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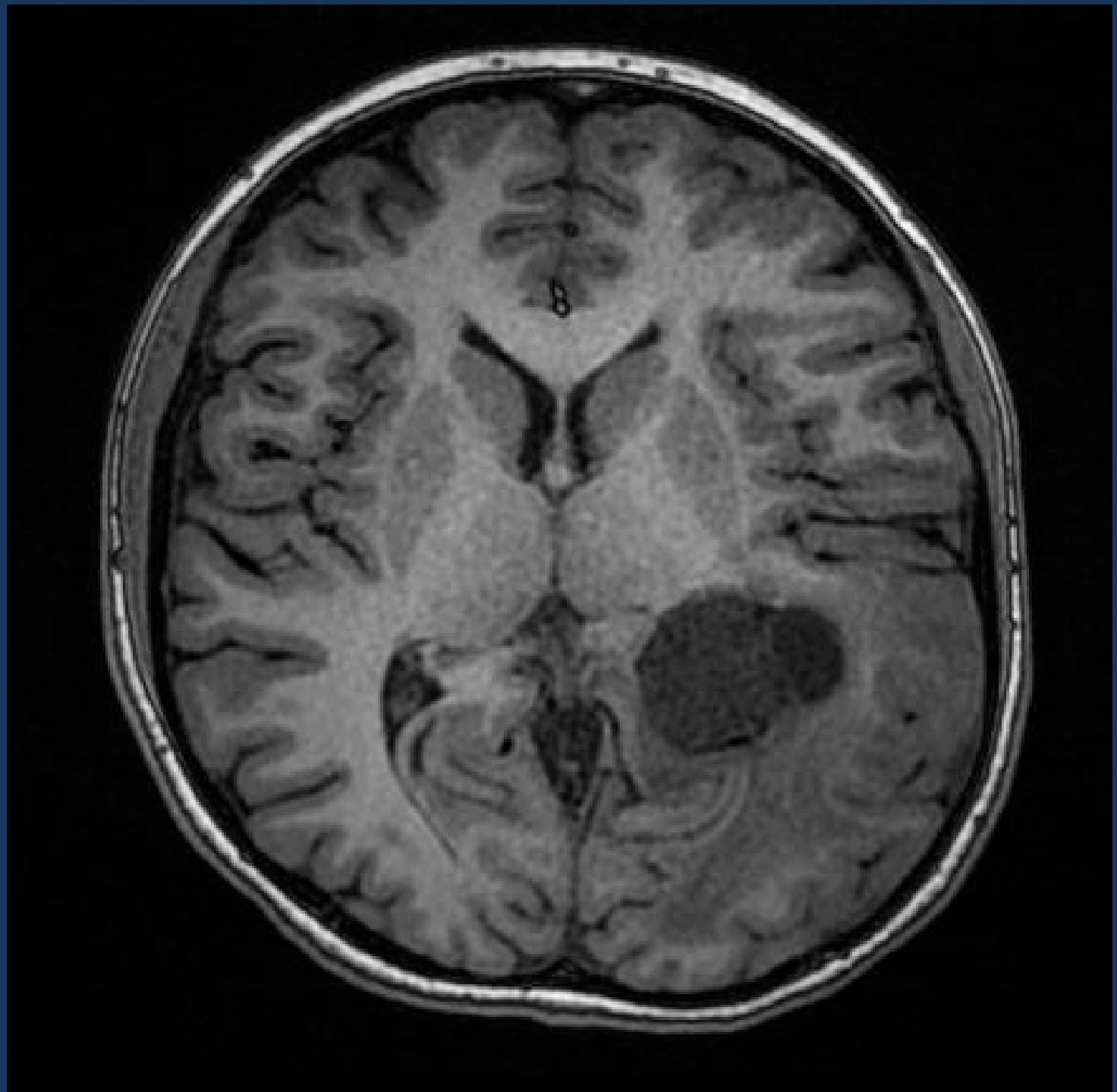
Cases 8a and 8b

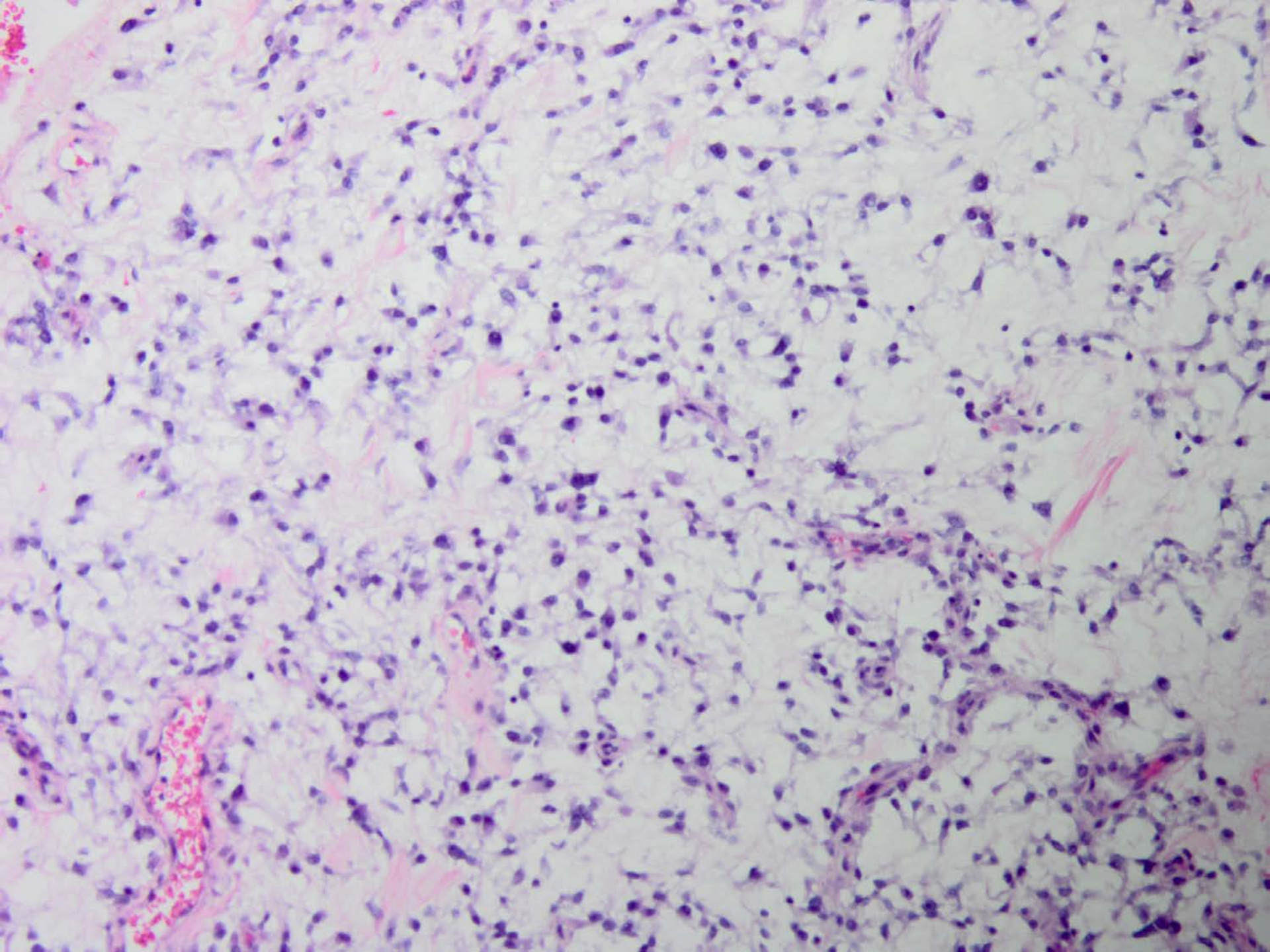
Tejus A. Bale, MD, PhD; Angelica Oviedo, MD; Harry Kozakewich, MD;
Sanda Alexandrescu, MD
Boston Children's Hospital, Boston, MA; Dalhousie University Medical School, IWK Health Center, Halifax, NS Canada

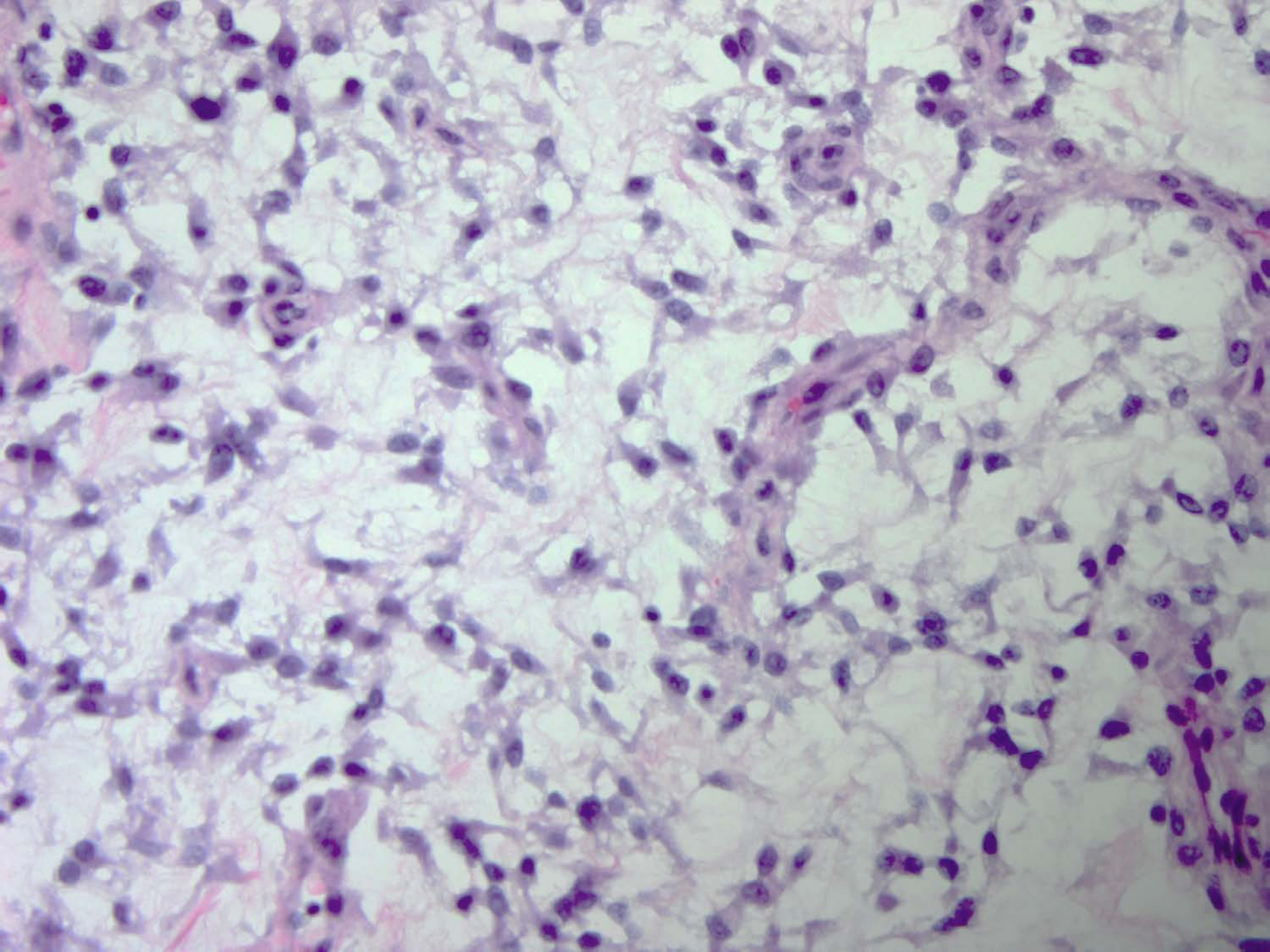
- The following faculty have nothing to disclose:
  - Tejus Bale
  - Angelica Oviedo
  - Harry Kozakewich
  - Sanda Alexandrescu

Case 8a – Clinical History

- 14 year old female presenting with intermittent nausea, vomiting and early morning headache of recent onset.

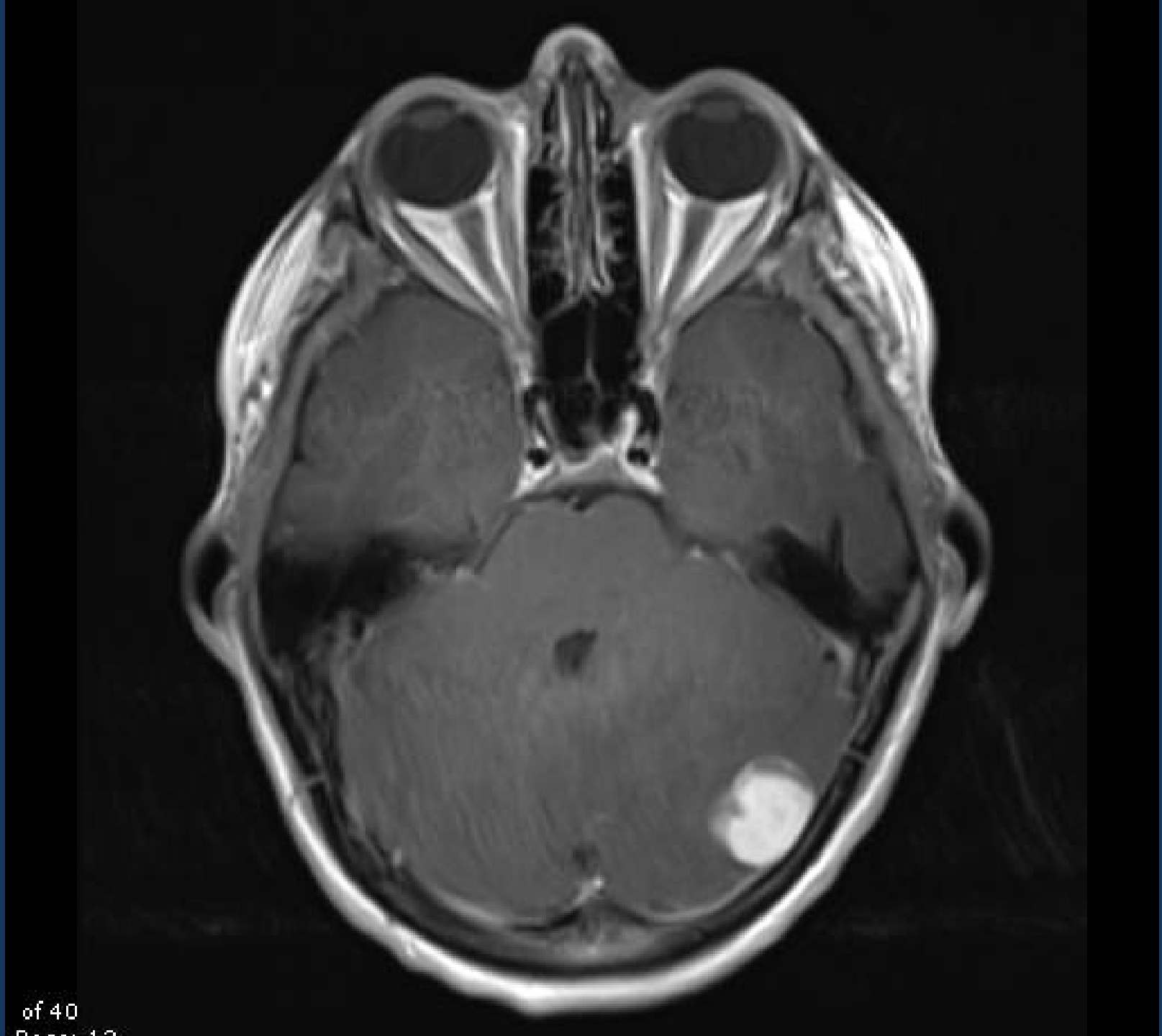


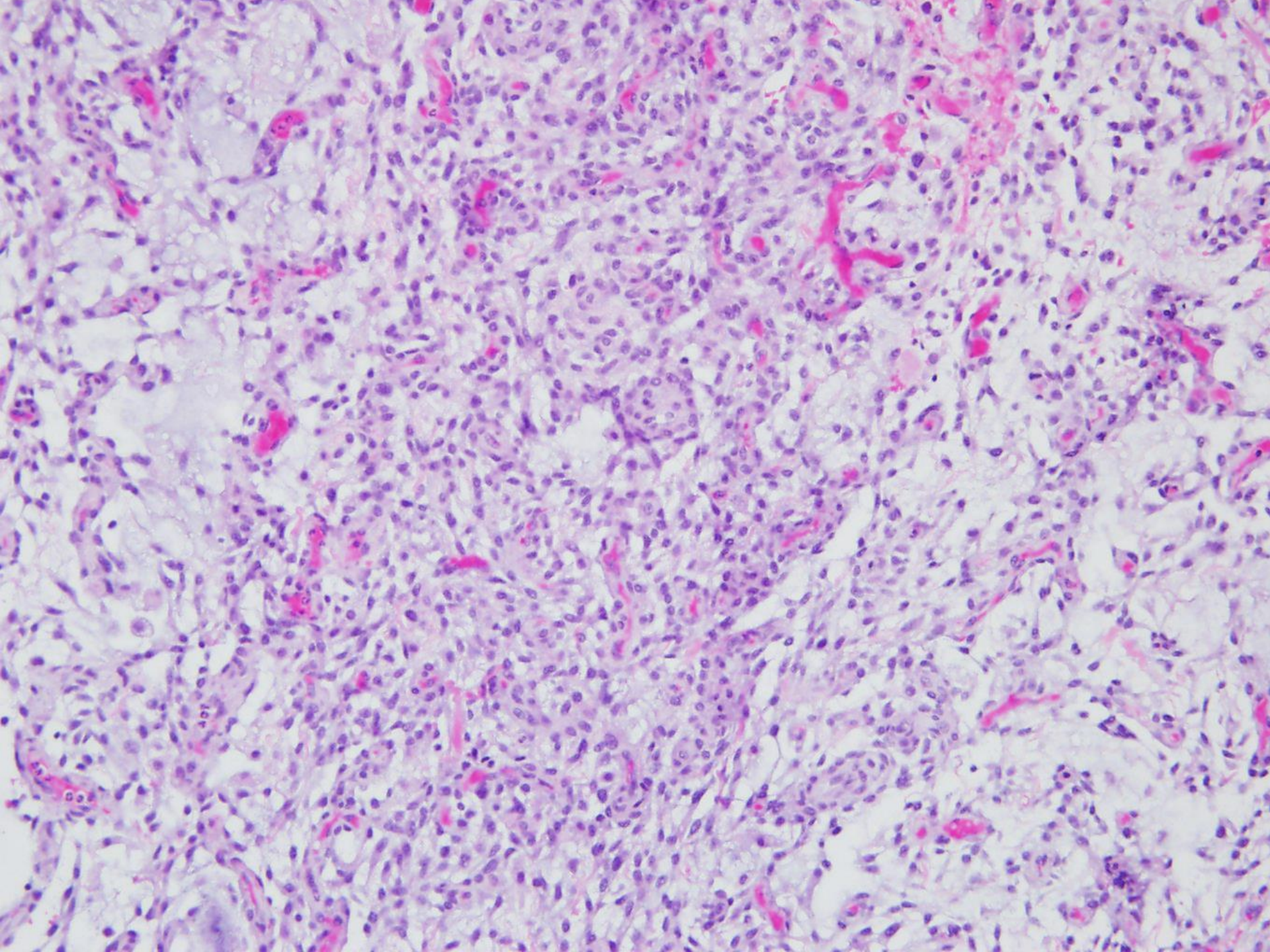


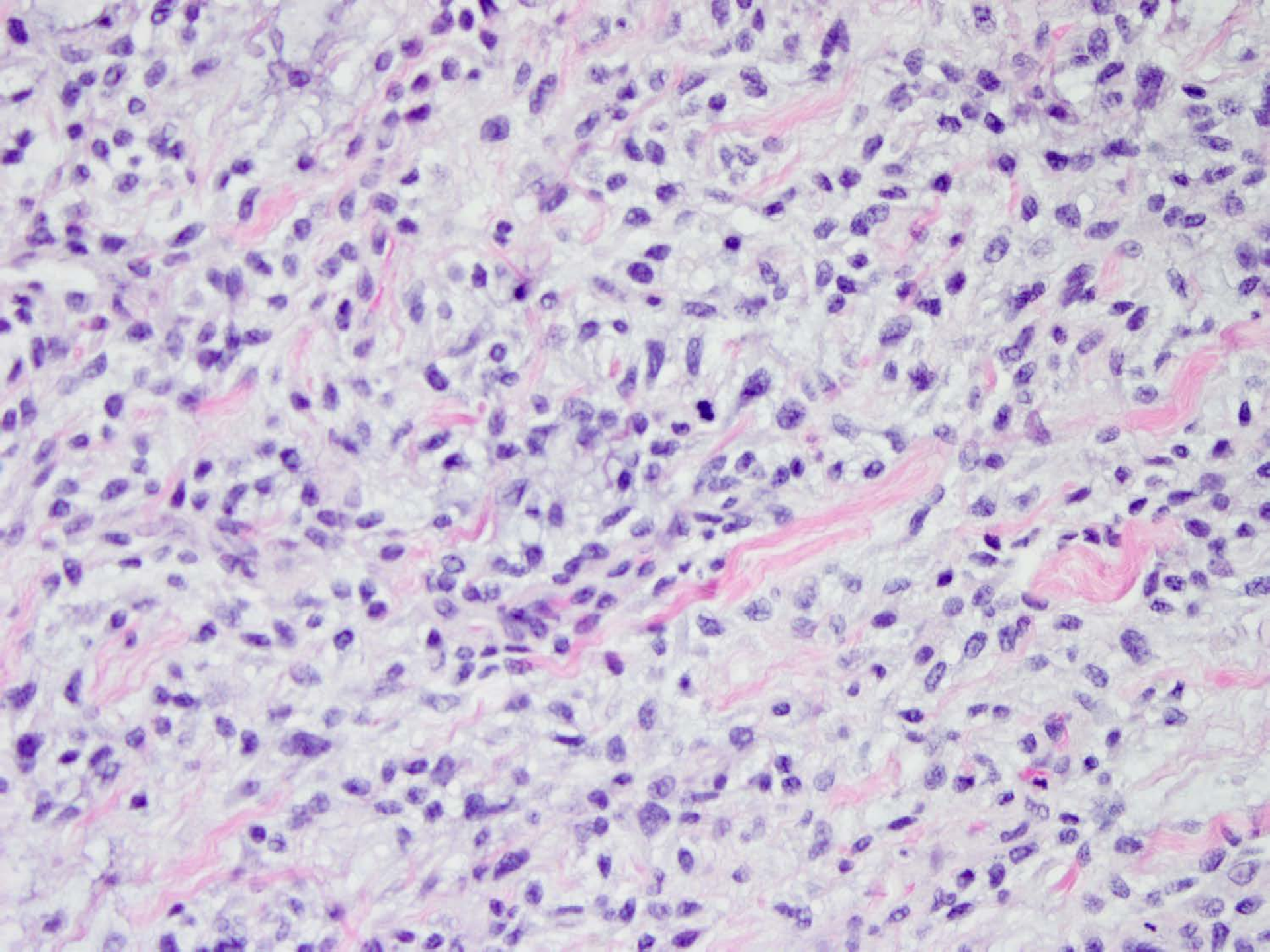


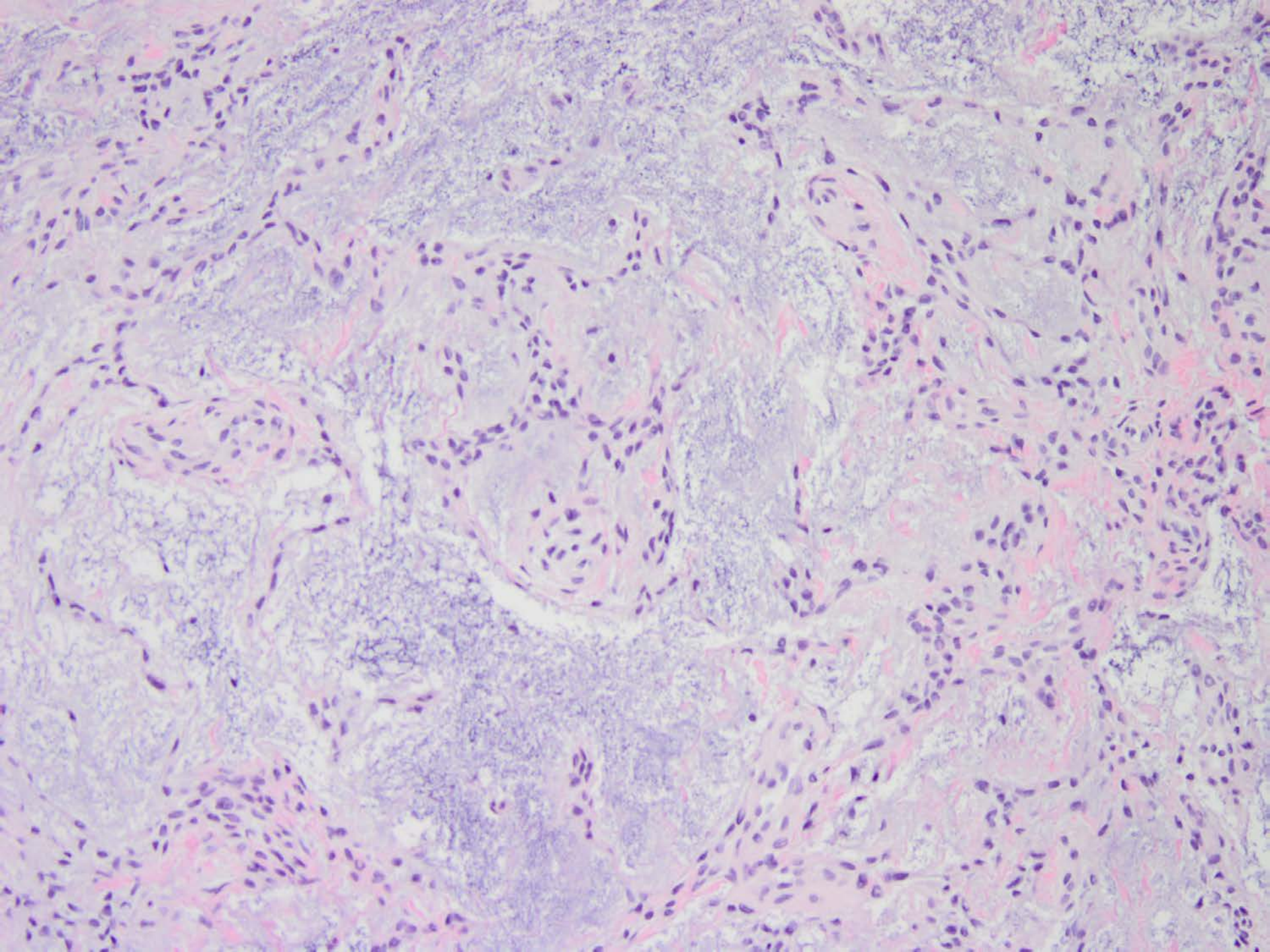
Case 8b - Clinical History

- 12-year-old boy with a past medical history of adrenal neuroblastoma diagnosed at the age of 7 and treated with chemotherapy, surgical resection, stem cell transplant and local radiotherapy.
- No evidence of recurrence.


of 40



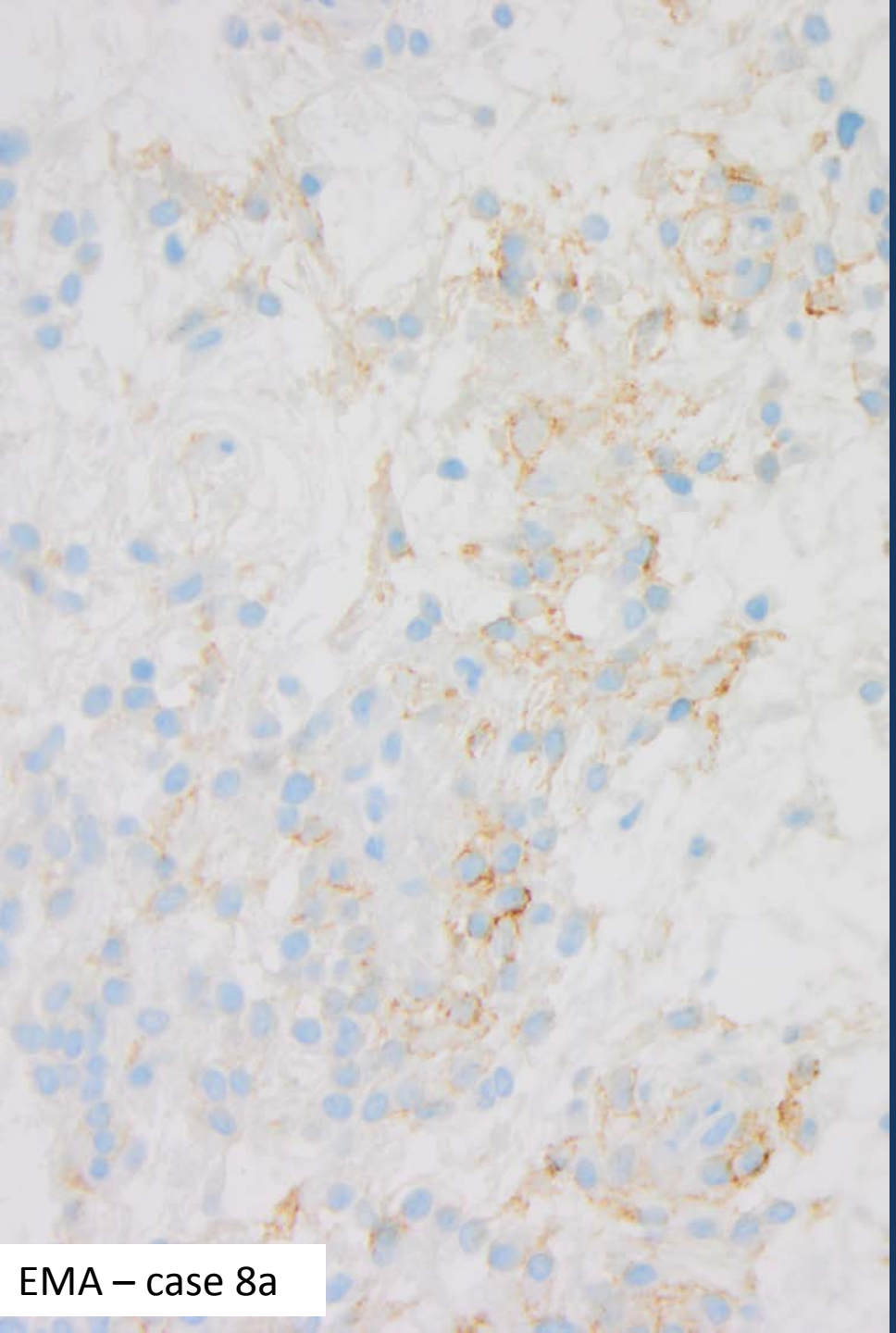




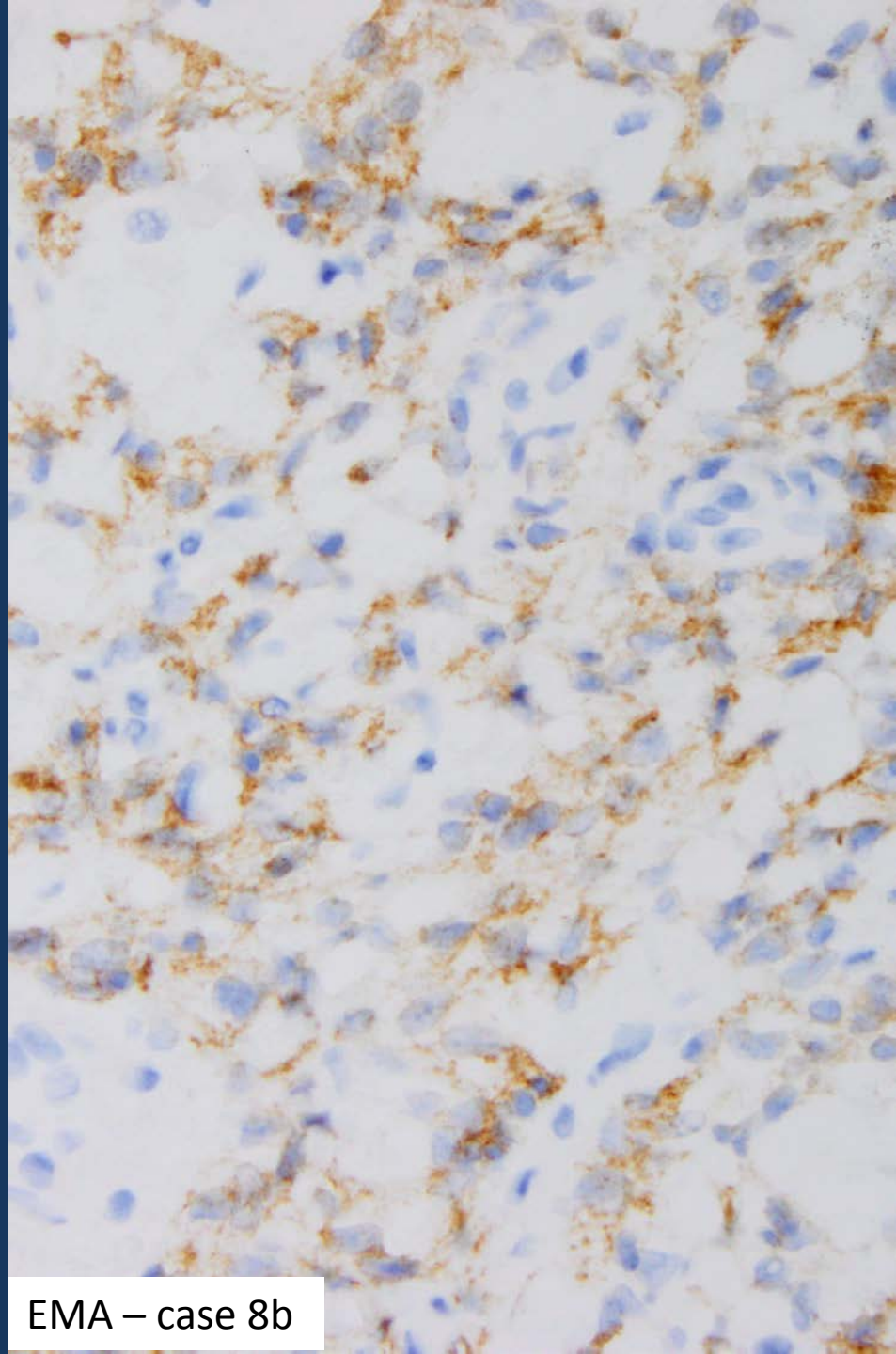
(Differential) Diagnosis?

Differential Diagnosis

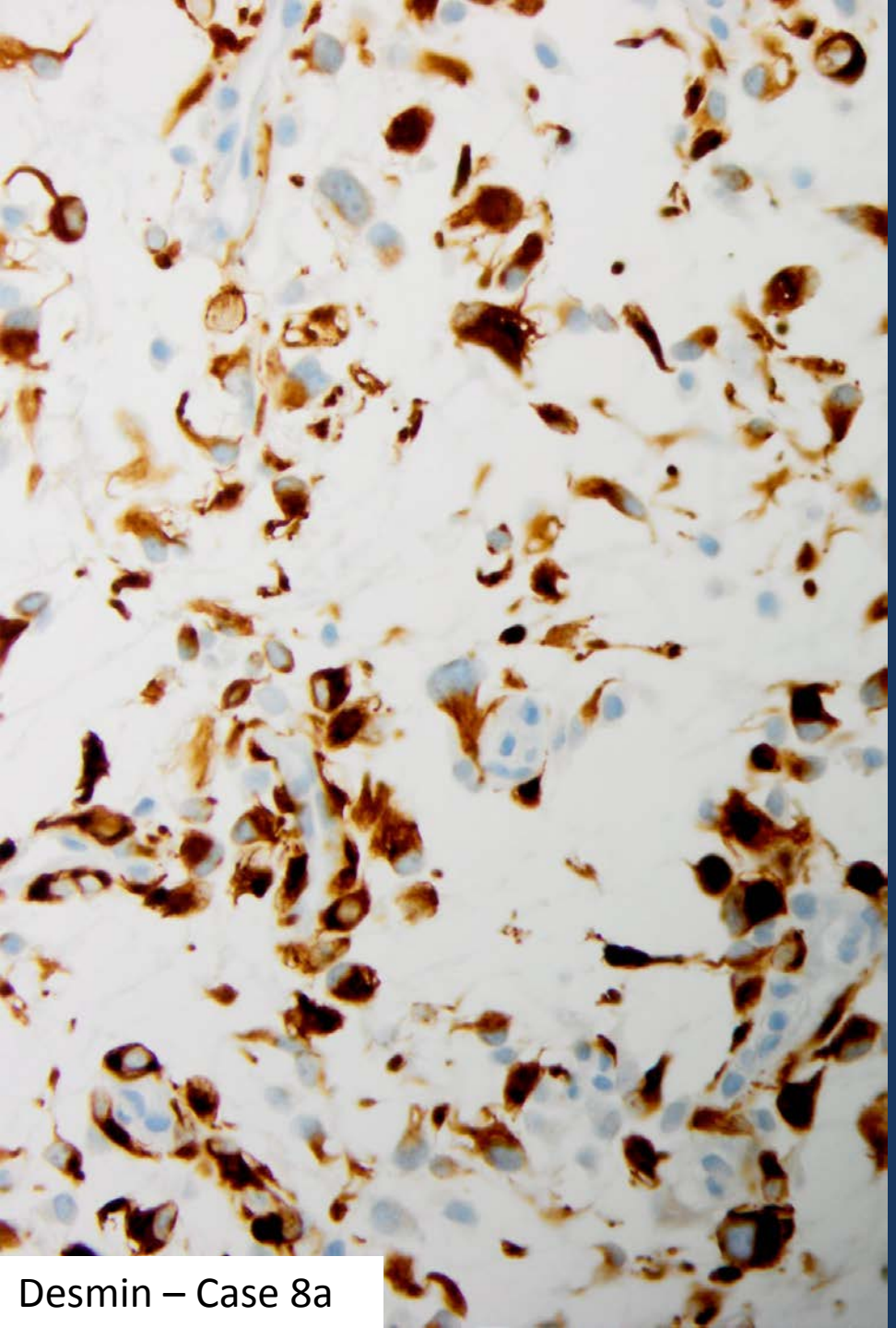
- Meningioma with prominent myxoid changes
- Chordoma
- Pilocytic astrocytoma
- Myoepithelioma/myoepithelial carcinoma
- Mesenchymal chondrosarcoma
- Extraskeletal myxoid chondrosarcoma
- Low grade myxofibrosarcoma
- Myxoid variant of angiomatoid fibrous histiocytoma
- An unusual synovial sarcoma
- Ewing sarcoma with myxoid changes
- Rhabdomyosarcoma



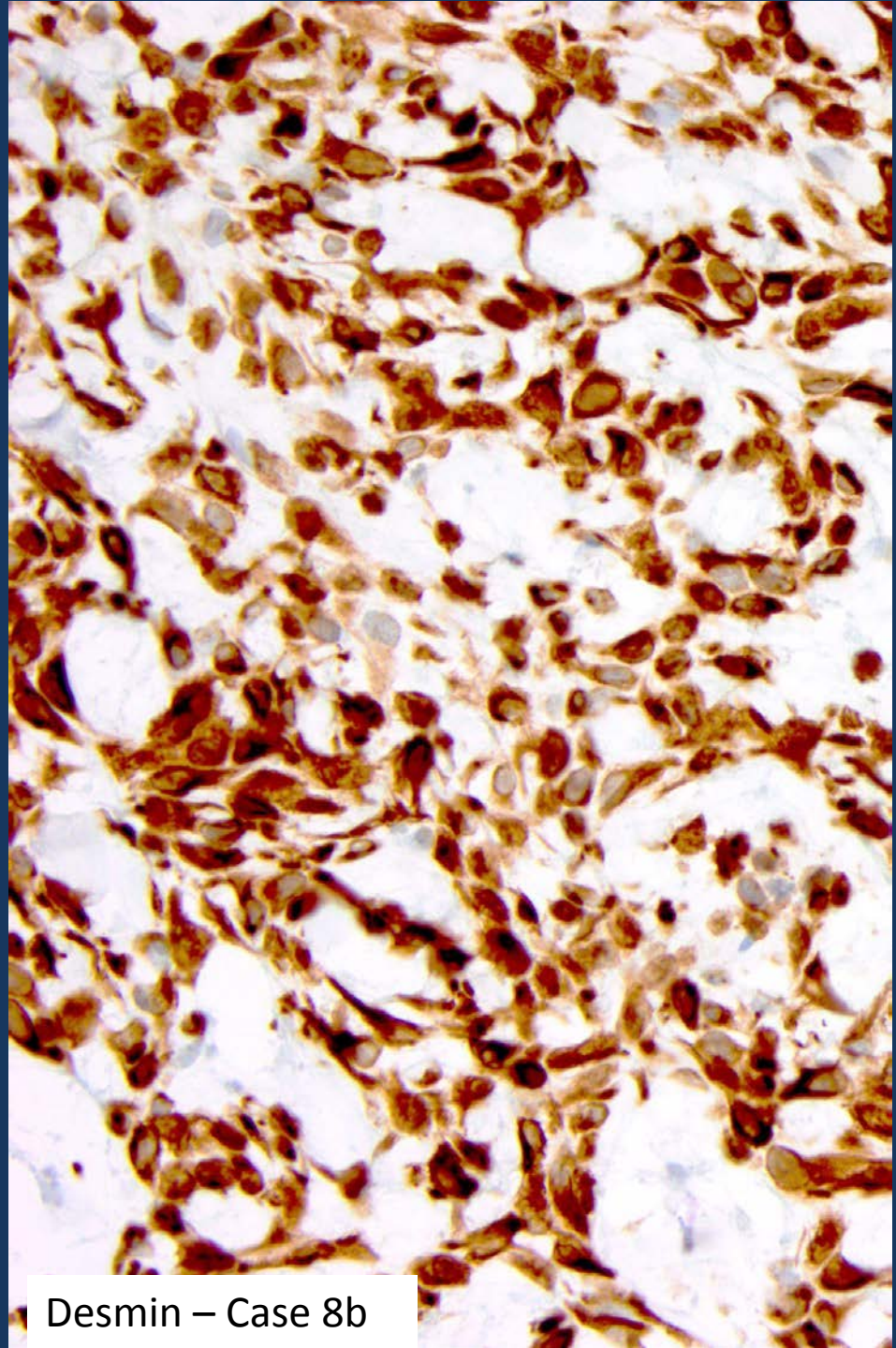
EMA – case 8a



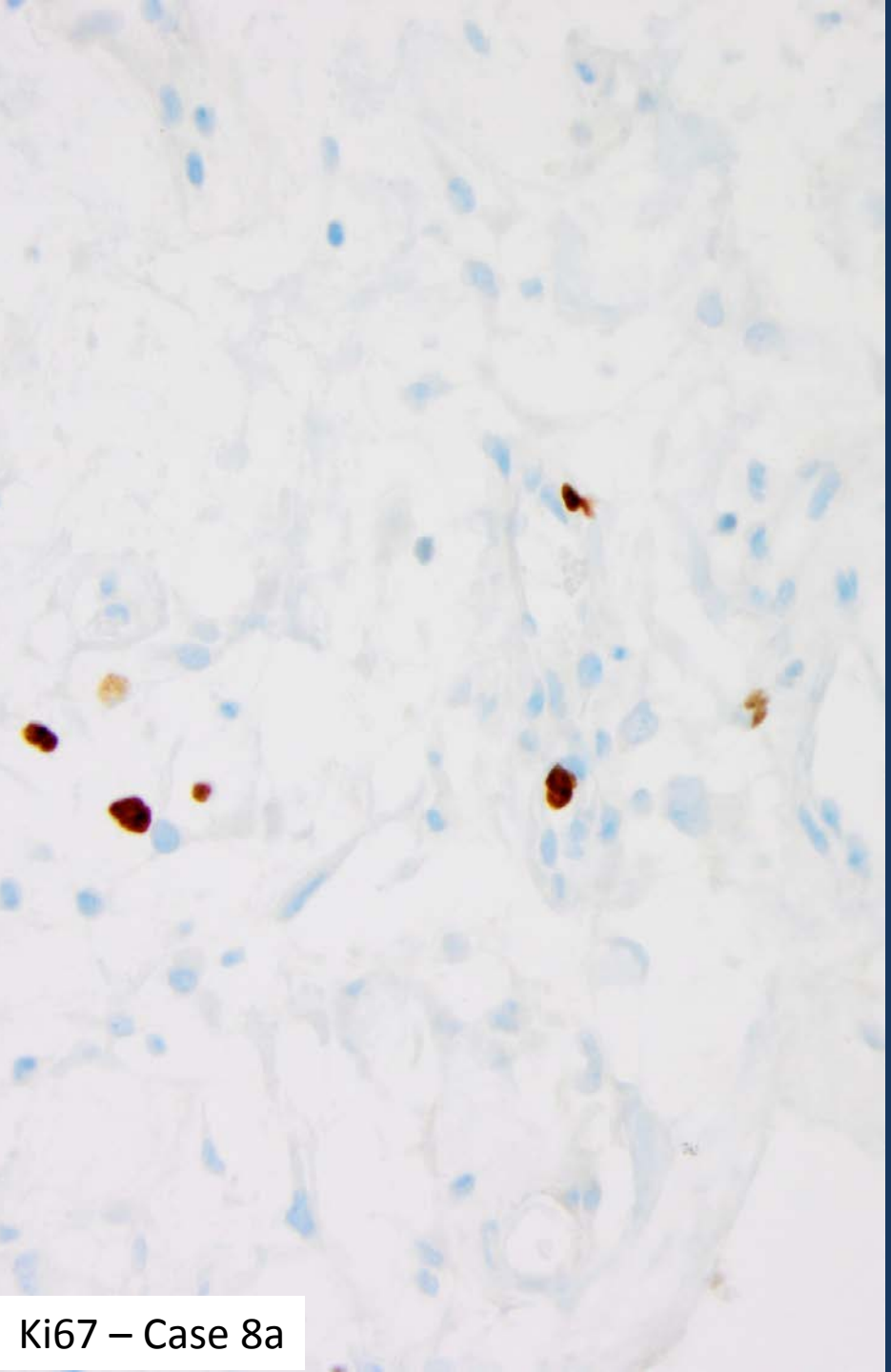
EMA – case 8b



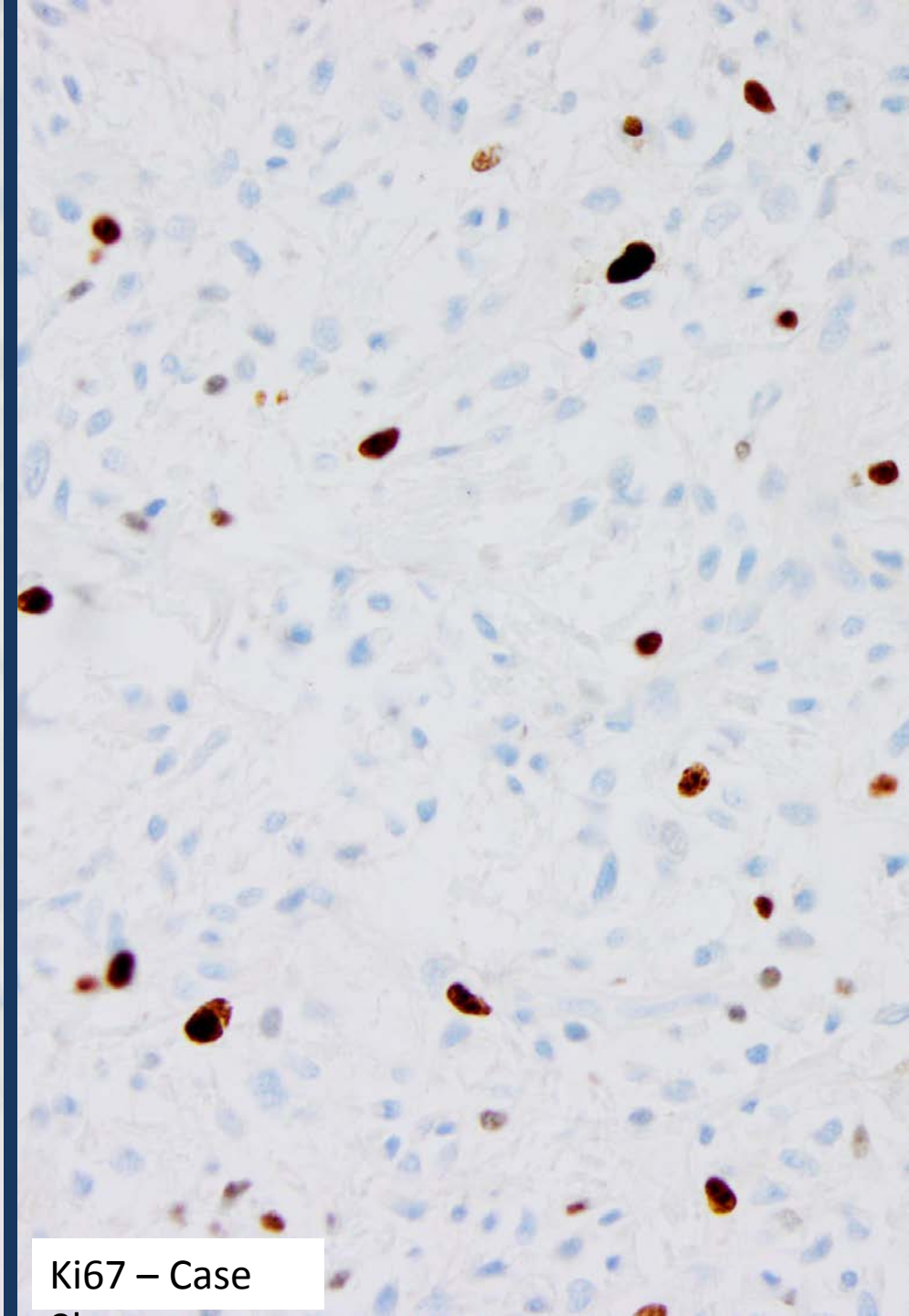
Desmin – Case 8a



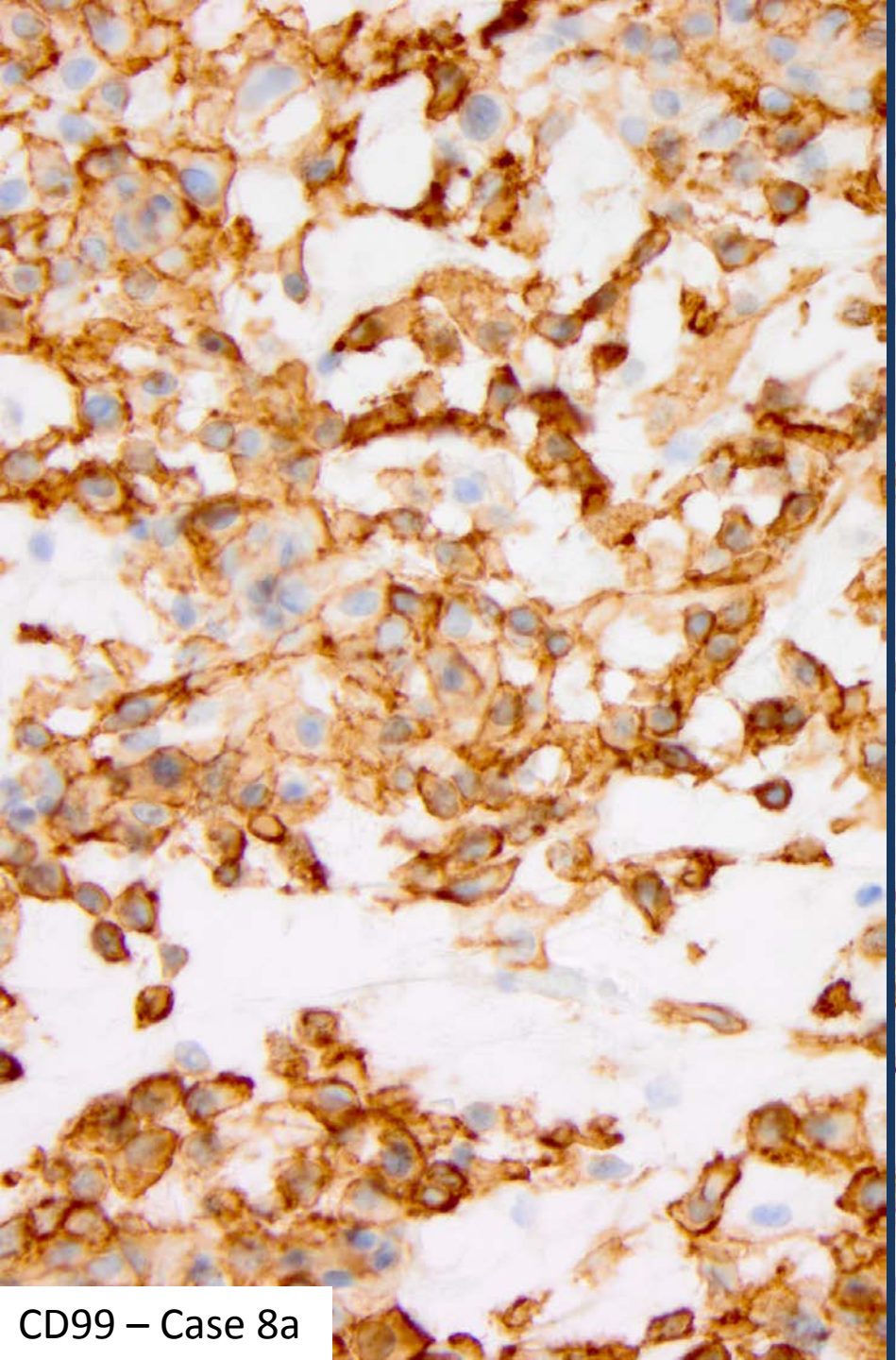
Desmin – Case 8b



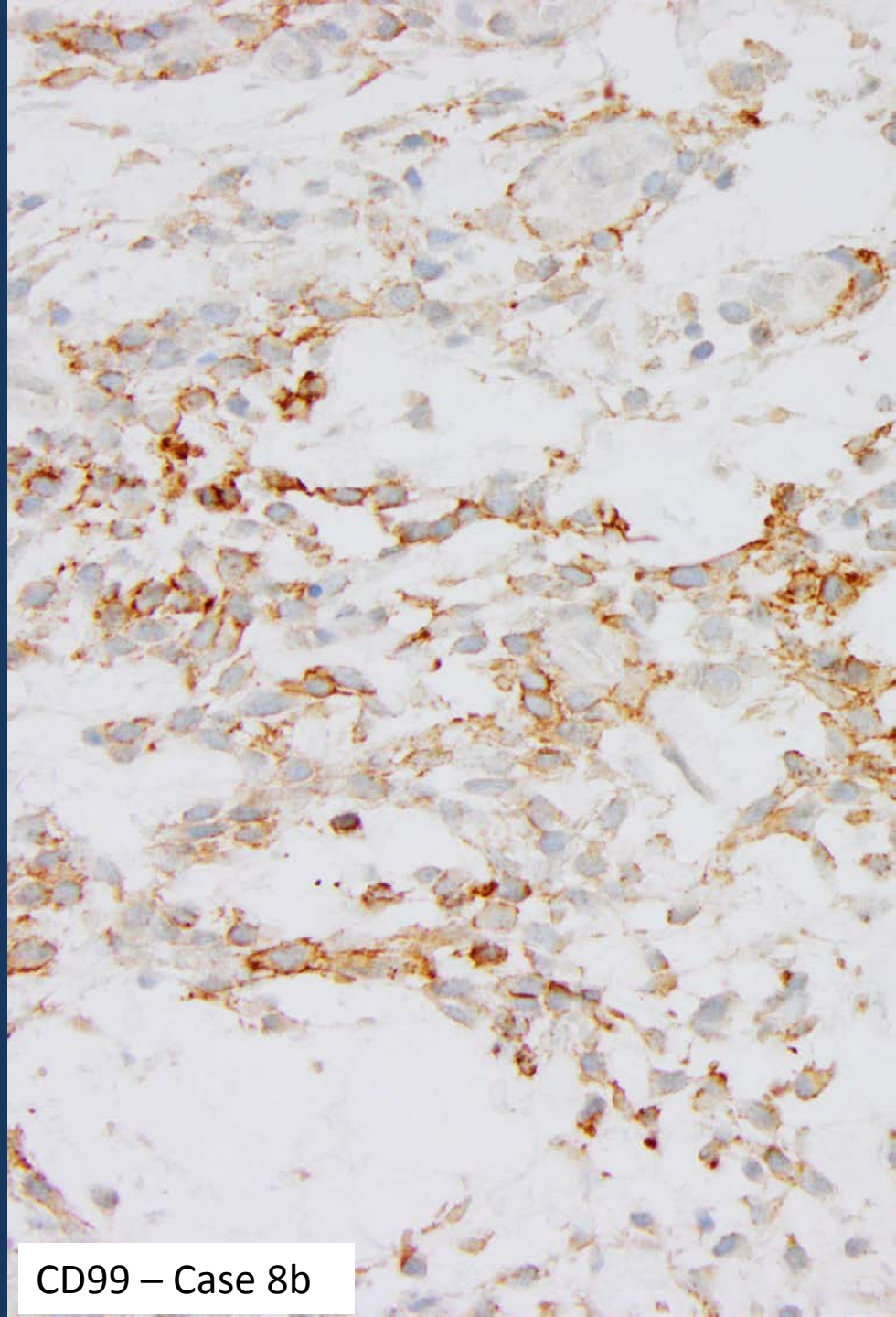
Ki67 – Case 8a



Ki67 – Case



CD99 – Case 8a

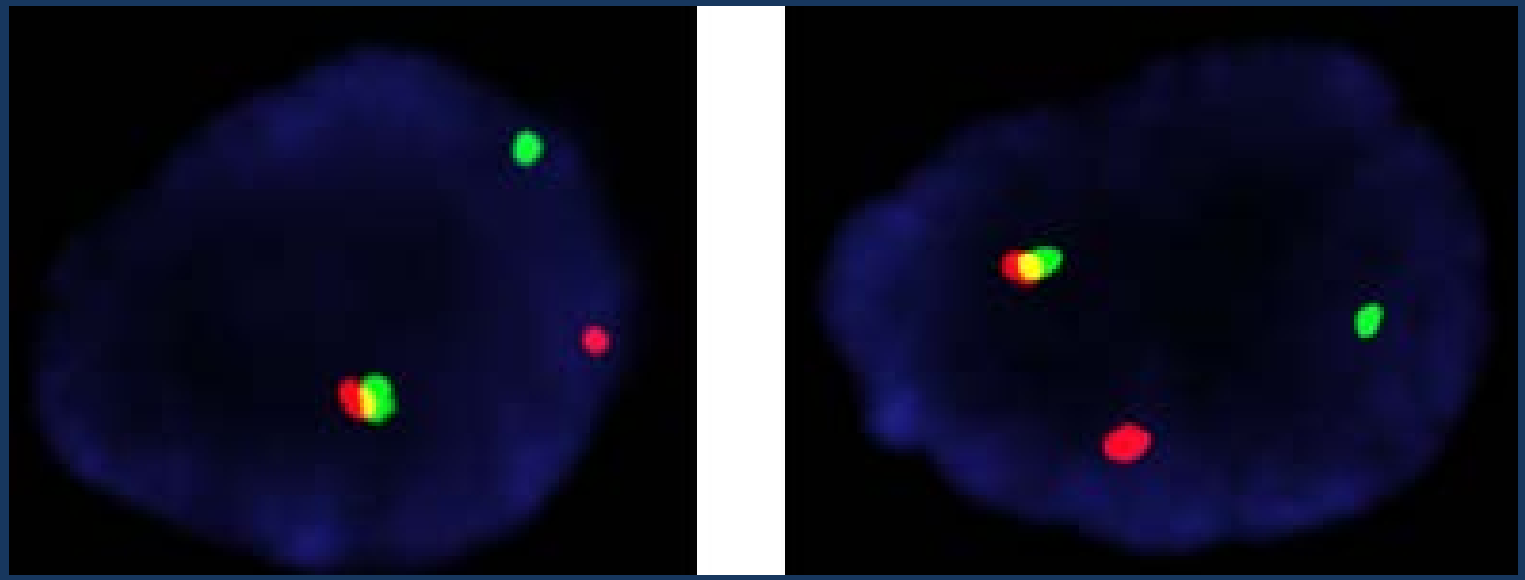


CD99 – Case 8b

The following immunostains were negative:

- Keratin
- S100
- Brachyury
- CD34
- Myogenin
- Olig2
- GFAP
- Fli1
- TLE
- CD68
- SMA (equivocal)
- Synaptophysin
- Chromogranin

Fluorescence in situ hybridization demonstrated EWSR1 (22q12) rearrangement in 93% nuclei in Case 8a, and in 88% nuclei in Case 8b.



Karyotype for Case 8a:

46, XX, t(2;22)(q34;q12)[3]/46,xx[25]

Targeted exome sequencing (OncoPanel) with subsequent structural variation analysis using breaKmer:

A reciprocal chromosome rearrangement between chromosome 2 (mapping to intron 6 in case 1 and intron 7 in case 2) of *CREB1* and chromosome 22 (mapping to intron 8 in both cases) of *EWSR1*.

Copy Number Variations

- Case 8a

Low copy number gain of:

5q35.1 (*KCNIP1*)
11q13.3(*CCND1*)
15q25.3 (*NTRK3*)
18q11.2 (*GATA6*)

- Case 8b

Low copy number gain of:

5q53.1 (*KCNIP1*)
11q13.3 (*CCND1*)
5q32 (*CSF1R*)
5q32 (*PDGFRB*)
12p13.32 (*CCND2*)
19p12 (*ZNF708*)

Diagnosis

Myxoid variant of angiomatoid fibrous histiocytoma.

Angiomatoid fibrous histiocytoma (AFH)

- Intermediate malignant potential
- Most common location: limbs, trunk, head and neck
- In rare instances, presents as a primary intracranial lesion. (Dunham 2008, Hansen 2015, Ochalski 2010).
- Characteristic chromosomal rearrangements involving EWSR1: EWSR1-CREB1 t(2:22)(q33;q12), EWSR1-ATF1 t(12;22)(q13;q12), and FUS-ATF1 t(12;16)(q13;p11)
- Histological features include:
  - fibrous pseudocapsule with lymphoplasmacytic infiltrates
  - blood-filled cystic spaces
  - epithelioid or spindled tumor cells with a multinodular, whorled, sheet-like or fascicular growth pattern

- Characteristic morphologic features of AFH (at least focal) within a prominent myxoid stroma

– Expected immunoprofile: EMA, desmin, CD99, and, occasionally, CD68 expression

– Characteristic chromosomal rearrangements

– No intracranial cases

– No previous reports of primary intracranial myxoid AFH

Follow-up

- Both patients are doing well without evidence of recurrence after 5 months (patient 8a) and 7 months (patient 8b).