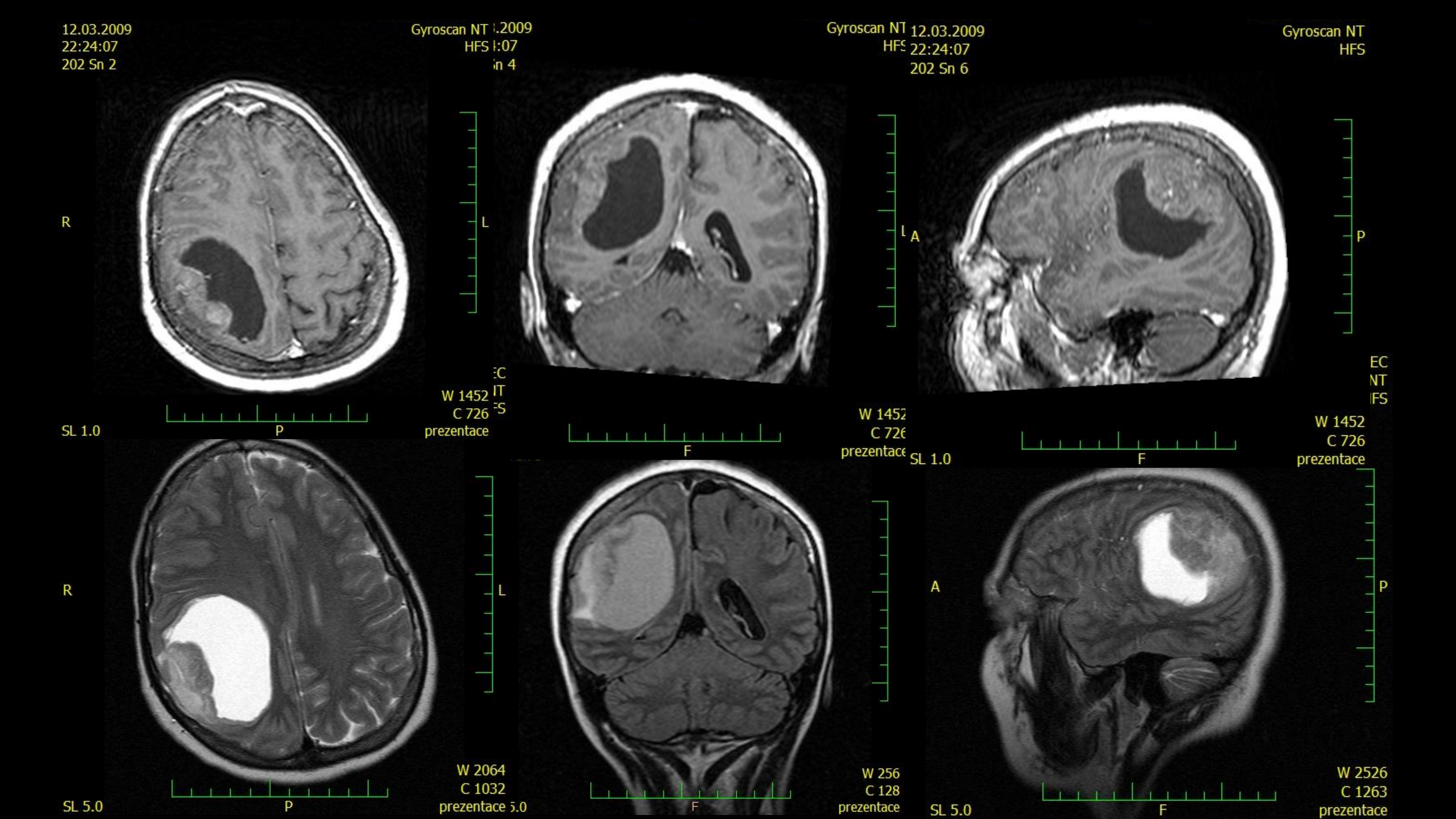
- Schwannómy sú jedným z najčastejších tumorov v oblasti miechy/miechového kanála
- Schwannóm os sacrum je však relatívne vzácny tumor, tvorí ~ 1-5% spinálnych schwannómov a menej ako 0,2% nádorov kostí
- Často asymptomatický tumor, ktorý sa prejaví až v neskoršom štádiu
  - „giant sacral schwannoma“ - s výrazným radiologickým nálezom
- Resekcia je komplikovaná anatomickými pomermi, ale možná

Prípad č. 2

- 44 ročná žena

- 9 rokov od operácie nádoru mozgu (lokalita?)
- je v dobrom klinickom stave, bez známok recidívy

- Na žiadosť klinika revízia pôvodného nálezu (prípad láskavo poskytol Doc.MUDr. Tomáš Jirásek, Liberec)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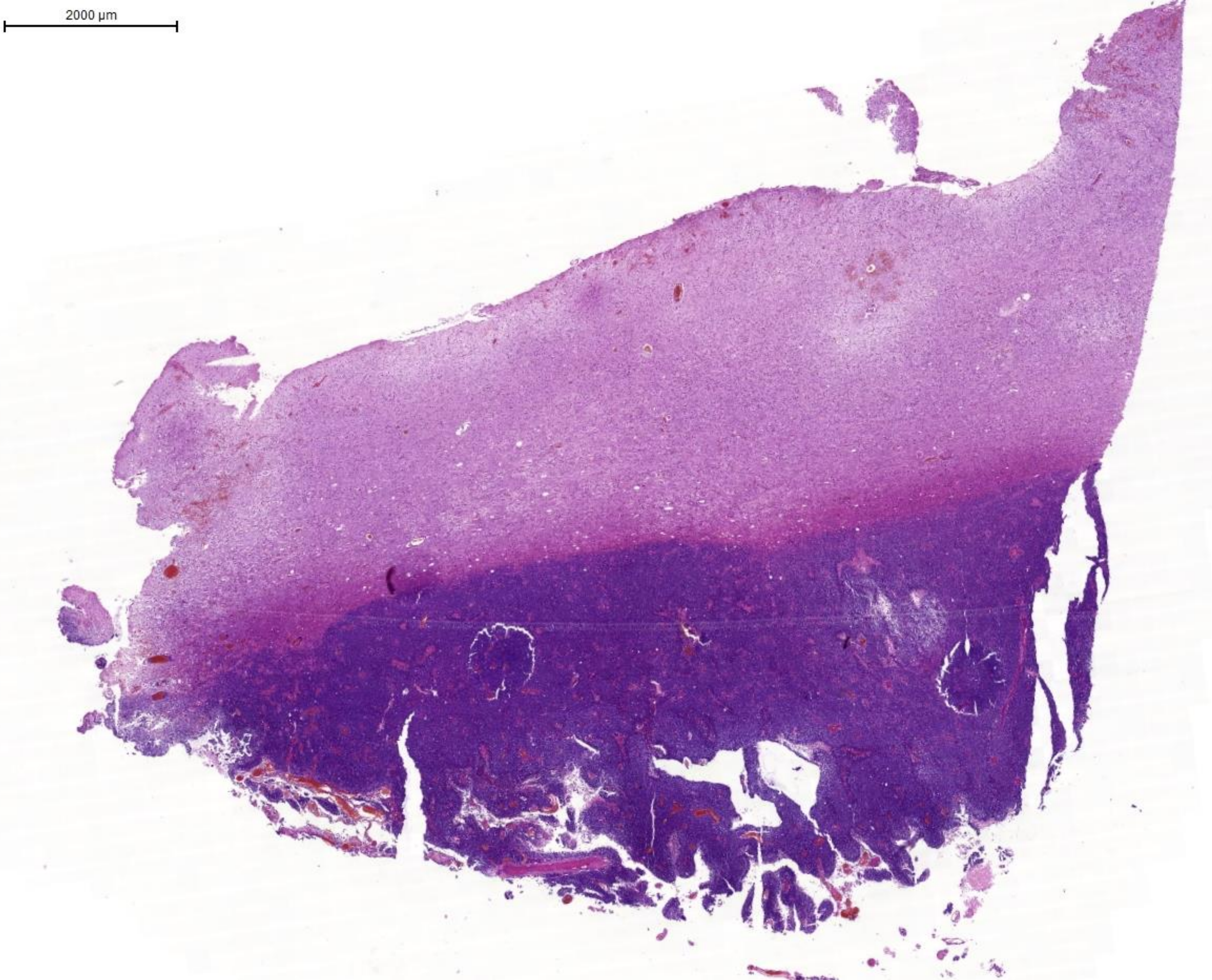
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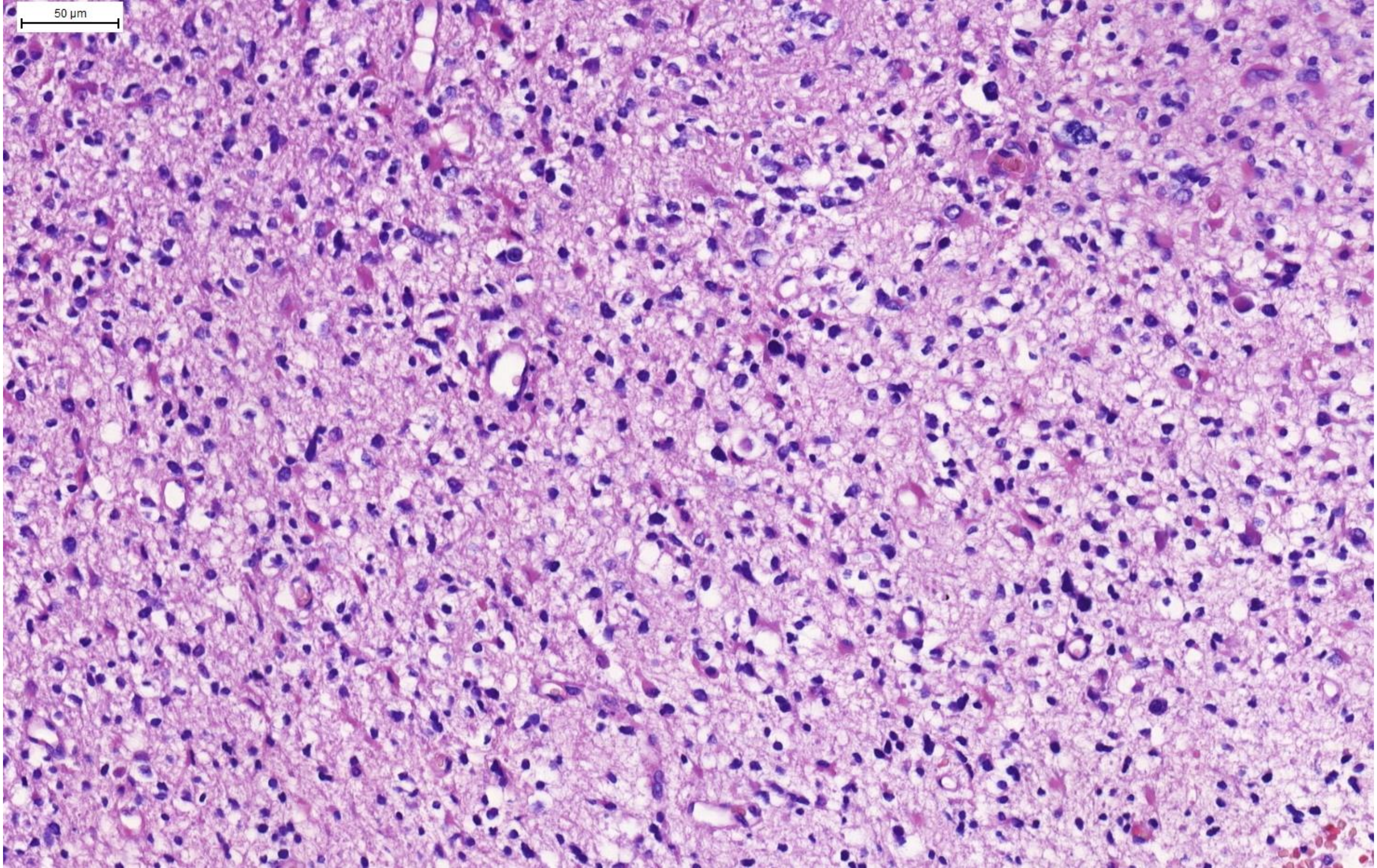
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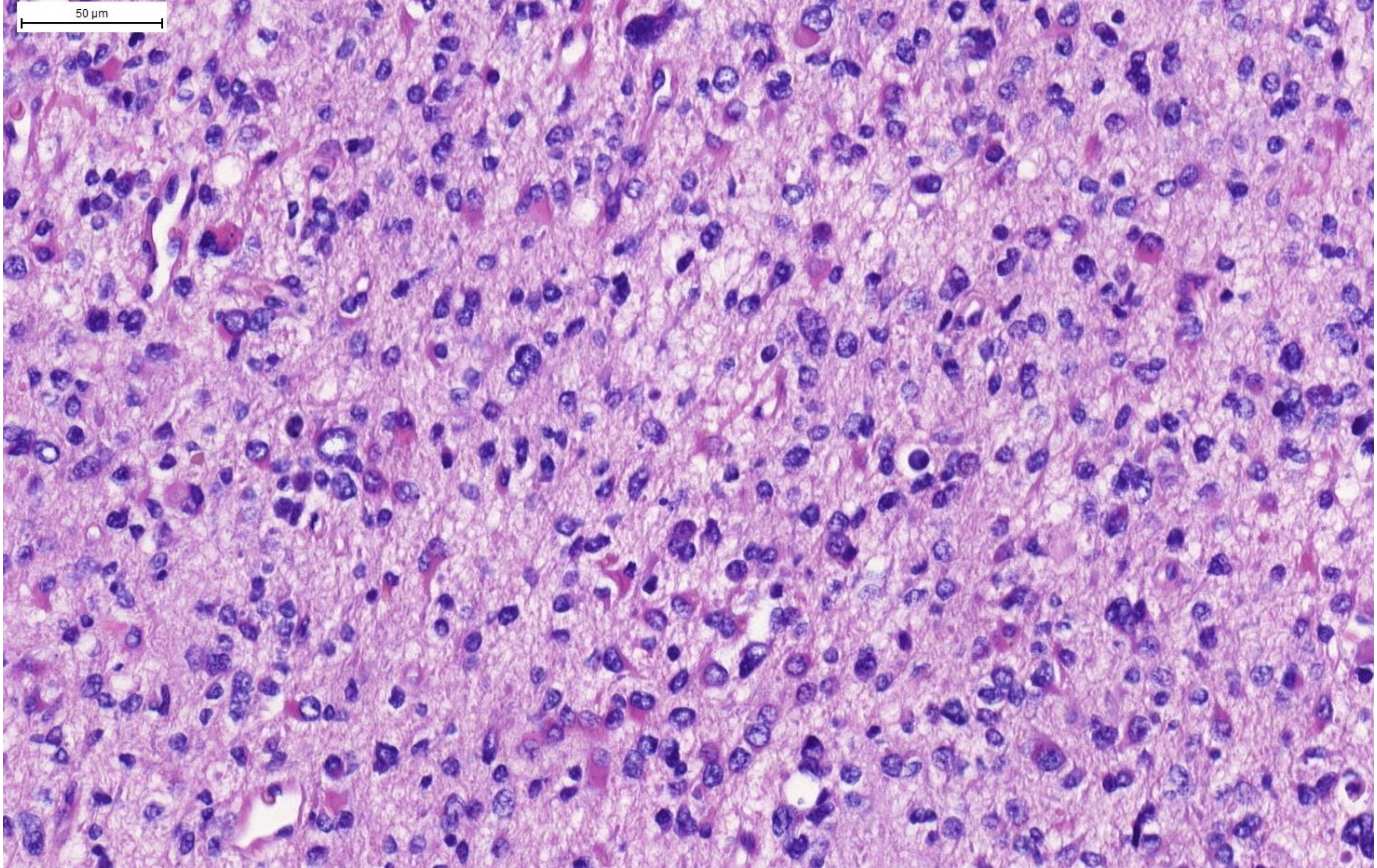
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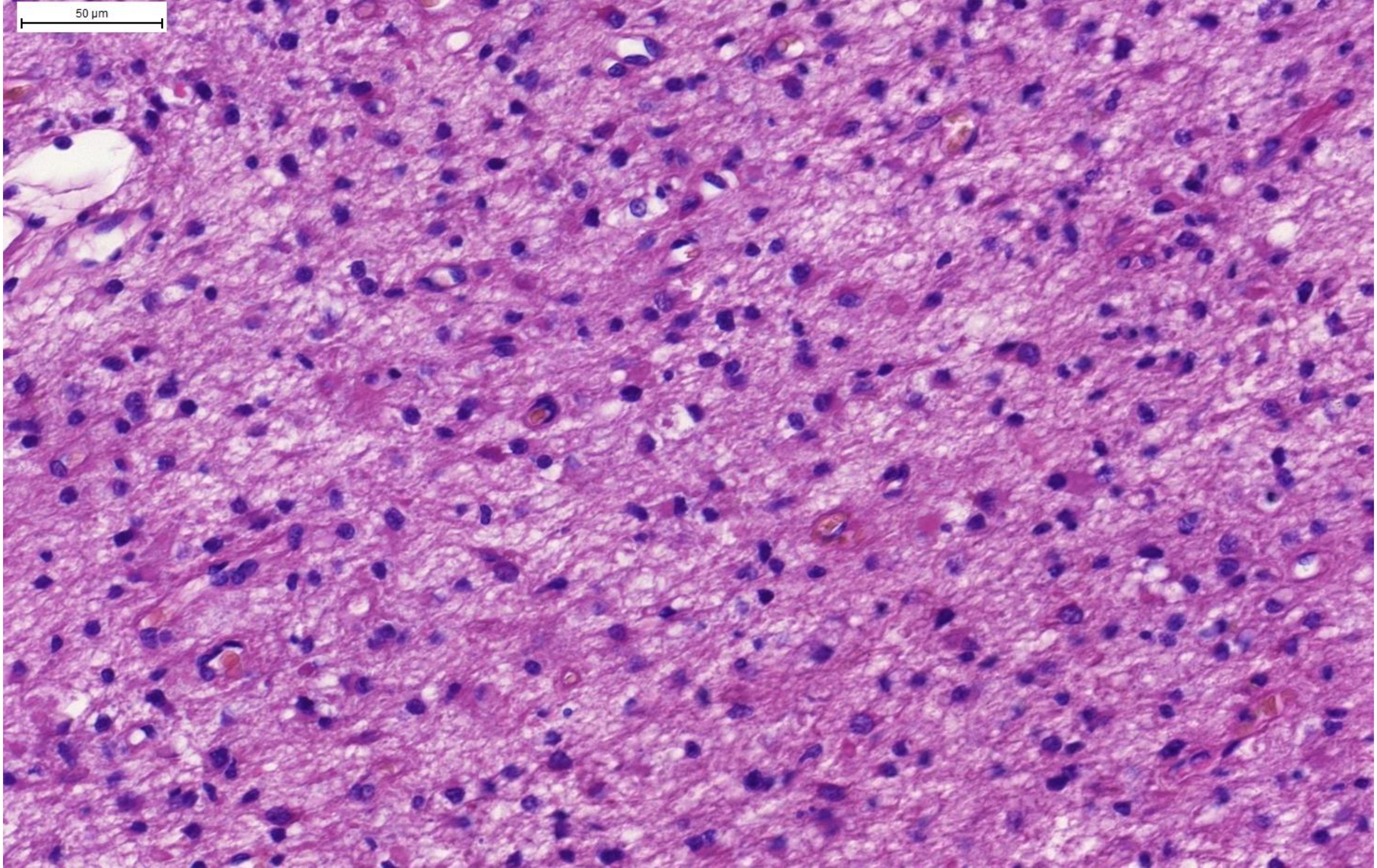
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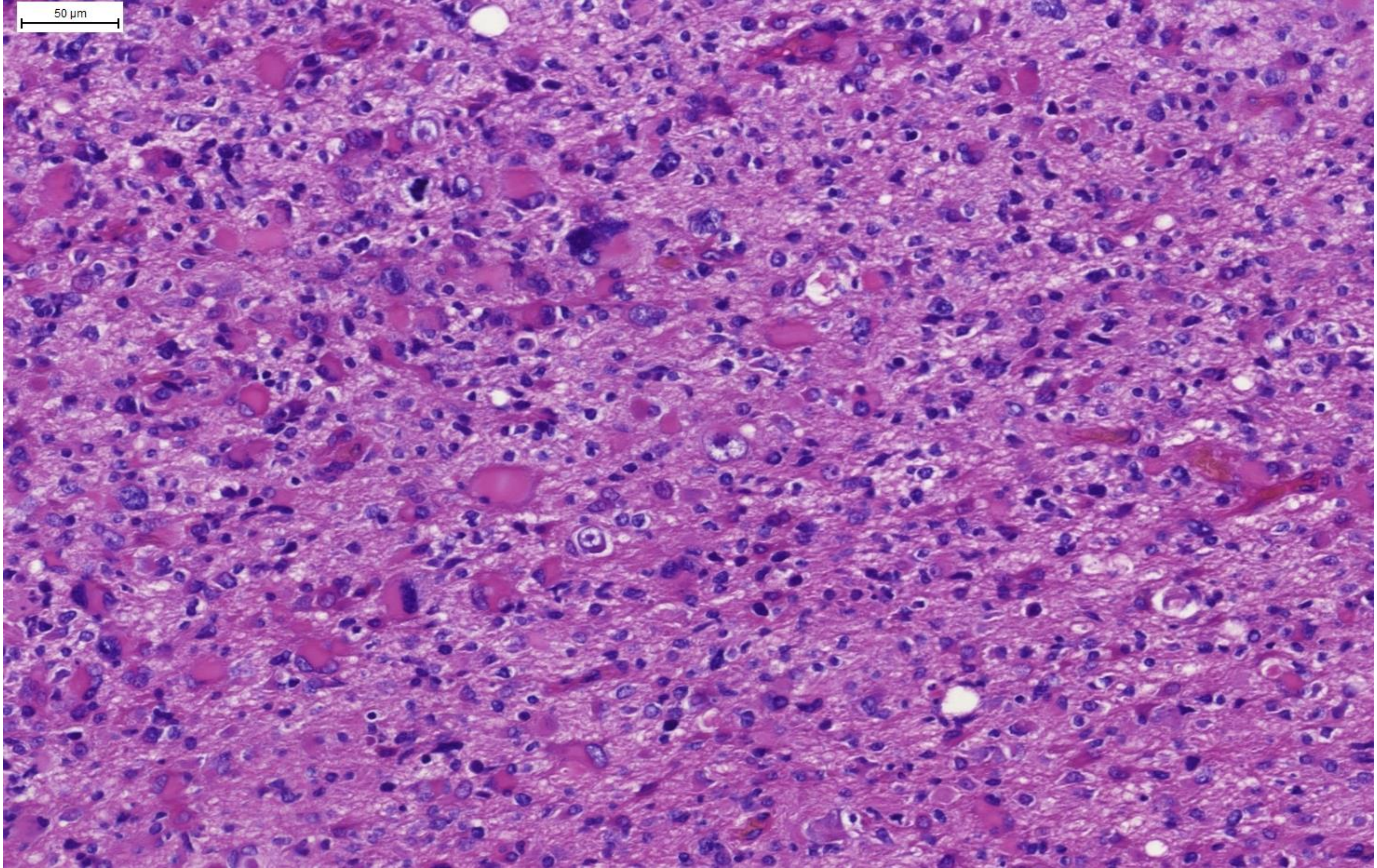
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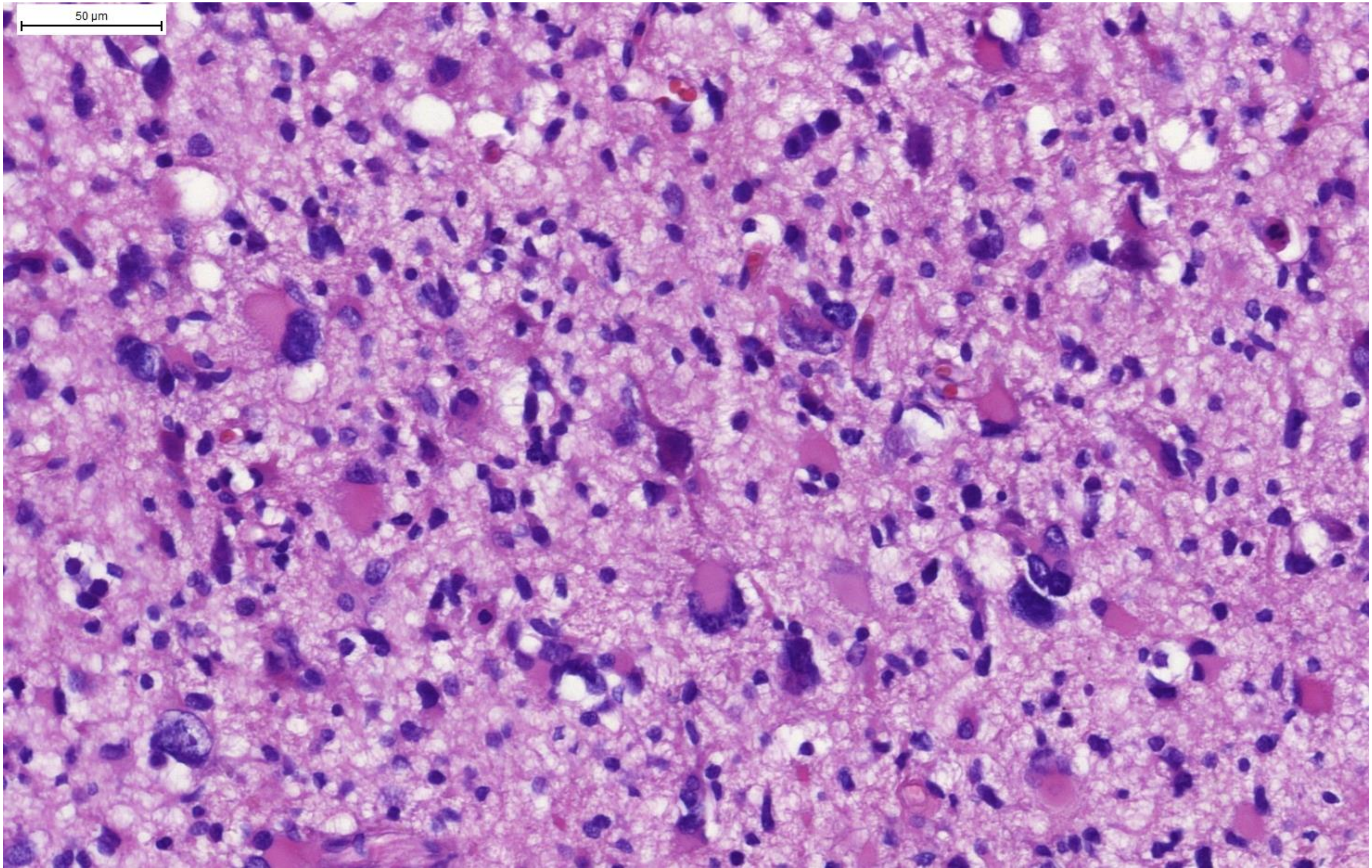
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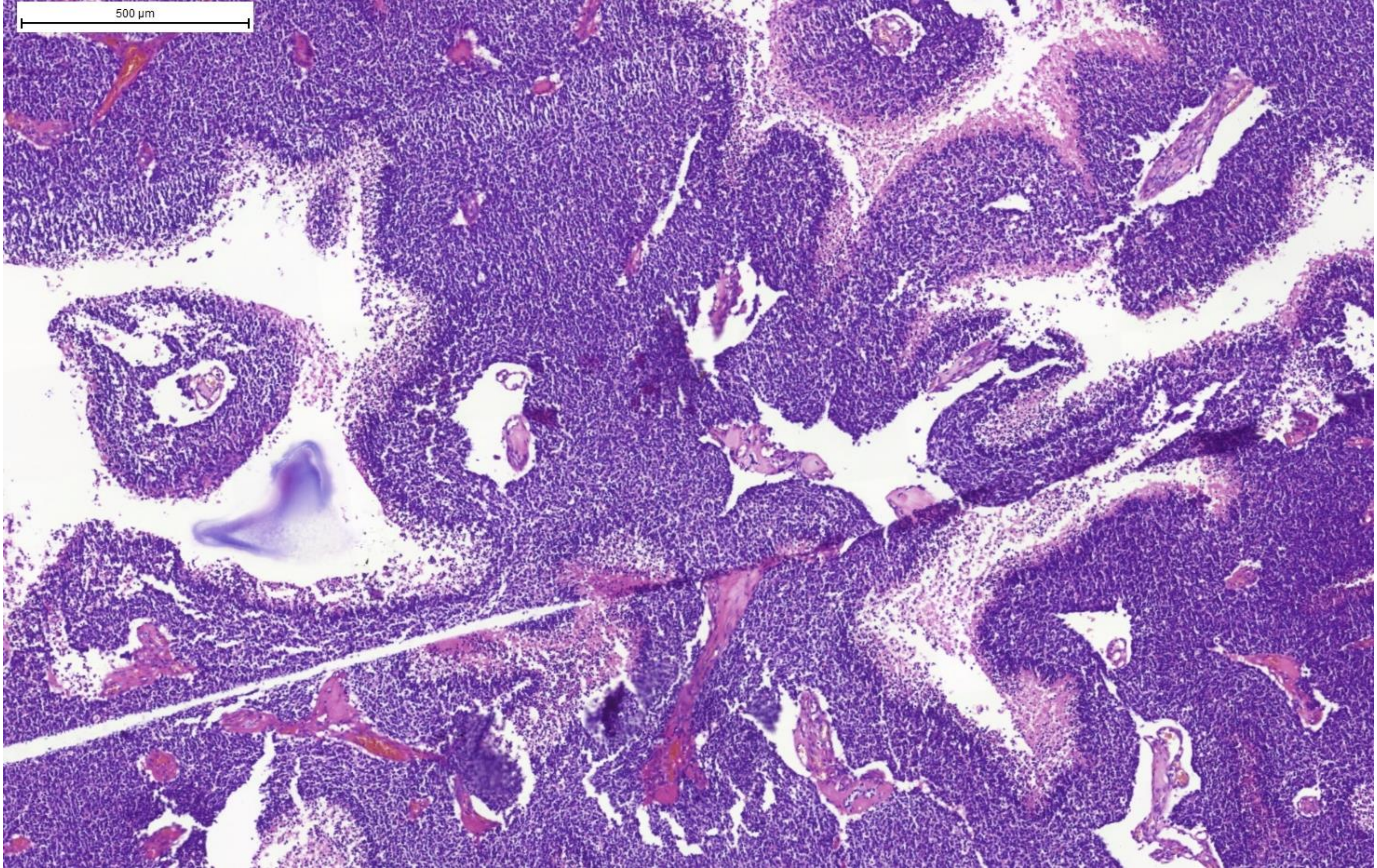
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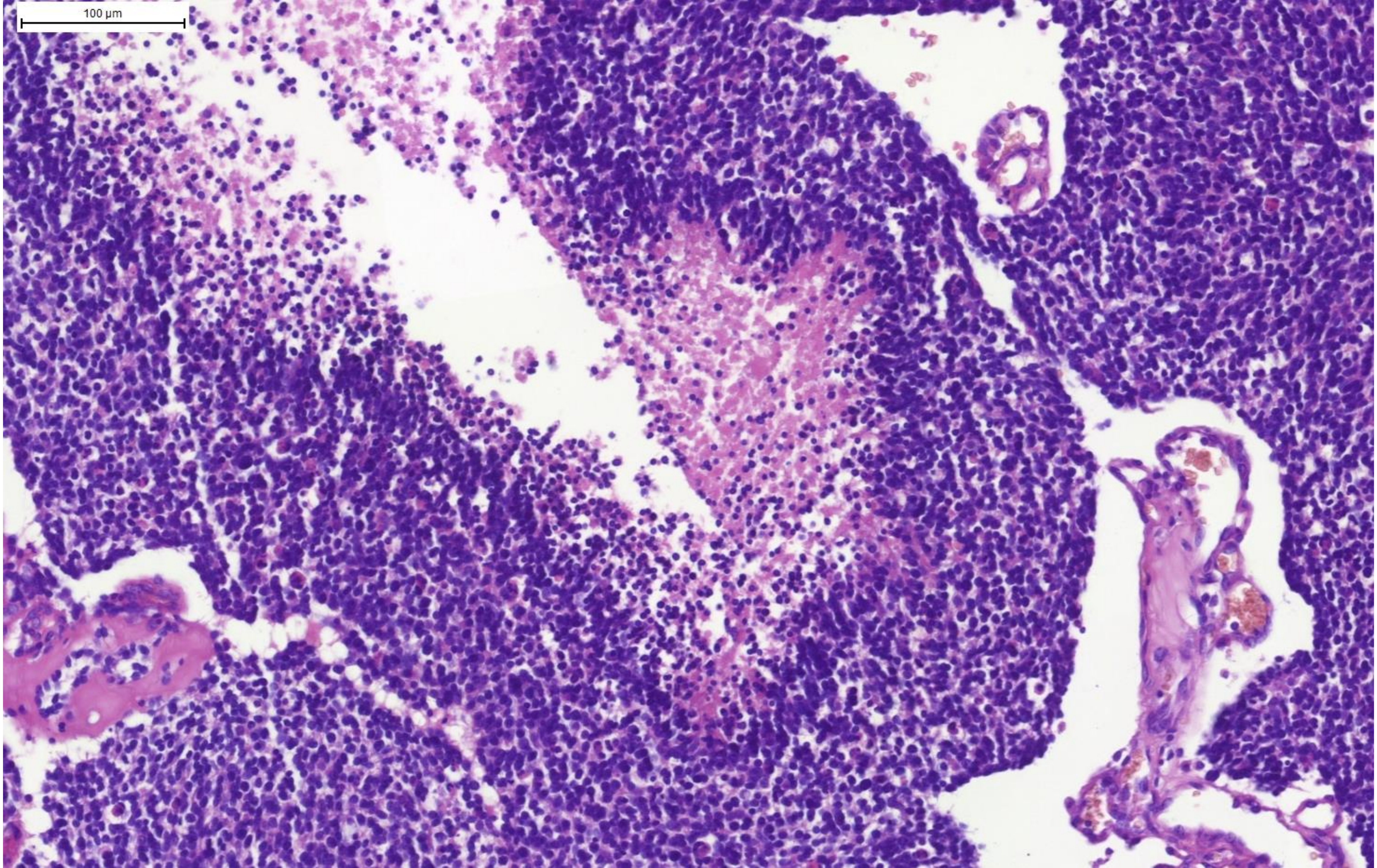
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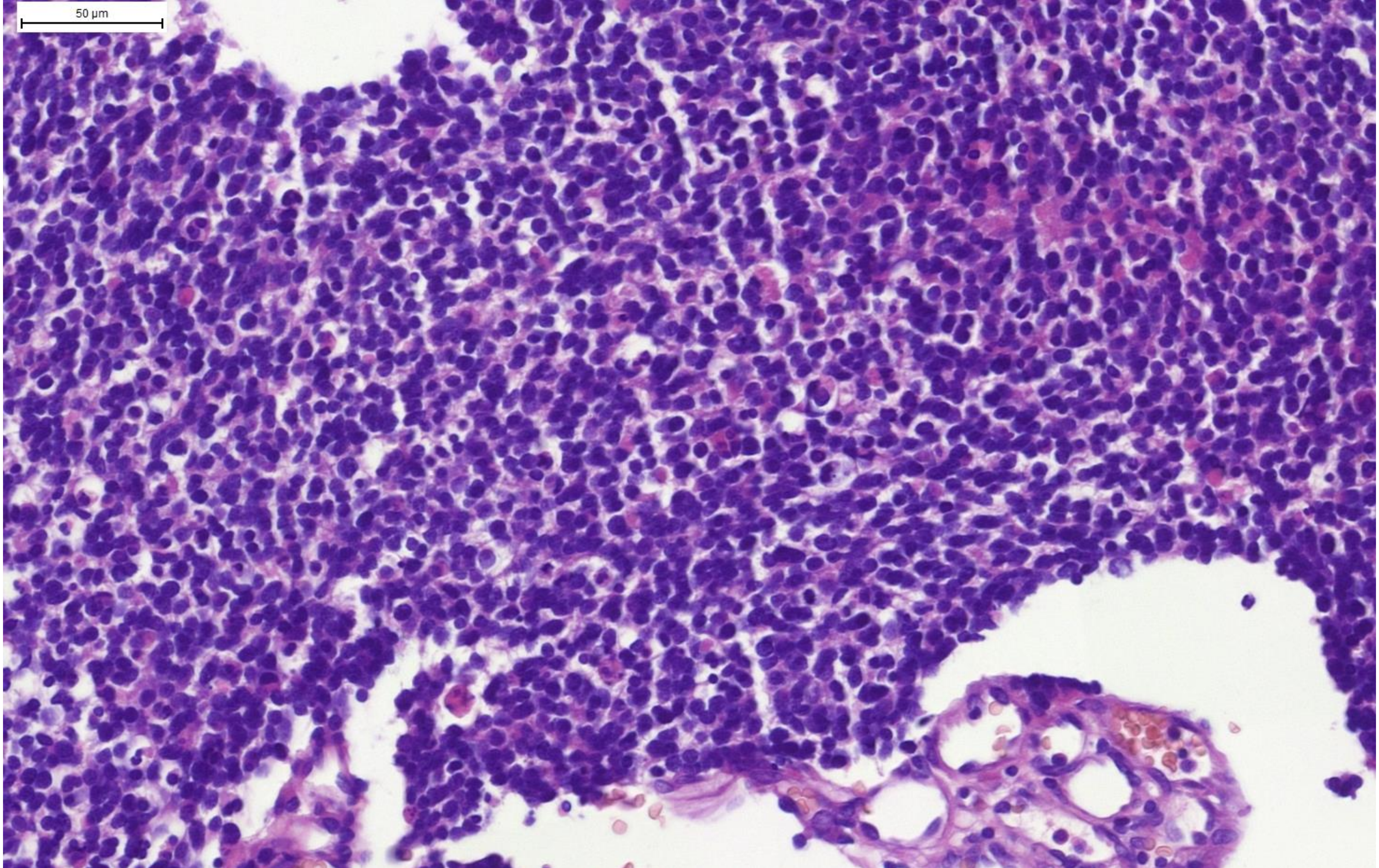
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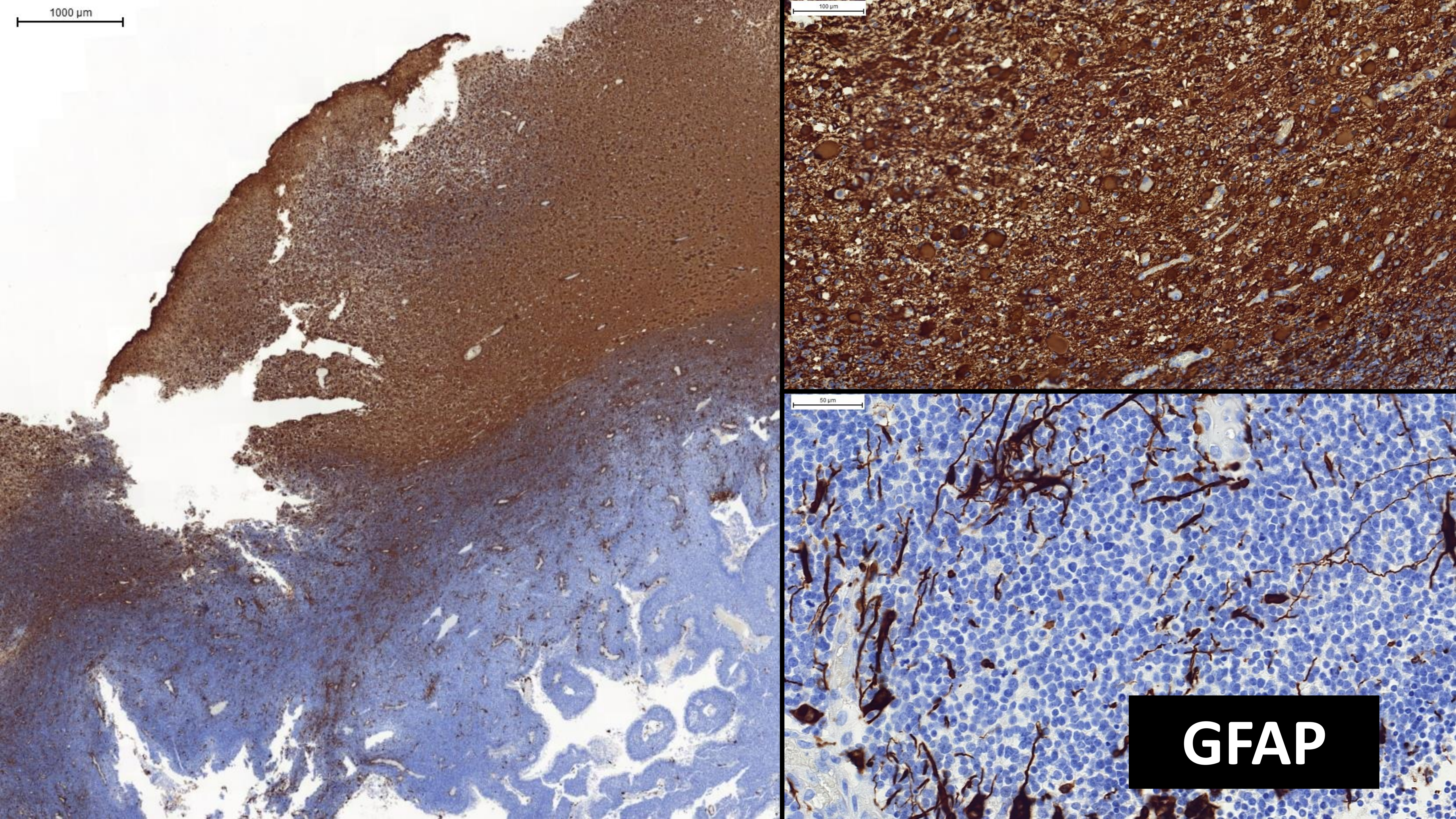
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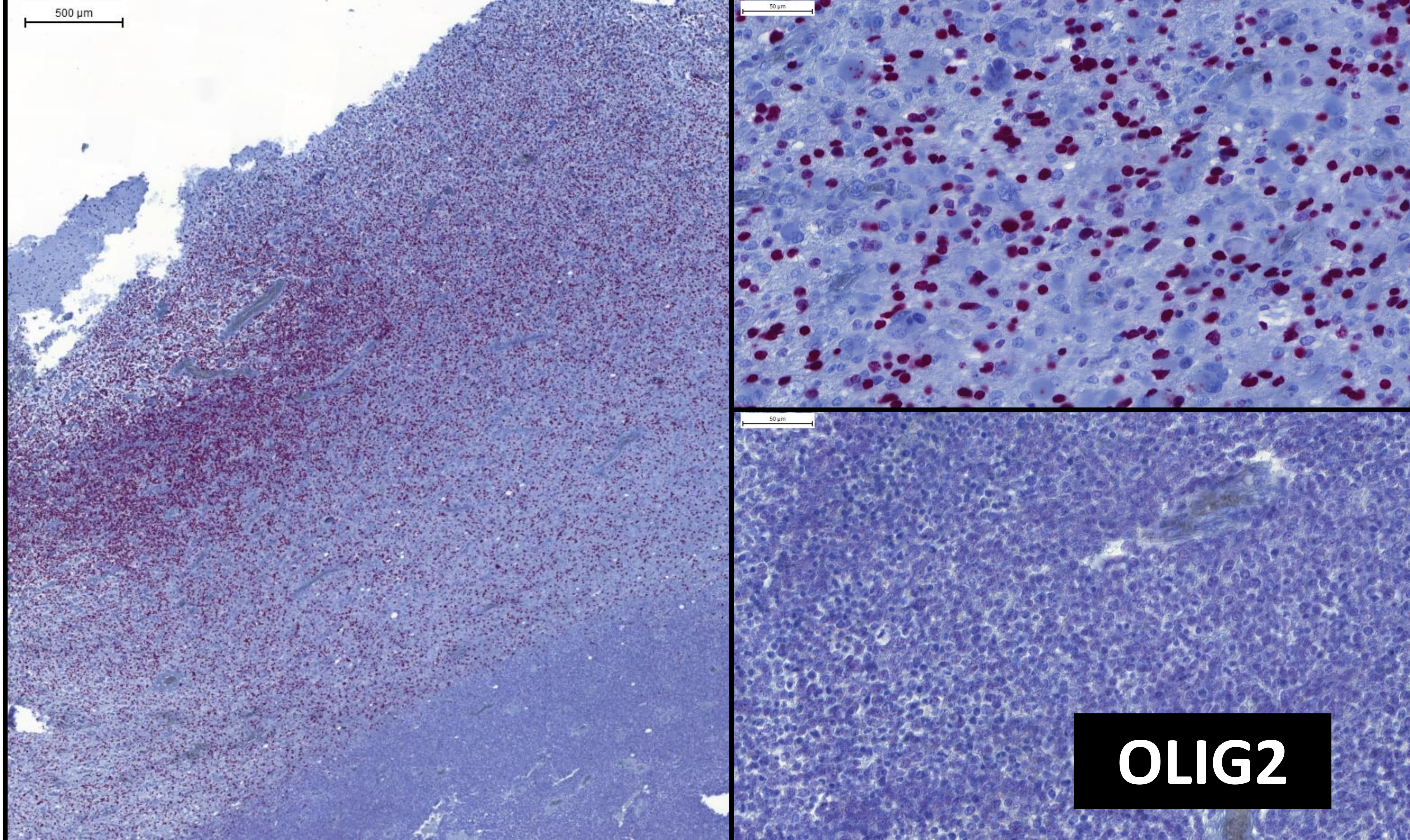
GFAP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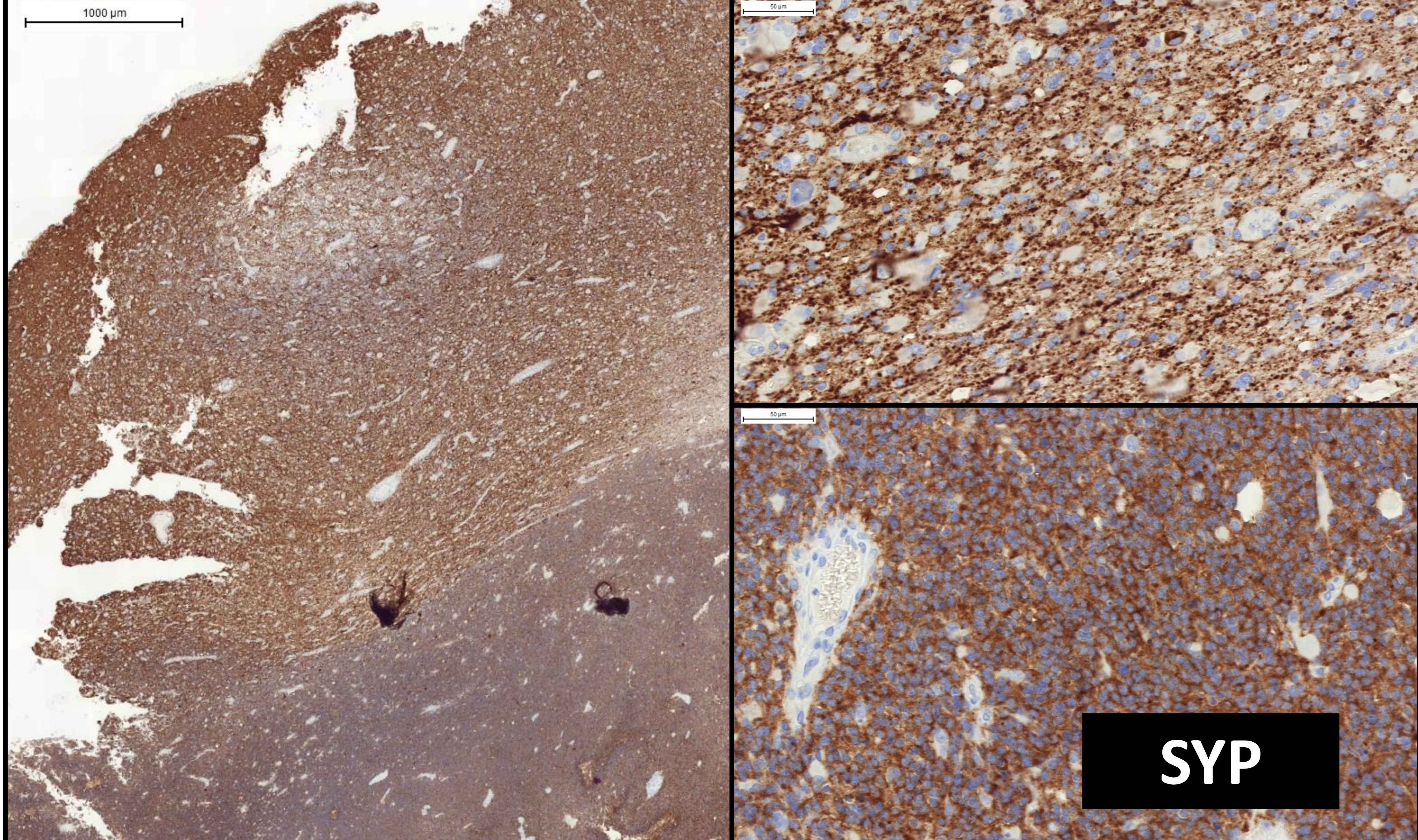
OLIG2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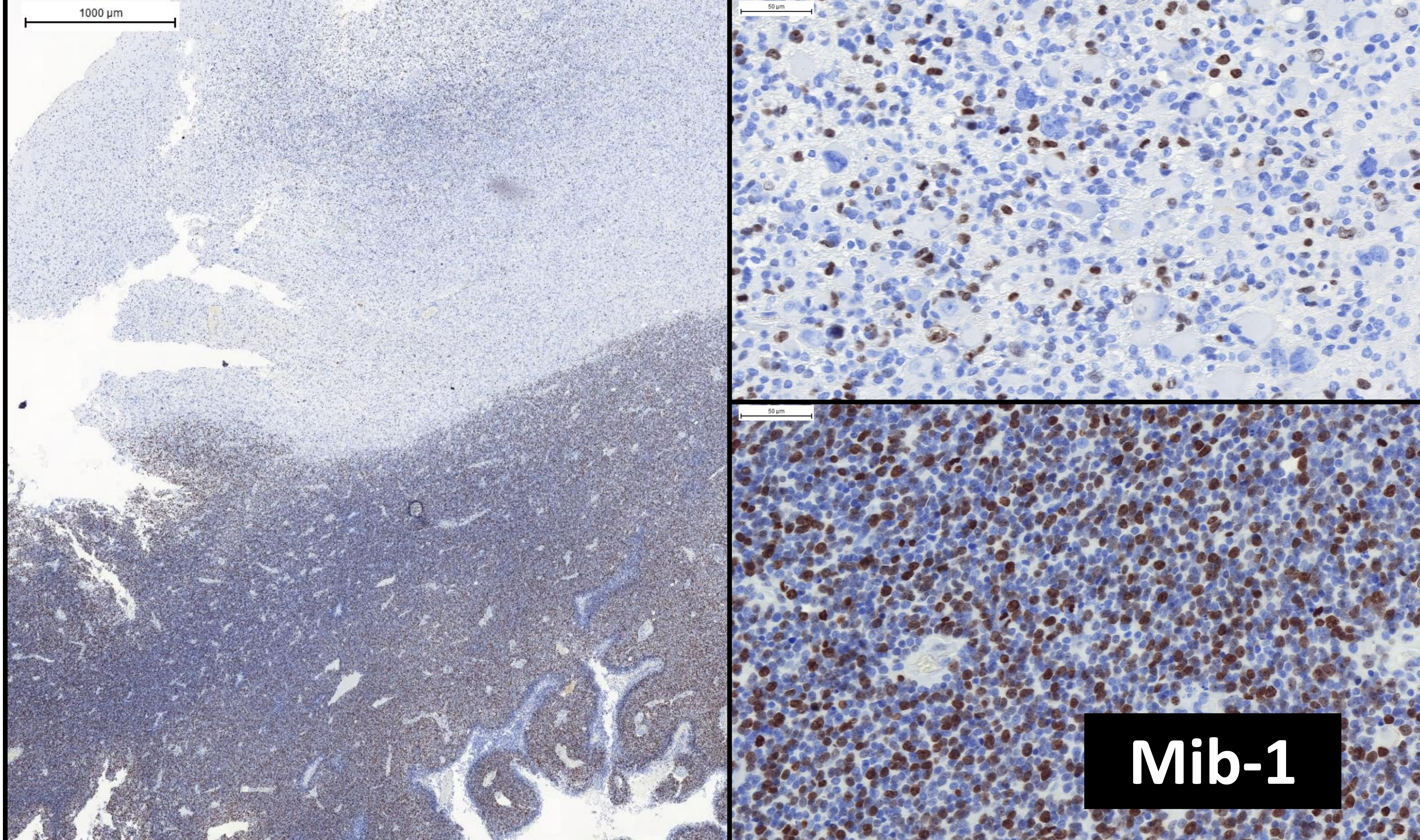
SYP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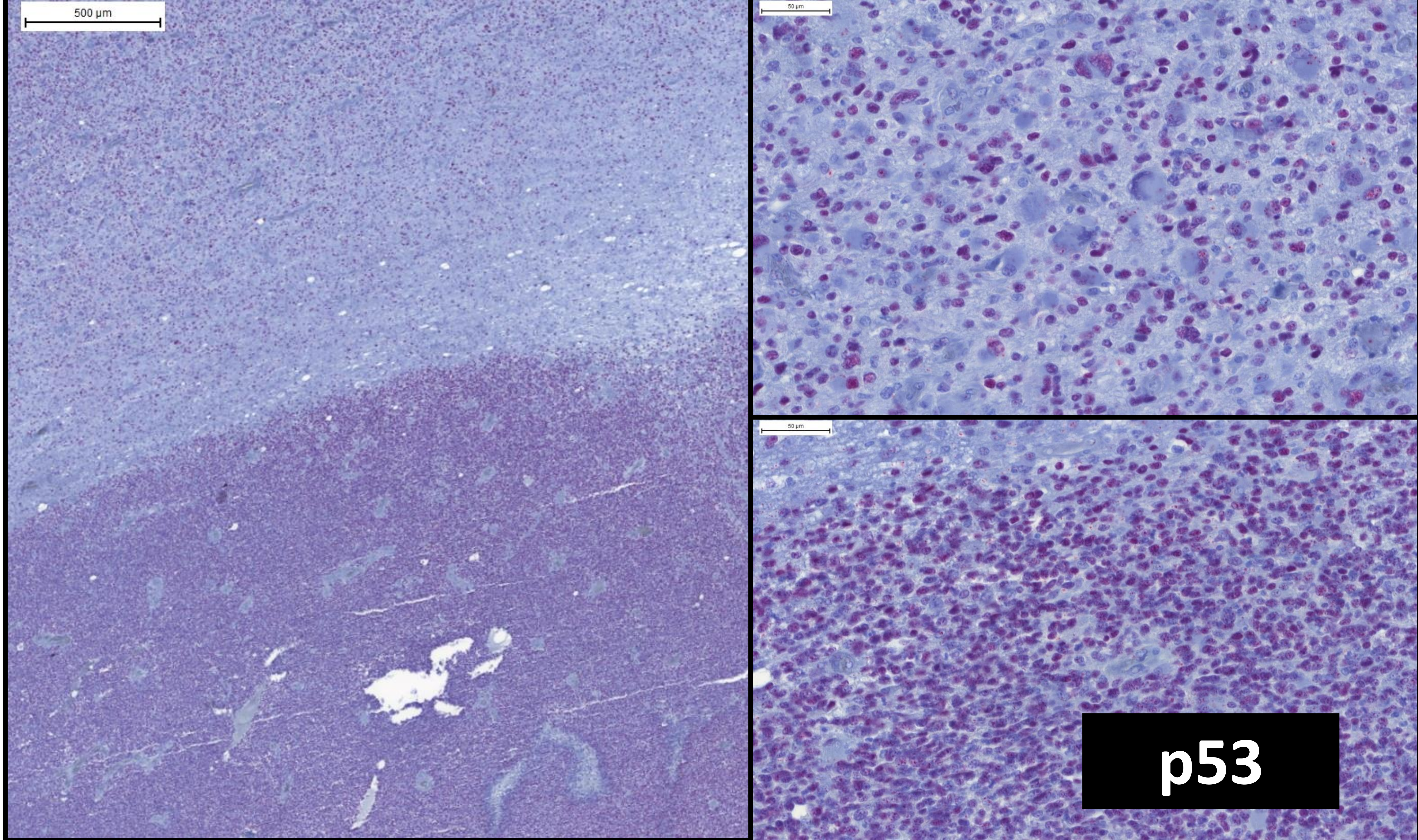
Mib-1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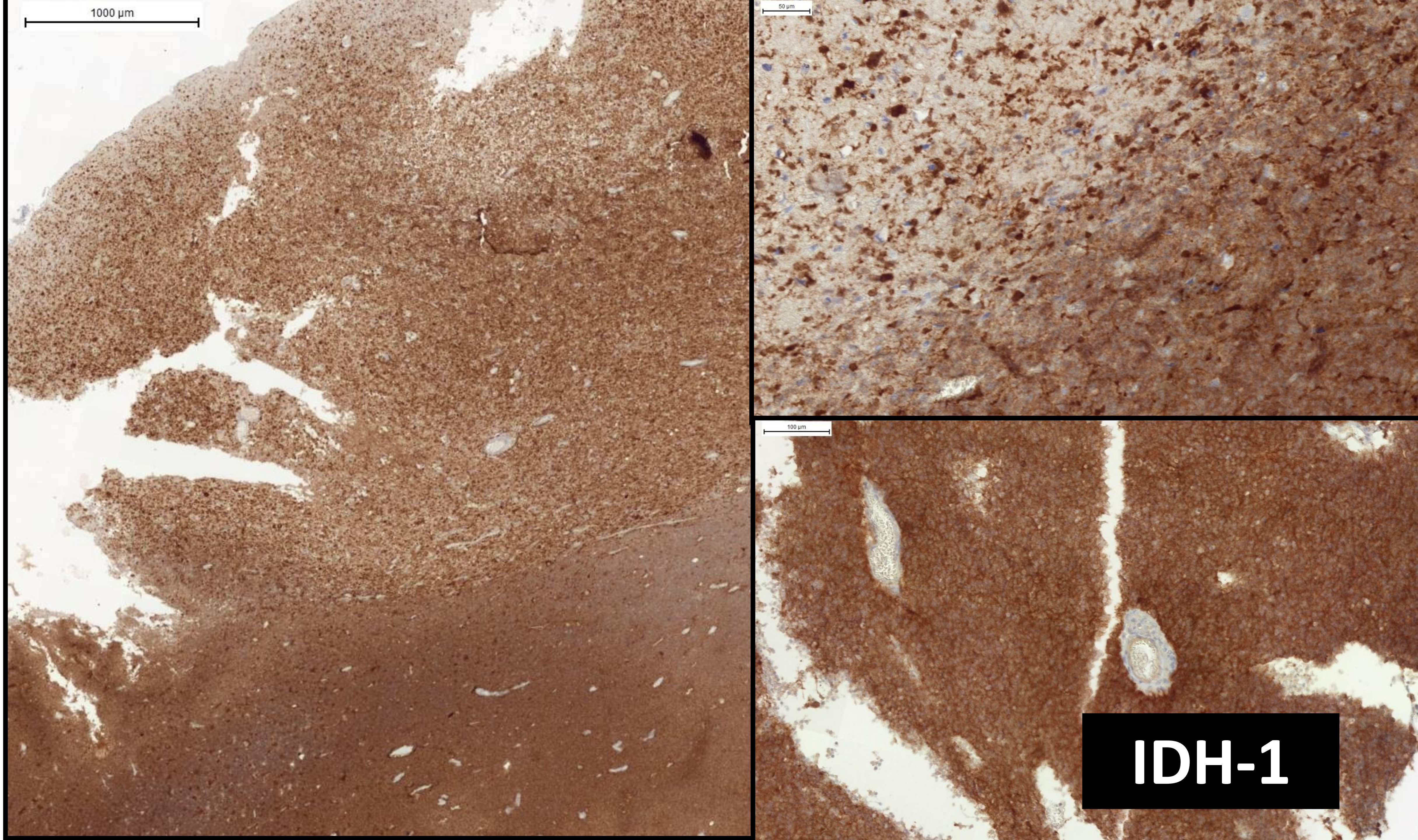
p53


1000 µm
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100 µm
IDH-1

DIAGNÓZA?

Genetika

- **Mutácia c.395G>A, p.Arg132His génu IDH1**
- Bez delécie 1p36
- **Dokázaná delécia 19q13**
- Bez amplifikácie génu EGFR
- Bez delécie lokusu PTEN
- Bez mutácie promotora génu TERT
- Bez aneuploídie chromozómu 7
- Bez amplifikácie C-MYC a N-MYC

Glioblastoma with a primitive neuronal component

- Nový „pattern“ glioblastómu
- Ostro ohraničené PNET-like fókusy v difúznom glióme, HW rozety +/-

- Neuronálne markery iba v PNET-like fókusoch
- Obe zložky majú alterácie typické pre GBM (p53, PTEN, EGFR...)
- ~40 % má MYCN / MYC amplifikáciu, iba v PNET-like zložke

- Prognóza je podobná „konvenčnému“ GBM, ale má tendenciu k diseminácii likvorom.... **Iná liečba (cisplatina, RT)**

MODERN PATHOLOGY (2013) 26, 315–326

Diagnostic implications of IDH1-R132H and OLIG2 expression patterns in rare and challenging glioblastoma variants

Nancy M Joseph[1], Joanna Phillips[1,2], Sonika Dahiya[3], Michelle M Felicella[1], Tarik Tihan[1], Daniel J Brat[4] and Arie Perry[1,2]

- 34 glioblastomas with primitive neuroectodermal tumor-like foci (PNET-like foci)
- **IDH1 was expressed in 15% (5/34)** of glioblastomas with PNET-like foci

Int J Clin Exp Pathol 2011;4(7):651-660
www.ijcep.com /IJCEP1108017

Original Article

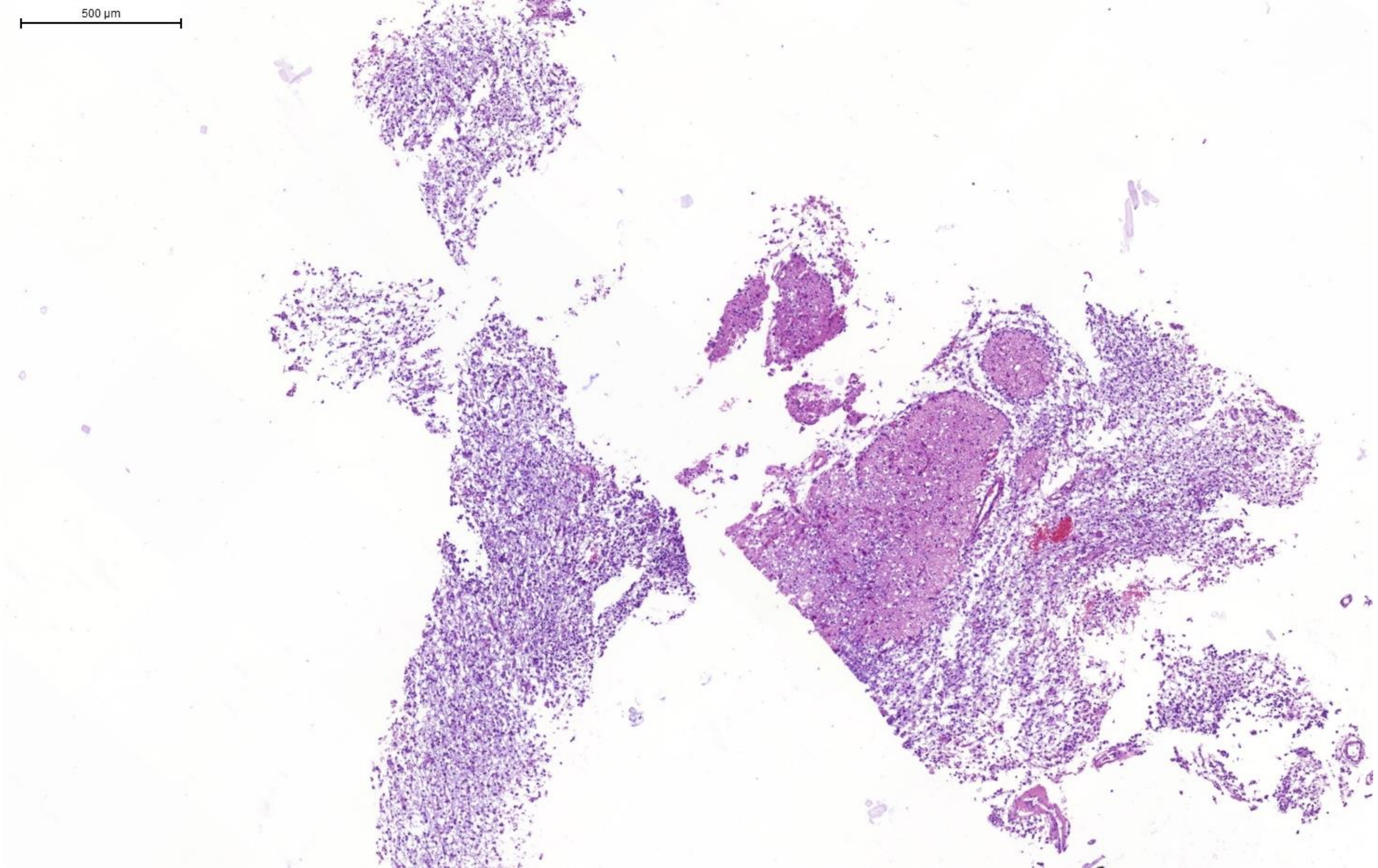
Glioblastoma with PNET-like components has a higher frequency of isocitrate dehydrogenase 1 (*IDH1*) mutation and likely a better prognosis than primary glioblastoma

Xianyuan Song[1], R Andrew Allen[2], S Terence Dunn[2], Kar-Ming Fung[2], Peter Farmer[3], Shital Gandhi[4], Tulika Ranjan[5], Alexis Demopoulos[6], Marc Symons[7], Michael Schulder[8], Jian Yi Li[3]

- **Two out of 8 cases** harbored isocitrate dehydrogenase 1 (*IDH1*) R132H mutation

Prípad č. 3

- 38-ročná žena
- intramedulárny tumor C2-Th4 (maximum zmien v C2-Th1)
- Konzultácia, MUDr. Boris Rychlý, Cytopathos s.r.o., Bratislava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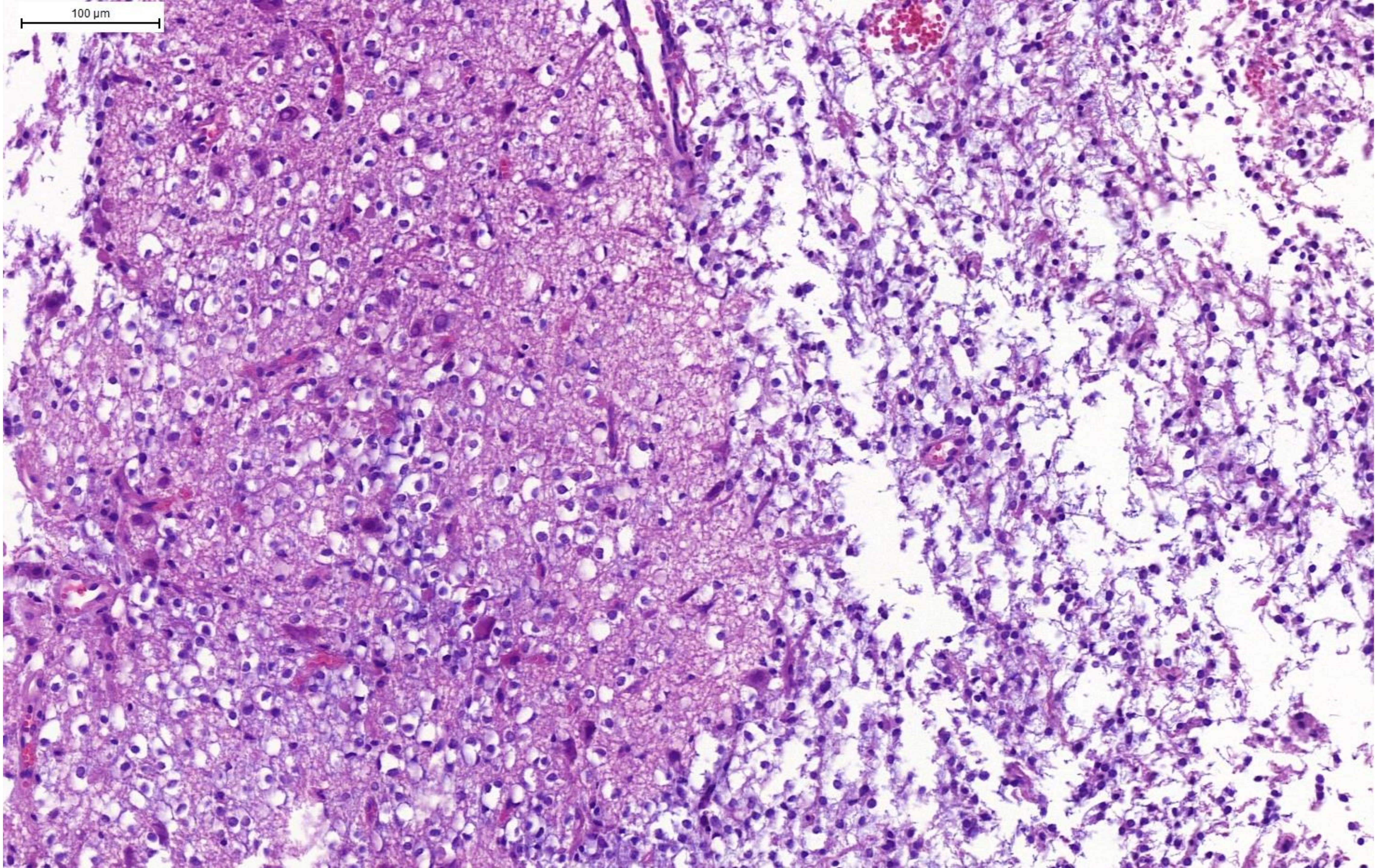
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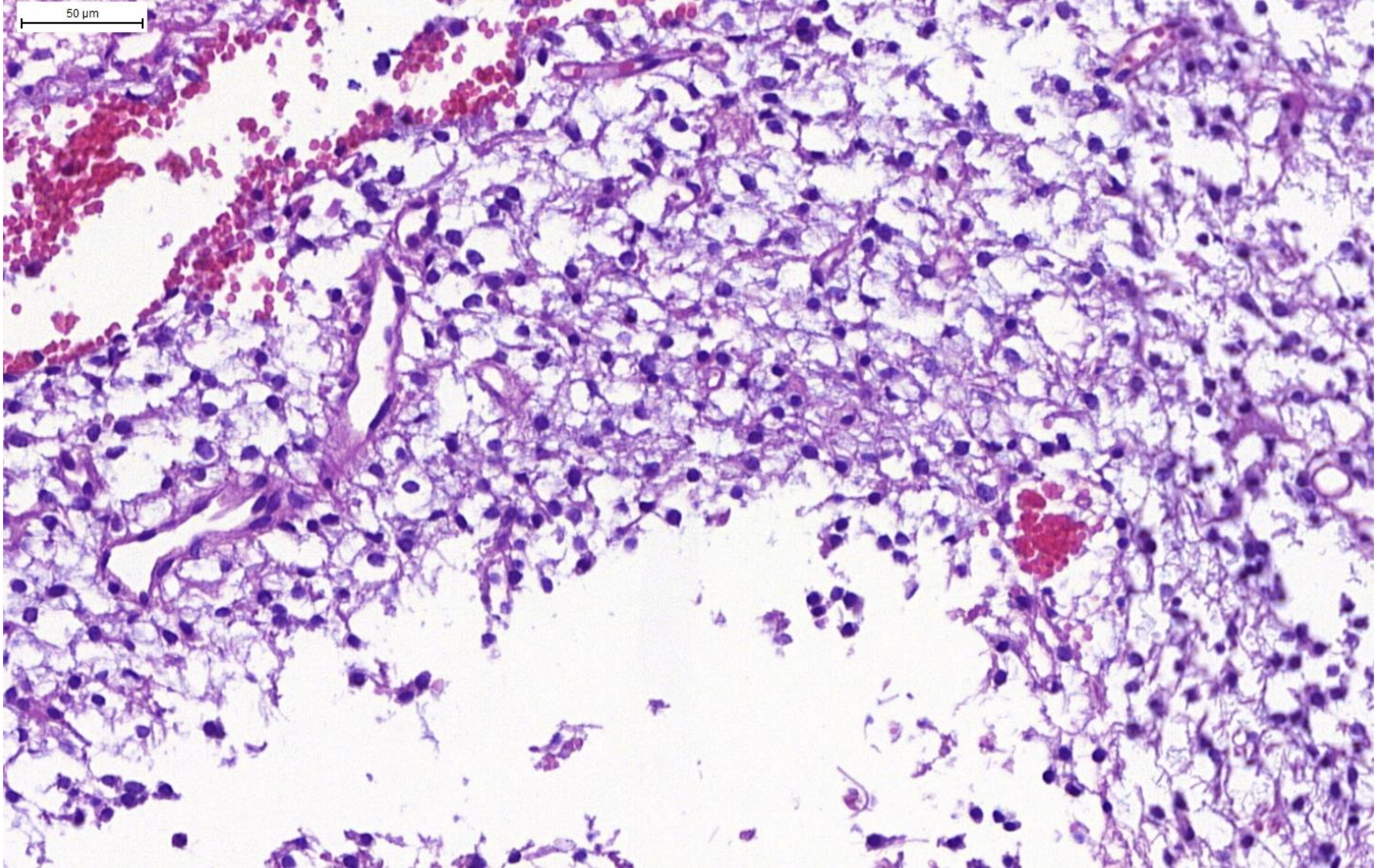
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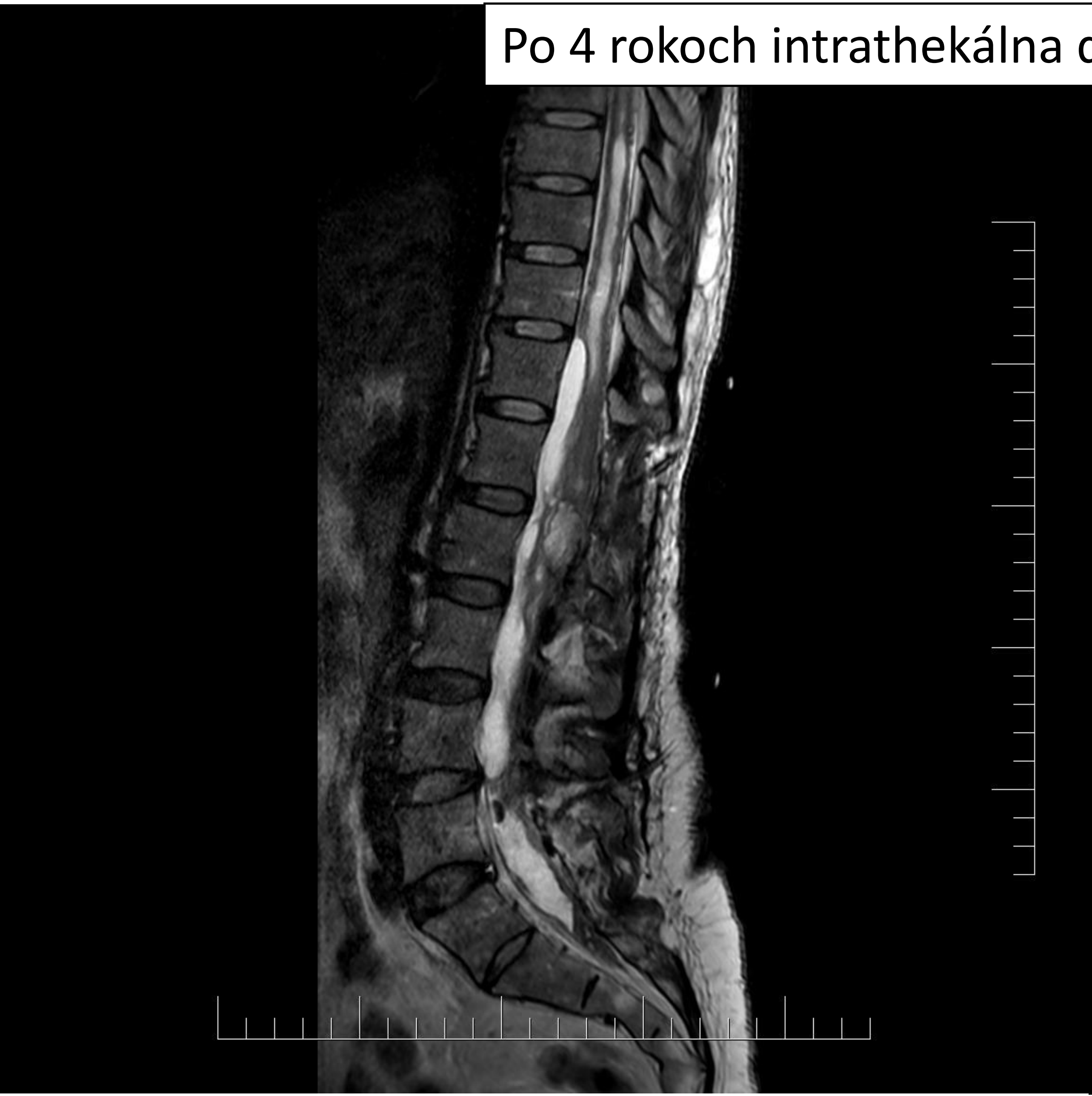
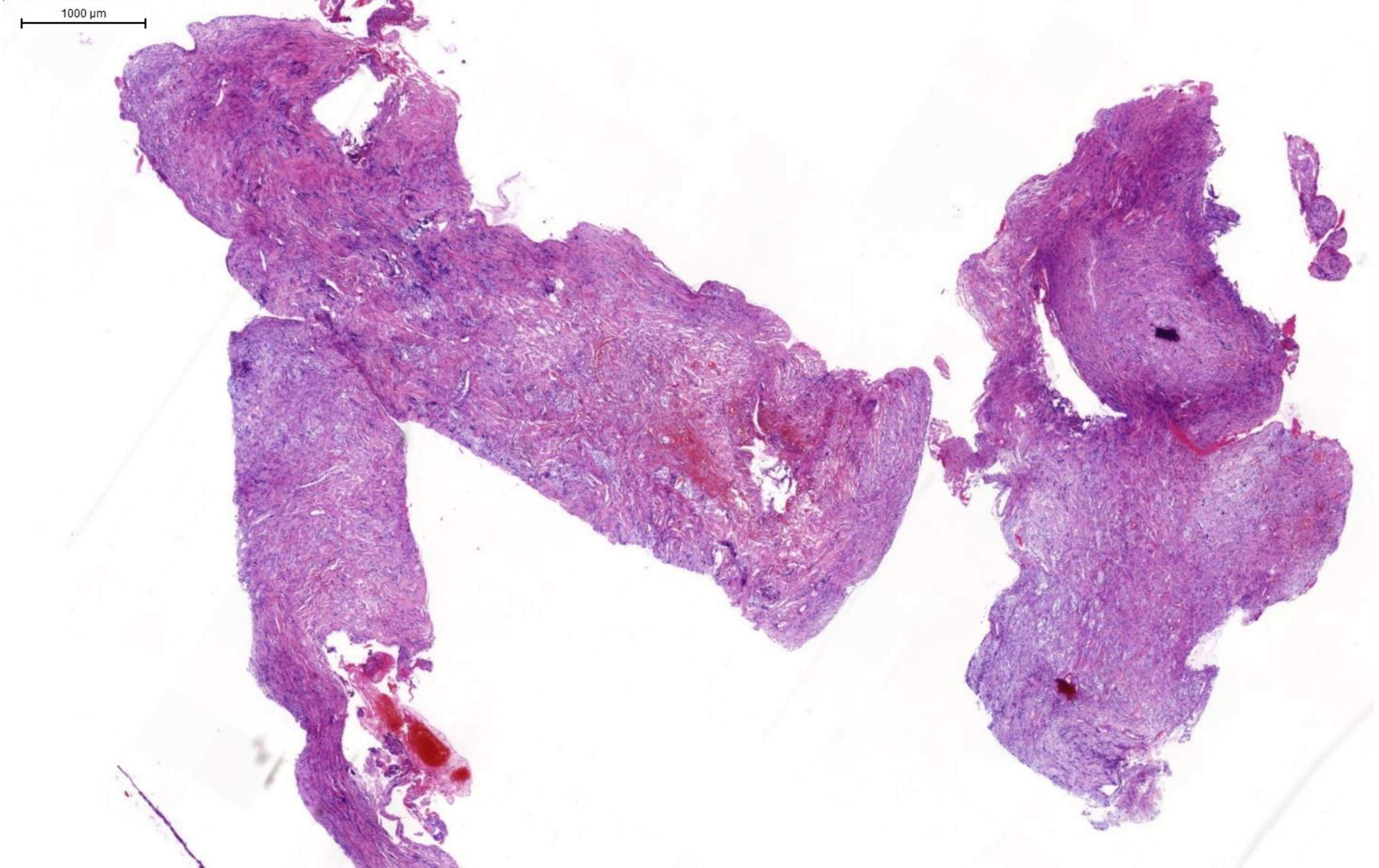
Po 4 rokoch intrathekálna diseminácia v oblasti L1, L5

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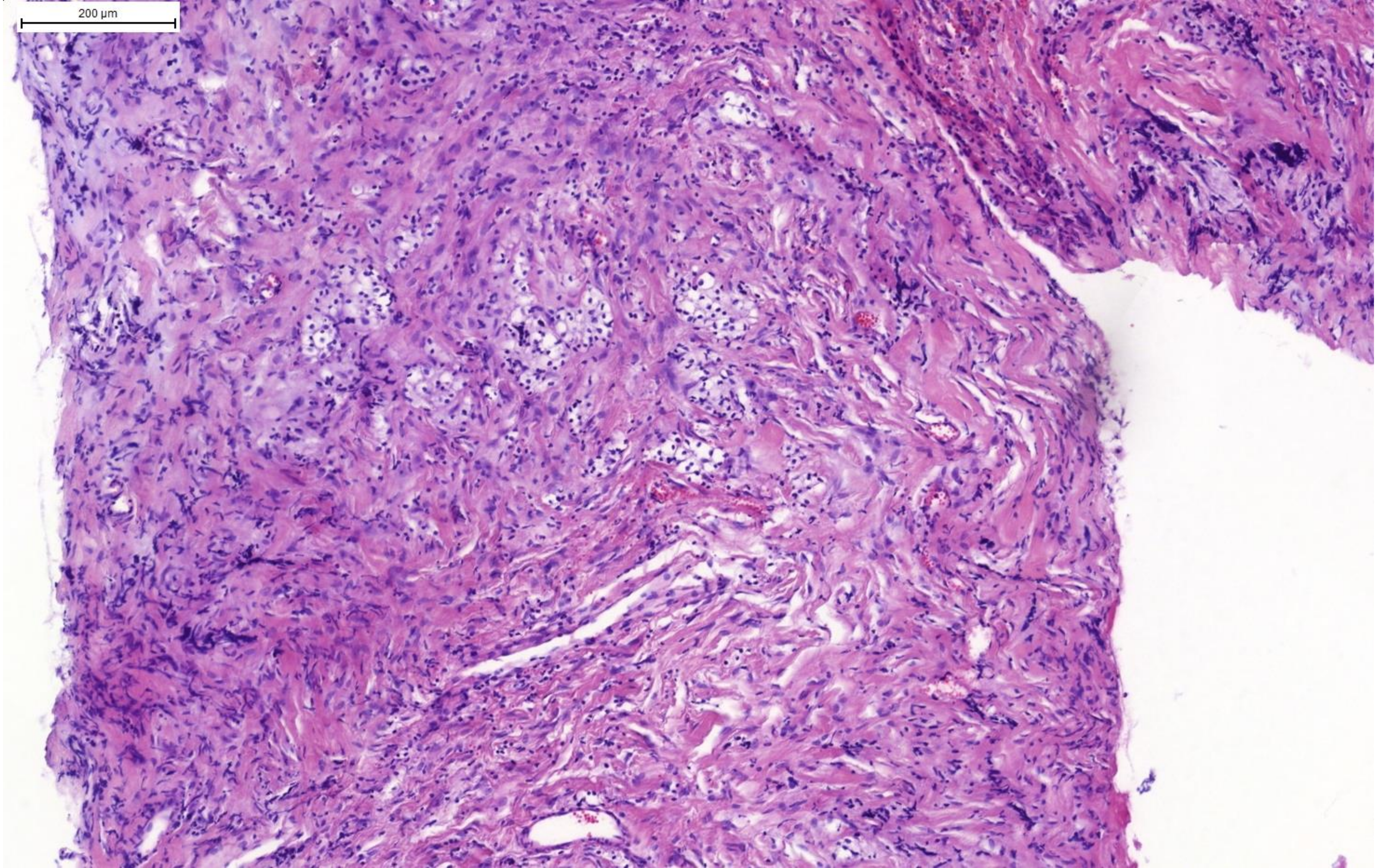
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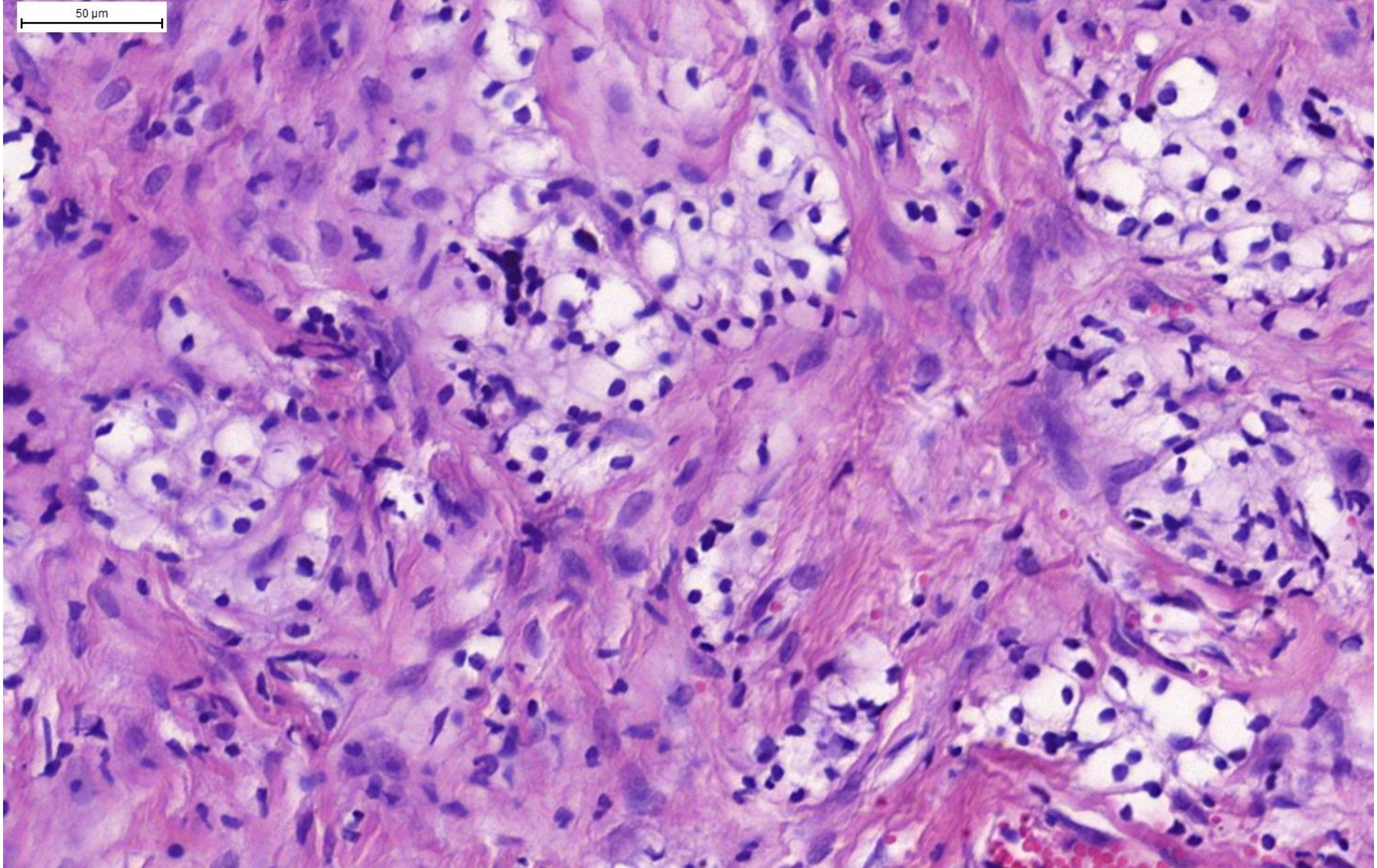
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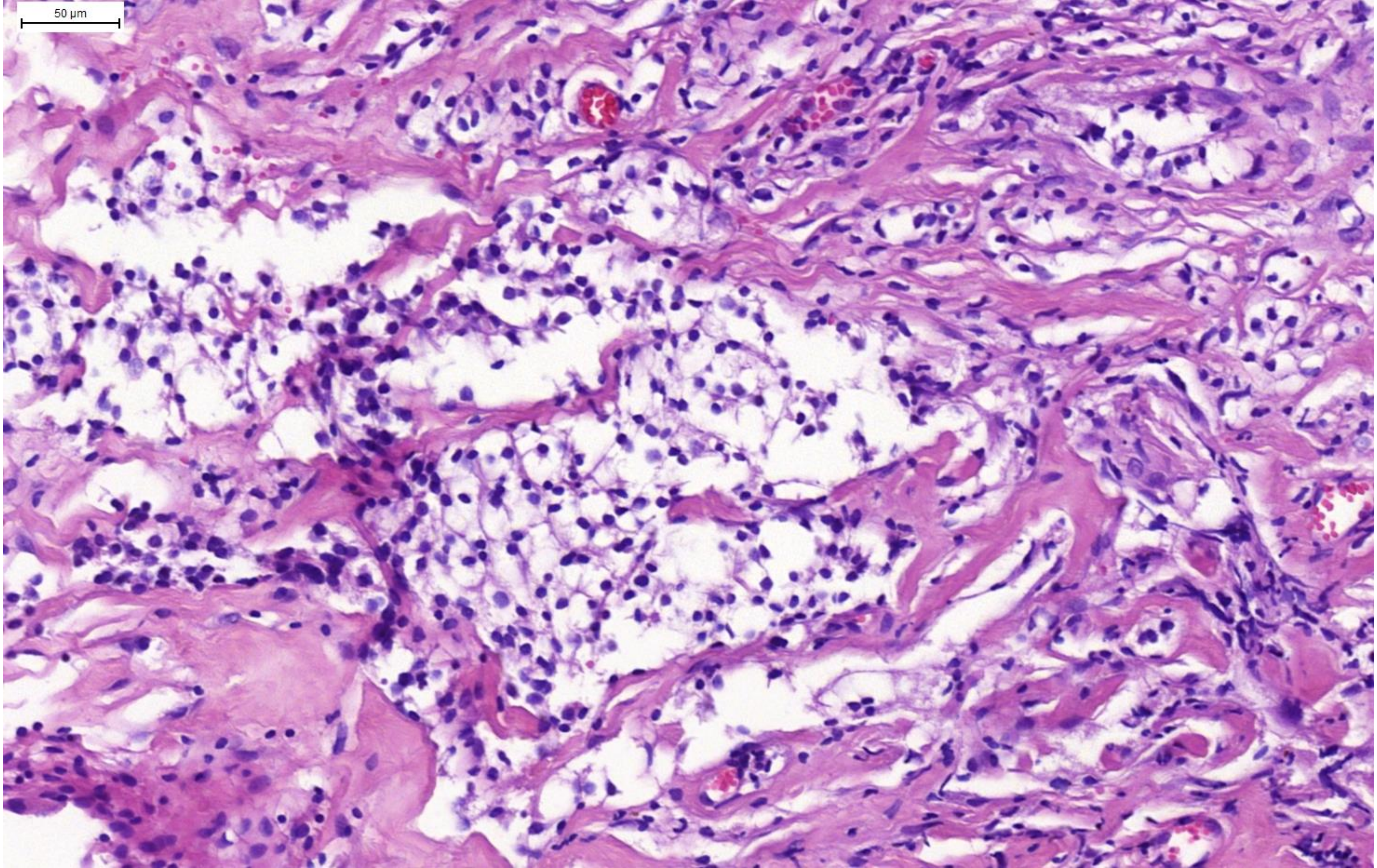
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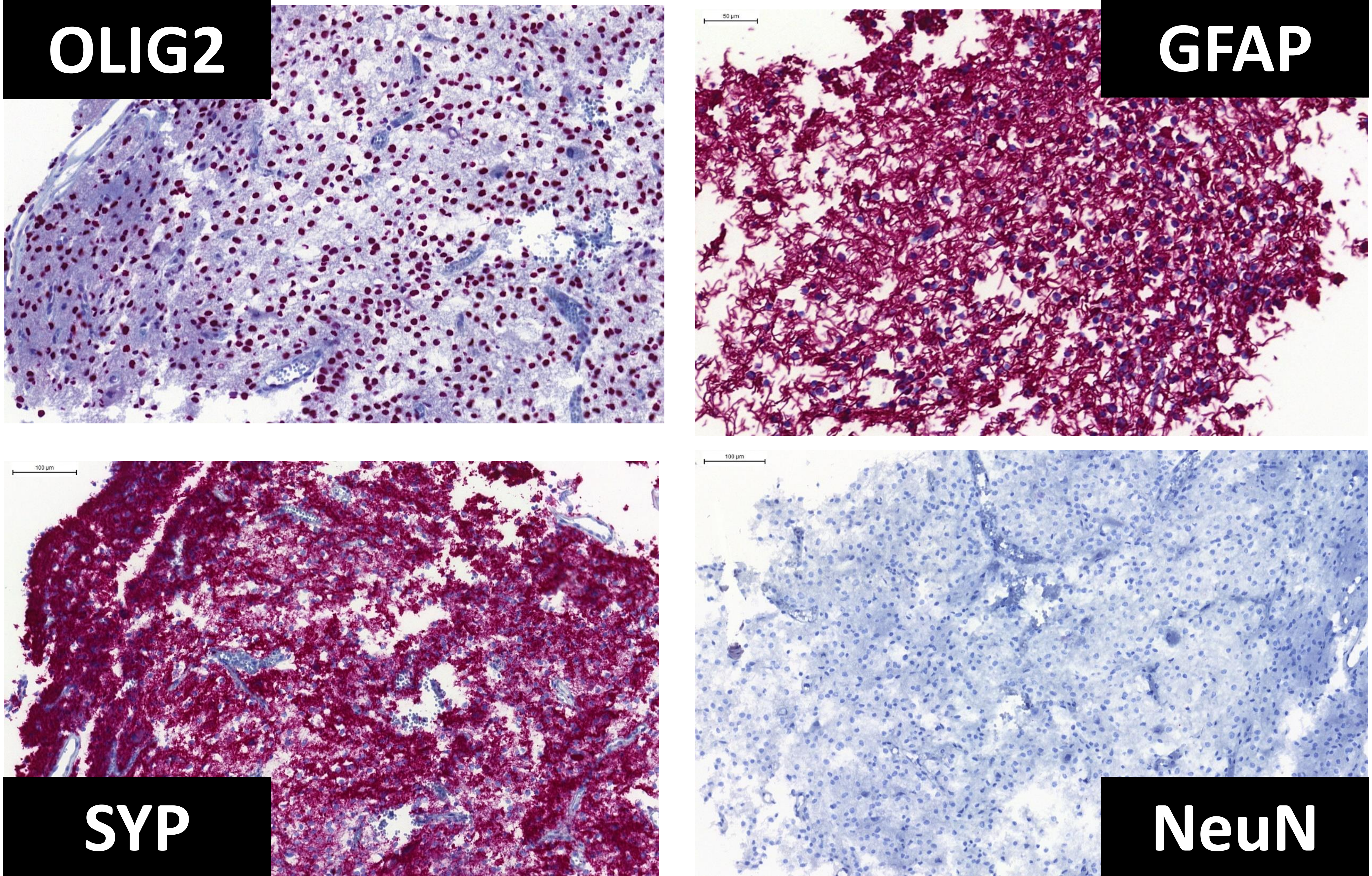
DIAGNÓZA?


OLIG2
GFAP
SYP
NeuN

Genetika

- KIAA1549-BRAF
- delécia 1p (bez kodelécie 19p)

Diffuse leptomeningeal glioneuronal tumor

- ODG-like nádor s leptomeningeálnym rozsevom a pomalou progresiou

- Táto „jednotka“ je známa > 70 rokov
  - Primary leptomeningeal oligodendrogliomatosis, disseminated oligodendroglioma-like leptomeningeal neoplasm....

- Zatiaľ nemá grade (väčšina vyzerá ako LG tumor, ale môže mať HG morfológiu)
- Prevažne u detí / mladých dospelých
- Parenchýmová zložka (častejšie v mieche) má ODG-like morfológiu bez dezmoplastickej reakcie, DNT-like morfológiu, alebo menej často PA-like morfológiu (vzácne gangliocytárna diferenciácia)

- *IDH* – wildtype
- KIAA-BRAF fúzia (~75 %), vzácne mutácia *BRAF*, del 1p (~50-60 %), codel 1p/19q (~20 %)

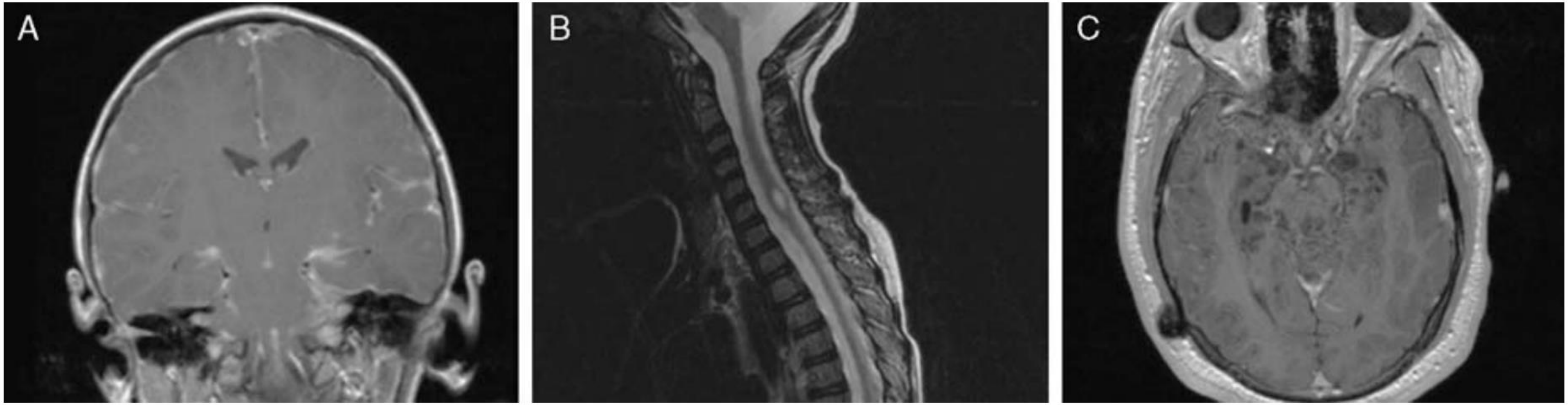
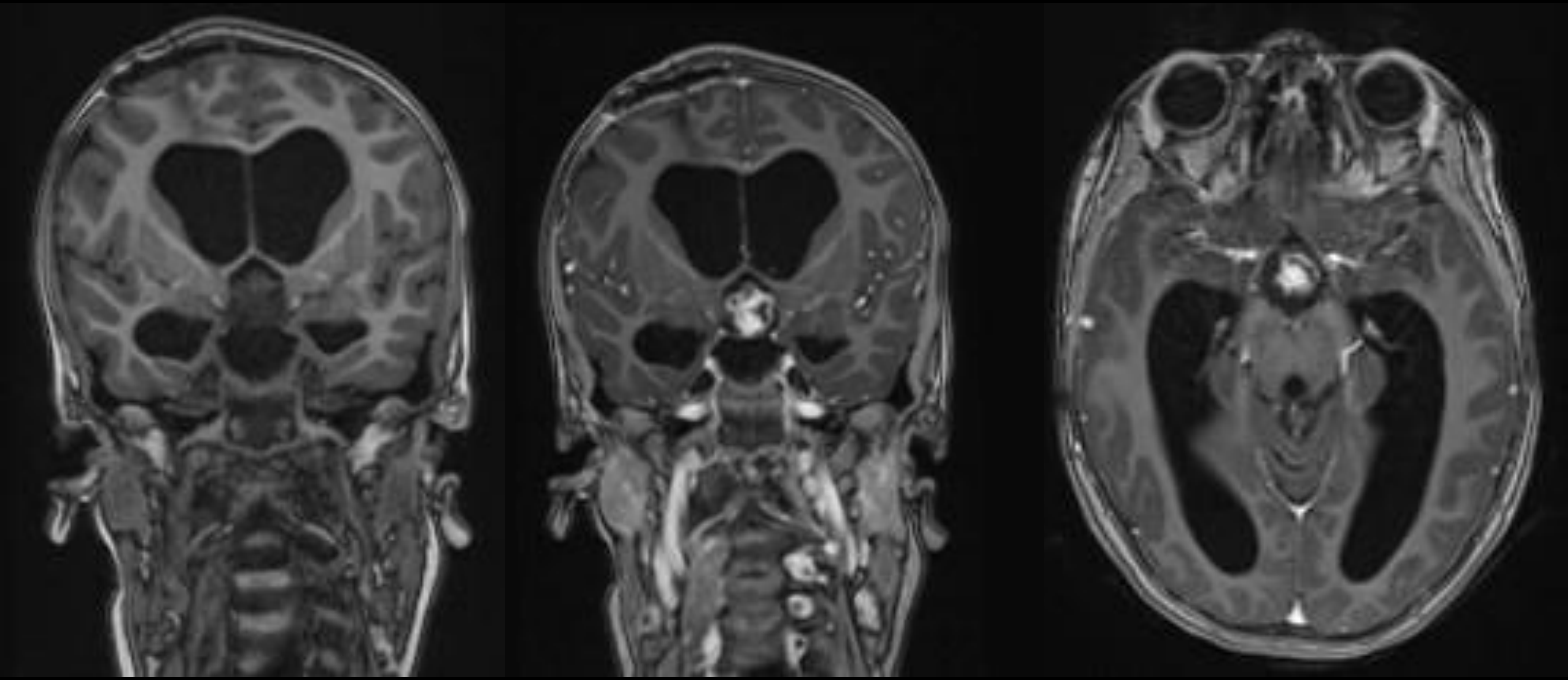


FIGURE 1. A, Coronal T1-weighted MRI showing diffuse leptomeningeal thickening and contrast enhancement over the brain surface. B, Sagittal T2-weighted MRI showing an intramedullary mass at C6-7 (case 2). C, Axial T1-weighted MRI showing cystic lesions around the midbrain and medial temporal lobes.

Schniederjan et al. Am J Surg Pathol 2013;37:763–771

Prípad č. 4

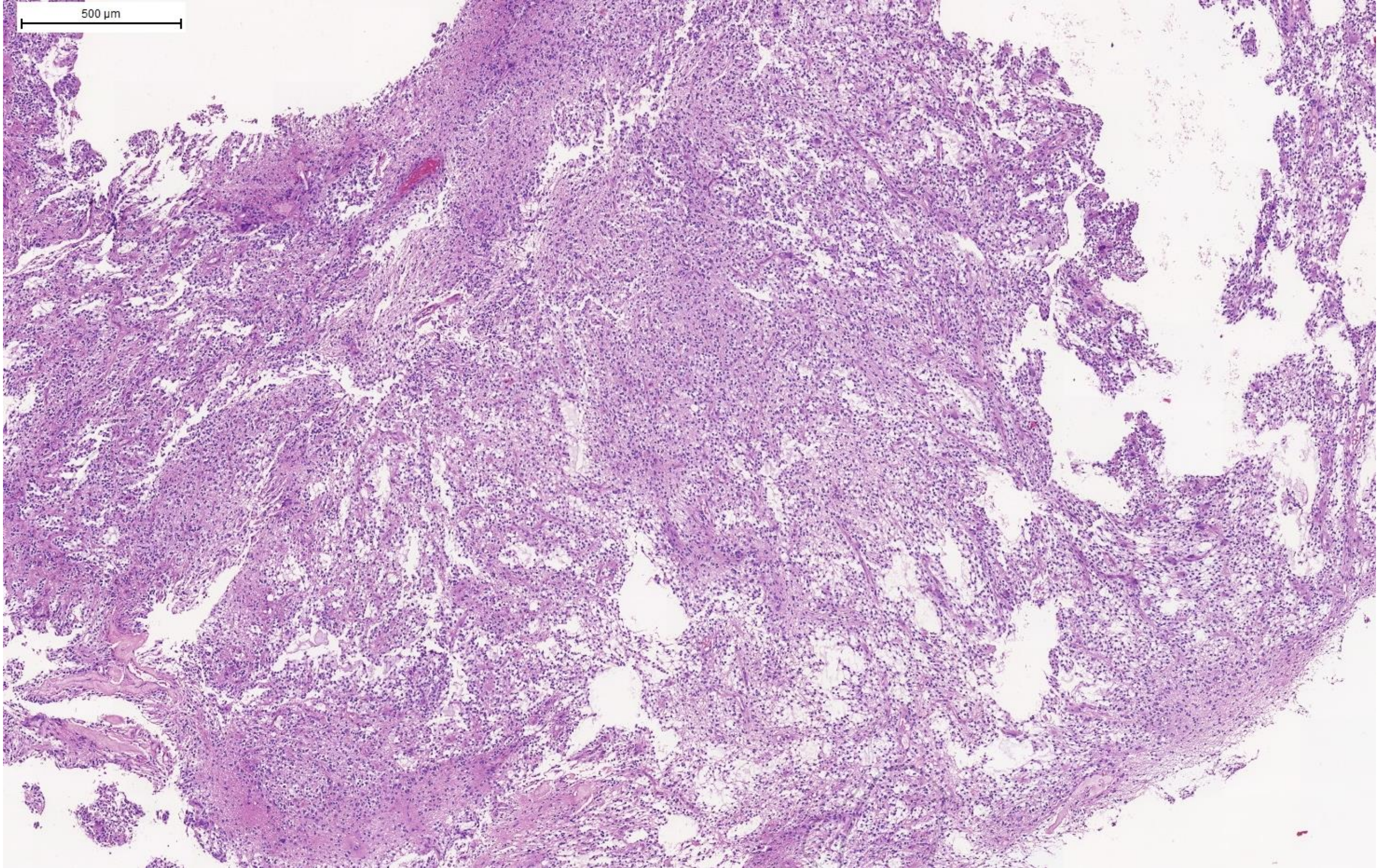
- 7 ročné dievča
- tumor III. komory s rozsevom v bočných komorách, IV. komore a difúznym leptomeningeálnym rozsevom v mieche
- konzultácia (prípad láskavo poskytla MUDr. Marta Ježová, Ph.D., FN Brno)



Doc. MUDr. J. Skotáková, CSc., KDR, FN Brno




Doc. MUDr. J. Skotáková, CSc., KDR, FN Brno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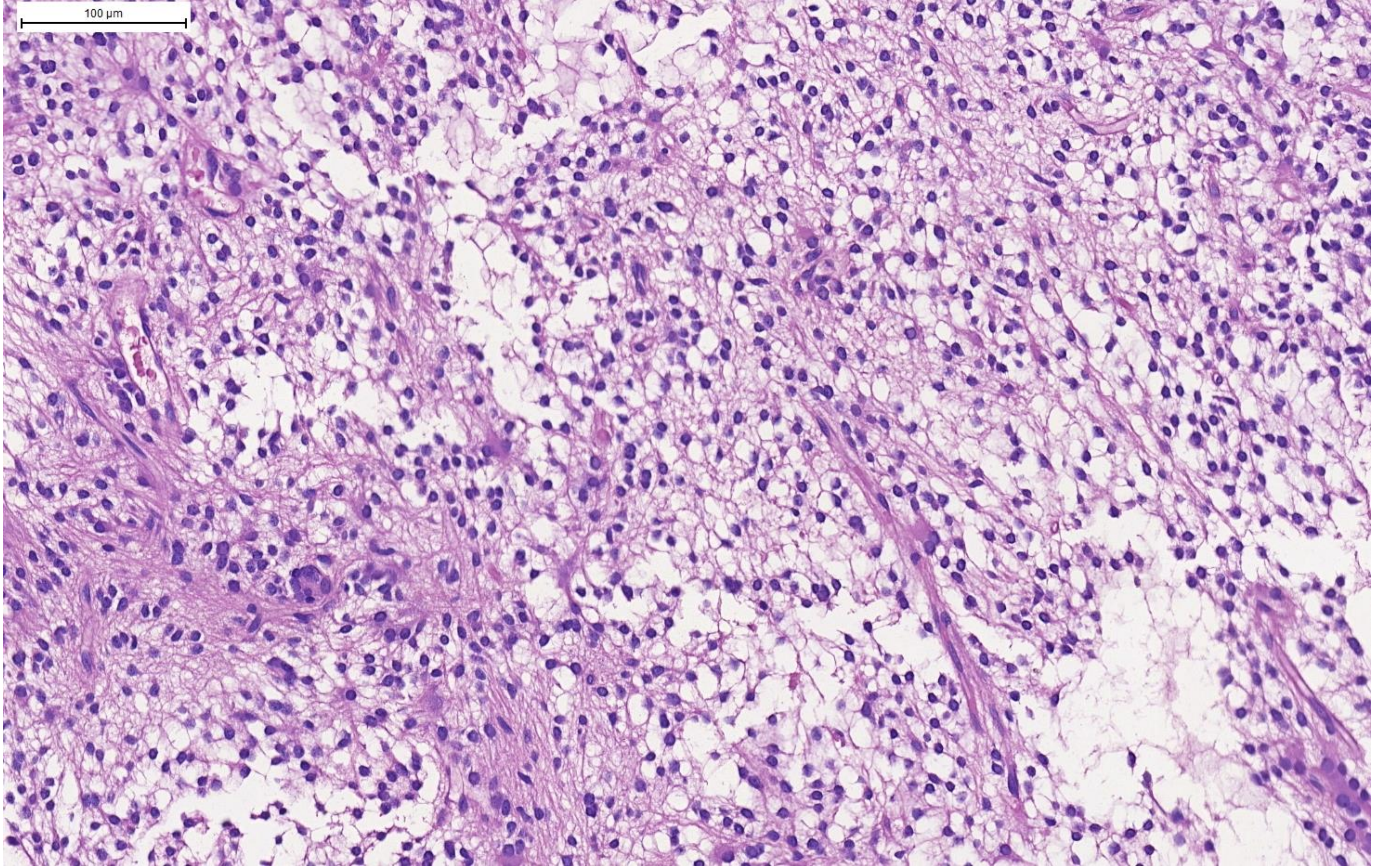
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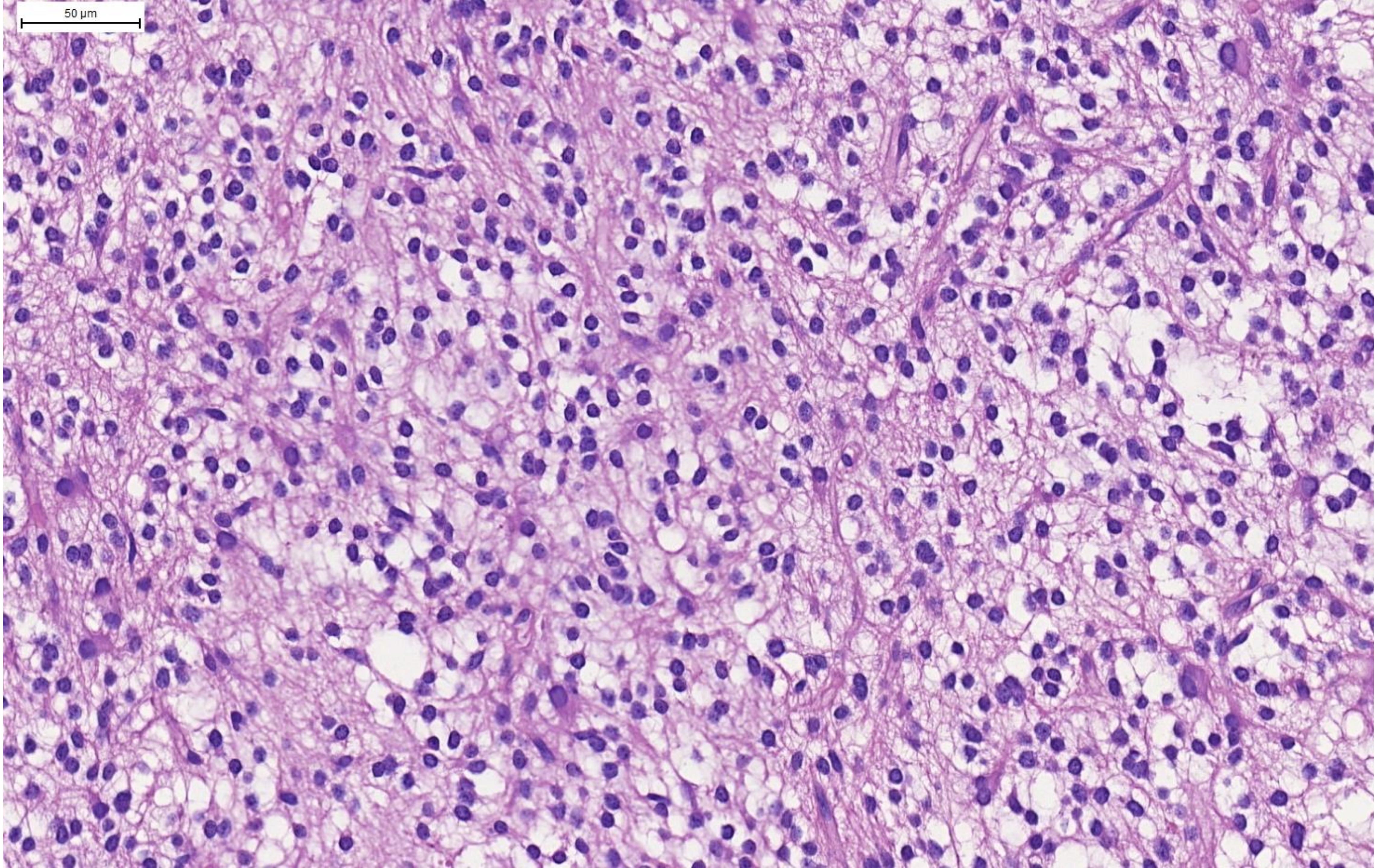
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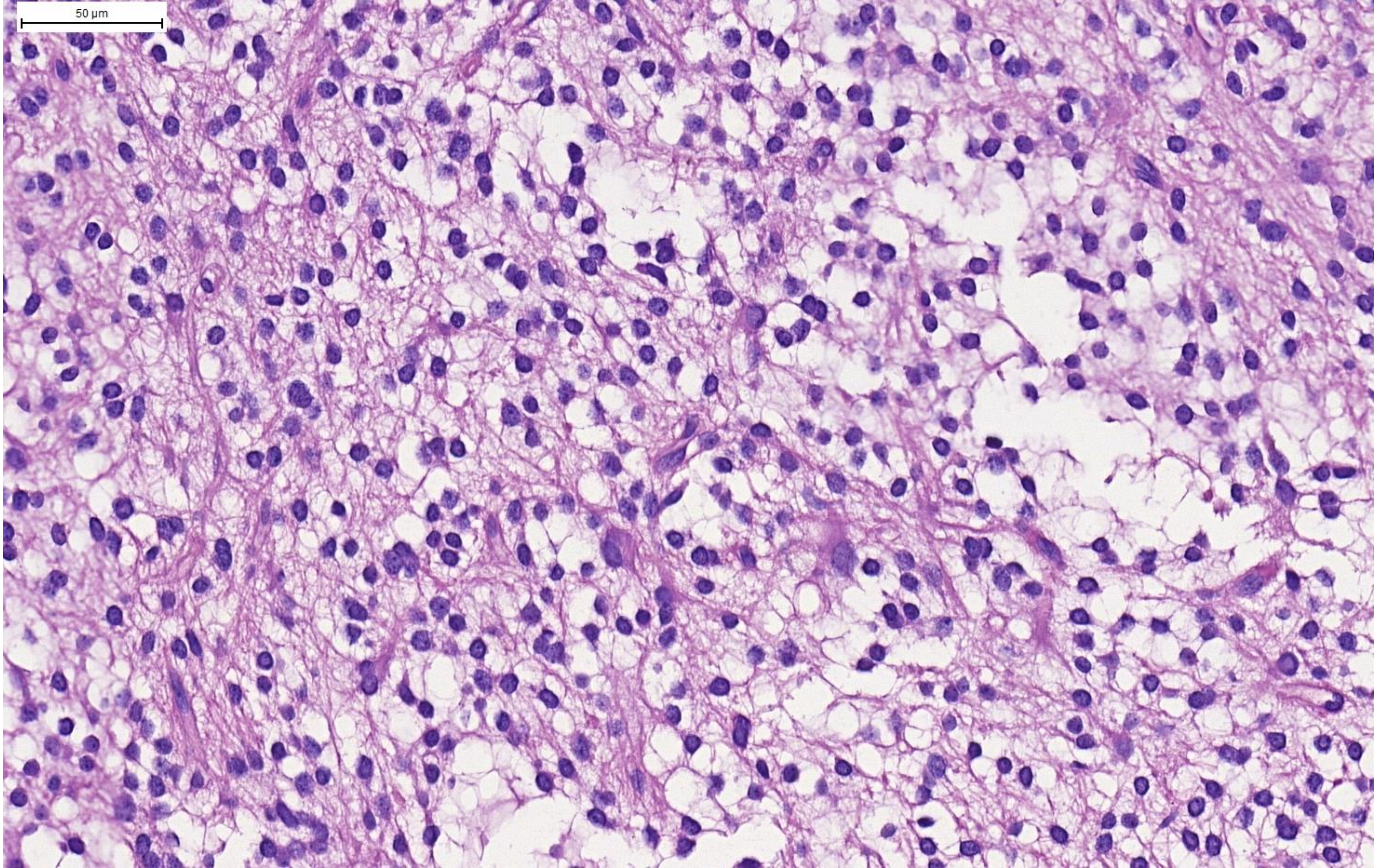
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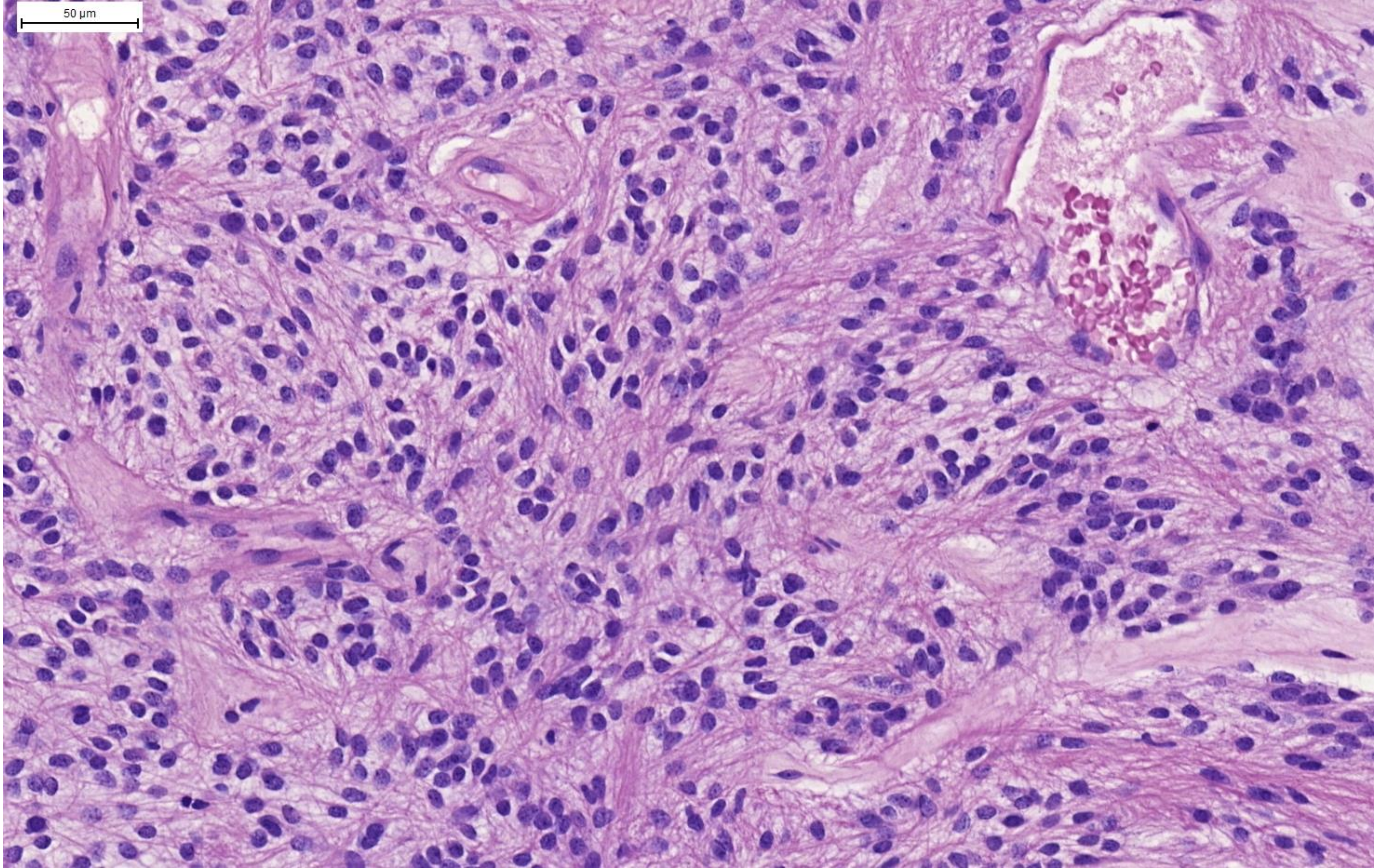
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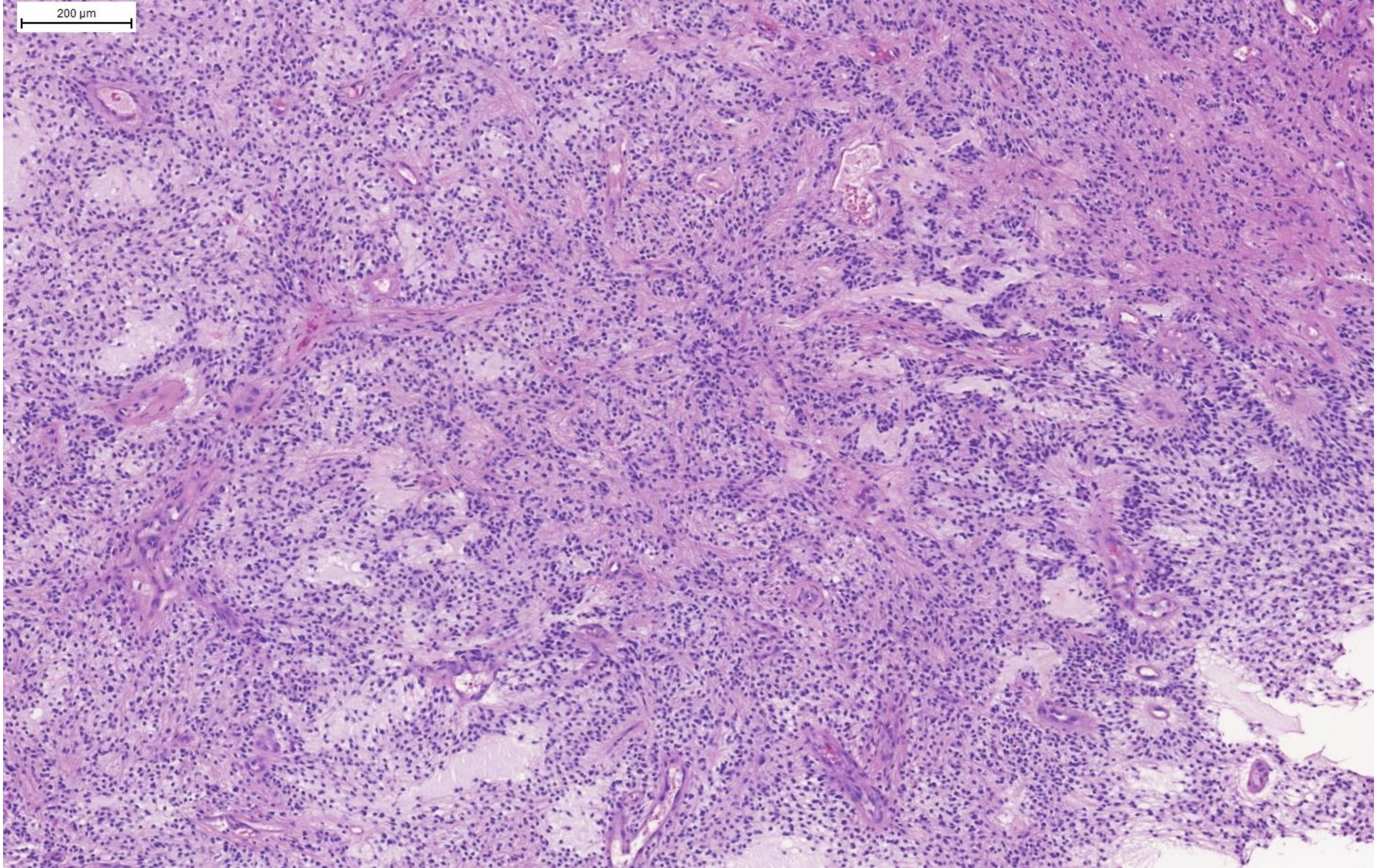
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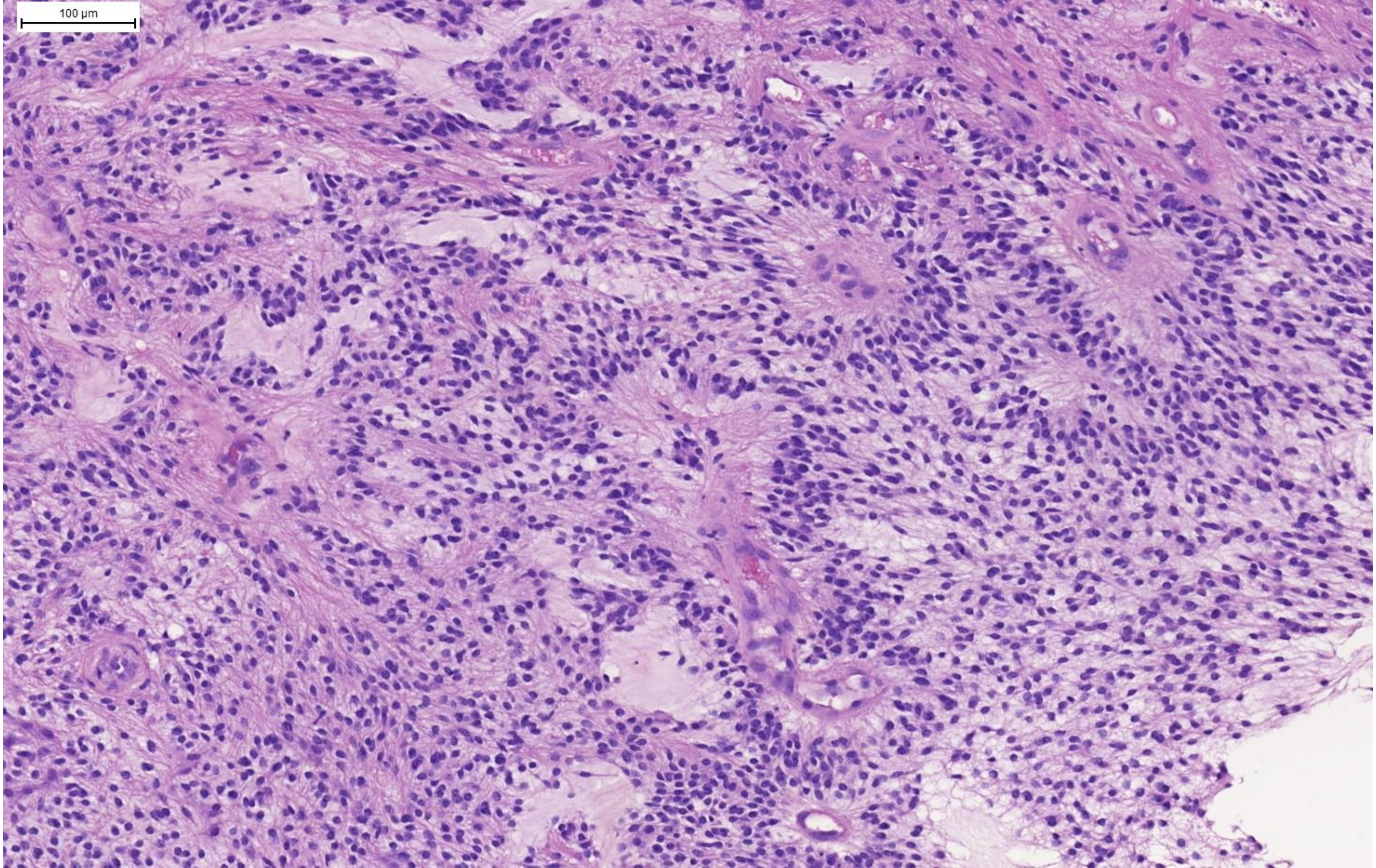
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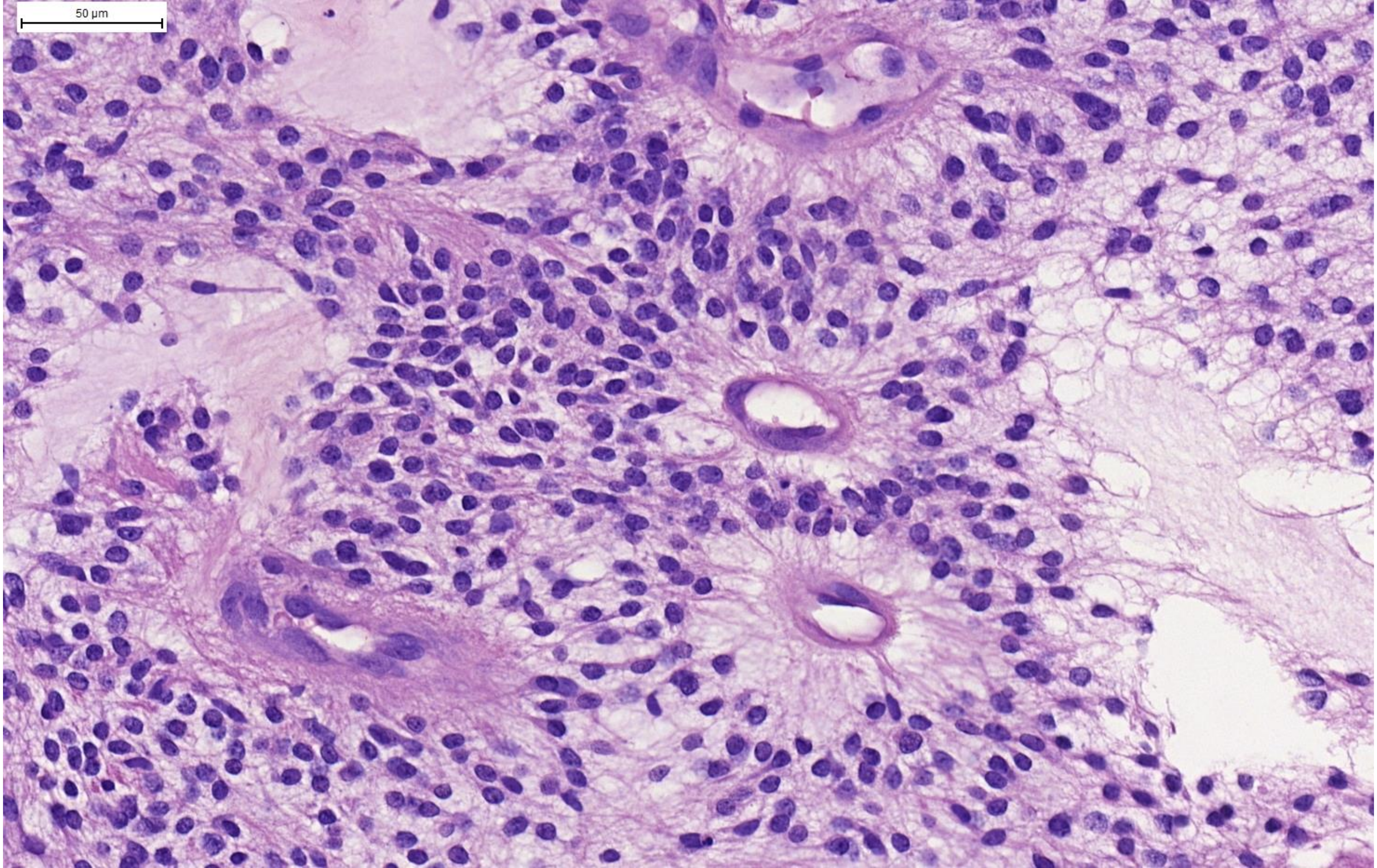
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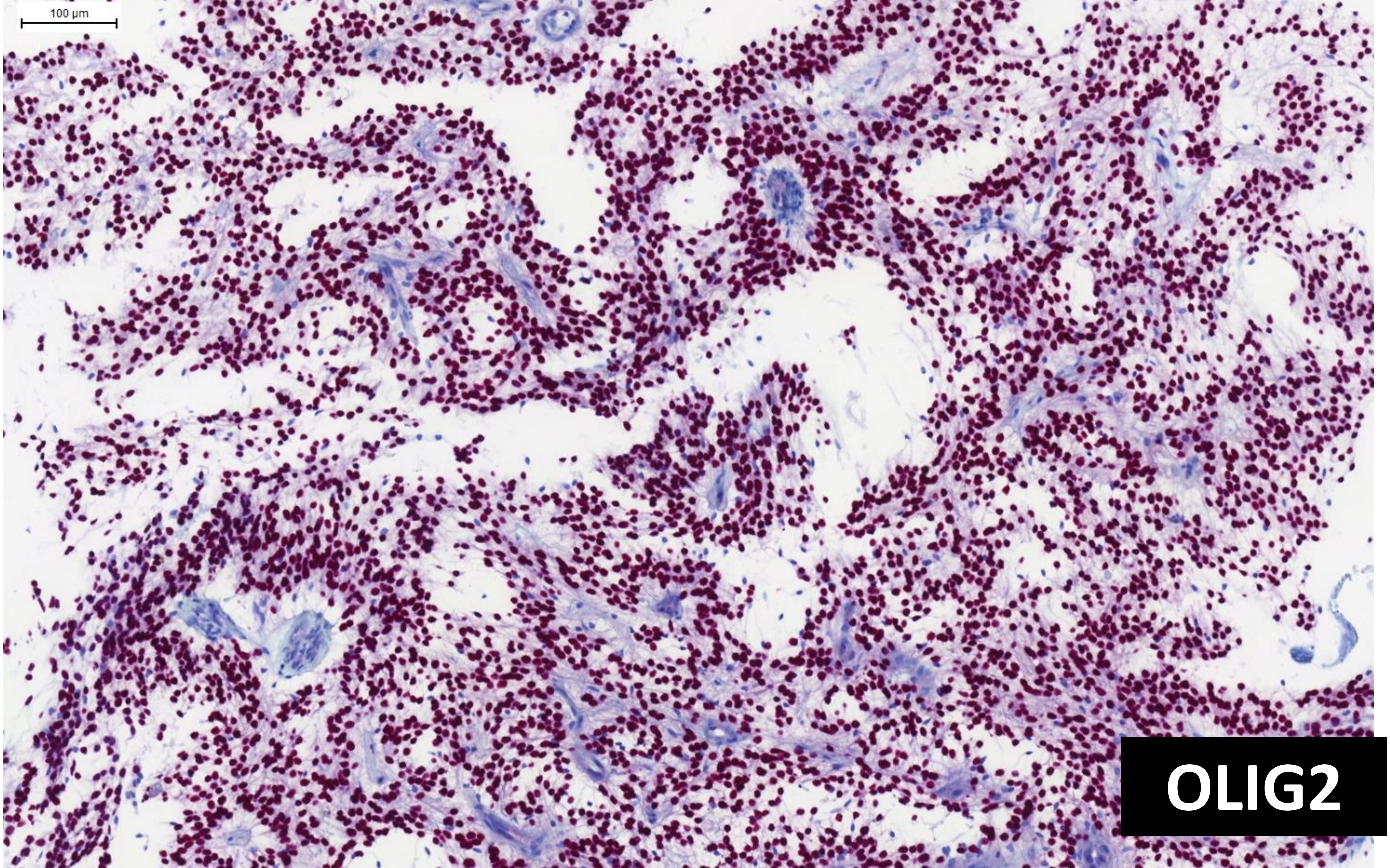
DIAGNÓZA?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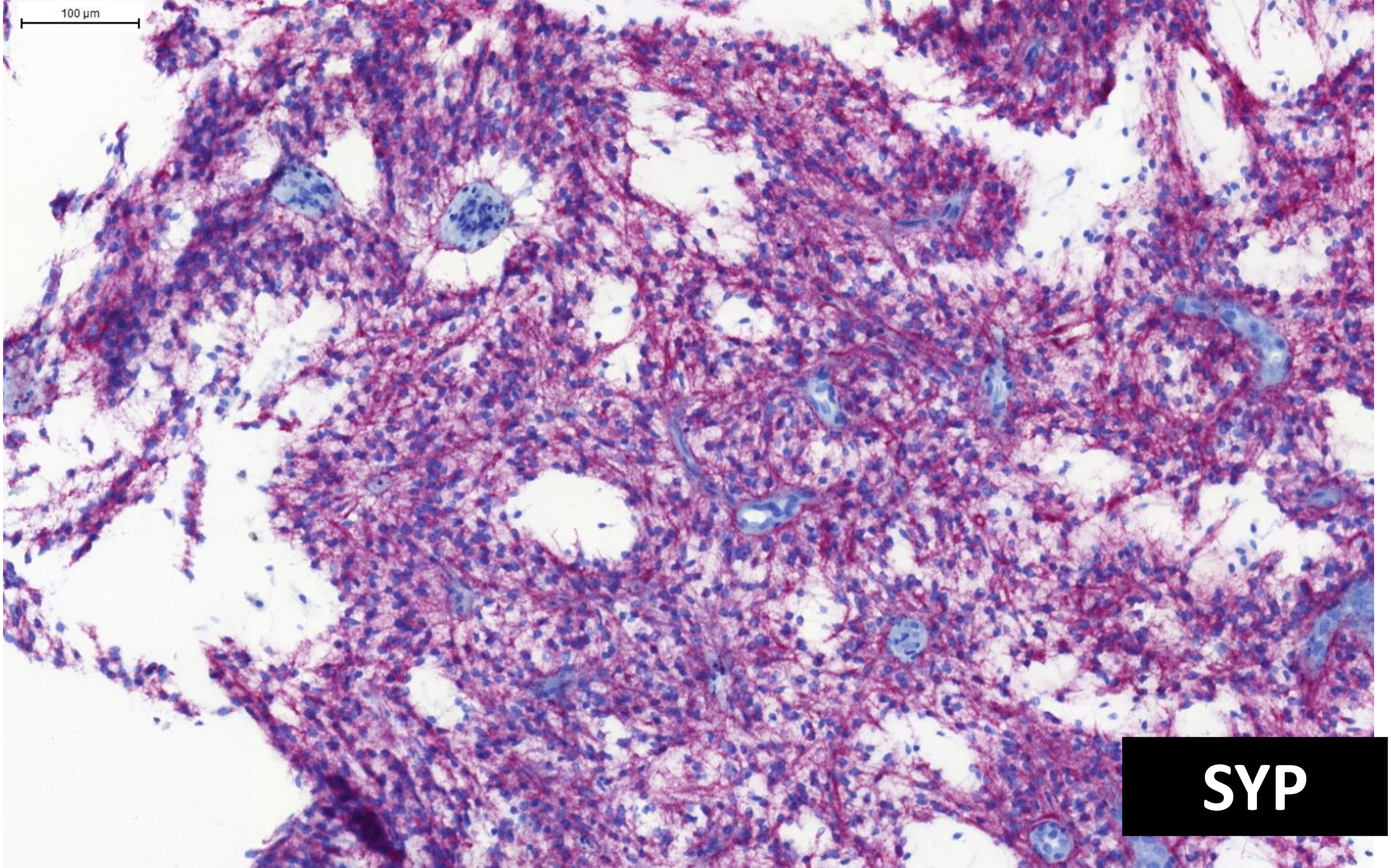
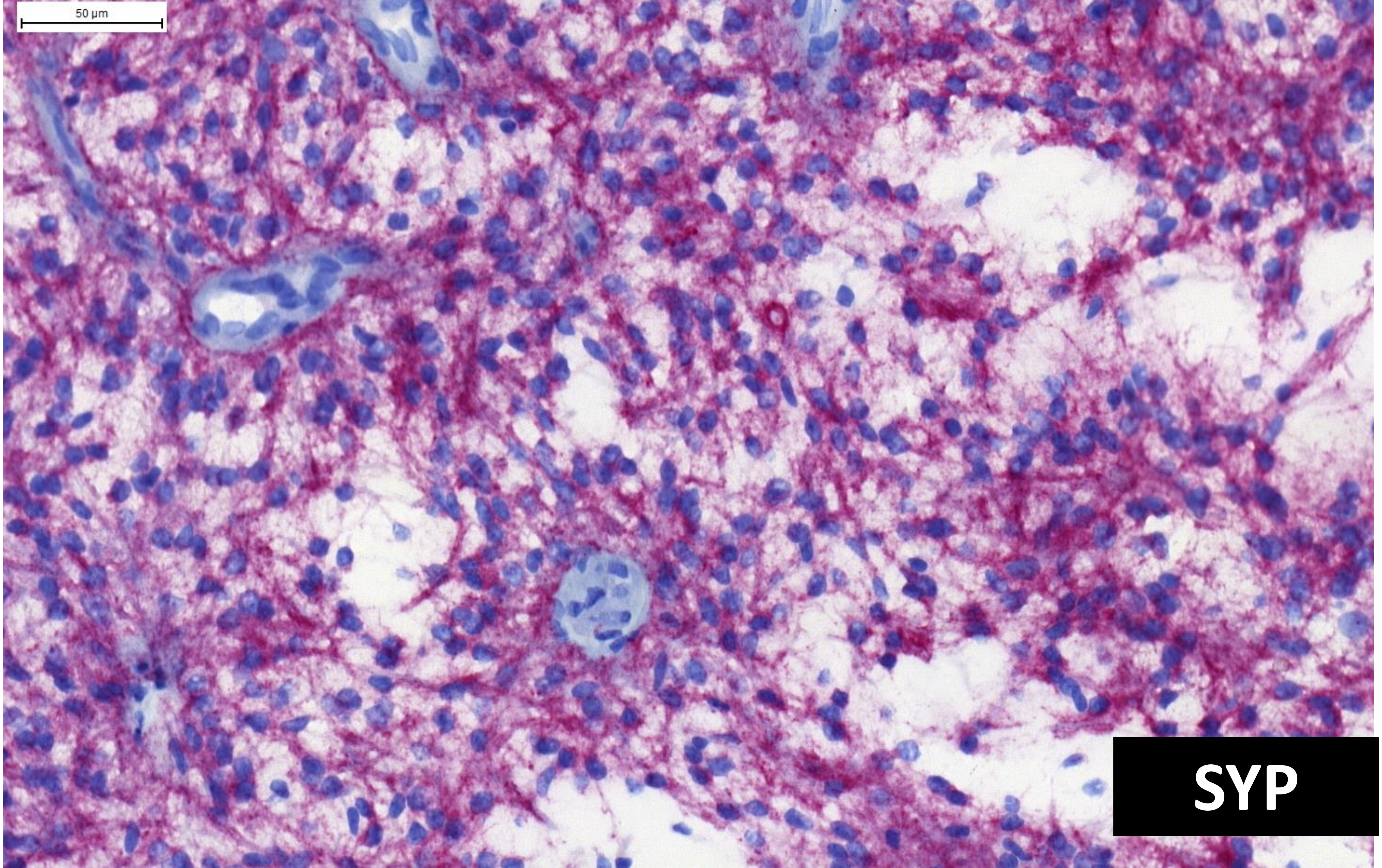
OLIG2


100 µm
SYP


50 µm
SYP

IMUNO

- Olig2, SOX10 a SYP difúzne pozitívne
- NF a Neu-N negatívne
- IDH1 negatívne
- K27M negatívne
- Mib-1 < 1%

Genetika

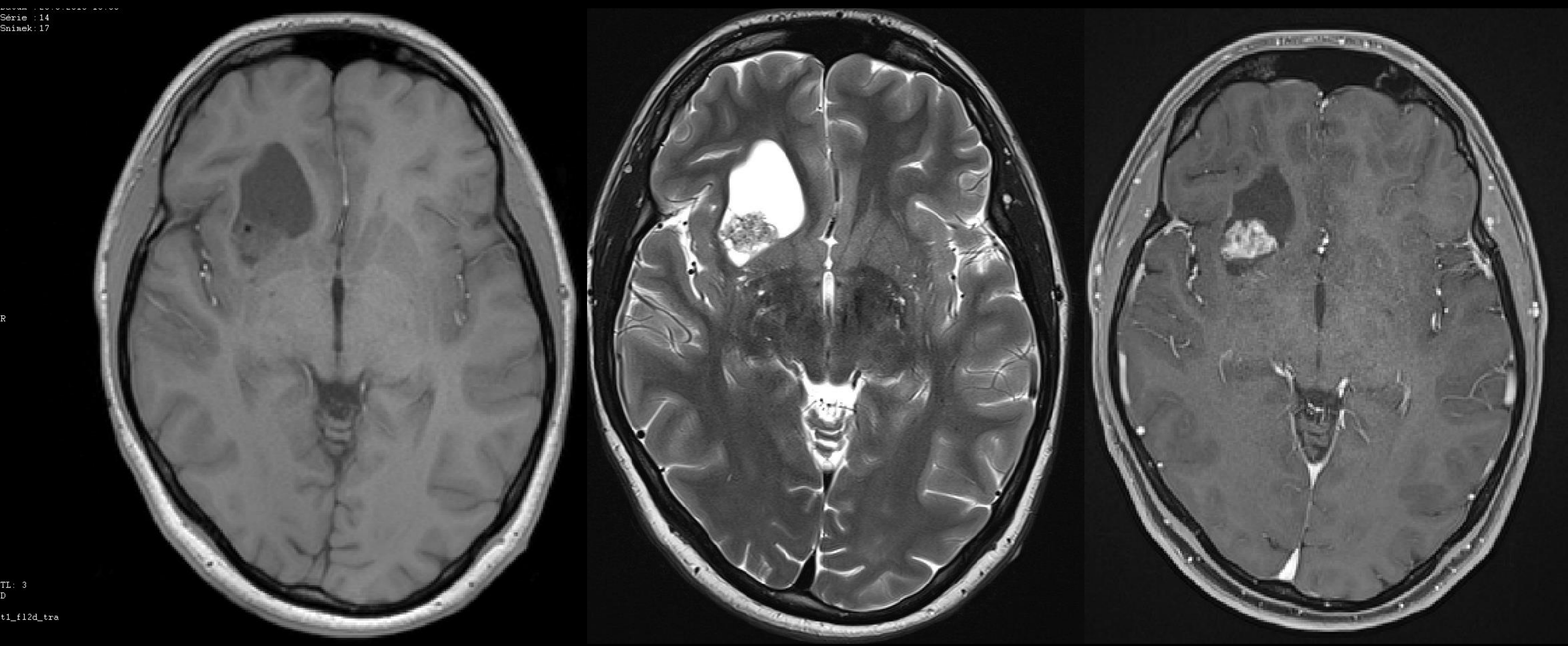
- KIAA1549-BRAF – negatívne
- Del 1p/19q – negatívne
- **Mutácia FGFR-1**

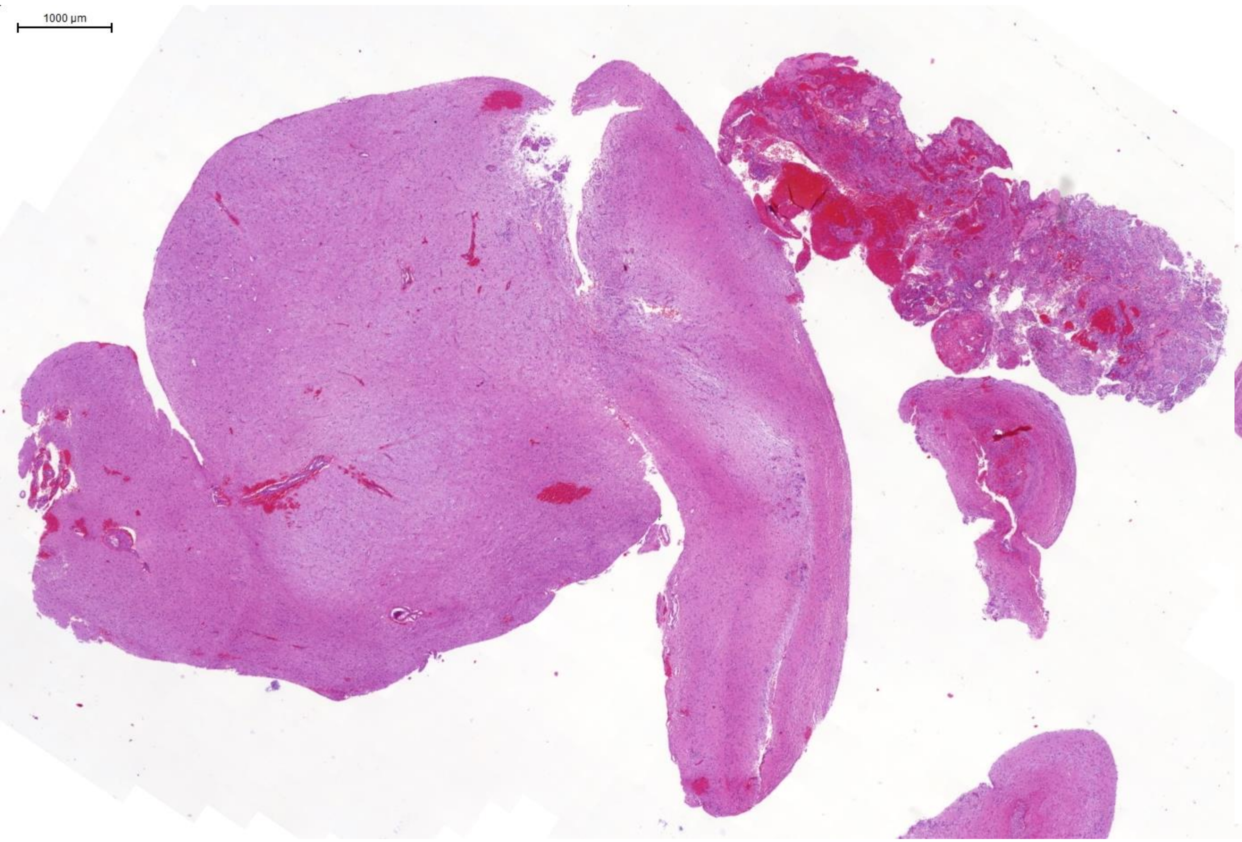
Diffuse leptomeningeal glioneuronal tumor

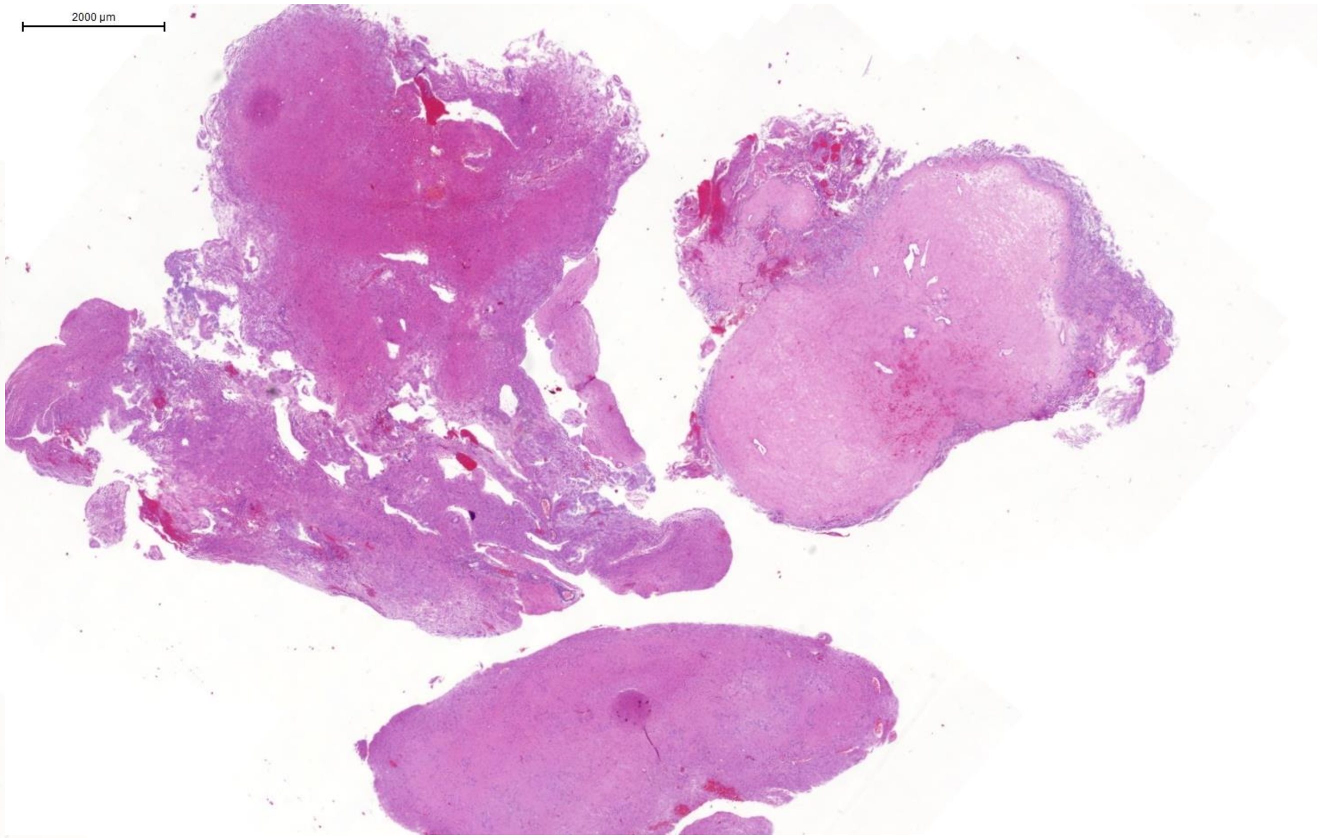
- Popísaný 1 prípad agresívneho tumoru s H3 K27M mutáciou (+ ***FGFR1***, *ATRX*, ...)
- .... Dif dg. leptomeningeálna diseminácia oligodendrogliómu, pilocytického astrocytómu alebo difúzneho astrocytómu

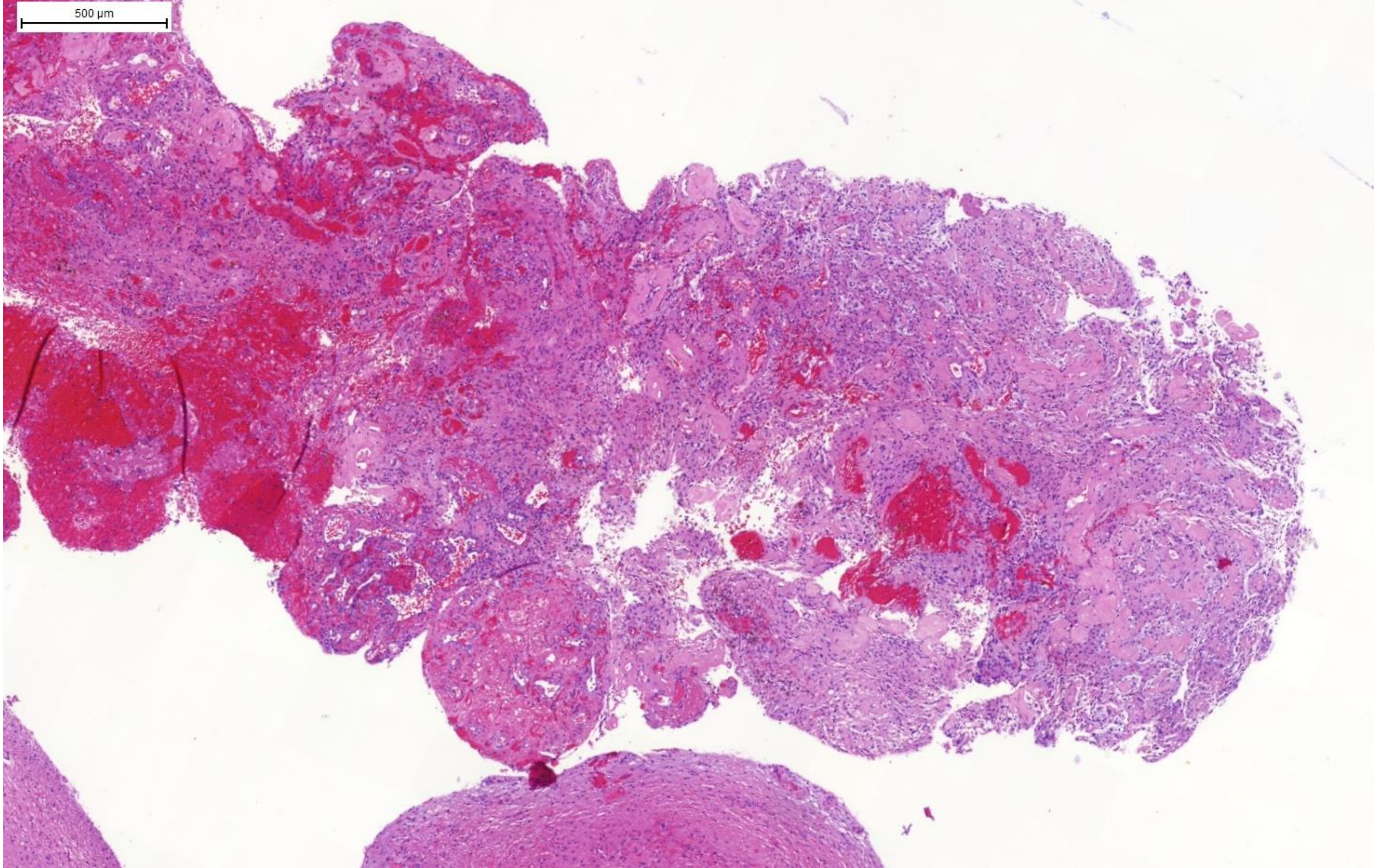
Prípad č. 5

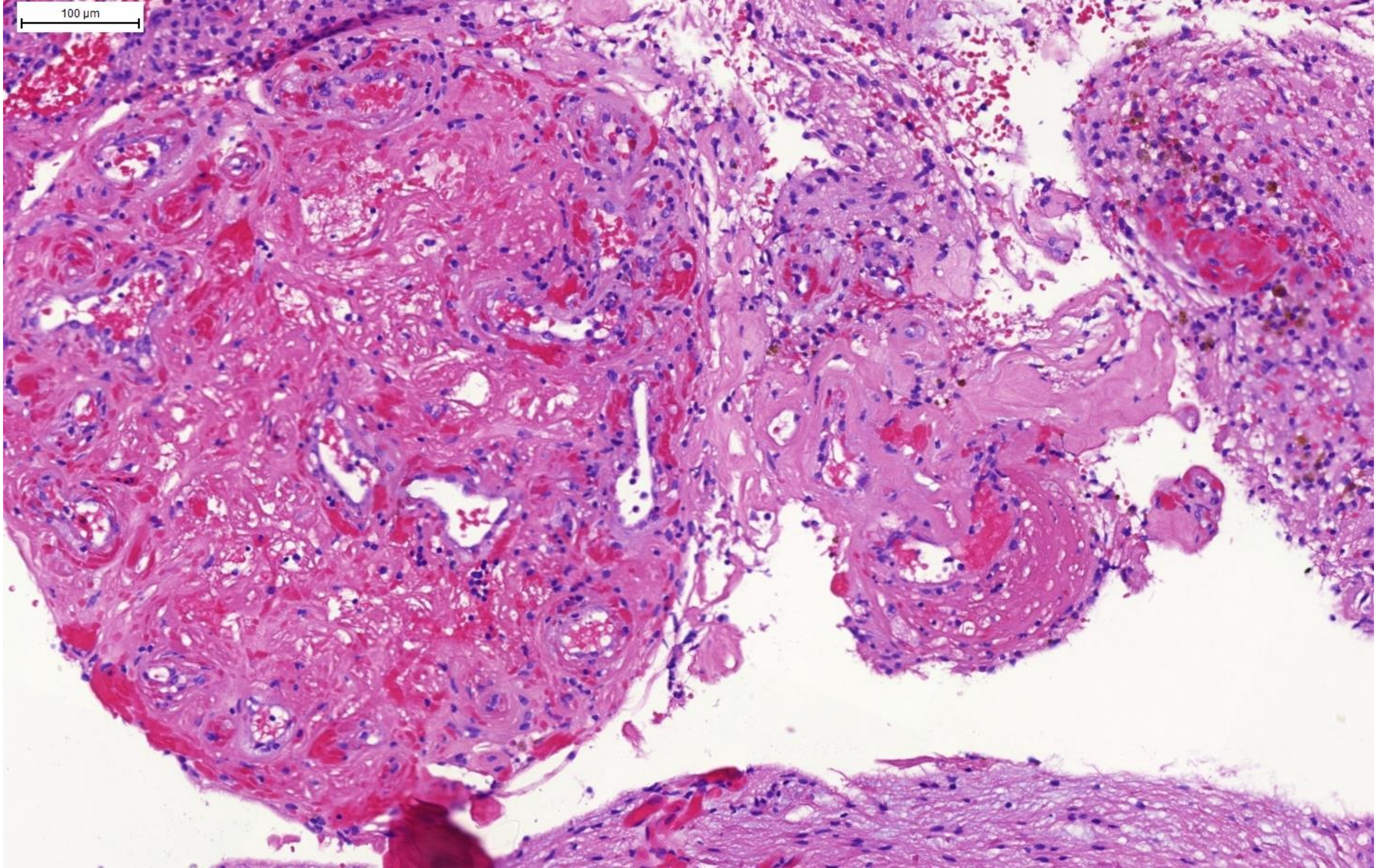
- 19-ročný muž
- v rozšírenom frontálnom rohu pravej postrannej komory je solídno-cystický tumor 45 x 39 x 23 mm
- pravdepodobne sa jedná o SEGA

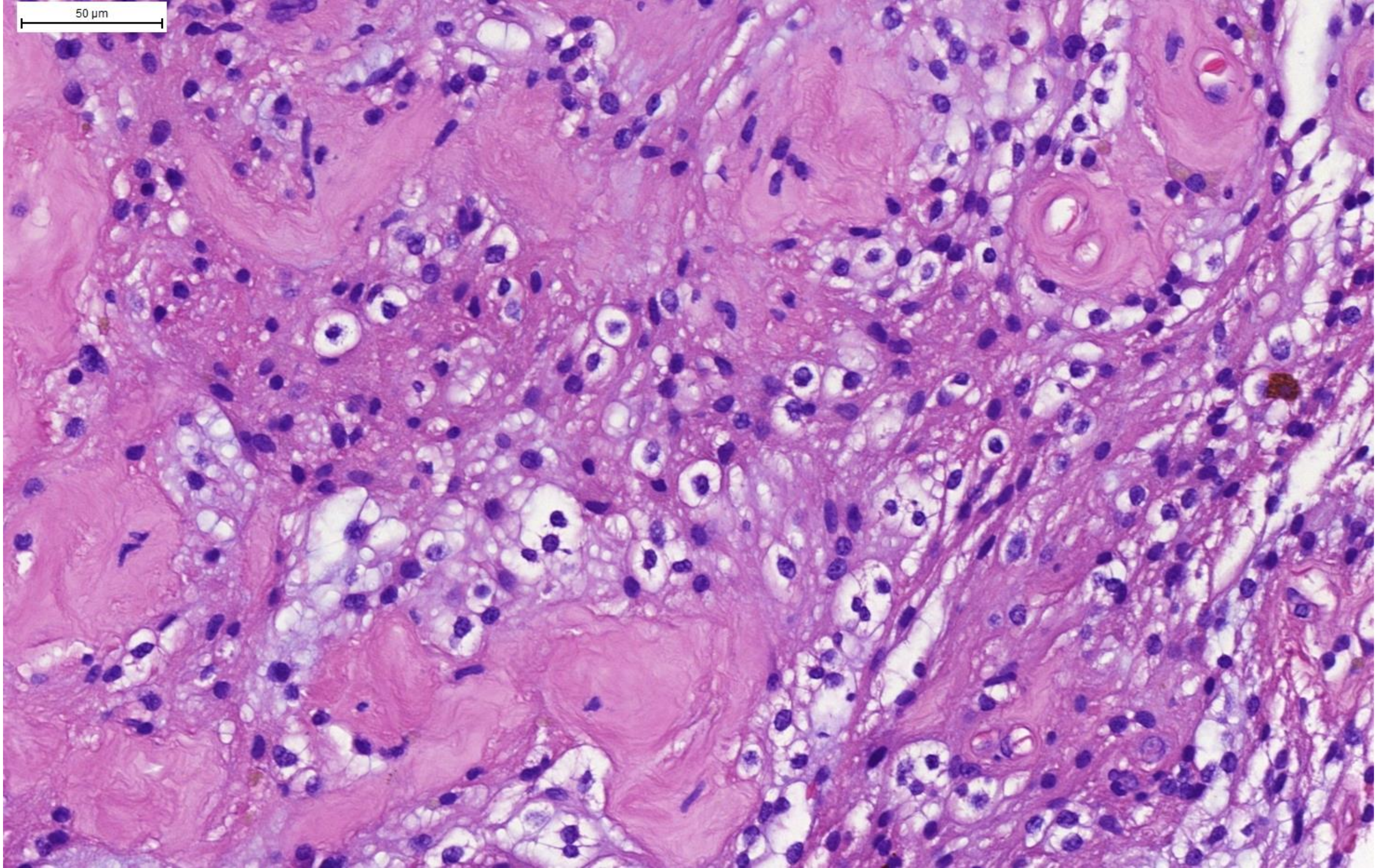

Série : 14
Snímek: 17
R
TL: 3
D
t1_fl2d_tra


1000 µm


2000 µm


500 µm


100 µm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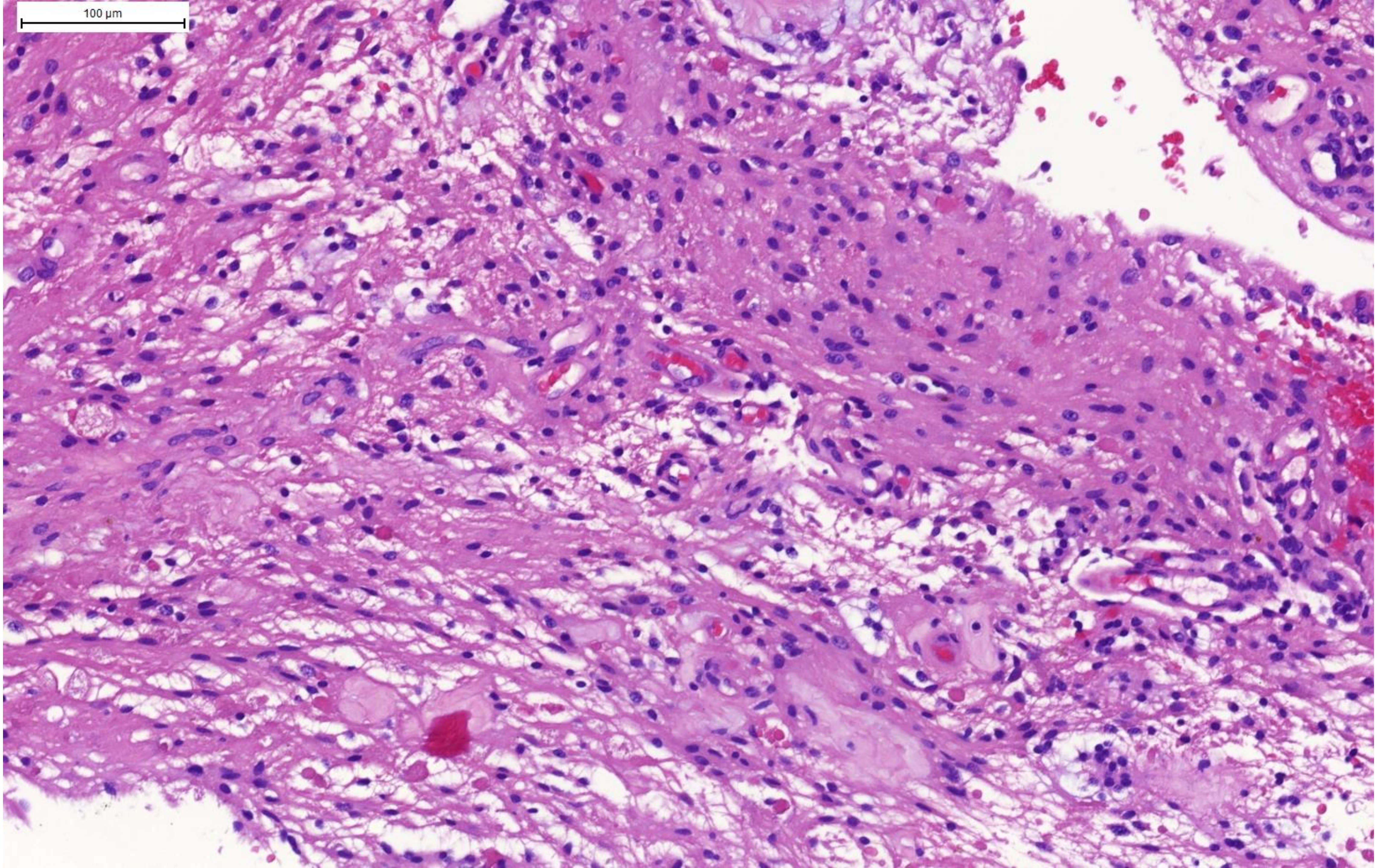
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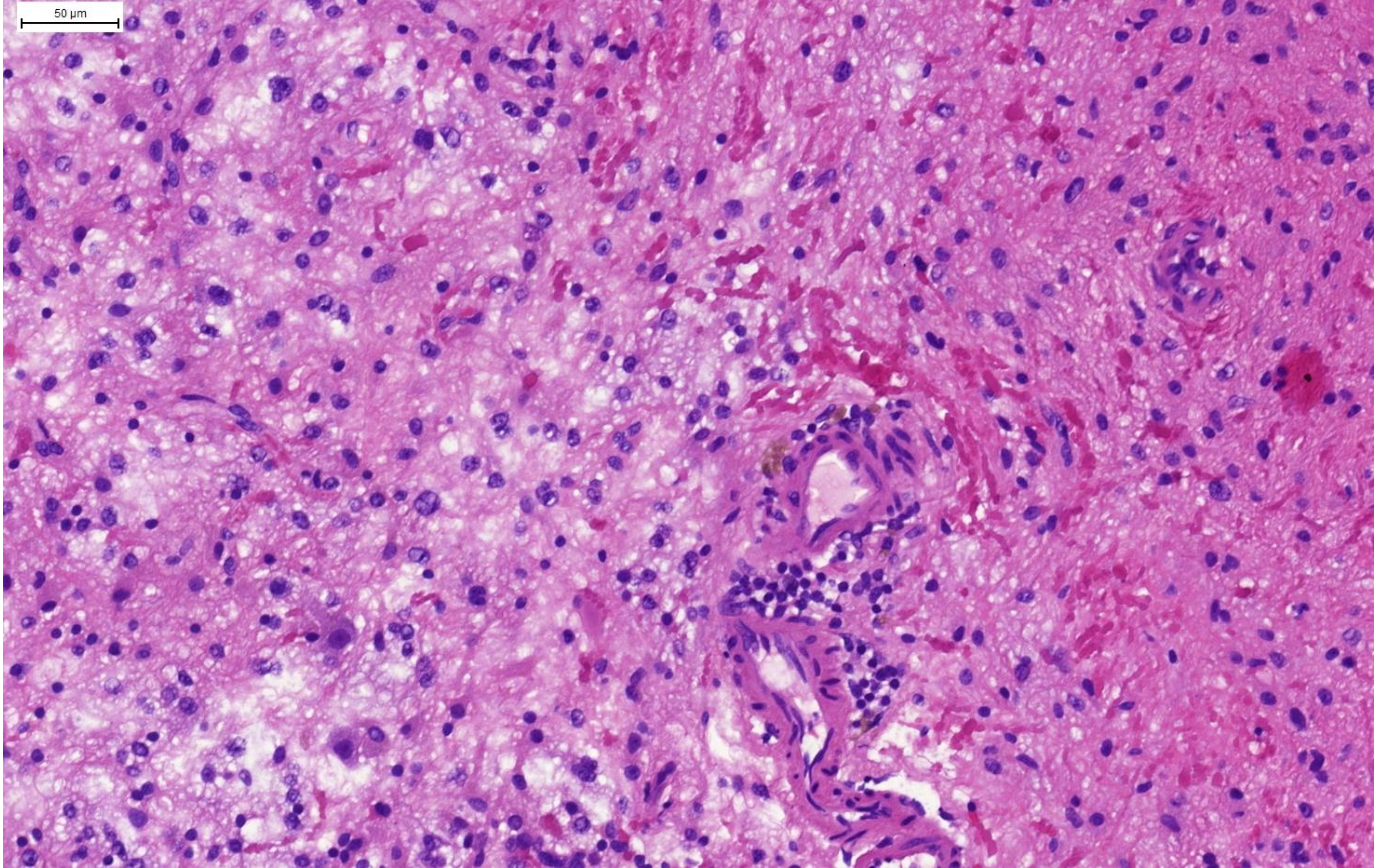
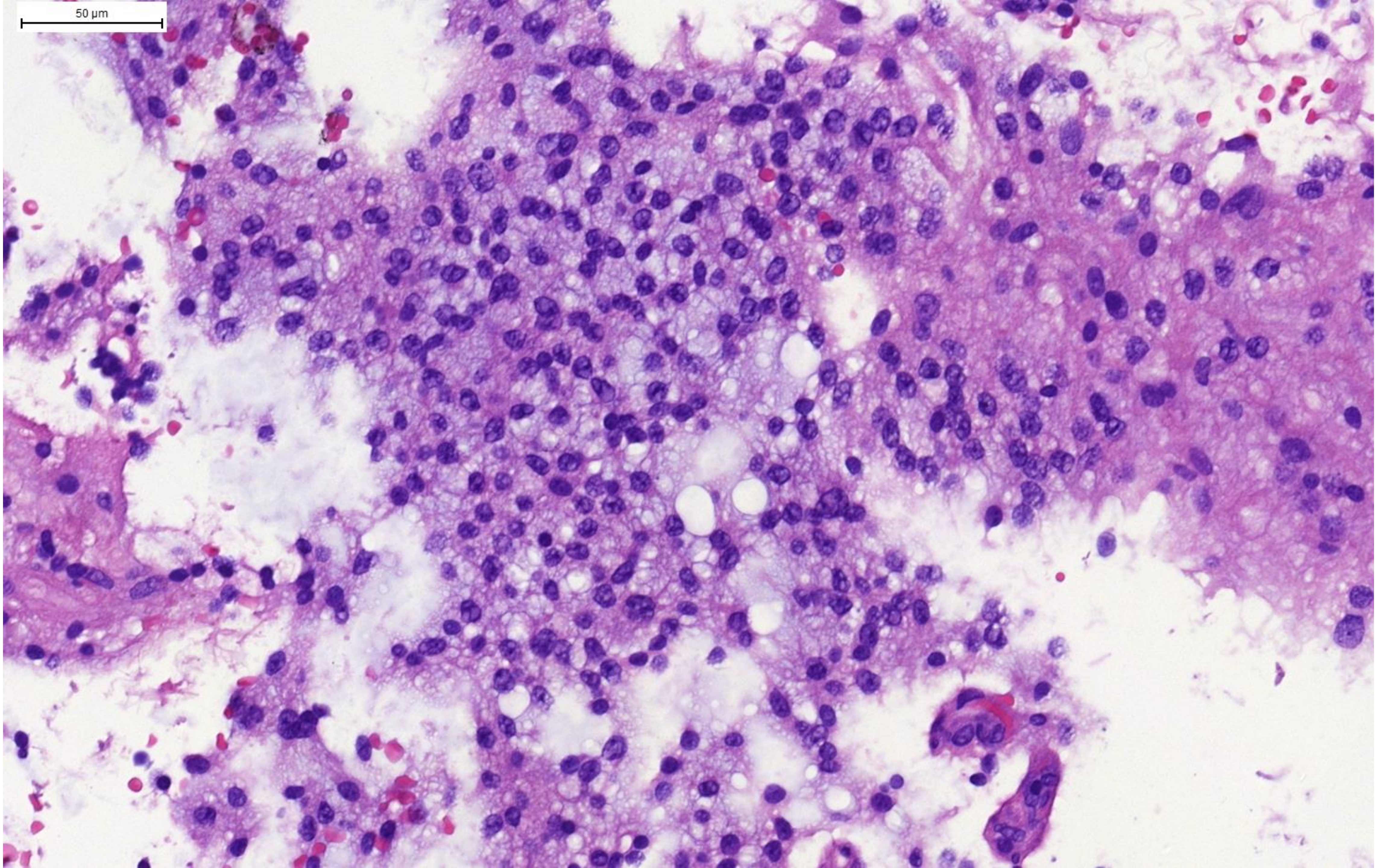
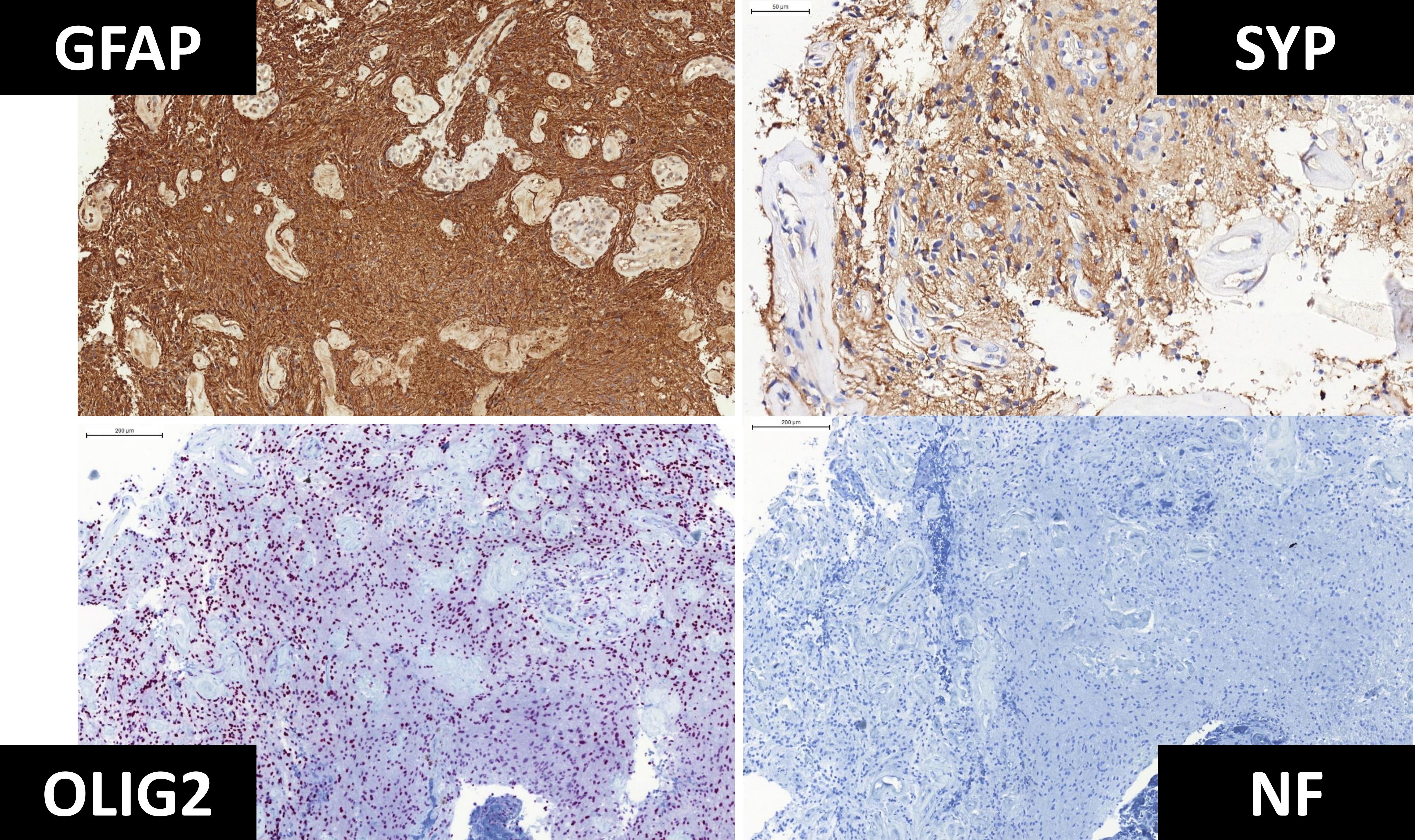

50 µm


50 µm


GFAP
50 µm
SYP
200 µm
200 µm
OLIG2
NF

DIAGNÓZA?

Genetika - NGS

- KIAA1549-BRAF negat
- bez fúzie/mutácie BRAF, FGFR1, NTRK

- Fúzia *RAF1-TRIM2*
- bez del 1p a del 19q

Pilocytický astrocytóm

(fúzia *RAF1-TRIM2* doposiaľ nebola popísaná)

Table 2.01 Genetic alterations affecting the MAPK pathway in pilocytic astrocytomas and their diagnostic utility; adapted from Collins VP et al. {482}

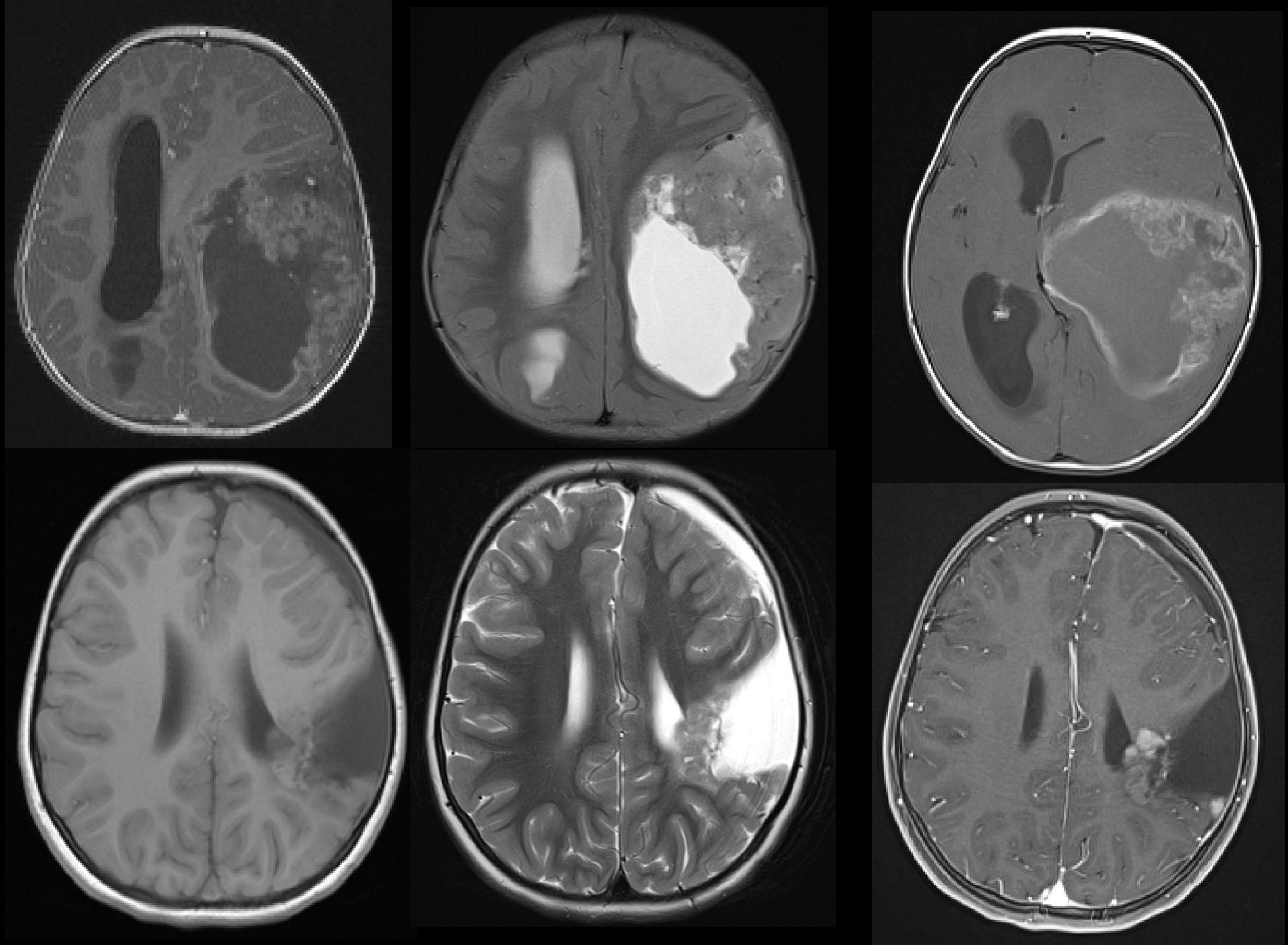
Gene	Change	% of tumours	Diagnostic utility	References
BRAF and *KIAA1549*	Tandem duplications resulting in KIAA1549-BRAF fusion proteins, all having the BRAF kinase domain and with the BRAF N-terminal regulatory domain replaced by the N-terminal end of KIAA1549	> 70%	Common in pilocytic astrocytomas, particularly cerebellar; rare in other tumour forms	{1176,1178,2
BRAF and various other genes	Deletions or translocations resulting in BRAF fusion proteins, all having the BRAF kinase domain and with the BRAF regulatory domain replaced by the N-terminal part of another gene	~5%	Occur in pilocytic astrocytomas; extremely rare in other entities	{1176,2855}
BRAF	V600E mutation	~5%	Occurs mainly in supratentorial pilocytic astrocytomas; also in gangliogliomas, pleomorphic xanthoastrocytomas, and dysembryoplastic neuroepithelial tumours	{1176,2855}
NF1	Loss of wild type and retained inherited mutation	~8%	Typically germline; closely associated with optic pathway pilocytic astrocytoma	{1176,2855}
FGFR1	Mutation	< 5%	Found mainly in midline pilocytic astrocytomas; frequency not established in other entities	{1176,2855}
FGFR1	Fusions / internal tandem duplication	< 5%	Rare in pilocytic astrocytoma; also observed in other low-grade gliomas	{1176,2855}
NTRK family	Fusions	~2%	Rare in pilocytic astrocytoma; frequency not established in other entities	{1176,2855}
KRAS	Mutation	Single cases	Rare in pilocytic astrocytoma; frequency not established in other entities	{1176,2855}
RAF1	Fusions with consequences similar to those of BRAF fusions, i.e. the loss of the regulatory domain and its replacement by the N-terminal end of SGRAP3	Single cases	Rare in pilocytic astrocytoma; frequency not established in other entities	{1176,2855}

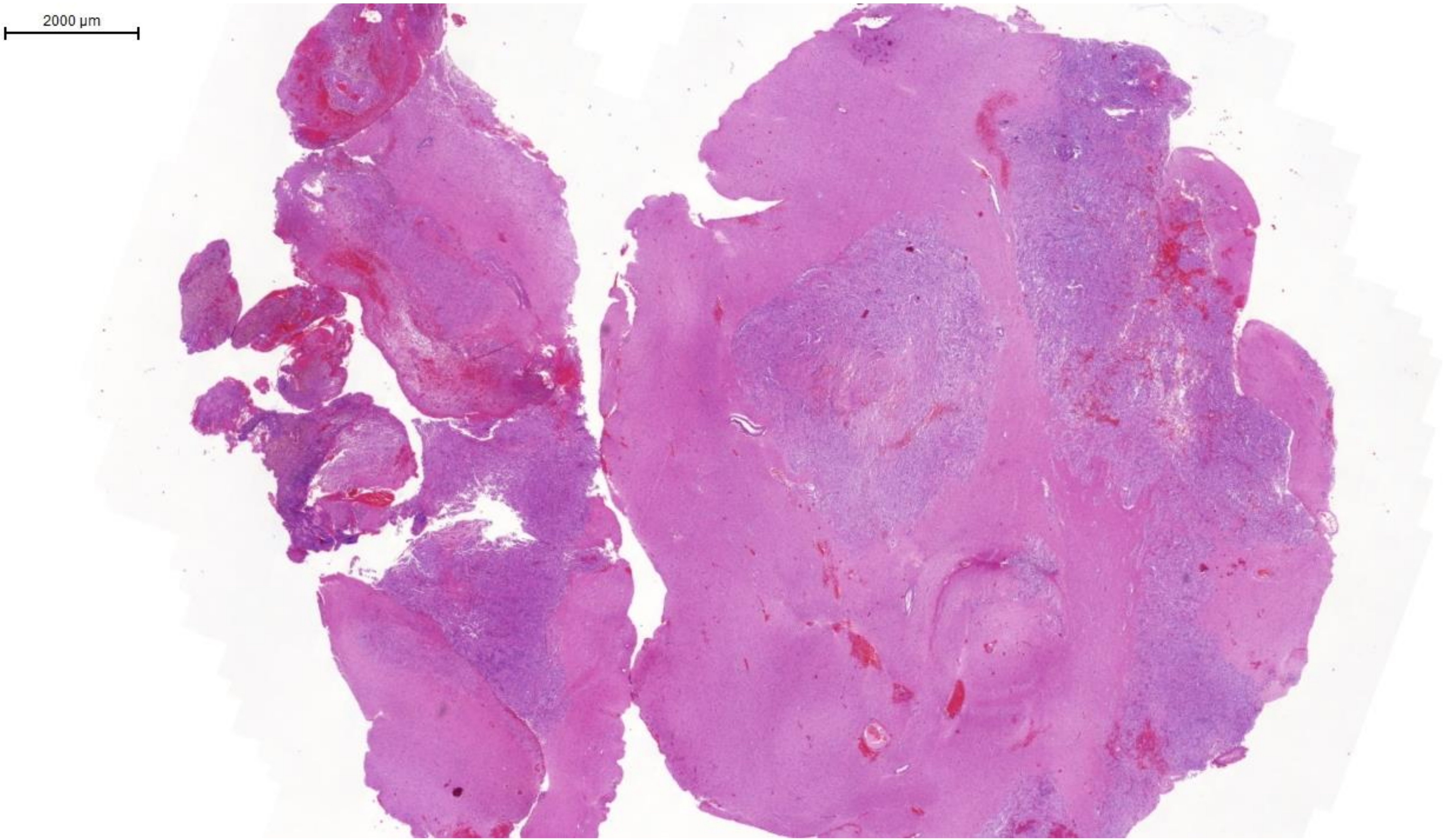
Prípad č. 6

- dievčatko, 1 rok a 7 mesiacov, glióm ľavej hemisféry (histologická diagnóza EPN grade III)
- resekcia a terapia podľa protokolu Infant Ependymoma 2004 CNS 2007 (VRC, Carboplatina, MTX, Cisplatina) - chemoterapia dokončená 2013
- reziduum/recidíva po 7. rokoch (vek 8 rokov a 7 mesiacov), periventrikulárne parietálne vľavo
- kompletná resekcia nádoru v 2 dobách

2011

2018

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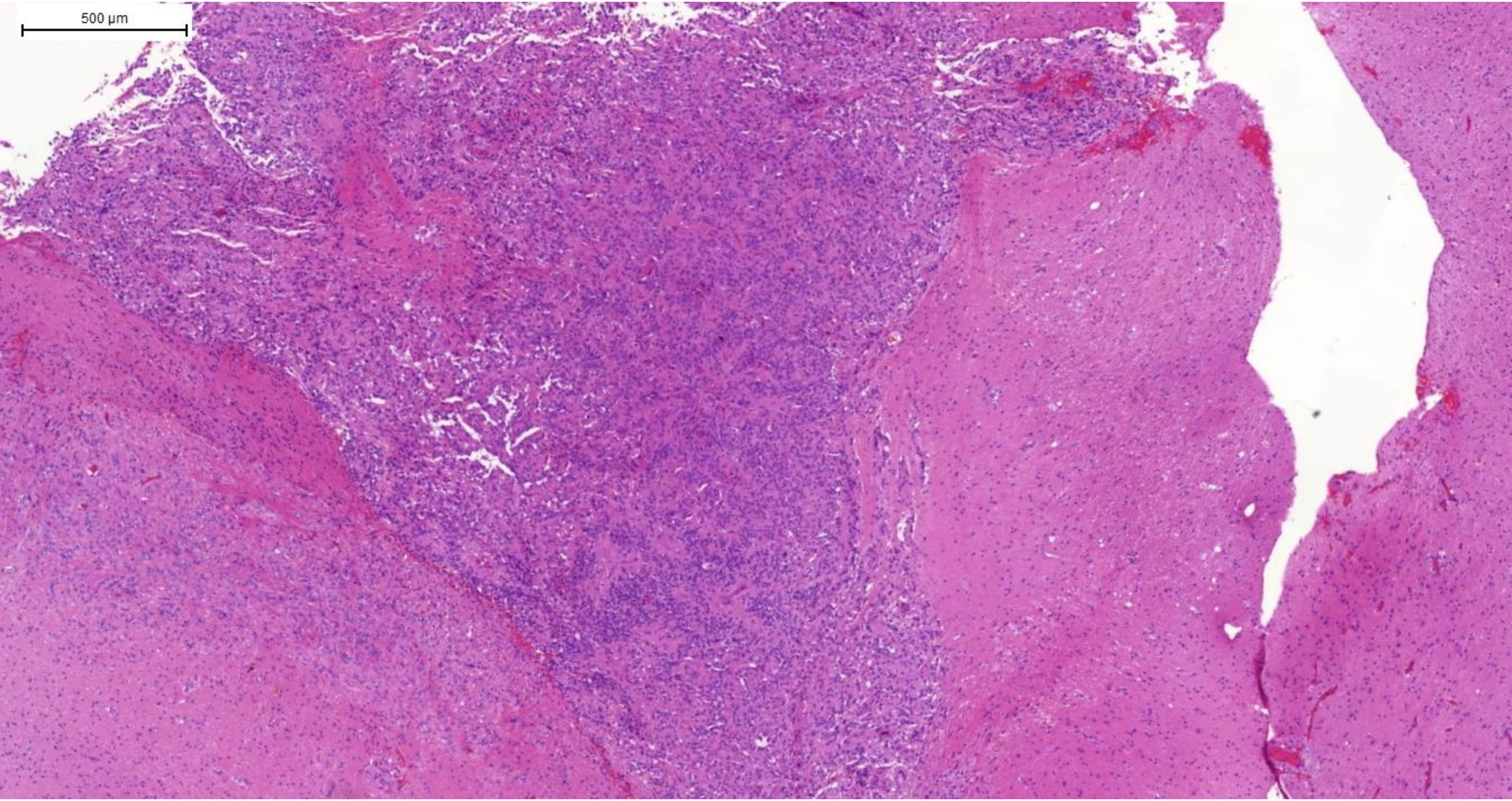
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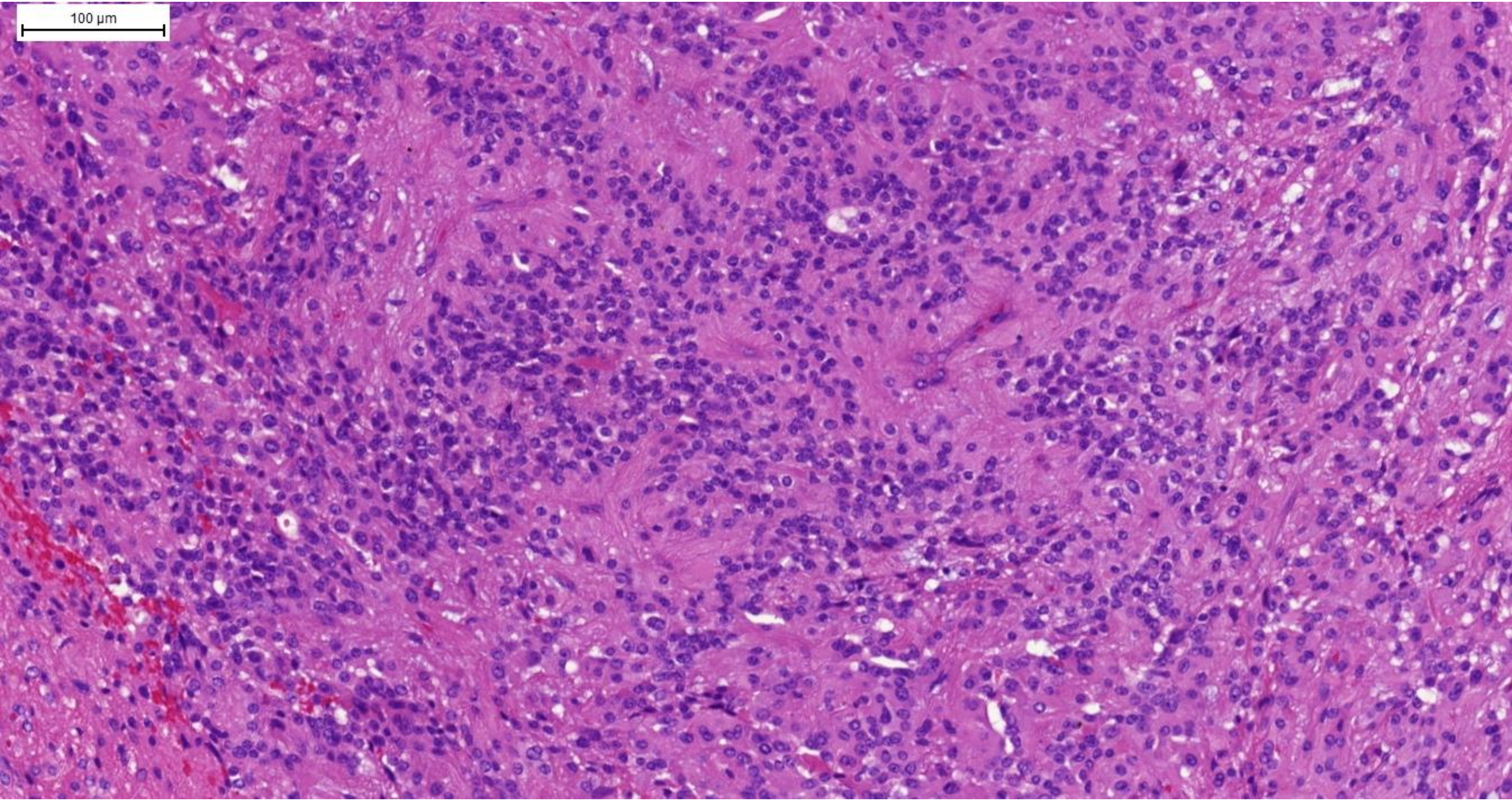
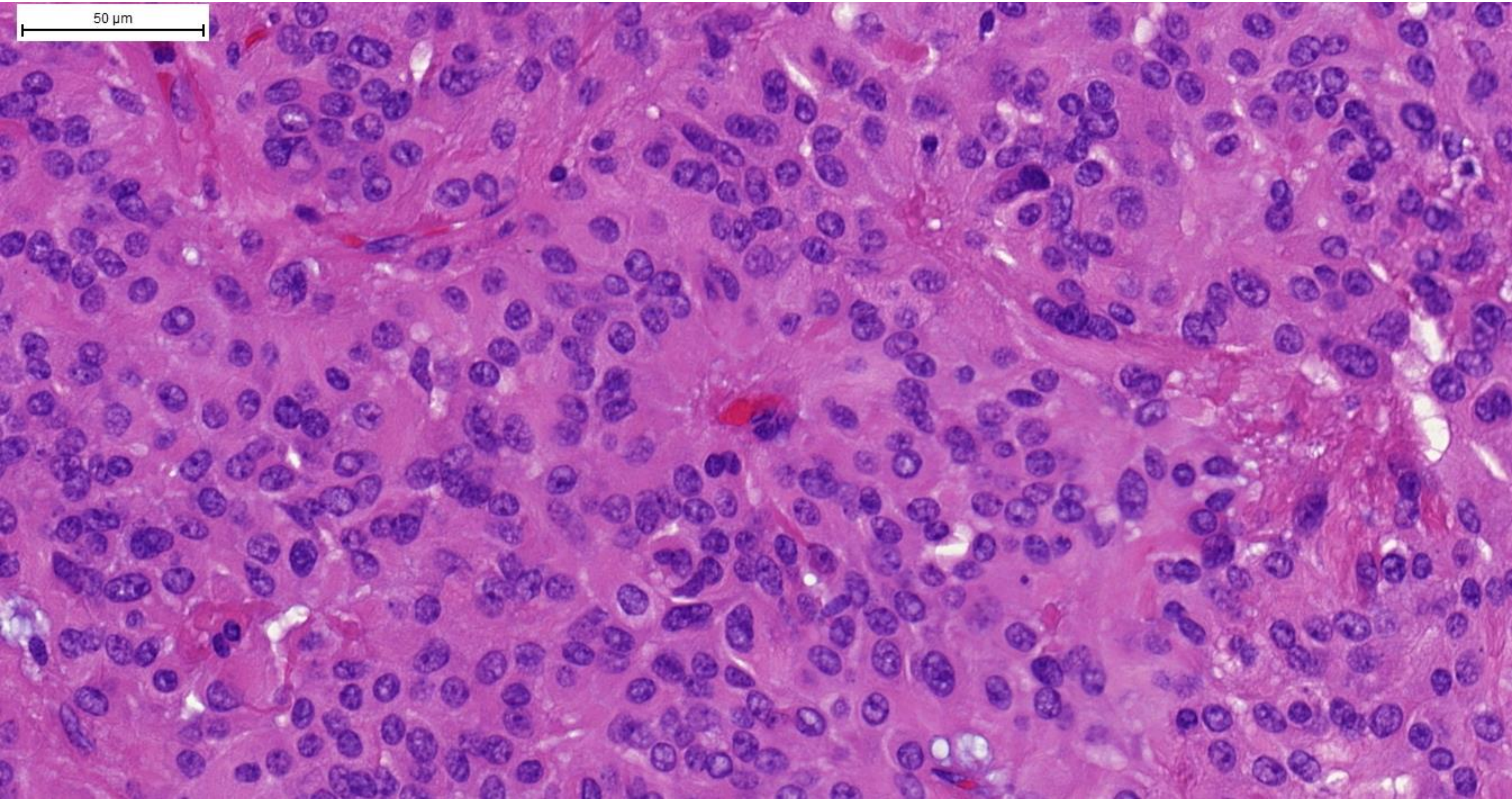
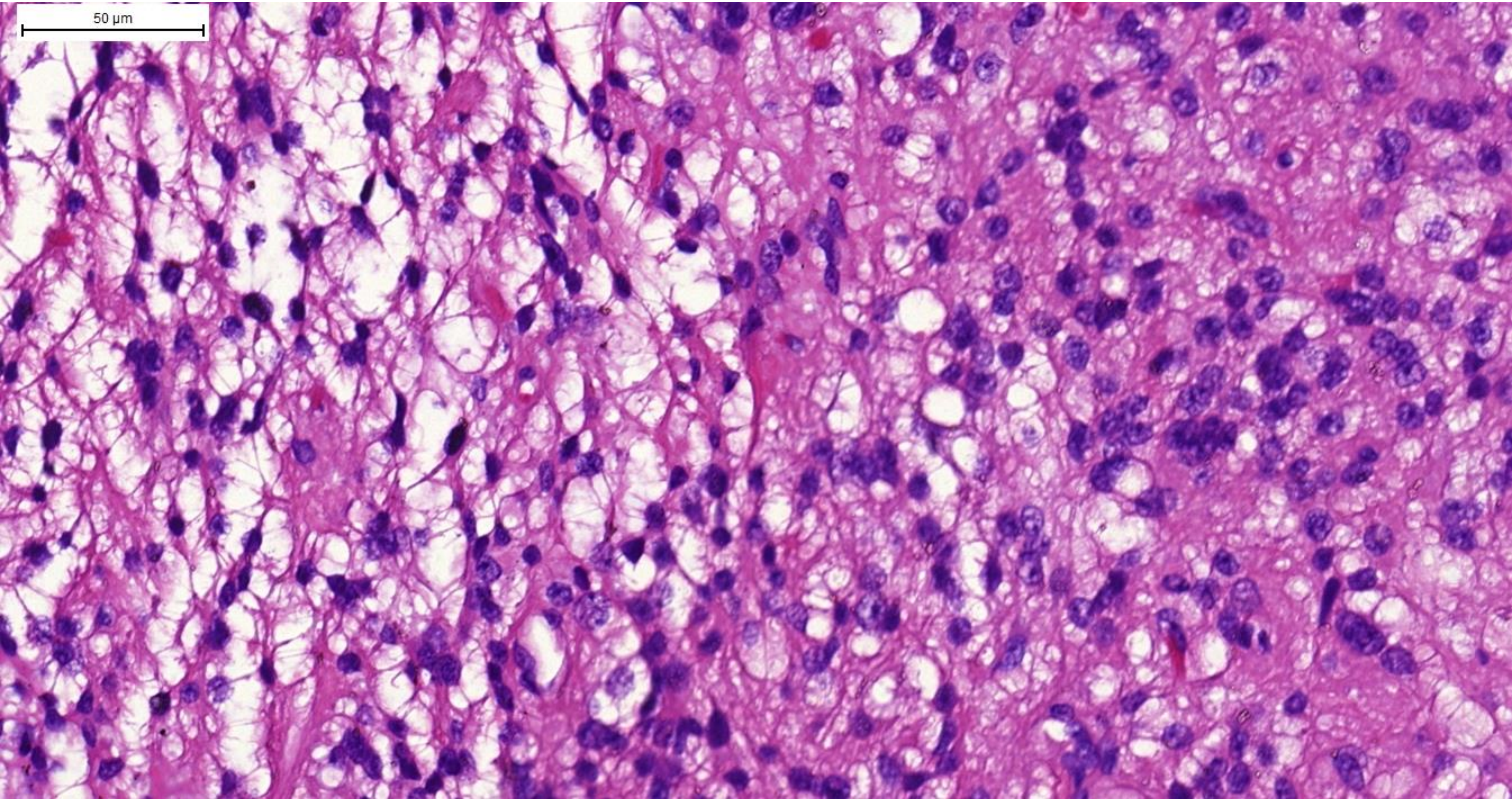

100 μm


50 µm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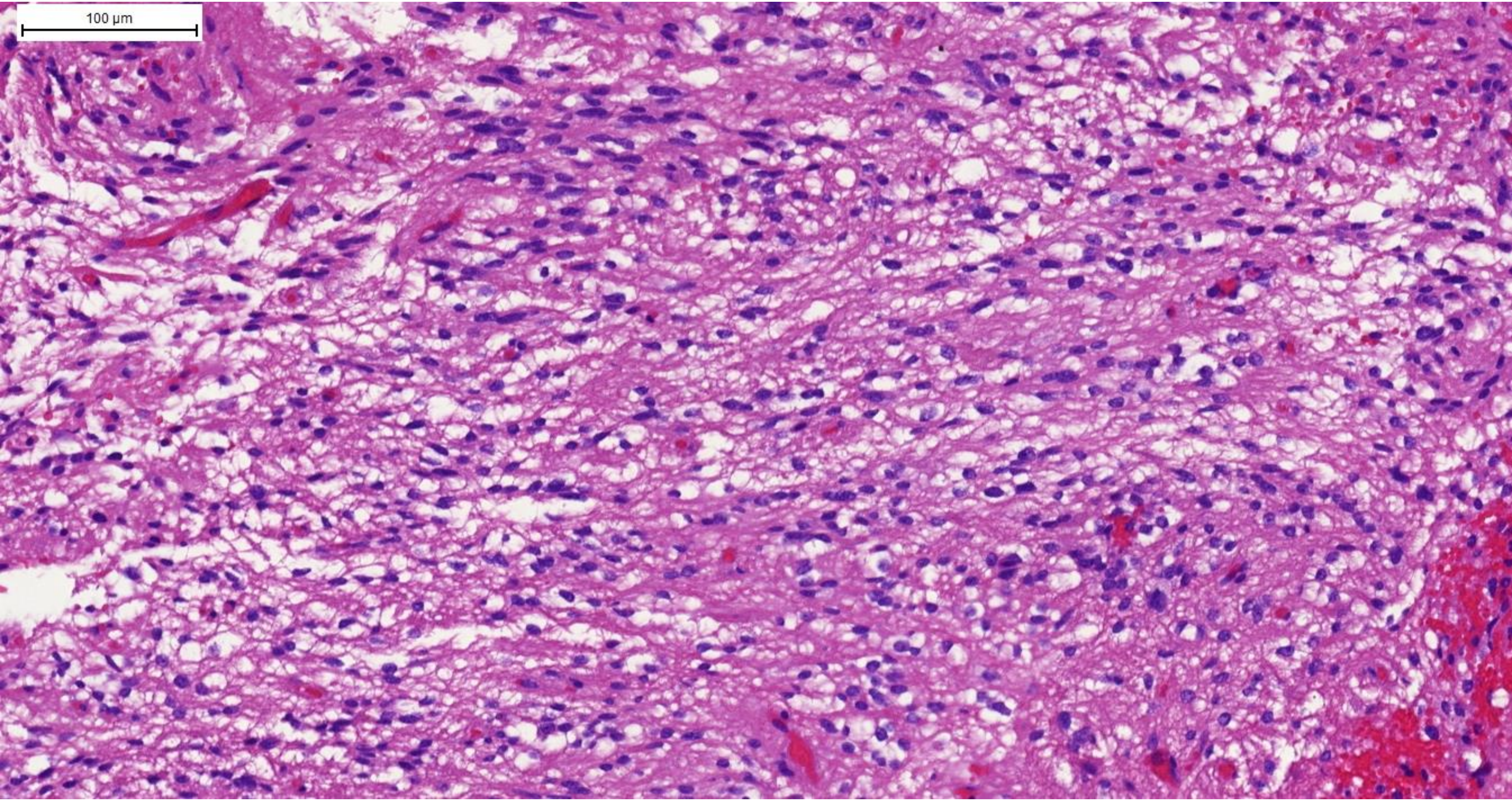
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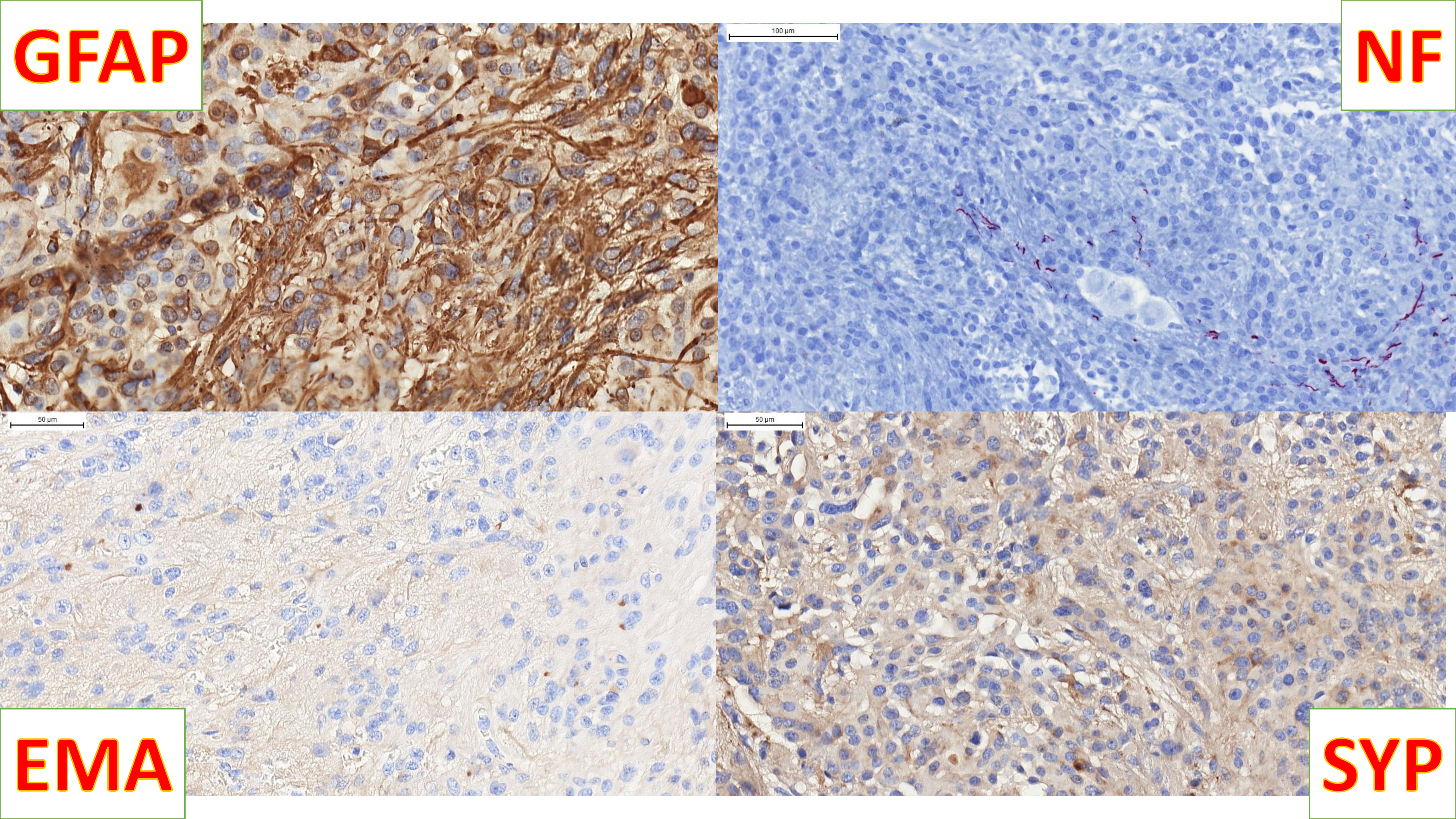

GFAP
NF
100 µm
EMA
50 µm
SYP
50 µm

DIAGNÓZA?

NGS

- *EWSR1-PLAGL1*
- bez *RELA* fúzie, žiadne iné aberácie...

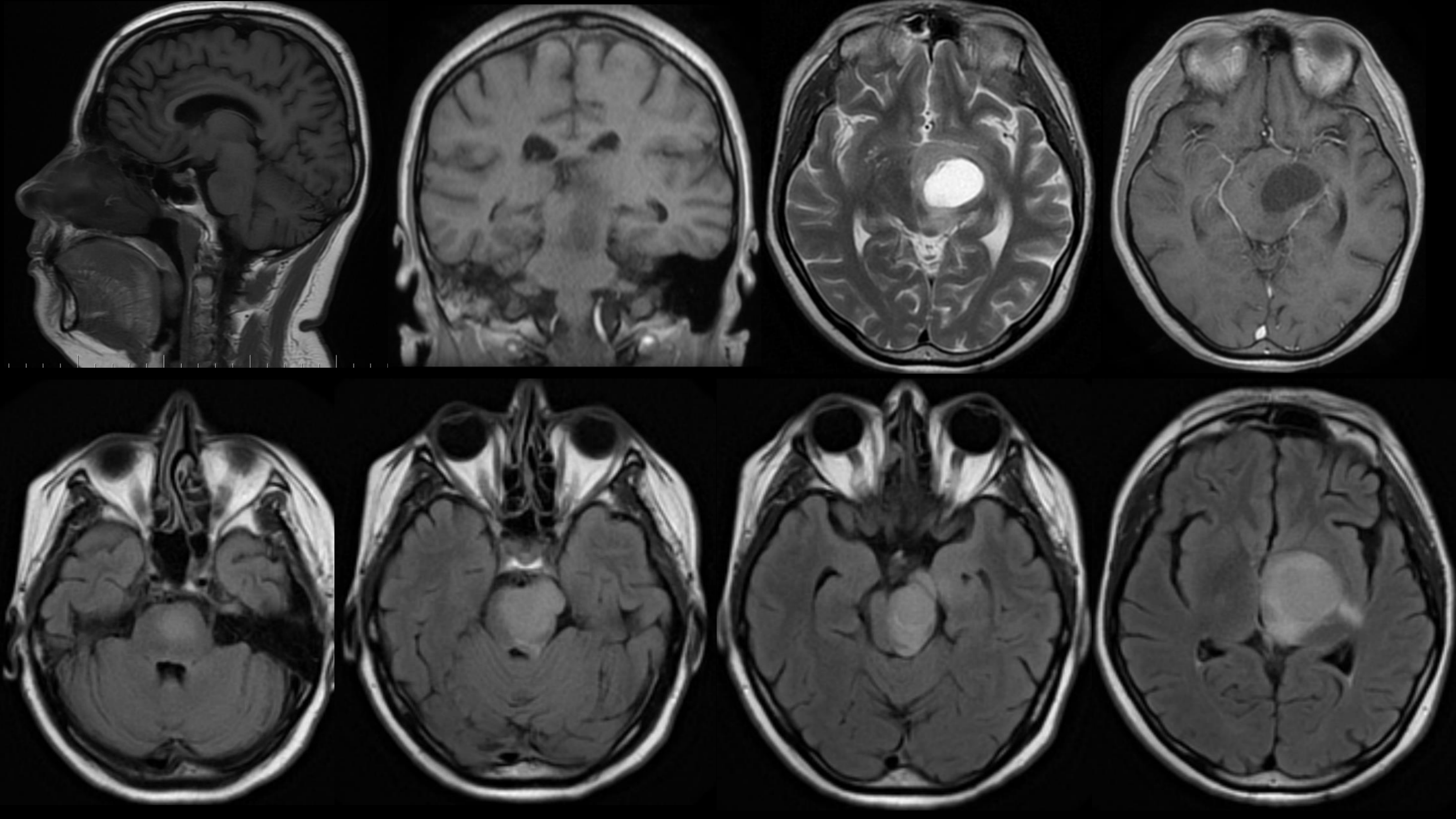
- Diagnóza???

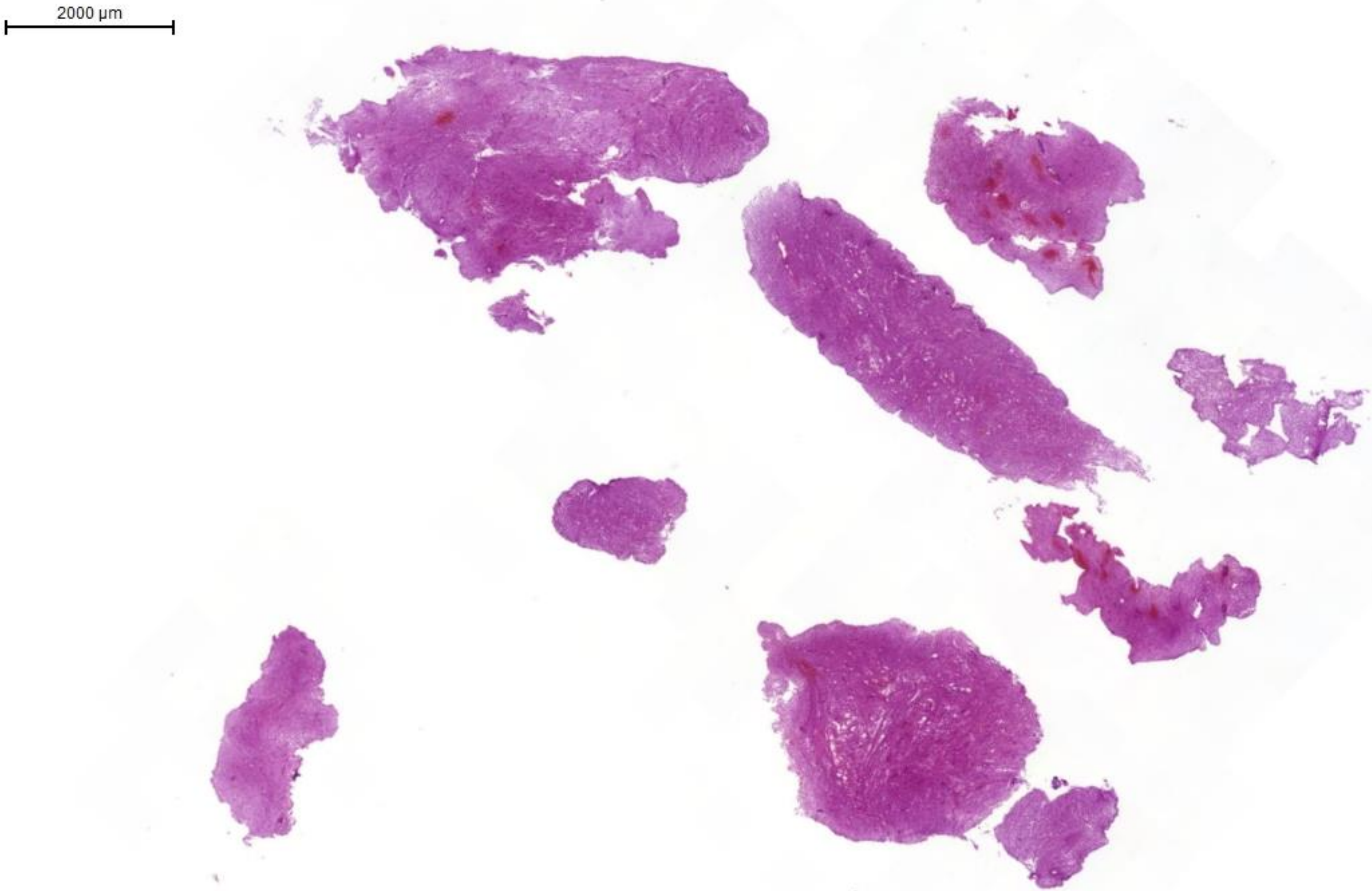
Iba deskriptívna:

„Ohraničene rastúci, low-grade (?) gliálny/glioneuronálny tumor s translokáciou *EWSR1-PALGL1,* NEC (not elsewhere classified)“

Prípad č. 7

- 38 ročná žena
- Tumor ponsu, mezencefala a temporálneho laloka vľavo
- Ožarovaná s klinickou diagnózou LG glióm kmeňa
- Konzultácia (Odd. patológie UNLP Košice)

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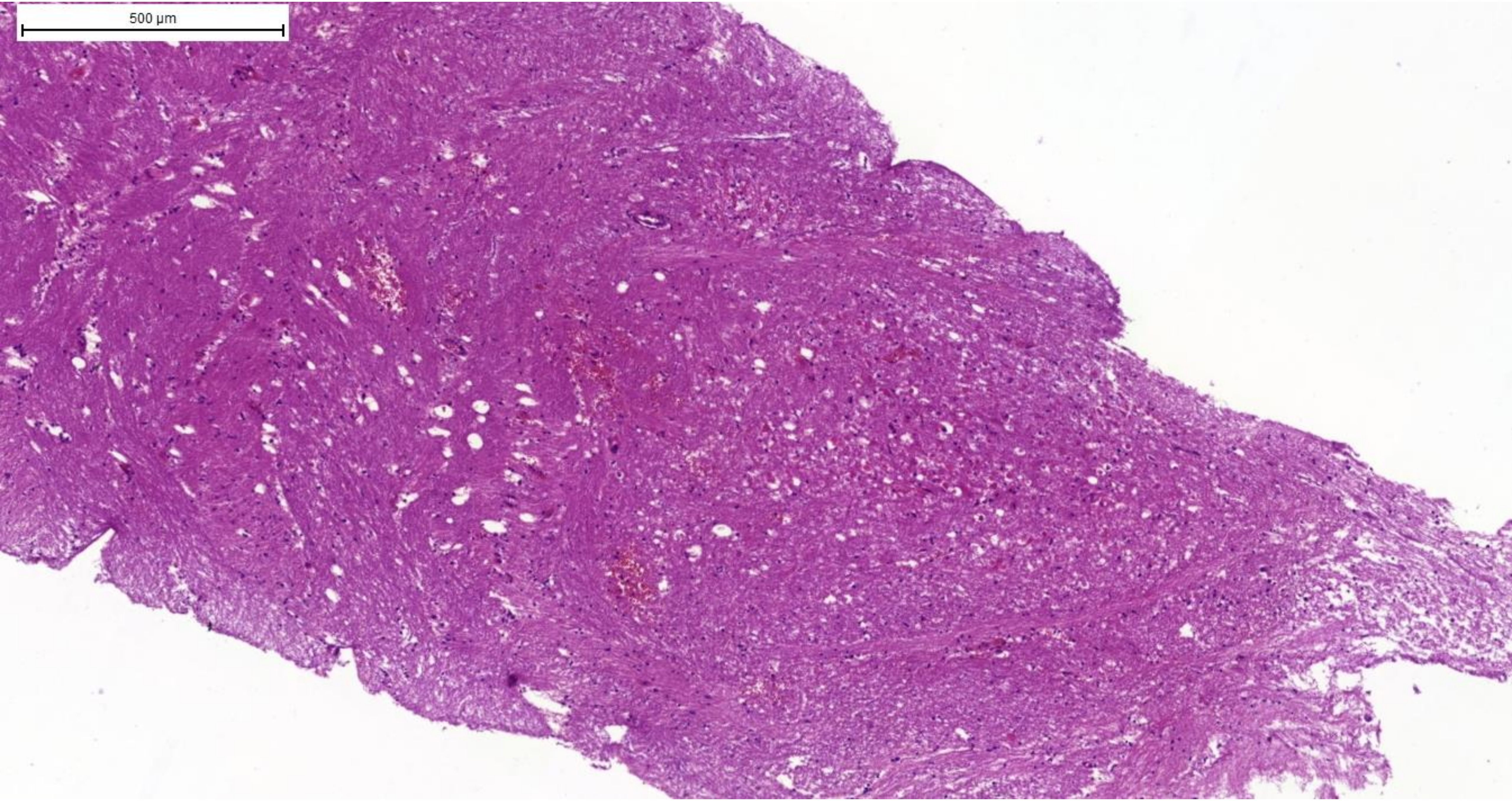
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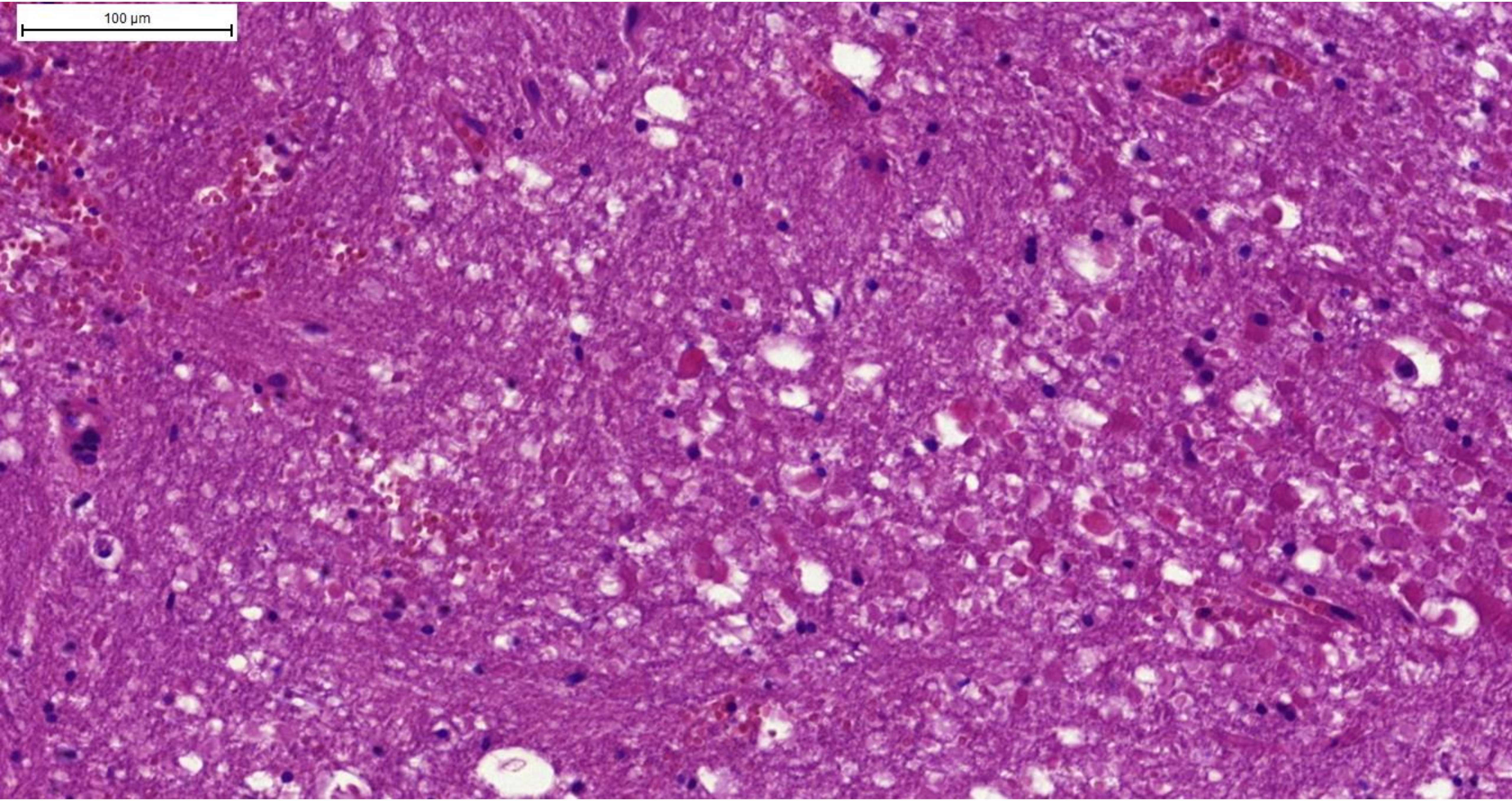
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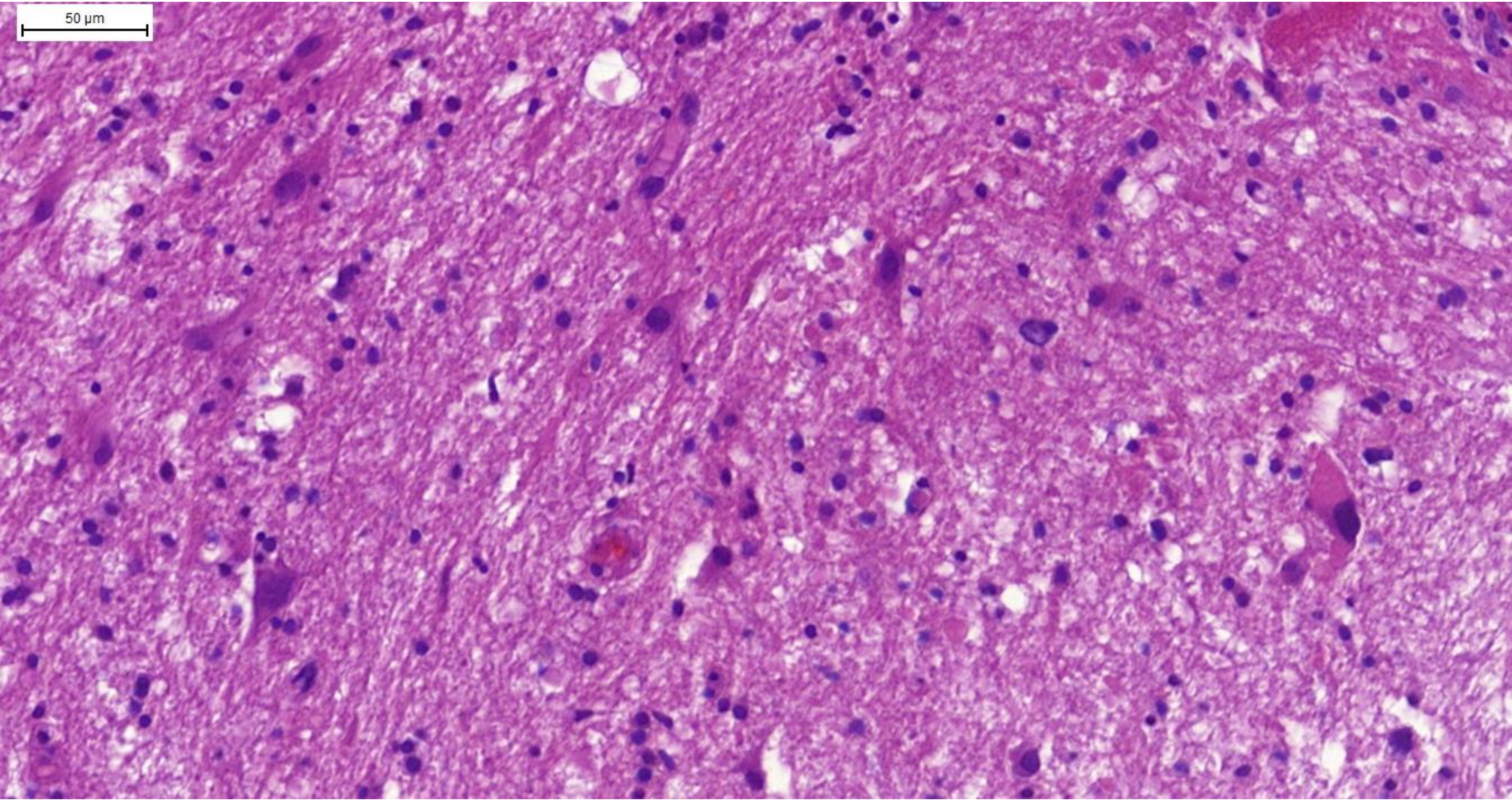
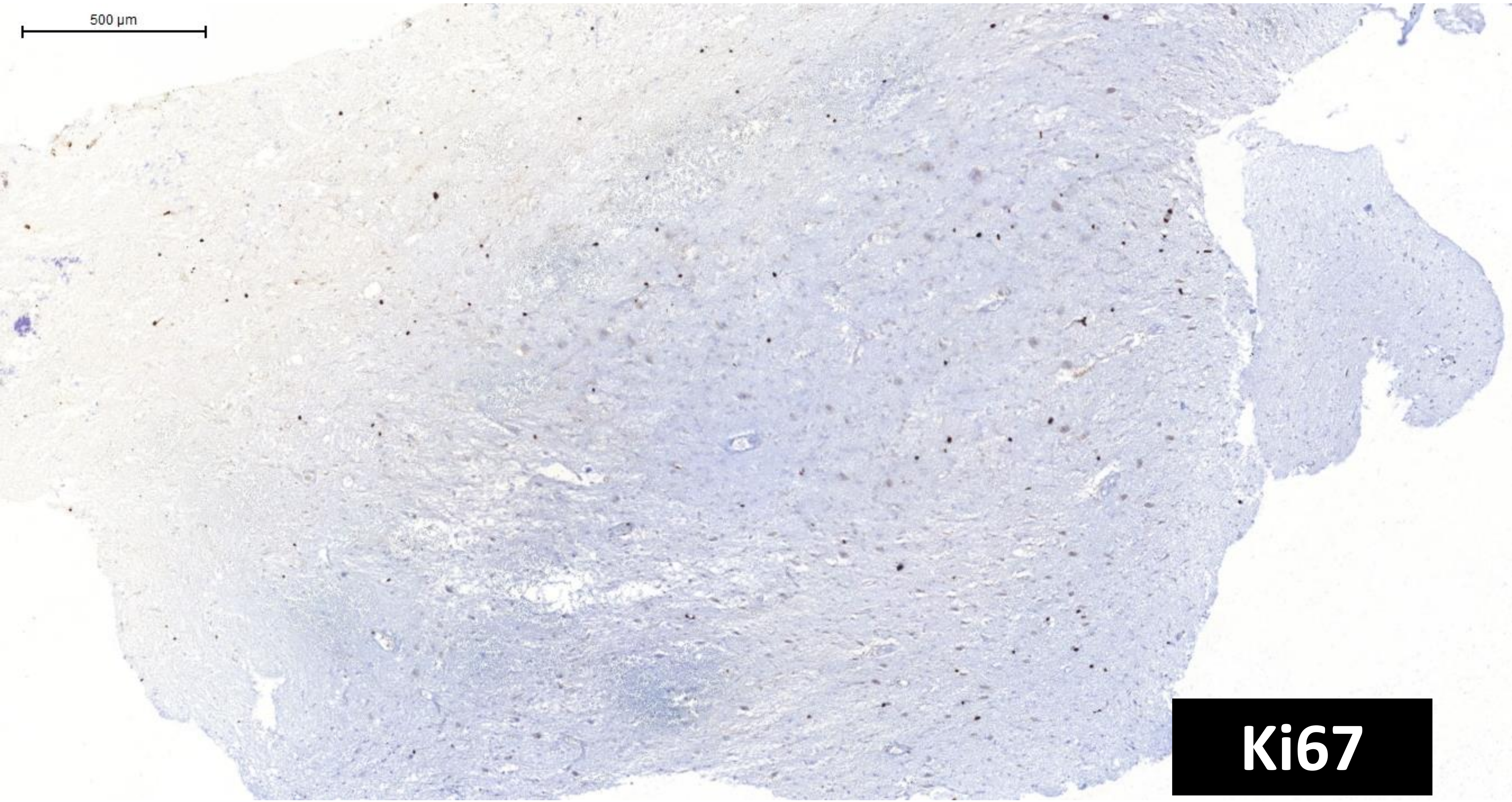
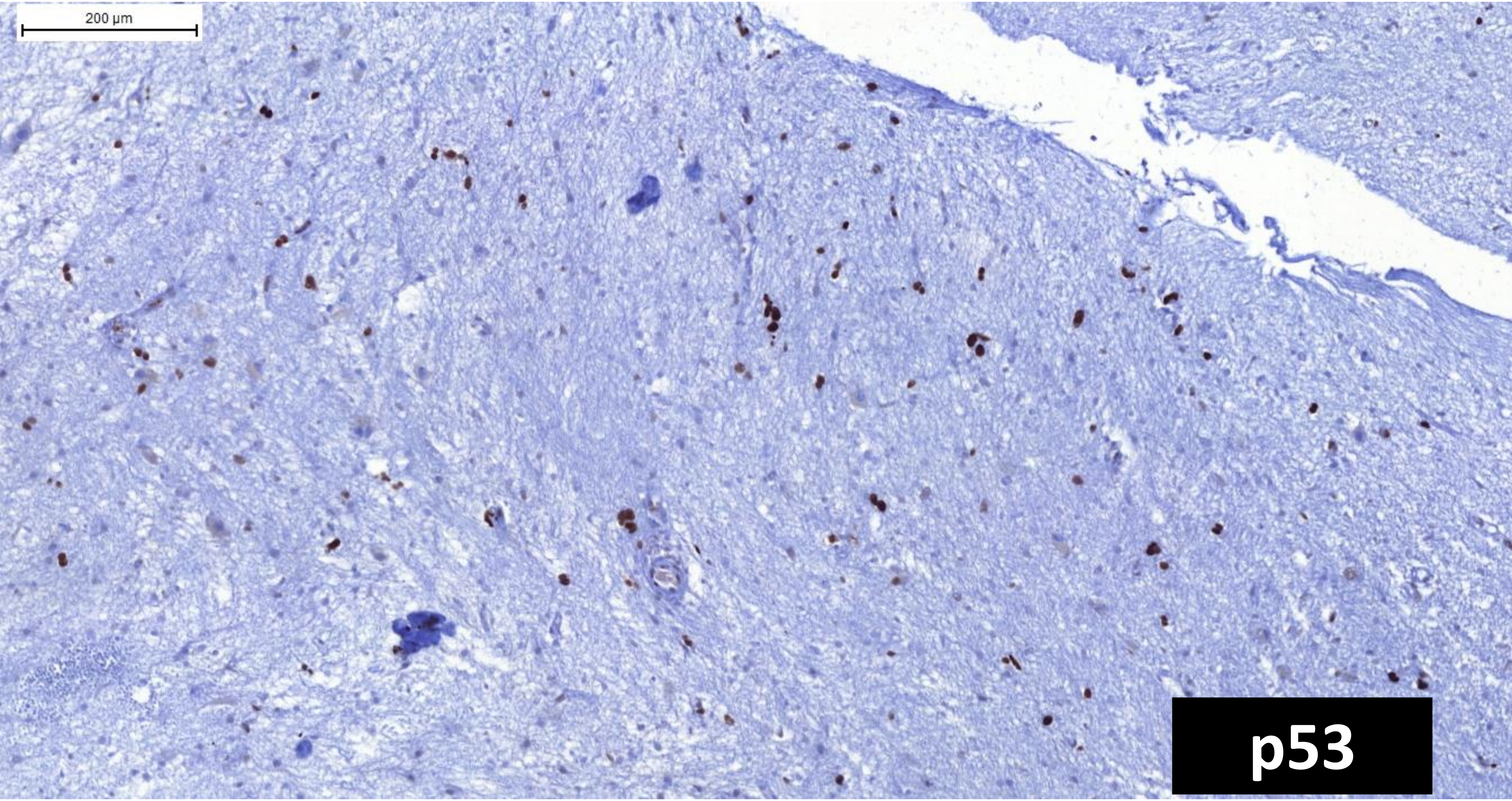

50 µm

DIAGNÓZA?

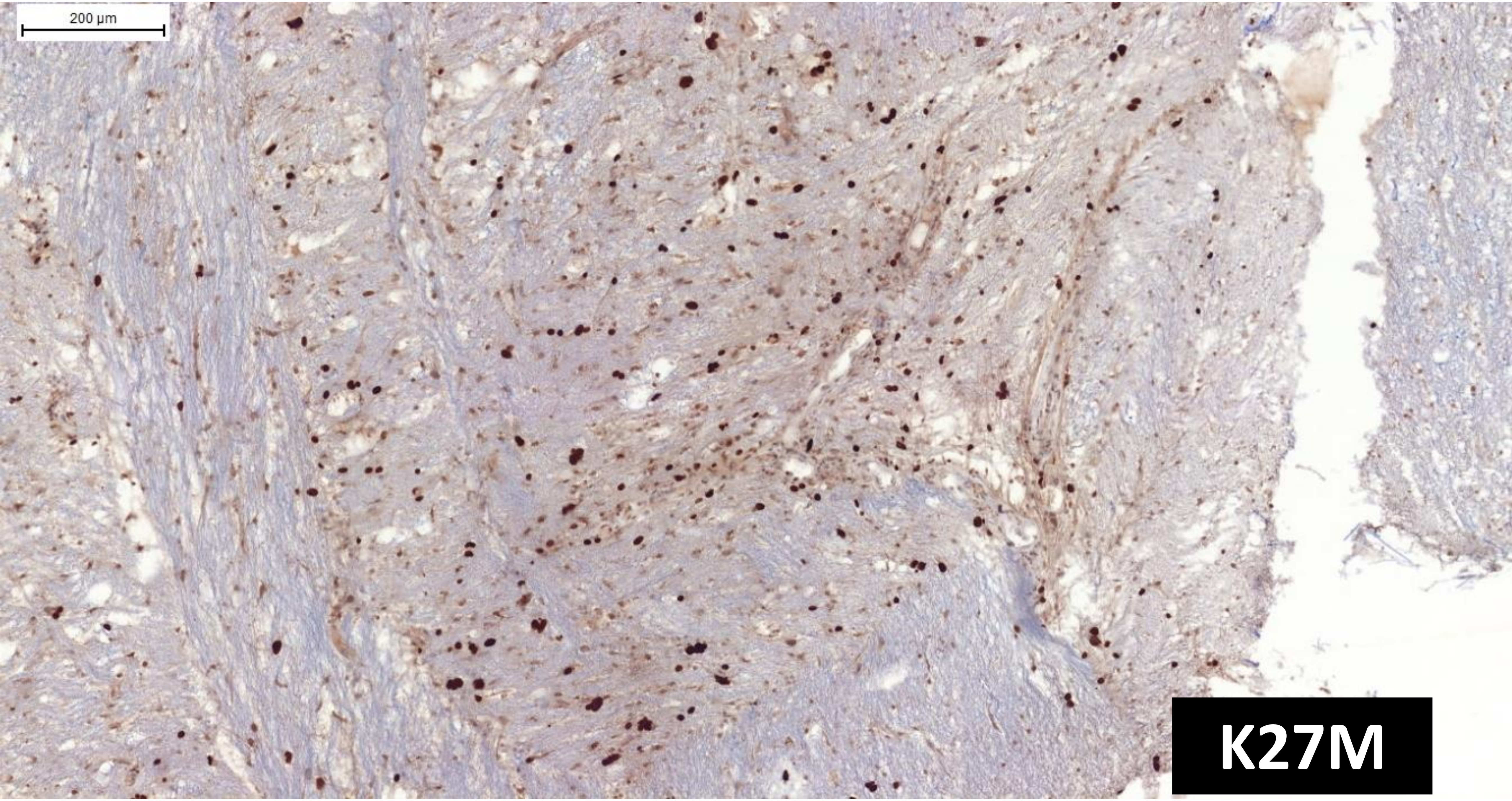

500 µm
Ki67

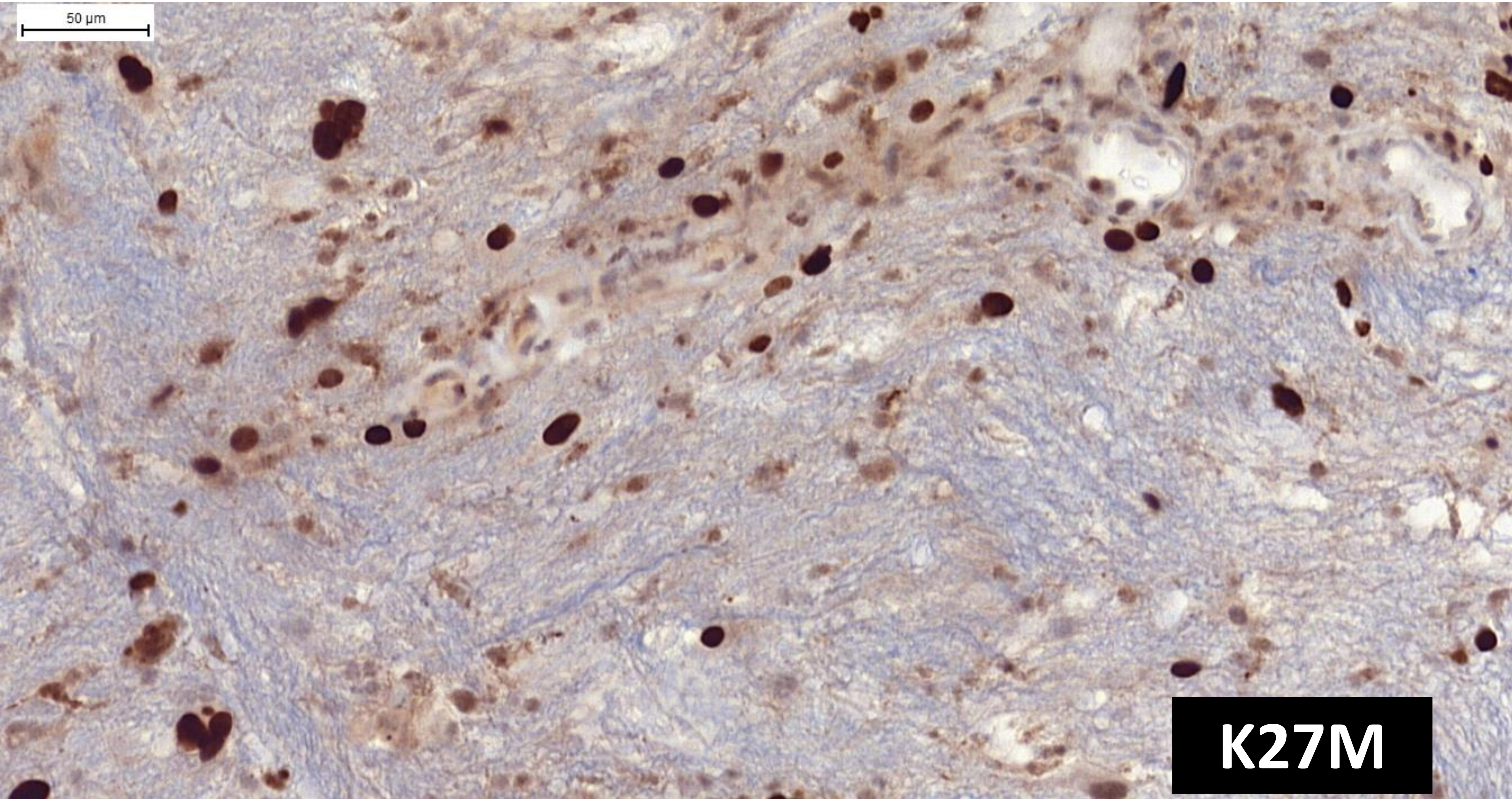

200 µm
p53

Imuno

- Ki67 nízke...
- Overexpresia p53

- Expresia ATRX zachovaná
- IDH-1 negatívne


200 μm
K27M


50 µm
K27M

Diffuse midline glioma, H3 K27M-mutant

- nová „pediatrická“ jednotka
- **Vyskytuje sa ale aj u dospelých pacientov, prevažne mladšieho veku**
- majú prevažne astrocytárnu morfológiu (spektrum morfológie!)
- Približne 10 % týchto nádorov nemá prítomné mitózy, mikrovaskulárnu proliferáciu ani nekrózy a histologicky by teda mohli byť klasifikované ako grade II

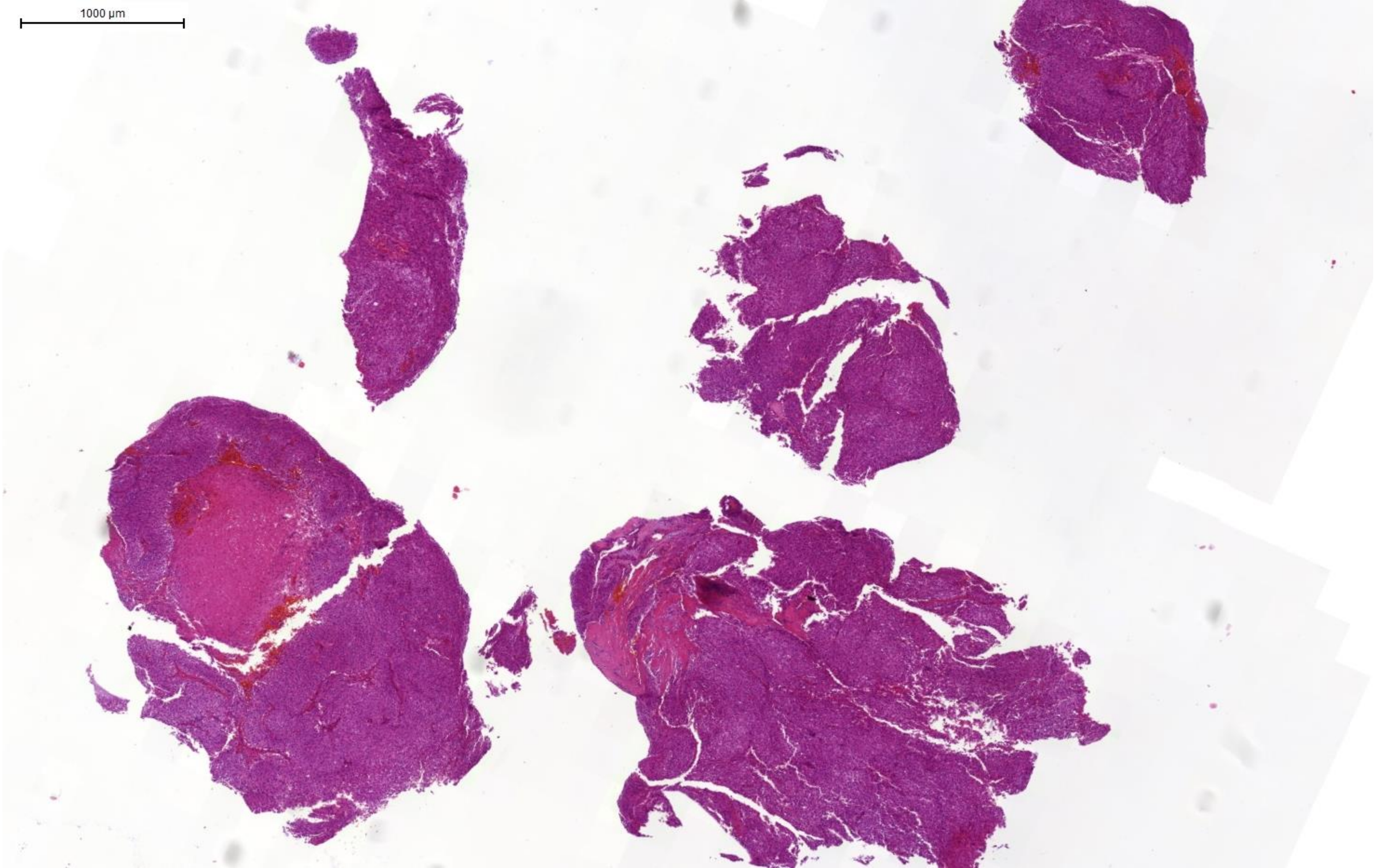
- Bez ohľadu na morfológiu majú mimoriadne zlú prognózu, čo platí aj pre dospelých pacientov a K27M mutované ohraničené gliómy

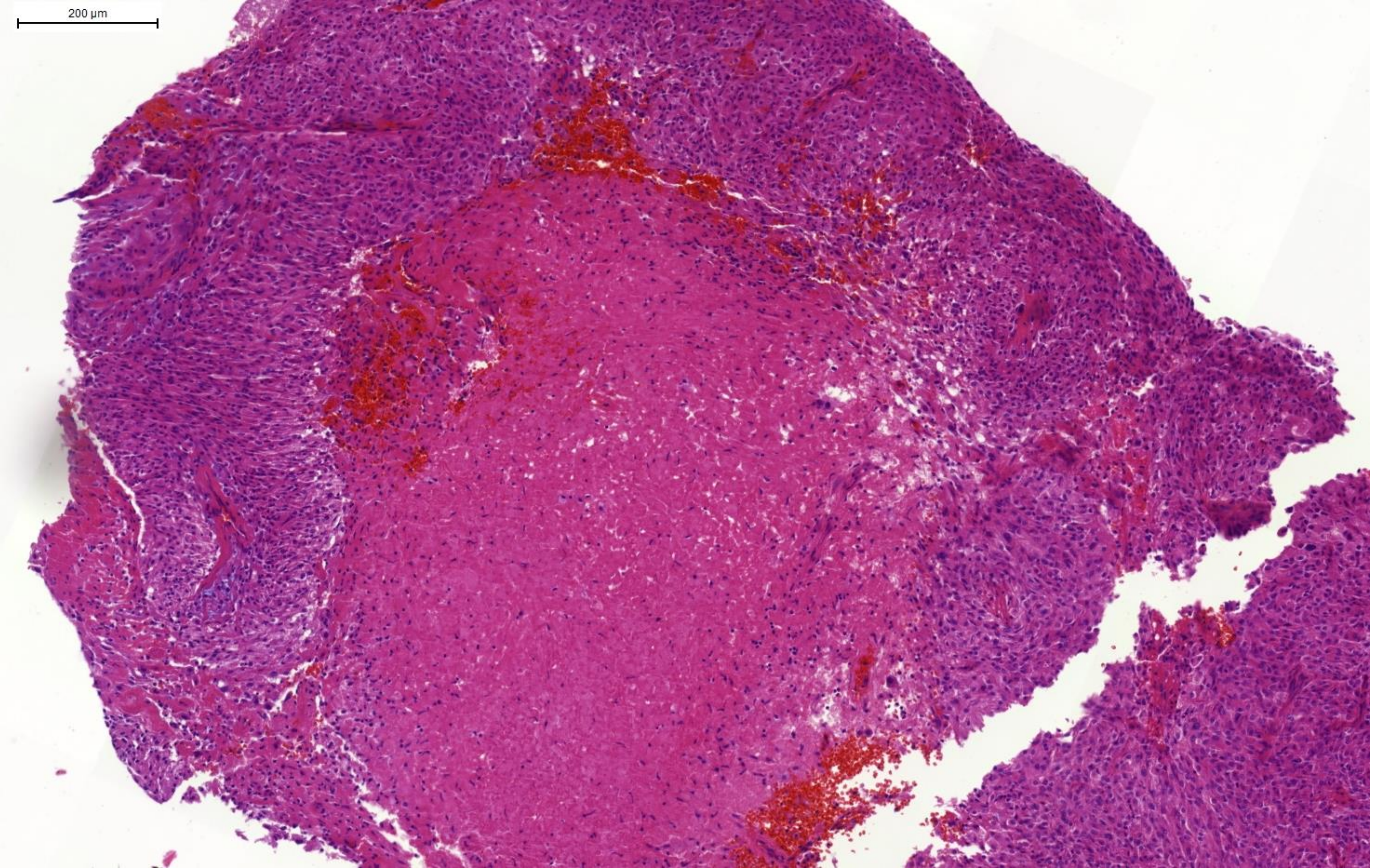
- K27M-mutované gliómy sú **klasifkované ako grade IV, bez ohľadu na histopatologický grade**

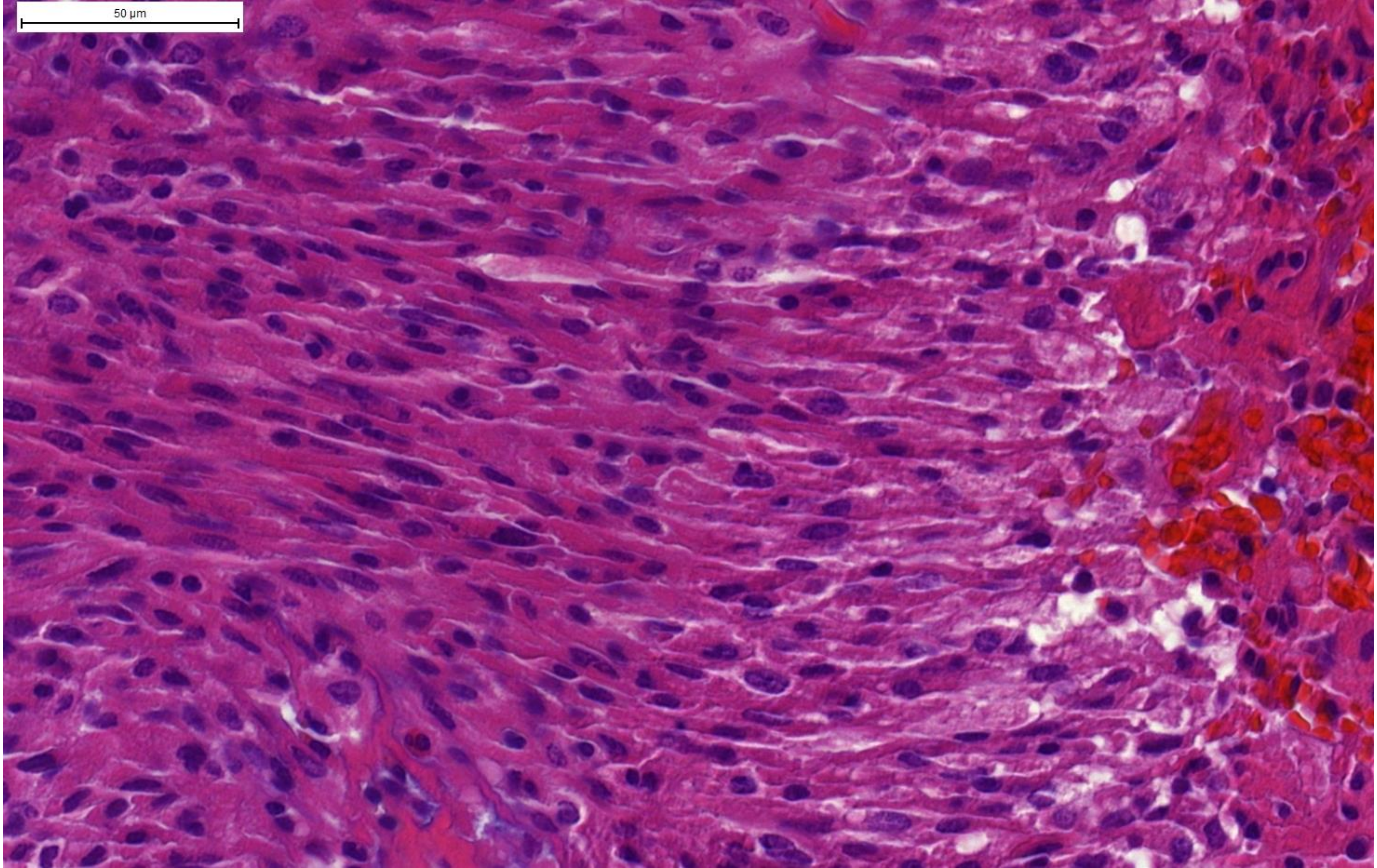
Prípad č. 8

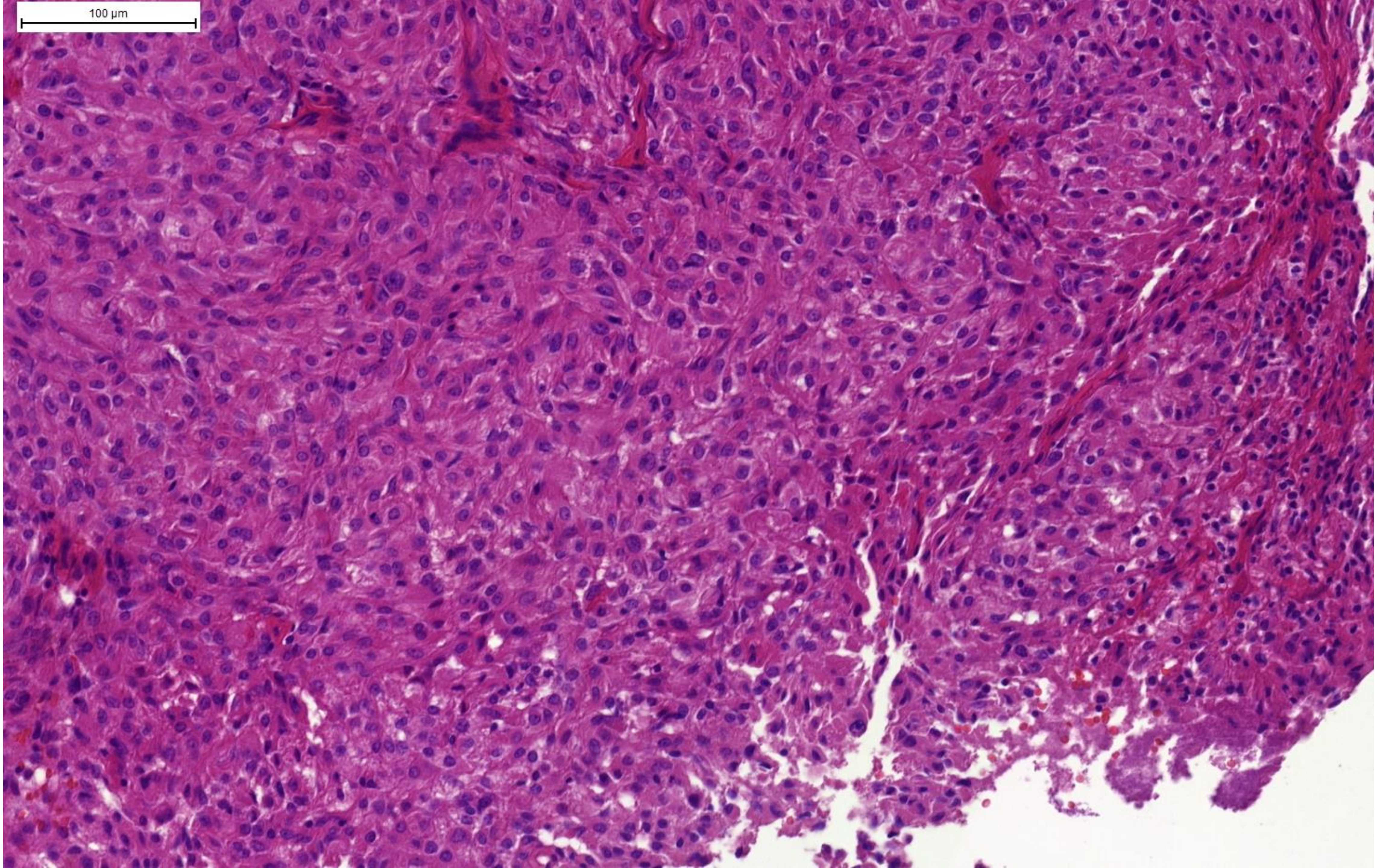
- 50 ročný muž
- Klinická diagnóza: recidíva adenómu hypofýzy, liečený RAT

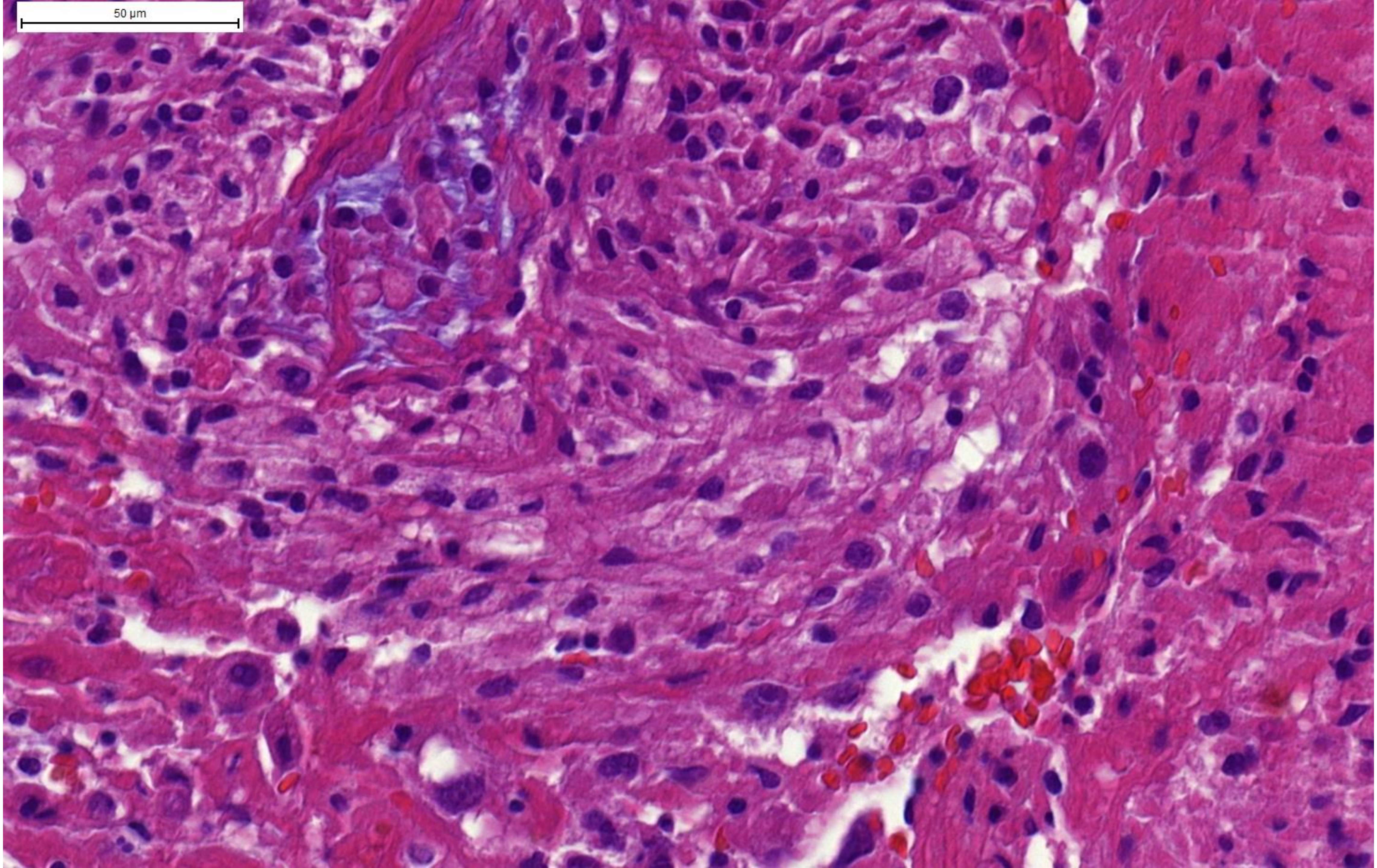
- Konzultácia (Odd. patológie UNLP Košice)


1000 µm


200 µm


50 µm

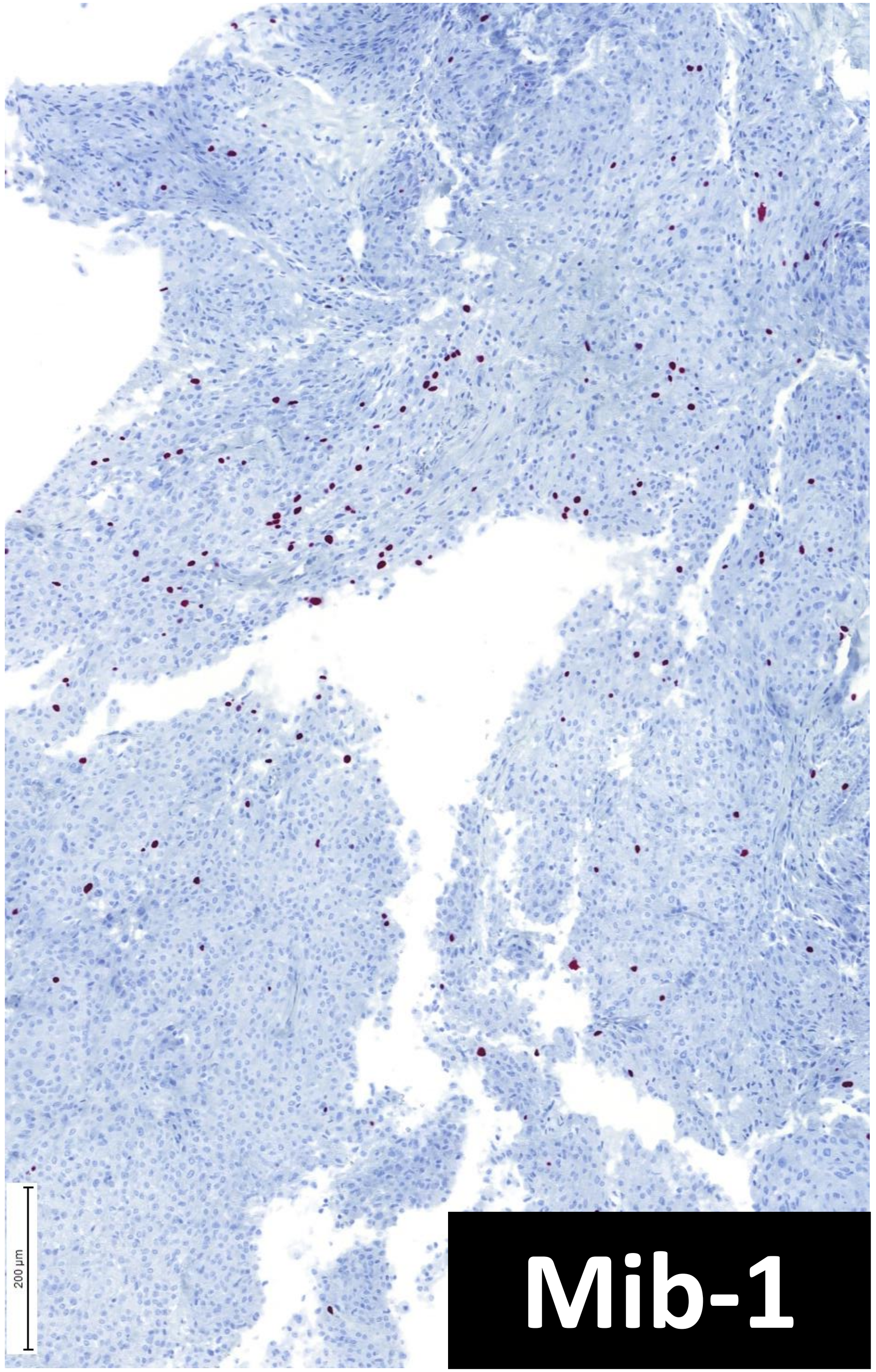

100 µm


50 µm

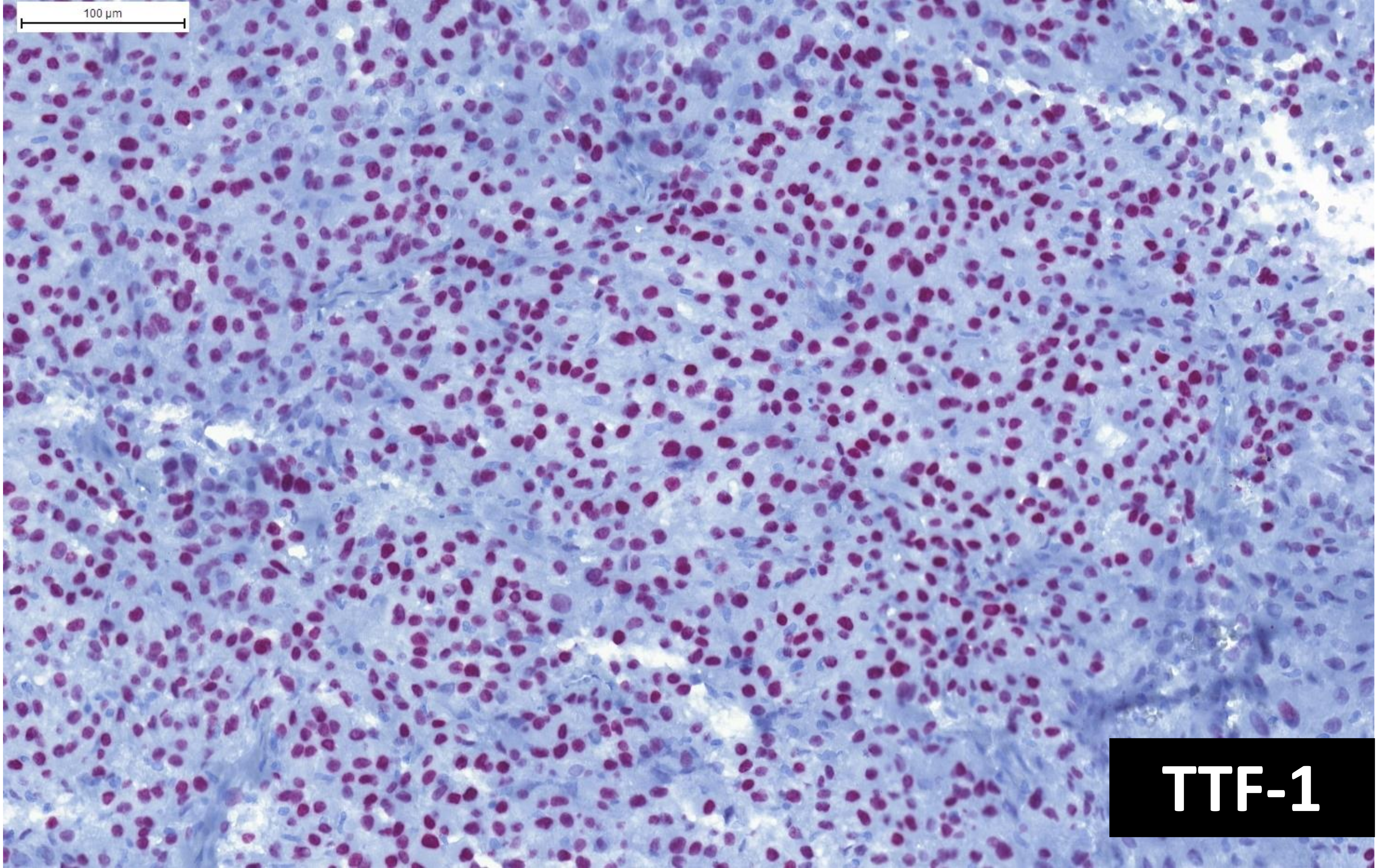
- mitotická aktivita je nízka (0-1 mitóza/10 hpf)
- proliferačný index cca 3-5% (Mib-1) v „hot-spots“

Negatívne IHC:

- CAM5.2, OSCAR
- chromogranin, SYP
- EMA, progesterone receptor
- GFAP, Olig2, S100, SOX10



DIAGNÓZA?


100 µm
TTF-1

SPINDLE CELL ONCOCYTOMA, WHO grade I

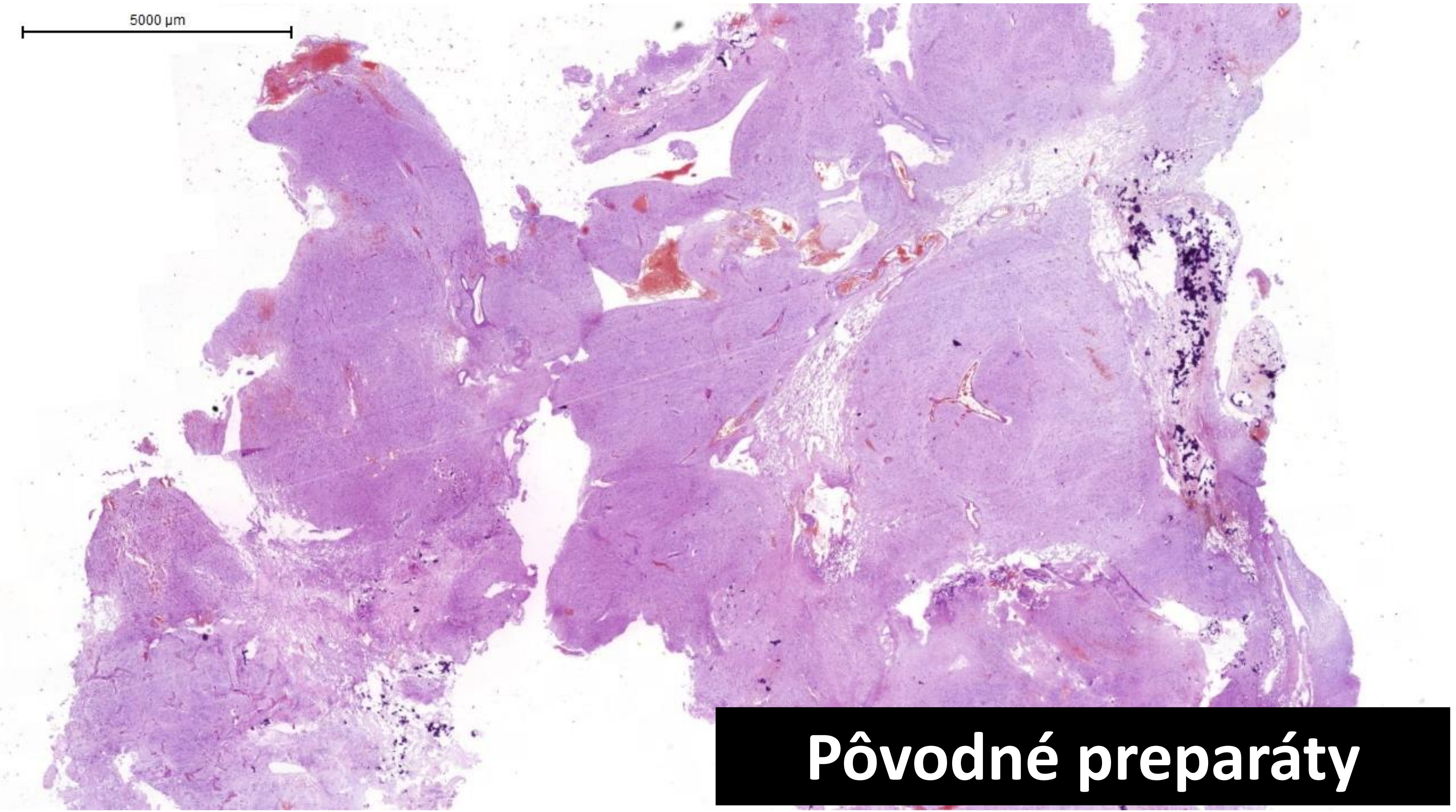
- vzácny tumor neurohypofýzy zo spektra pituicytoma-spindle cell oncocytoma-granular cell tumor of the sellar region

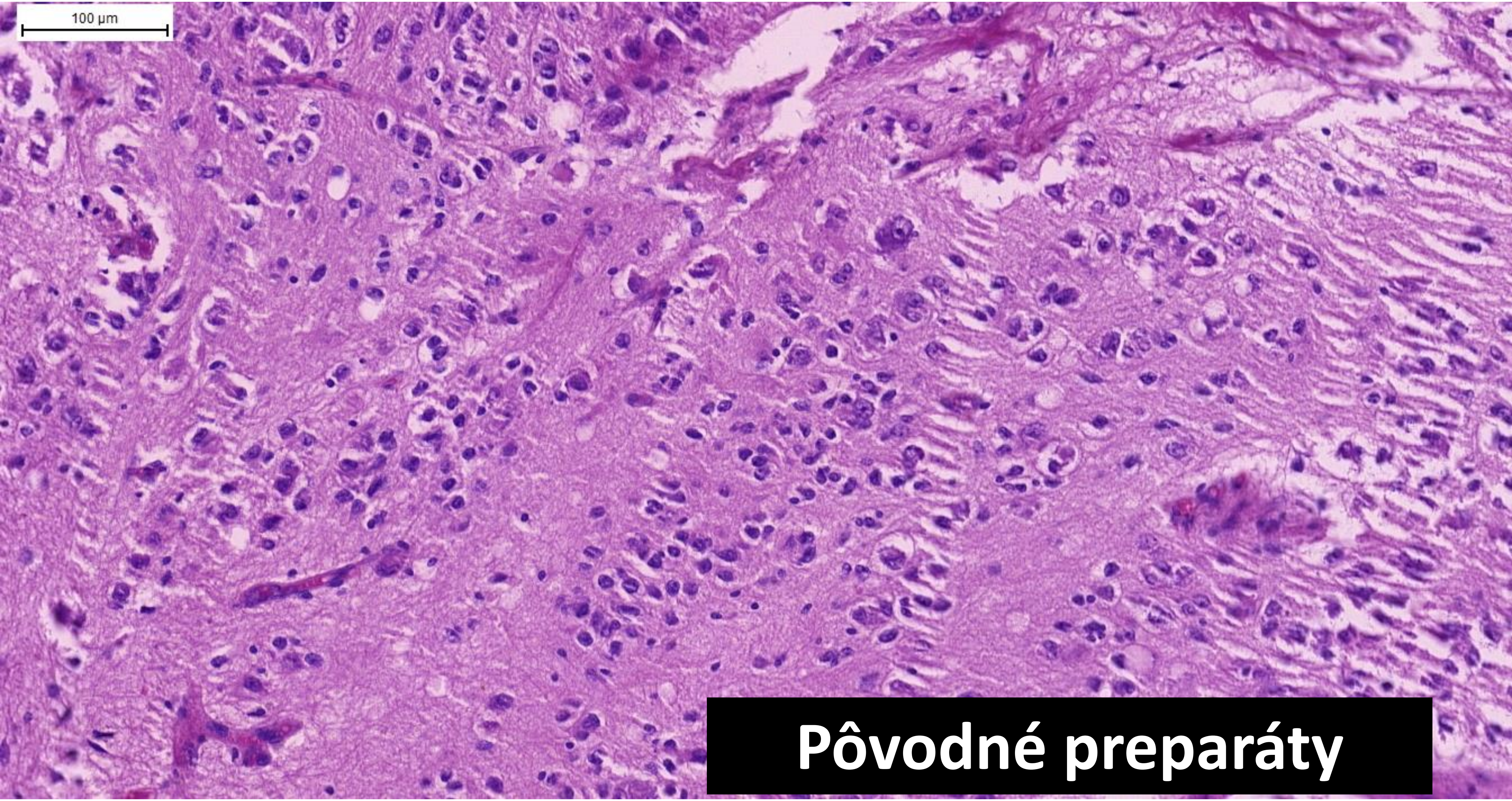
- Mierne sa líšia morfologicky
- Variabilný imunoprofil
  - Granullar cell tumor: CD68+, S100+, GFAP -/+, **TTF-1 +**
  - Pituicytóm: S100+, GFAP +/-, **TTF-1 +**
  - Spindle cell oncocytoma: S100 +, EMA +/-, GFAP -/+, **TTF-1+**

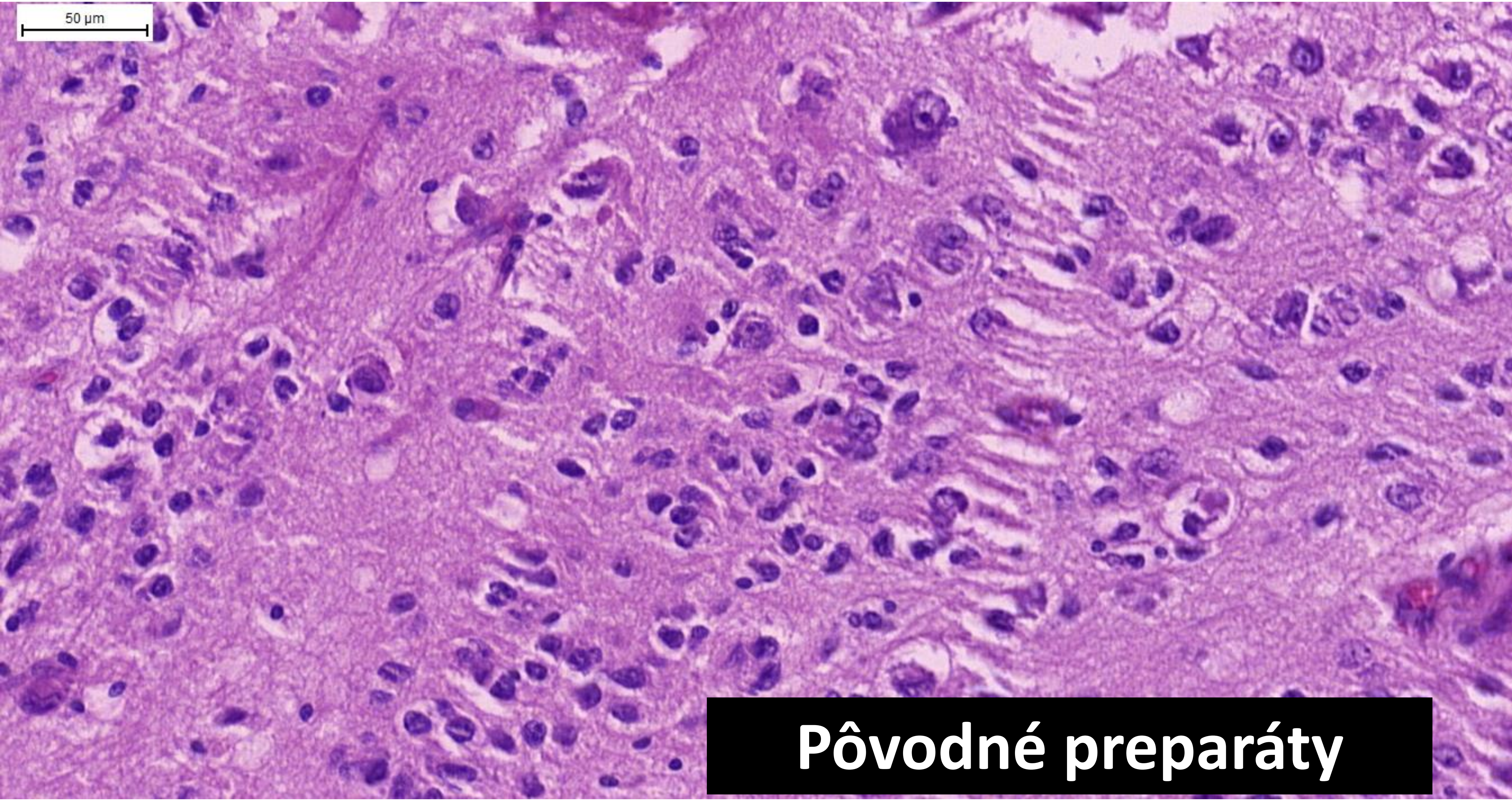
- Klinicky benígne lézie, rekurencie veľmi vzácne (náš prípad rekuroval po 9 rokoch) – rekurentné lézie môžu byť klinicky agresívnejšie

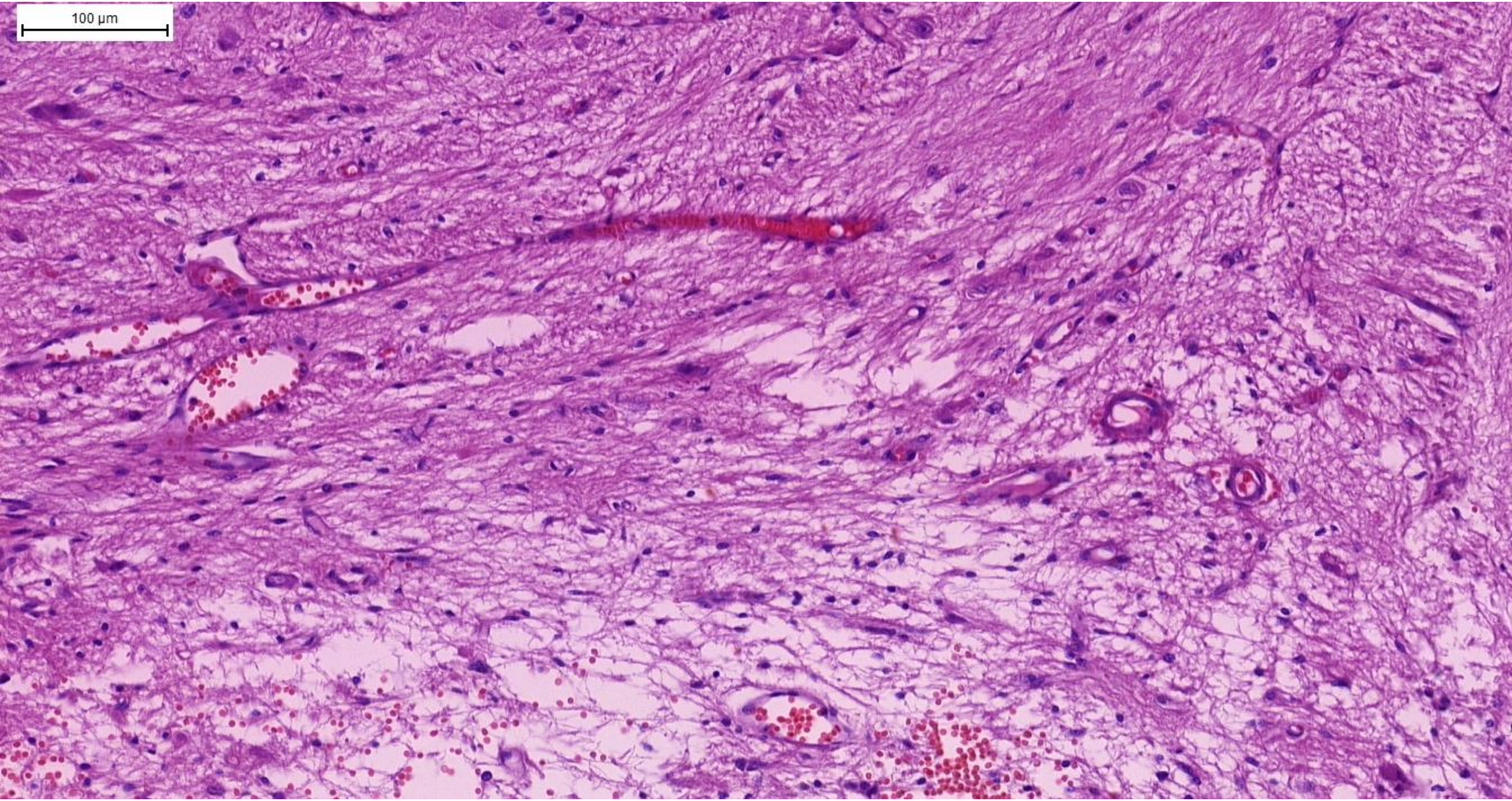
Prípad č. 9

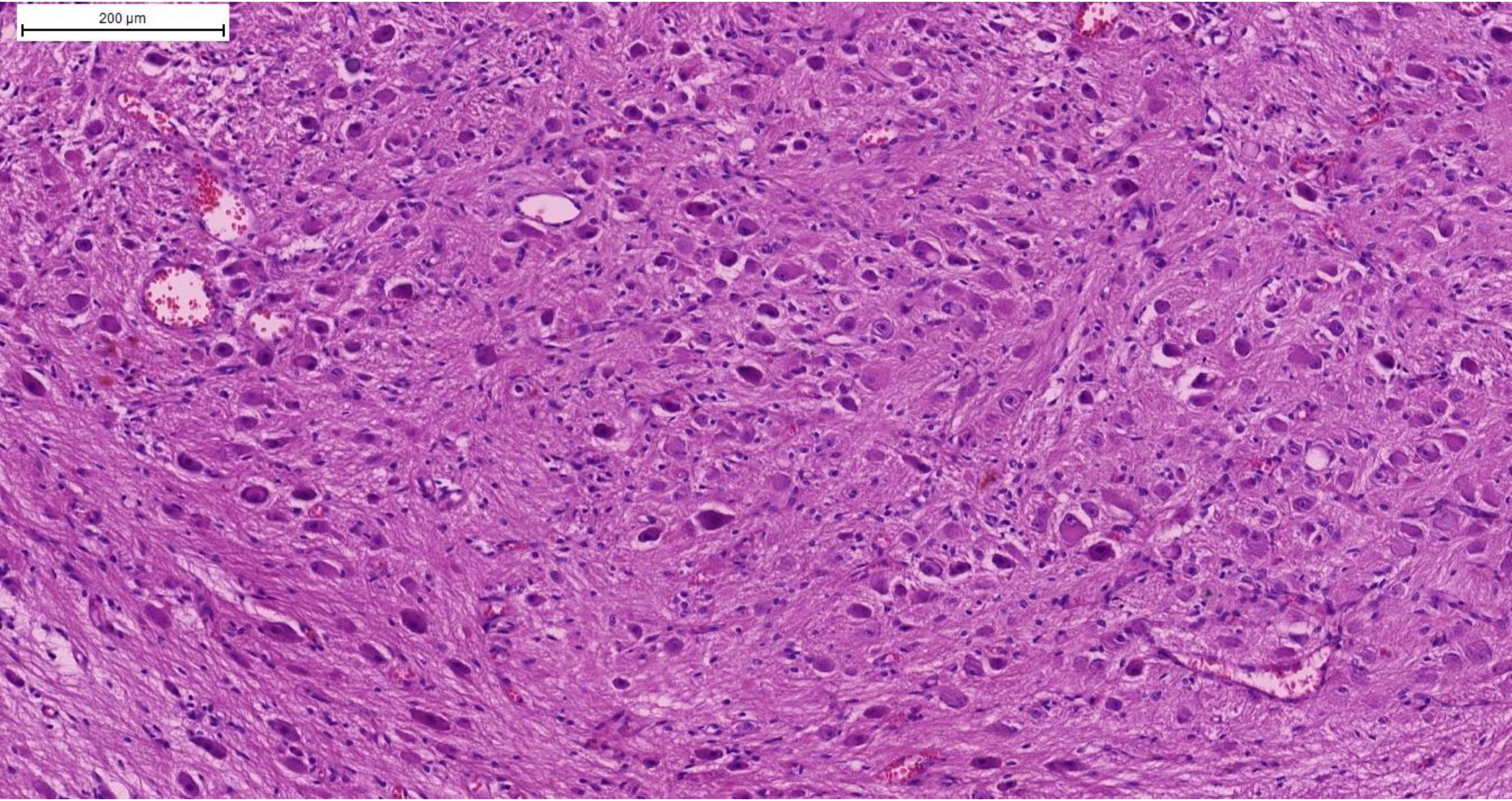
- 22 ročný muž
- Tumor mozgu – bez udania lokality
- Konzultácia, Cytopathos Bratislava – revízia nálezu z roku 2010 (dg. oligoastrocytóm G II)

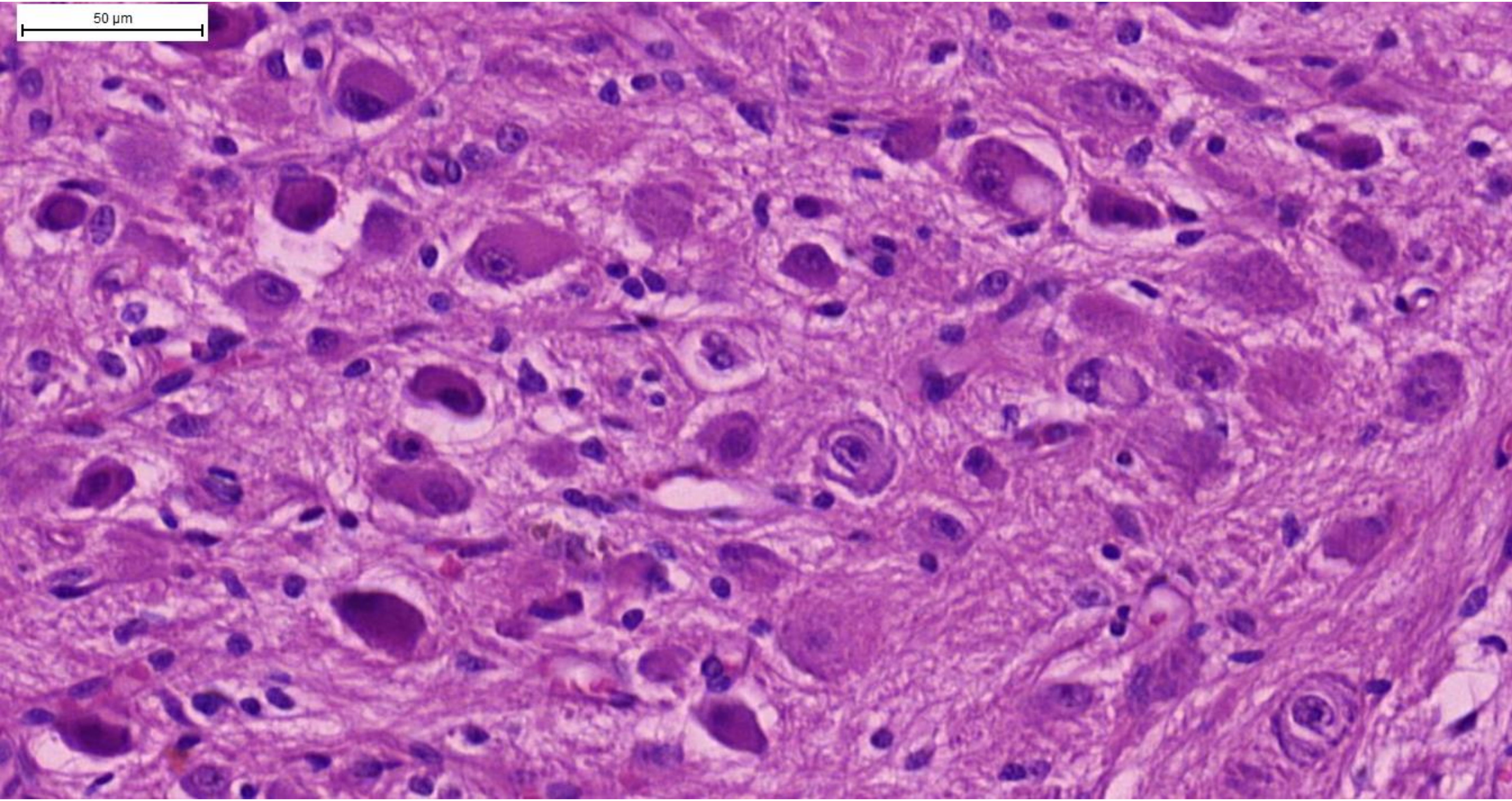

5000 µm
Pôvodné preparáty


100 µm
Pôvodné preparáty

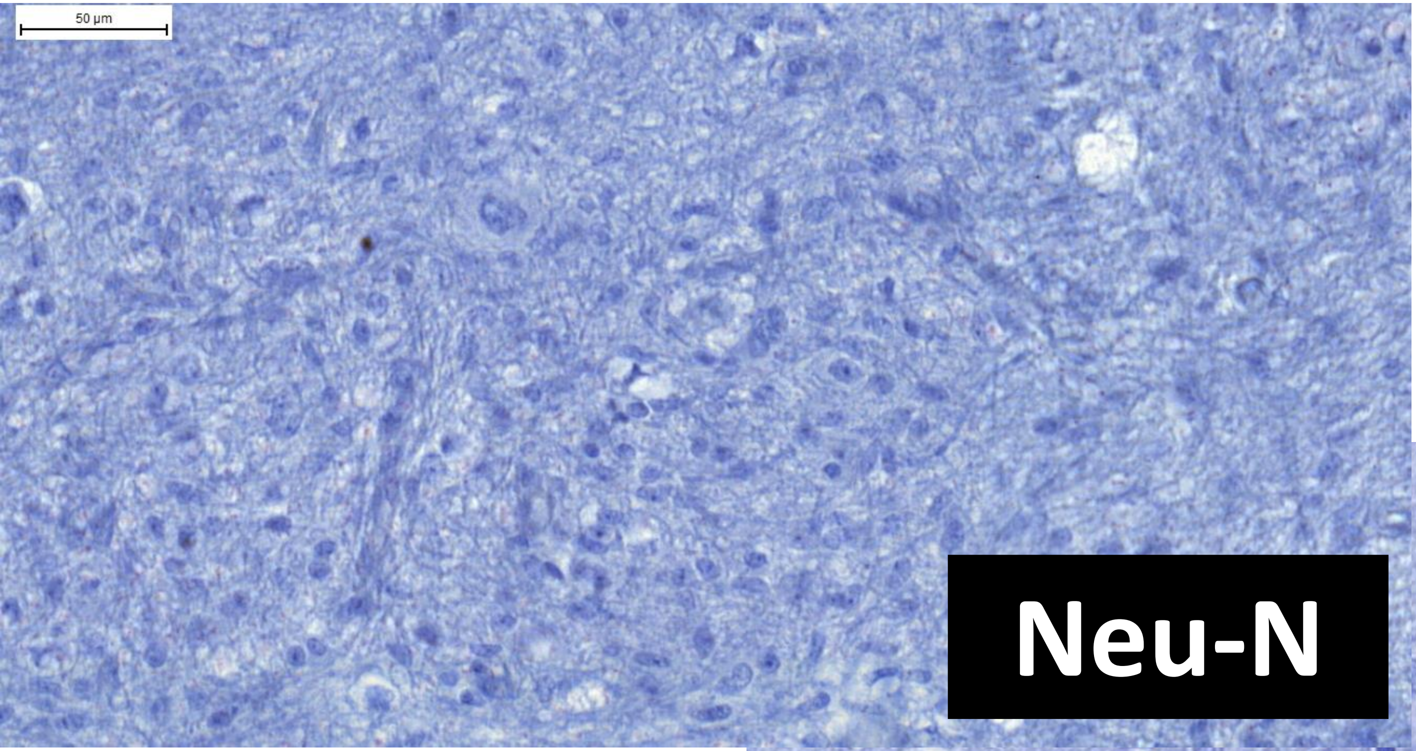

50 µm
Pôvodné preparáty

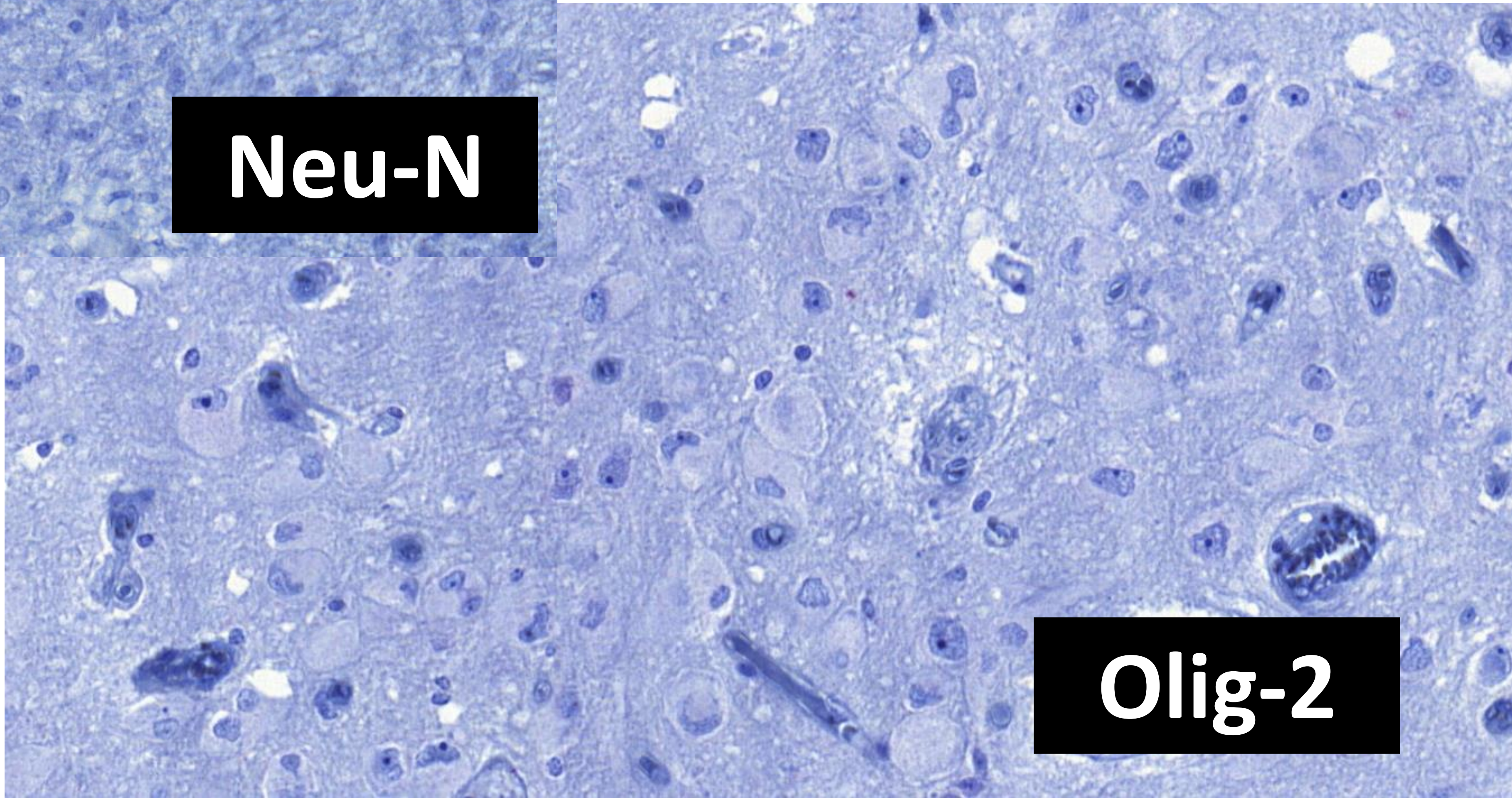

100 µm

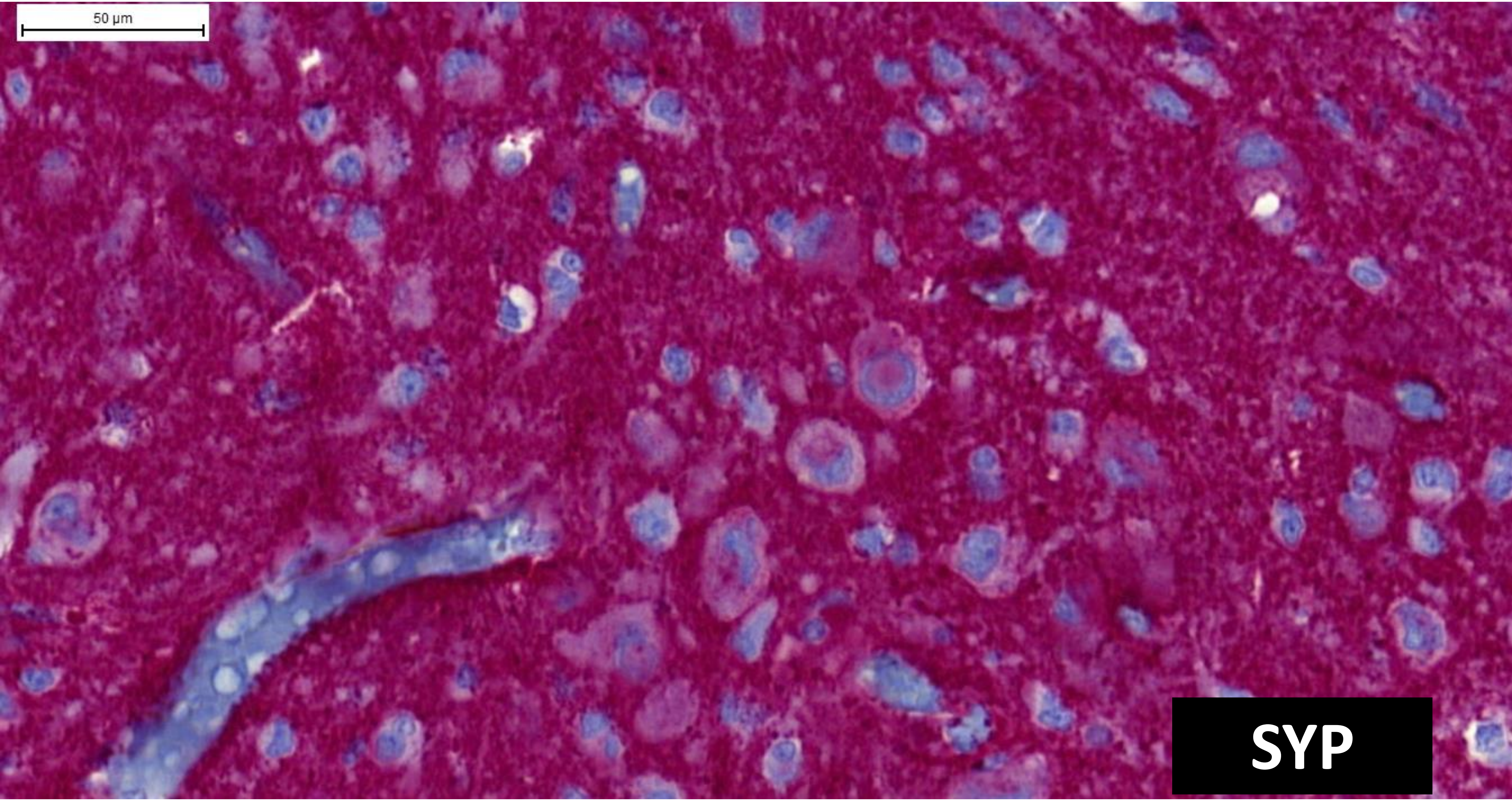

200 µm

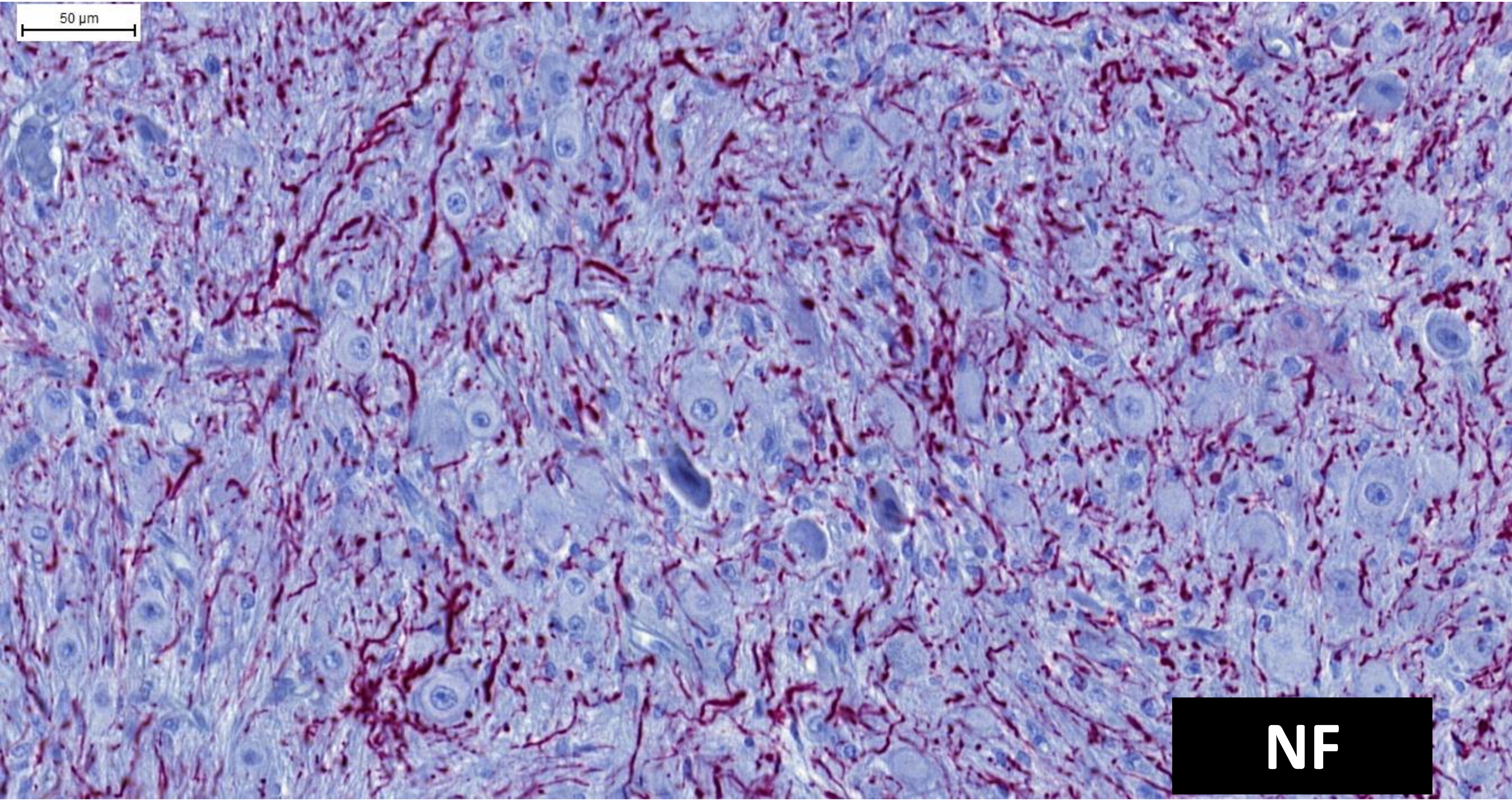

50 µm

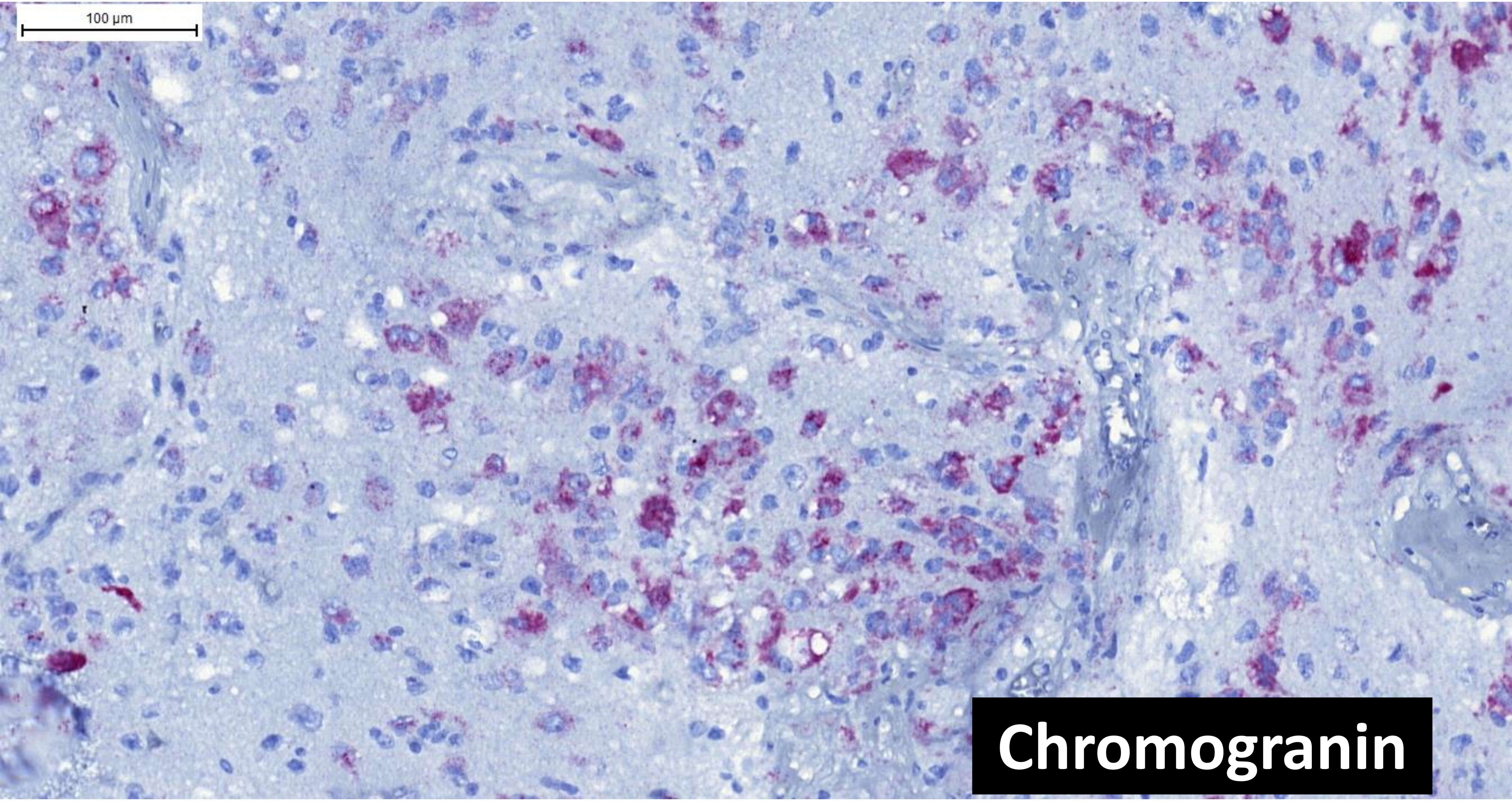
DIAGNÓZA?

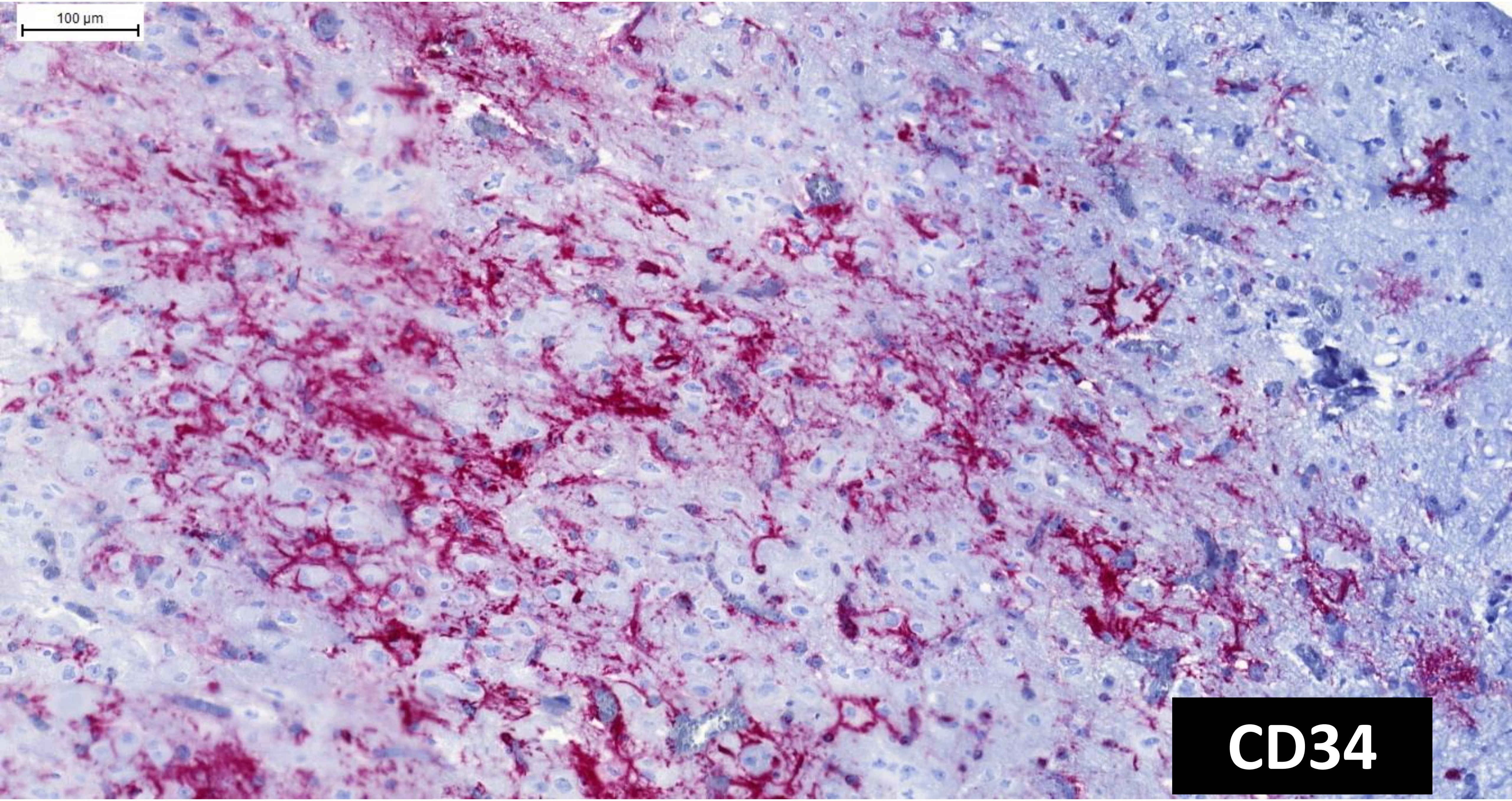

50 µm
Neu-N


Olig-2


50 µm
SYP


50 µm
NF


100 μm
Chromogranin


100 µm
CD34

Ganglioglioma, Grade I

- proliferačná aktivita (Mib1 index) prakticky nulová
- zachovaná expresia ATRX, IDH1-negatívny
- bez overexpresie p53

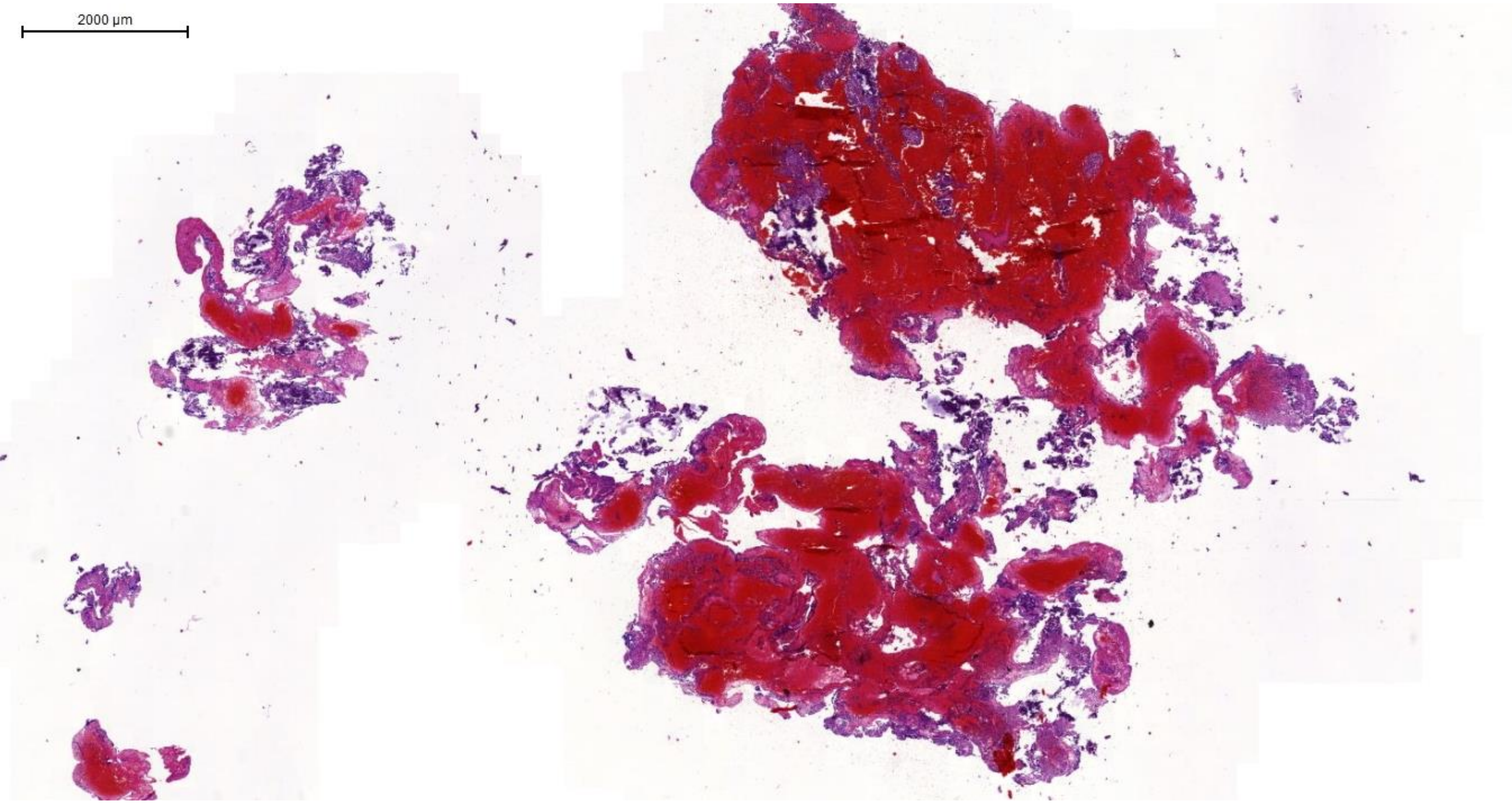
- v gliovej komponente exprimuje GFAP a OLIG2
- gangliocytárna zložka je SYP, NF, CHROM a CD34 pozitívna

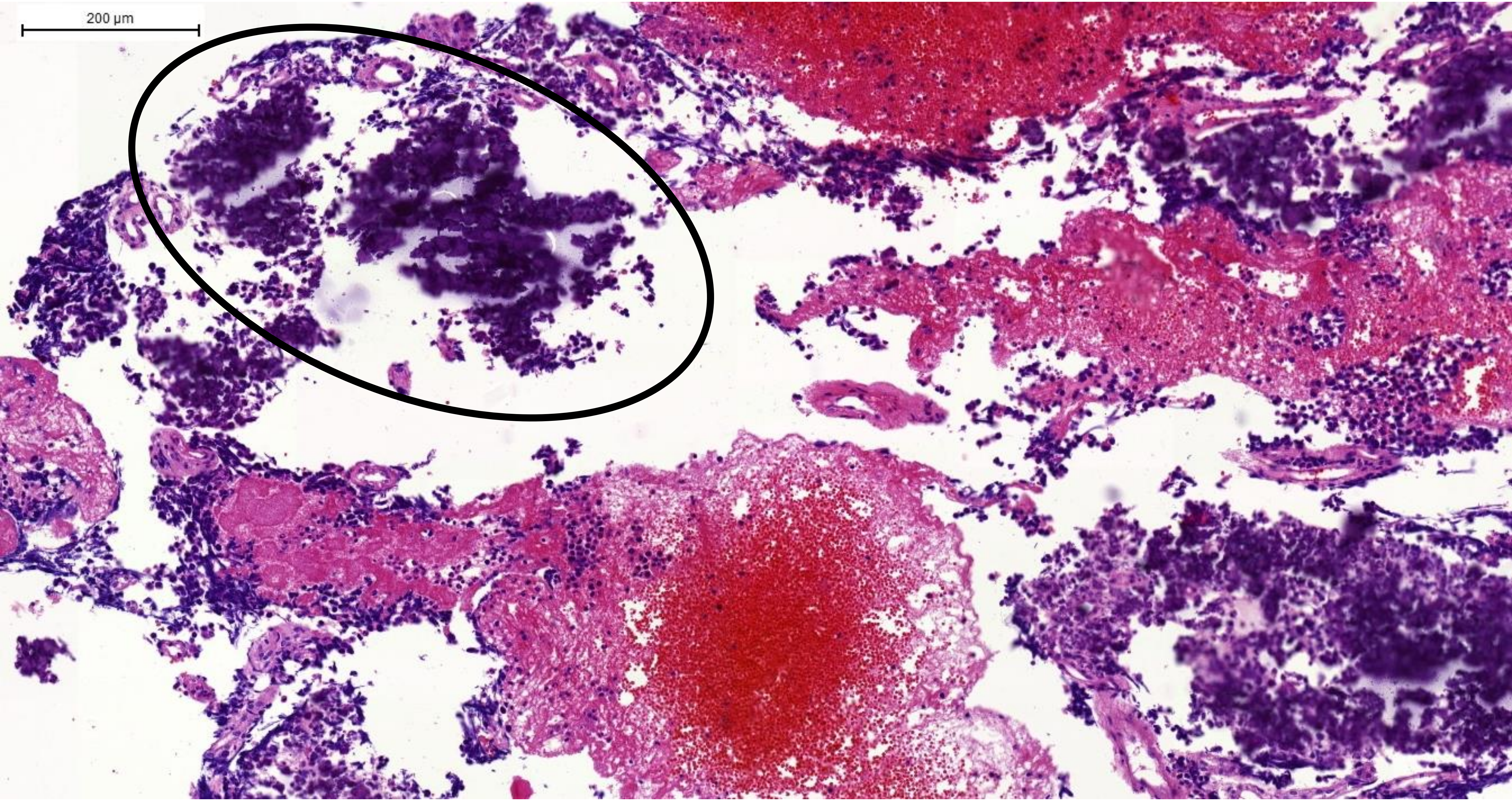
- BRAF (V600E) negatívna

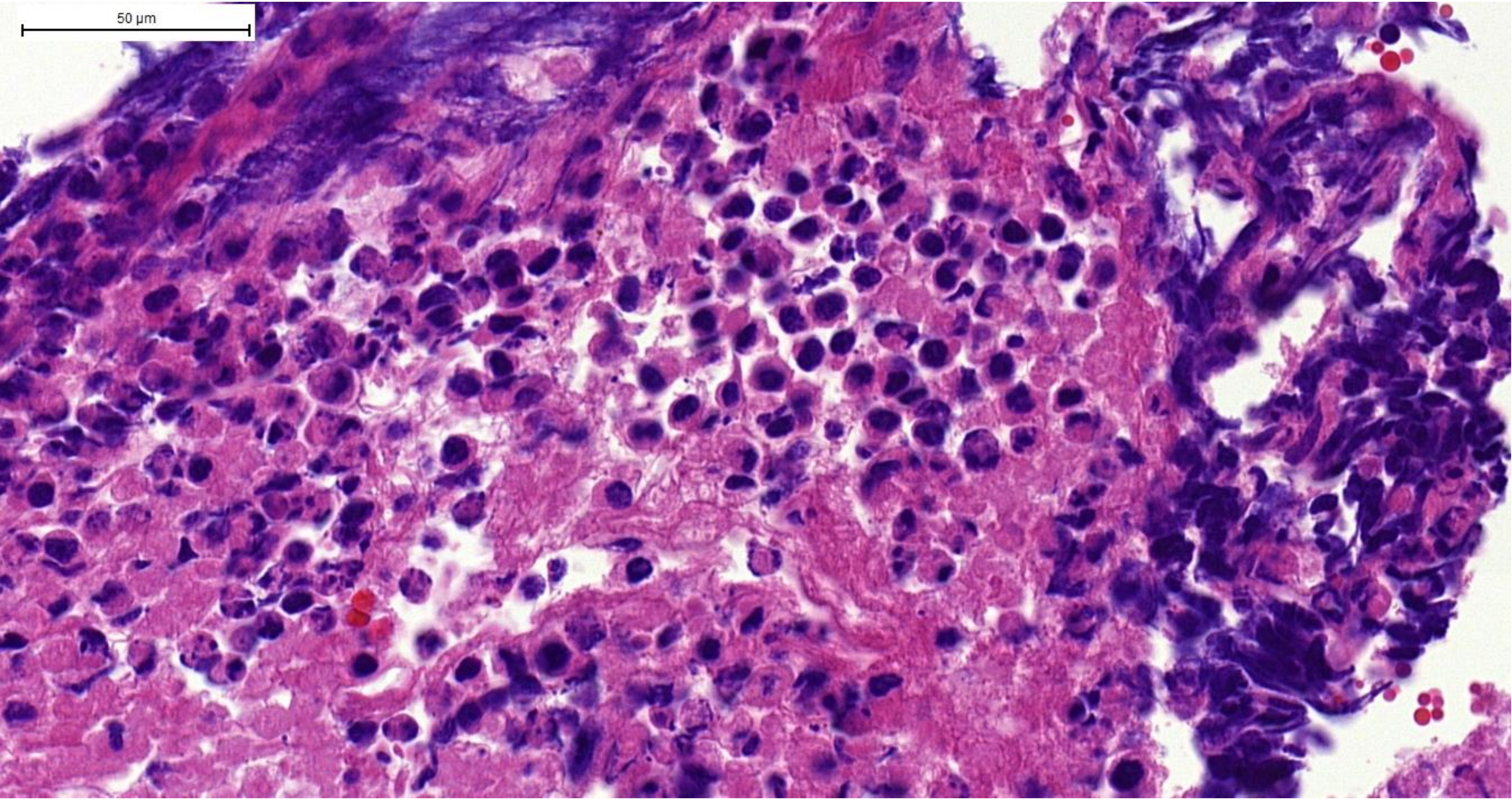
Prípad č. 10

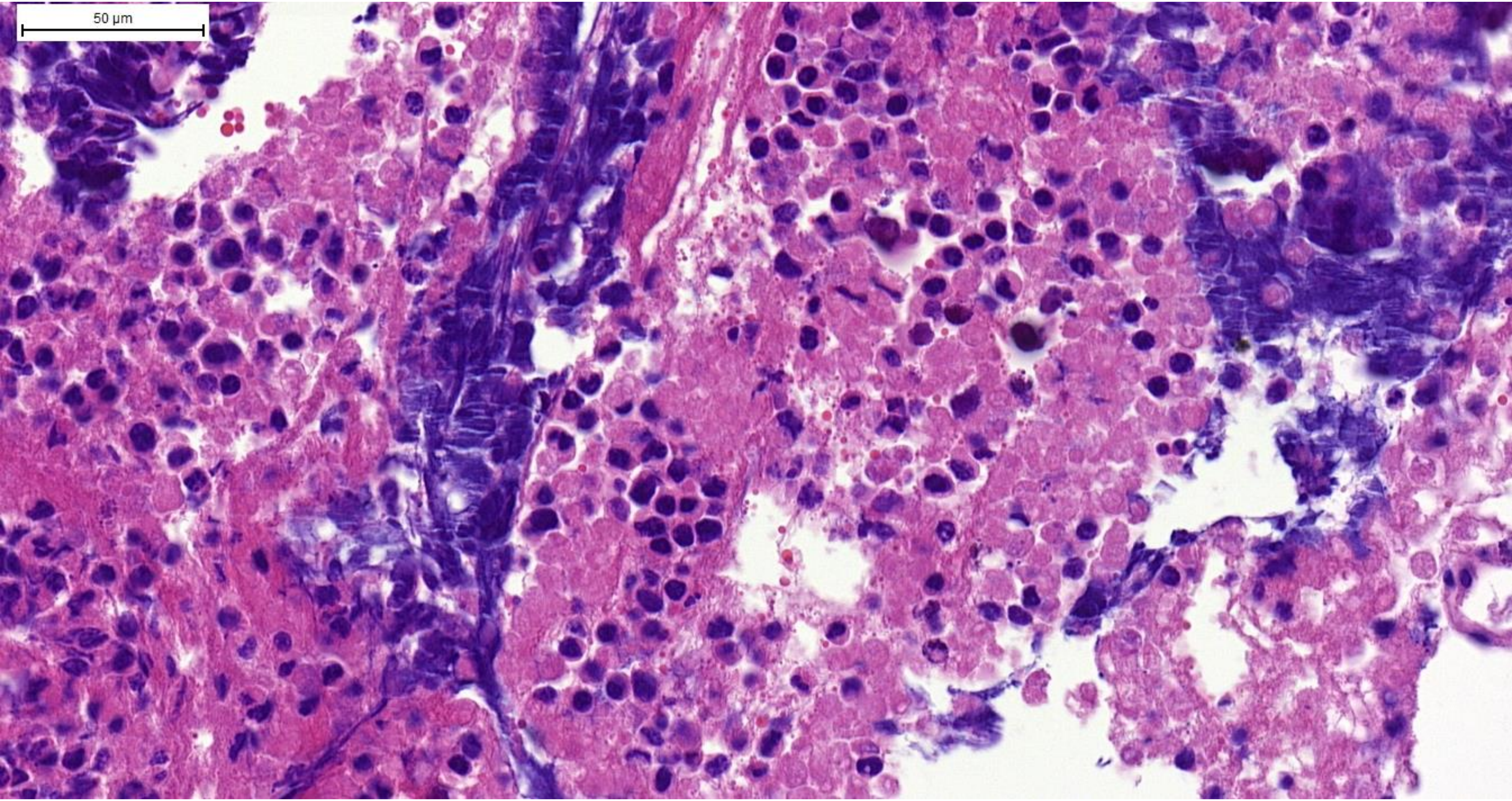
- 5 ročný chlapec
- Tumor pineálnej oblasti

- Druhé čítanie na žiadosť klinika, Cytopathos Bratislava (diagnóza v.s. pineocytóm)
- Radiologicky rekurencia tumoru po niekoľkých týždňoch


2000 µm


200 µm


50 µm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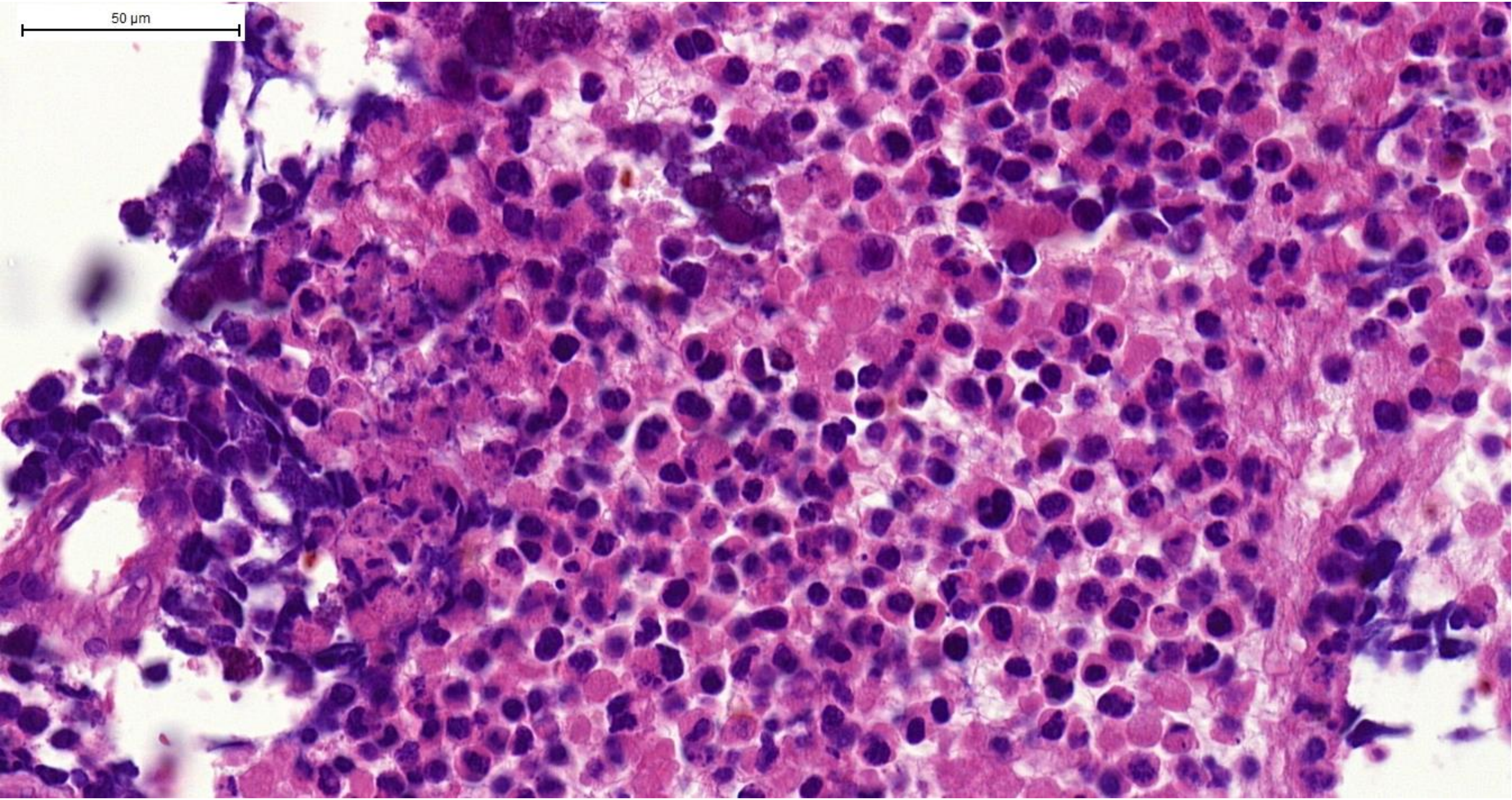
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Imuno

- Pozitívna expresia SYP, MAP2, PGP, INI-1 (všetko dodané IHC preparáty)

- Negatívna expresia SMA, EMA, PLAP, Glypican 3, NF, hCG, CD117, IDH1, chromogranin A, GFAP, NeuN, LCA (výrazná prímes lymfocytov), CD3, CD20 (všetko dodané IHC preparáty)

- Proliferačný index je obtiažne hodnotiteľný, niektoré pravdepodobne nádorové bunky sú Ki-67-pozitívne
- PHH3 značí iba ojedinelé mitózy, niektoré snáď v nádorových bunkách, mnohé mitózy sú v zápalových elementoch

DIAGNÓZA?

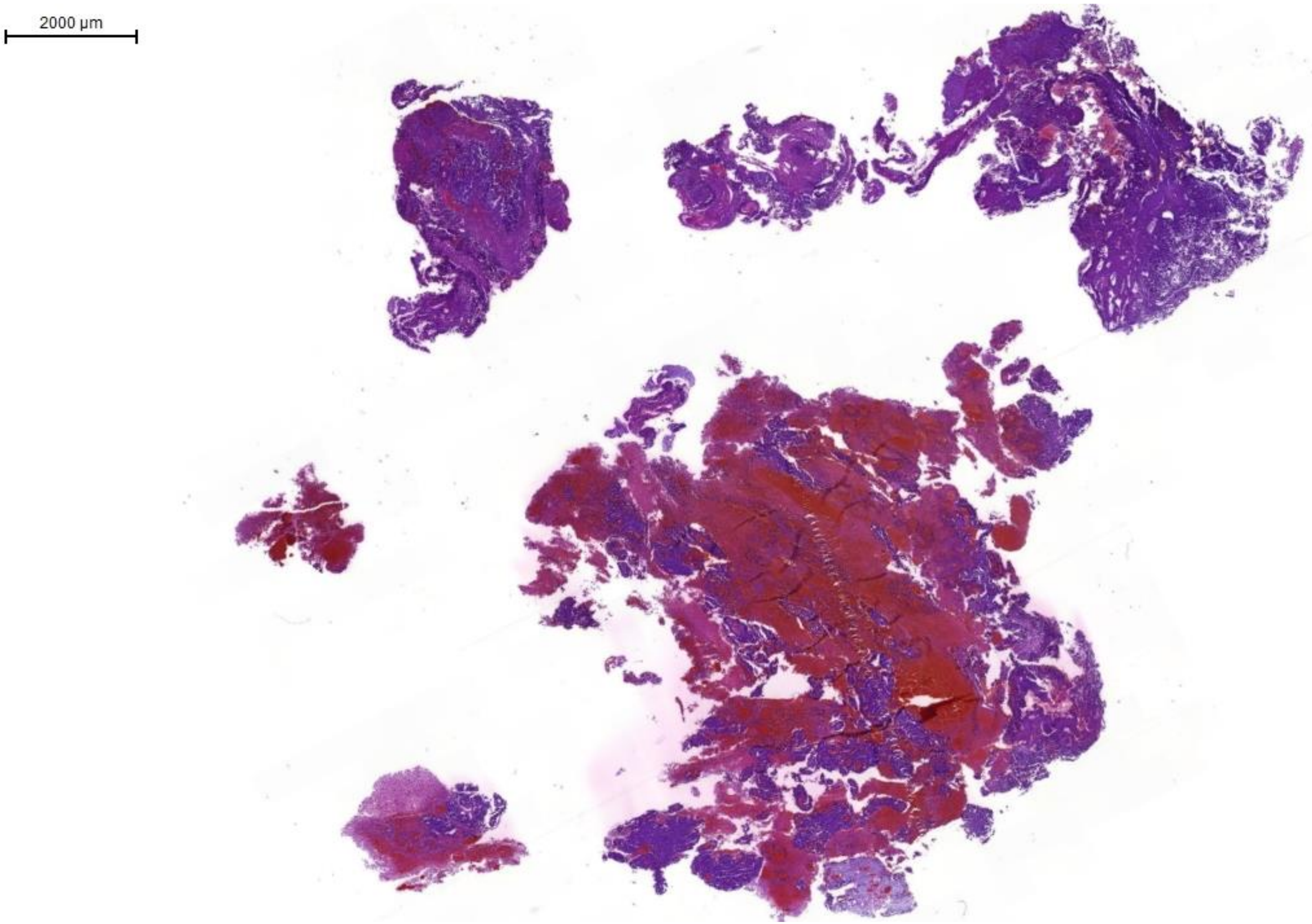
Pineoblastoma, WHO grade IV

- Vzácny tumor pineálnej oblasti, prevažne detského/adolescentného veku (priemerný vek ~18 rokov)
- Výskyt sporadicky a u pacientov s Rb-syndrómom („trilateral retinoblastoma“) a u pacientov s *DICER1* zárodočnou mutáciou
- Kalcifikácie sú bežné v normálnej žľaze, +/- v benígnych léziách (skôr vo zvyškoch normálneho corpus pineale), ale mimoriadne vzácne v pineoblastóme – ich prítomnosť by ale nemala odviesť pozornost od morfológie nádorových buniek

Prípad č. 11

- 22 ročný muž
- Tumor PO l. sin

- Konzultácia Odd. patológie UNLP Košice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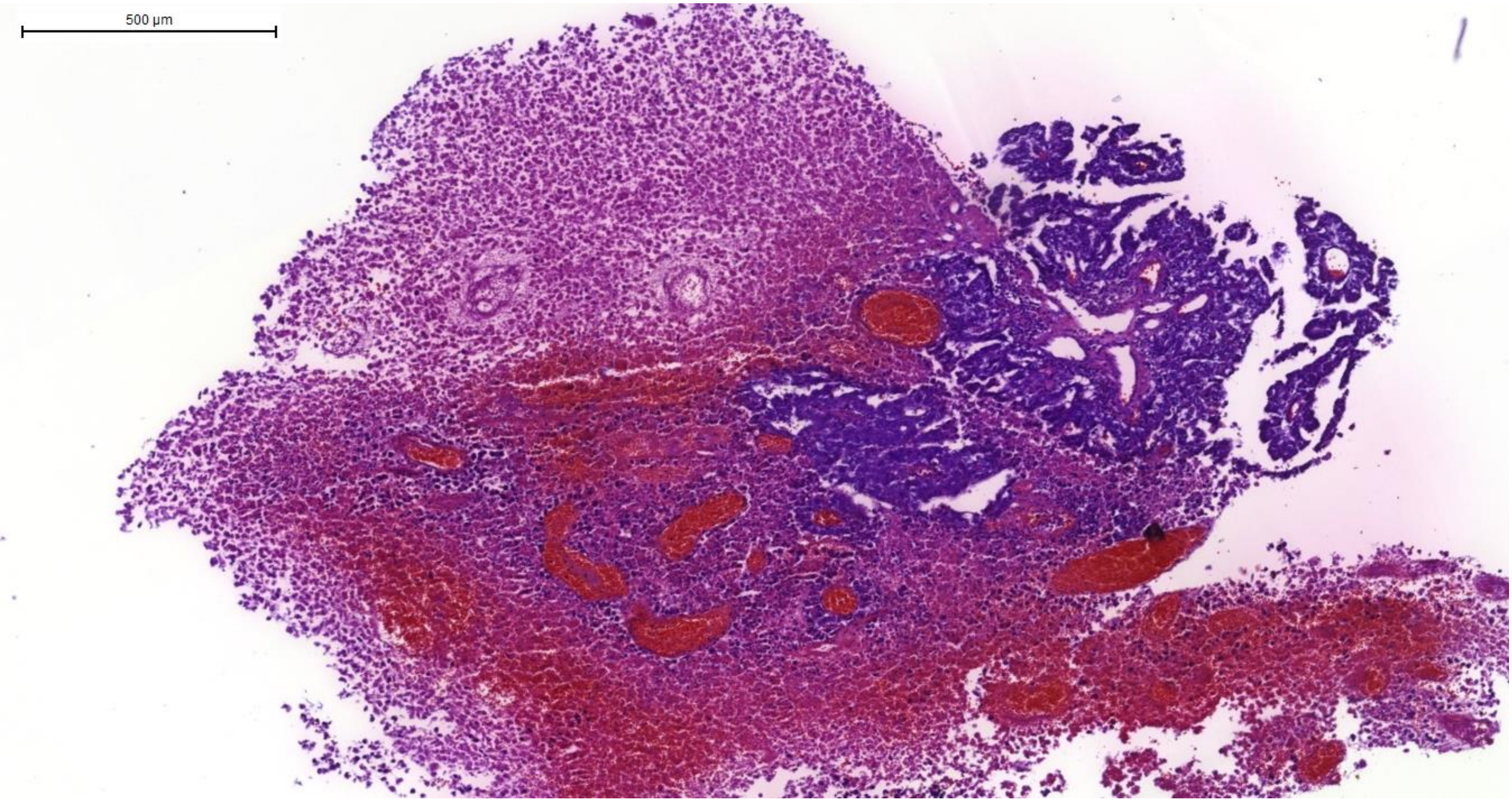
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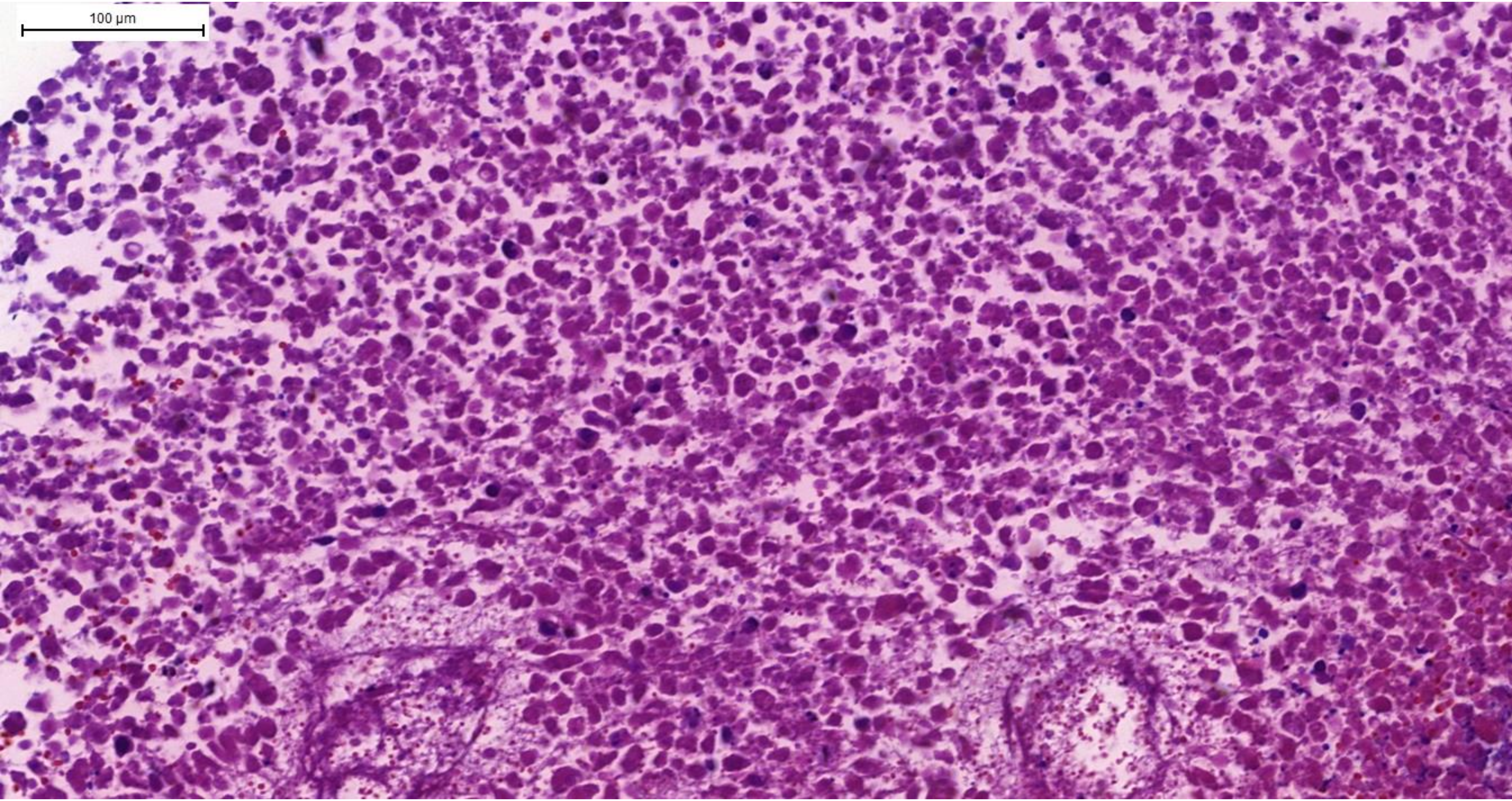
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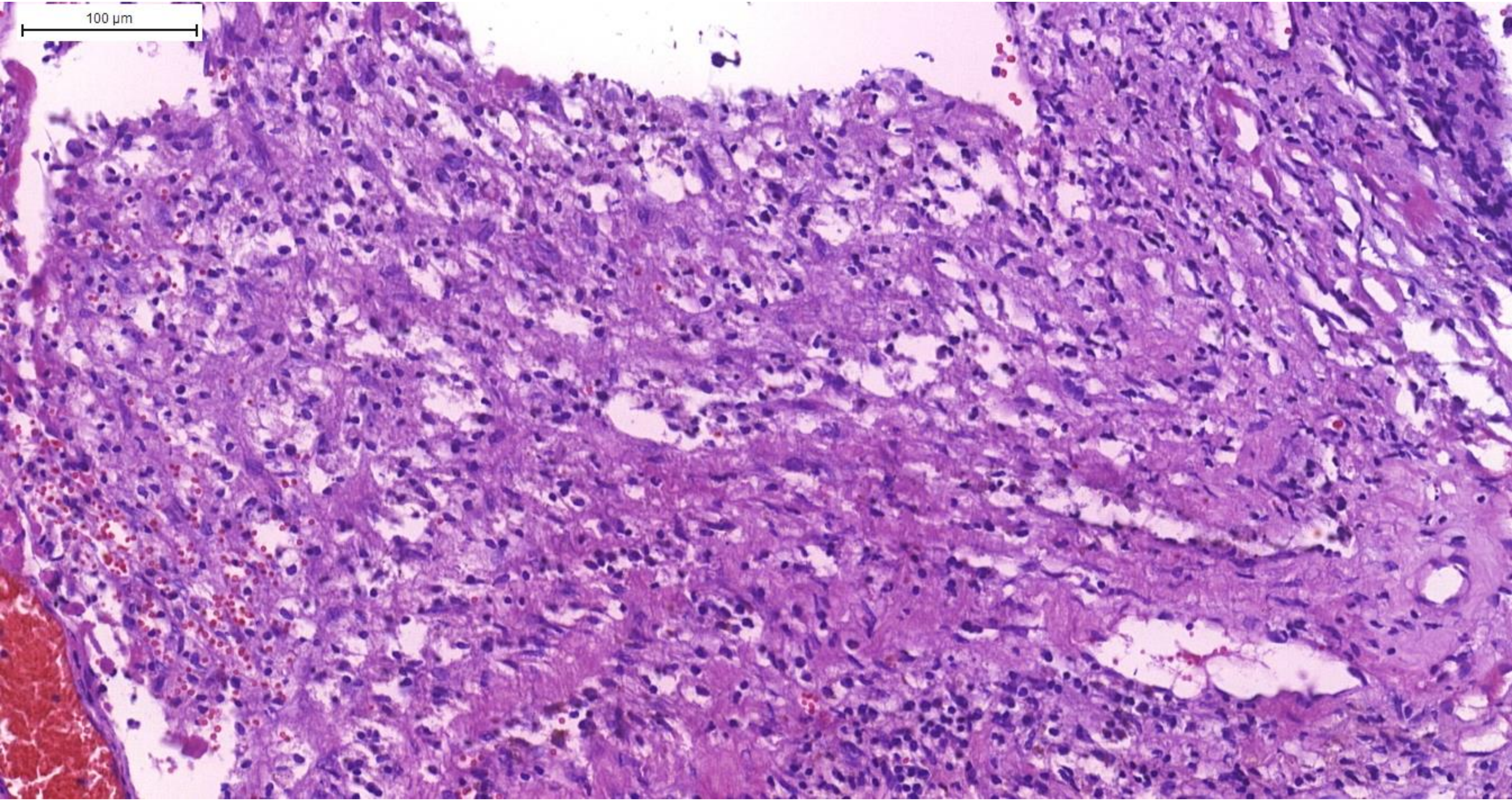
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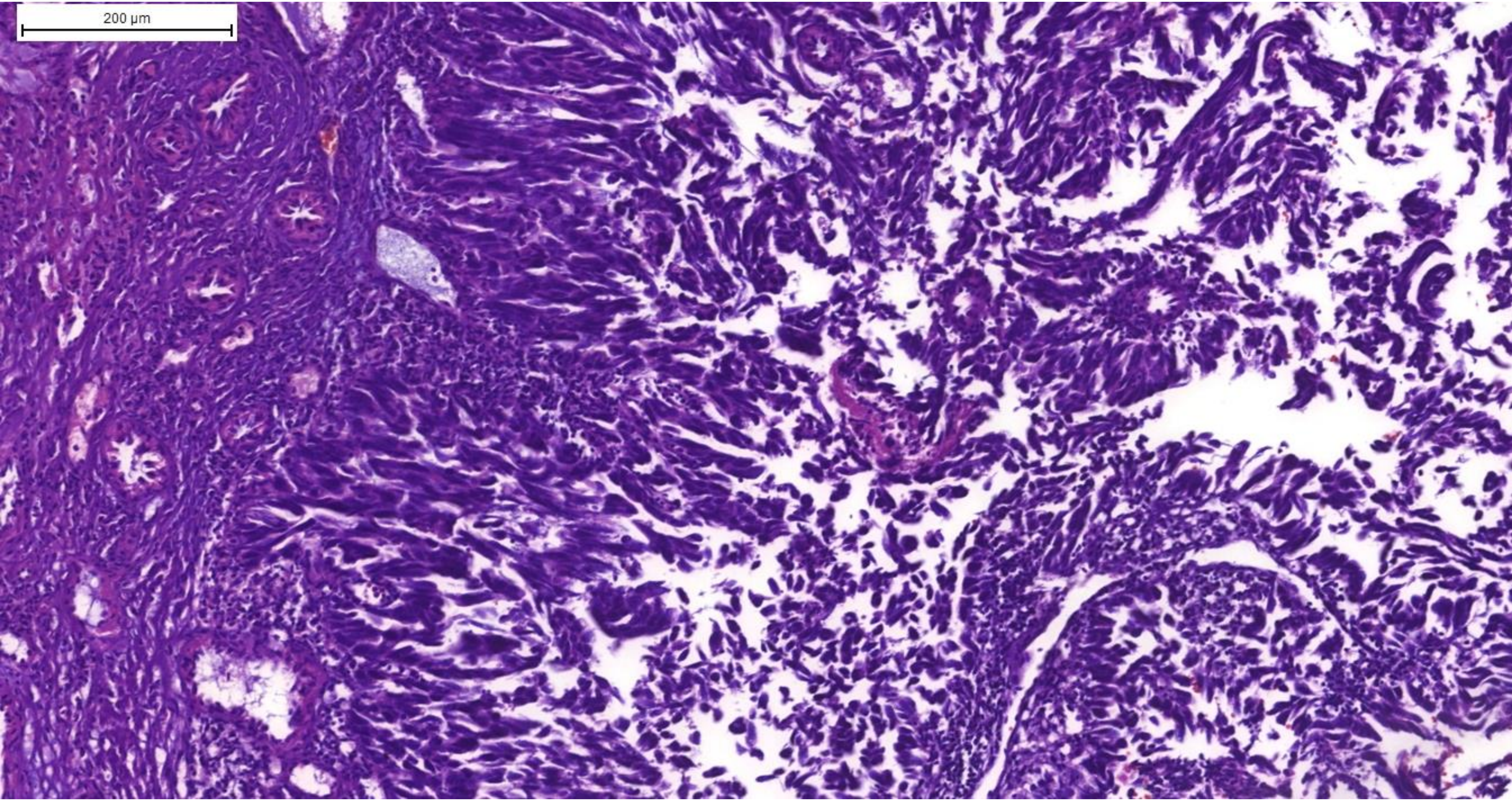
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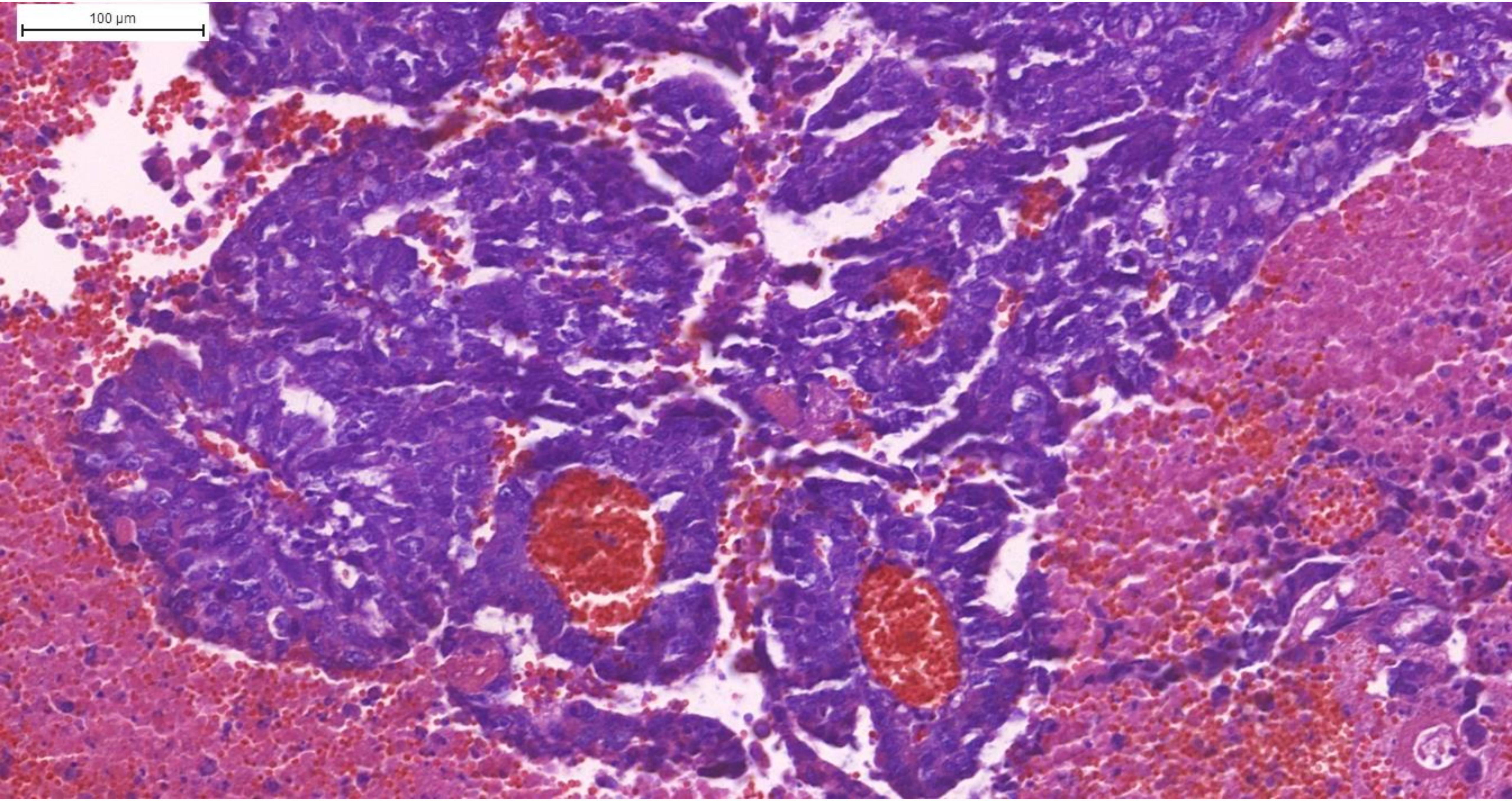
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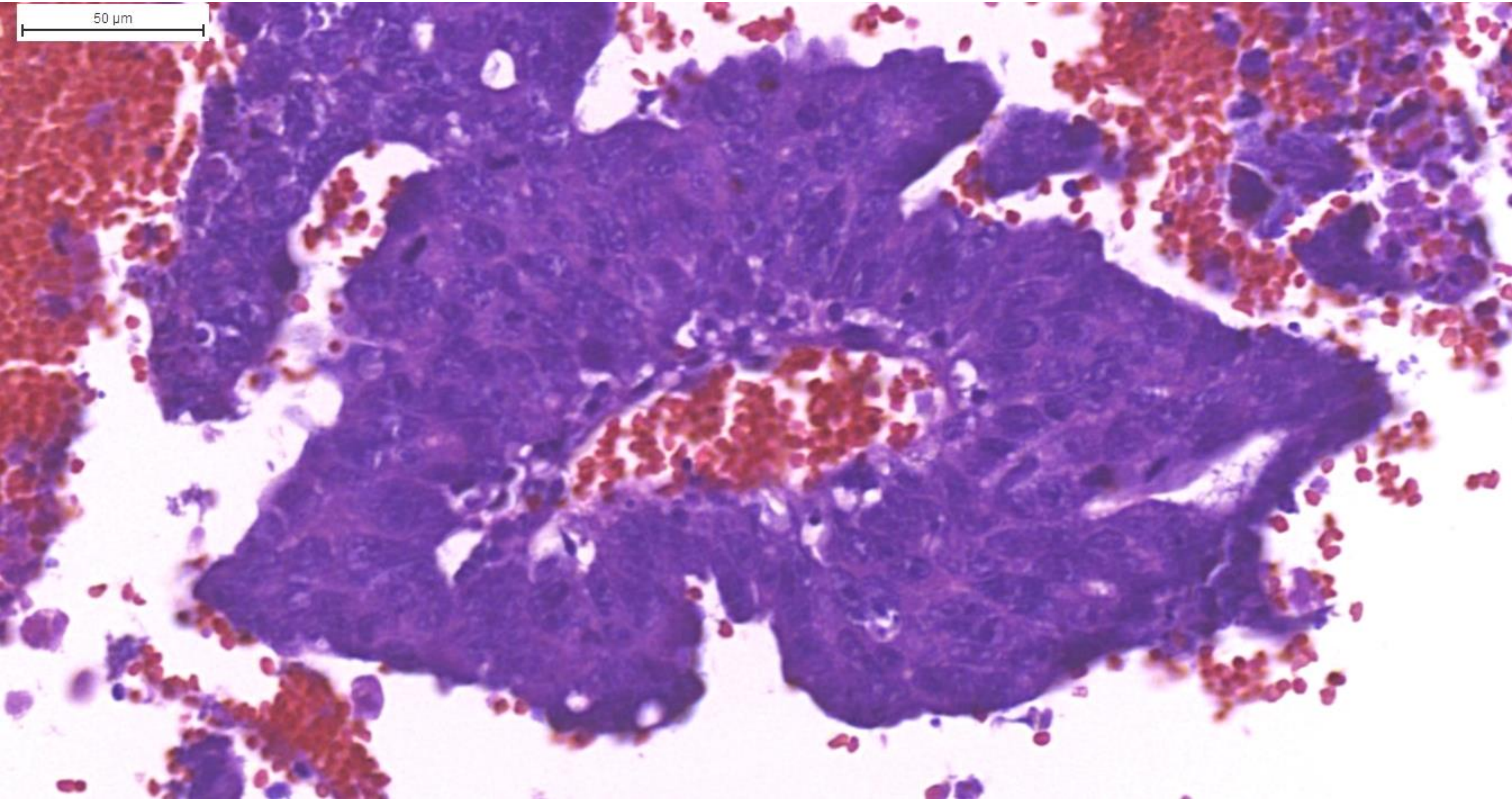
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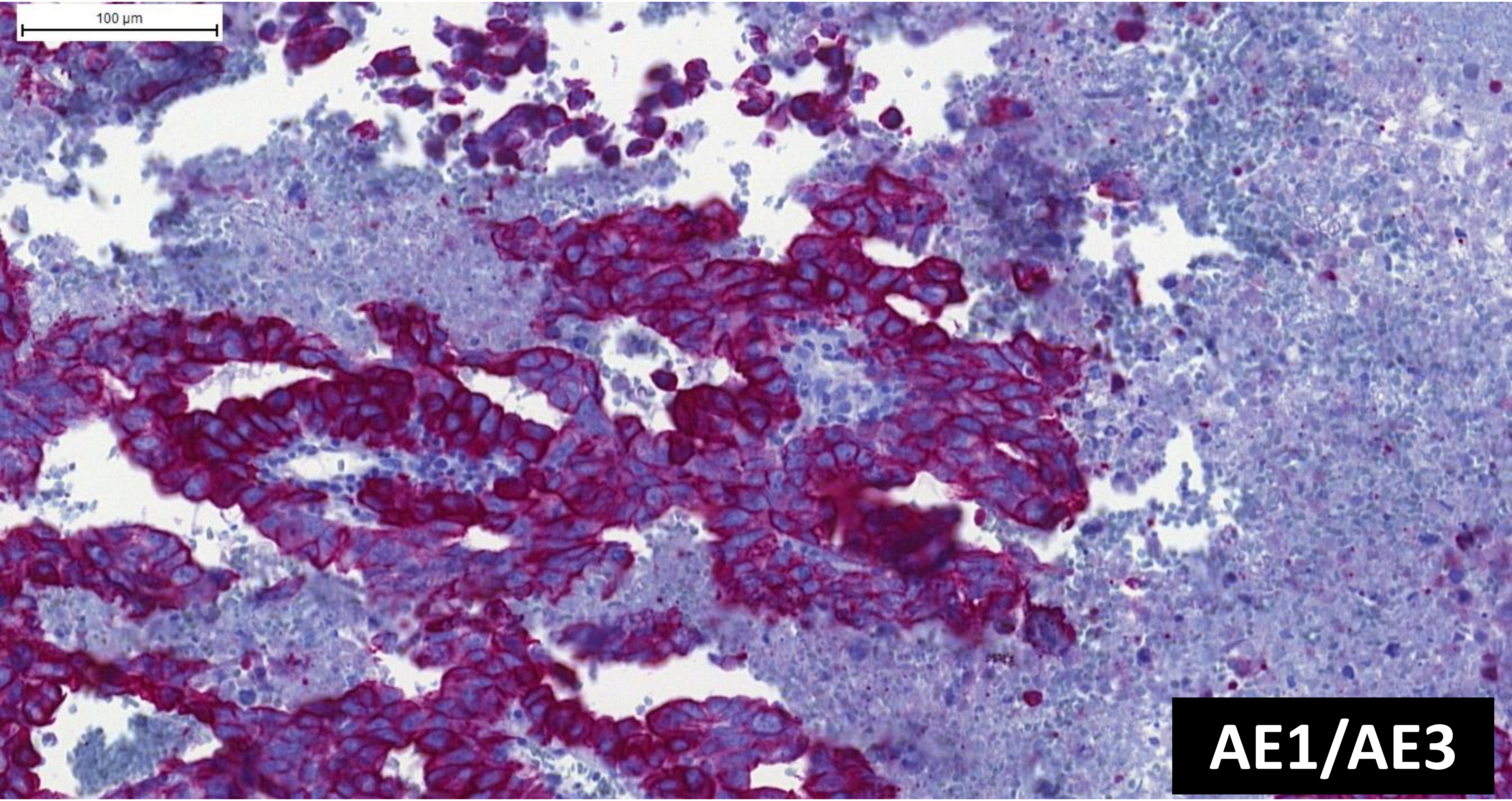
Imunoprofil

Dodané imuno

- GFAP –
- OLIG2-
- SYP –
- NF fokálne +
- CK8/18 +
- SMA –
- Desmin –
- Myogenin –
- LCA –
- Beta catenin –
- INI-1 +
- Mib-1 takmer 100%

DIAGNÓZA?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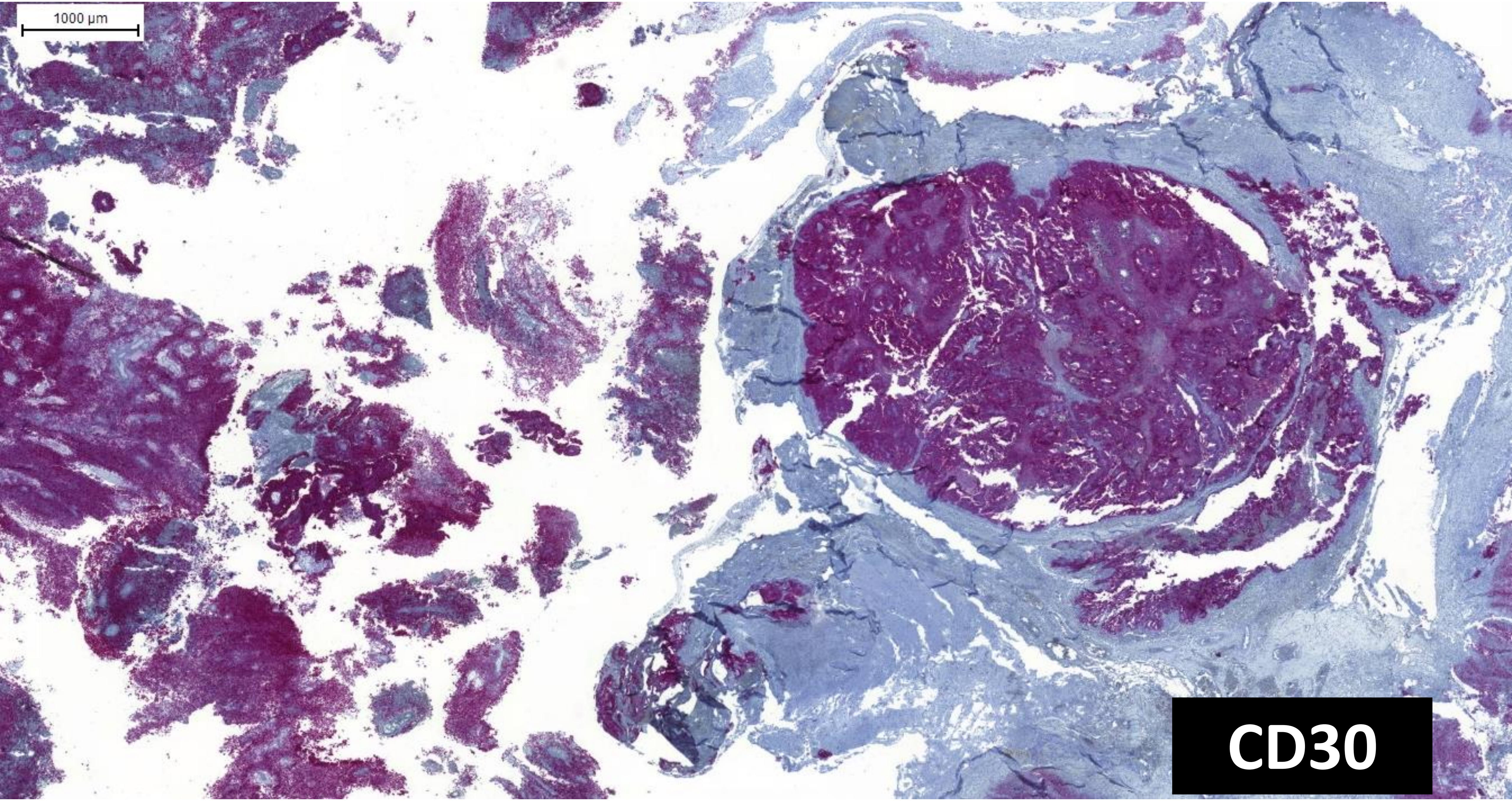
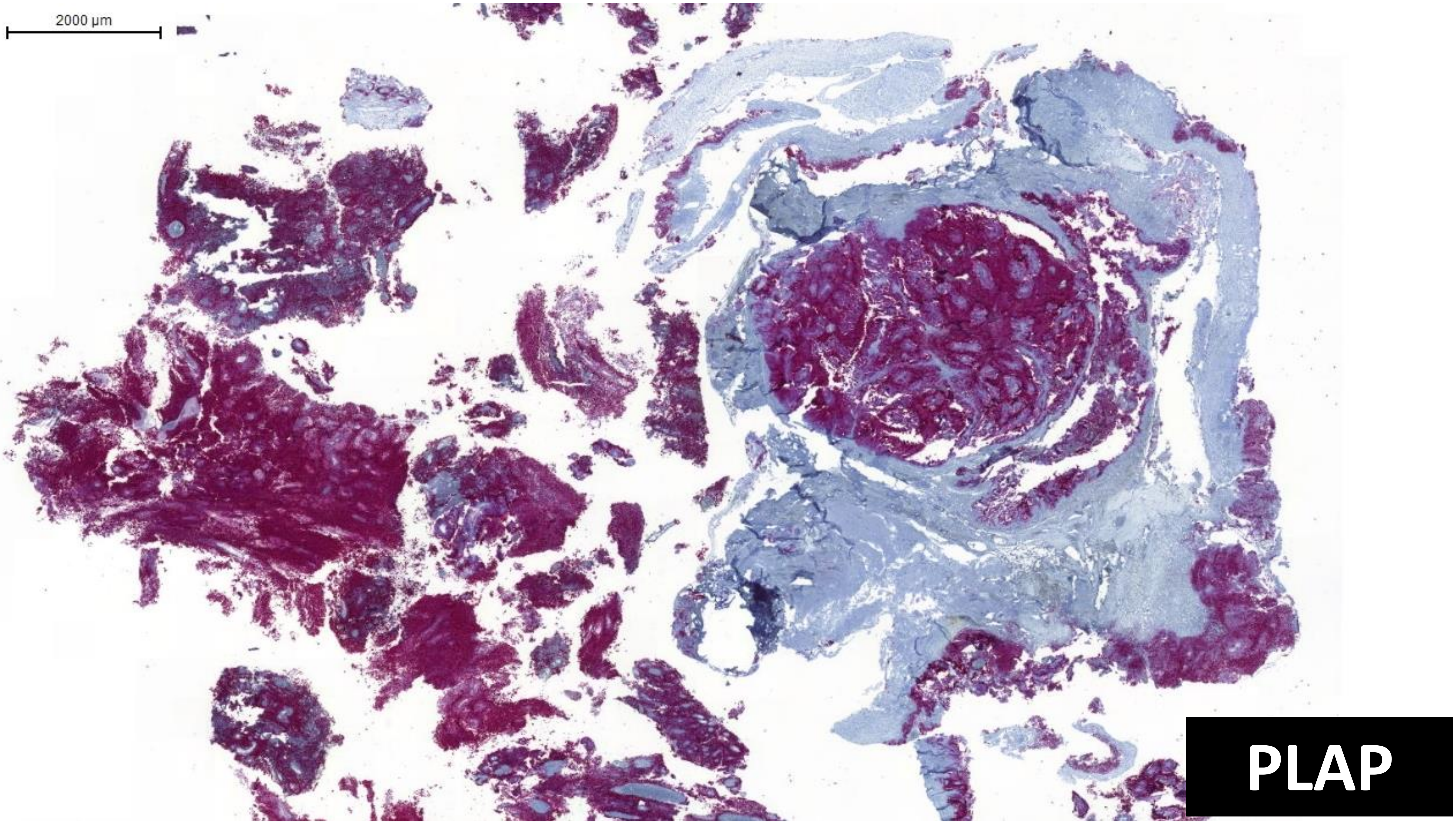
AE1/AE3


1000 µm
CD30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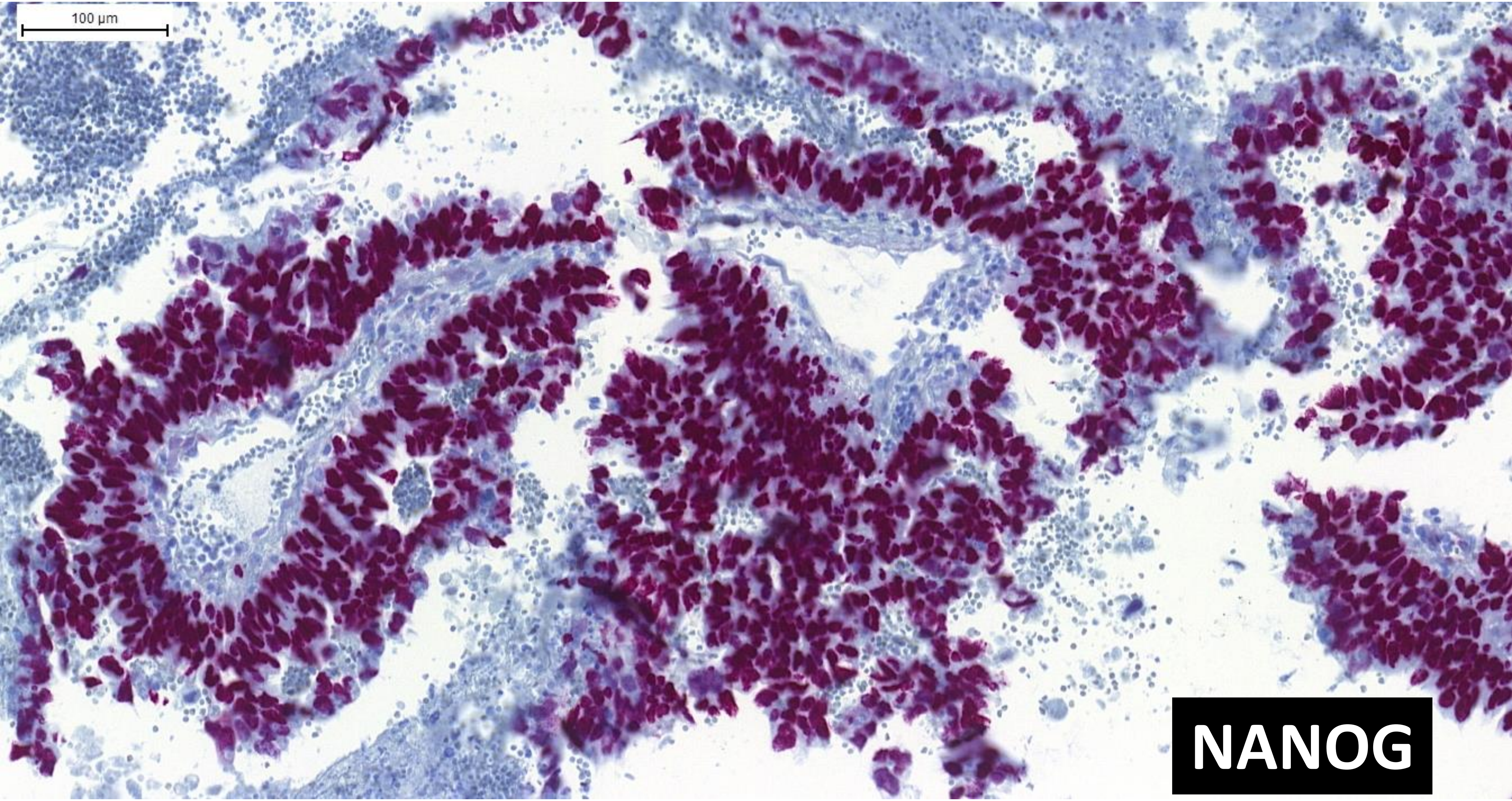
PLAP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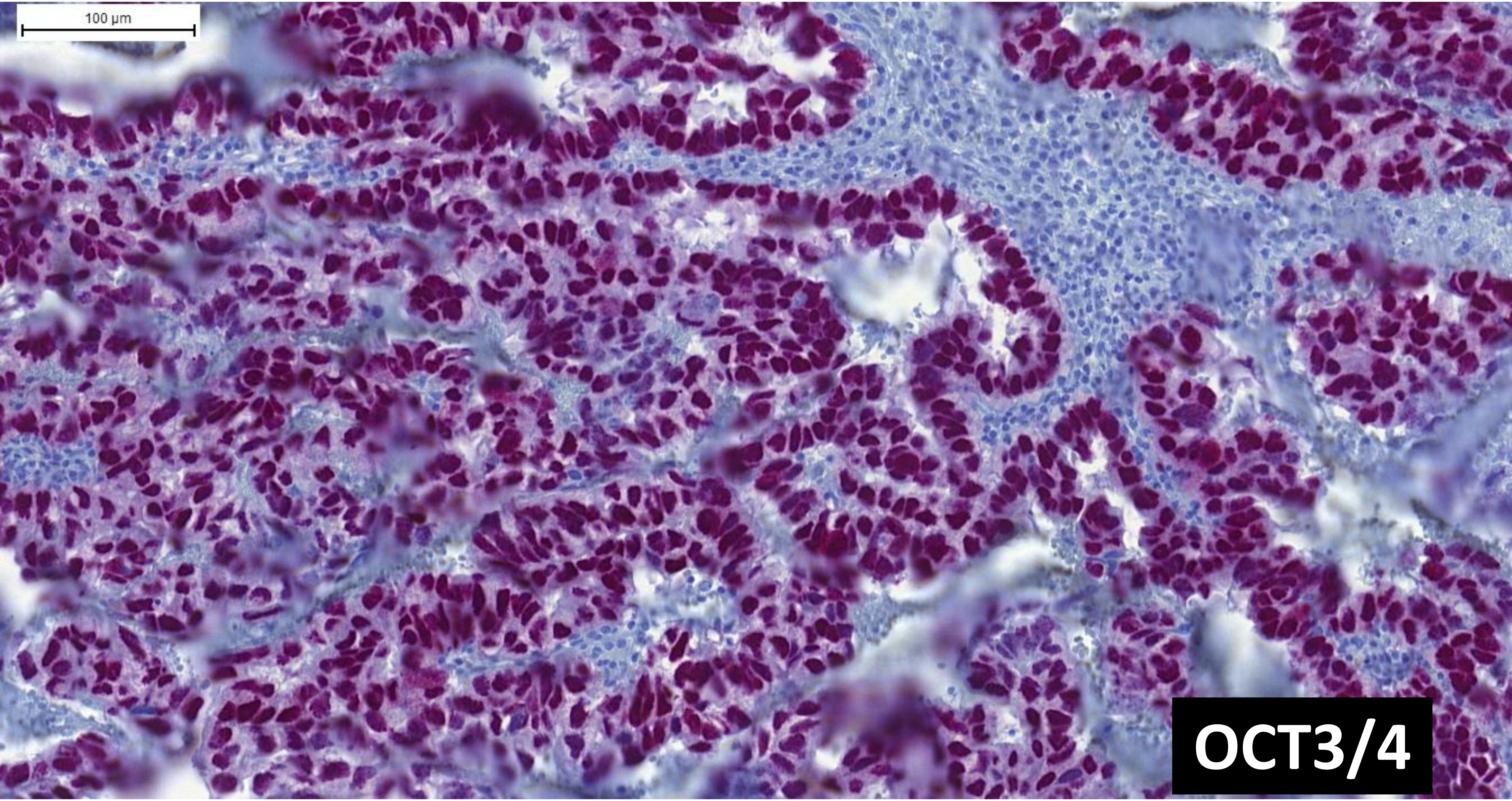
NANOG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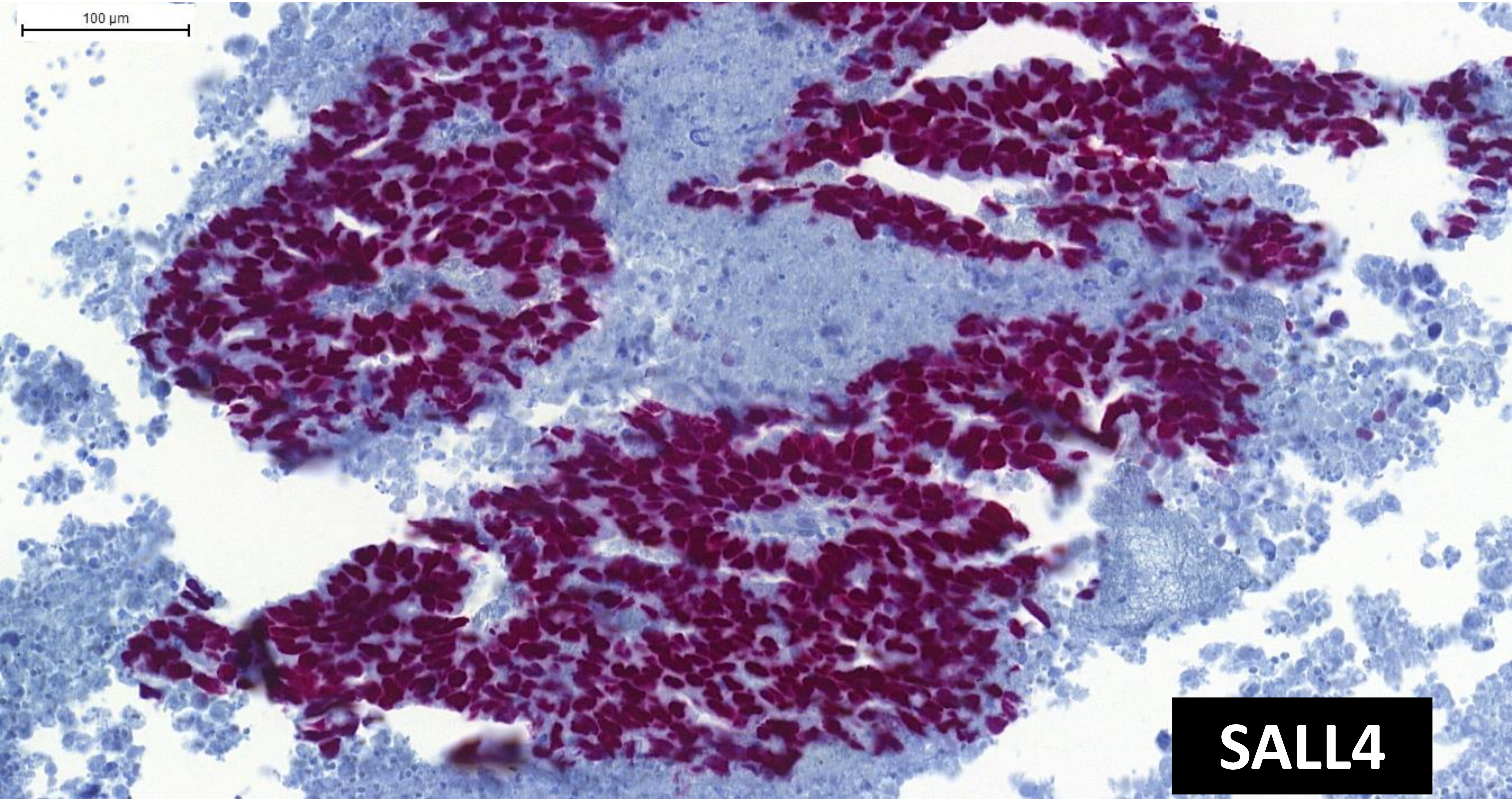
OCT3/4


100 µm
SALL4

Imunoprofil

Doplnené imuno

- AE1/AE3 +
- CD30 +
- PLAP +
- NANOG +
- OCT3/4 +
- SALL4 +
- Beta-HCG –
- Glypican3 –
- AFP –

Dodané imuno

- GFAP –
- OLIG2-
- SYP –
- NF fokálne +
- CK8/18 +
- SMA –
- Desmin –
- Myogenin –
- LCA –
- Beta catenin –
- INI-1 +
- Mib-1 takmer 100%

Embryonal carcinoma

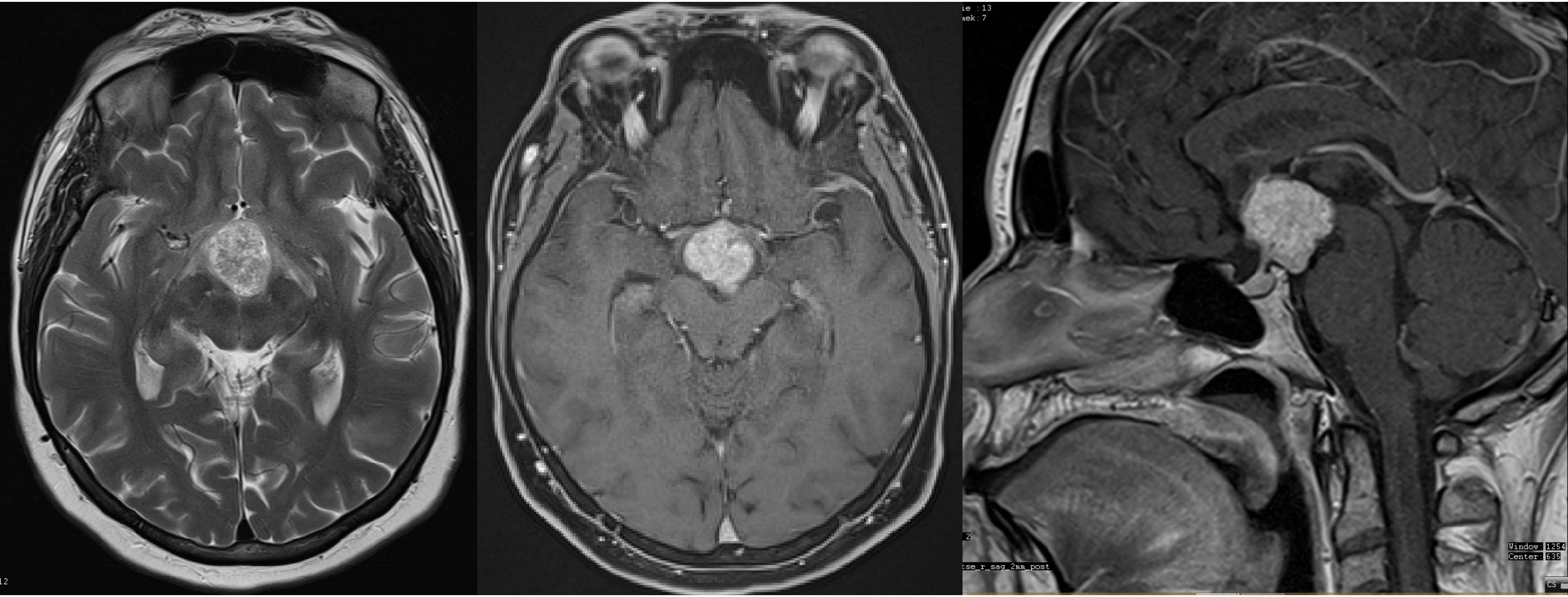
- Je nutné vylúčiť možnosť metastázy, vrátane možnosti regresie origa v testis

- Vykonaná orchiektomia
    - atrofické testis s jazvou
    - mikroskopicky IGCN (germ cell neoplasia in situ), kalcifikácie v tubuloch, bez invazívnej komponenty

	Seminom	EC	YST	ChorioCa	Teratóm
AFP	-	+/- (do 30%)	+/- (70-100%)	-	+/-
CD30	-	+/- (80-90%)	-	-	-
Glypican 3	-	-/+ (do 5%)	+ (100%)	+/- (80%)	+/- (do 20%)
CD117	+ (100%)	-	+/- (60%)	-	-
NANOG	+ (100%)	+ (100%)	-	-	-
OCT3/4	+ (100%)	+ (100%)	-	-	-
PLAP	+ (90-100%)	+ (80-90%)	+/- (do 90%)	+	-
D2-40	+ (100%)	-	-	-	+/-
SALL4	+ (100%)	+ (100%)	+ (100%)	+/- (70%)	+/- (50%)
SOX17	+ (95%)	-	+/- (50%)	-	+/-
SOX2	-	+ (96%)	-	-	+/-
βHCG	-	-	-	+ (100%)	-

Prípad č. 12

- 36-ročná žena
- interhemisferický TU – pravdepodobne ependymóm III.komory, v dif. dg. TU hypothalamu s propagáciou kraniálne, alebo TU stopky hypofýzy - makroadenom s propagáciou do obl. III. komory
- pooperačný diabetes insipidus (hyperosmolalita, hypernatriémia, dehydratácia)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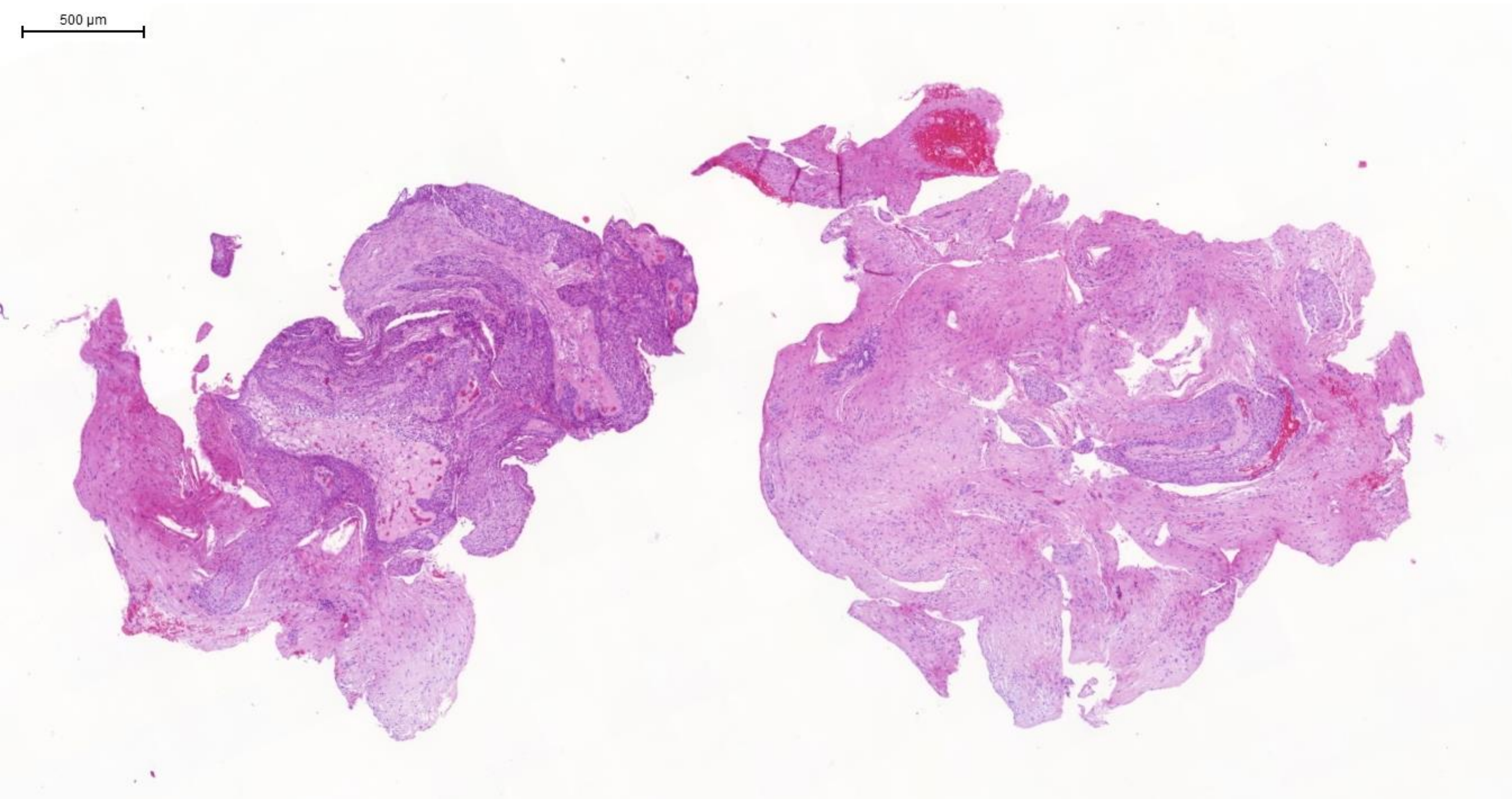
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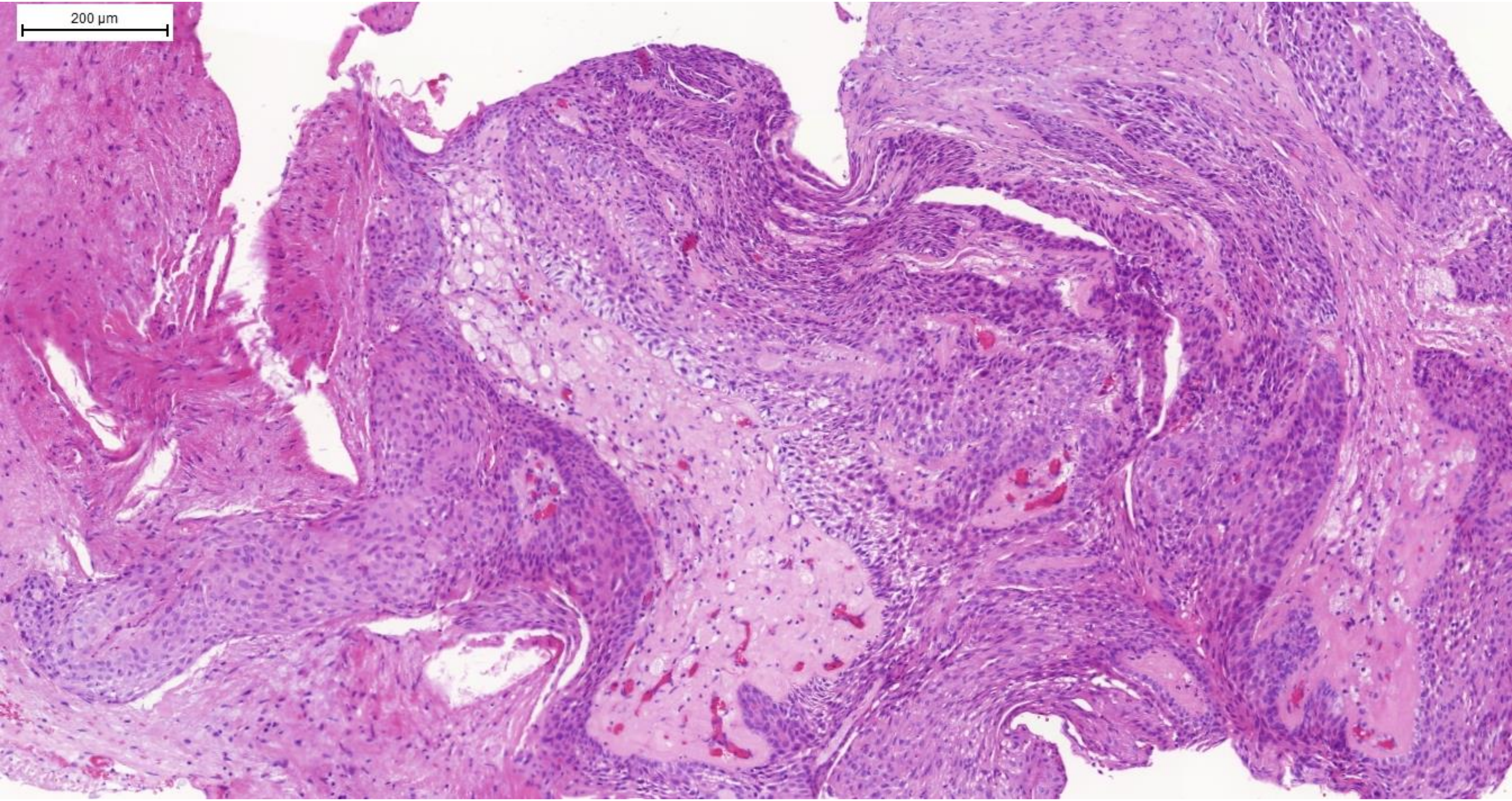
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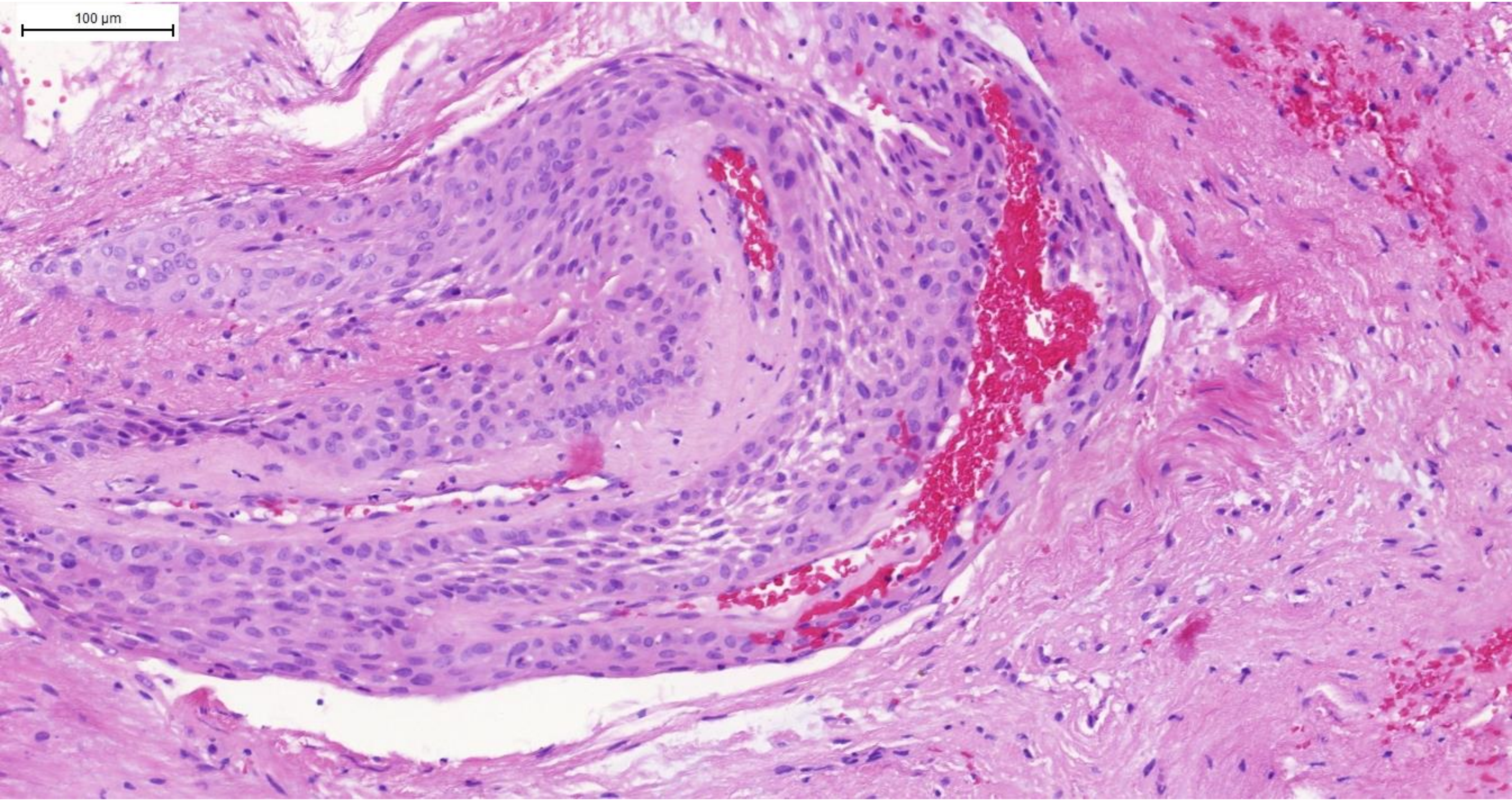
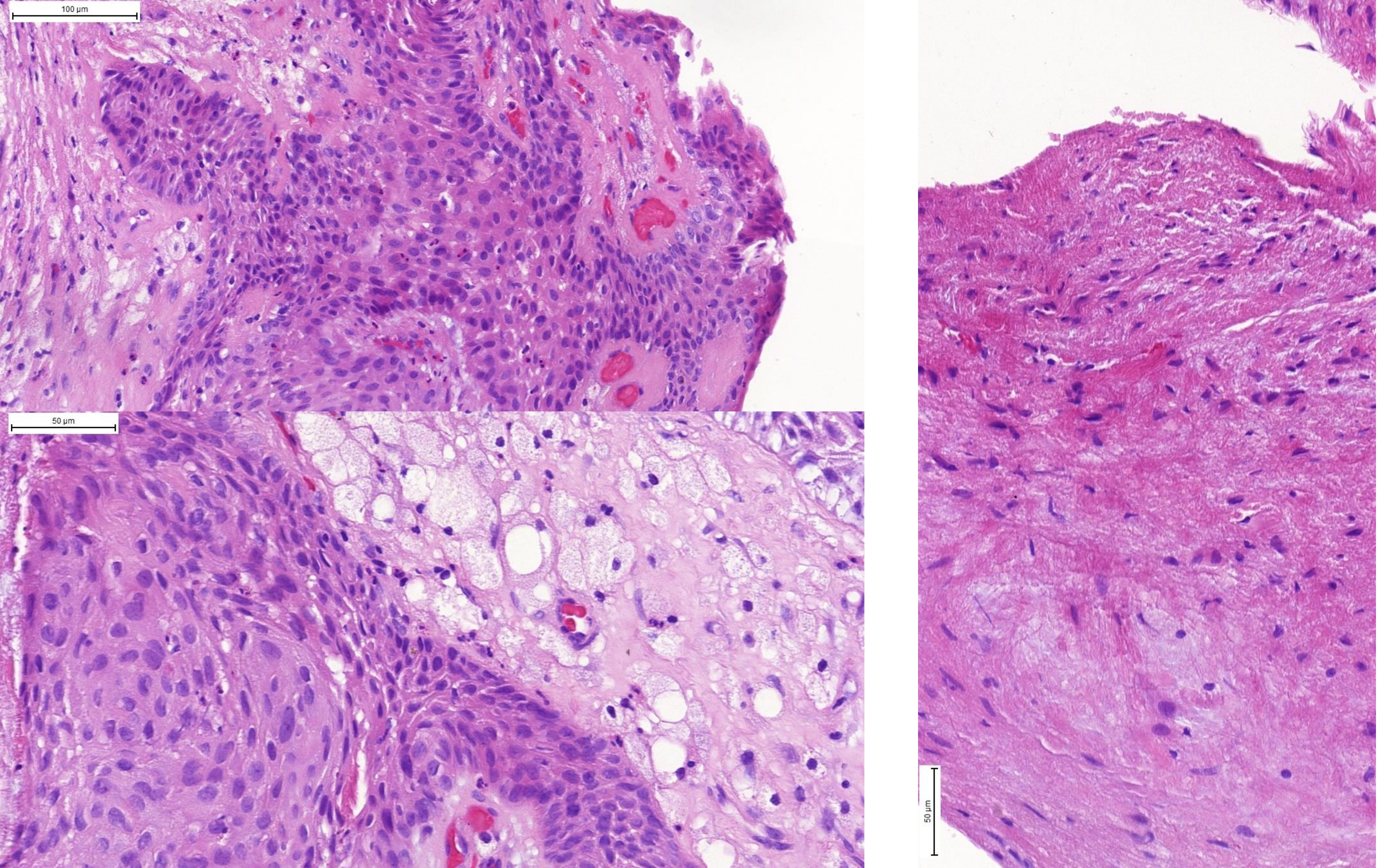
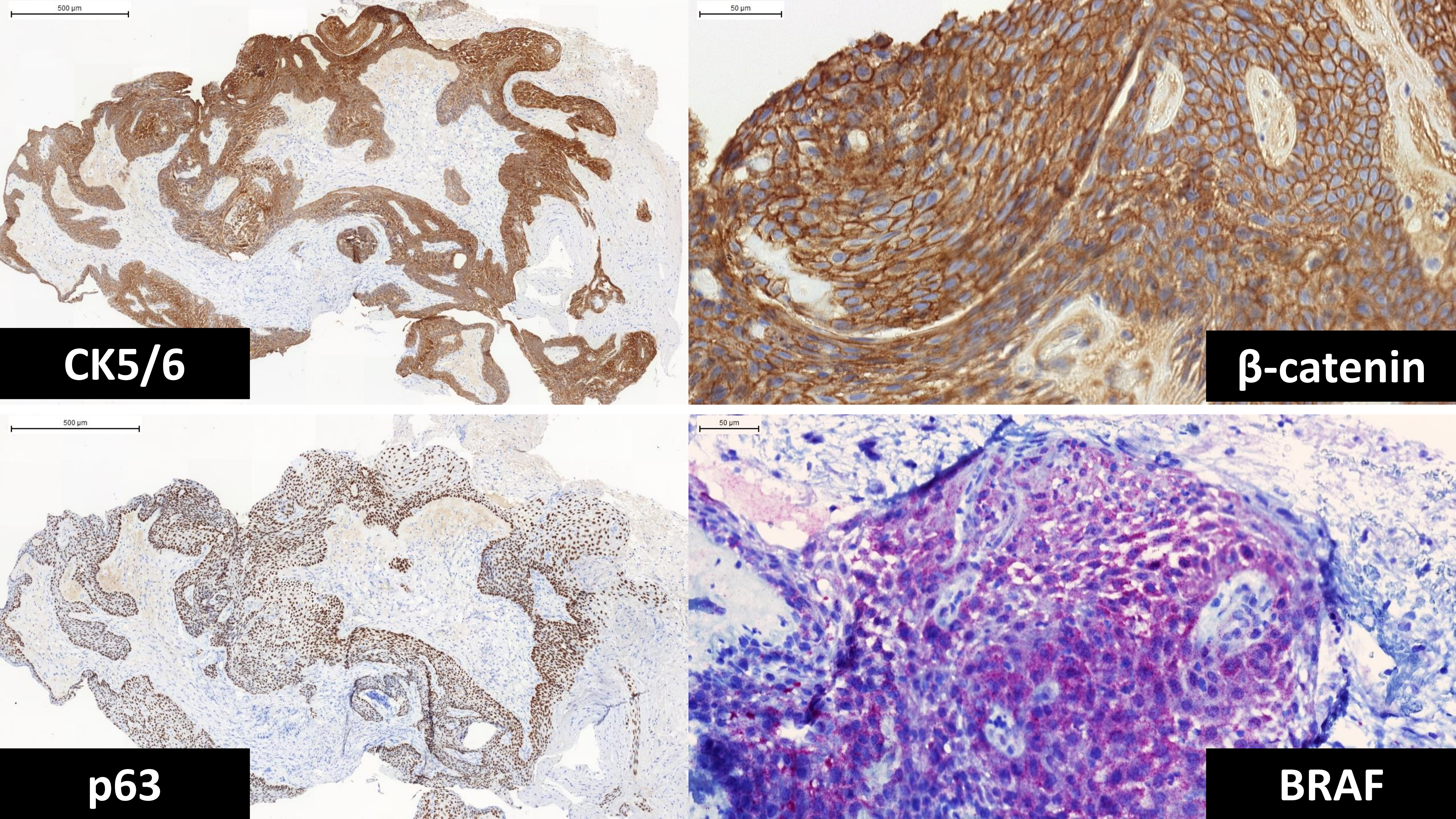
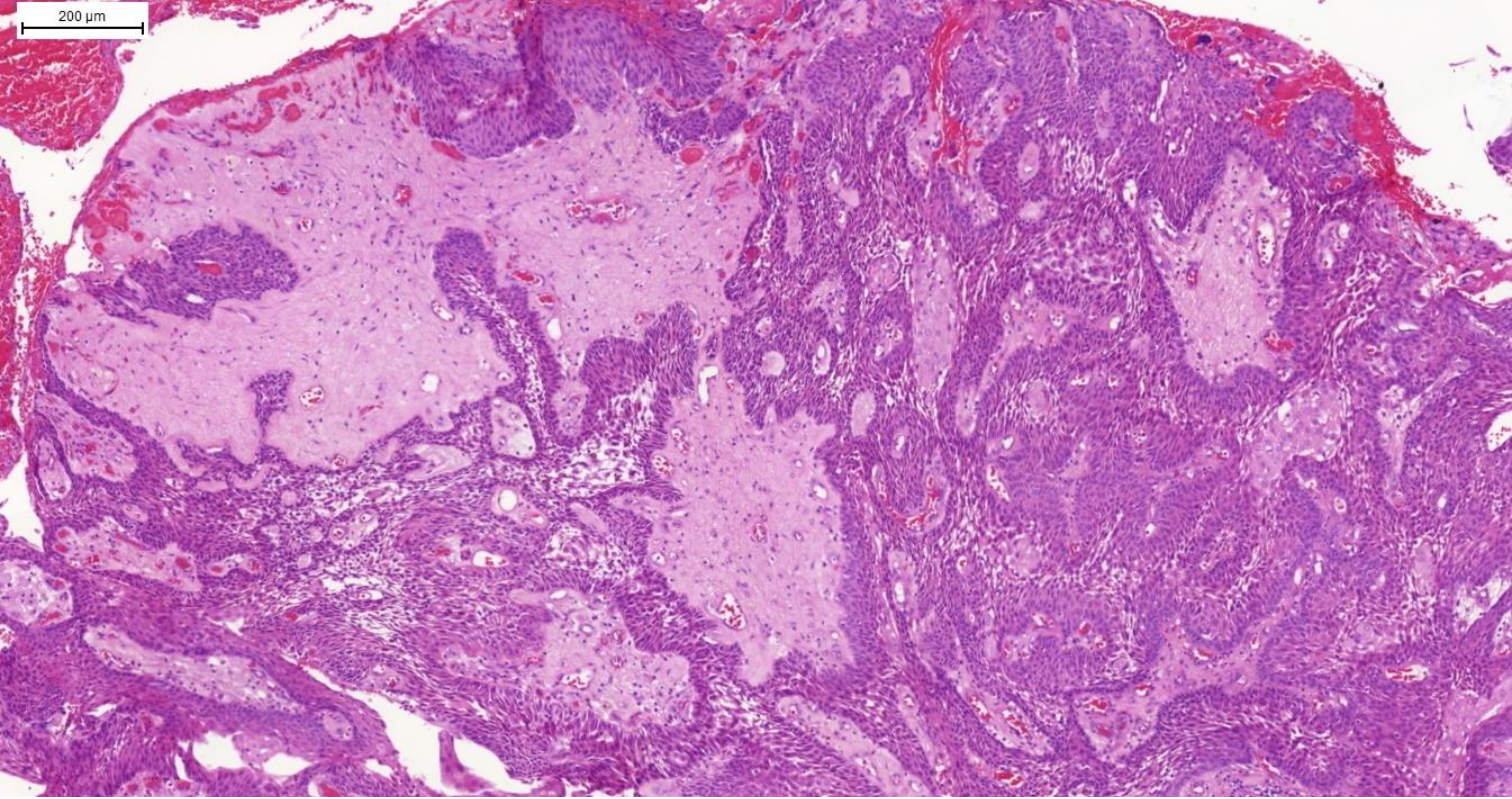

100 µm


100 µm
50 µm
50 µm

DIAGNÓZA?


500 µm
CK5/6
50 µm
β-catenin
500 µm
p63
50 µm
BRAF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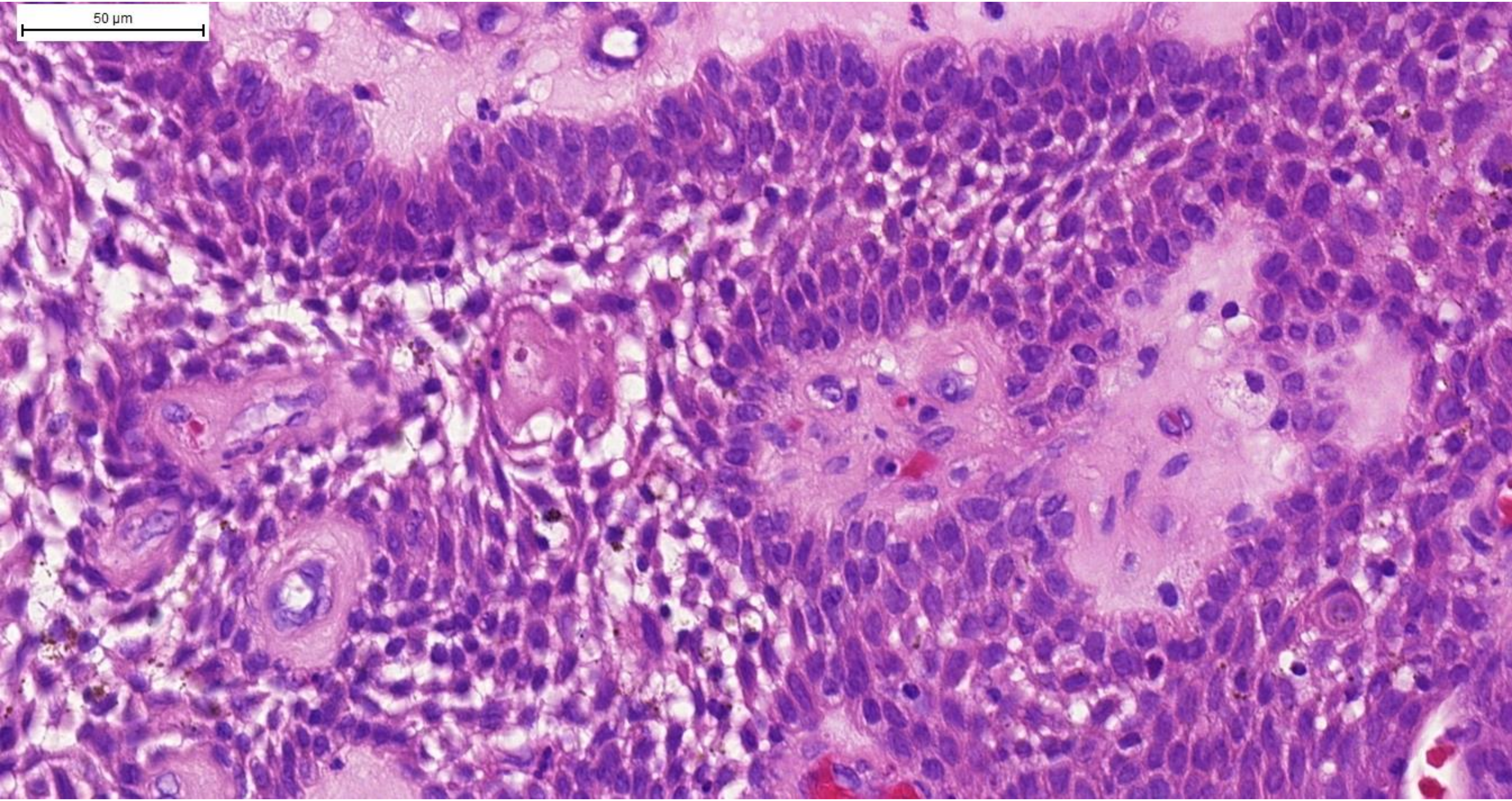
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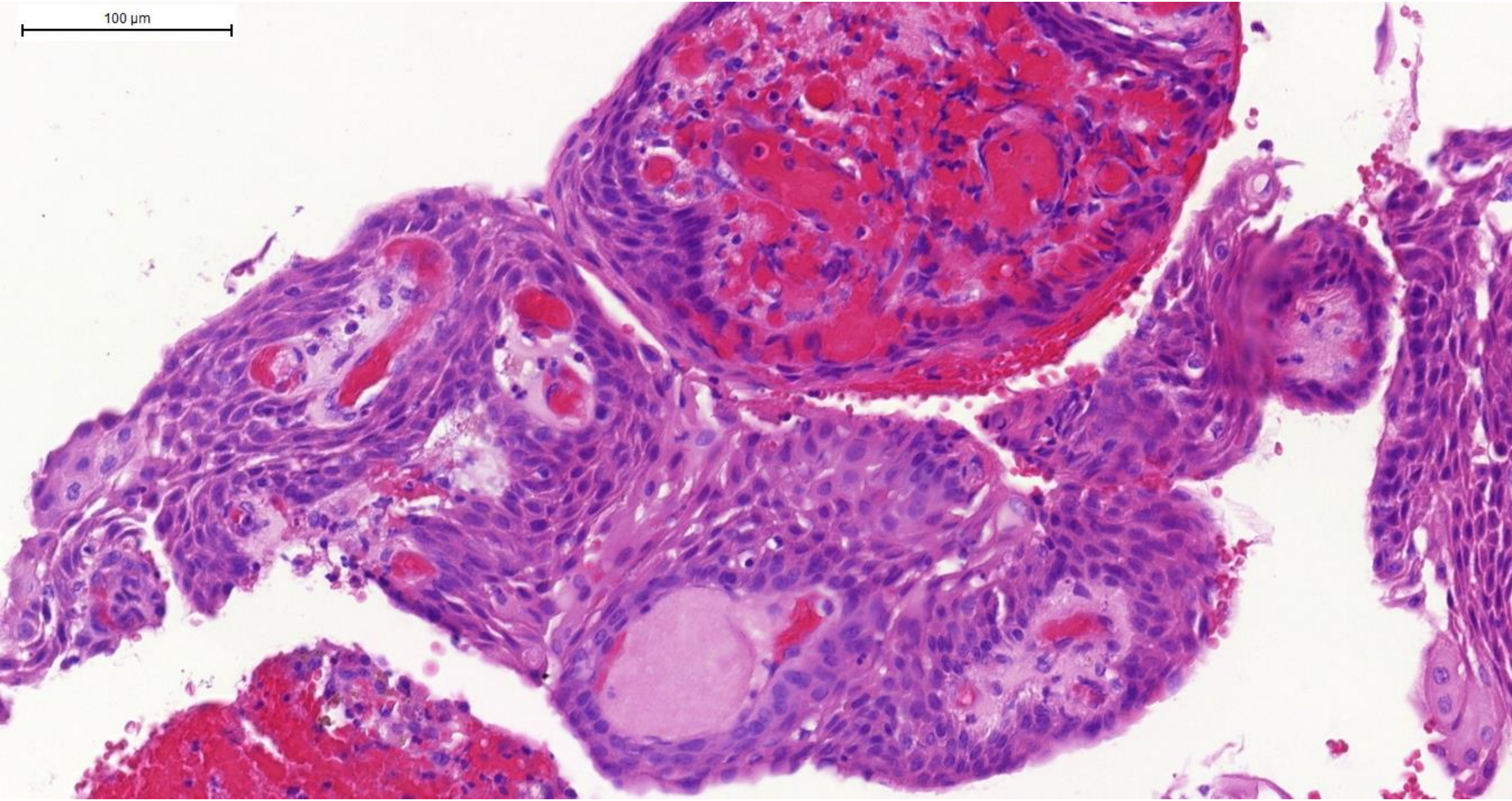
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Papillary craniopharyngioma, WHO grade I

- väčšinou supraselárny tumor, alebo oblasť III. komory
- solídny, menej často cystický
- takmer bez výnimky nádor dospelého veku
- +/- lepšia prognóza ako adamantinózny kraniofyrangeóm

- fibrovaskulárne jadro a blandný skvamózny epitel, vzácne pohárikovité bunky alebo riasinkový epitel
- bez palisádovania jadier na periférii, nemá „wet keratin“ a „whorling“ štruktúry, bez kalcifikácií

Papillary craniopharyngioma, WHO grade I

- Histologicky benígne lézie (WHO grade I), ale lokálne agresívne, s tendenciou k rekurenciám s neurologickým/endokrinologickým deficitom

- štandardom postoperačnej terapie po subtotálnej resekcii je radioterapia

- 80-95% má mutáciu BRAF V600E
- v „case reportoch“ dokázaná účinnosť cielenej liečby - dabrafenib + trametinib (BRAF + MEK inhibítor)

JNCI J Natl Cancer Inst (2016) 108(2): djv310

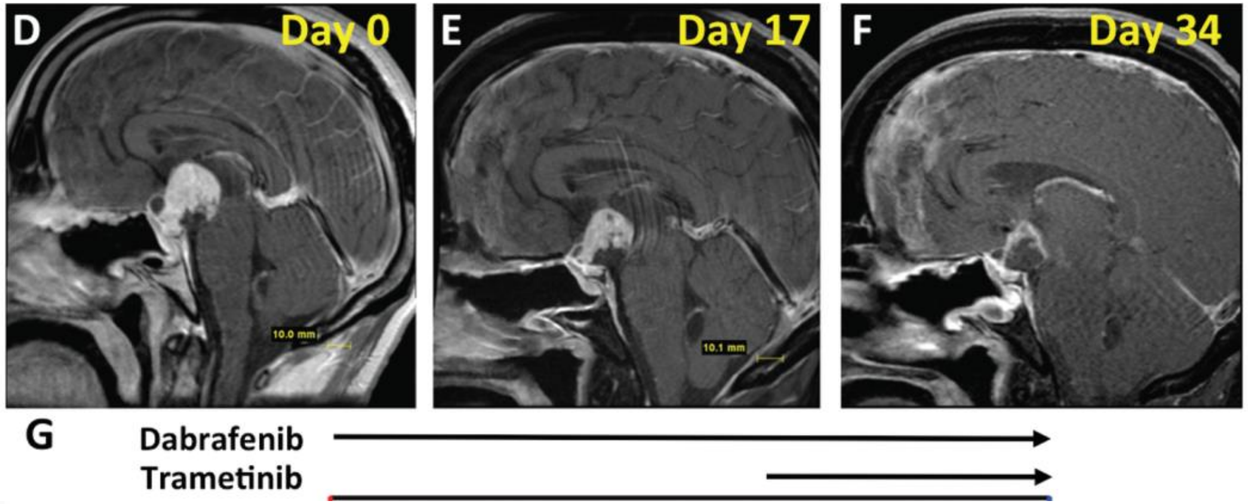
doi:10.1093/jnci/djv310
First published online October 23, 2015
Brief Communication

OXFORD

BRIEF COMMUNICATION

Dramatic Response of BRAF V600E Mutant Papillary Craniopharyngioma to Targeted Therapy

Priscilla K. Brastianos*, Ganesh M. Shankar *, Corey M. Gill*, Amaro Taylor-Weiner, Naema Nayyar, David J. Panka, Ryan J. Sullivan, Dennie T. Frederick, Malak Abedalthagafi, Pamela S. Jones, Ian F. Dunn, Brian V. Nahed, Javier M. Romero, David N. Louis, Gad Getz, Daniel P. Cahill†, Sandro Santagata†, William T. Curry Jr†, Fred G. Barker II†



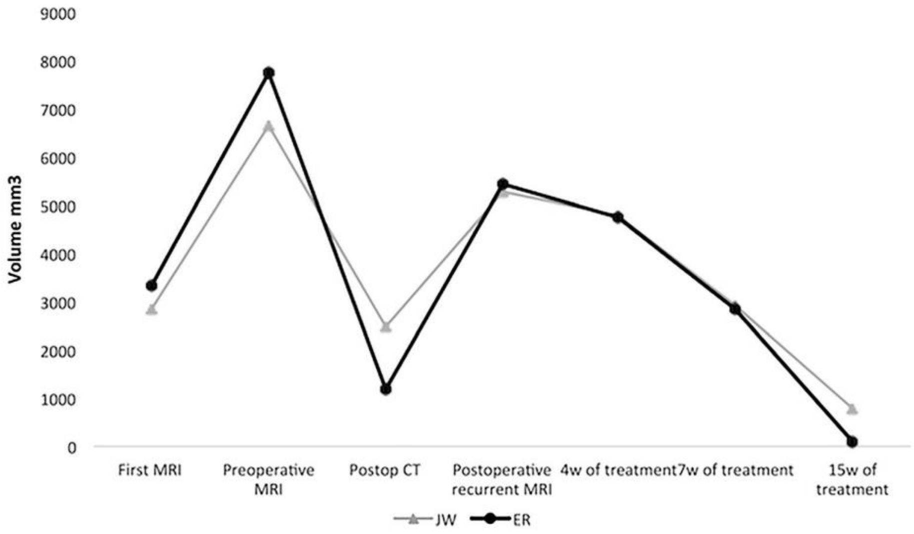
Acta Neurochir (2017) 159:2217–2221
DOI 10.1007/s00701-017-3311-0

CASE REPORT - BRAIN TUMORS

Recurrent papillary craniopharyngioma with BRAFV600E mutation treated with neoadjuvant-targeted therapy

Elham Rostami[1] · Petra Witt Nyström[2,3] · Sylwia Libard[4,5] · Johan Wikström[6] · Olivera Casar-Borota[4,5] · Olafur Gudjonsson[1]

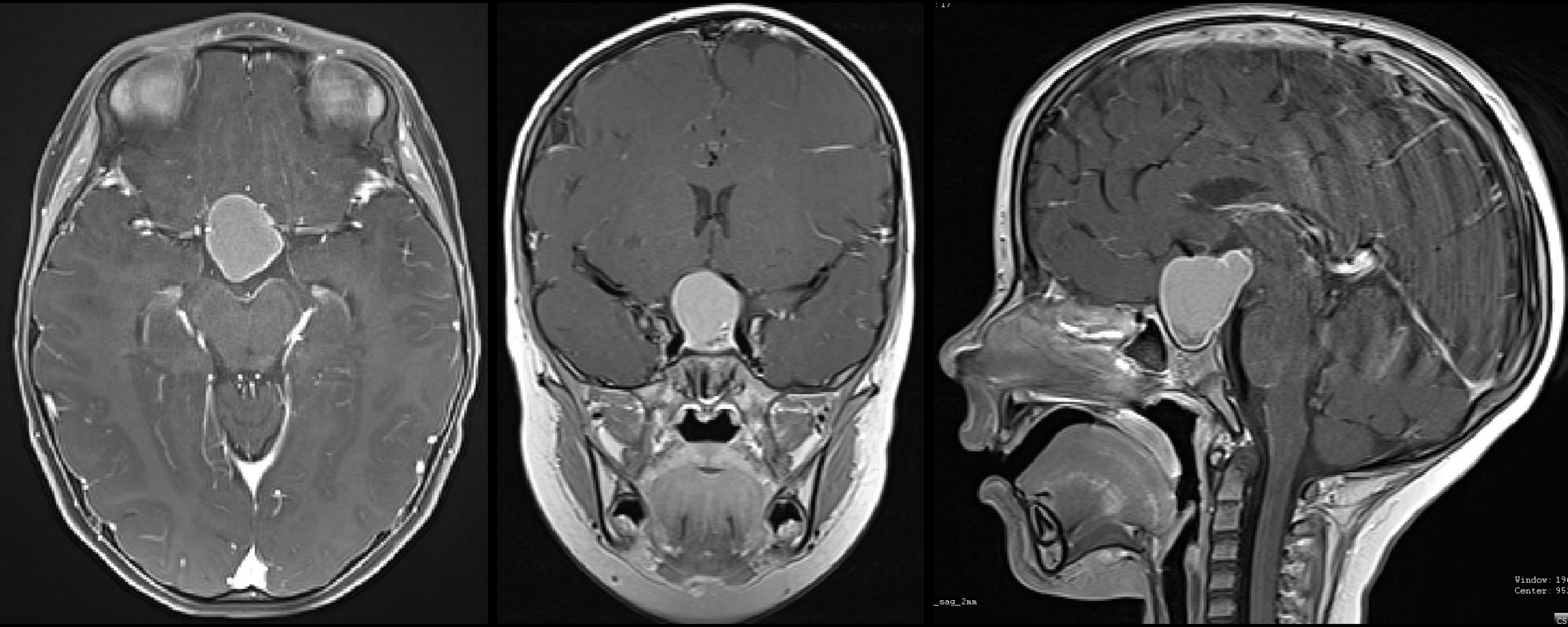
Fig. 2 Radiological evaluation of the two readers, one neurosurgeon (ER) and one neuroradiologist (JW), who independently evaluated the CT and MRI scans. The neuroradiologist was blinded to the diagnosis and the treatment plan



Prípad č. 13

- 4-ročné dievčatko
- zvracanie, polyúria, polydipsia - susp. diabetes insipidus
- atrofia papily zrakového nervu vpravo

- MRI: objemná, prevažne cystická expanzia hypofýzy zasahujúca supraselárne
- Vzhľadom k charakteru signálu v T1 sa môže jednať o koloidnú cystu rathkeho výchlipky, skôr ako cysticky degenerovaný kraniopharyngeom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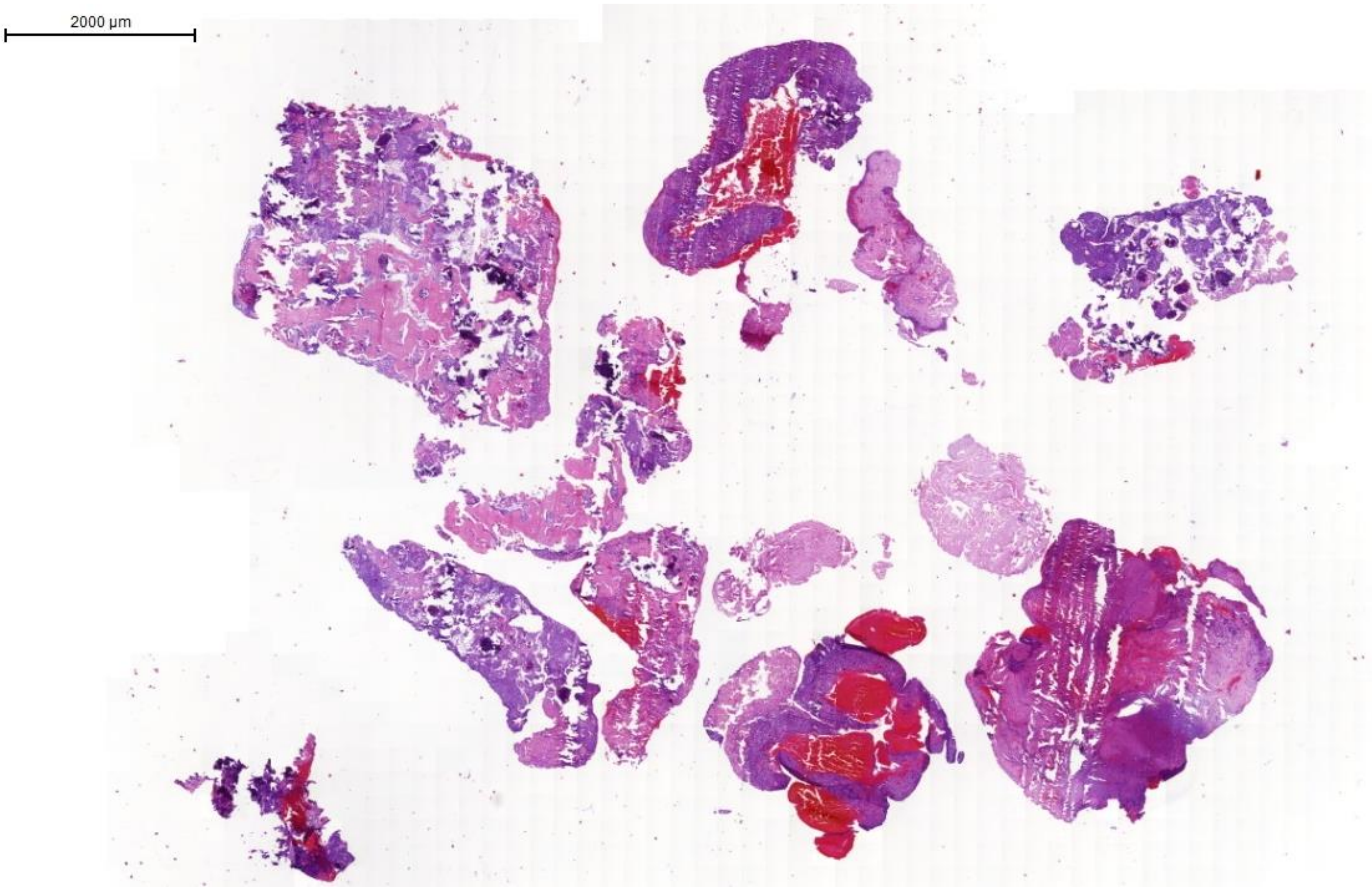
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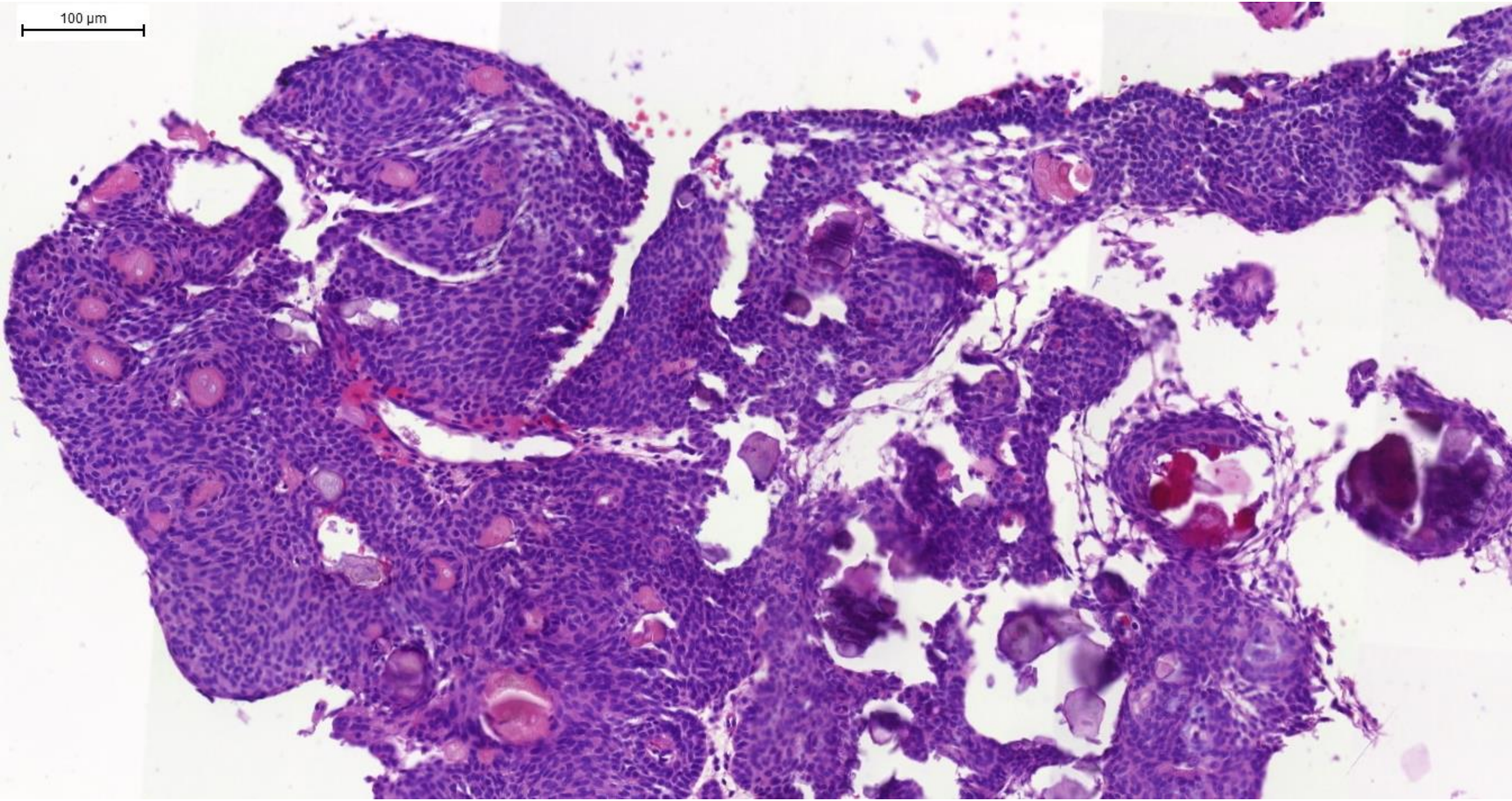
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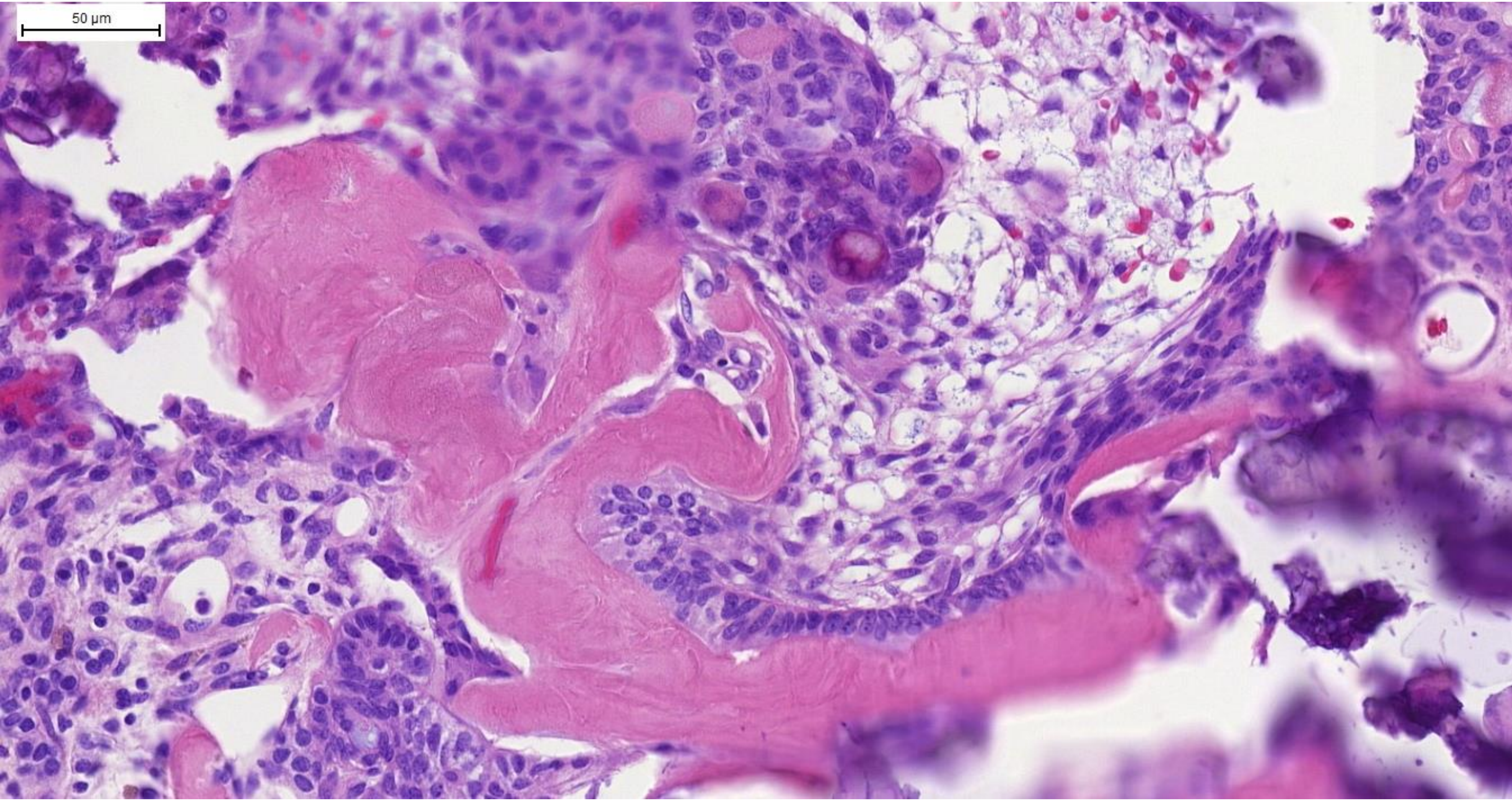
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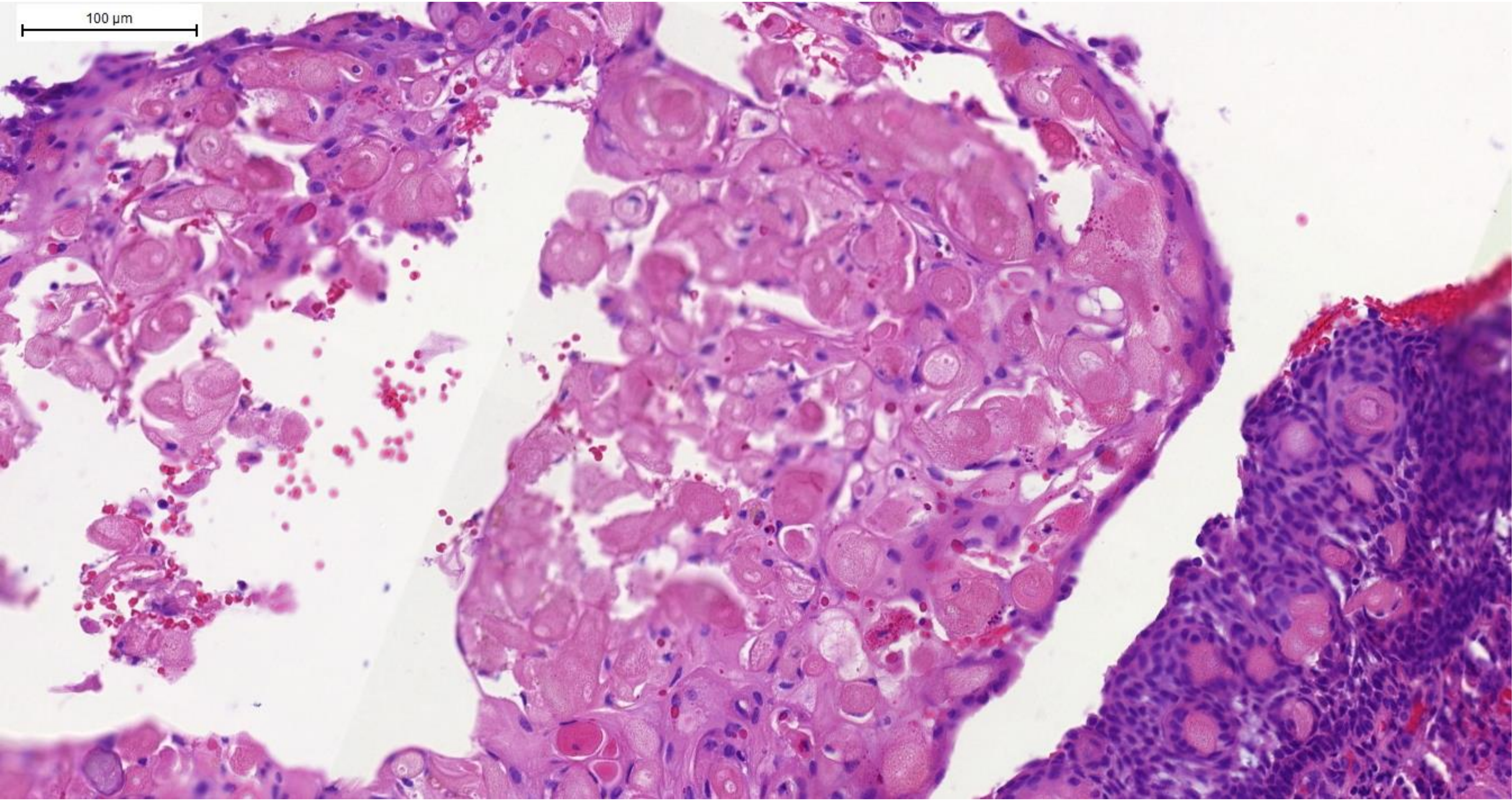
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Imuno

- BRAF negat.
- Beta- catenin ložiskovo v cytoplazme a jadre

Adamantinous craniopharyngioma, WHO grade I

- postihuje deti (5-15 rokov) aj dospelých (45-60 rokov)
- mutácia *CTNNB1* ~ 95%
- nukleárna expresia β-cateninu (nie je difúzna, najčastejšie vo výbežkoch a vírovitých „whorl-like“ štruktúrach na periférii tumoru a bunkách okolo „wet“ keratínu)

- epitel s palisádovaním na periférii
- kompaktnejšie časti + rozvoľnené časti - „stellate reticulum“
- tieňovité bezjadrové keratínové hmoty - „wet keratin“
- kalcifikácie
- piloidná glióza v okolí

Adamantinous craniopharyngioma, WHO grade I

- cielená liečba pri aktivácii cesty Wnt je komplikovaná a účinné inhibitory sú stále vo vývoji

- Mutácie *BRAF* a *CTNNB1* sú vzájomne exkluzívne a špecifické pre podtyp kraniofaryngeómu

Acta Neuropathol (2014) 127:927–929
DOI 10.1007/s00401-014-1270-6

CORRESPONDENCE

BRAF V600E mutations are characteristic for papillary craniopharyngioma and may coexist with CTNNB1-mutated adamantinomatous craniopharyngioma

Sarah Jane Larkin · Veronica Preda · Niki Karavitaki · Ashley Grossman · Olaf Ansorge

Of 16 aCP cases, 14 (88 %) were BRAF wild type by sequencing and IHC. We observed BRAF V600E mutation in two aCP cases. This finding was validated by

Acta Neuropathologica (2018) 135:757–777
https://doi.org/10.1007/s00401-018-1830-2

ORIGINAL PAPER

Tumour compartment transcriptomics demonstrates the activation of inflammatory and odontogenic programmes in human adamantinomatous craniopharyngioma and identifies the MAPK/ERK pathway as a novel therapeutic target

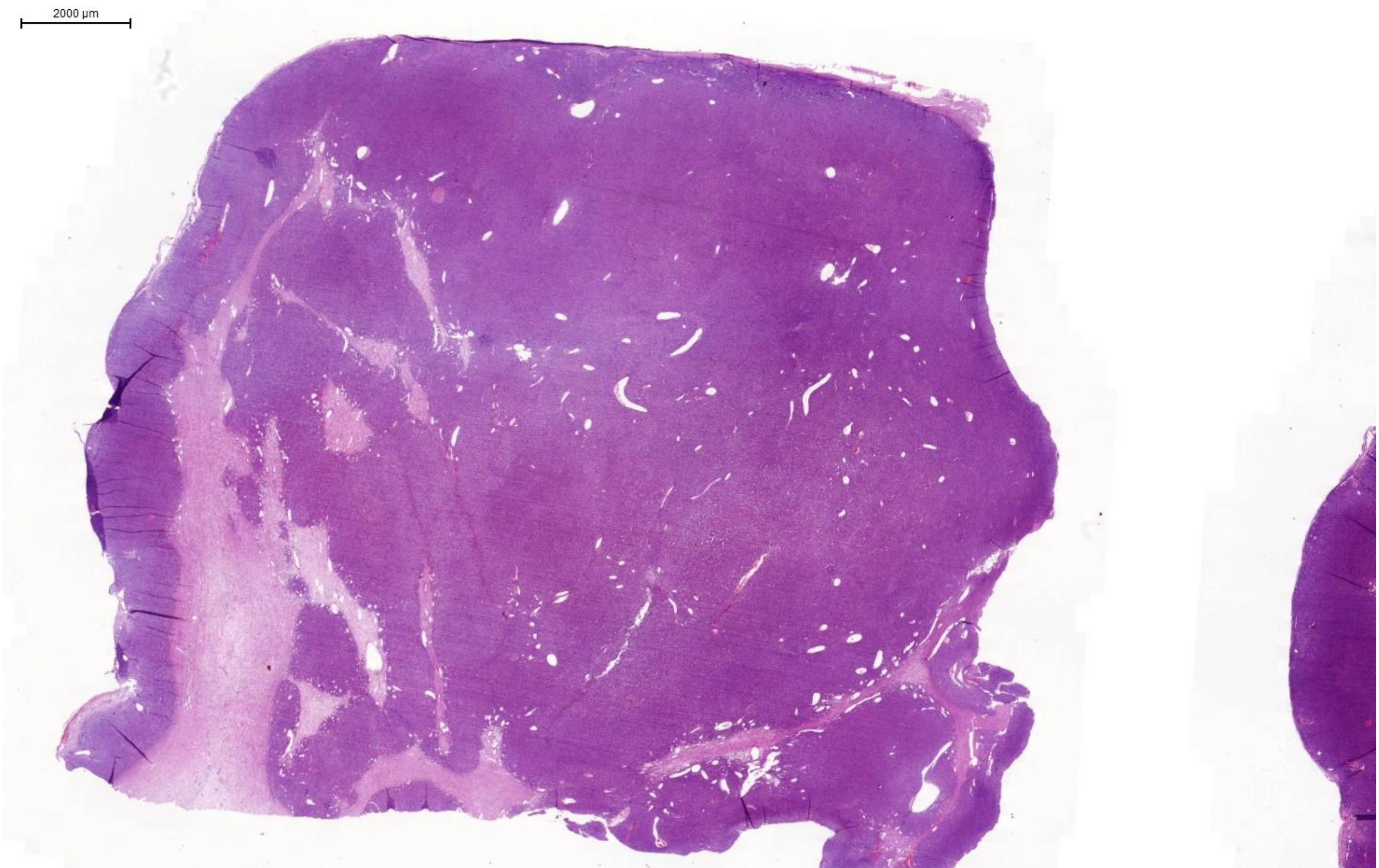
John R. Apps[1,2] · Gabriela Carreno[1] · Jose Mario Gonzalez-Meljem[1,3] · Scott Haston[1] · Romain Guiho[1] · Julie E. Cooper[1] · Saba Manshaei[1] · Nital Jani[4] · Annett Hölsken[5] · Benedetta Pettorini[6] · Robert J. Beynon[7] · Deborah M. Simpson[7] · Helen C. Fraser[1] · Ying Hong[8] · Shirleen Hallang[9] · Thomas J. Stone[1,2] · Alex Virasami[2] · Andrew M. Donson[10] · David Jones[11] · Kristian Aquilina[12] · Helen Spoudeas[13] · Abhijit R. Joshi[14] · Richard Grundy[15] · Lisa C. D. Storer[15] · Márta Korbonits[16] · David A. Hilton[17] · Kyoko Tossell[18] · Selvam Thavaraj[19] · Mark A. Ungless[18] · Jesus Gil[18] · Rolf Buslei[5,20] · Todd Hankinson[10] · Darren Hargrave[21] · Colin Goding[22] · Cynthia L. Andoniadou[23,24] · Paul Brogan[8,25] · Thomas S. Jacques[1,2] · Hywel J. Williams[4] · Juan Pedro Martinez-Barbera[1]

Trametinib, a clinically approved MEK inhibitor, results in reduced proliferation and increased apoptosis in explant cultures of human and mouse ACP

Prípad č. 14

- 83-ročná žena
-
- Klinická diagnóza: tentoriálny meningiom, dif. dg. MTS Ca prsníka
- Prof. Hes, FN Plzeň


SAG HEAD_KLIV 3.0
AX HEAD KLIV 3.0
Window: 80
Center: 35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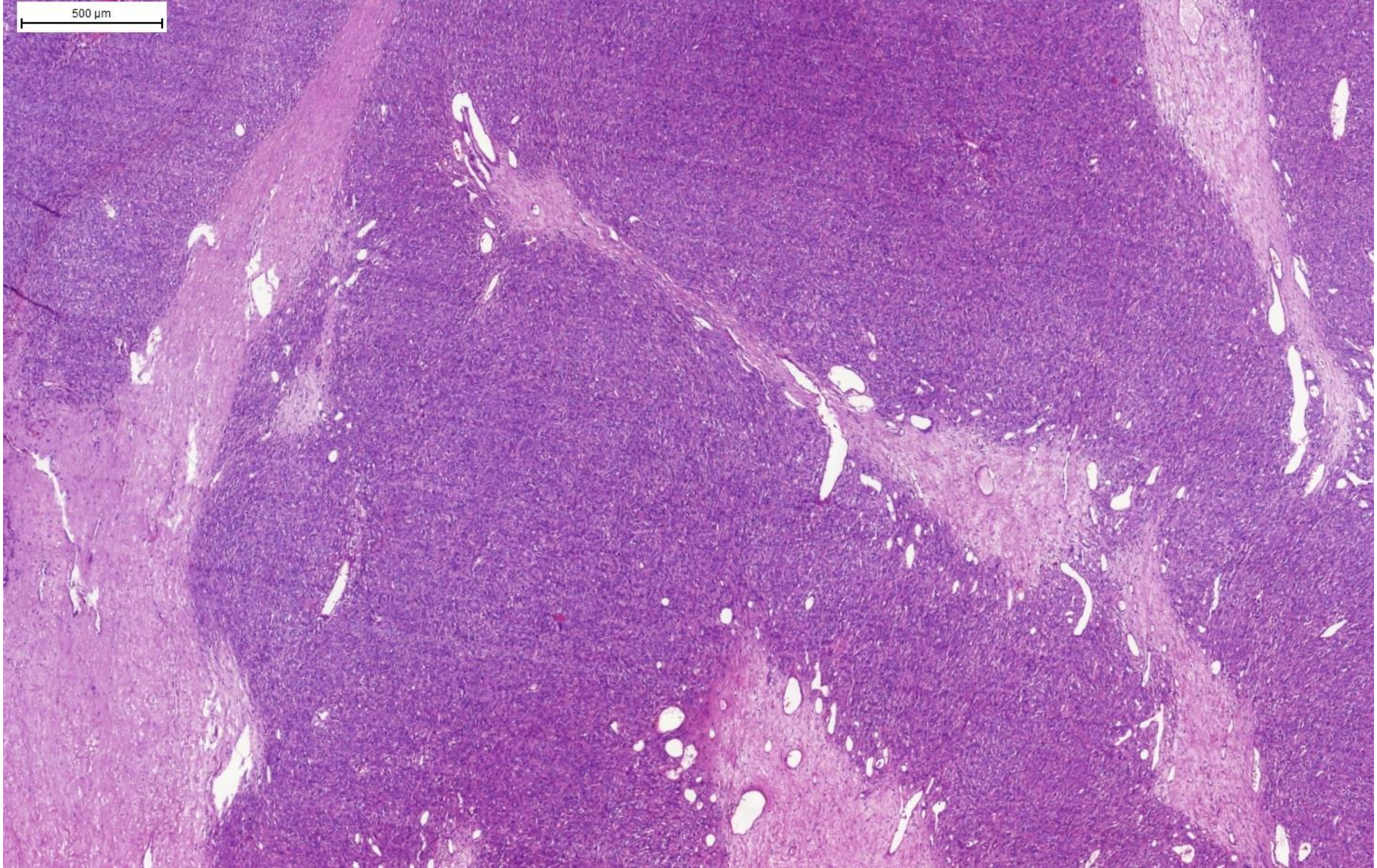
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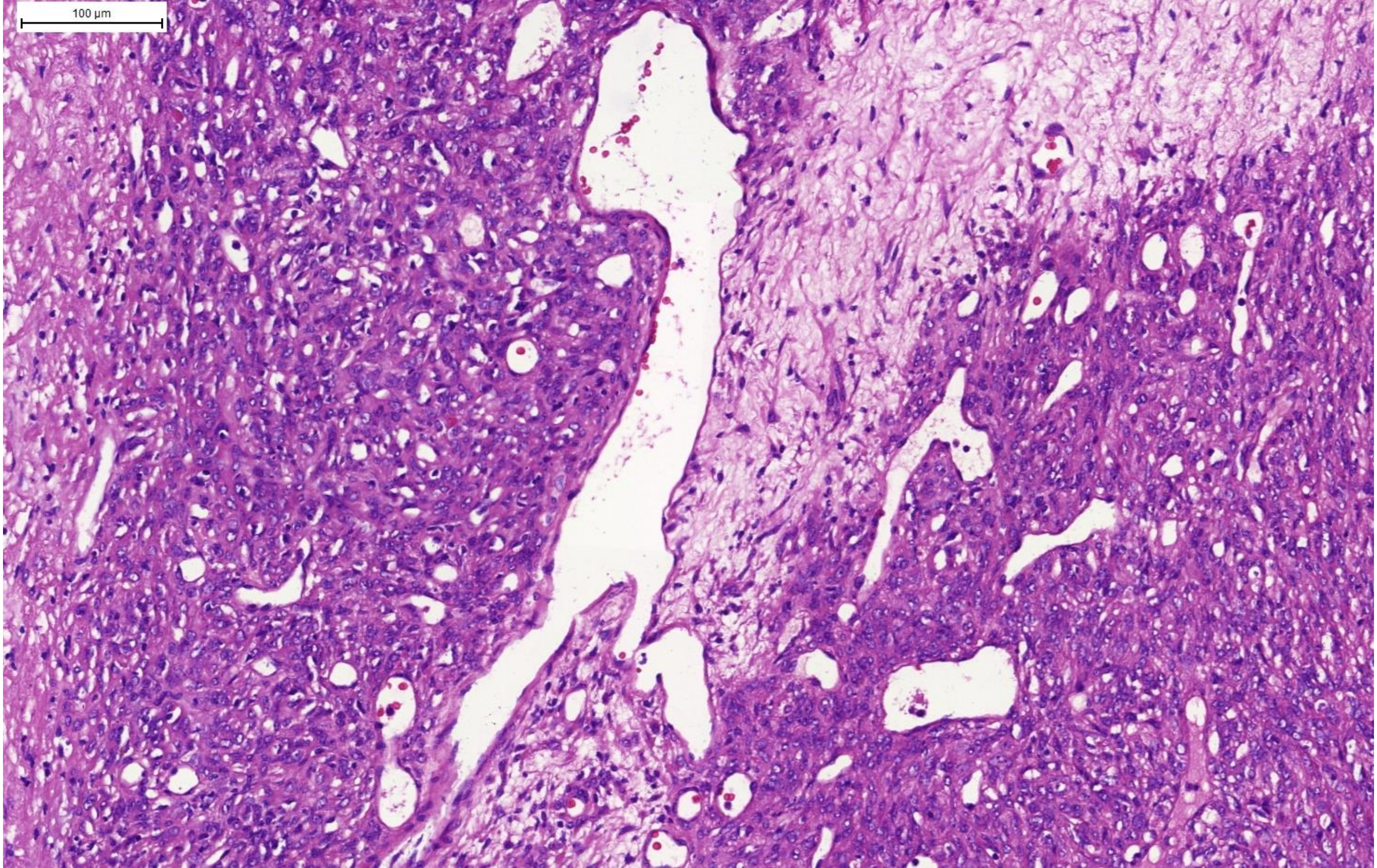
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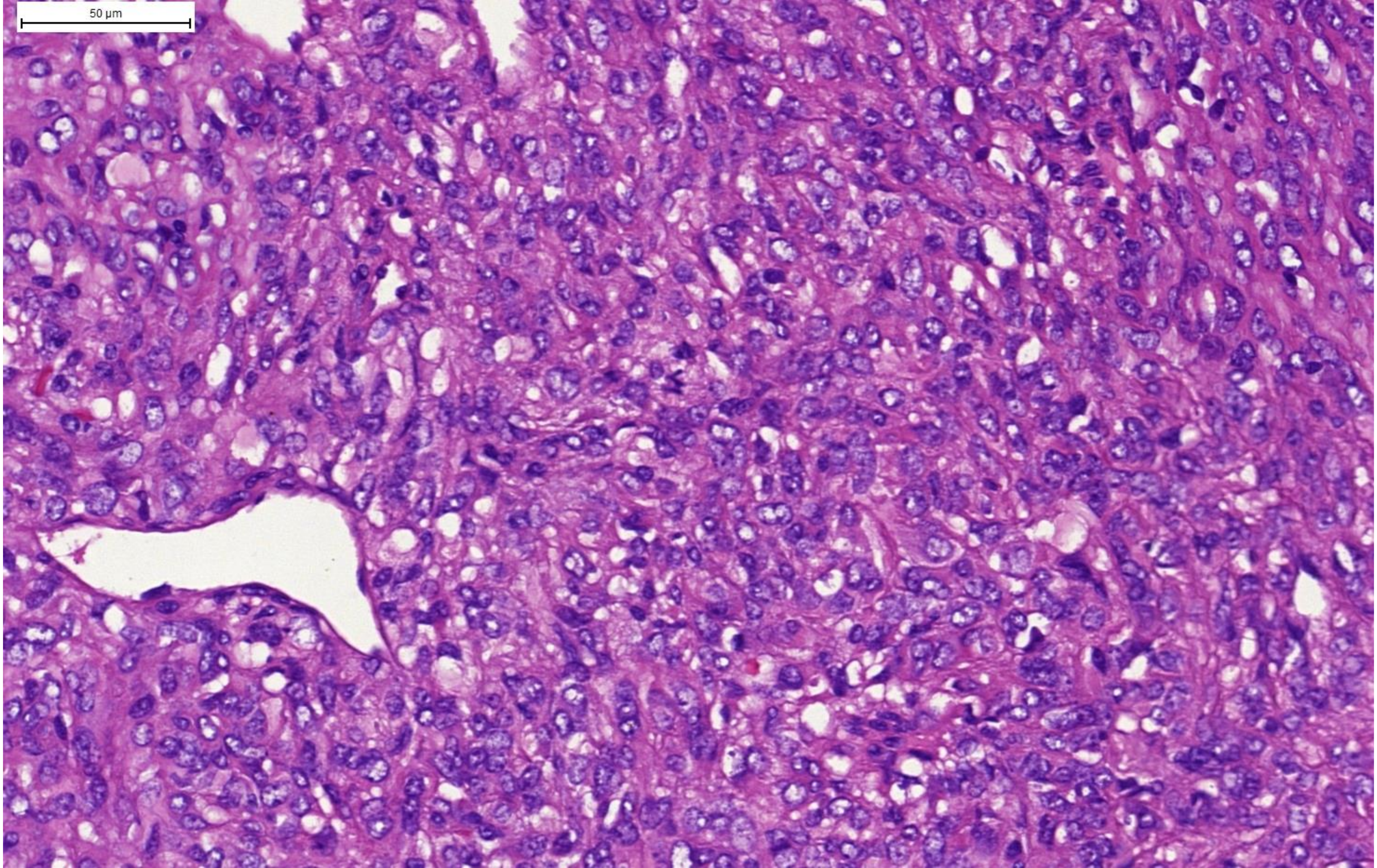
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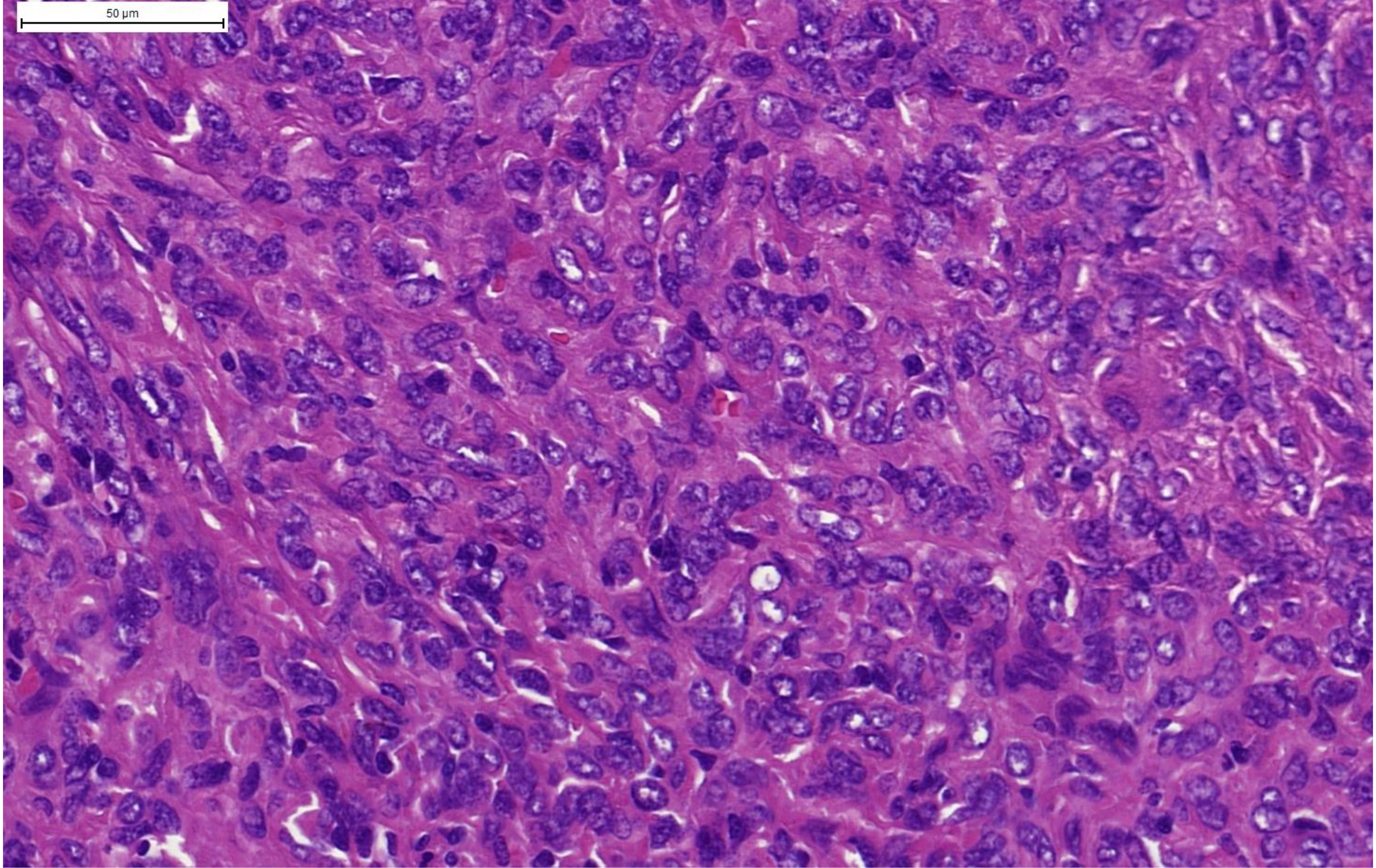
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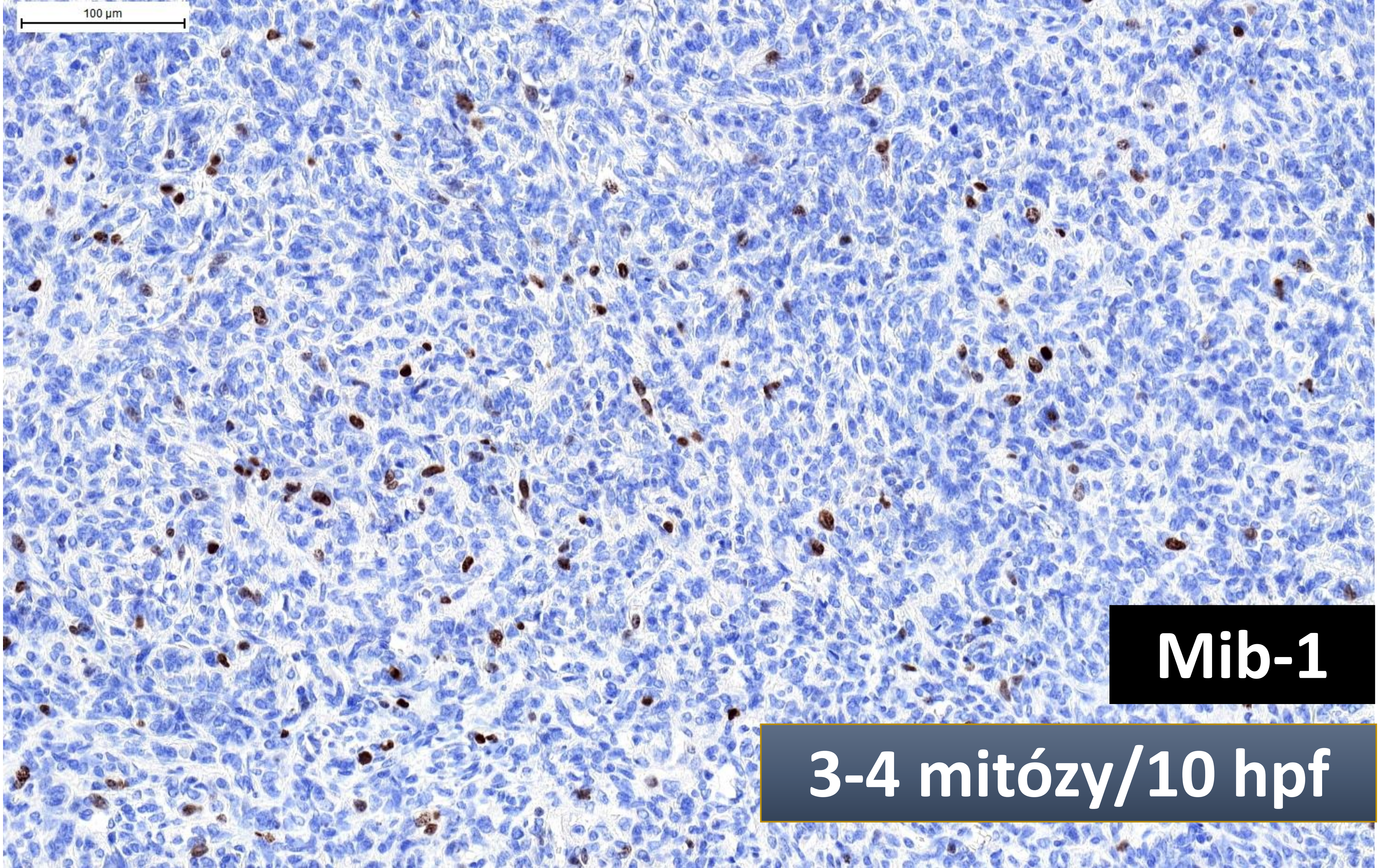
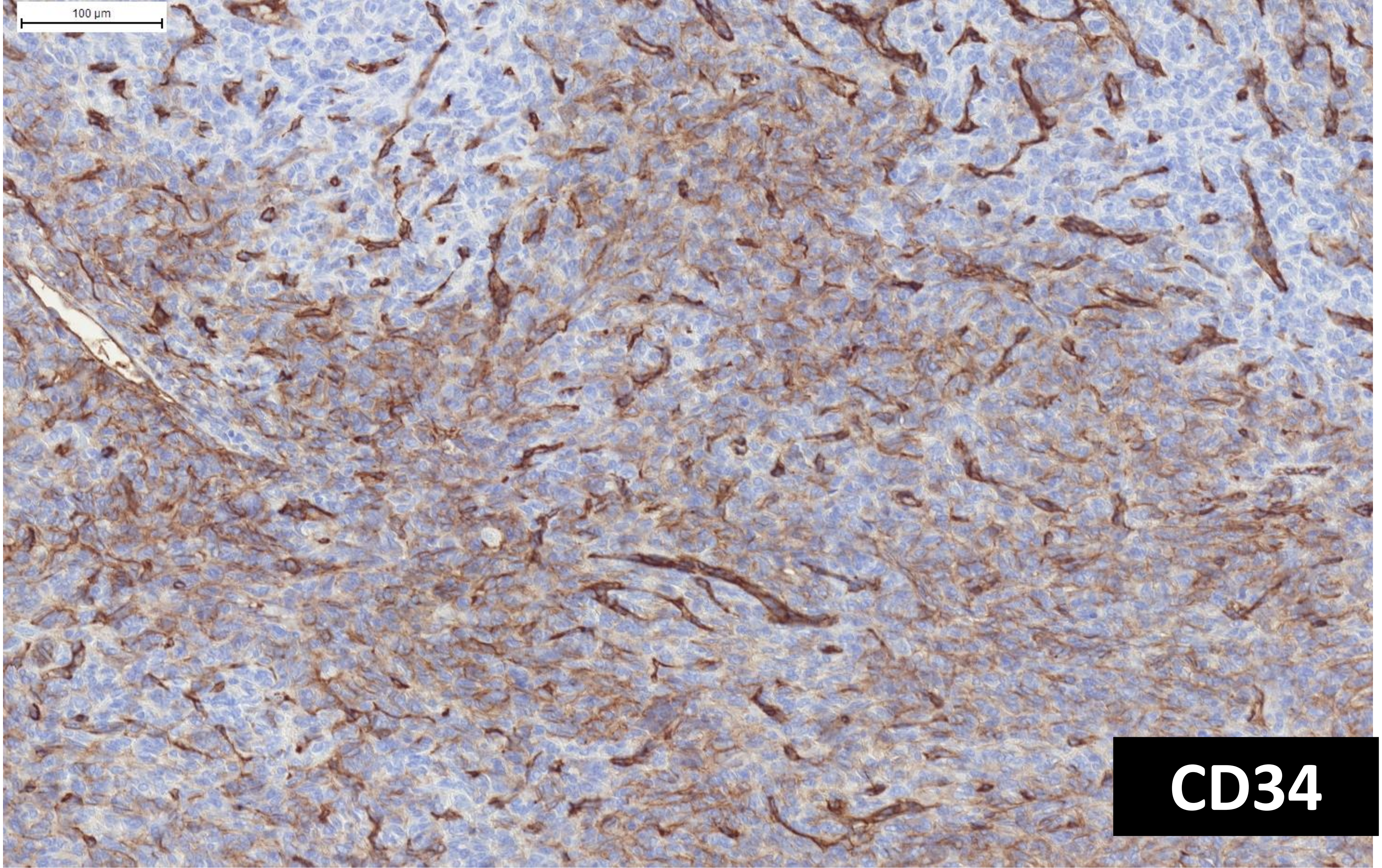

100 µm
Mib-1
3-4 mitózy/10 hpf

DIAGNÓZA?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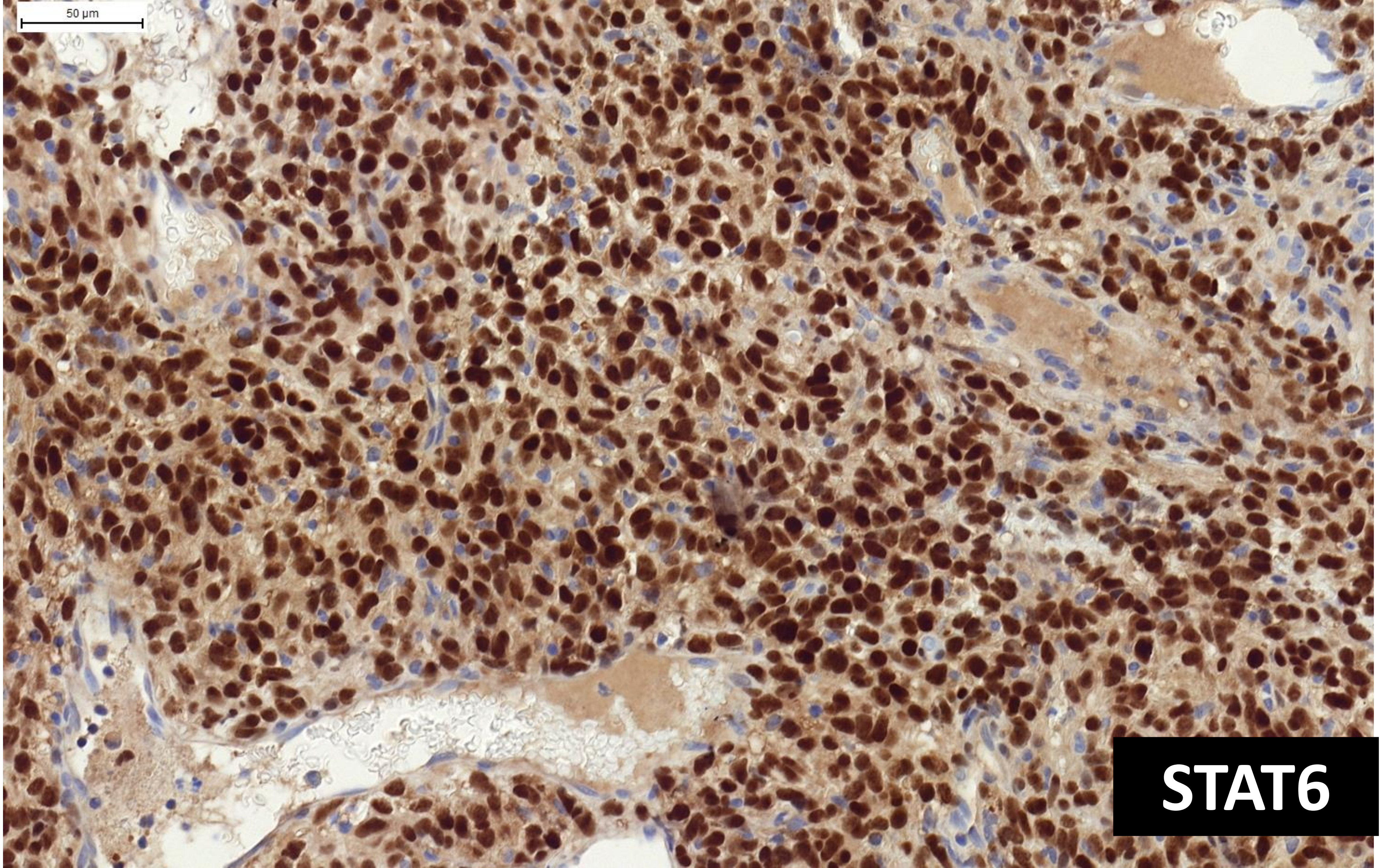
CD34


50 µm
STAT6

Solitary fibrous tumor/hemangiopericytoma

- SFT = GI
- HPC <5 mitóz = GII
- HPC ≥5 mitóz = GIII

Analysis of *NAB2-STAT6* Gene Fusion in 17 Cases of Meningeal Solitary Fibrous Tumor/Hemangiopericytoma

Review of the Literature

Sayaka Yuzawa, MD, Hiroshi Nishihara, MD, PhD,†‡ Lei Wang, PhD,† Masumi Tsuda, PhD,* Taichi Kimura, MD, PhD,†‡ Mishie Tanino, MD, PhD,* and Shinya Tanaka, MD, PhD*†*

Abstract: Solitary fibrous tumor/hemangiopericytoma (SFT/HPC) is a mesenchymal tumor that can affect virtually any region of the body. SFT/HPC of the thoracic cavity and soft tissue

Key Words: solitary fibrous tumor, hemangiopericytoma, *NAB2*, *STAT6*, genetic analysis

(*Am J Surg Pathol* 2016;40:1031–1040)

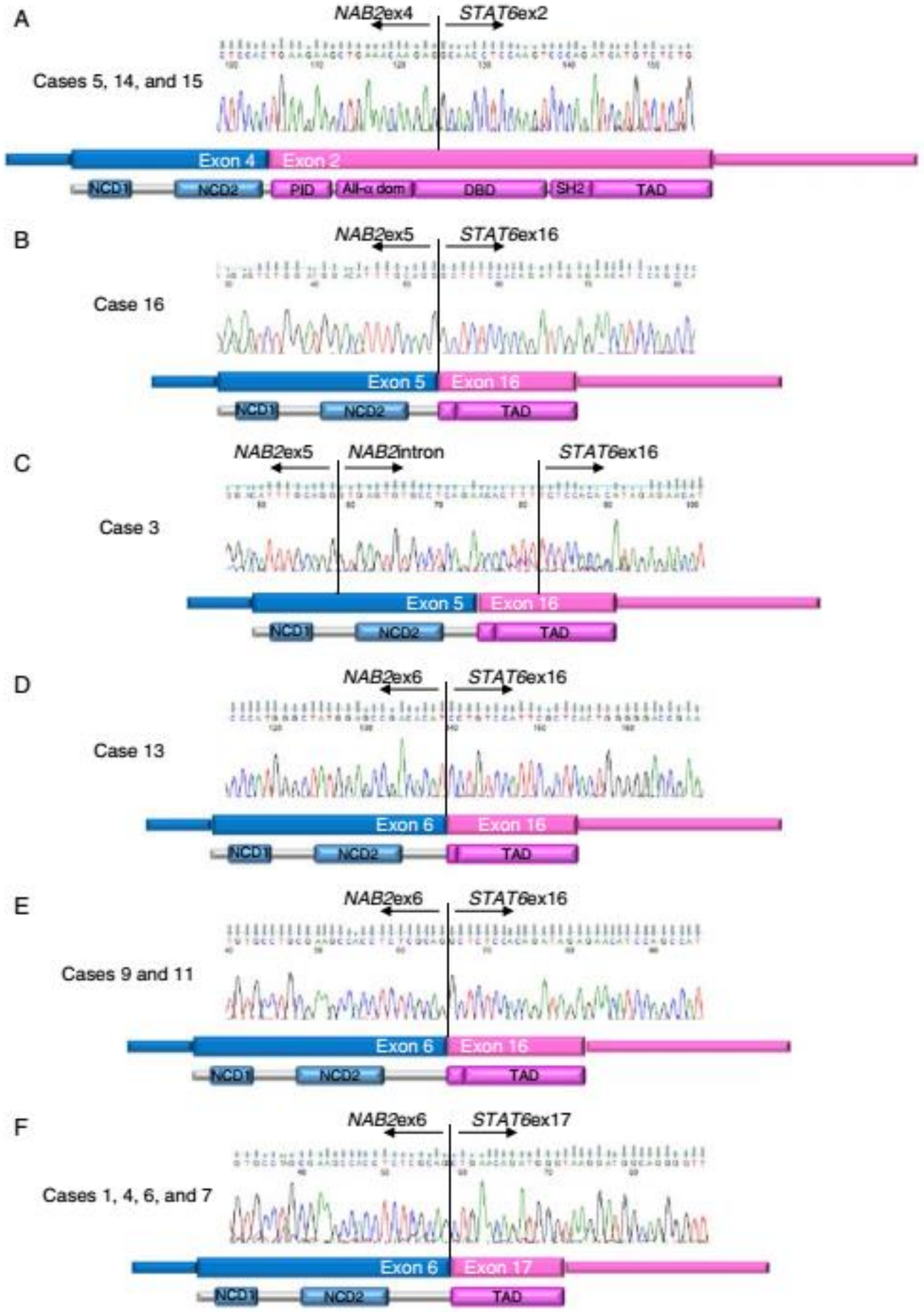
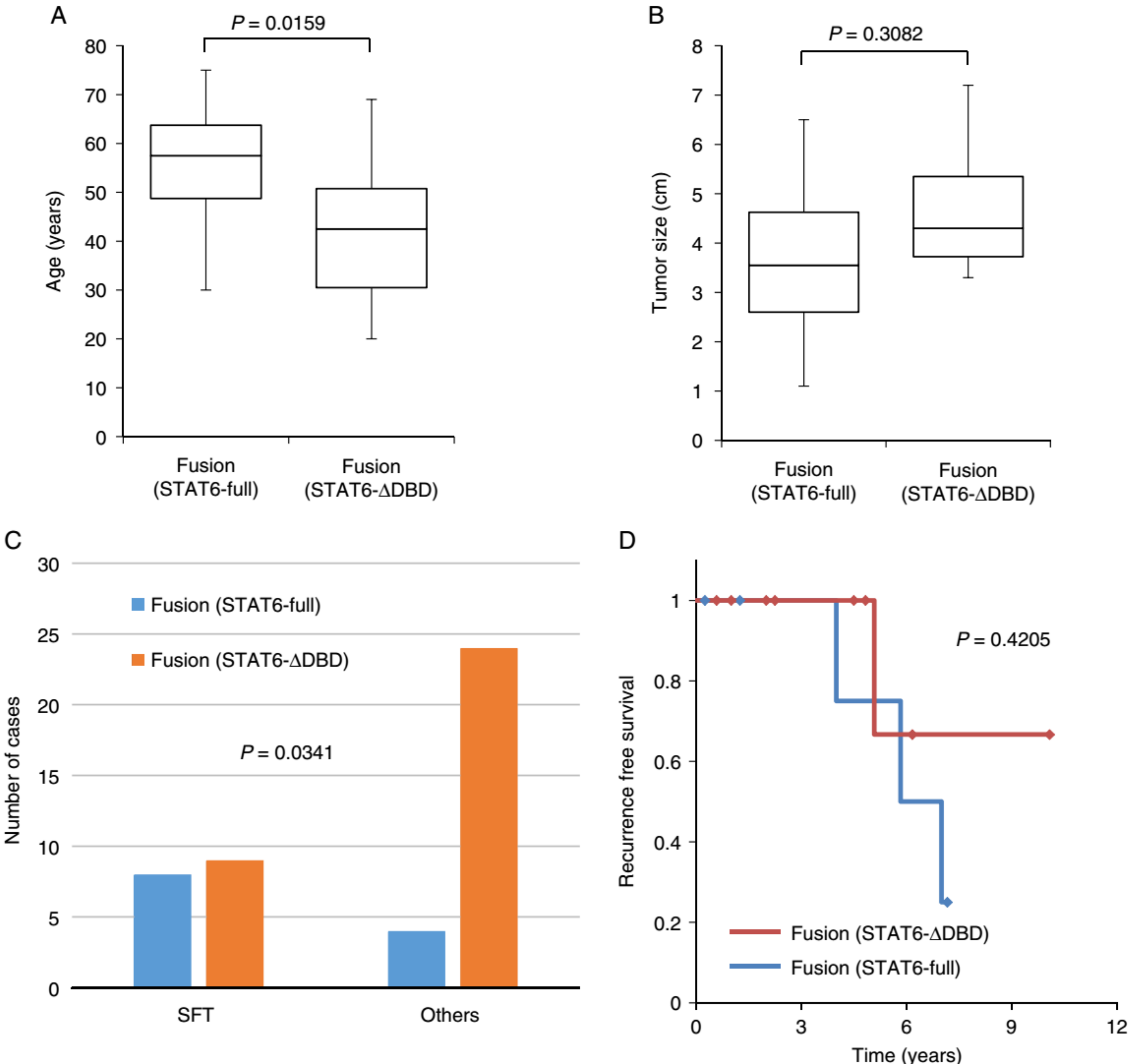


TABLE 1. Pathologic and Genetic Findings

Case	Diagnosis	Papillary Pattern	Necrosis	Hemorrhage	Nuclear Atypia	High Cellularity	Mitosis (/10 HPF)	CD34	MIB-1 Index (%)	STAT6 IHC	Fusion Variant
1	SFT	–	–	–	–	–	1	+	6	+	6-17
2	HPC	+	–	+	–	–	1	–	2	+	–
3	Anaplastic HPC	–	–	+	–	+	5	–	22	+	5-16
4	Anaplastic HPC	+	+	+	+	–	1	–	7	+	6-17
4’	Anaplastic HPC	+	–	+	+	–	7	f+	16	+	6-17
4R	Anaplastic HPC	–	–	+	+	–	1	–	5	+	6-17
5	SFT	–	–	+	–	–	0	+	1	+	4-2
6	Anaplastic HPC	+	–	+	+	–	5	f+	14	+	6-17
7	HPC	–	–	–	–	–	1	f+	9	+	6-17
8R1	Anaplastic HPC	–	–	+	–	+	30	–	30	+	–
8R2	Anaplastic HPC	–	–	+	+	+	47	+	28	+	–
8R3	Anaplastic HPC	–	–	+	–	+	18	+	24	+	–
9	Anaplastic HPC	–	–	+	+	–	5	f+	30	+	6-16
10R	Anaplastic HPC	–	+	+	+	–	6	f+	20	+	–
11	HPC	–	–	+	–	–	1	f+	6	+	6-16
12R	Anaplastic HPC	–	+	+	+	–	8	f+	35	+	–
13	Anaplastic HPC	–	–	+	+	–	16	–	14	+	6-16
14R	HPC	–	+	+	–	–	1	f+	4	+	4-2
15	SFT	–	+	+	–	+	4	+	9	+	4-2
16	HPC	–	+	+	–	–	2	f+	3	+	5-16
17	SFT	–	–	+	–	–	2	+	8	+	–

f+ indicates focally positive; HPF, high-power fields; R, recurrence.

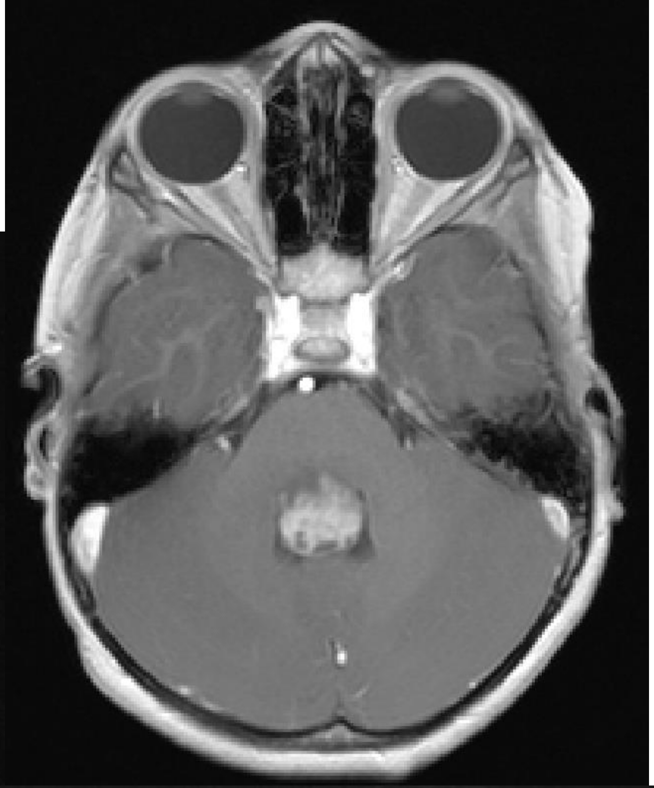
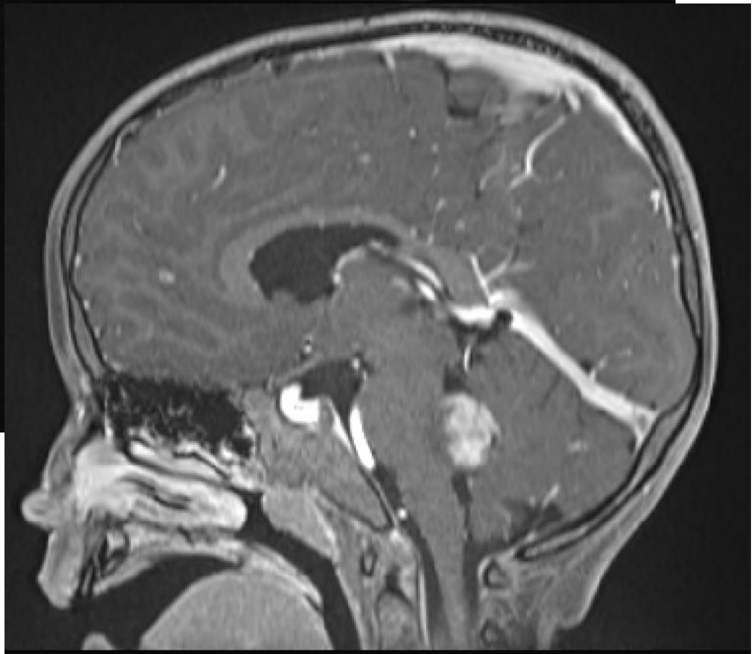
Focusing on *meningeal* SFT/HPC, *NAB2*ex6-*STAT6*ex16 was observed most frequently (21 cases, 39%), followed by *NAB2*ex4-*STAT6*ex2 (9 cases, 17%) and *NAB2*ex6-*STAT6*ex17 (8 cases, 15%) (Table 2). Seven of 9 cases (78%) harboring *NAB2*ex4-*STAT6*ex2 exhibited a pure SFT pattern. Fusion variants significantly correlated with age (1-way ANOVA, $P = 0.0389$), whereas the rate of recurrence was not associated with fusion variants. When divided into 2 fusion types, fusion (STAT6-full) and fusion (STAT6-ΔDBD), meningeal SFT/HPC carrying fusion (STAT6-full) occurred in older patients than fusion (STAT6-ΔDBD) (median age 58 vs. 43 y, $P = 0.0159$) (Fig. 4A) just as with SFT in the entire body, whereas the type of fusion variants did not correlate with tumor size (median size 3.6 vs. 4.3 cm, $P = 0.3082$) in meningeal SFT/HPC (Fig. 4B). In terms of histopathology, aggressive histology such as malignant SFT, HPC, and anaplastic HPC tended to harbor fusion (STAT6-ΔDBD) rather than fusion (STAT6-full) (Fisher exact test, $P = 0.0341$) (Fig. 4C), whereas the types of fusion variants did not show any correlation with prognosis (Fig. 4D).

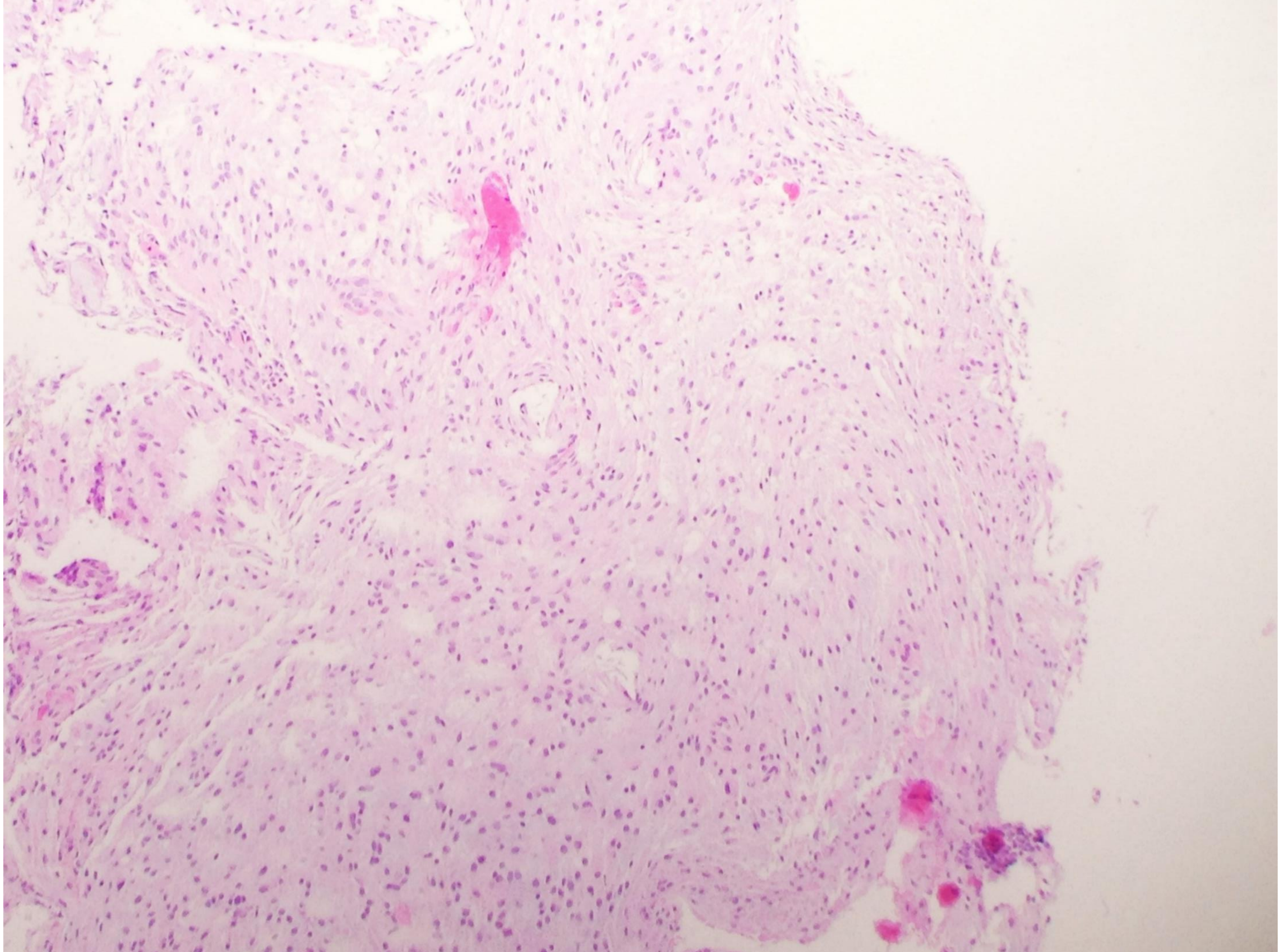


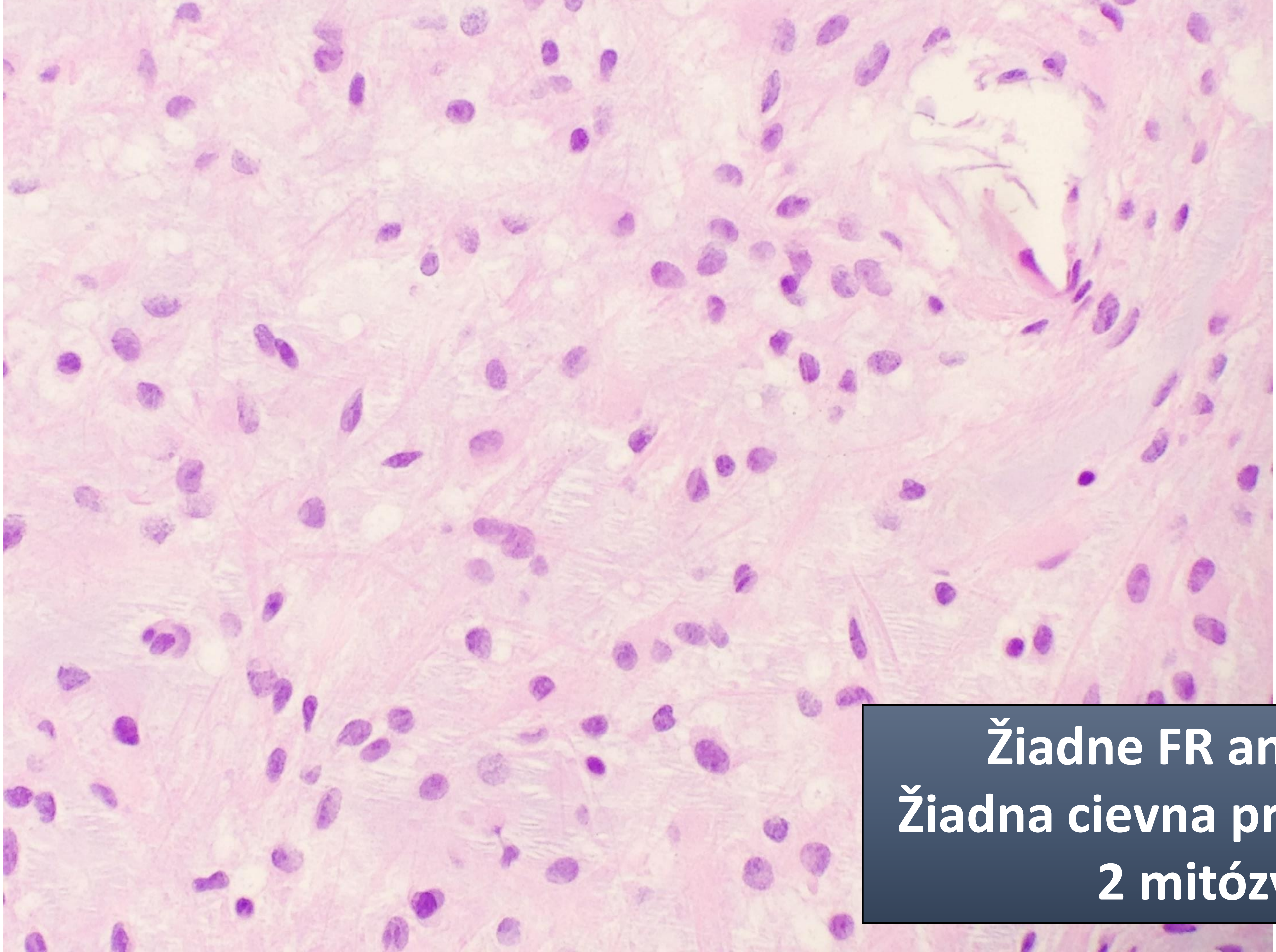
Prípad č. 15

- 6-ročný chlapec, zadná jama
- MRI: Tumor 4. komory so znakmi malignity, najskôr ependymóm alebo meduloblastóm
- Dr. Ondič, FN Plzeň

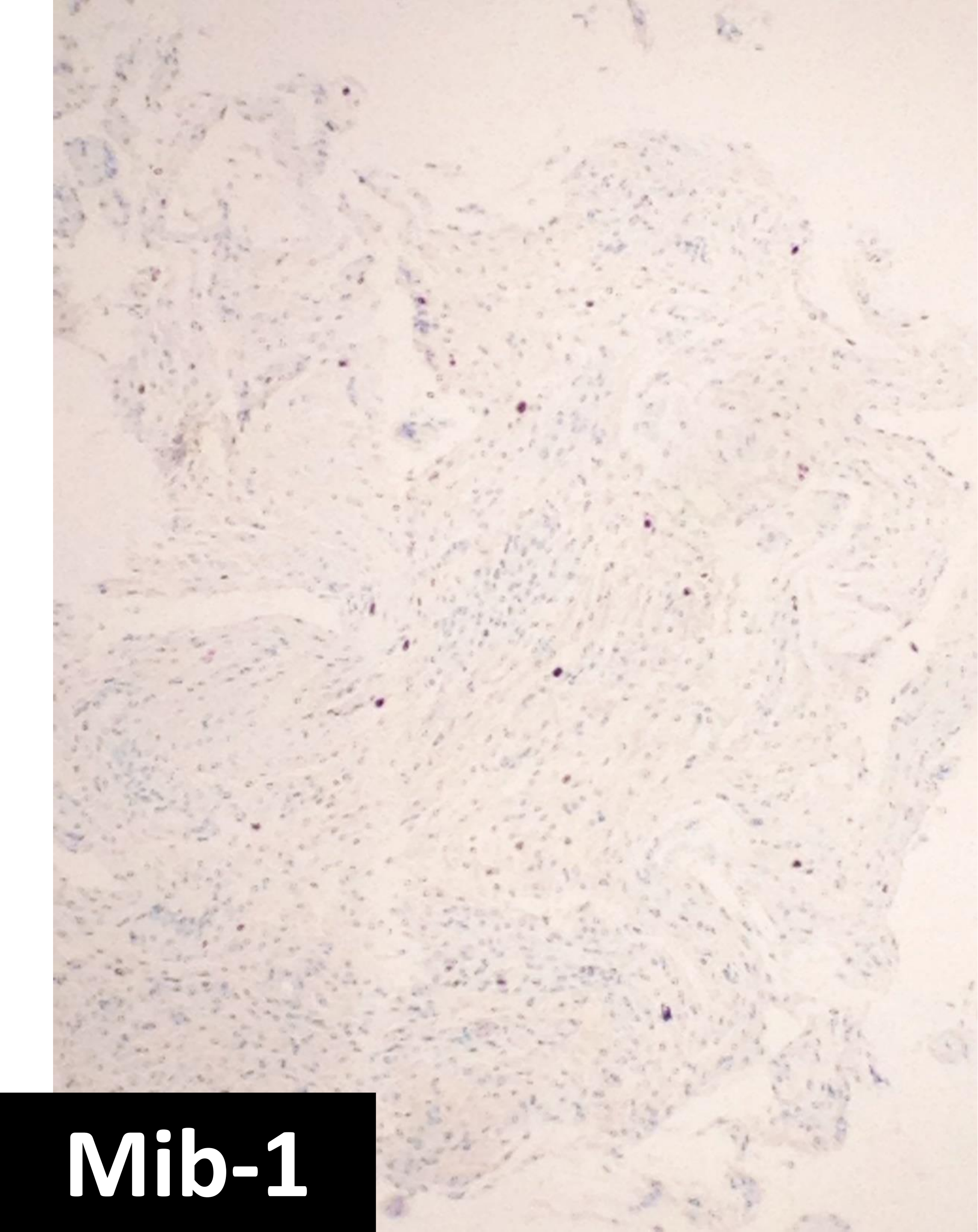


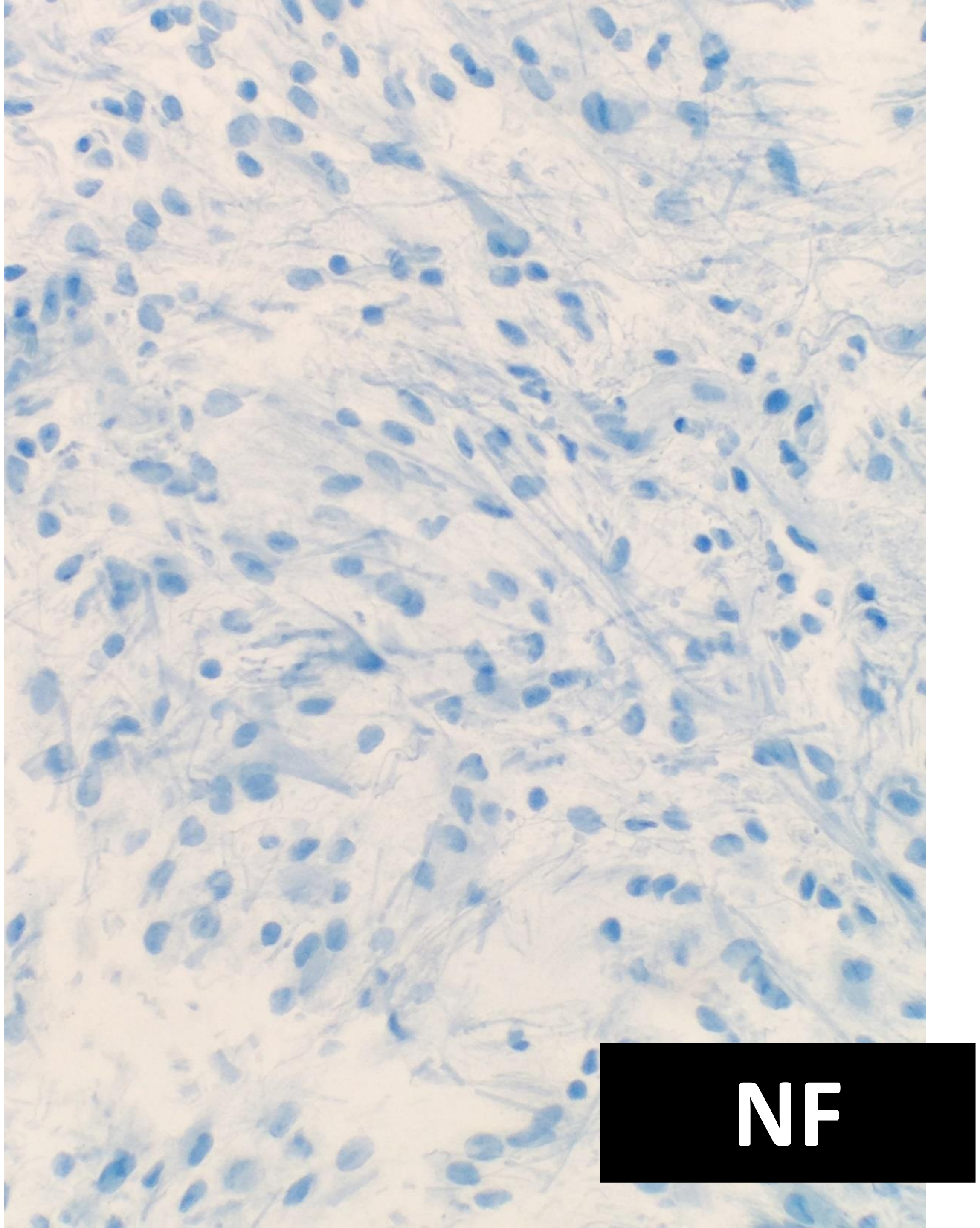







Žiadne FR ani EGB
Žiadna cievna proliferácia
2 mitózy


Mib-1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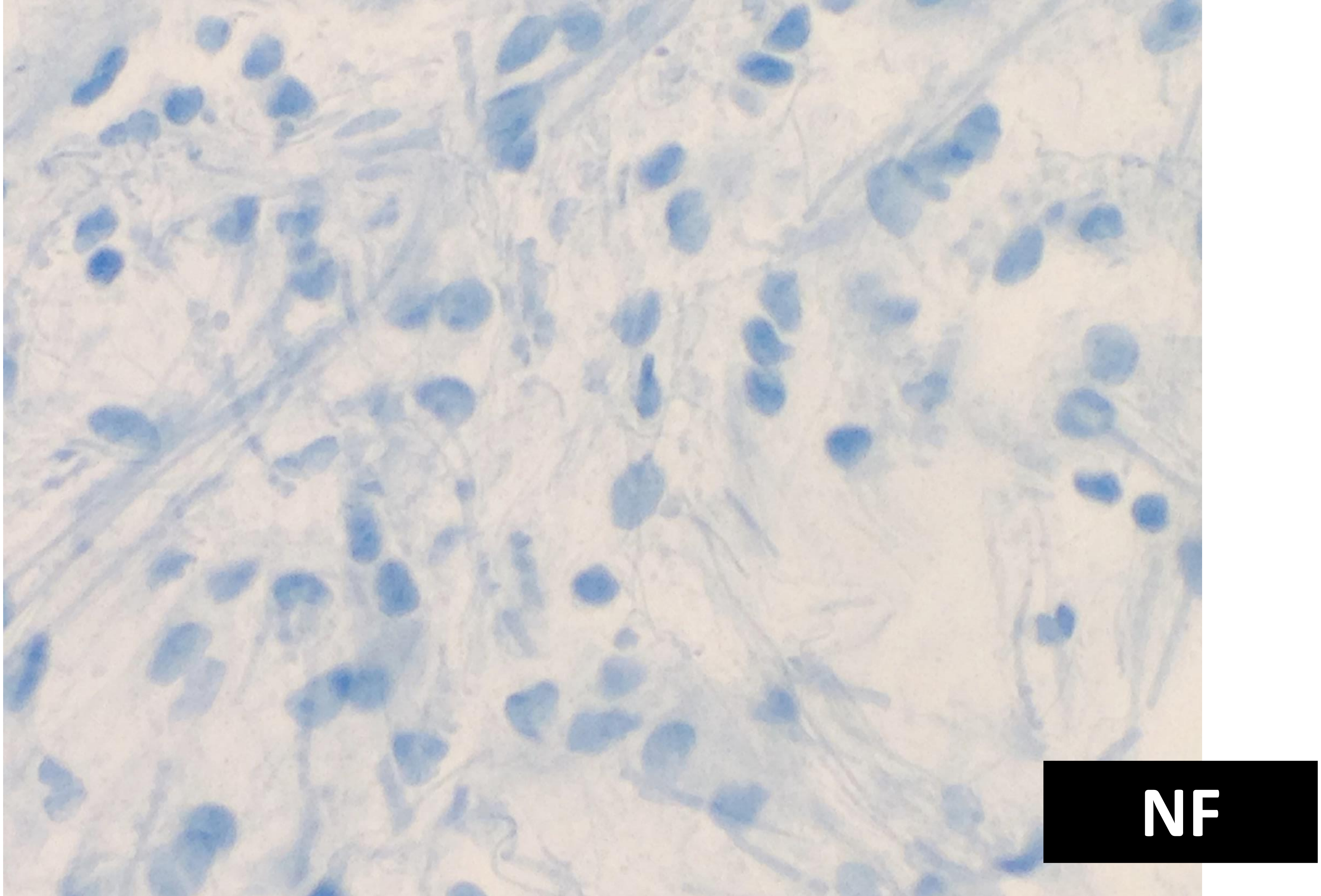
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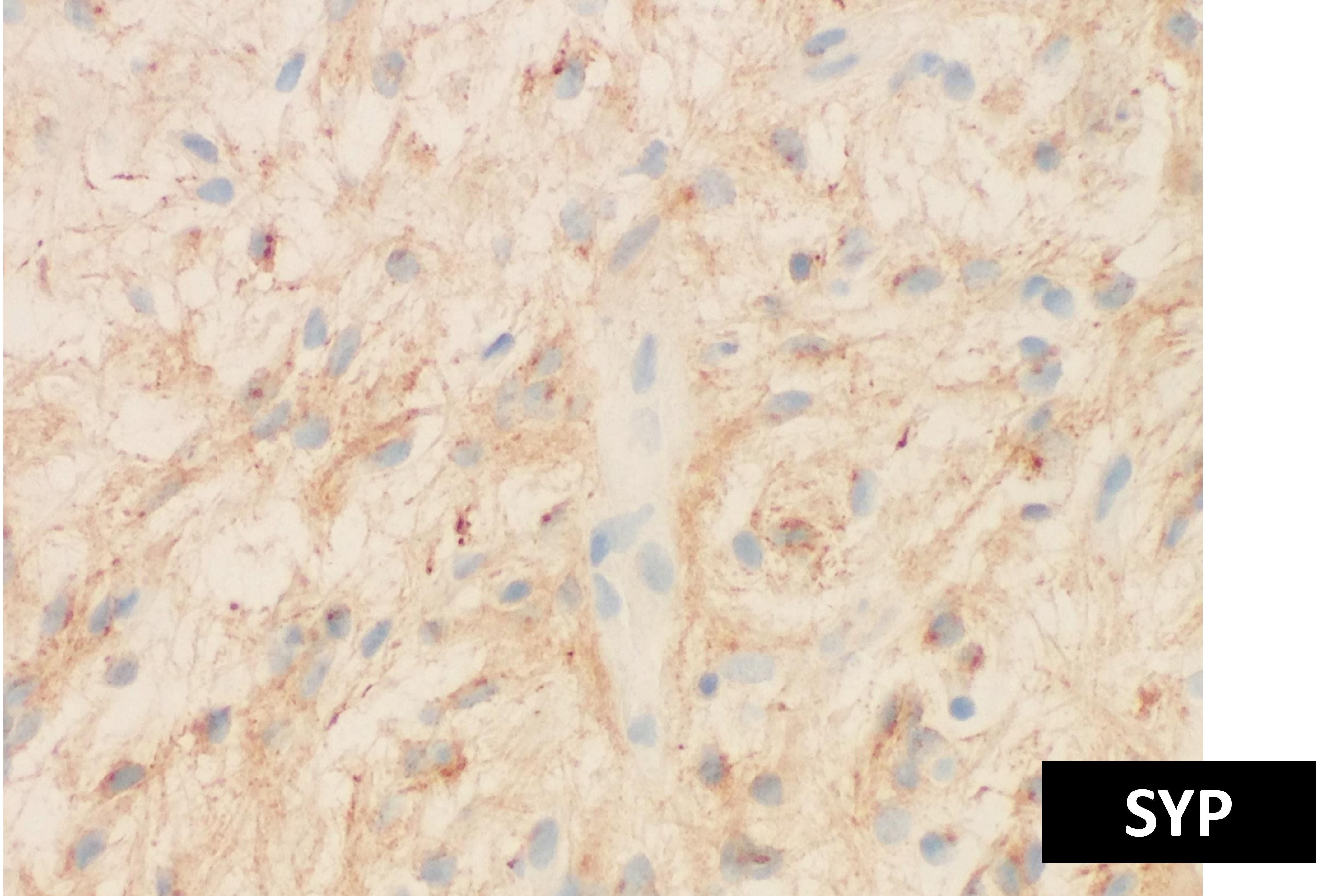
SYP

Imunofenotyp

- GFAP a Olig2 +
- SYP slabo +
- NF –
- IDH1 –
- P53-
- K27M-

Genetika: fúzia KIAA1549-BRAF

Pilocytický astrocytóm, grade I