UCSF
University of California
San Francisco

DSS 2015 - 8

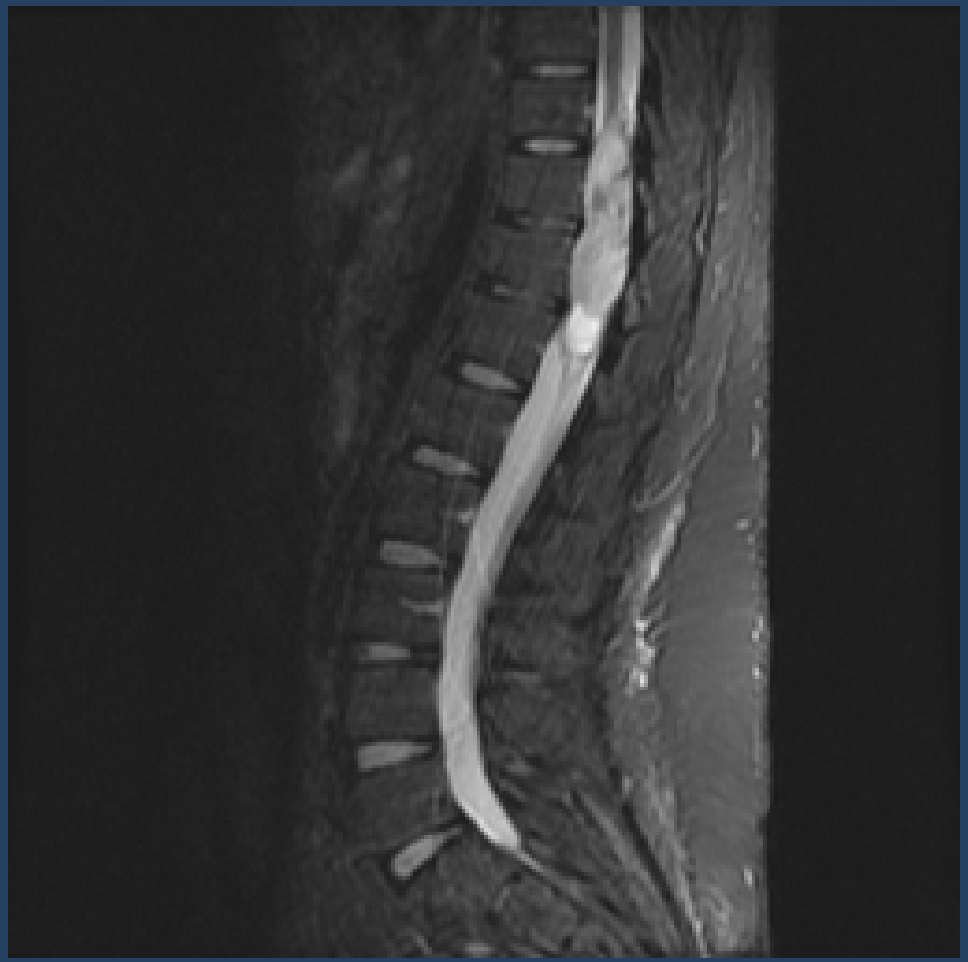
S. Alexandrescu, MD, M. Wood, MD, PhD, A. Bollen, MD, E. Du, MD, A. Perry, MD.

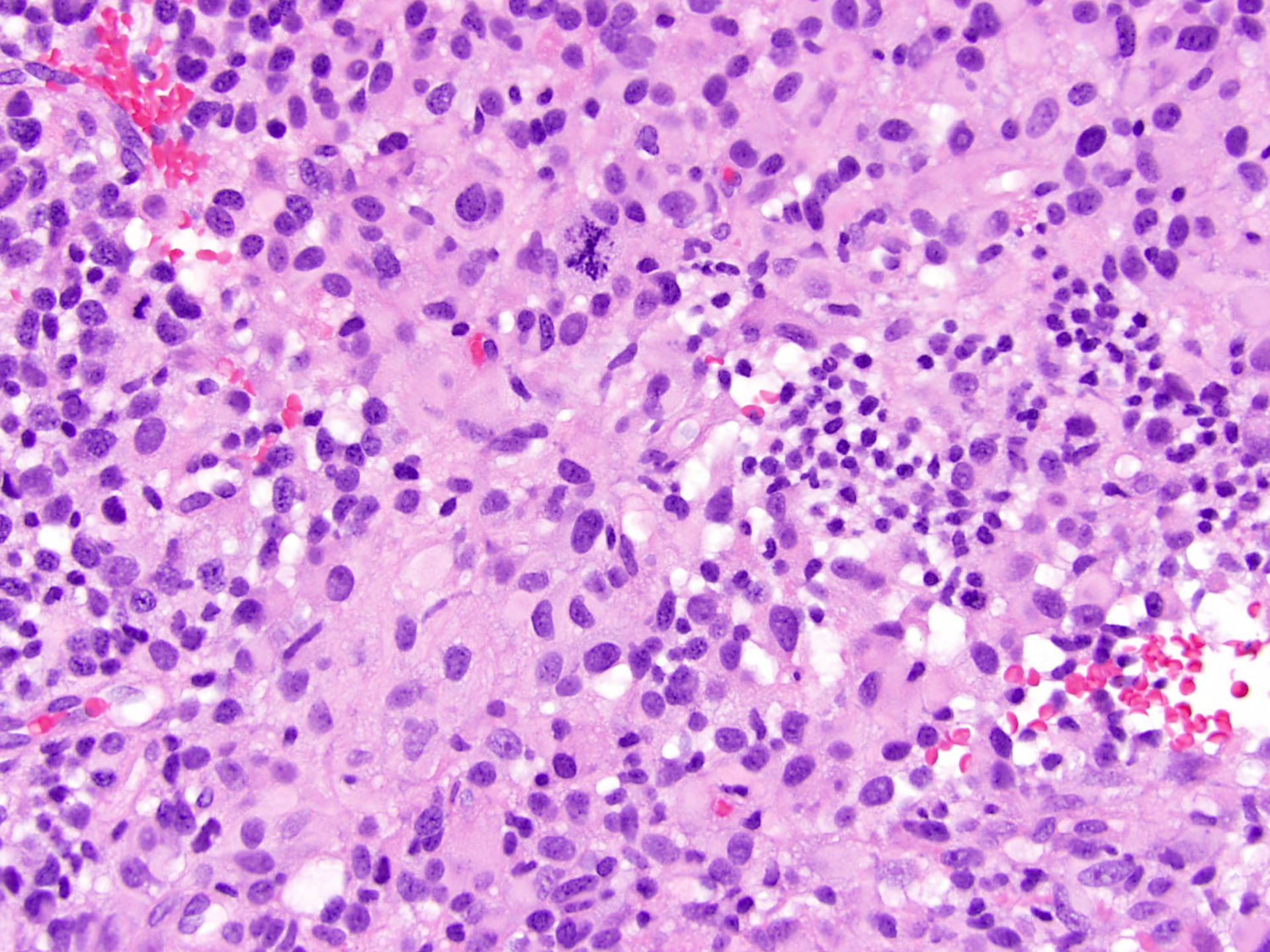
Division of Neuropathology, University of California San Francisco

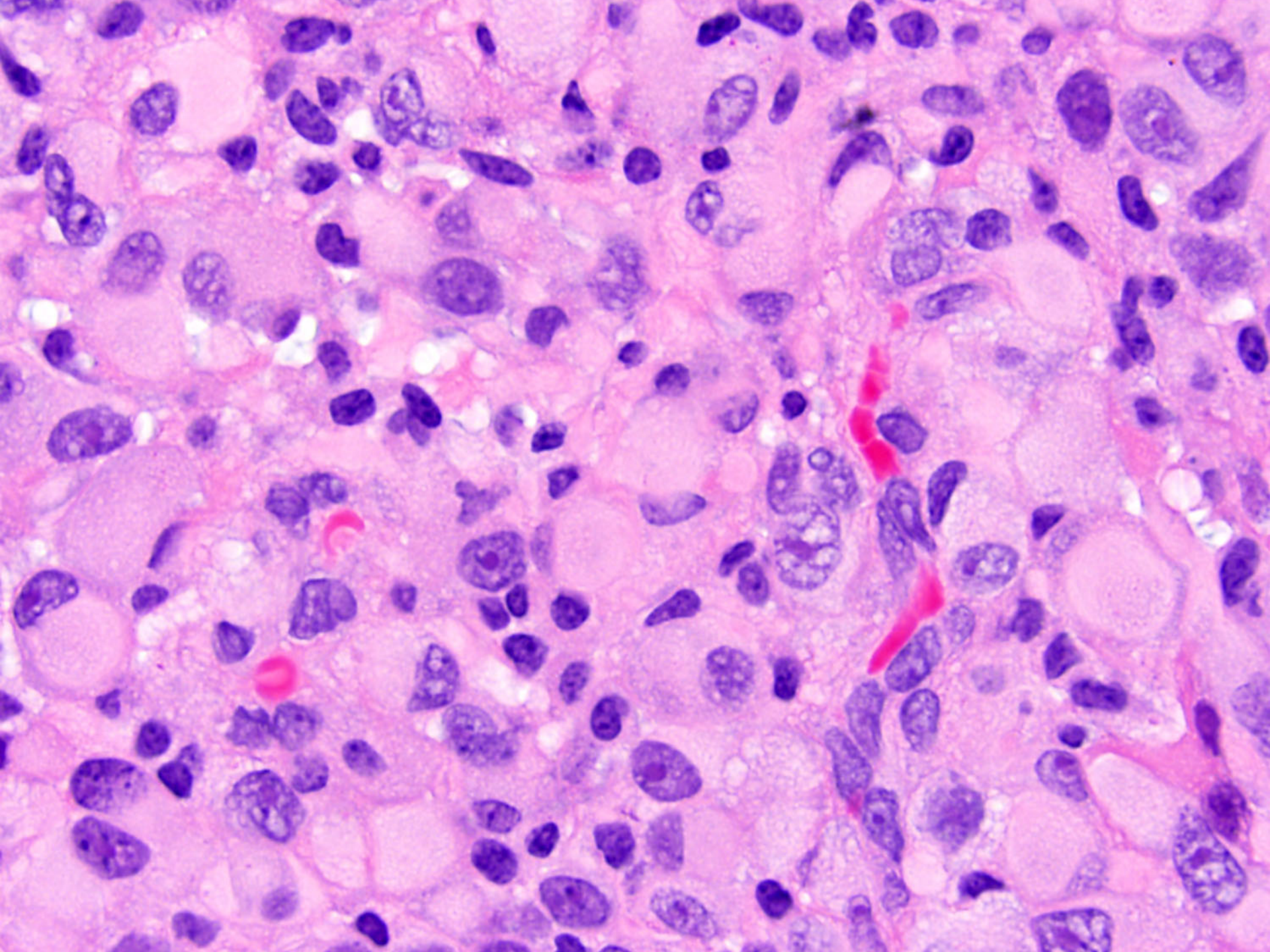
Clinical History

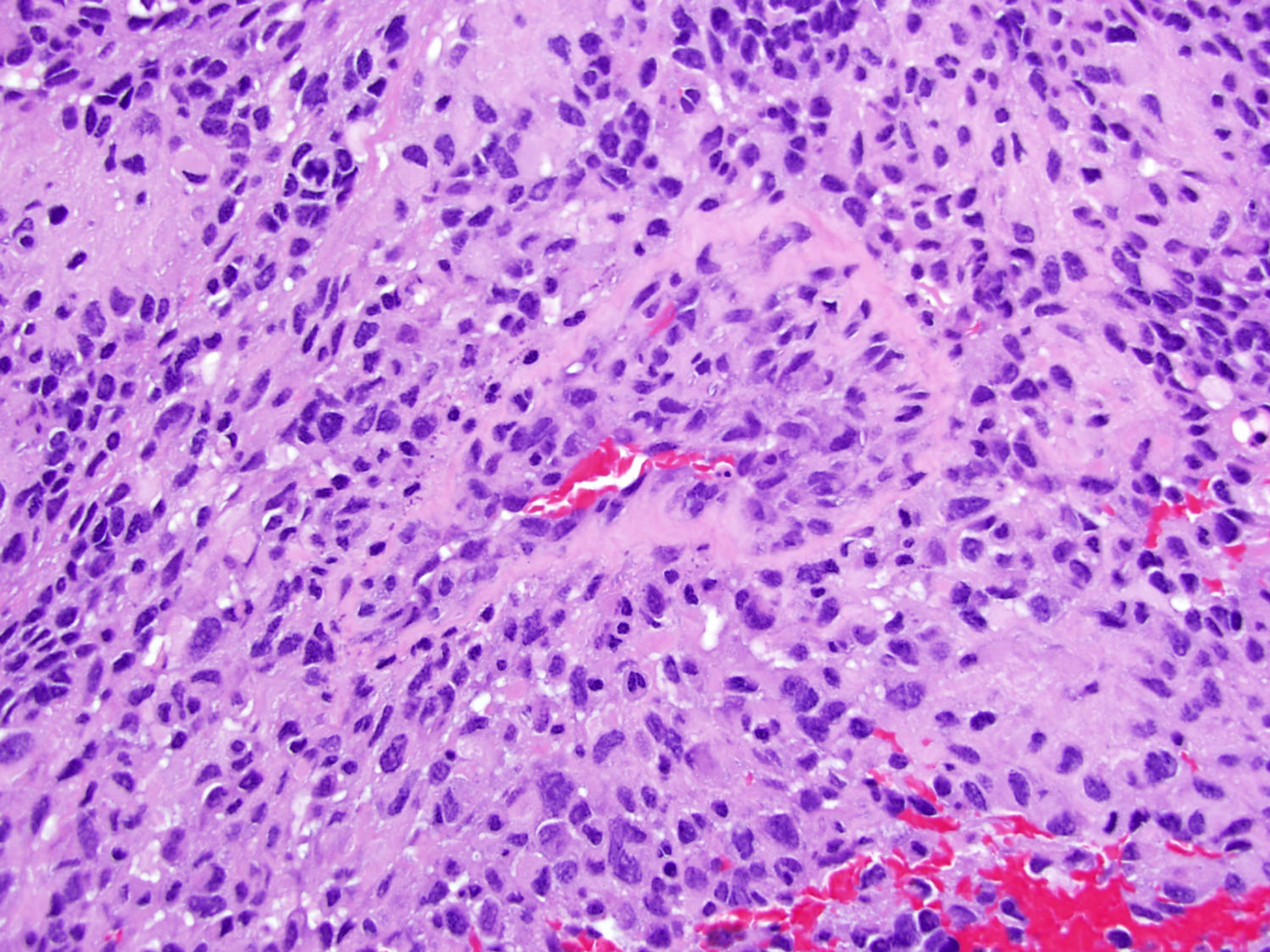
- 26 year-old man with a 10 year history of right leg weakness:
- Three week history of urinary retention

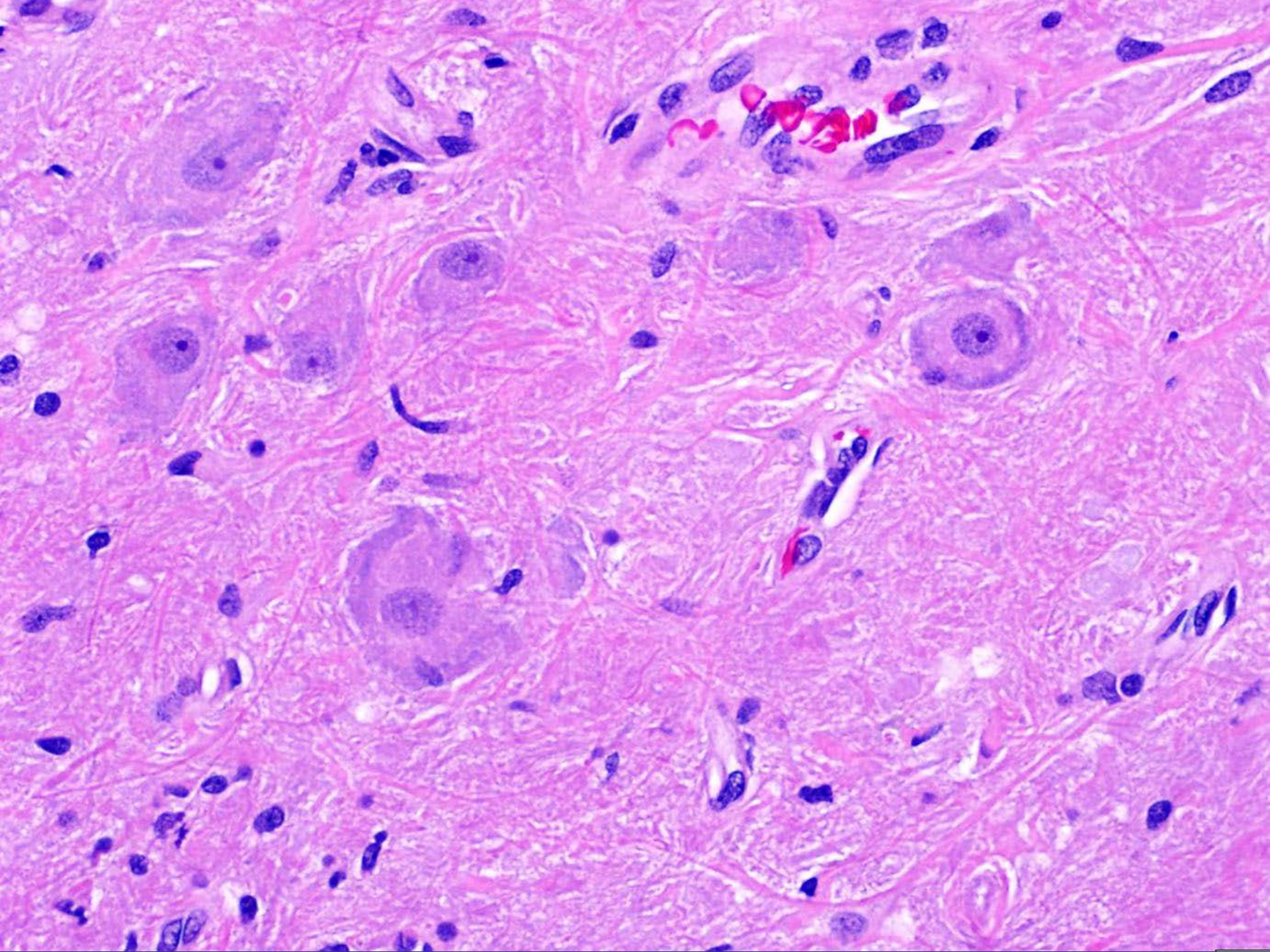
Non-Contrast Magnetic Resonance Imaging

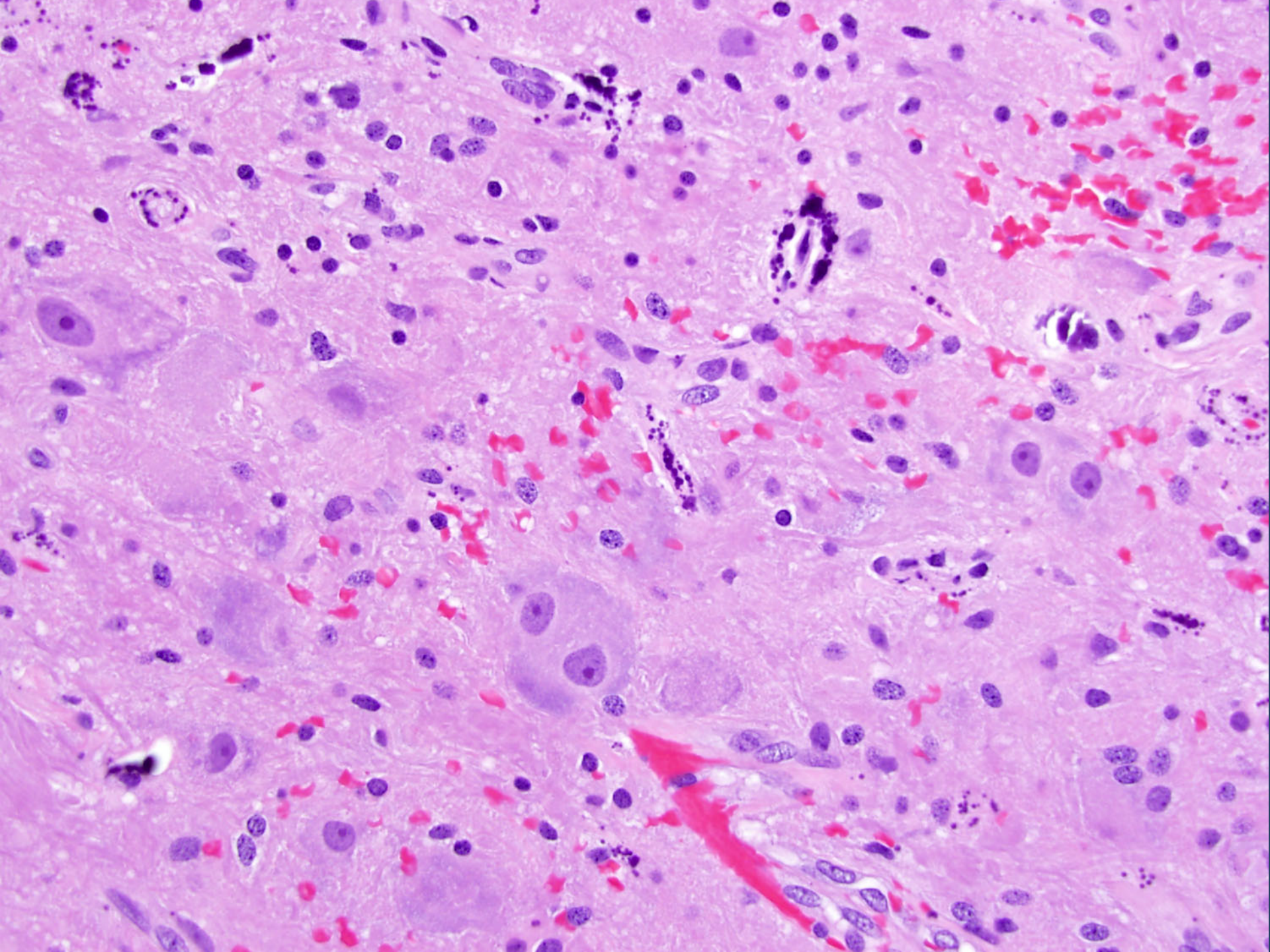


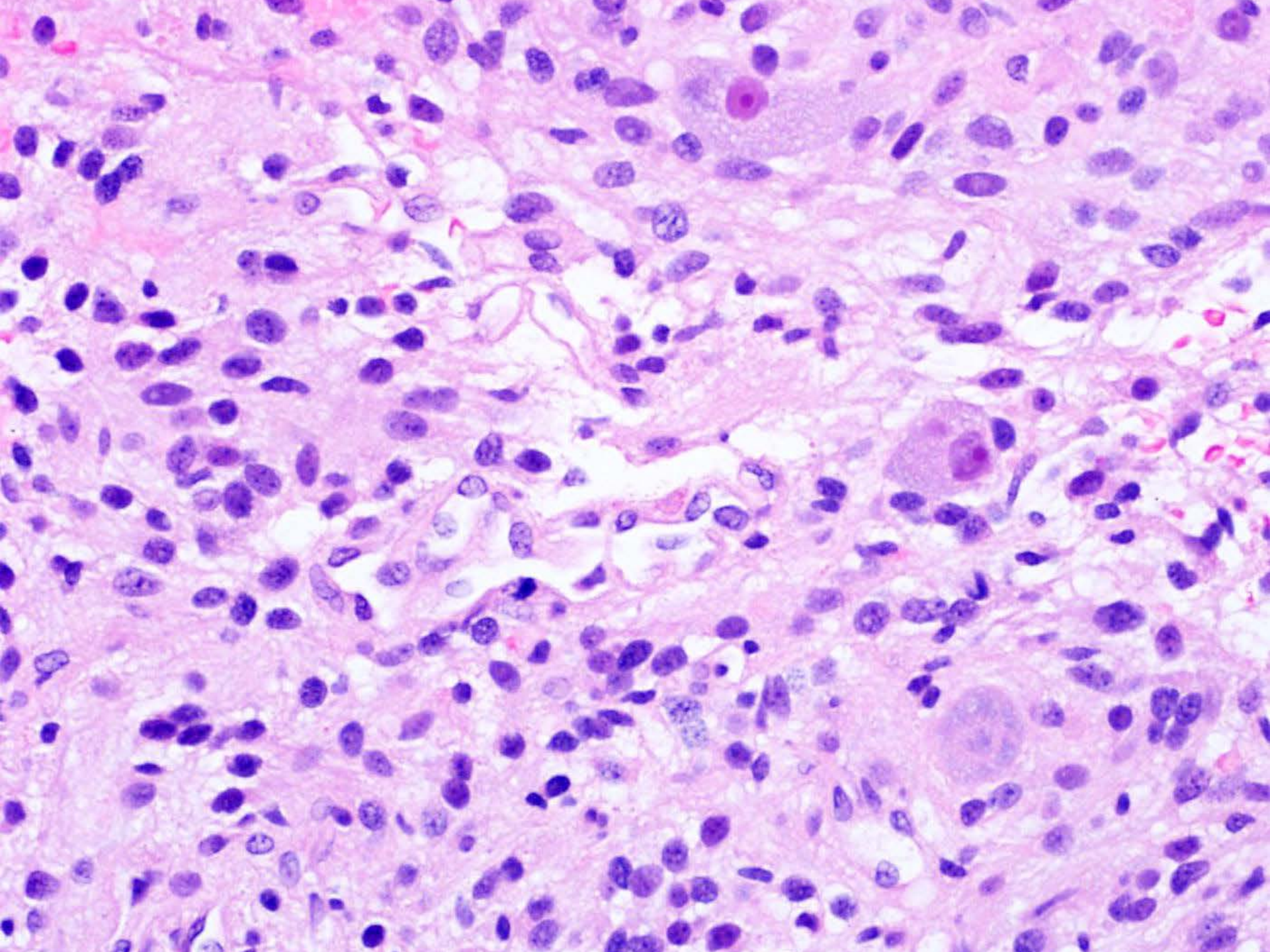








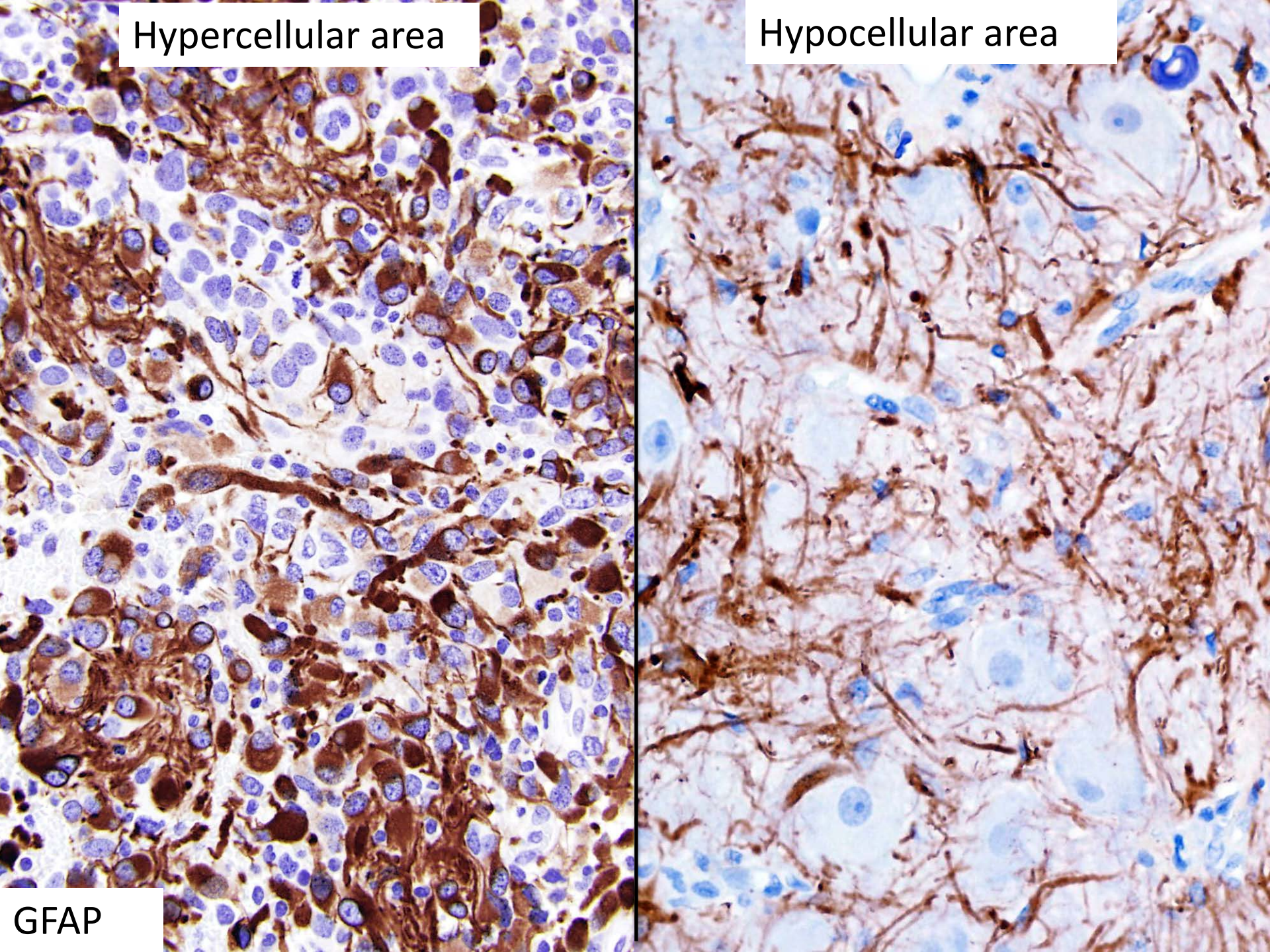


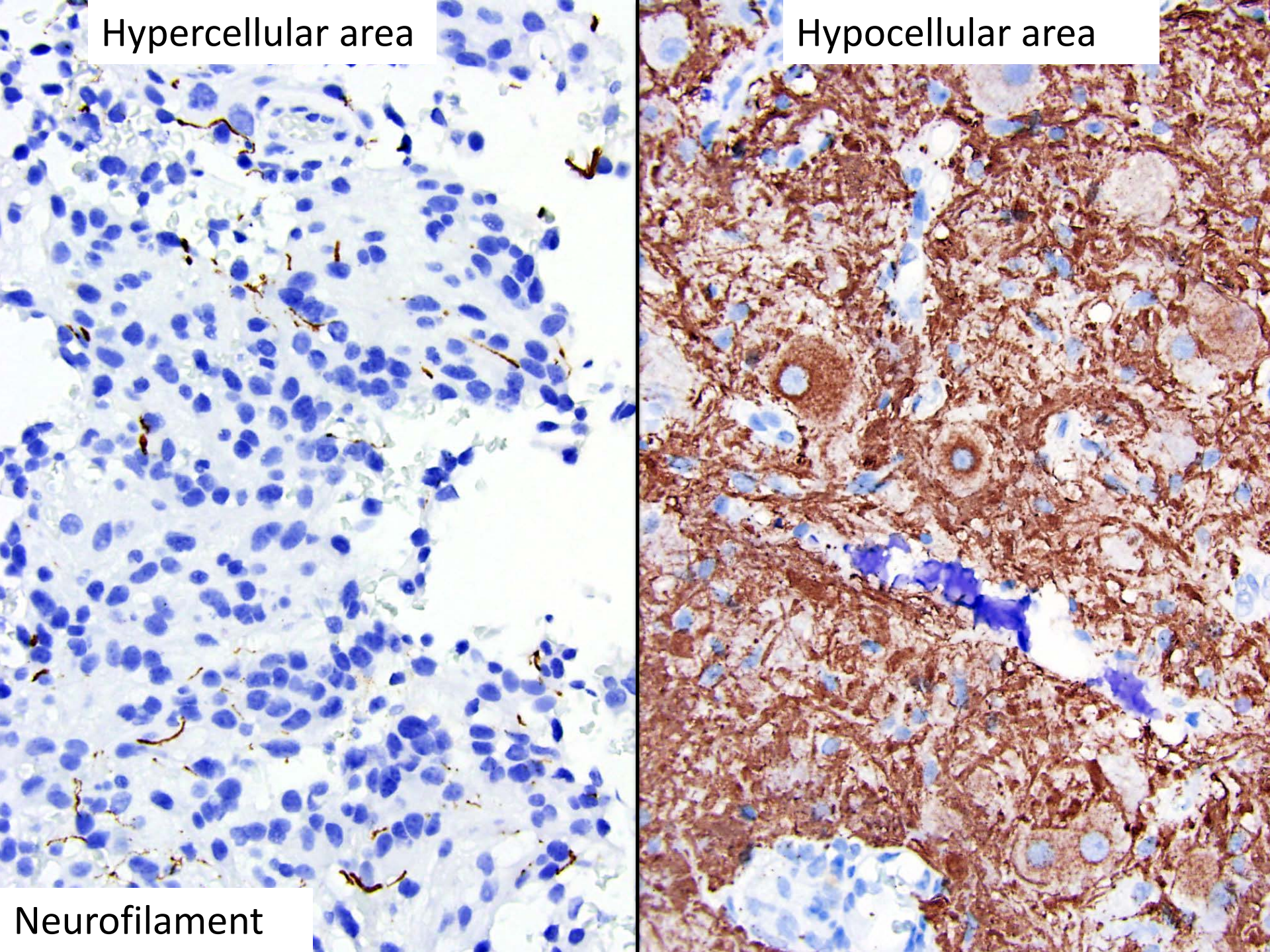


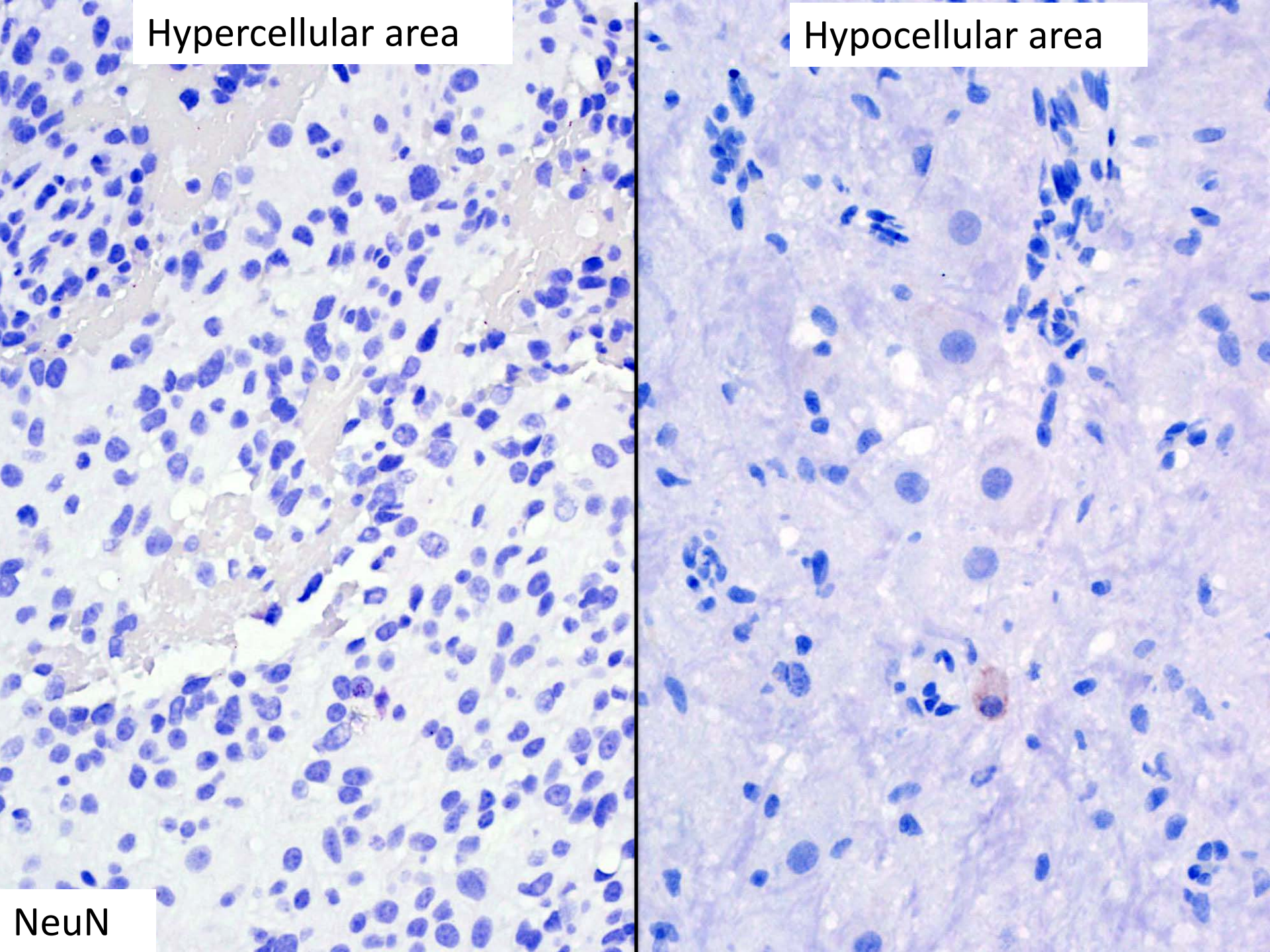
Diagnosis?

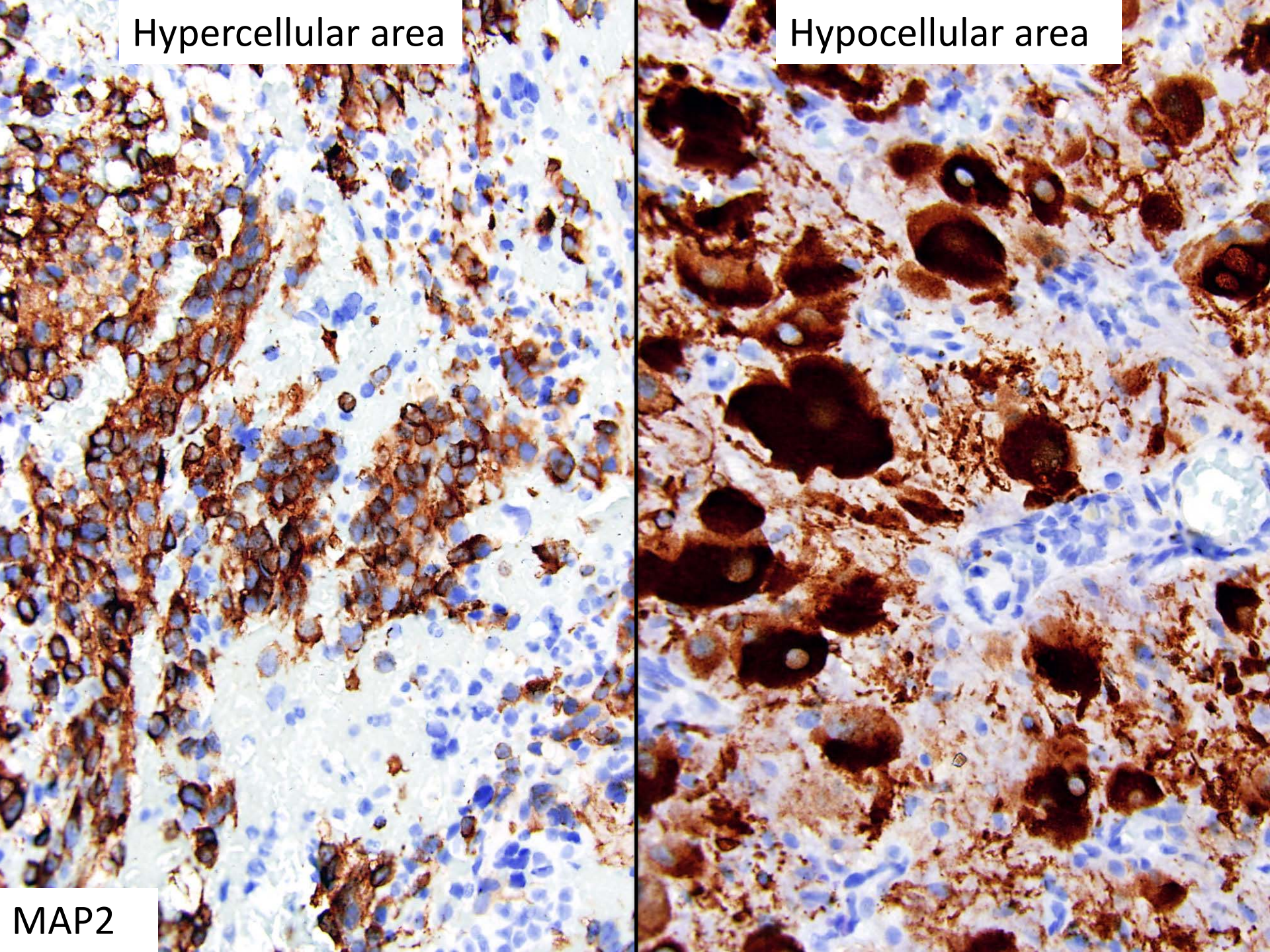
Differential Diagnosis

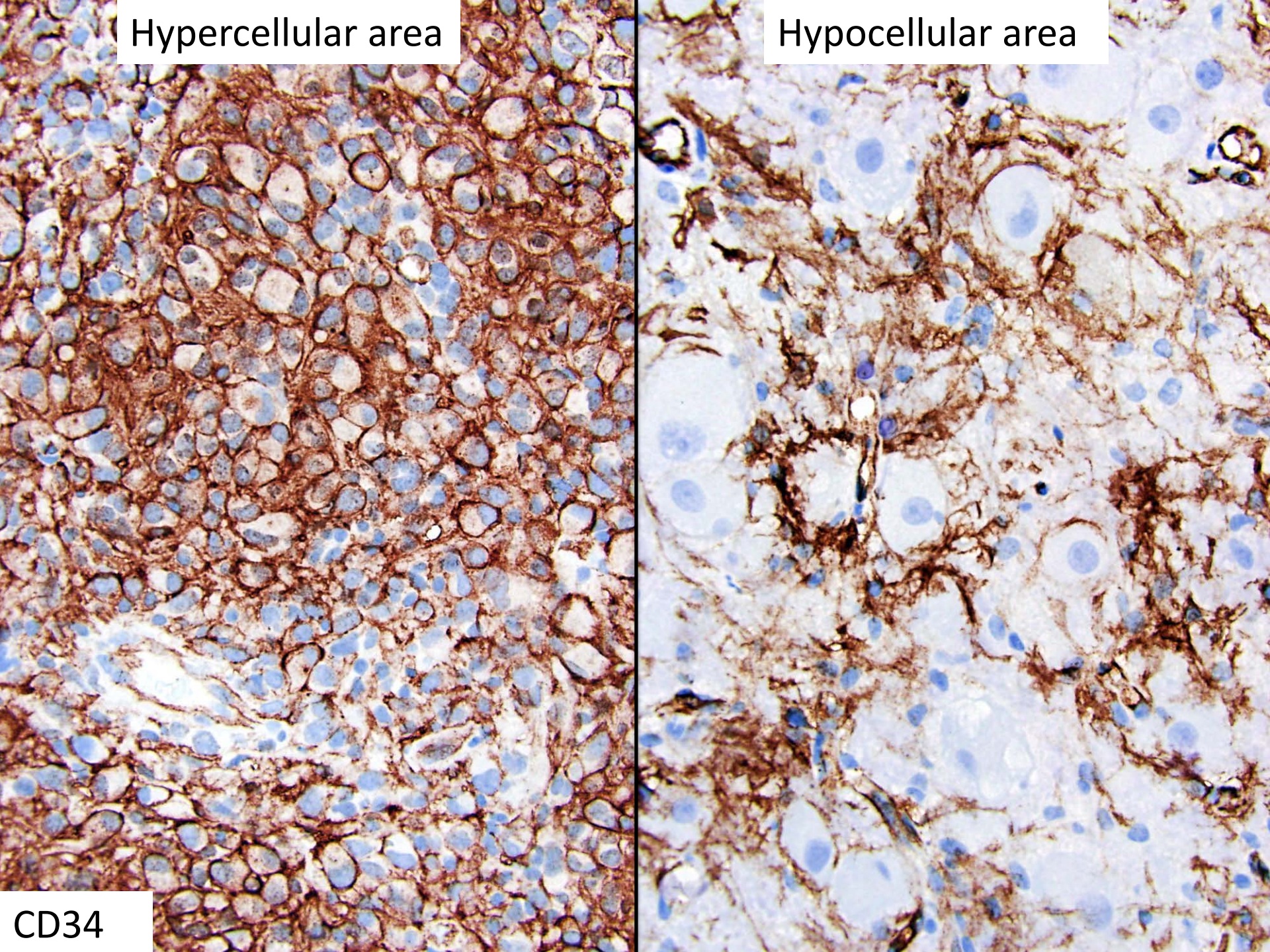
- Anaplastic ganglioglioma (WHO grade III)
- Atypical teratoid/rhabdoid tumor arising in ganglioglioma (WHO grade IV)
- Epithelioid glioblastoma with ganglioglioma-like foci (WHO grade IV)

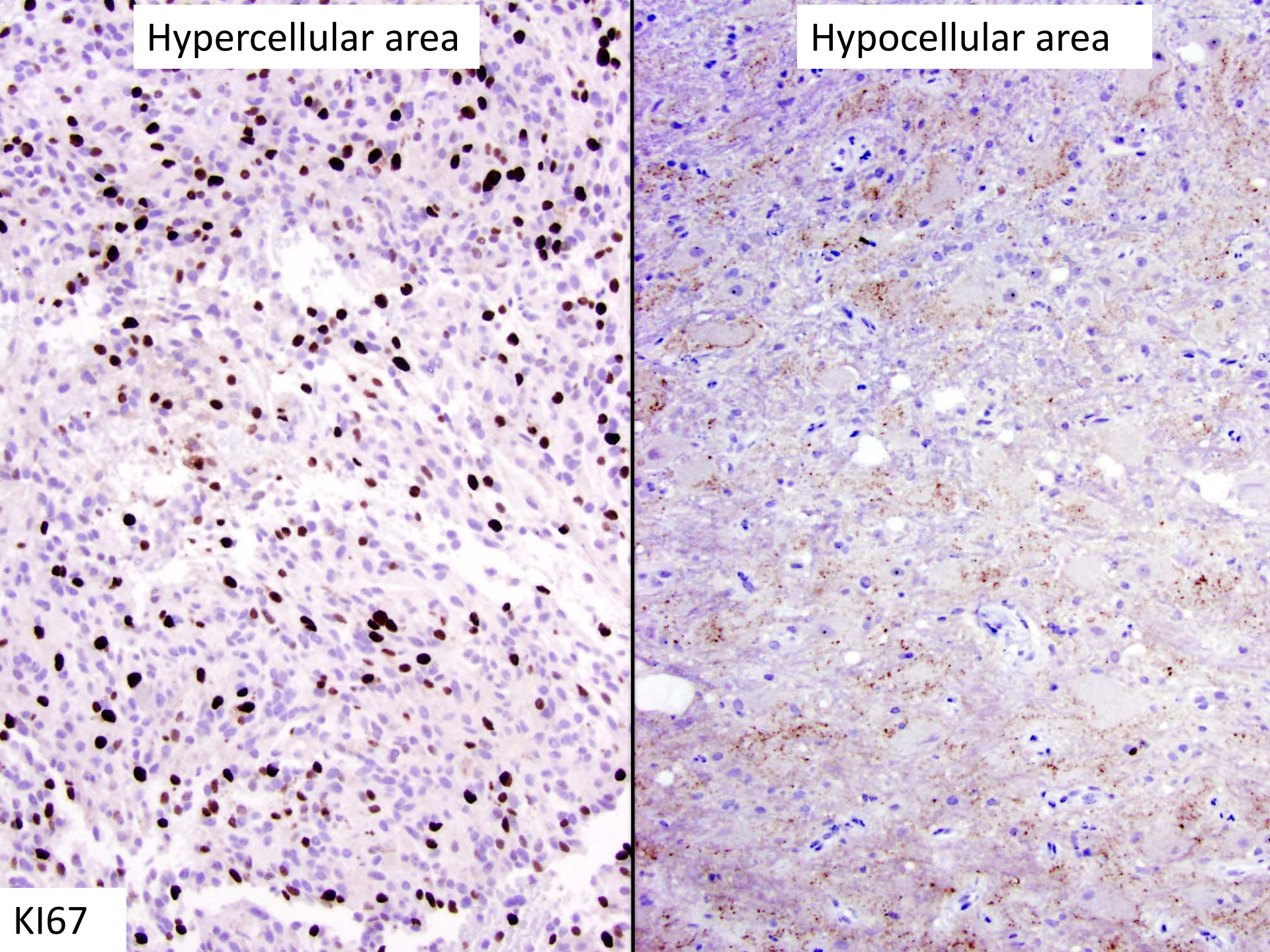

Hypercellular area
Hypocellular area
GFAP

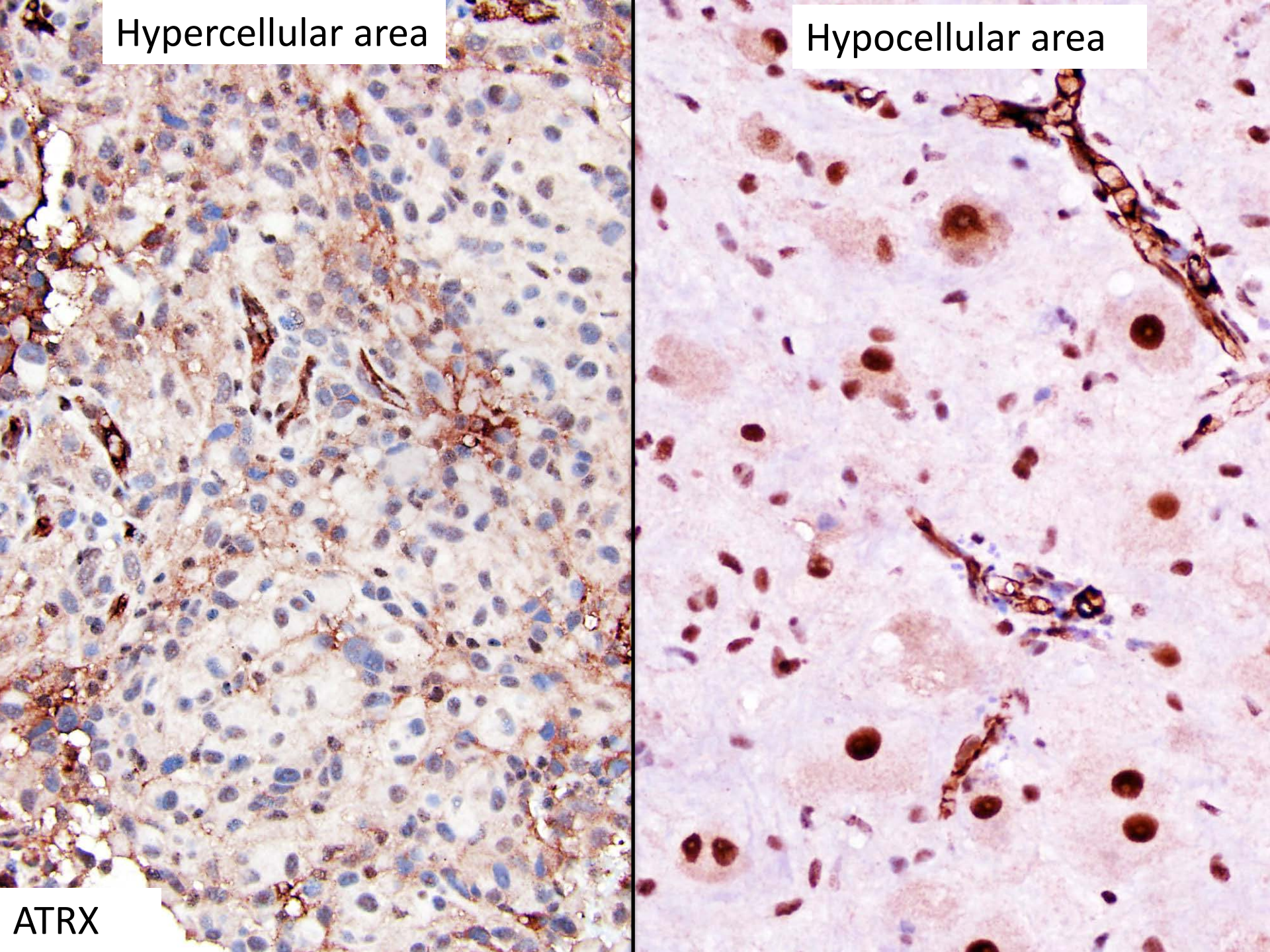

Hypercellular area
Hypocellular area
Neurofilament

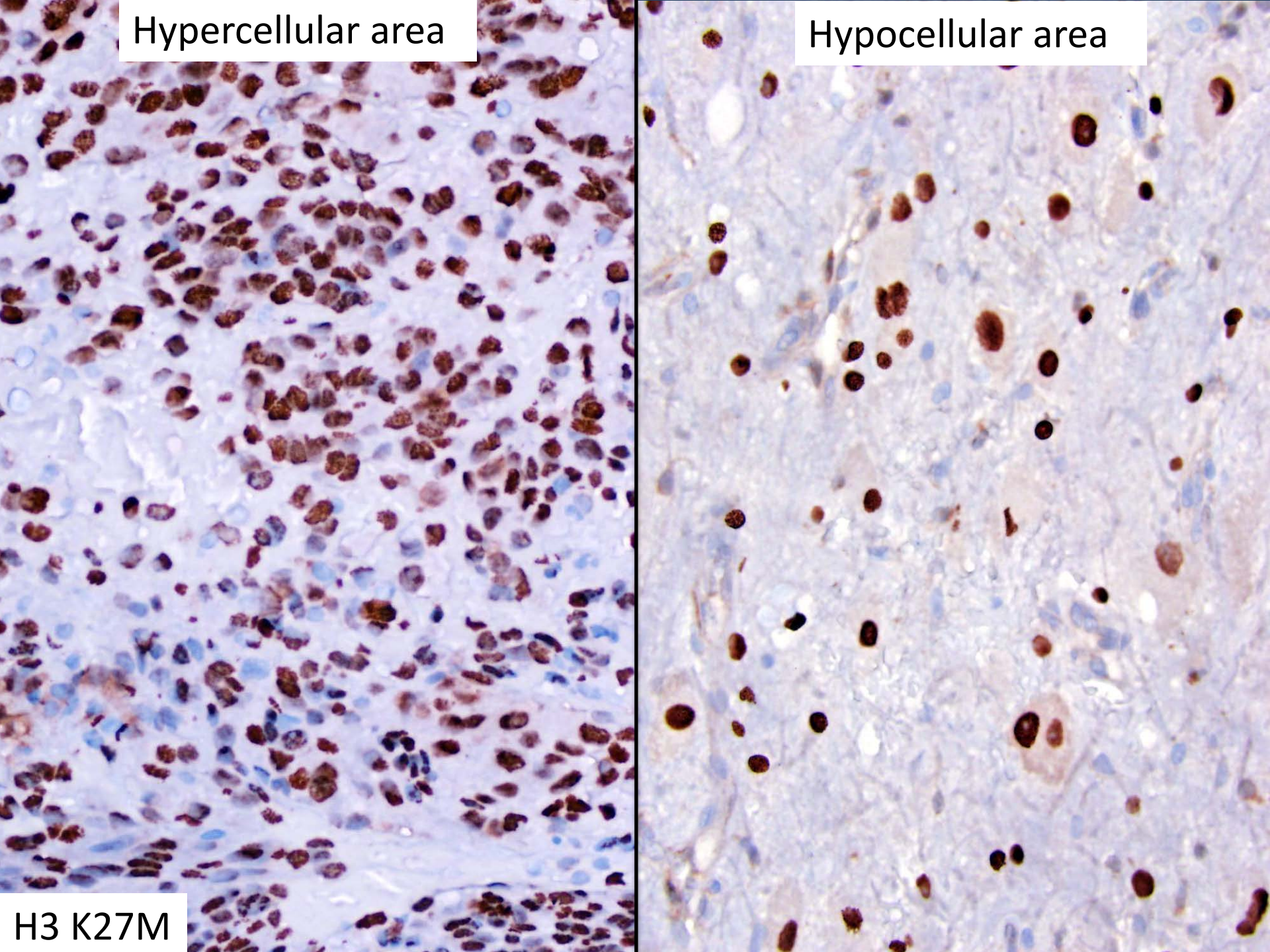

Hypercellular area
Hypocellular area
NeuN


Hypercellular area
Hypocellular area
MAP2


Hypercellular area
Hypocellular area
CD34


Hypercellular area
Hypocellular area
KI67


Hypercellular area
Hypocellular area
ATRX


Hypercellular area
Hypocellular area
H3 K27M

- The tumor was negative for BRAF V600E and IDH1(R132H) immunostains and INI1 was retained in the tumor nuclei.
- There was no *EGFR* amplification or *PTEN* deletion.

Diagnosis

- Spinal glioblastoma with epithelioid features, ganglioglioma-like foci and *H3 K27M* mutation

Discussion

- Epithelioid glioblastoma
  - Rare variant (Kleinschmidt-DeMasters BK et al. Am J Surg Pathol. 2013 May (37(5):685-98)
  - Primary glioblastoma
  - Leptomeningeal spread, short recurrence interval, metastases outside of CNS (Broniscer A. et al. Neuropathol Appl Neurobiol 2014 April;40(3):327-336)
  - Long survival in a subset (Kelinschmidt-Demasters BK et al. Am J Surg Pathol 2013 May;37(5):685-98)

Discussion

- *BRAF V600E* mutation in ~50% of cases
- Negative for *IDH1 (R132H)* mutation (one exception reported)
- Negative for *EGFR* amplification

Peculiar Findings in Our Case

- Symptoms of long duration
- Gangliioglioma – like foci
- Loss of ATRX in the glioma-like areas but retained ATRX in the gangliioglioma-like areas
- *H3 K27M* mutation

K27M Mutation

- Common in DIPG and in midline pediatric GBM (Wu G. et al. Nat. Genet. 2012;44(3):251-2530)
- Common in thalamic high grade gliomas in young adults (Aihara K. et al. Neuro-Oncol. 2014;16(1),140-146)
- Worse prognosis than high grade diffuse gliomas without *K27M* mutation (Korshunov A. et al. Acta Neuropathol (2015) 129;669-678

Follow-Up

- The patient underwent radiotherapy and treatment with temozolomide
- Vertebral fracture due to osteonecrosis (radiotherapy-related)
- Currently he has stable disease and is back to work (six months follow-up)


Thank you

References

- Broniscer A, Tatevossian RG, Sabin ND, Klimo P, Dalton J et al. Clinical, radiological, histological, and molecular characteristics of paediatric epithelioid glioblastoma. Neuropathol Appl Neurobiol 2014 April;40(3):327-336
- Kleinschmidt-DeMasters BK, Aisner DL, Birks DK, Foreman NK. Epithelioid GBMs show a high percentage of BRAF V600E mutation. Am J Surg Pathol. 2013 May (37(5):685-98
- Gielen GH, Gessi M, Hammes J, Kramm CM, Waha A. et al. *H3F3A* K27M mutation in pediatric CNS tumors. Am J Clin Pathol 2013;139:345-349
- Aihara K, Mukasa A, Gotoh K, Saito K, Nagae G. H3F3A K27M mutations in thalamic gliomas from young adult patients. Neuro-Oncology 16(1),140-146, 2014
- Korshunov A, Ryzhova M, Hovestadt V, Bender S, Sturm D et al. Integrated analysis of pediatric glioblastoma reveals a subset of biologically favorable tumors with associated molecular prognostic findings. Acta Neuropathol.2015 May;129(5):669-78.
- Kleinschmidt-DeMasters BK, Birks DK, Aisner DL, Hankinson TC, Rosenblum MK. Atypical teratoid/rhabdoid tumor arising in ganglioglioma: genetic characterization. Am J Surg Pathol 2011 Dec;35(12):1894-901