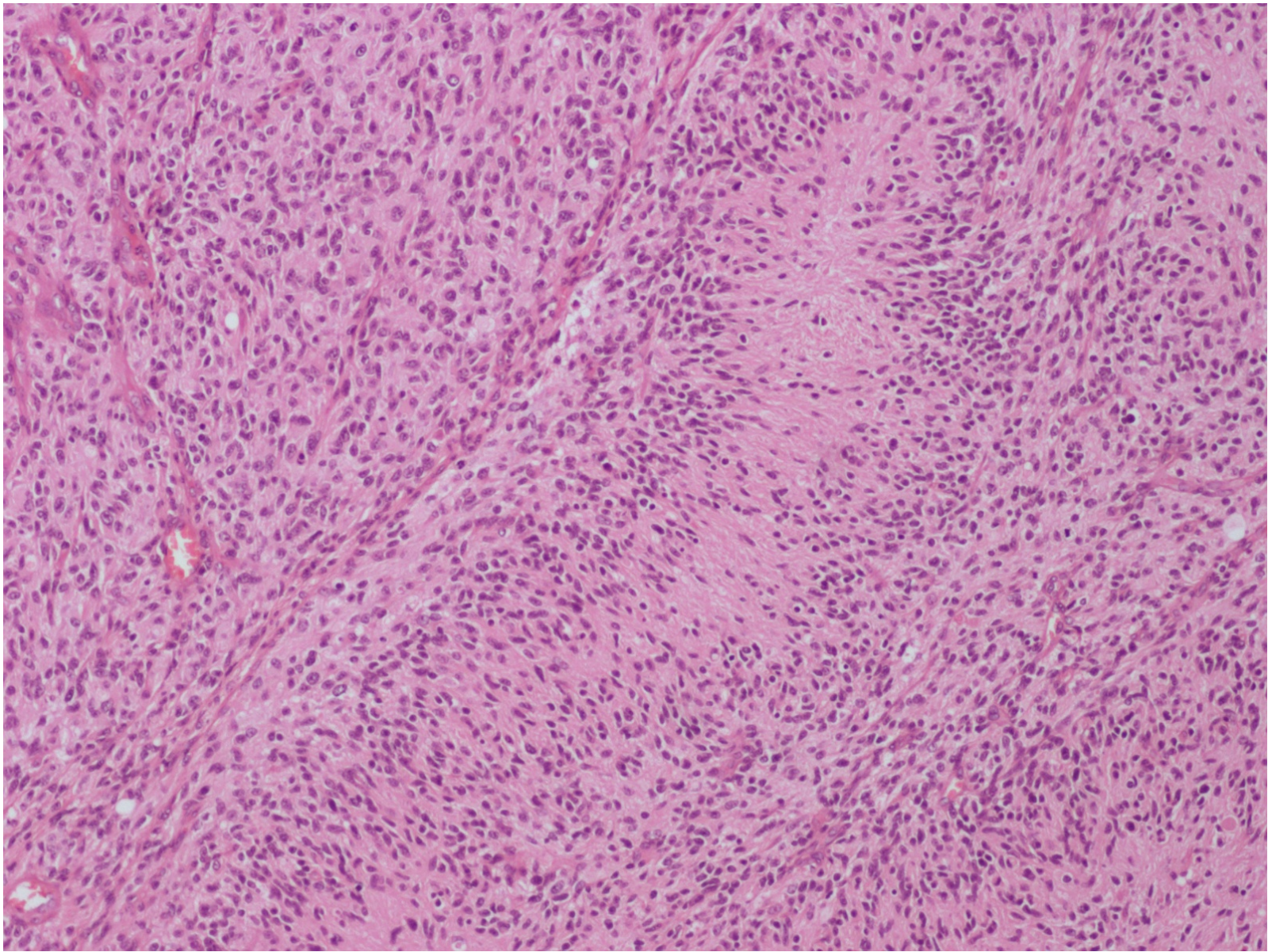


FRCPath teaching

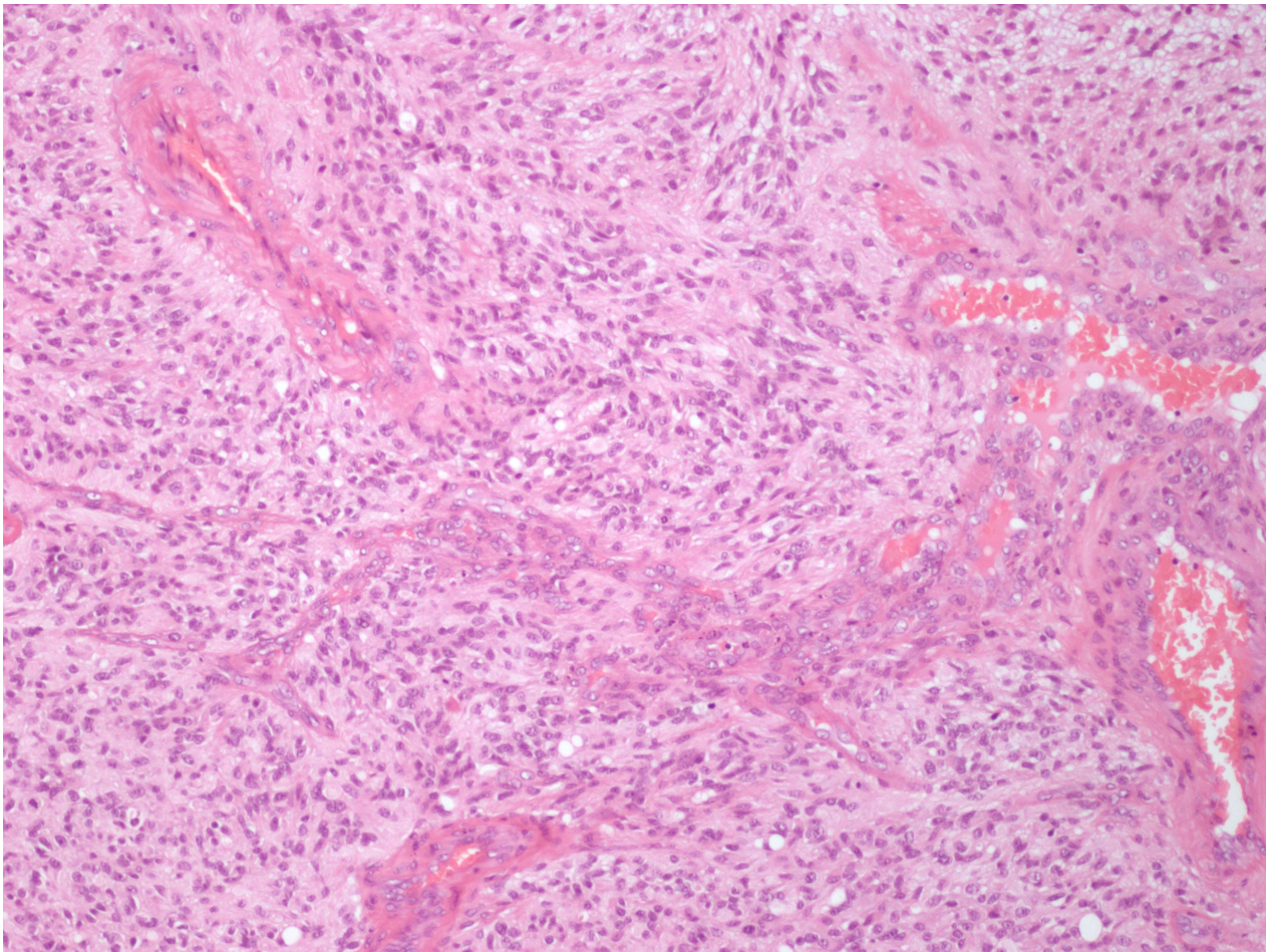
Kieren Allinson

Case 1

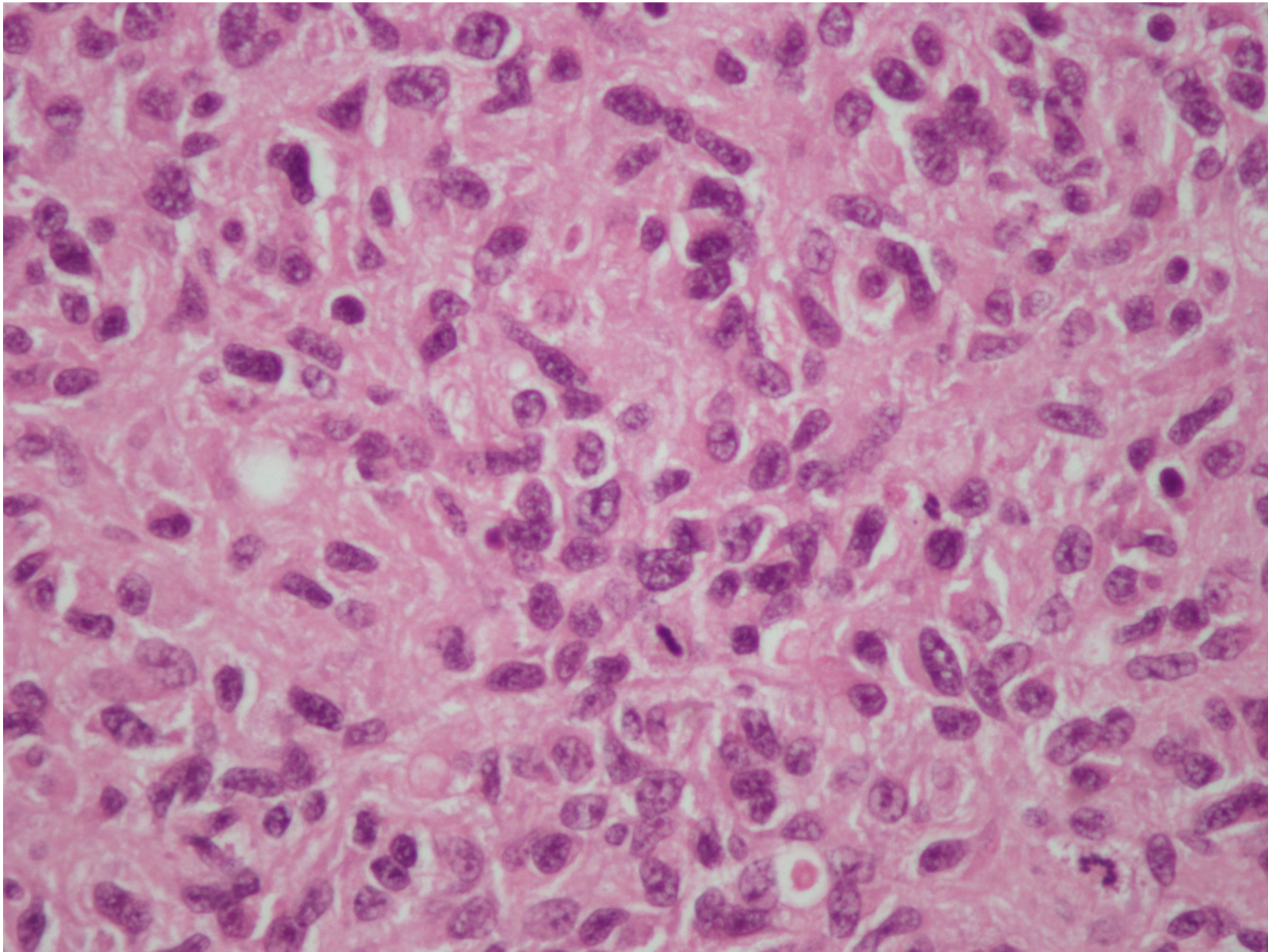
- 68M.
- Forgetful. Headache and left facial droop
- MRI – large enhancing tumour right insula



Palisading necrosis



Microvascular proliferation



Astrocytic neoplasm – nuclear atypia, mitotic figures

Glioblastoma (WHO grade 4)

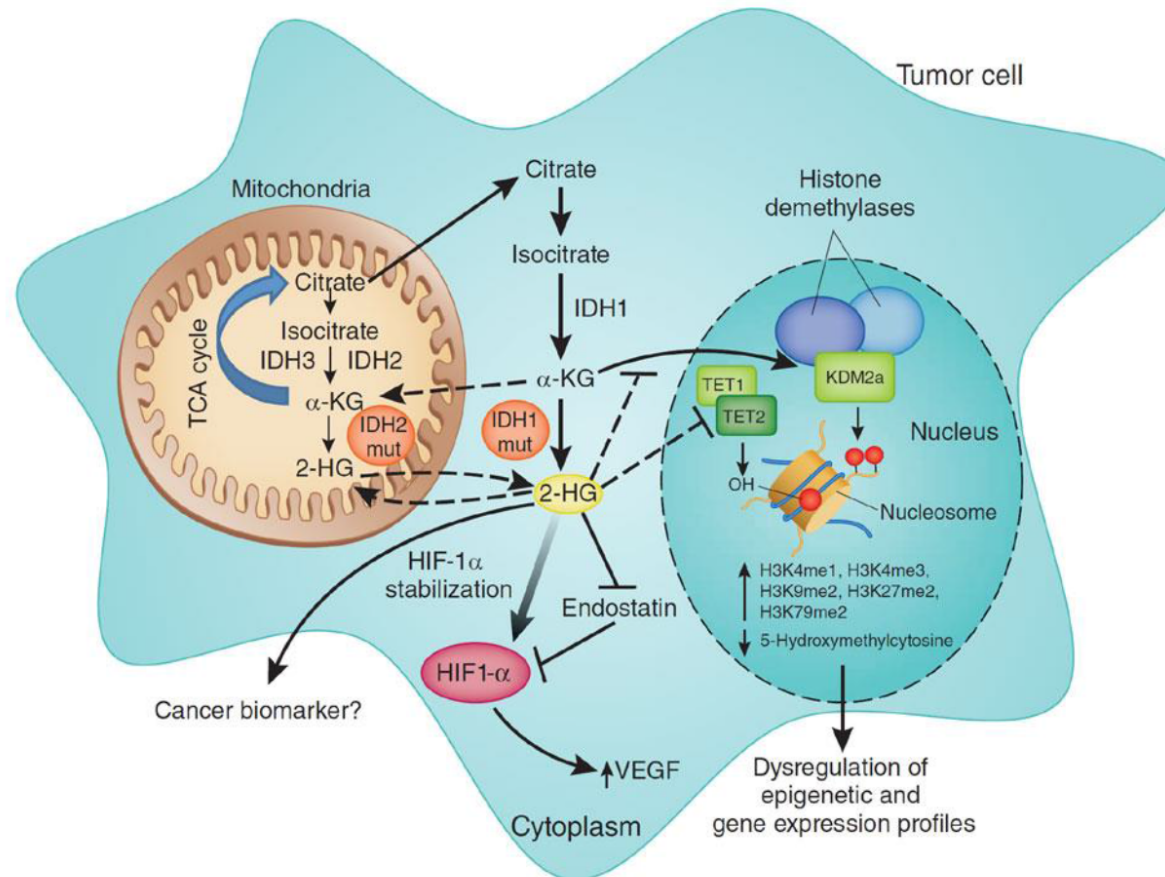
IHC

- GFAP
- Mib-1 (Ki67)
- IDH1 (R132H)

Molecular

- MGMT methylation

Isocitrate dehydrogenase (IDH)



[Metabolism unhinged: IDH mutations in cancer](#) John R Prensner¹ & Arul M Chinnaiyan² Nature Medicine Volume: 17, Pages: 291–293 Yea(2011)

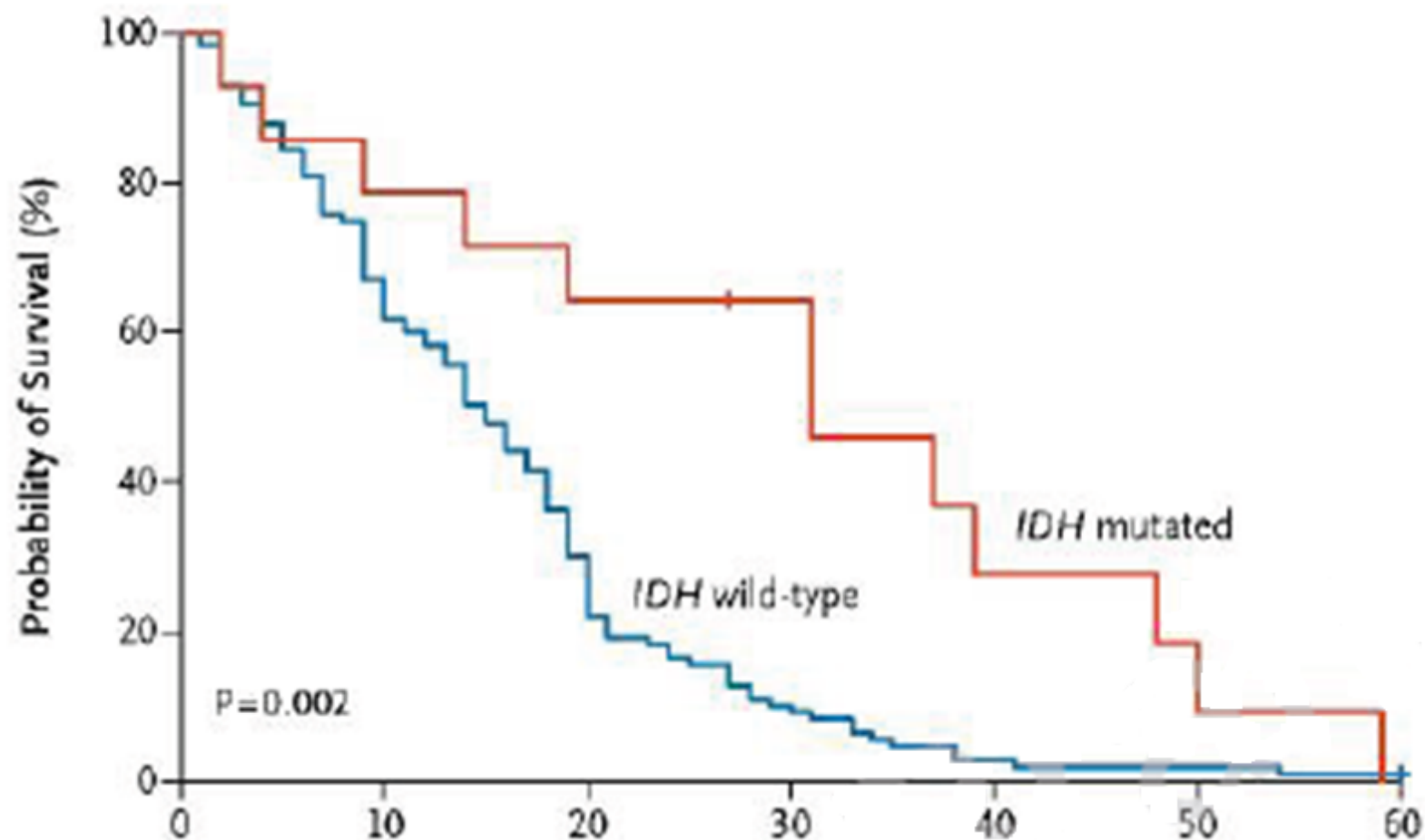
IDH-1 mutations in GBM

Characteristics of GBM patients with IDH1 mutations

Patient ID	Patient age (years) [±]	Sex	Recurrent GBM [±]	Secondary GBM [±]	Overall survival (years) [§]	IDH1 mutation		Mutation of TP53	Mutation of PTEN, RB1, EGFR, or NF1
						Nucleotide	Amino acid		
Br10P	30	F	No	No	2.2	G395A	R132H	Yes	No
Br11P	32	M	No	No	4.1	G395A	R132H	Yes	No
Br12P	31	M	No	No	1.6	G395A	R132H	Yes	No
Br104X	29	F	No	No	4.0	C394A	R132S	Yes	No
Br106X	36	M	No	No	3.8	G395A	R132H	Yes	No
Br122X	53	M	No	No	7.8	G395A	R132H	No	No
Br123X	34	M	No	Yes	4.9	G395A	R132H	Yes	No
Br237T	26	M	No	Yes	2.6	G395A	R132H	Yes	No
Br211T	28	F	No	Yes	0.3	G395A	R132H	Yes	No
Br27P	32	M	Yes	Yes	1.2	G395A	R132H	Yes	No
Br129X	25	M	Yes	Yes	3.2	C394A	R132S	No	No
Br29P	42	F	Yes	Unknown	Unknown	G395A	R132H	Yes	No
IDH1 mutant patients (n=12)	33.2	67% M	25%	42%	3.8	100%	100%	83%	0%
IDH1 wild- type patients (n=93)	53.3	65% M	16%	1%	1.1	0%	0%	27%	60%

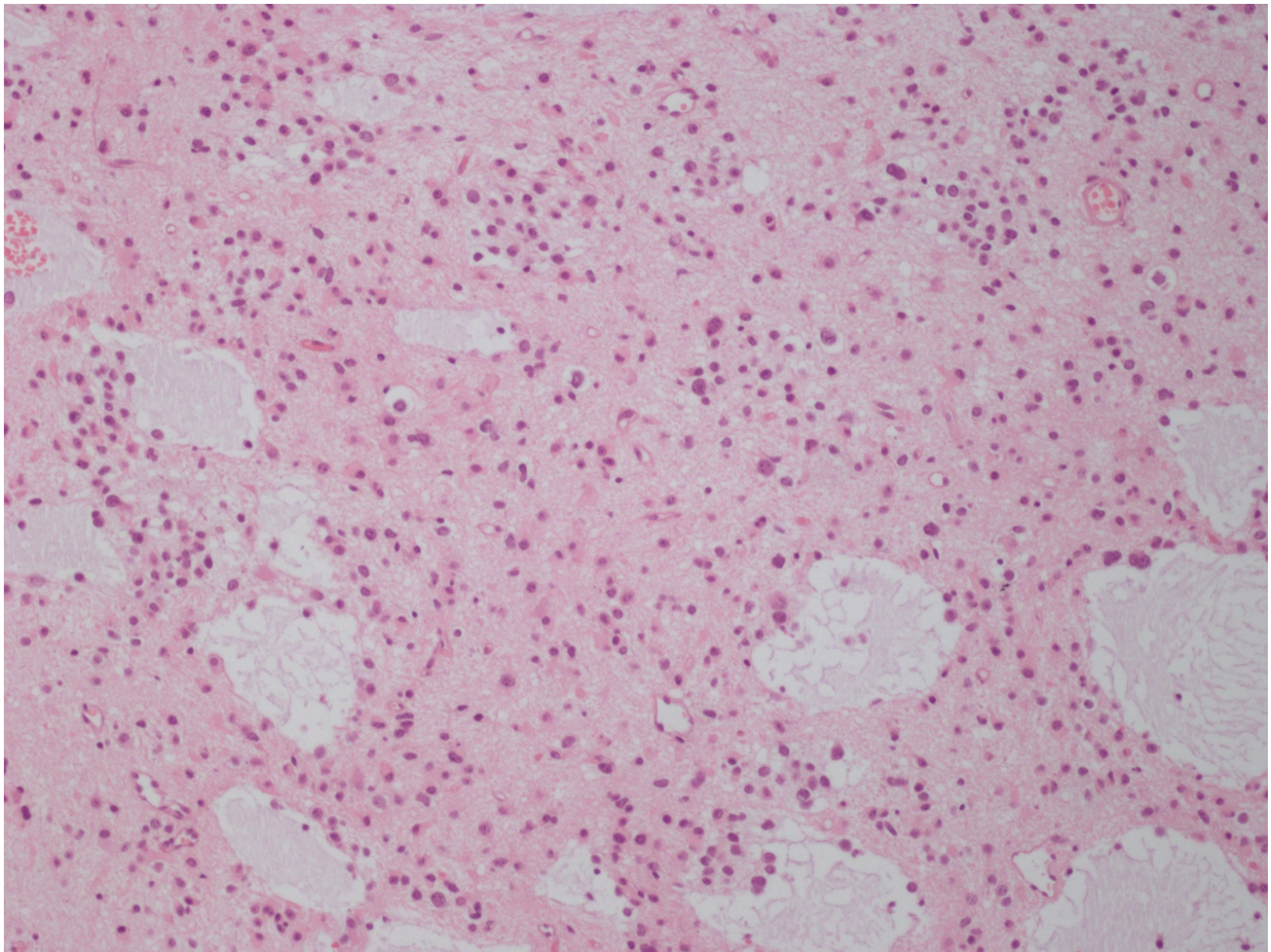
Parsons DW, Jones S, Zhang X, et al. An integrated genomic analysis of human glioblastoma multiforme. *Science*. 2008;321:1807–1812.
Sequenced 20,661 protein coding genes,

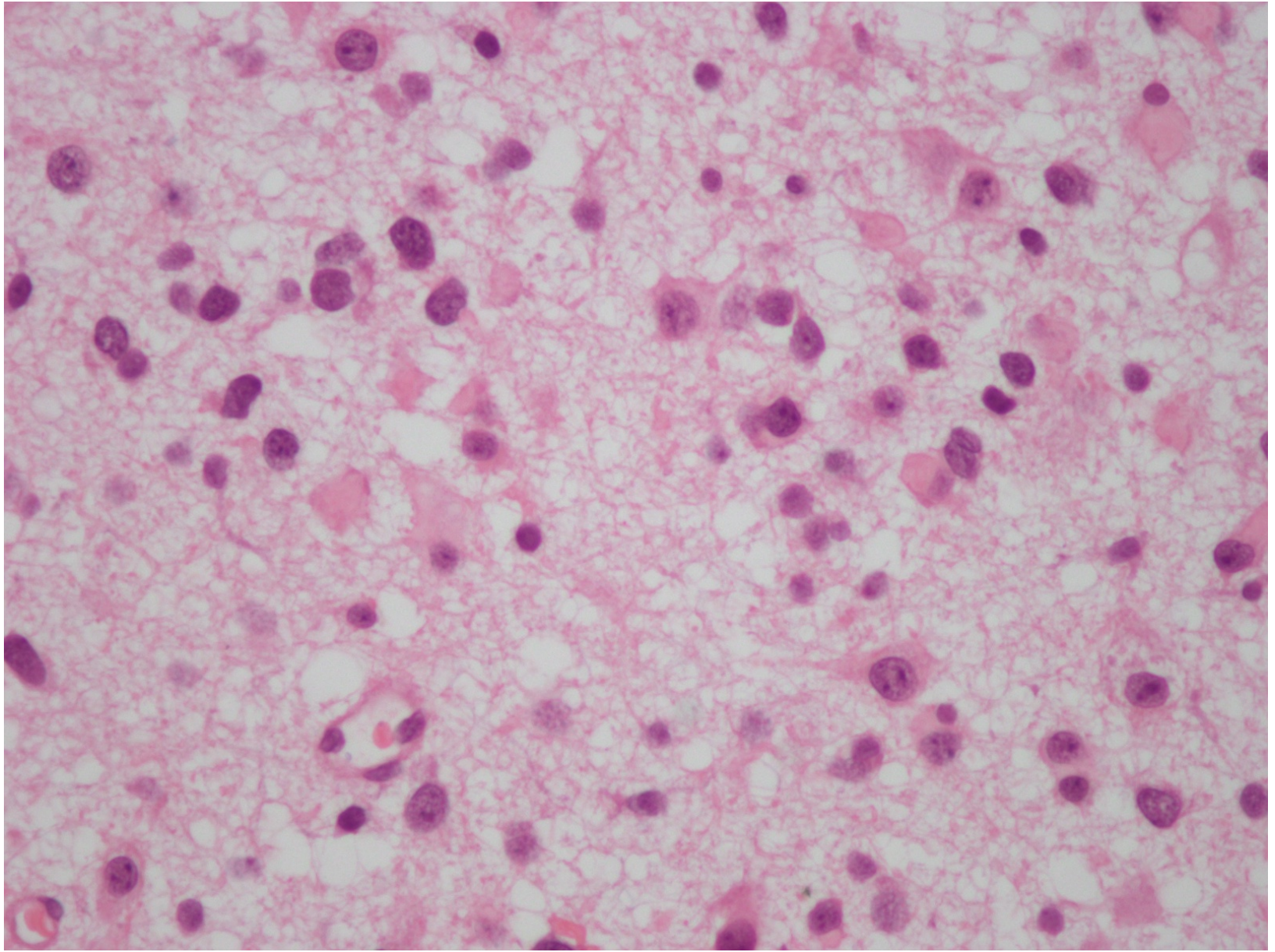
A Glioblastoma



Case 2

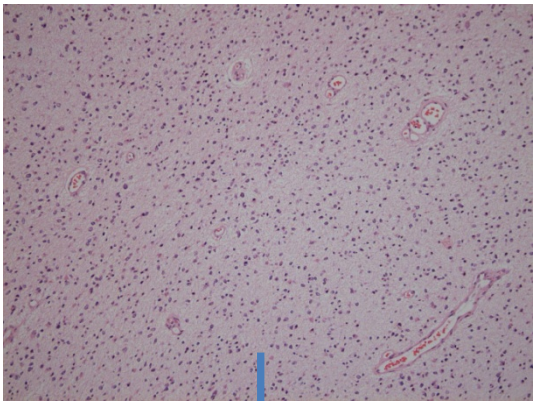
- 56M
- Right frontal tumour



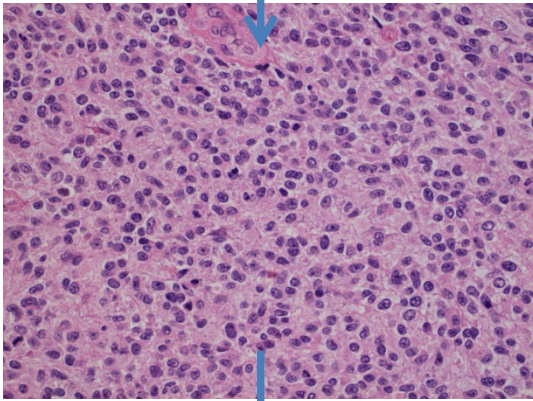


Glioma grading

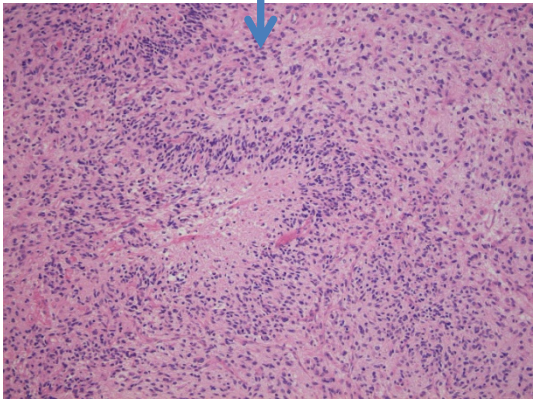
Grade 2
diffuse astrocytoma



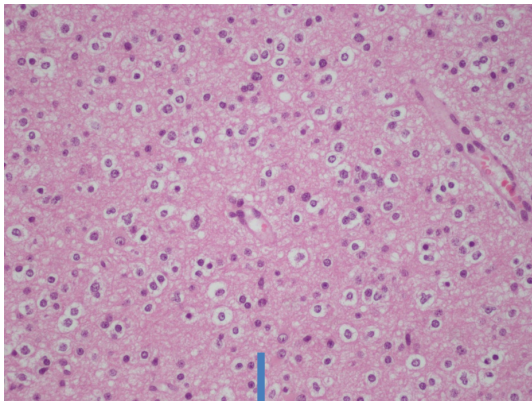
Grade 3
anaplastic astrocytoma



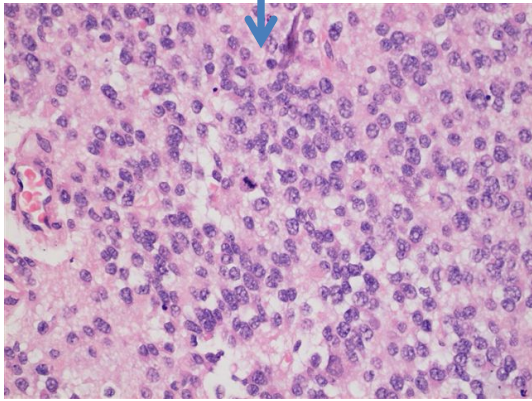
Grade 4
Glioblastoma (GBM)



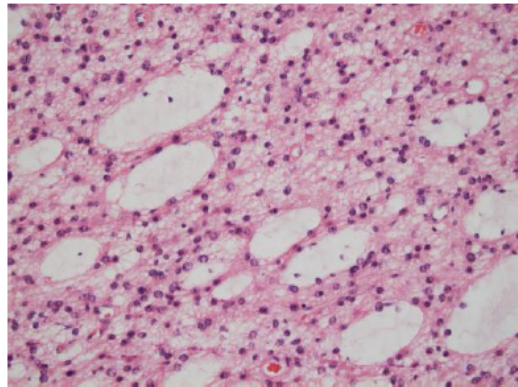
Grade 2
Oligodendroglioma



Grade 3
Anaplastic
oligodendroglioma

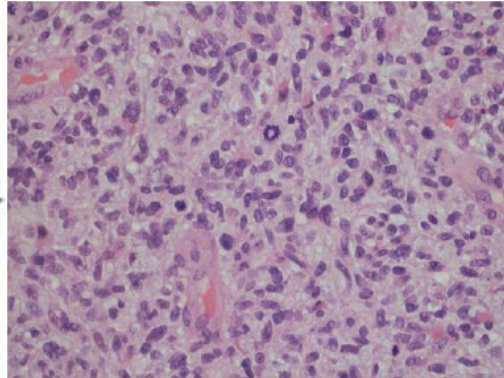


Primary versus secondary GBM



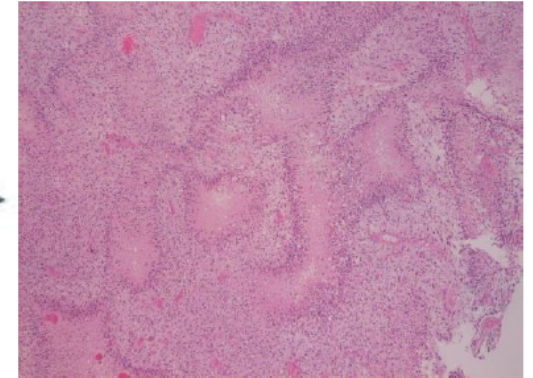
Astrocytoma

WHO II



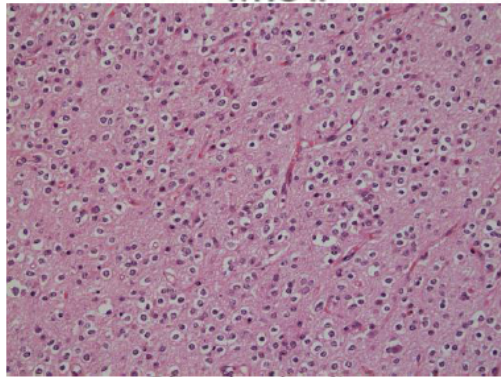
Anaplastic astrocytoma

WHO III

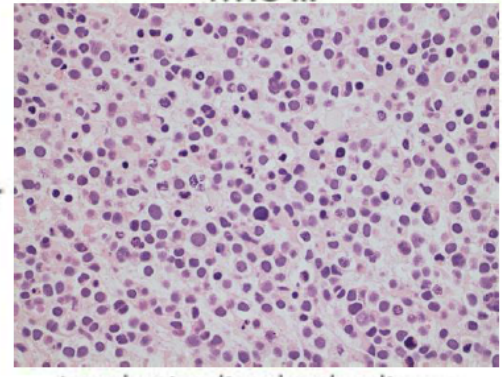


Secondary GBM

WHO IV



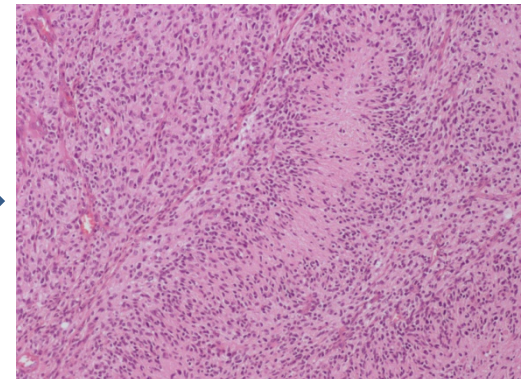
Oligodendroglioma



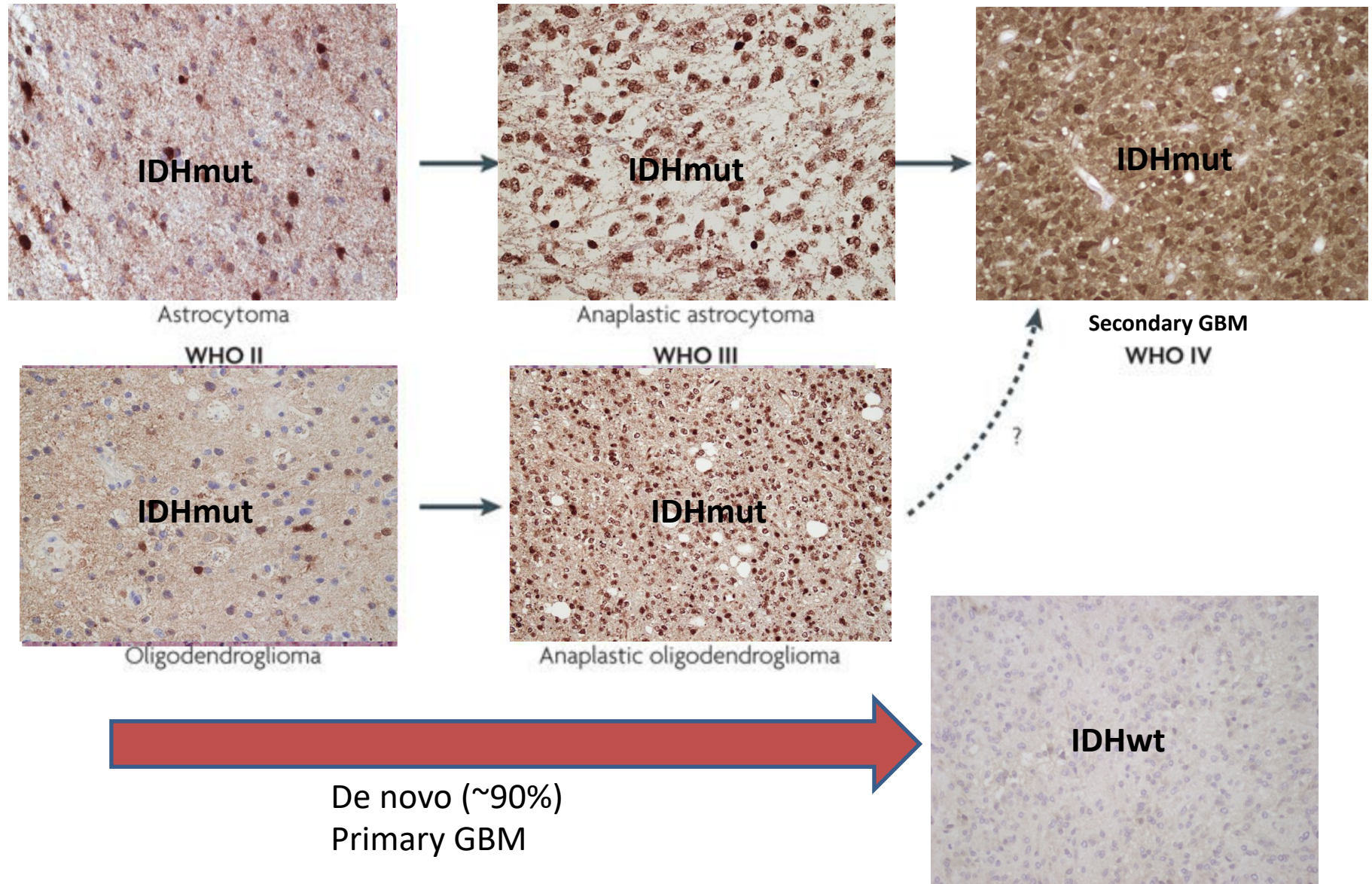
Anaplastic oligodendroglioma



De novo (~90%)
Primary GBM

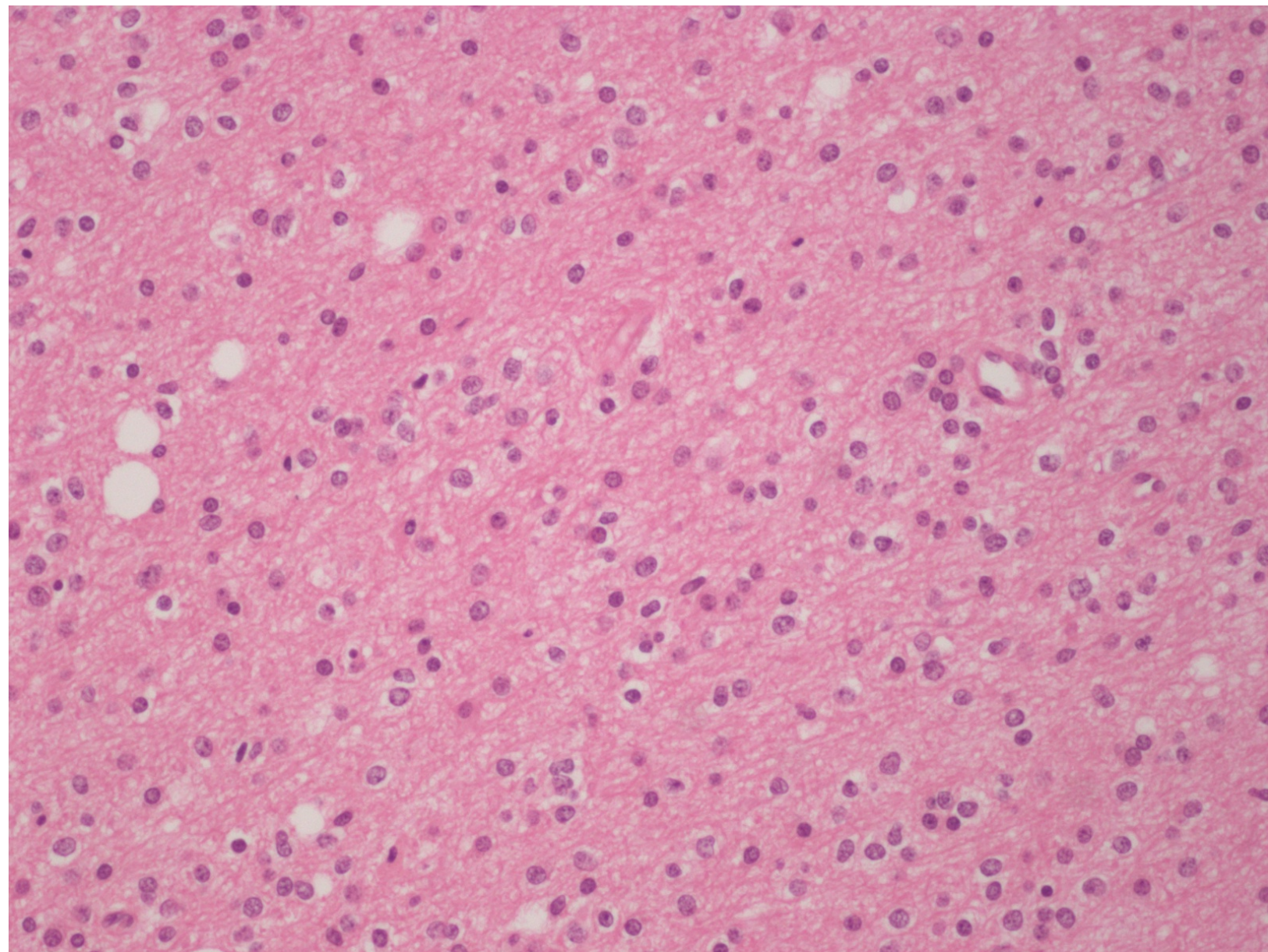


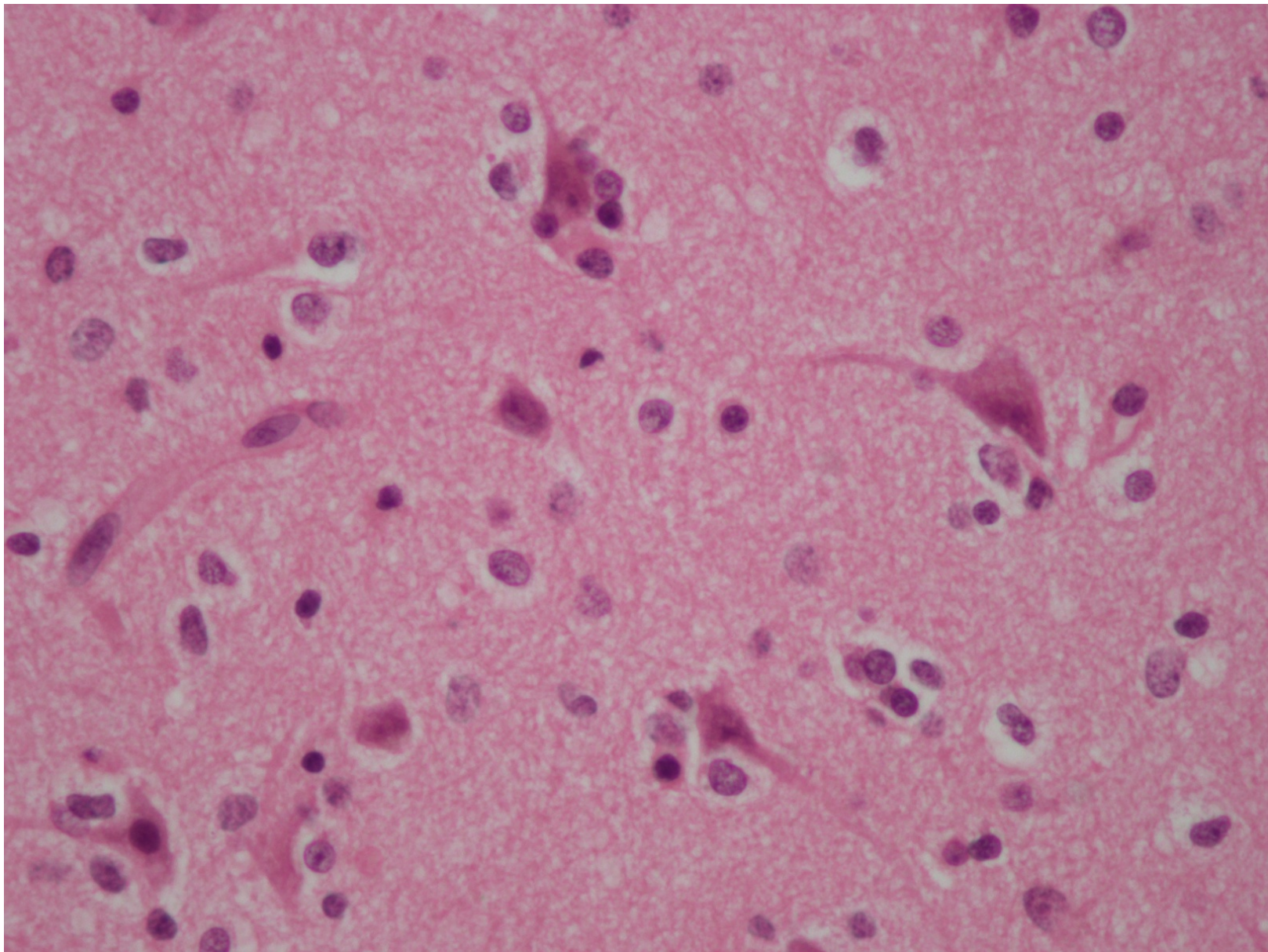
LGG and secondary GBM are IDH mutated



Case 3

- 47M
- Right parietal tumour
- p/w focal seizure with secondary generalisation
- MRI – non enhancing mass





Perineuronal satellitosis

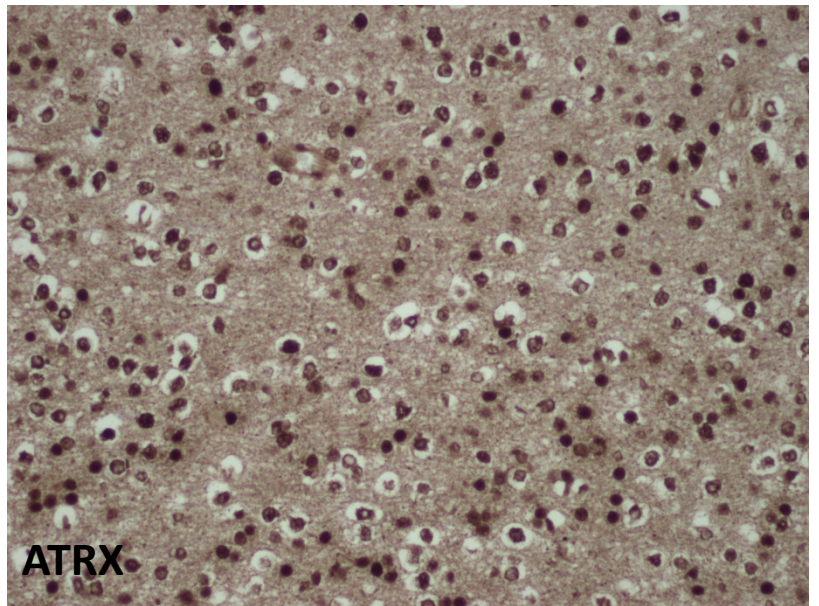
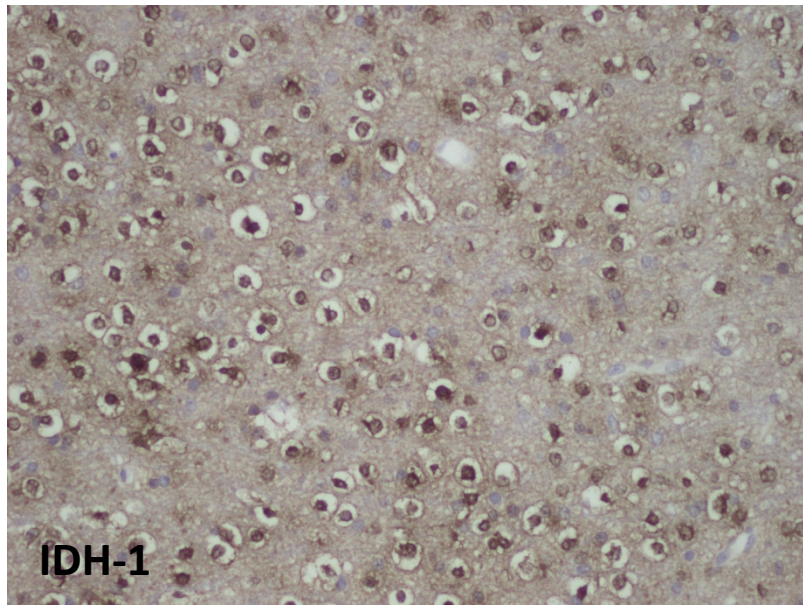
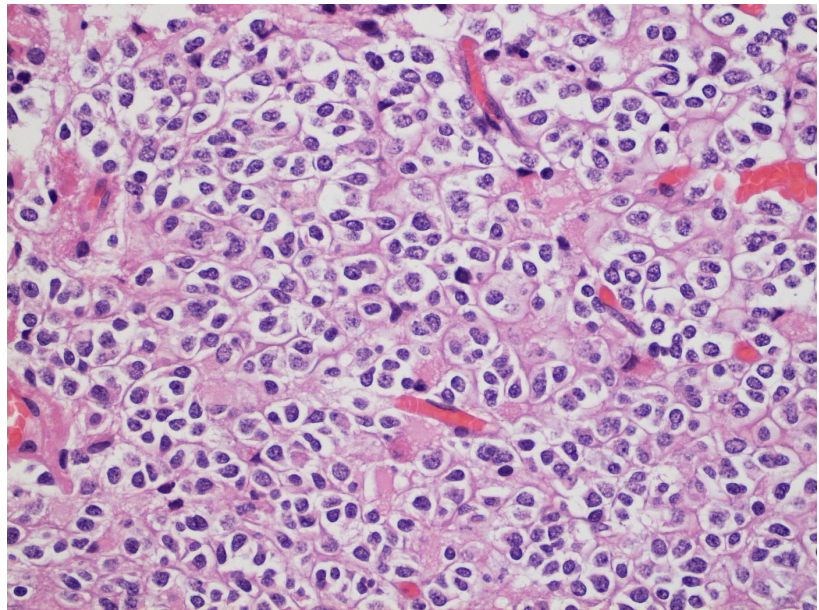
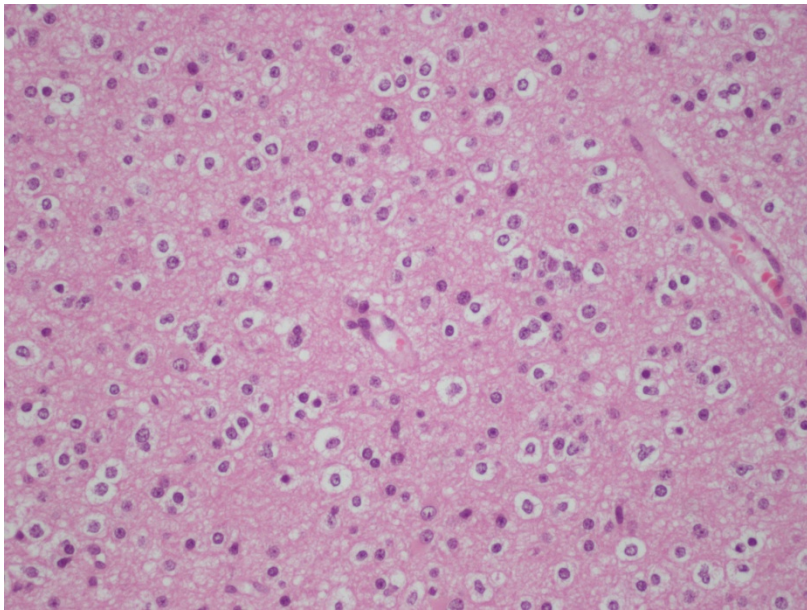
Oligodendroglioma (WHO grade 2)

IHC

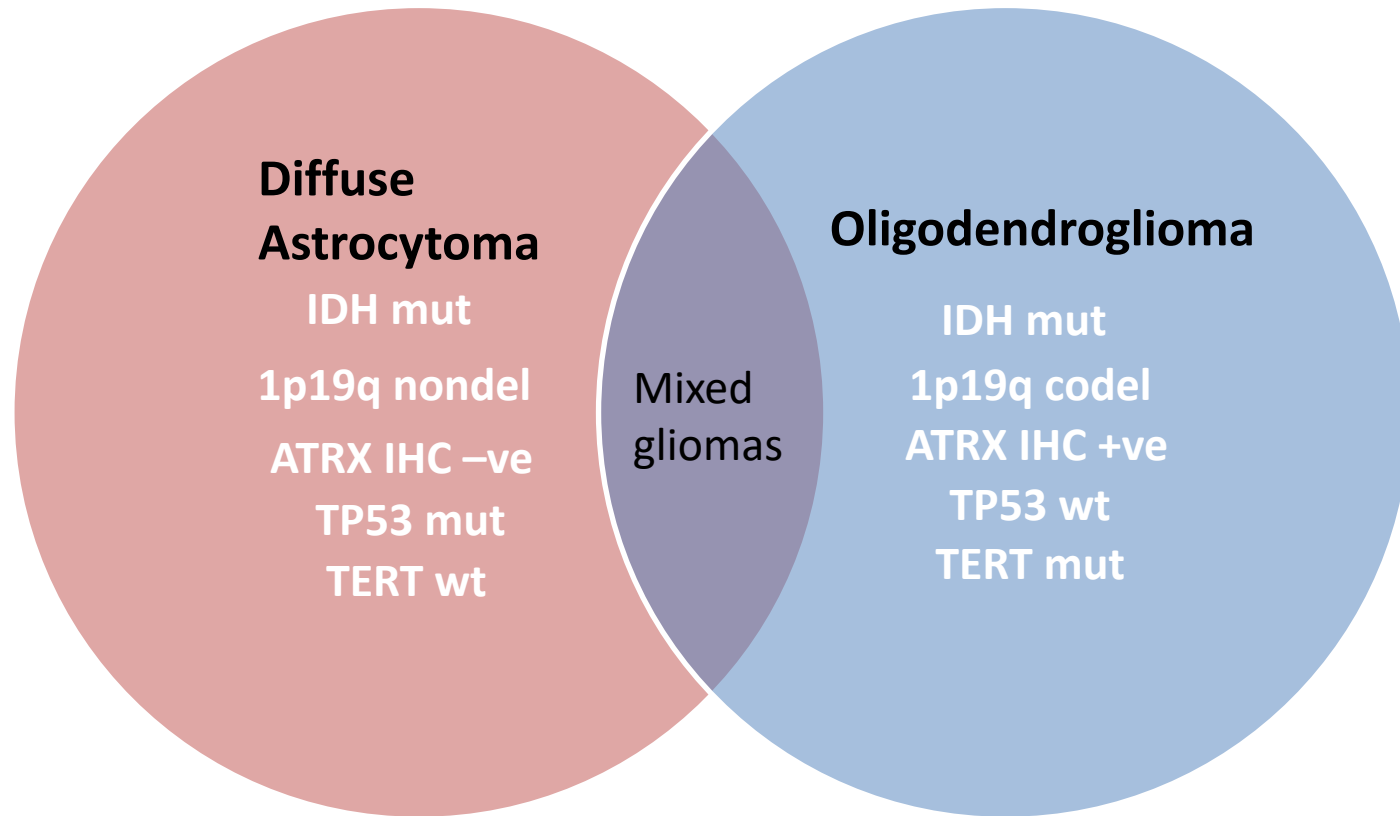
- GFAP
- Mib-1 (Ki67)
- IDH1 (R132H)
- ATRX

Molecular

- 1p / 19q FISH



low grade gliomas - molecular



low grade gliomas - molecular

Diffuse Astrocytoma

IDH mut
ATRX IHC –ve
TERT wt
TP53 mut

Oligodendroglioma

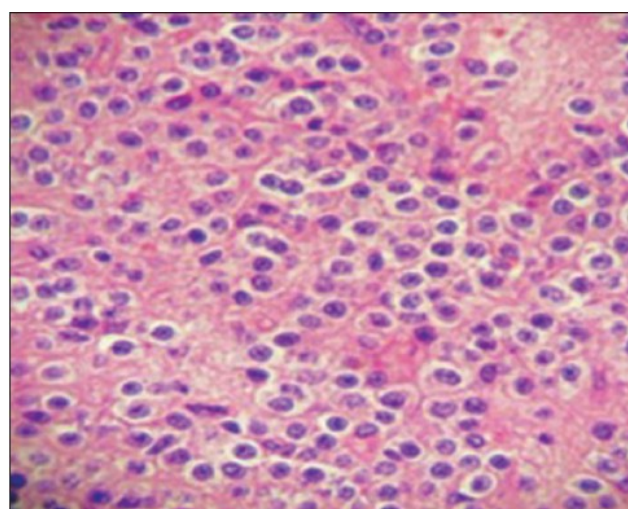
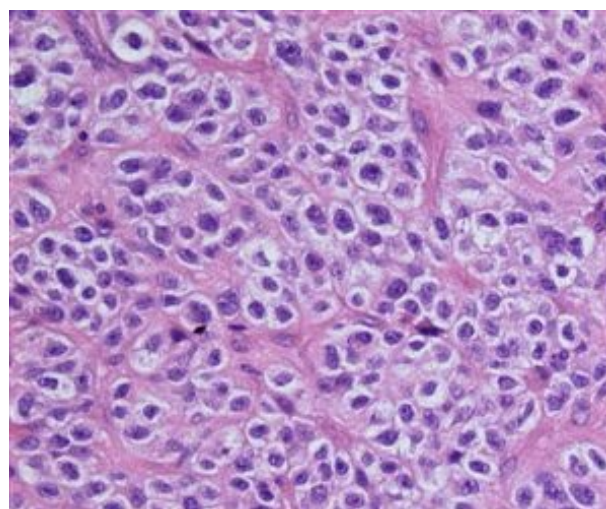
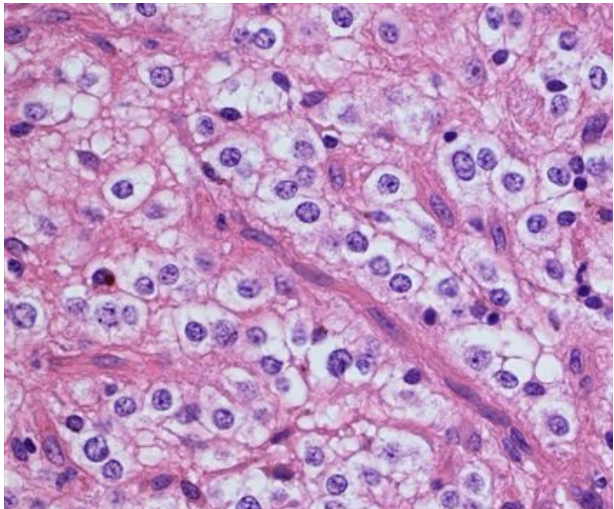
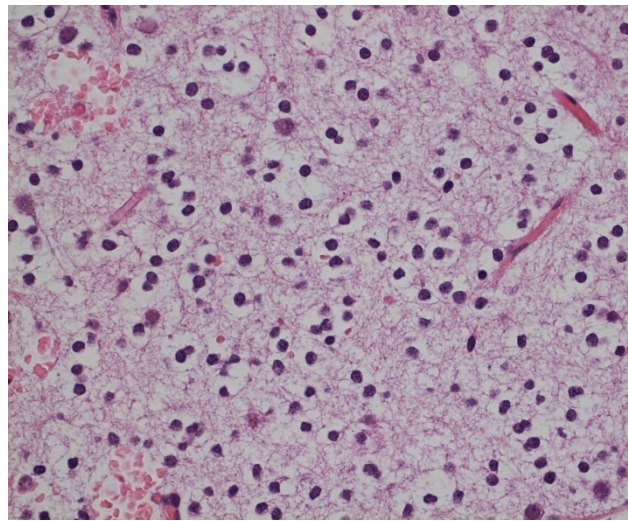
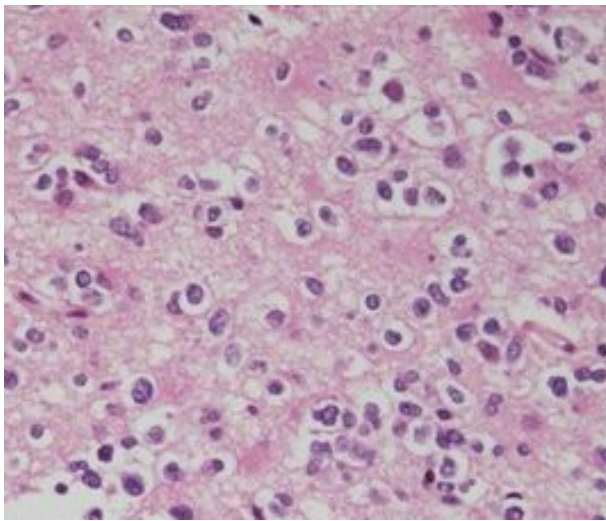
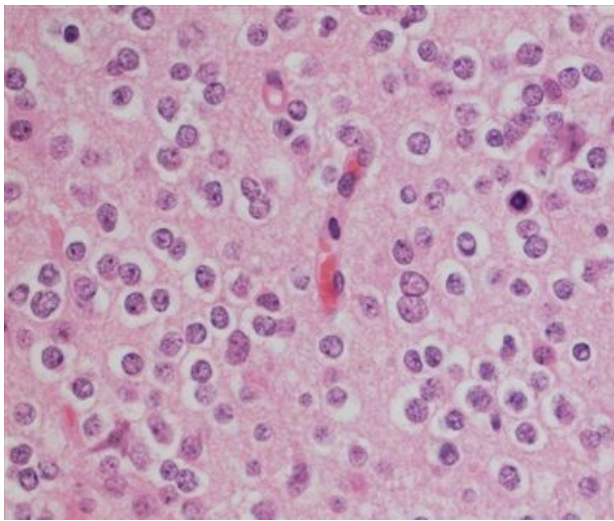
IDH mut
ATRX IHC +ve
TERT mut
TP53 wt

Acta Neuropathol (2014) 128:551–559
DOI 10.1007/s00401-014-1326-7

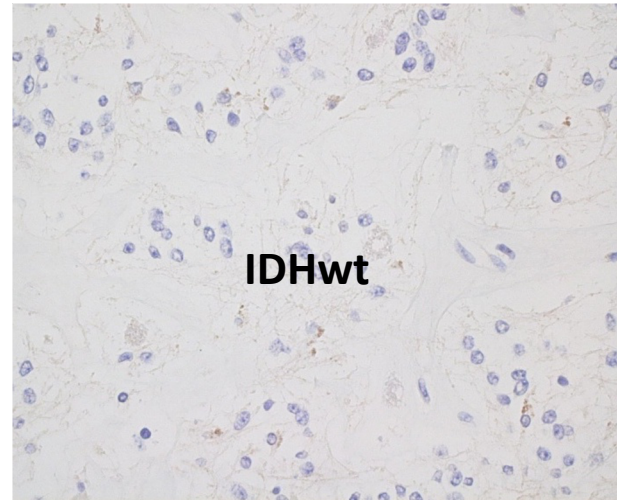
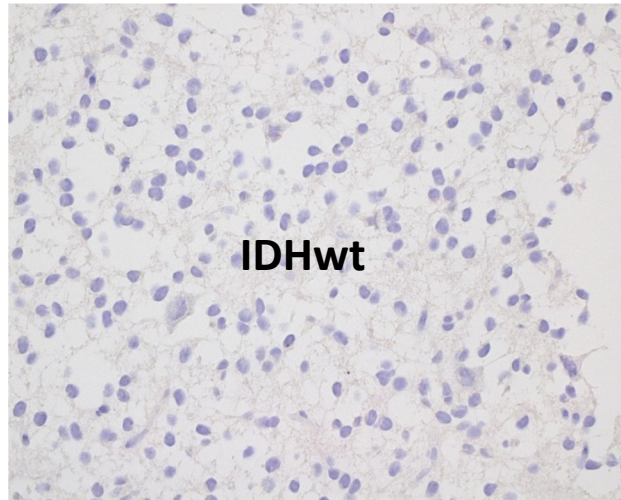
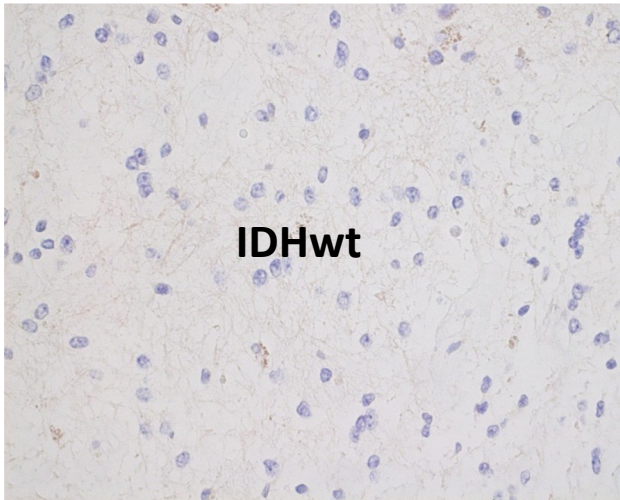
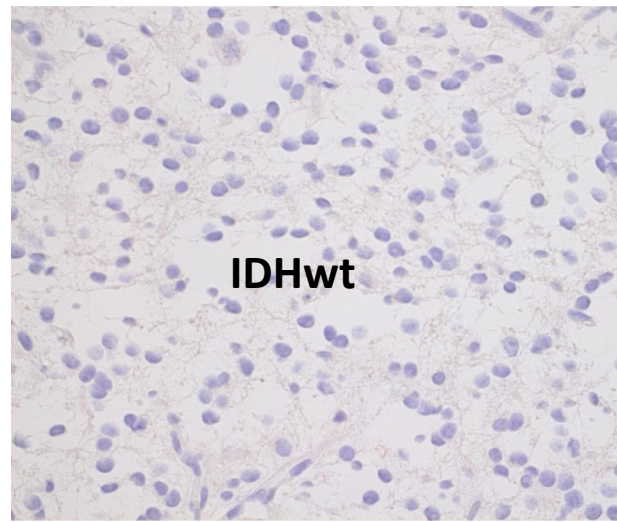
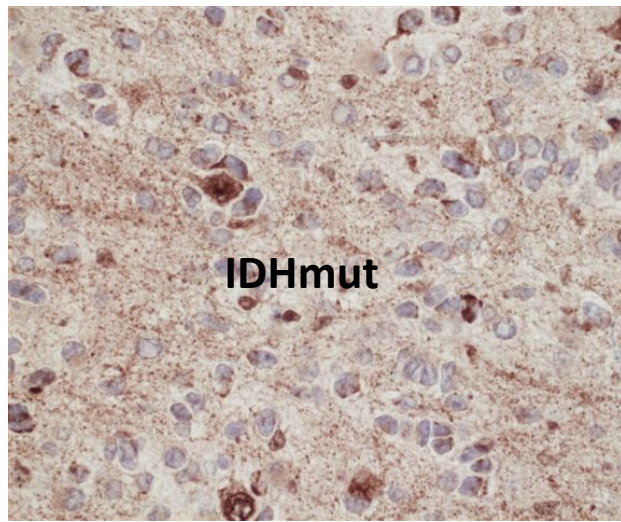
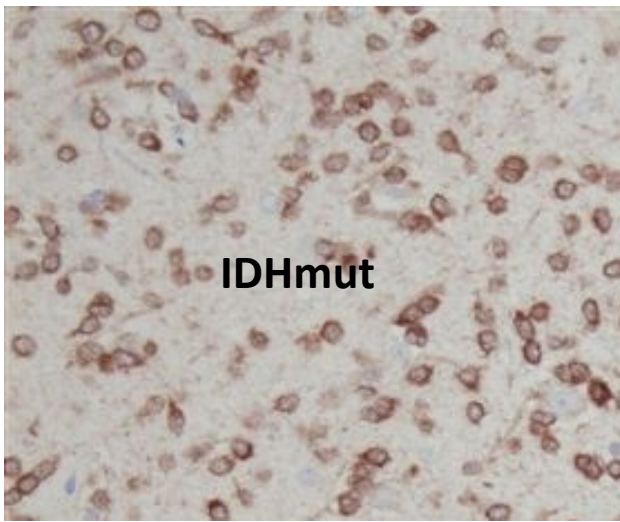
ORIGINAL PAPER

Farewell to oligoastrocytoma: in situ molecular genetics favor classification as either oligodendroglioma or astrocytoma

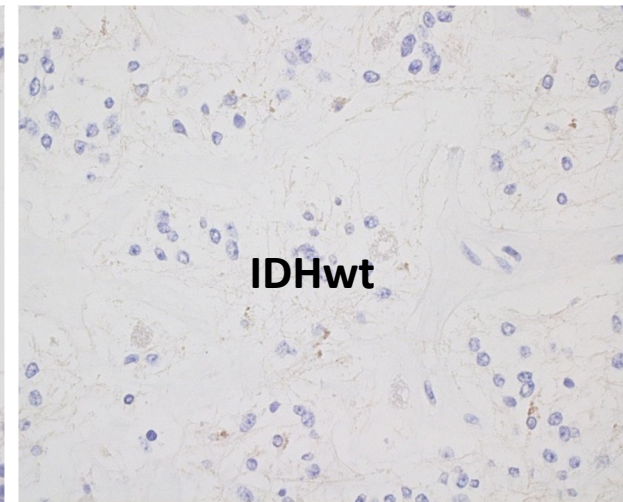
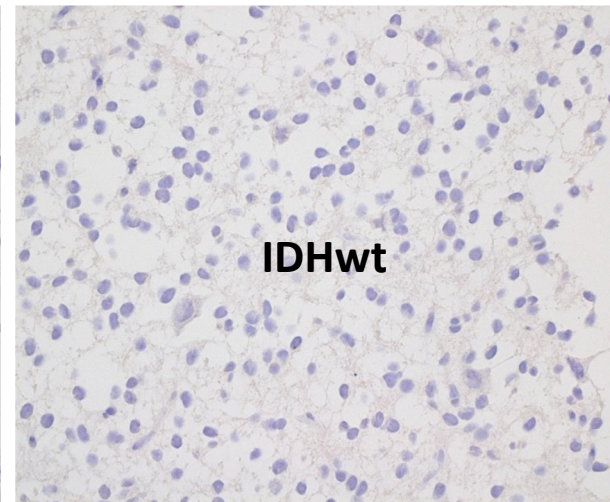
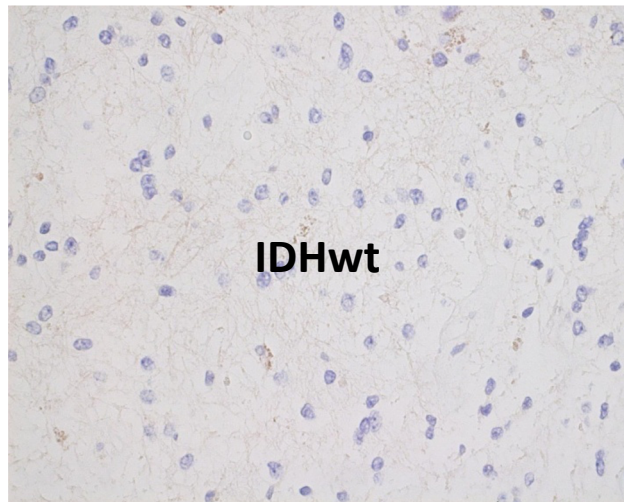
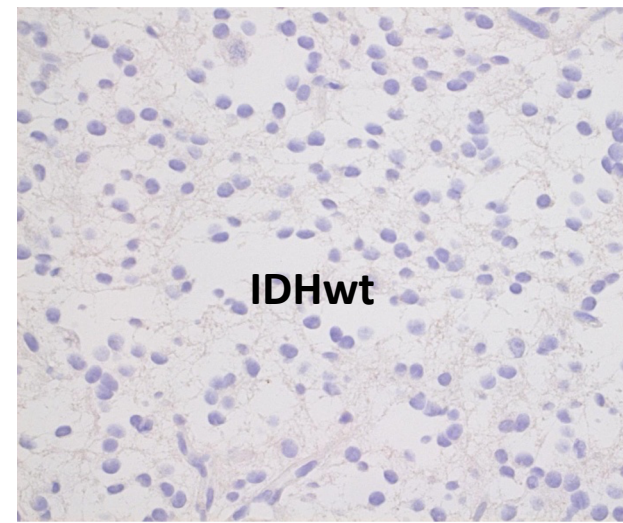
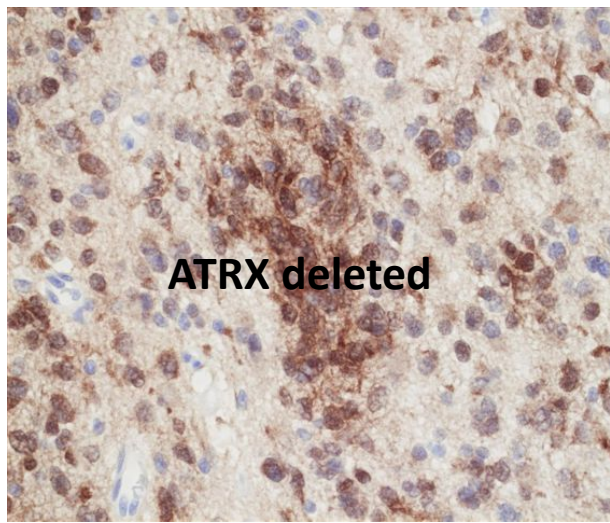
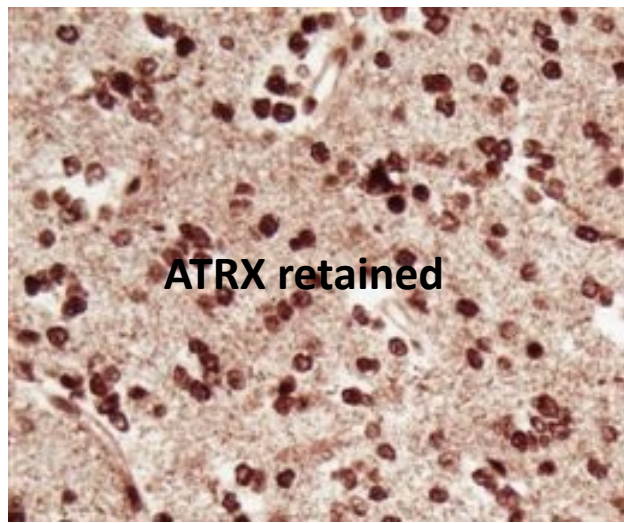
Felix Sahm · David Reuss · Christian Koelsche · David Capper · Jens Schittenhelm · Stephanie Heim · David T. W. Jones · Stefan M. Pfister · Christel Herold-Mende · Wolfgang Wick · Wolf Mueller · Christian Hartmann · Werner Paulus · Andreas von Deimling



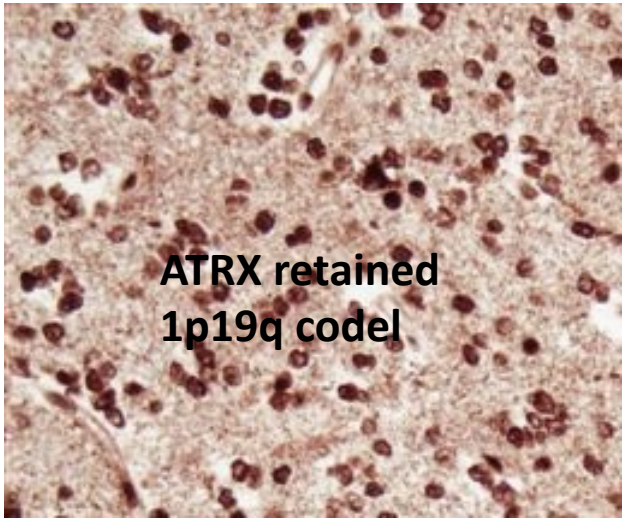
What's the diagnosis?



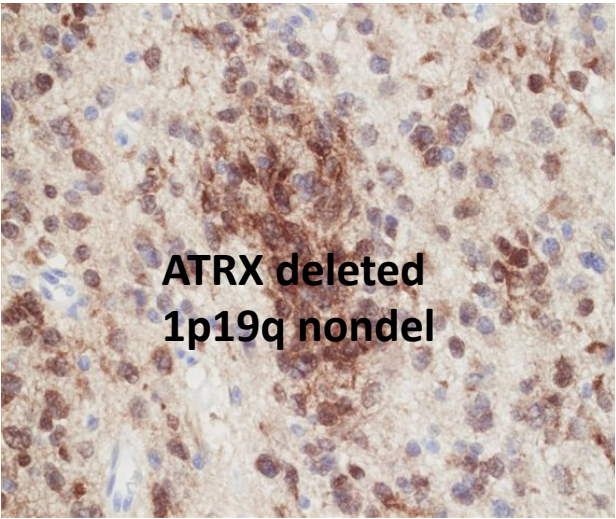
Oligodendrogliomas have IDH mutations



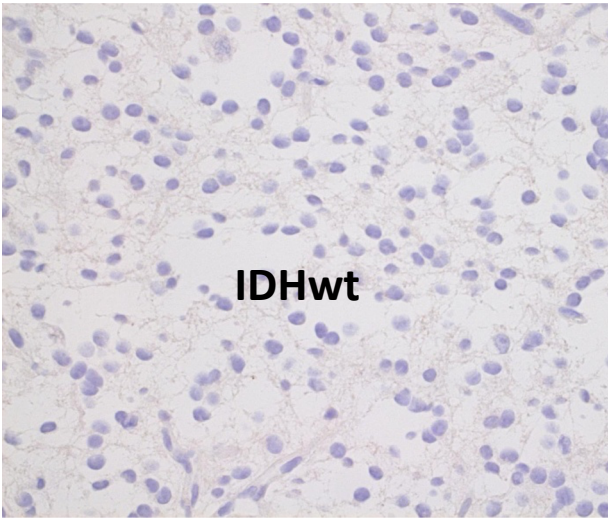
Oligodendrogliomas have IDH mutations and are not ATRX deleted



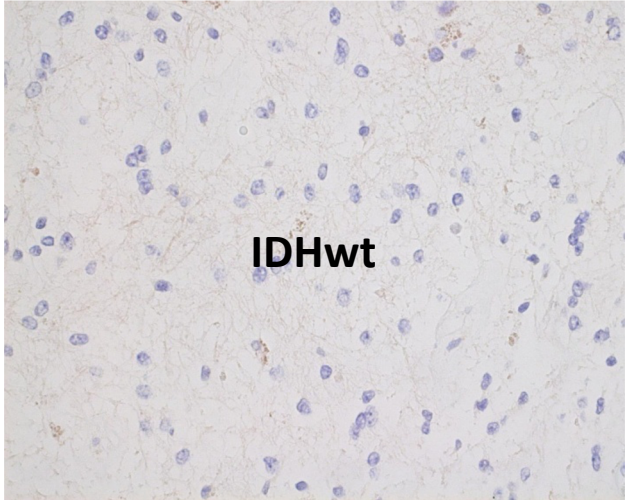
**ATRX retained
1p19q codeletion**



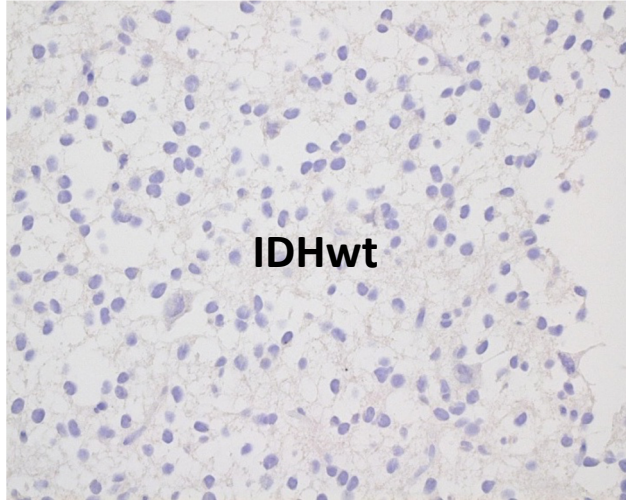
**ATRX deleted
1p19q nondel**



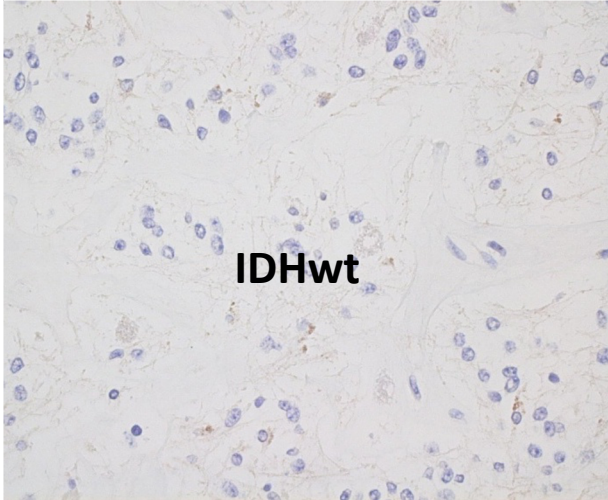
IDHwt



IDHwt

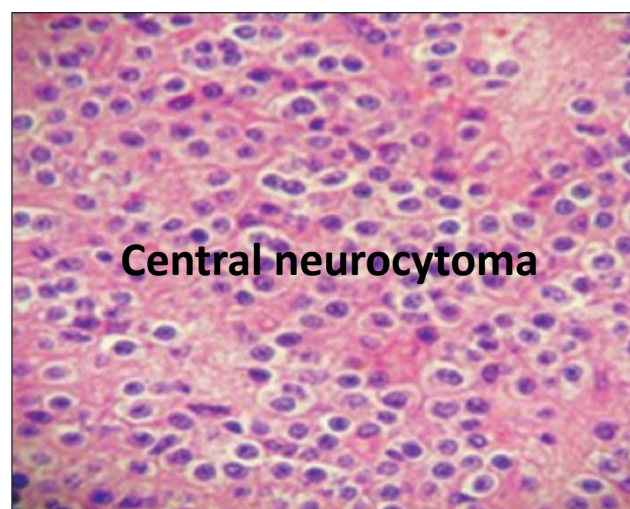
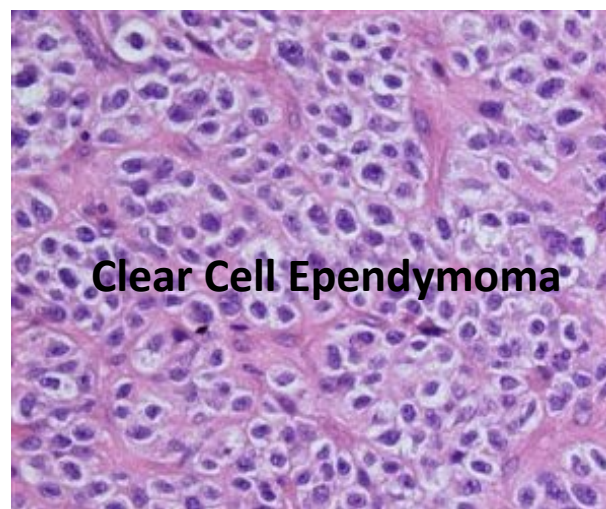
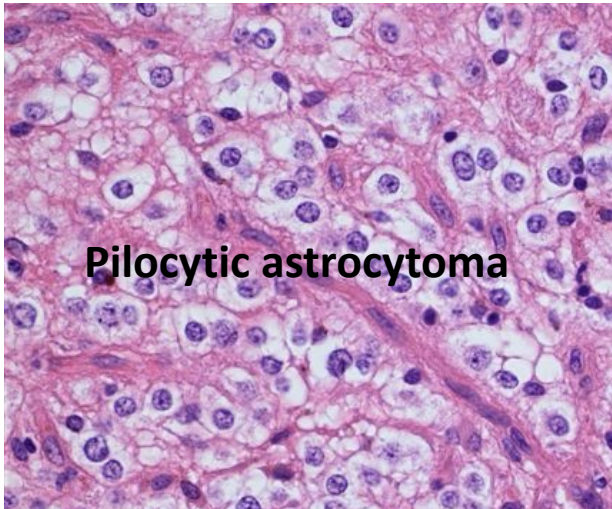
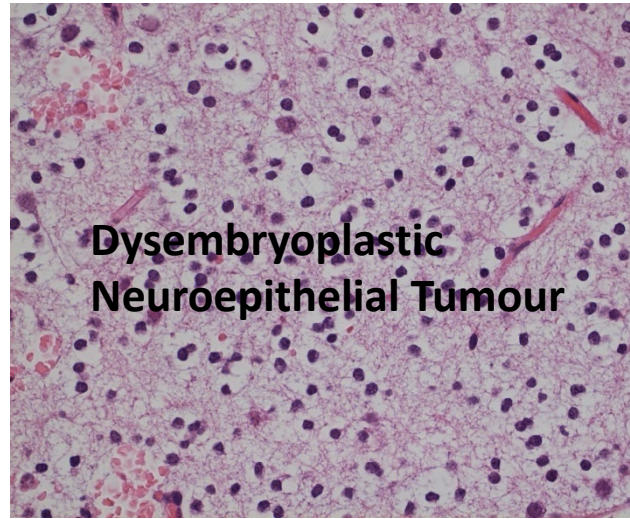
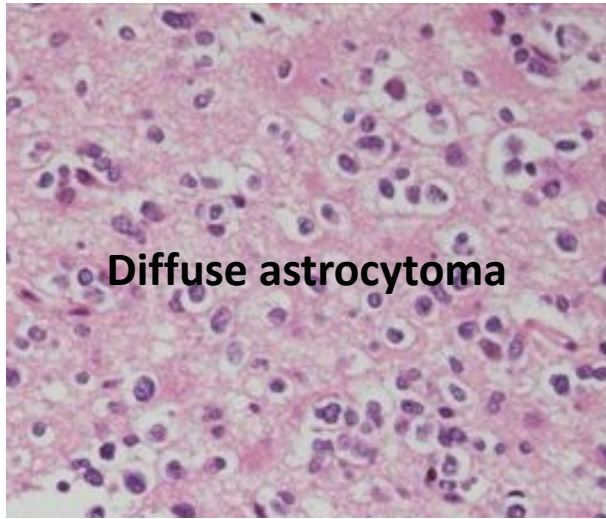
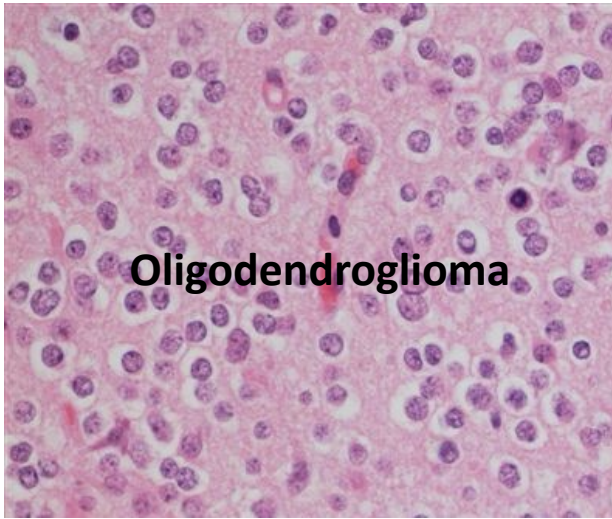


IDHwt



IDHwt

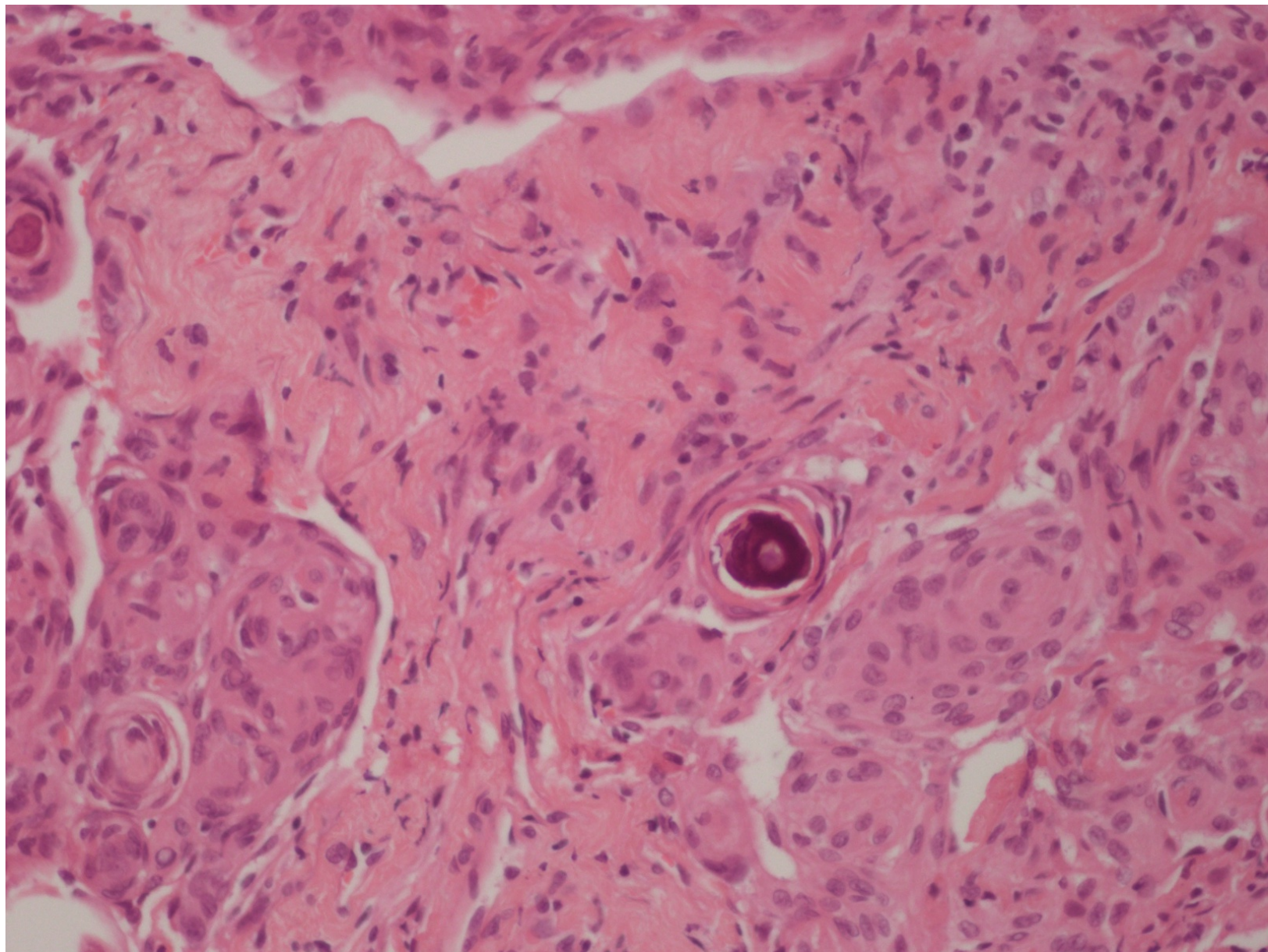
Oligodendrogliomas have IDH mutations and 1p19q codeletions and are not ATRX deleted

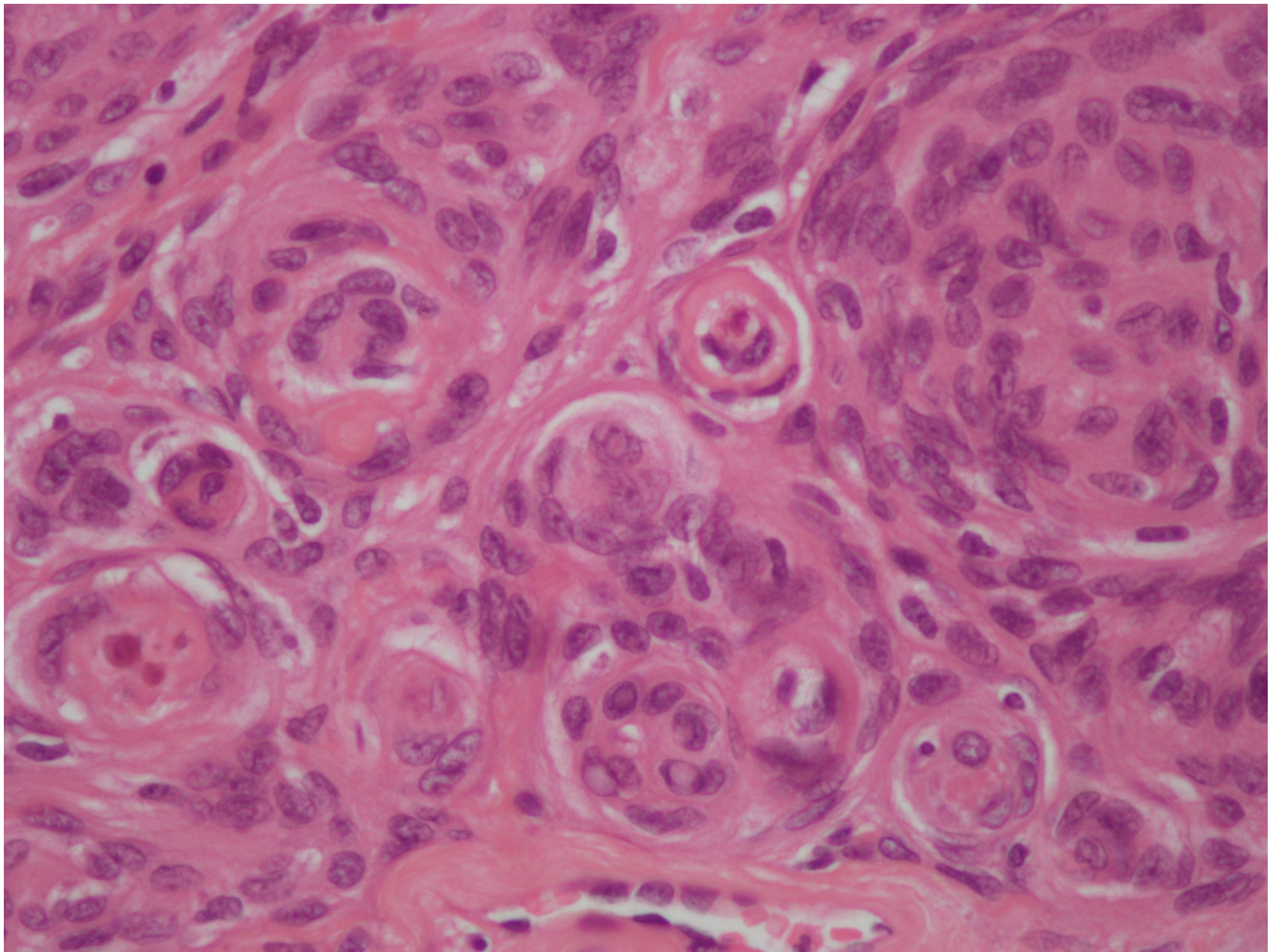


Oligodendrogliomas are now defined by IDH mutation and 1p19q co-deletion

Case 4

- 51F
- Suprasellar tumour encasing left carotid and left optic nerve





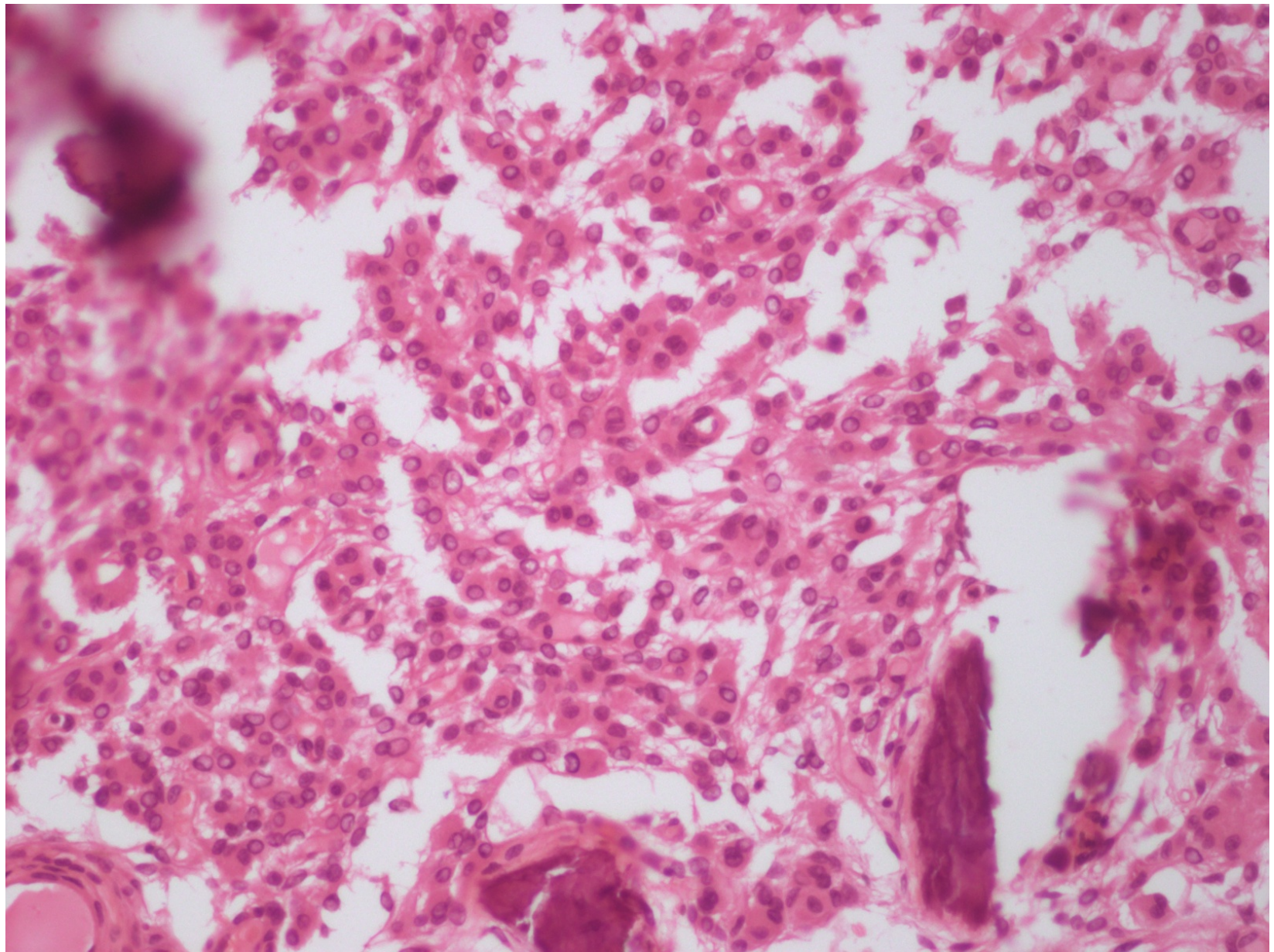
- Meningioma (Grade 1)
- IHC
 - Mib-1
 - (PR, EMA)

Meningioma grading

- Meningioma (WHO Grade 1)
- Atypical meningioma (WHO Grade 2)
 - 4 or more MFs per 10 HPF
 - Brain invasionOR
3 of 5:
 - Necrosis
 - Small cell change
 - Patternless sheet-like architecture
 - Hypercellularity
 - Prominent nucleoli
- Anaplastic meningioma (WHO Grade 3)
 - 20 or more MF per 10 HPFOR
 - Frank sarcomatous or carcinomatous appearance

Case 5

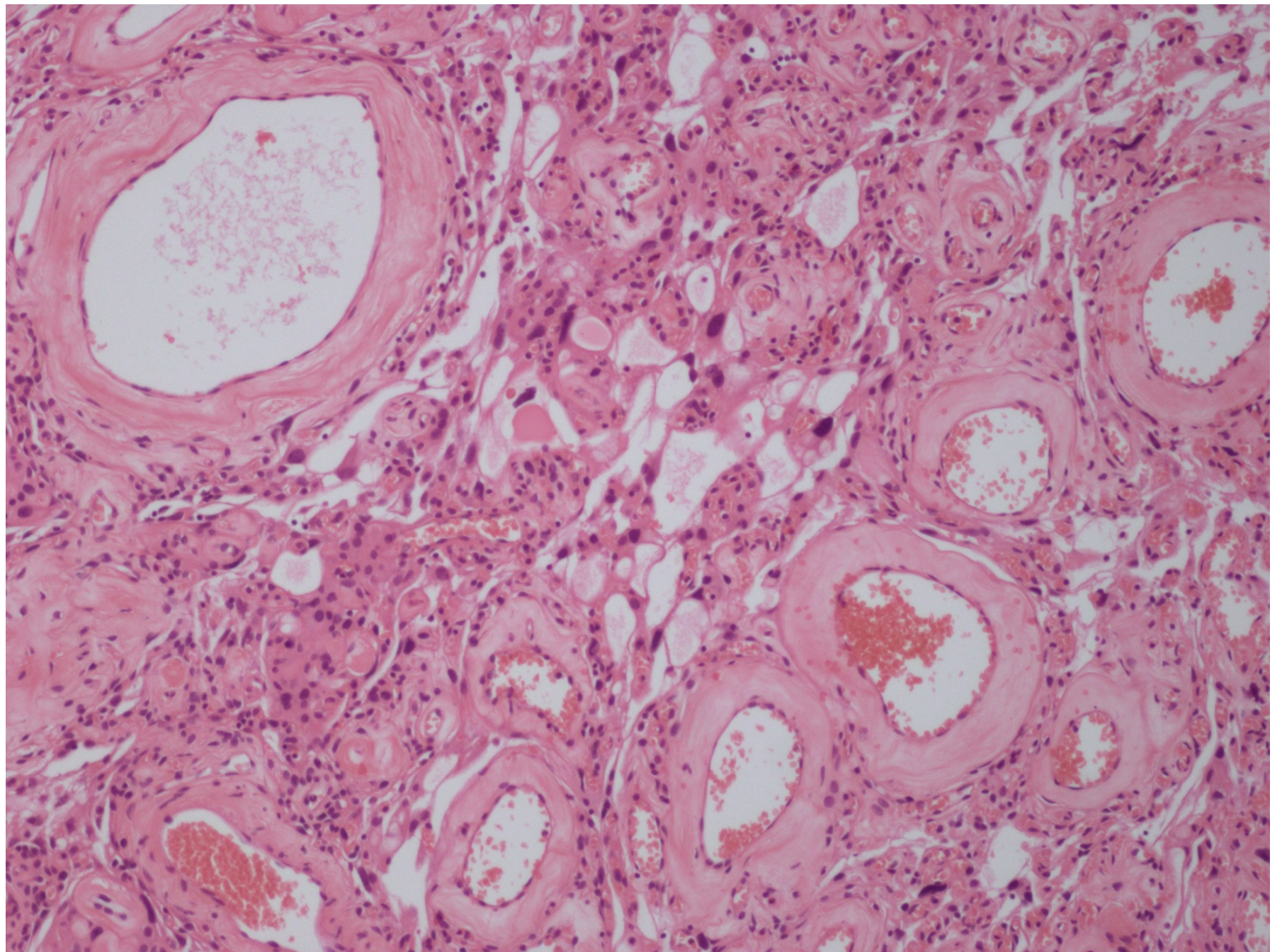
- 83F
- Tumour right sphenoid wing

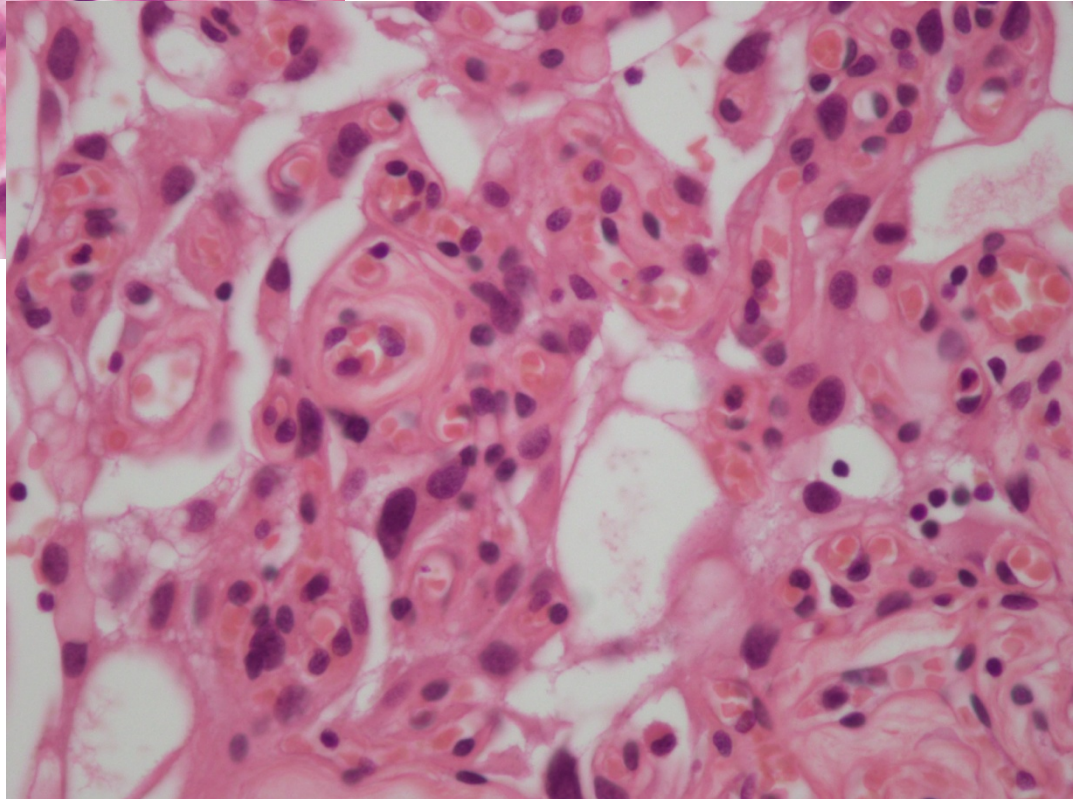
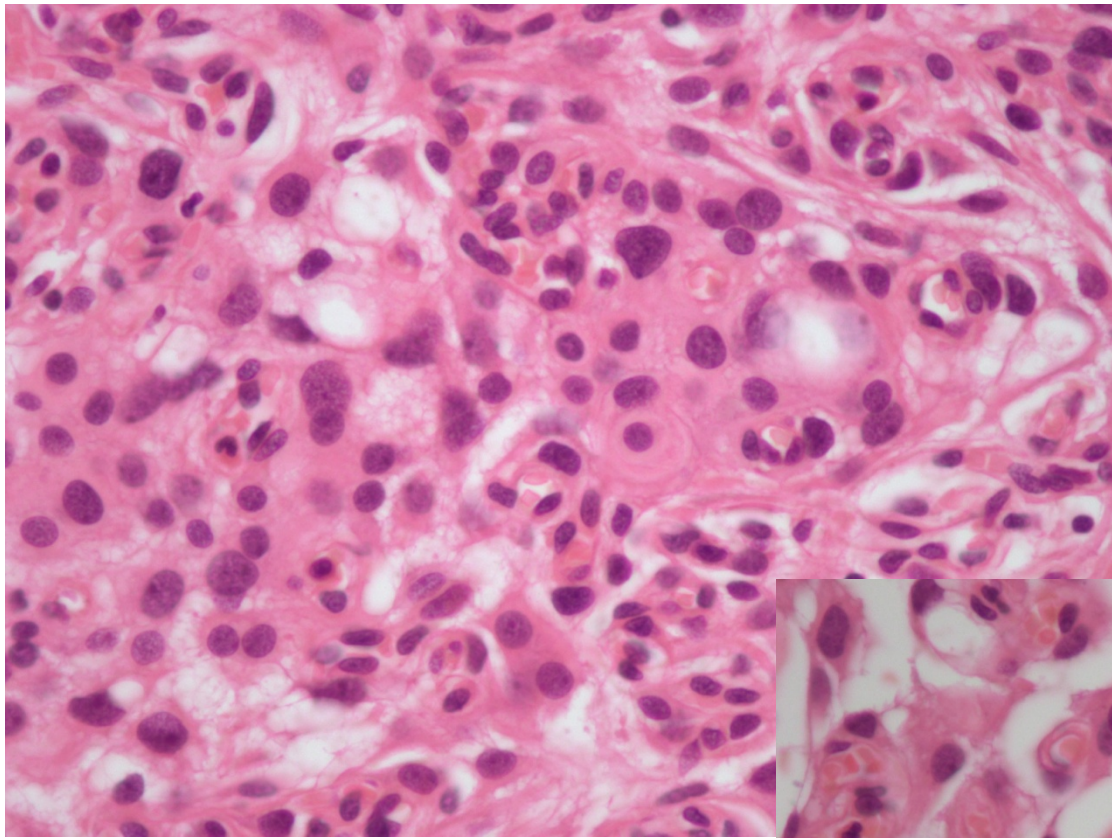


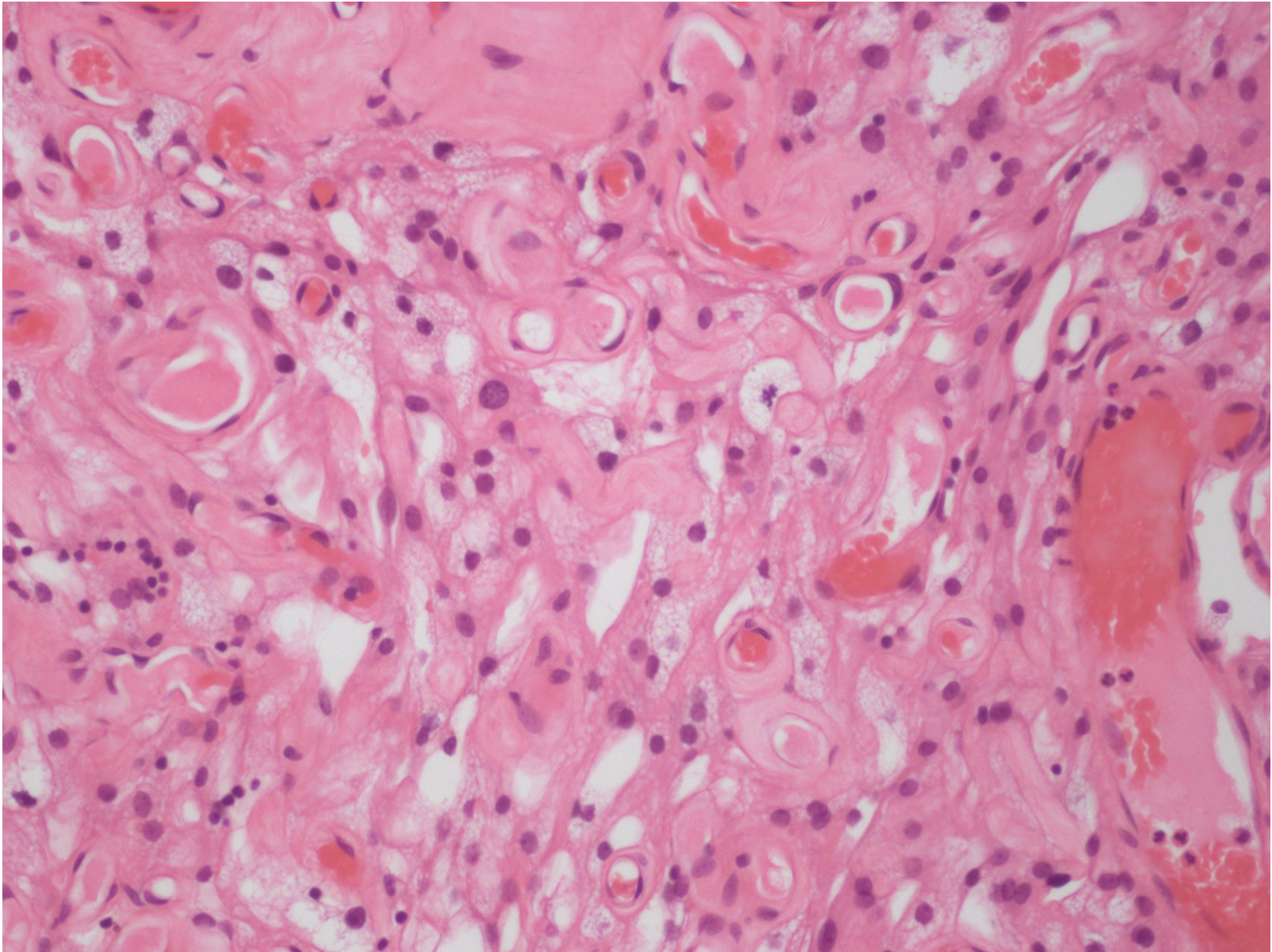
- Meningioma (Grade 1)
- IHC
 - Mib-1
 - (PR, EMA)

Case 6

- 55F
- Left parietal tumour



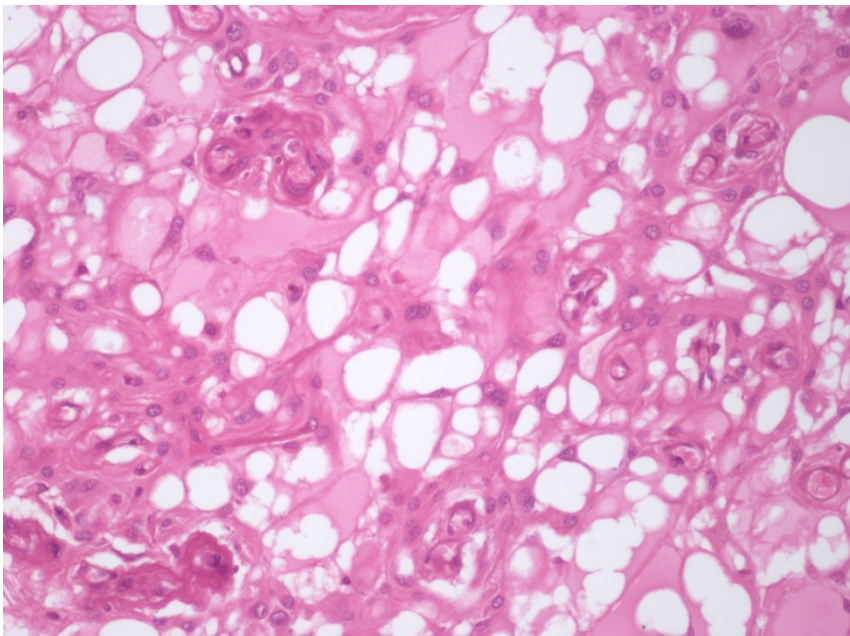
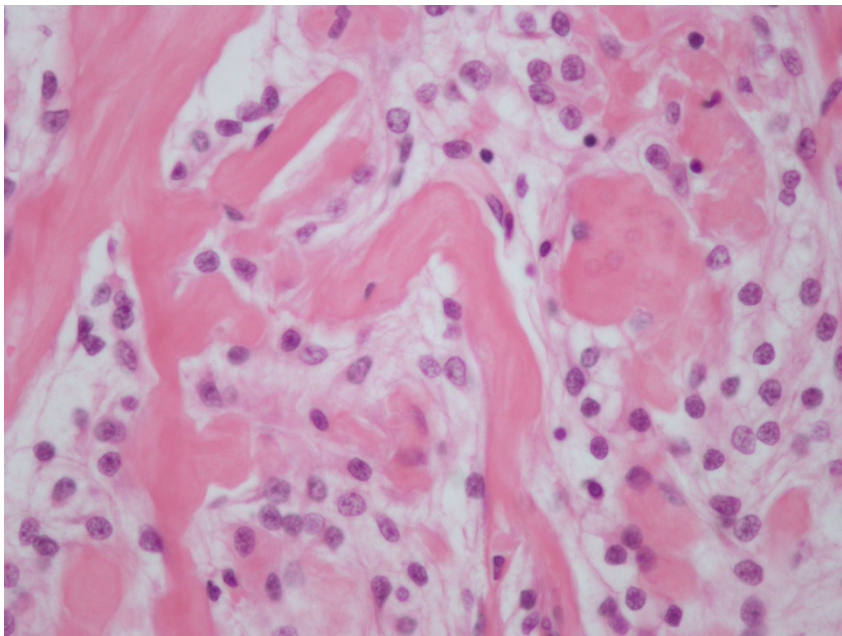
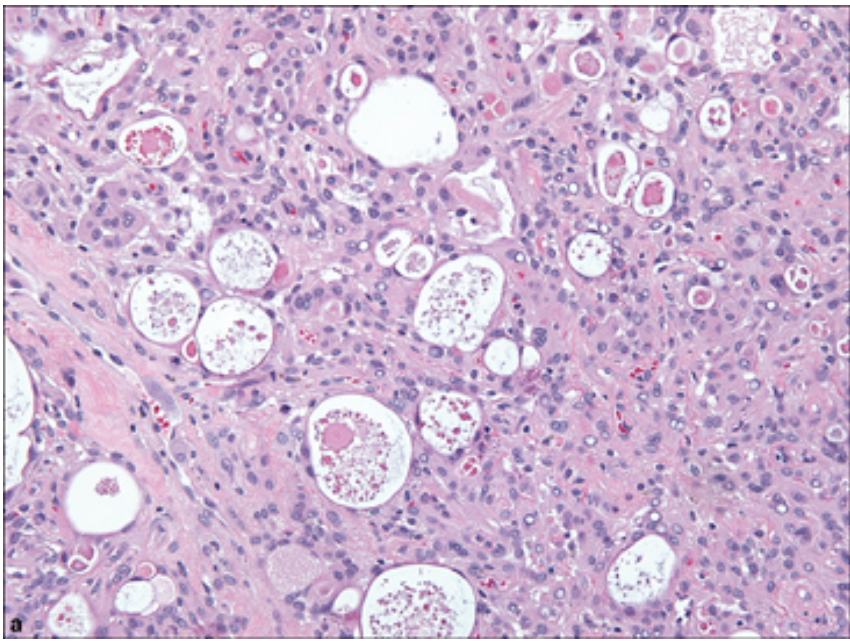
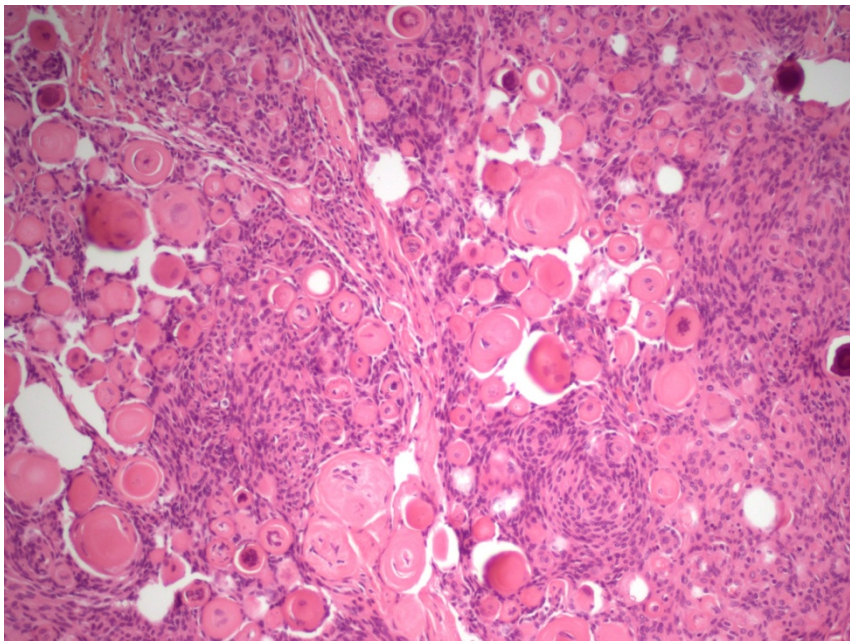




Angiomatous Meningioma (Grade 1) – different case

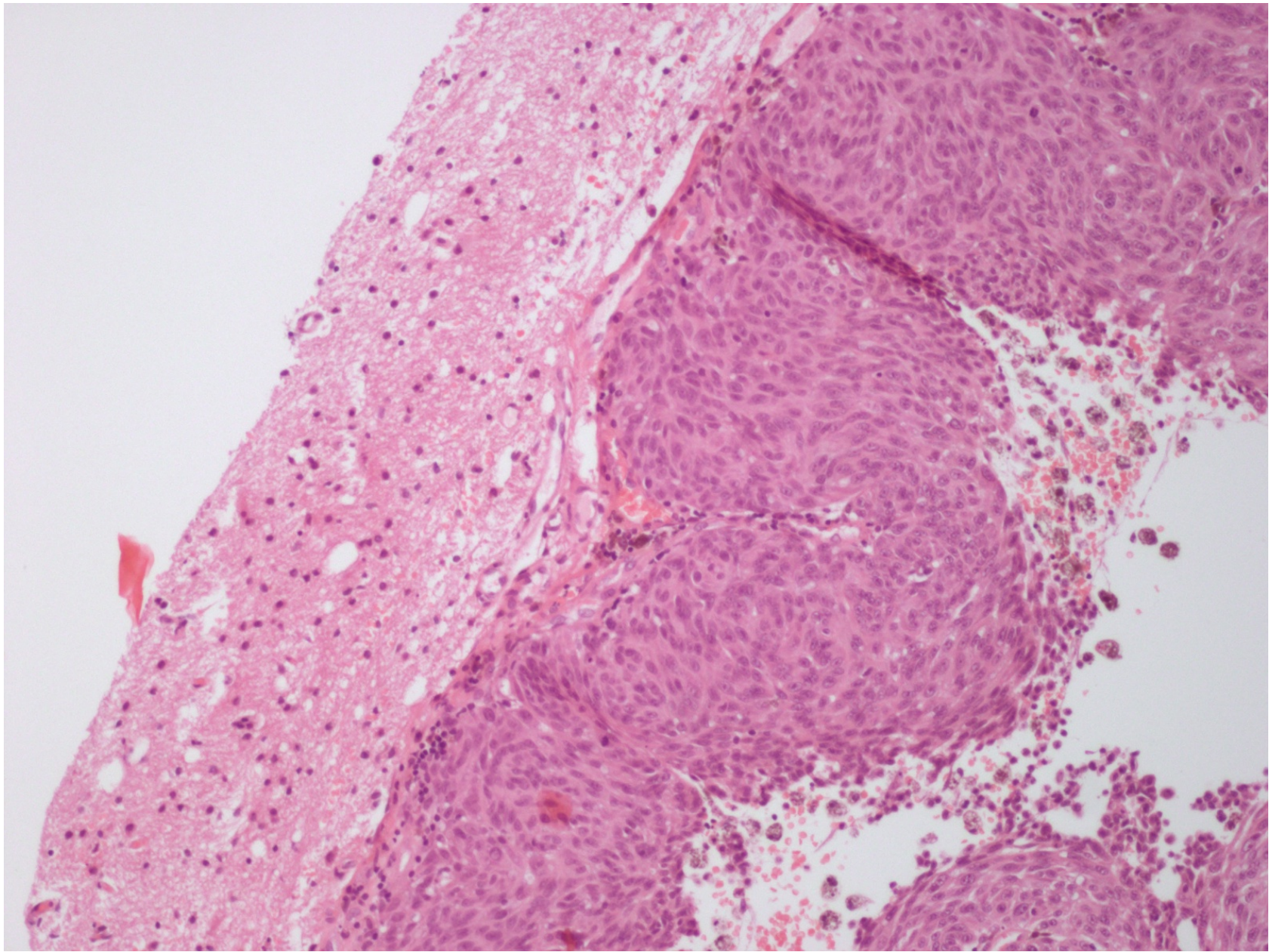
Meningioma subtypes

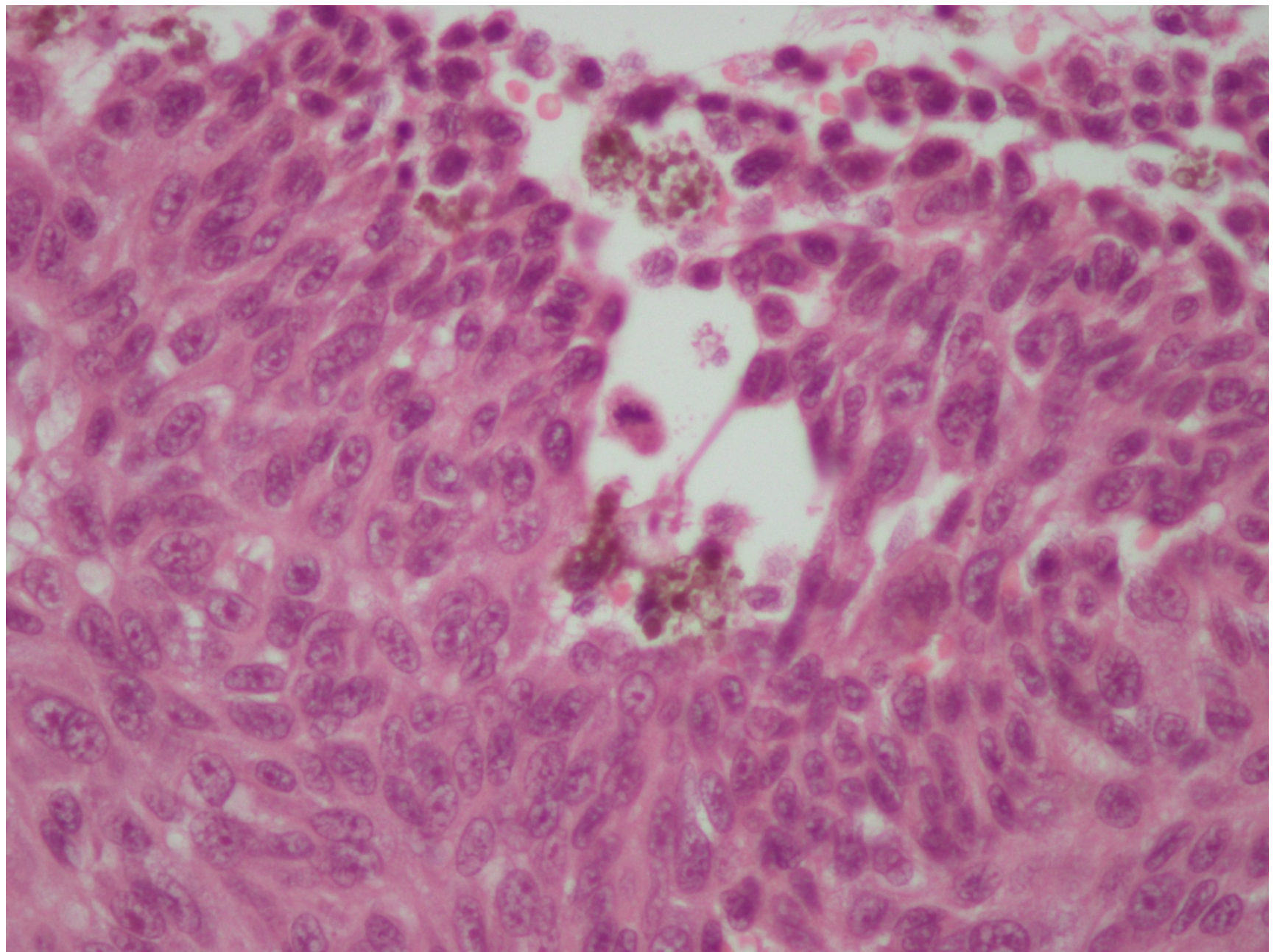
Grade	Grade 2	Grade 3
meningotheiomatous	Clear cell	Papillary
fibrous	chordoid	rhabdoid
transitional		
secretory		
angiomatous		
microcystic		
metaplastic		
psammomatous		



Case 7

- 69M
- Left frontal intrinsic SOL

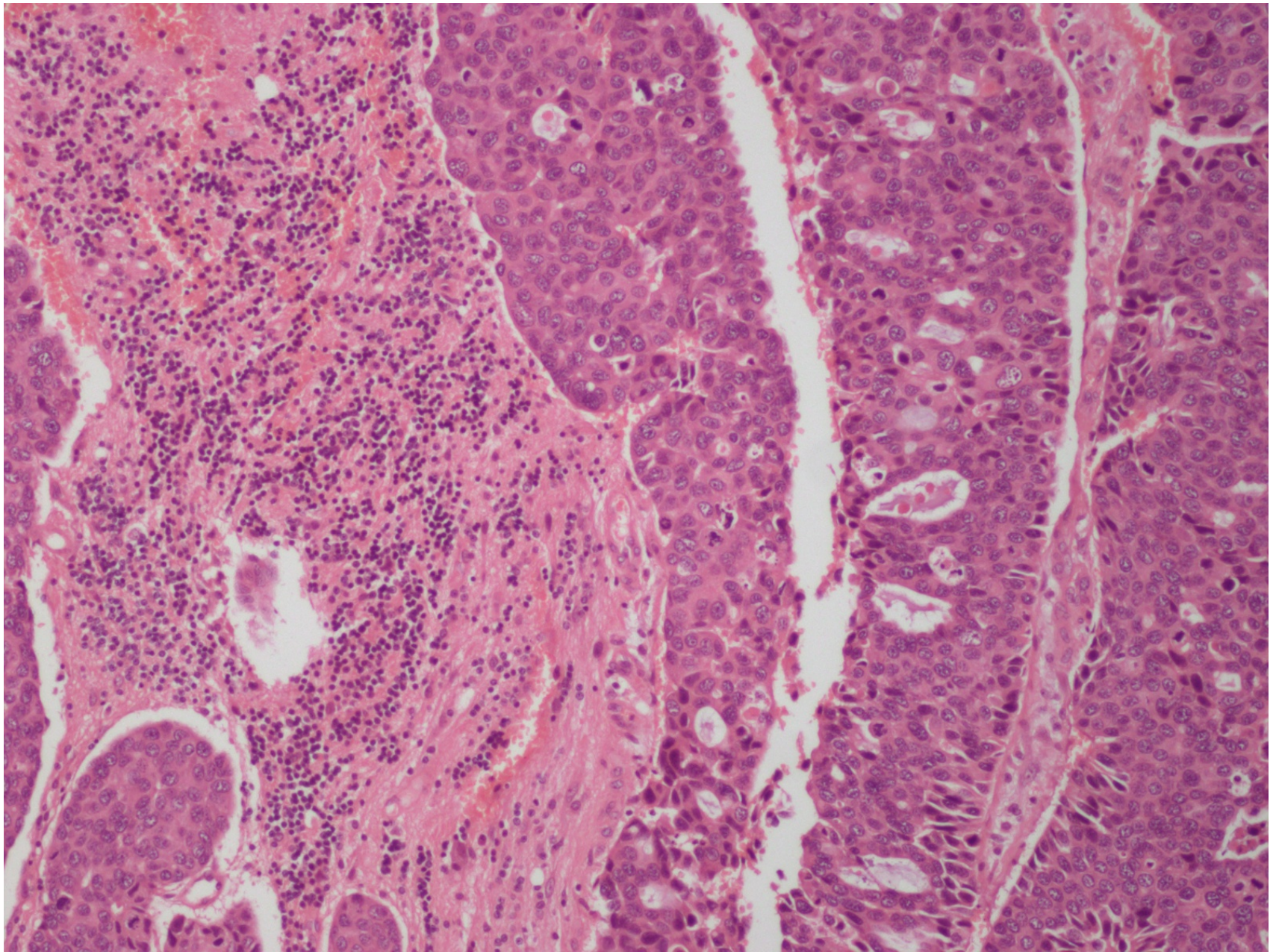




- Metastatic melanoma
- IHC
 - S100, HMB45, melanA
 - (SOX10, MART1)
- Molecular
 - BRAF V600

Case 8

- 61F
- Posterior fossa tumour



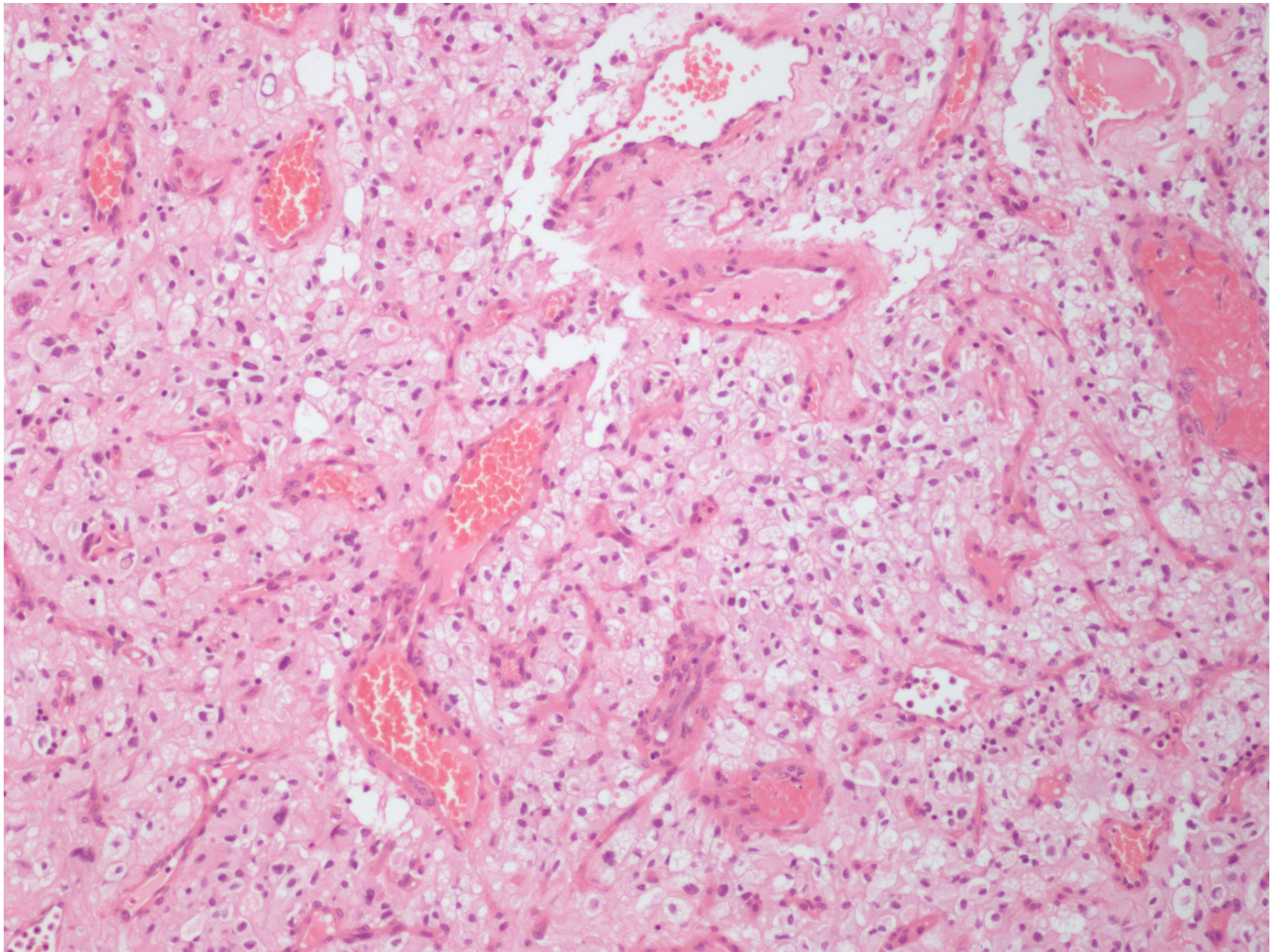
- Metastatic adenocarcinoma

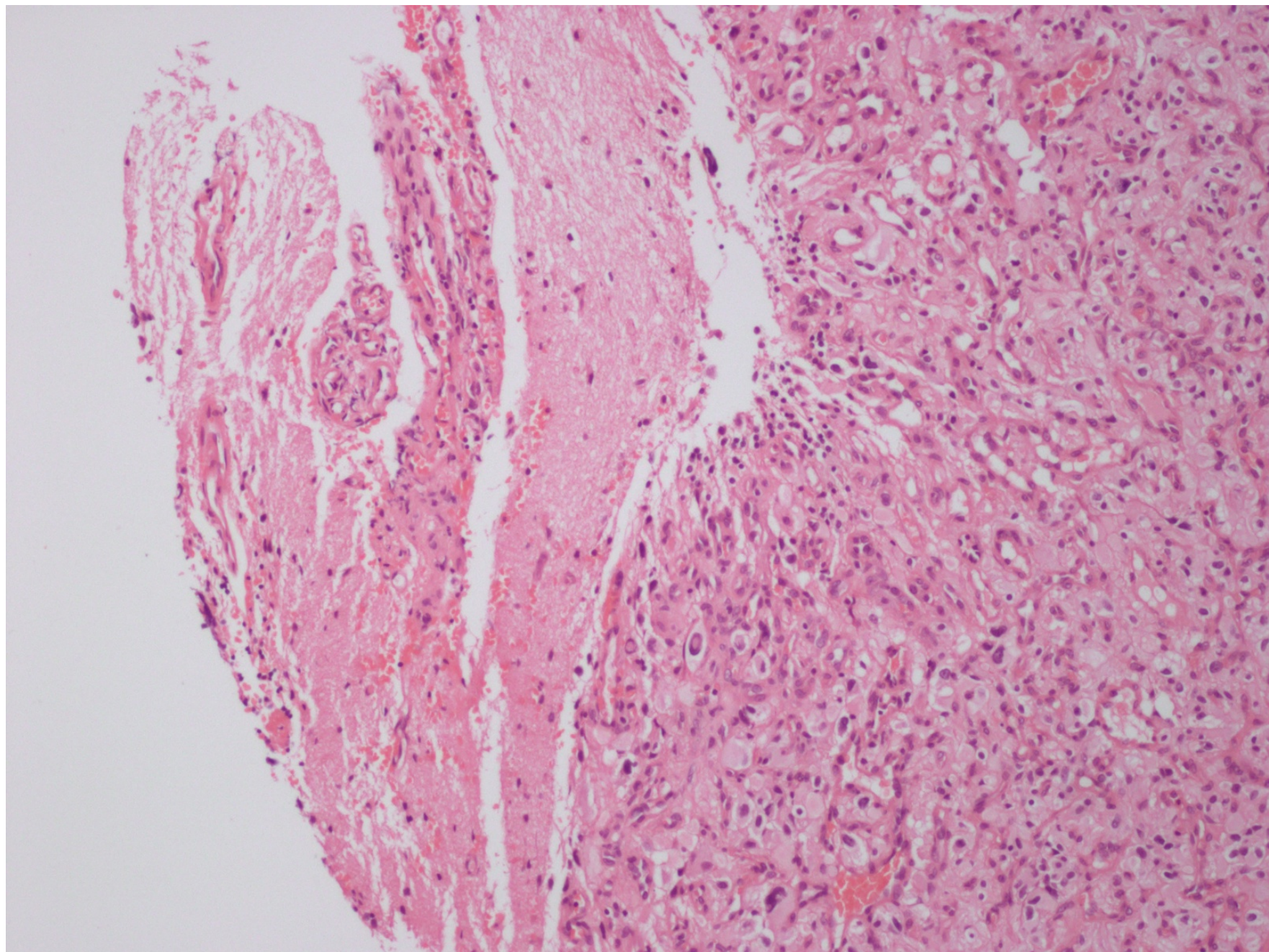
Common brain metastases

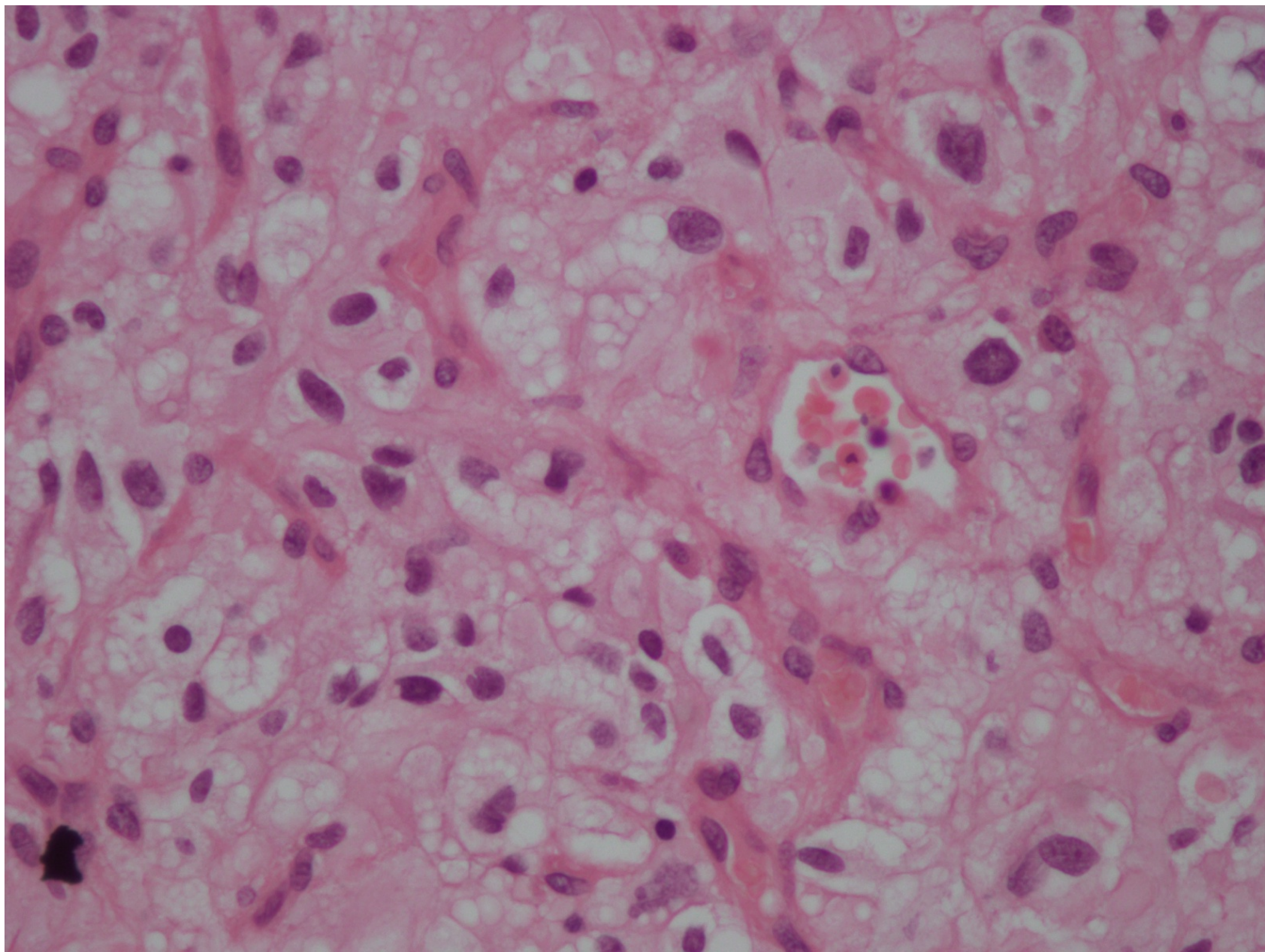
- Lung
- Breast
- Melanoma
- Renal
- Colorectal

Case 9

- 42M
- 1/12 h/o headache and giddiness
- MRI – cerebellar lesion



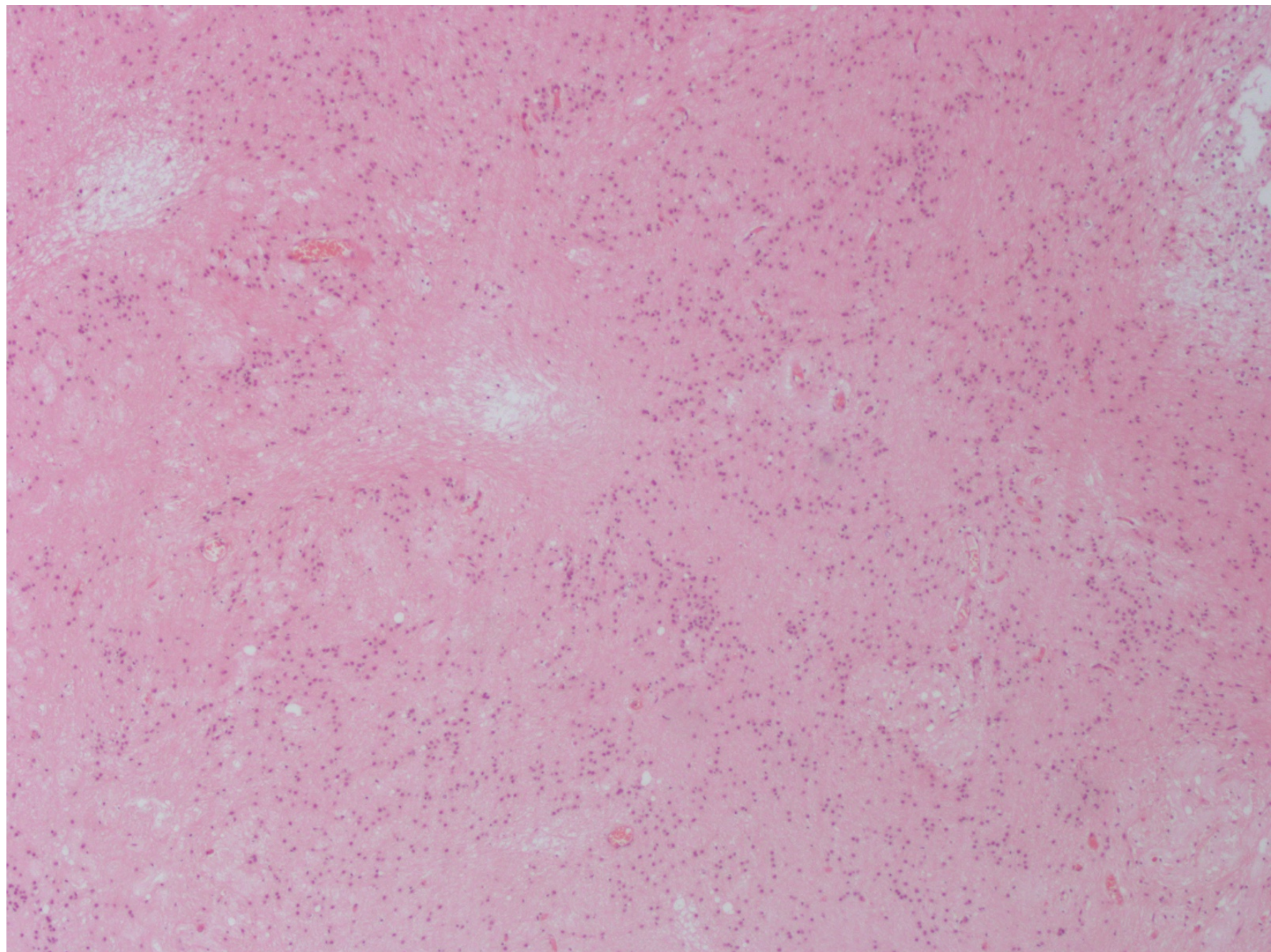


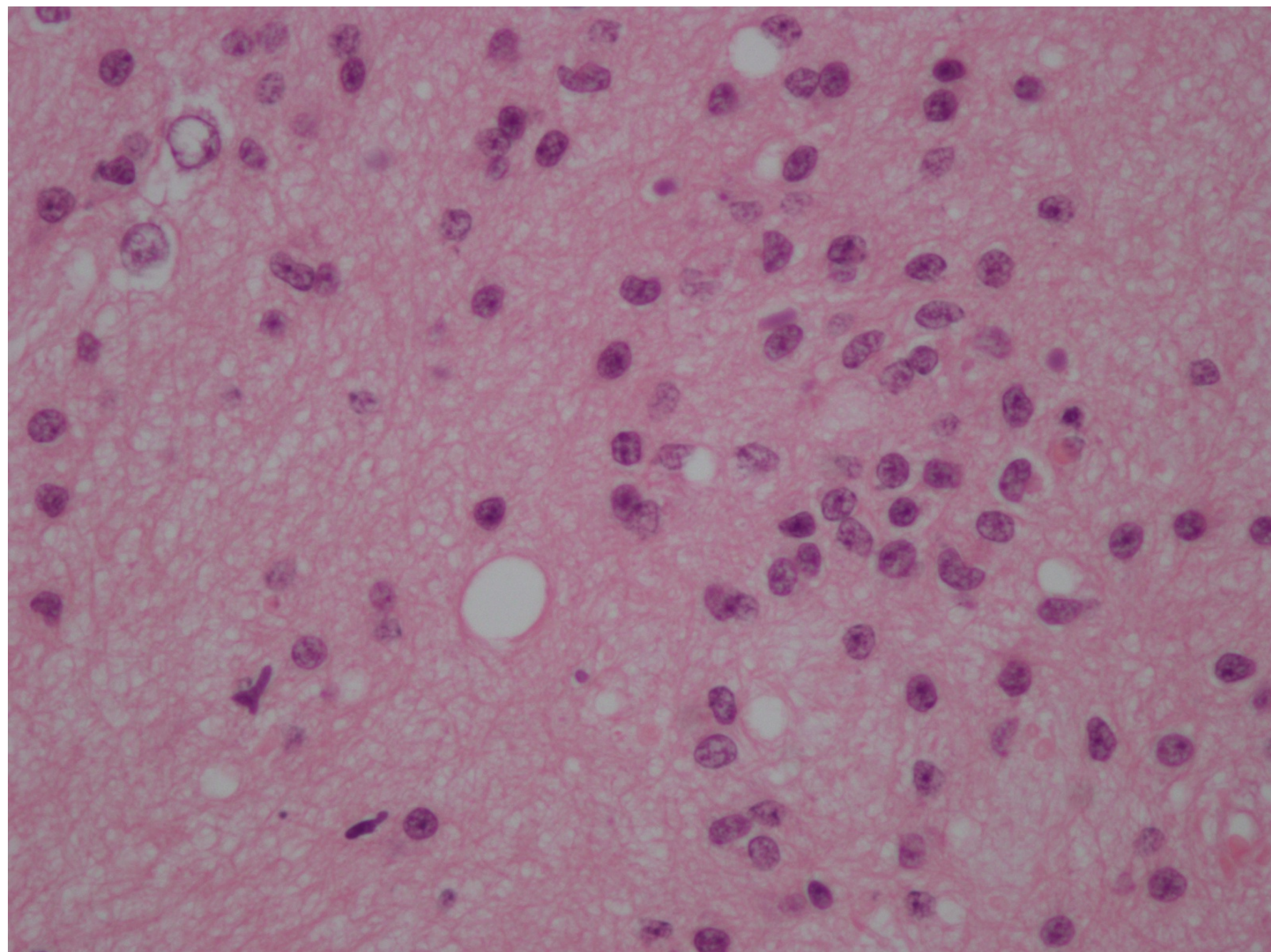


- Haemangioblastoma (WHO Grade 1)
- IHC
 - S100, inhibin, D240
- Associated with Von Hippel Lindau syndrome

Case 10

- 50F
- Headache & papilloedema
- CT & MRI – 3rd ventricle cyst

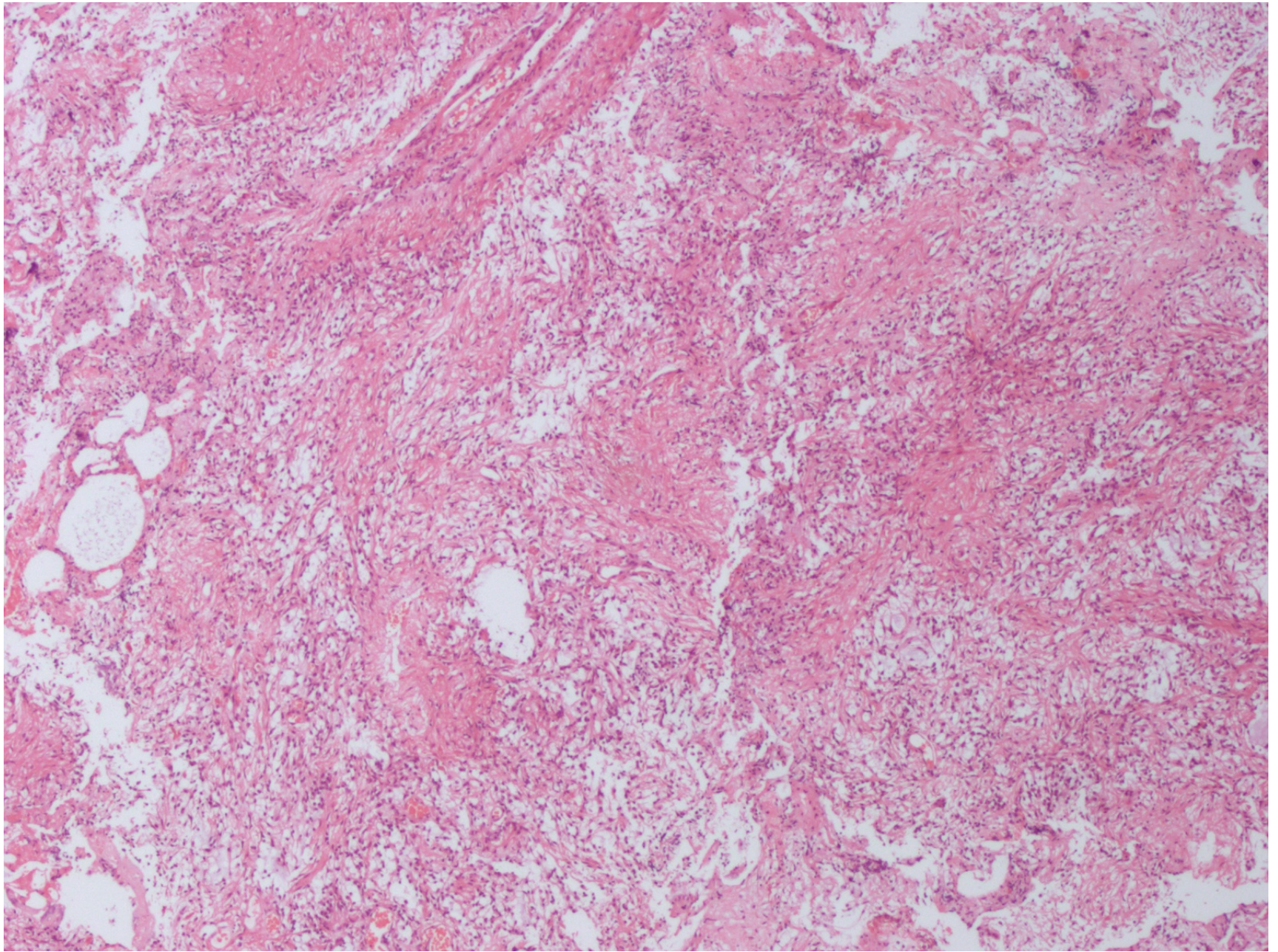


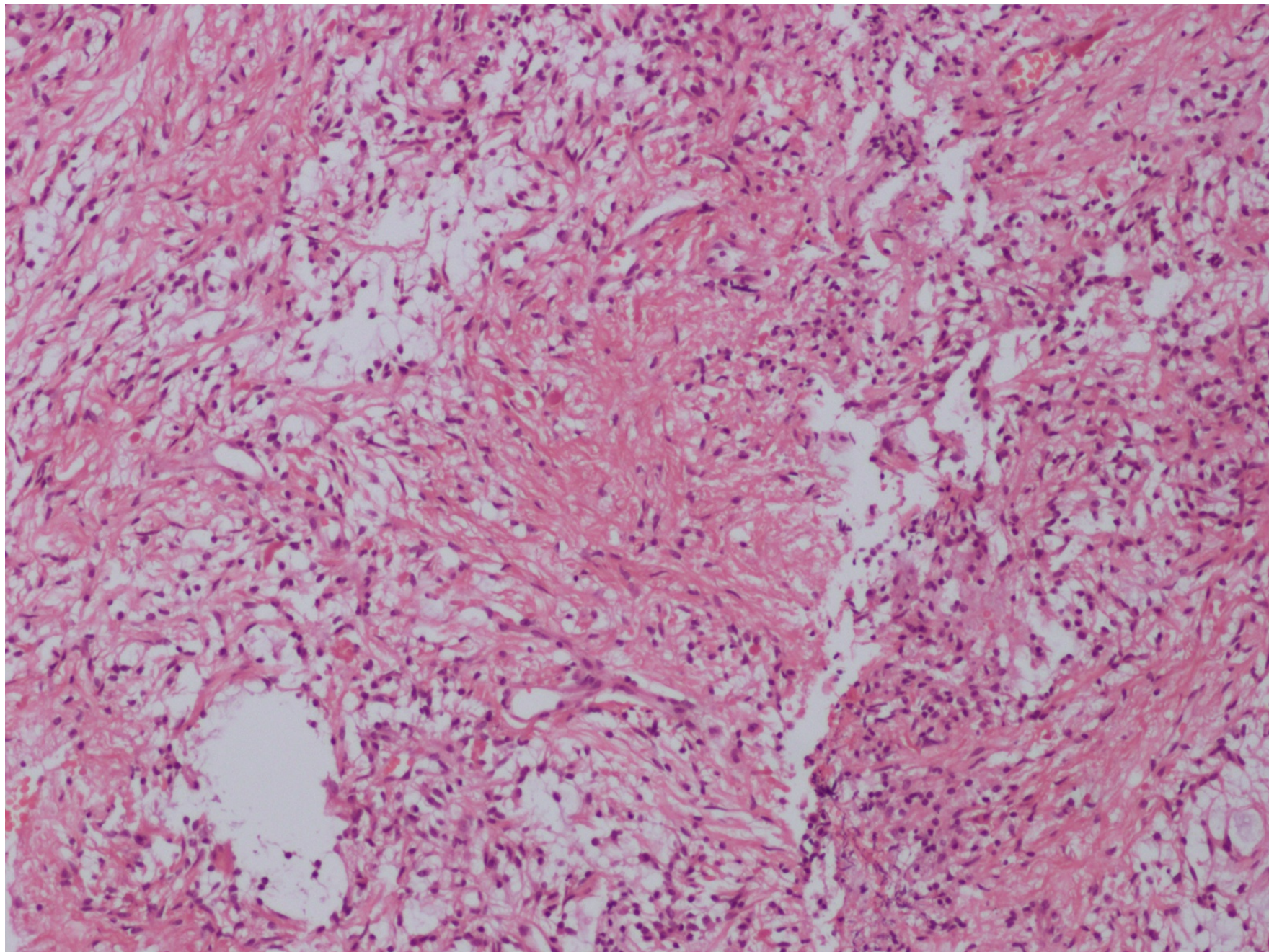


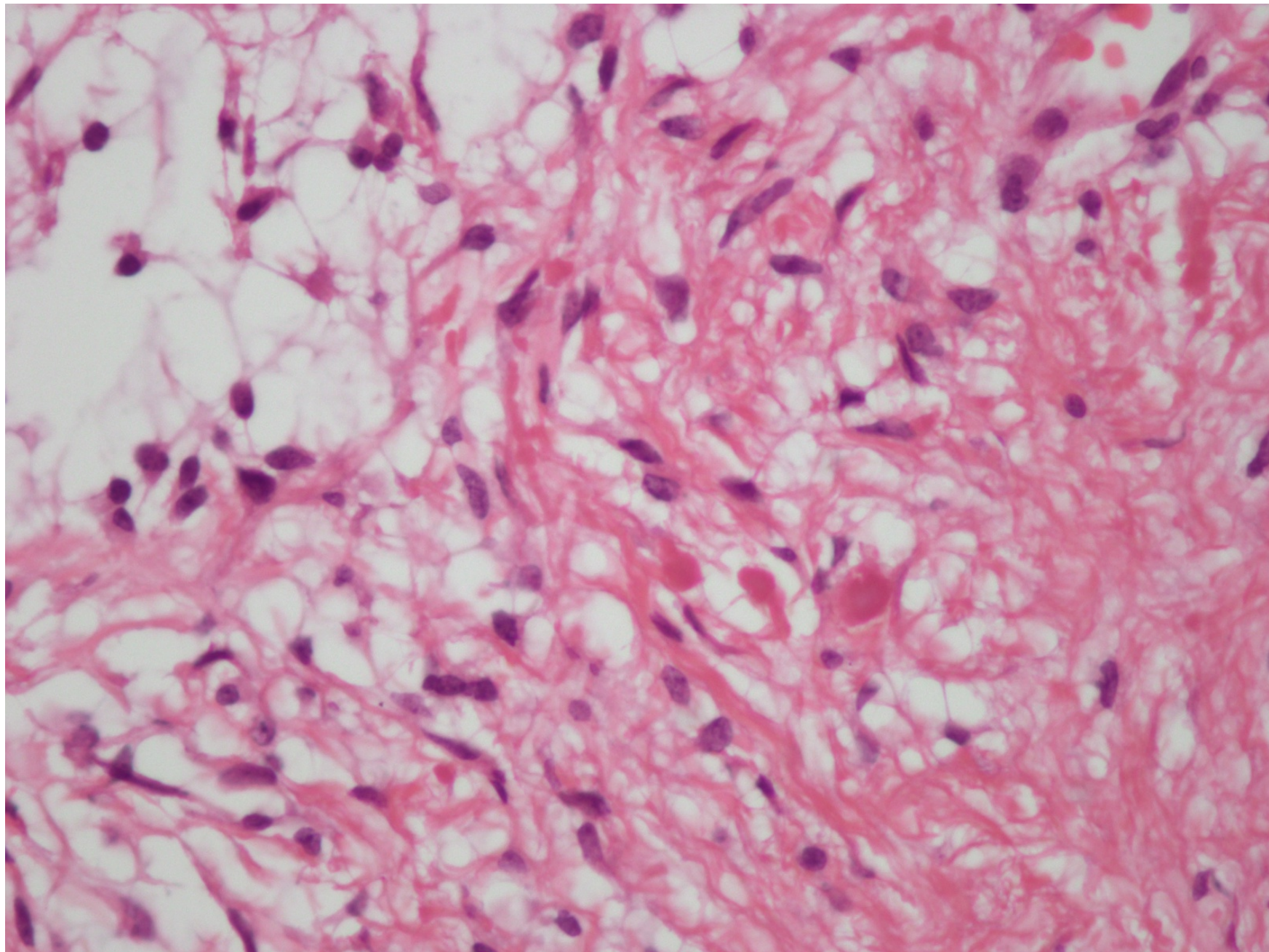
- Subependymoma (WHO Grade 1)
- IHC
 - GFAP
 - Mib-1

Case 11

- 5F
- Suprasellar tumour



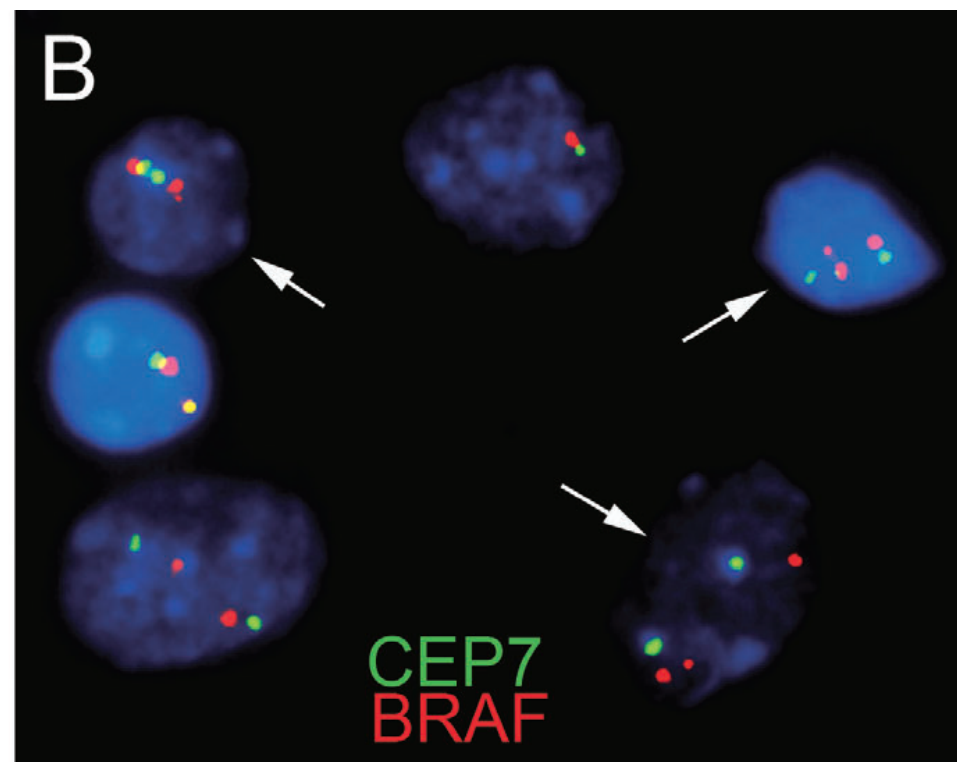
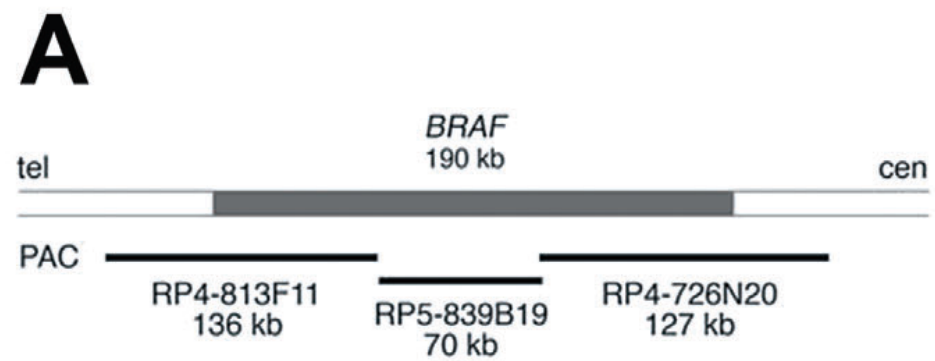




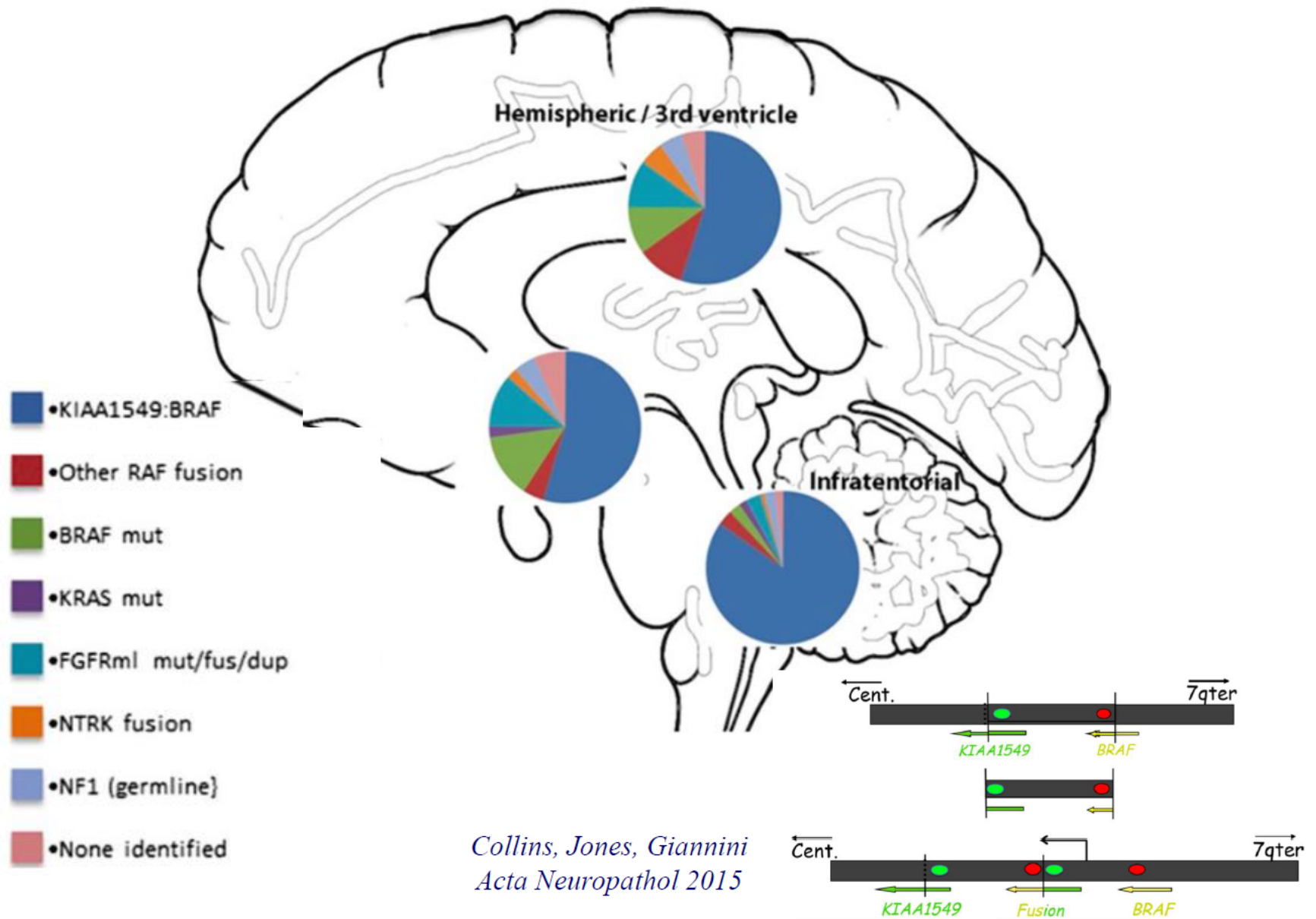
- Pilocytic astrocytoma (WHO grade 1)
- IHC
 - GFAP
 - Mib-1

Molecular

- BRAF-KIAA fusion (FISH) ~2/3

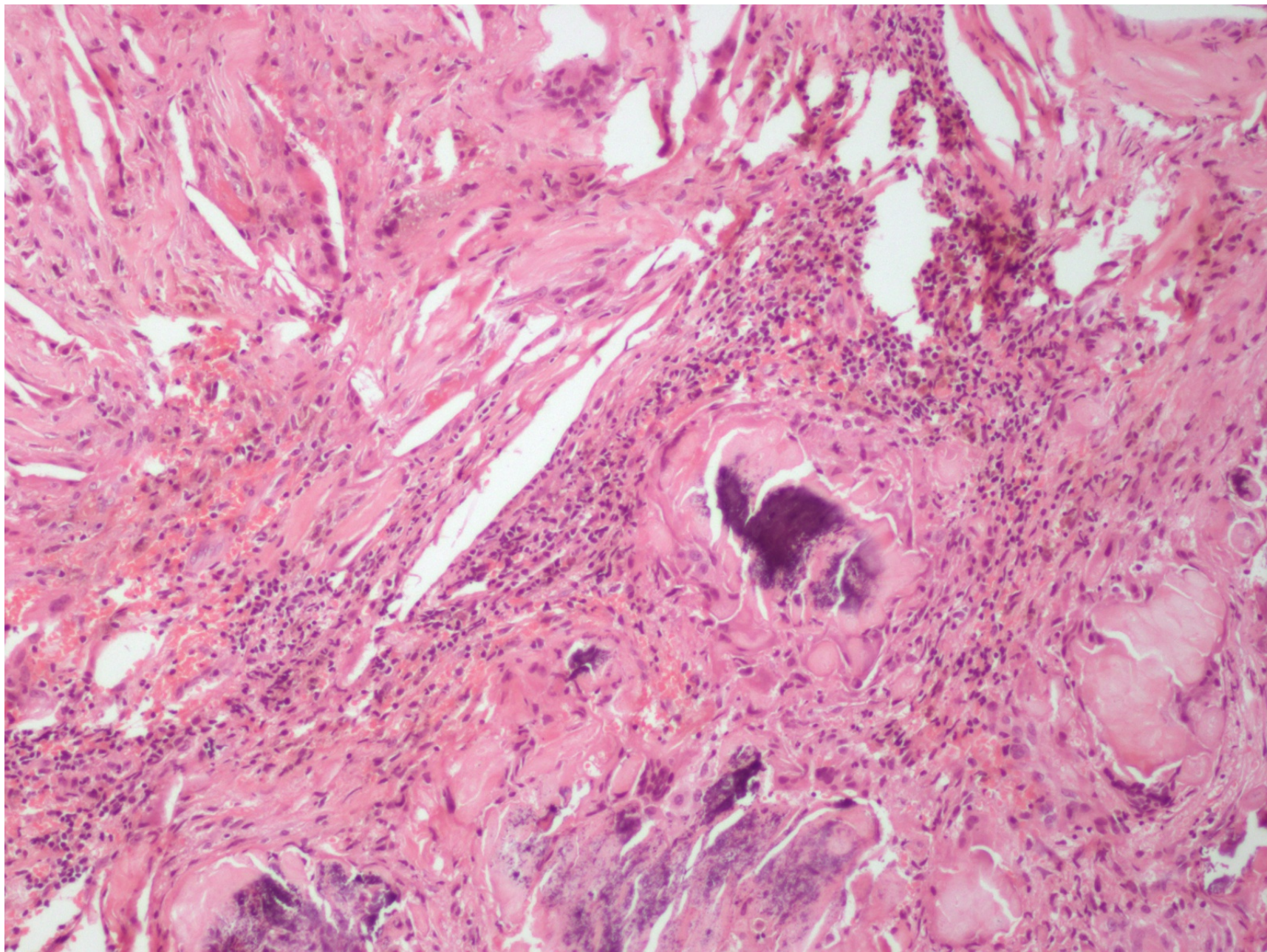


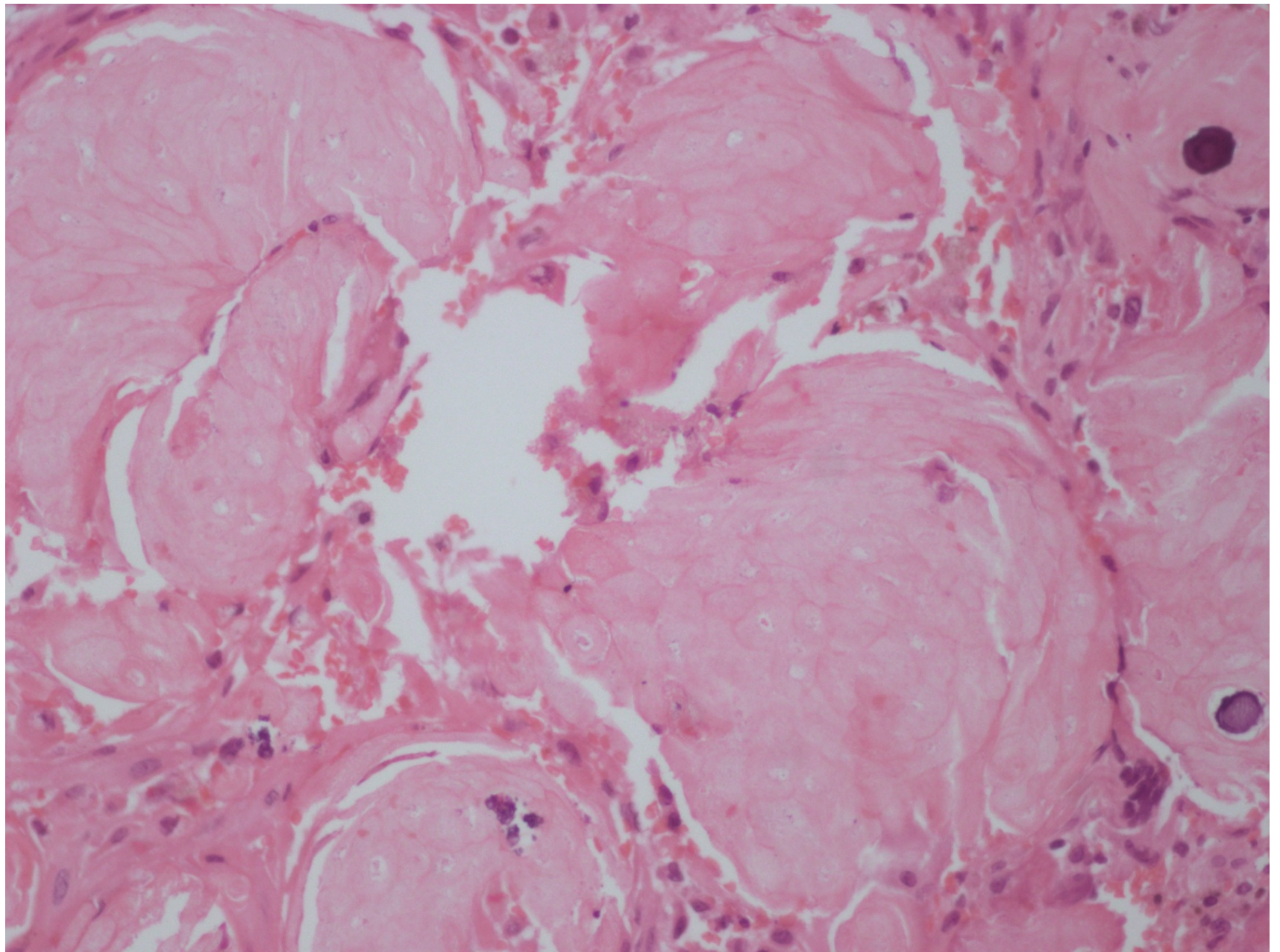
Pilocytic astrocytoma

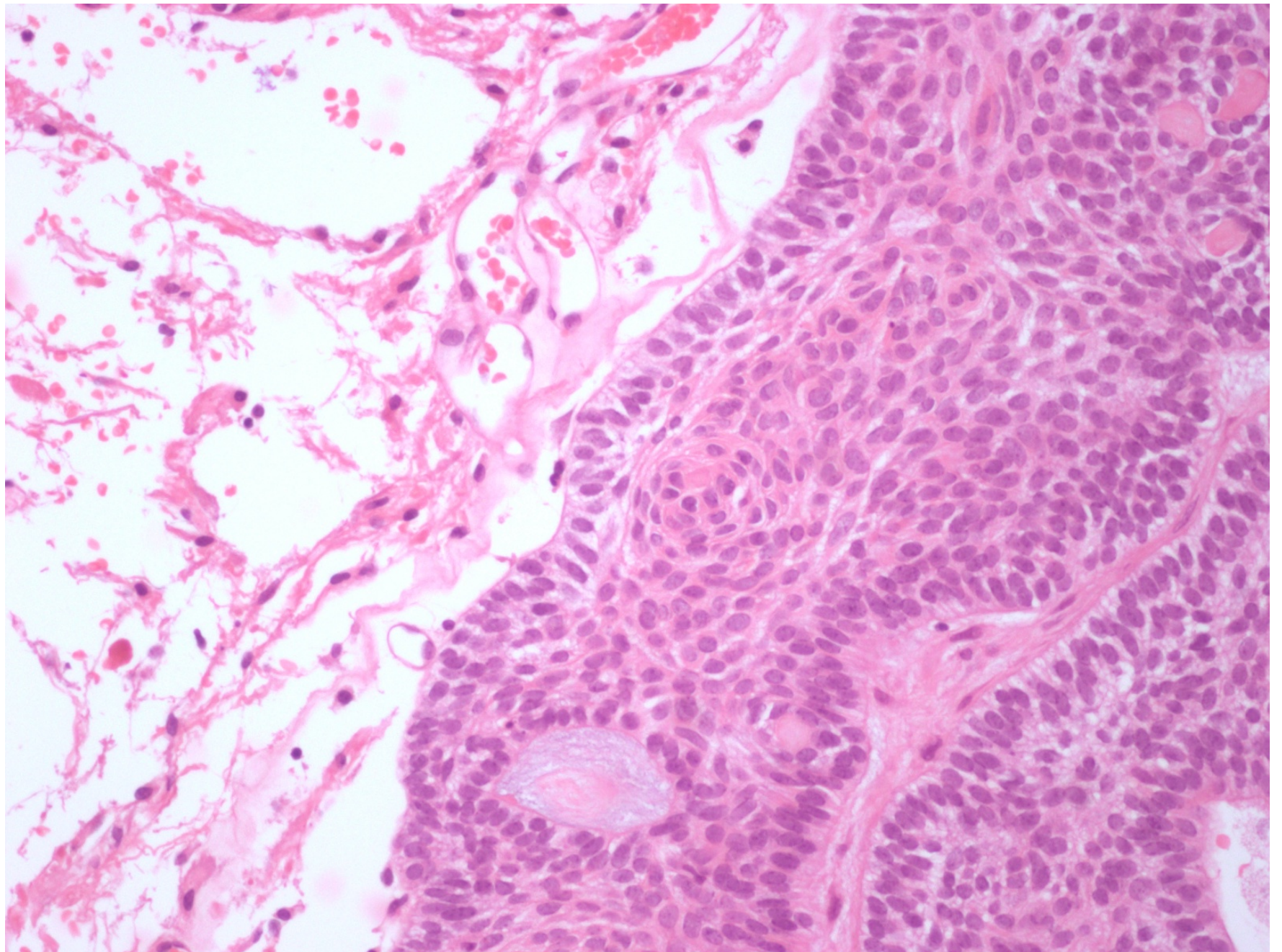


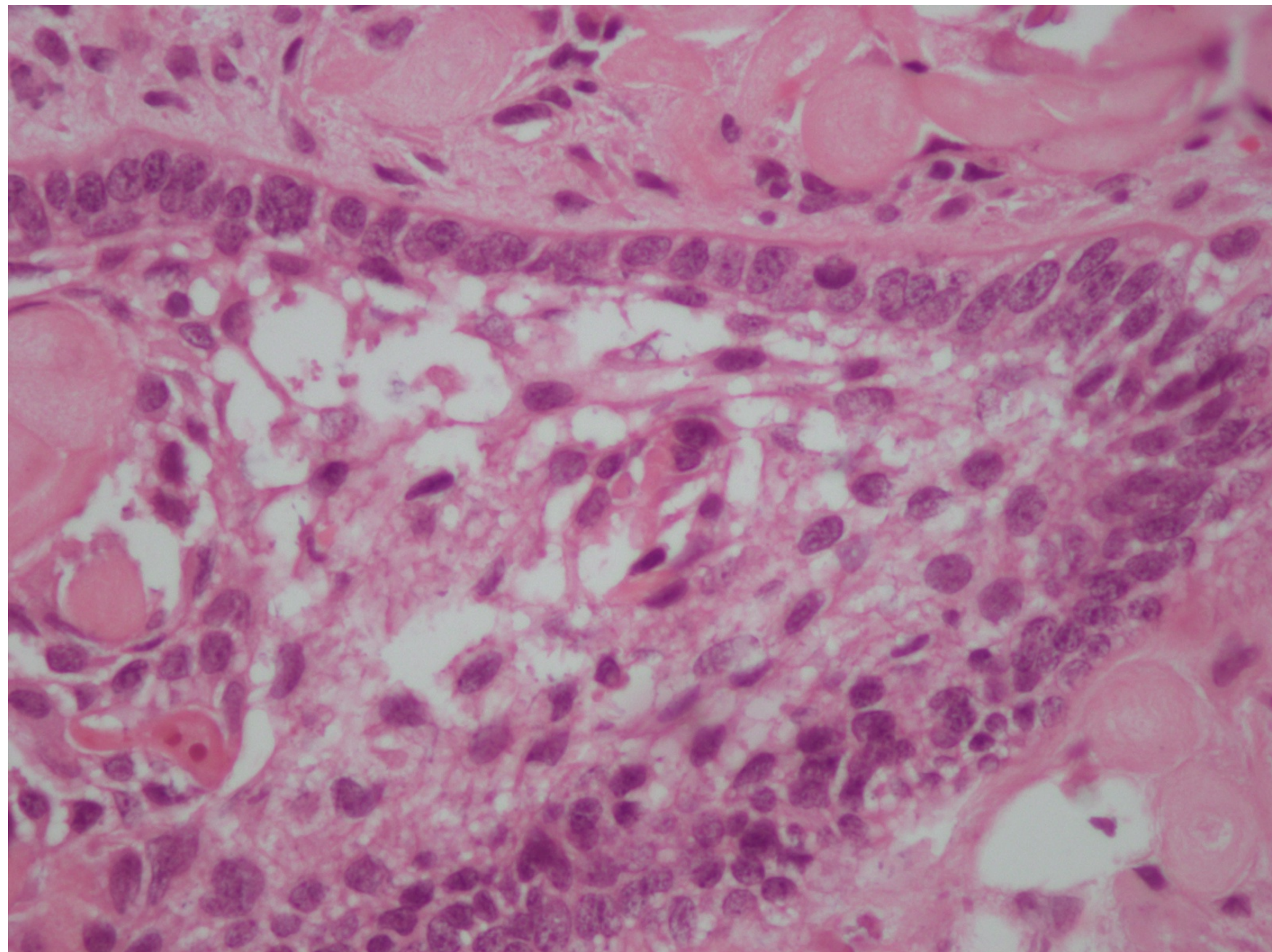
Case 12

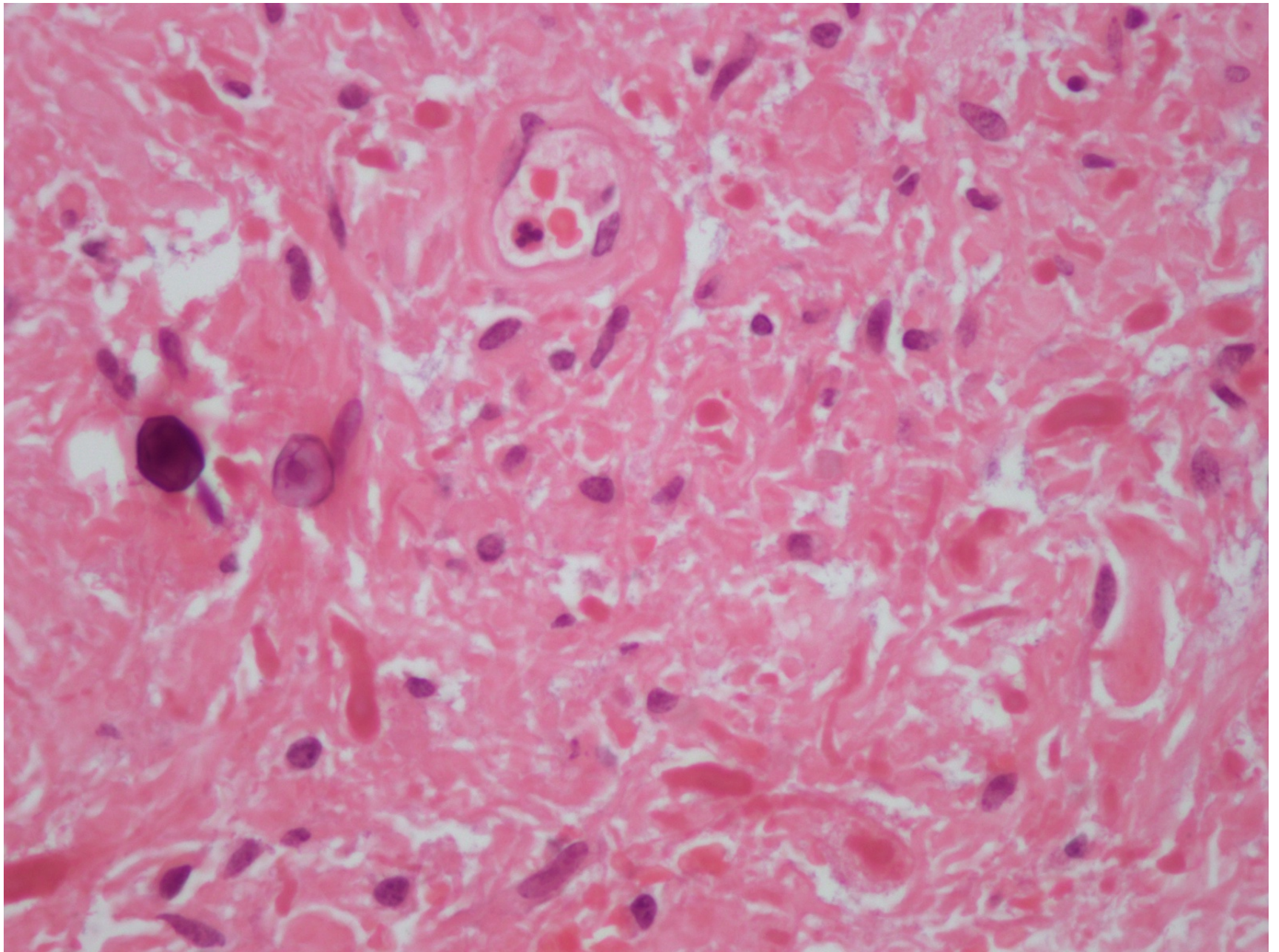
- ^{18}F
- Suprasellar biopsies







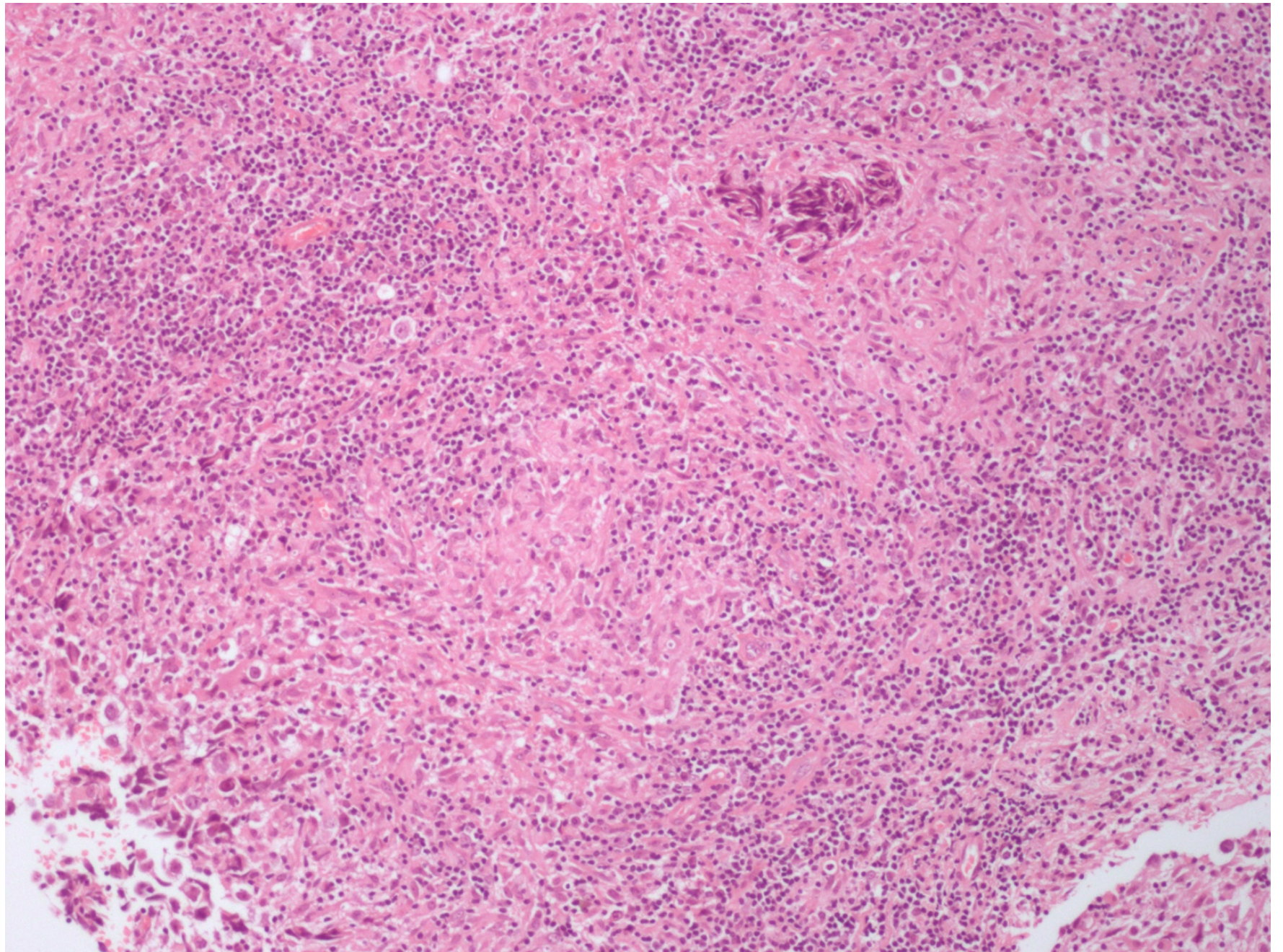


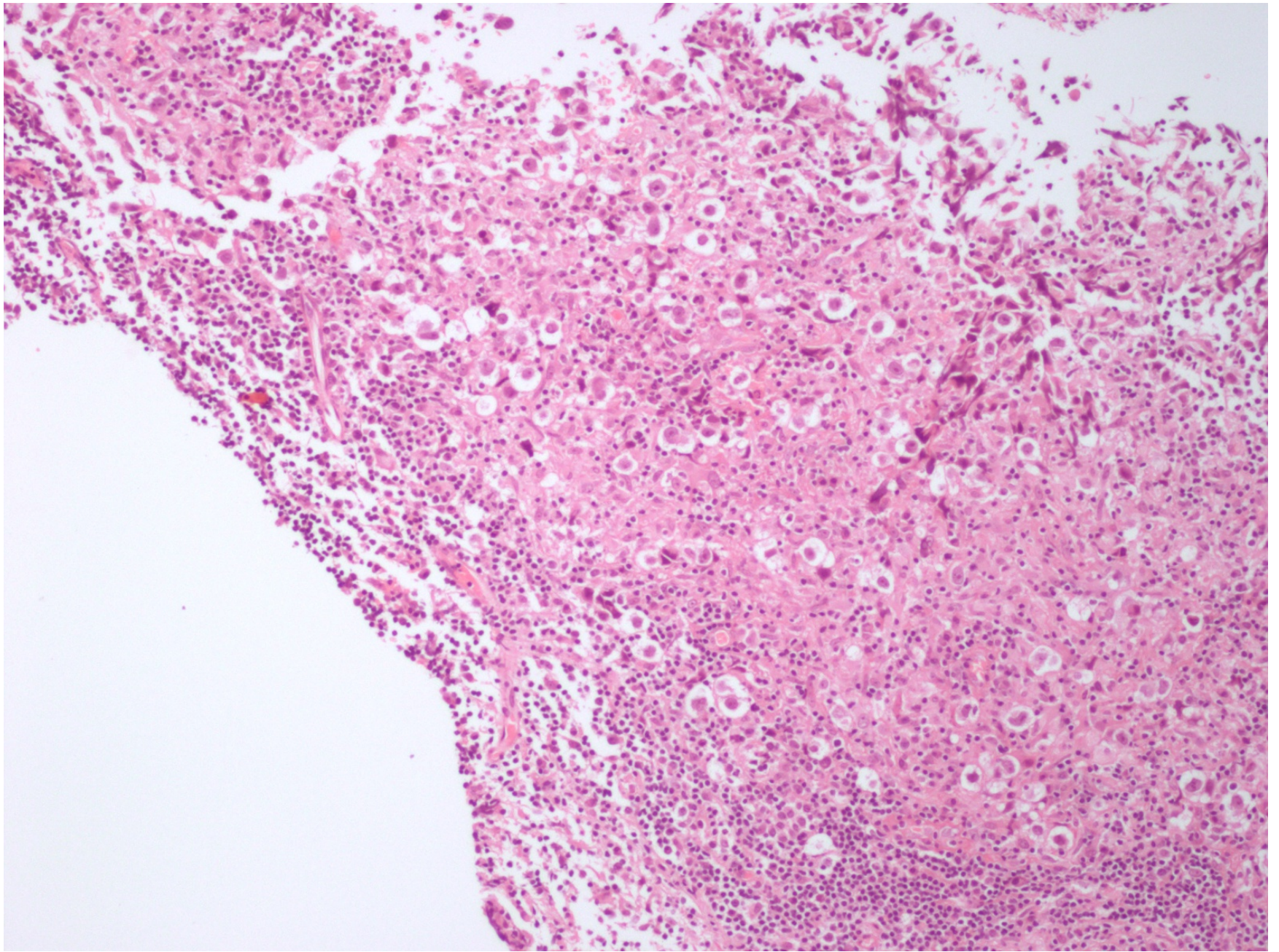


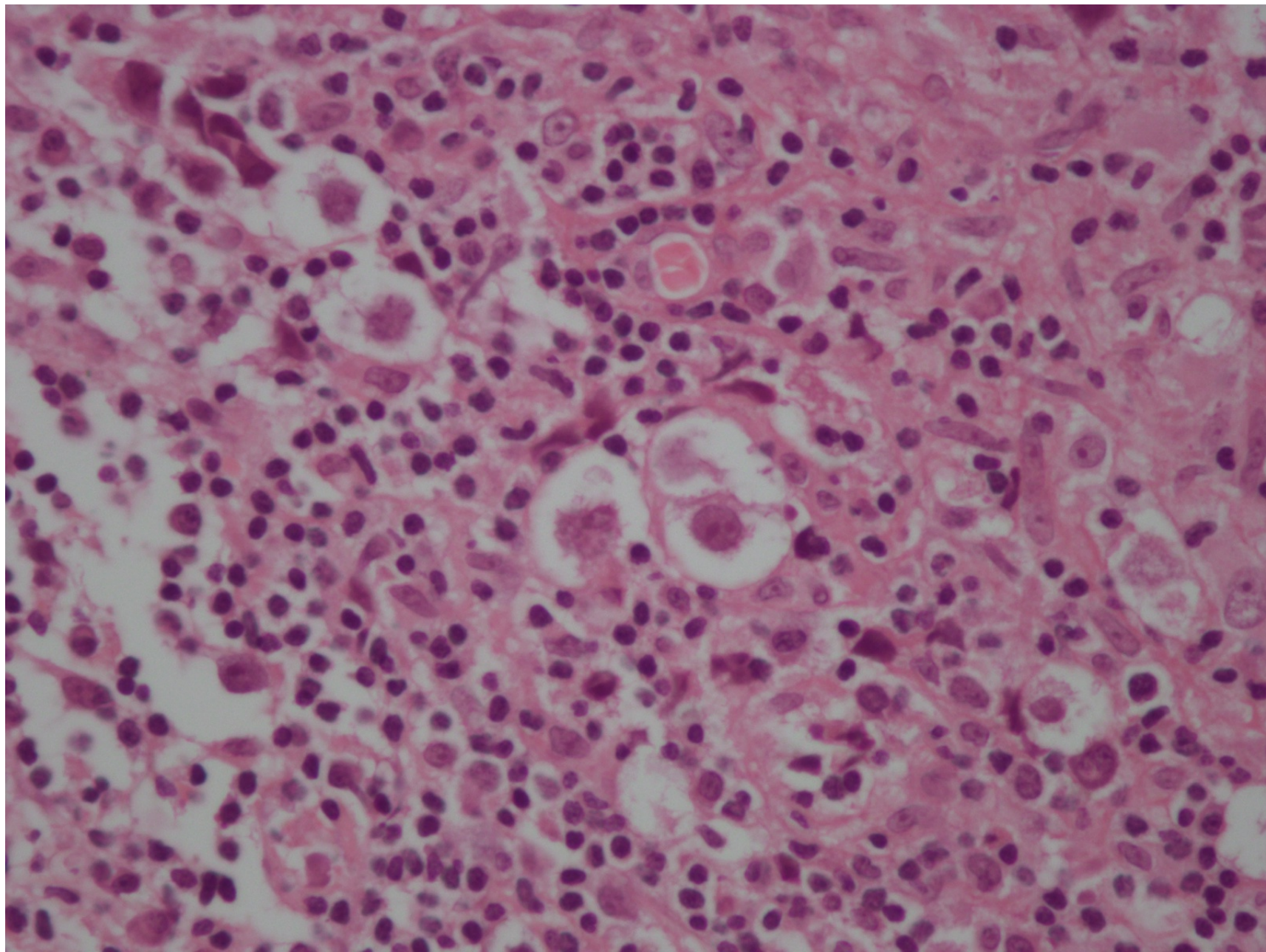
- Adamantinomatous craniopharyngioma (WHO grade 1)

Case 13

- 18M
- Pineal gland biopsy



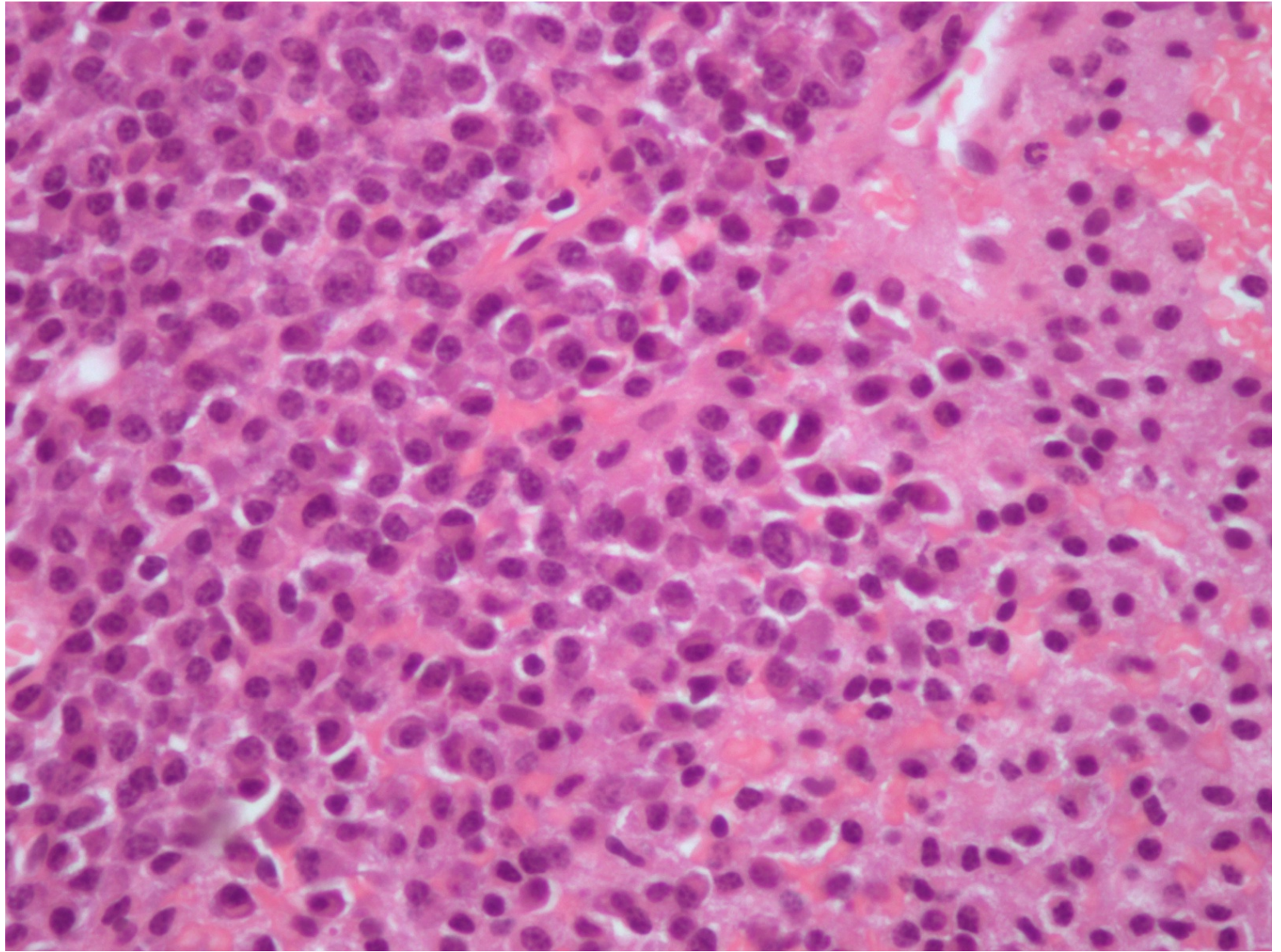




- Germinoma
- IHC
 - PLAP, OCT3/4, CD117
 - AFP, bHCG, CD30
- Correlate with plasma and CSF levels

Case 14

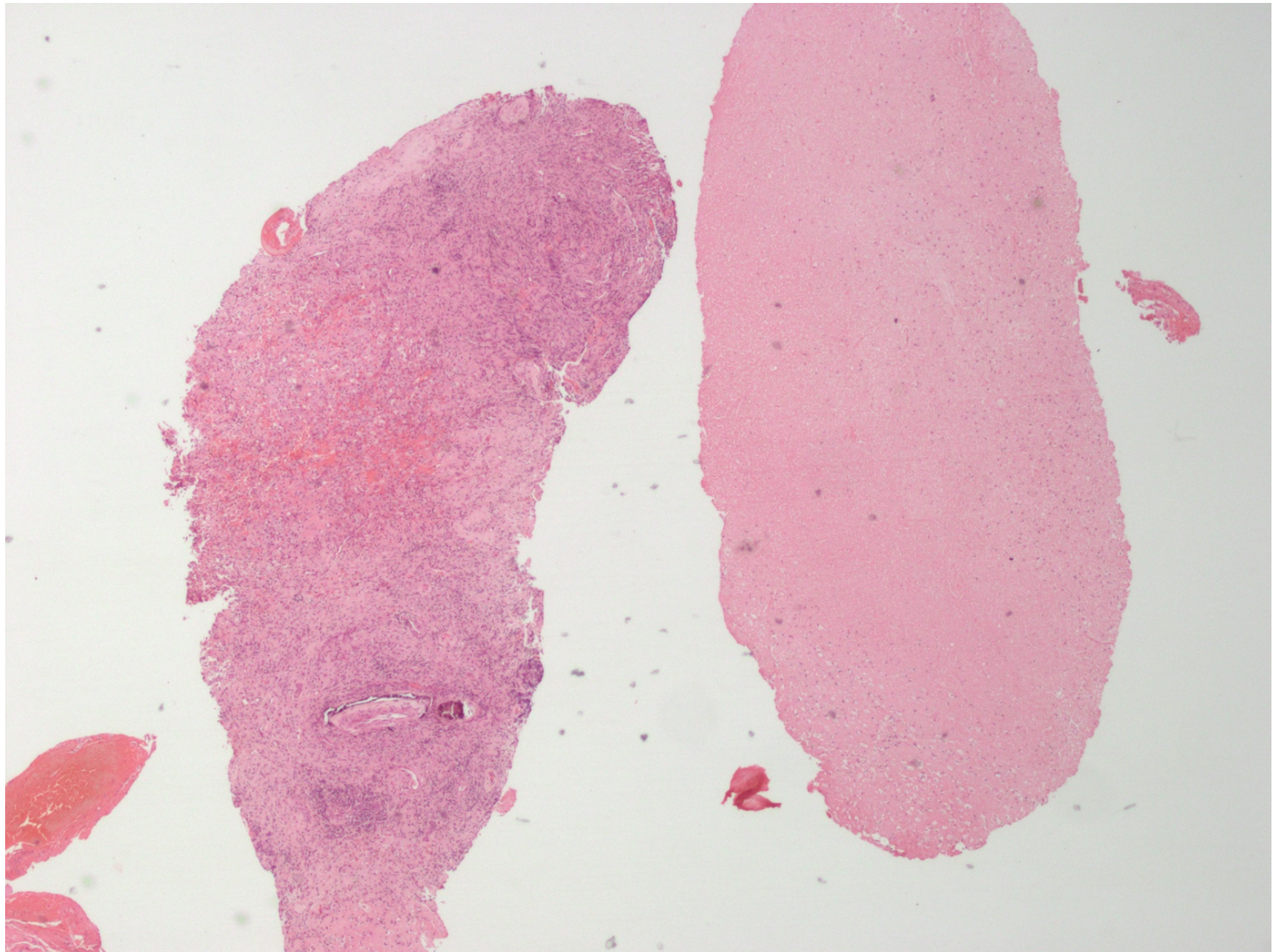
- 50M
- L4 vertebra

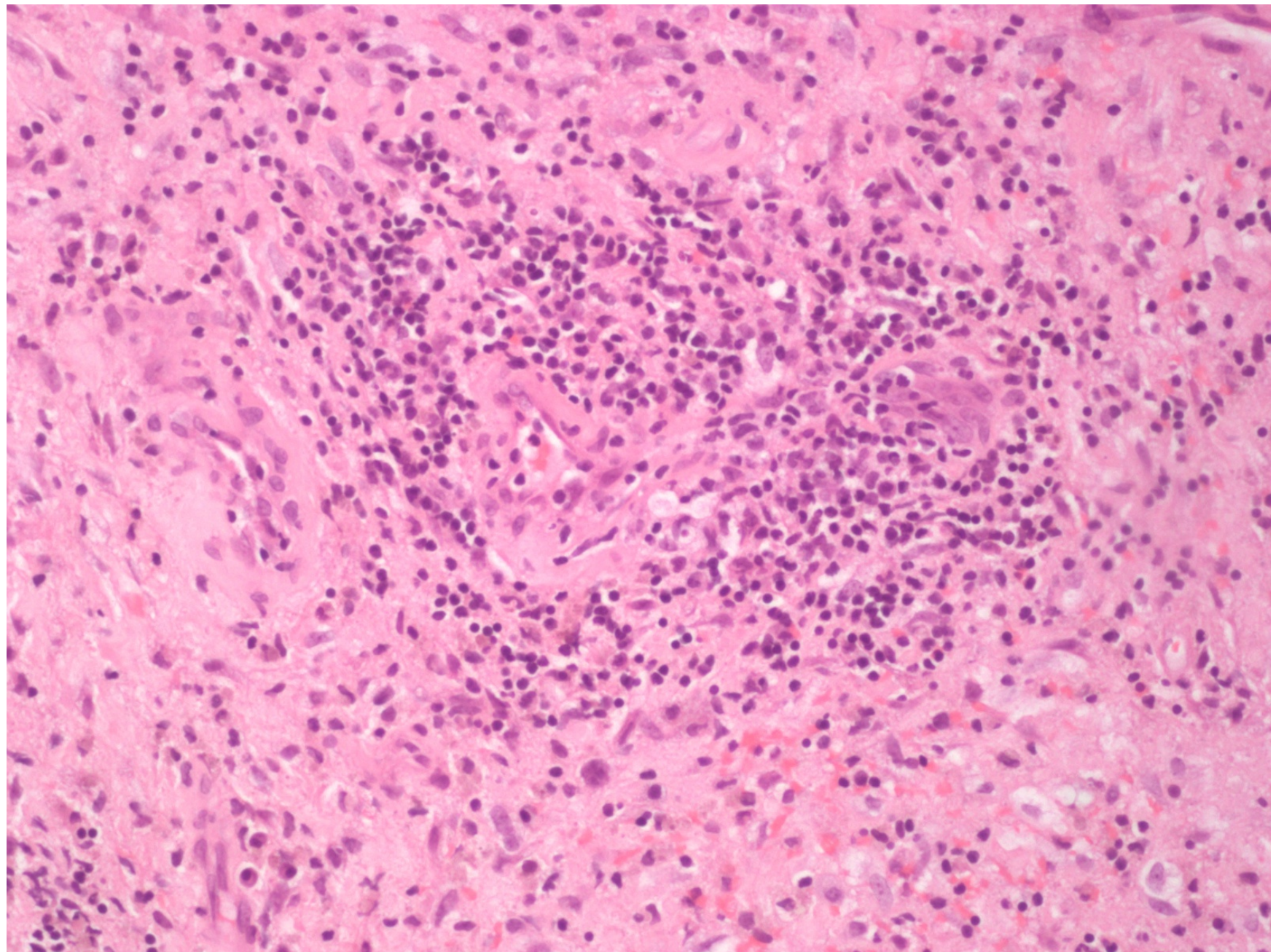


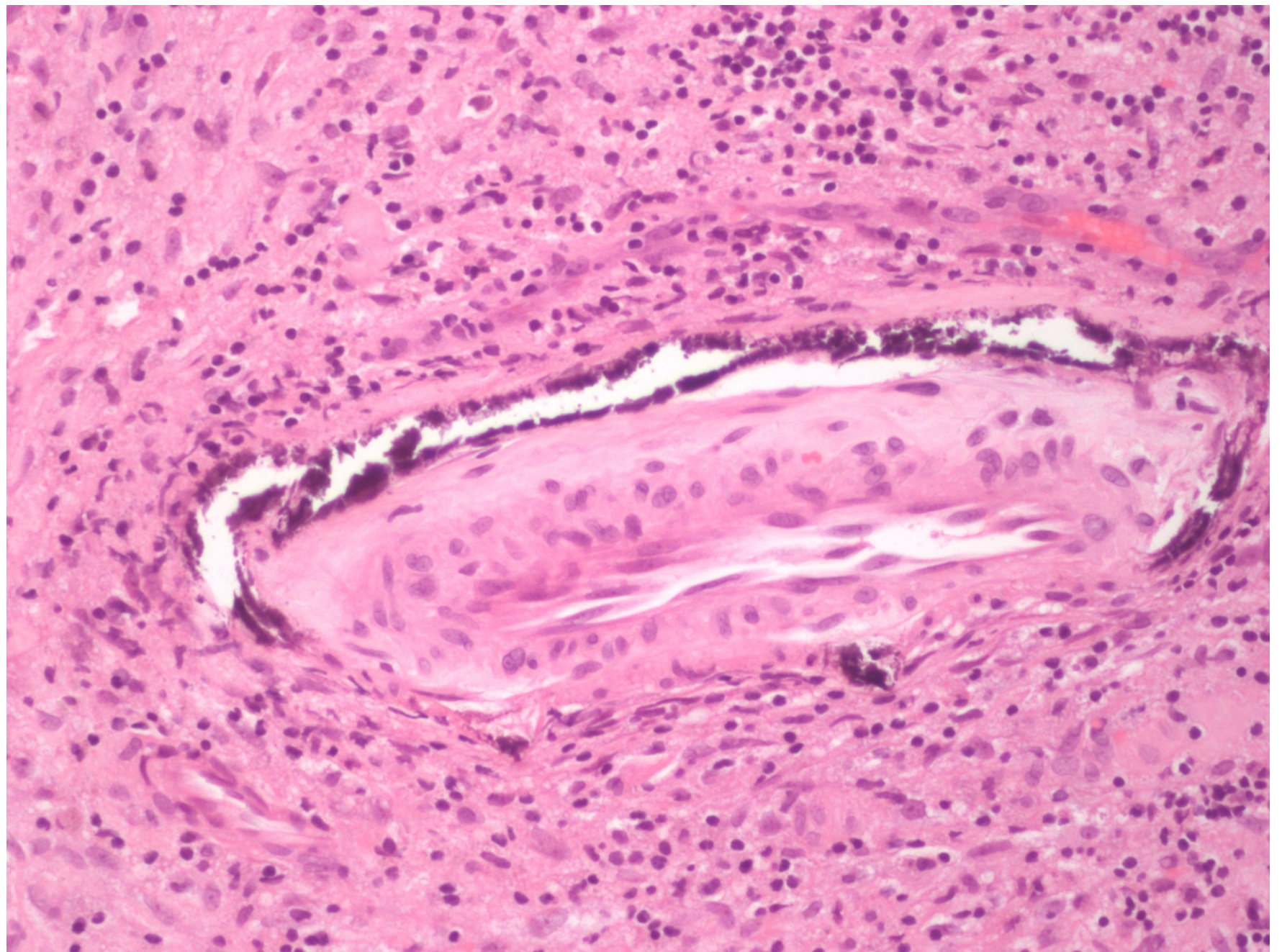
- Plasma cell neoplasm
- IHC
 - CD138
 - CD56
 - Kappa and lambda

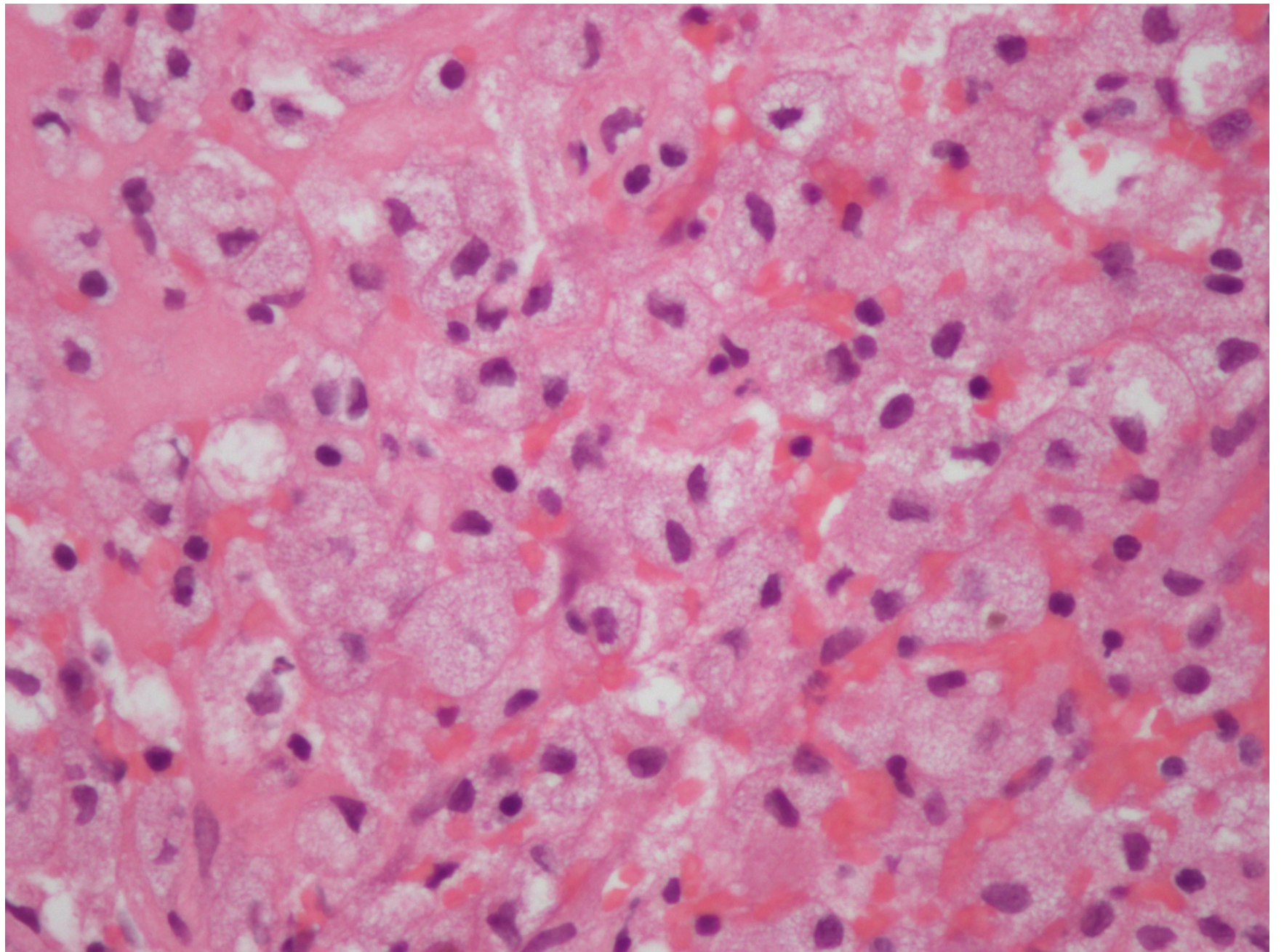
Case 15

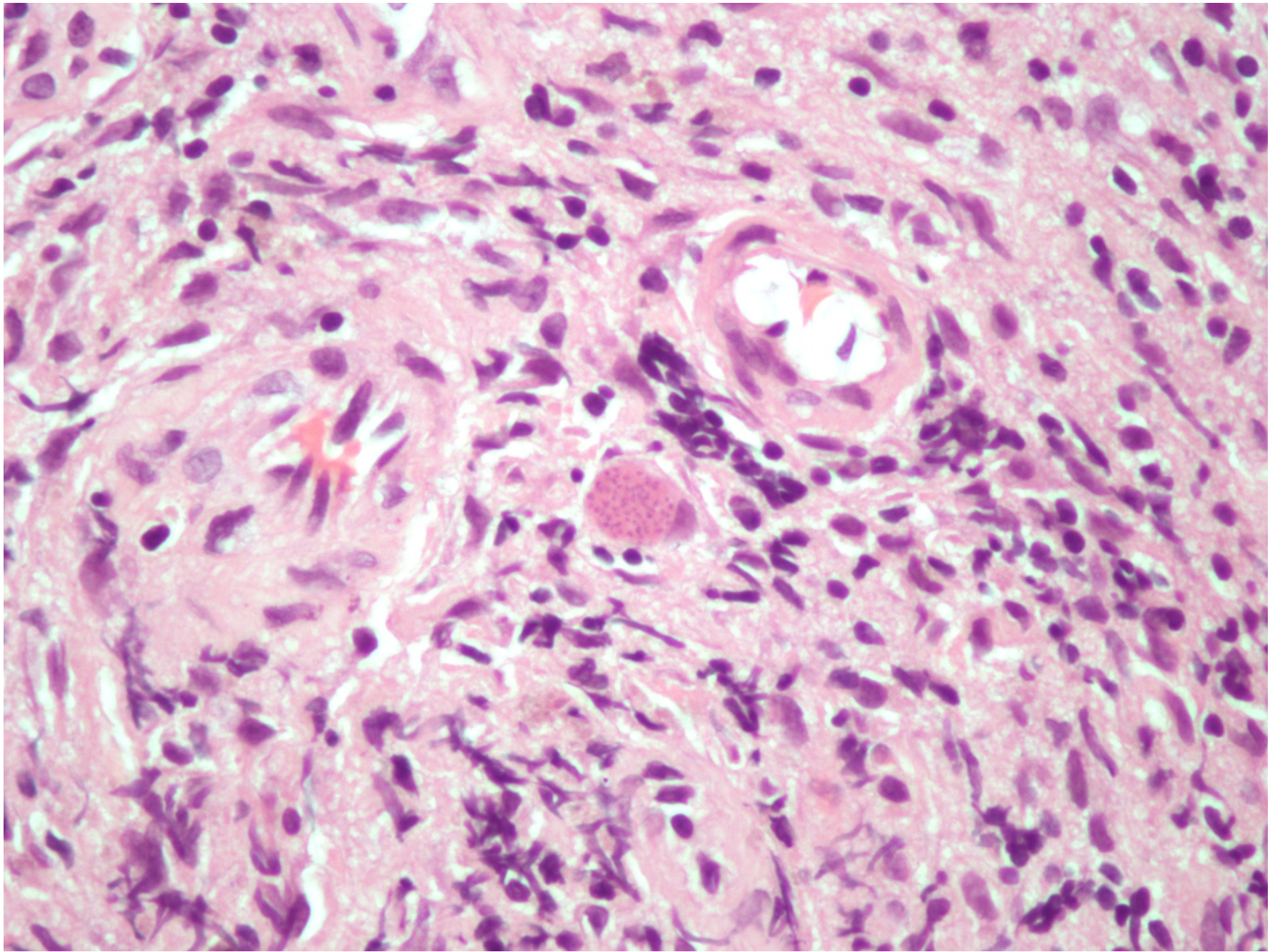
- 34M
- Hep B and HIV positive
- Multiple cerebral SOL











- Toxoplasmosis
- IHC
 - *T. gondii*