DSS 2024-9

June 8, 2024

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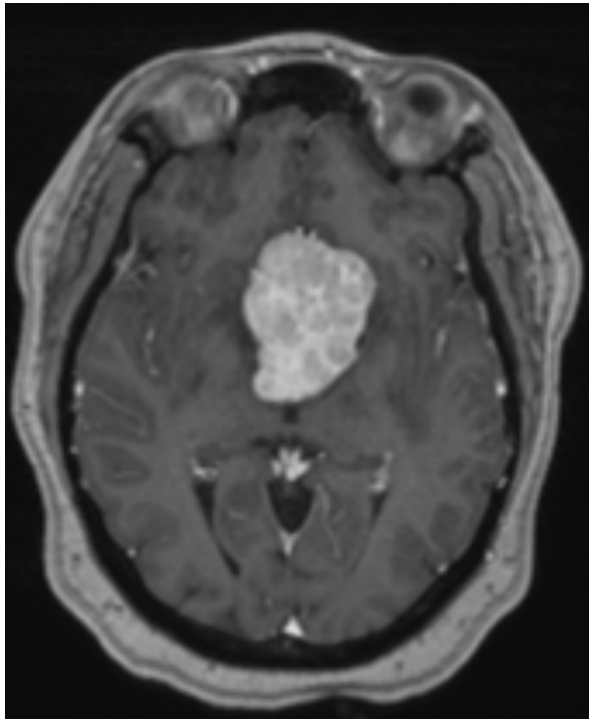
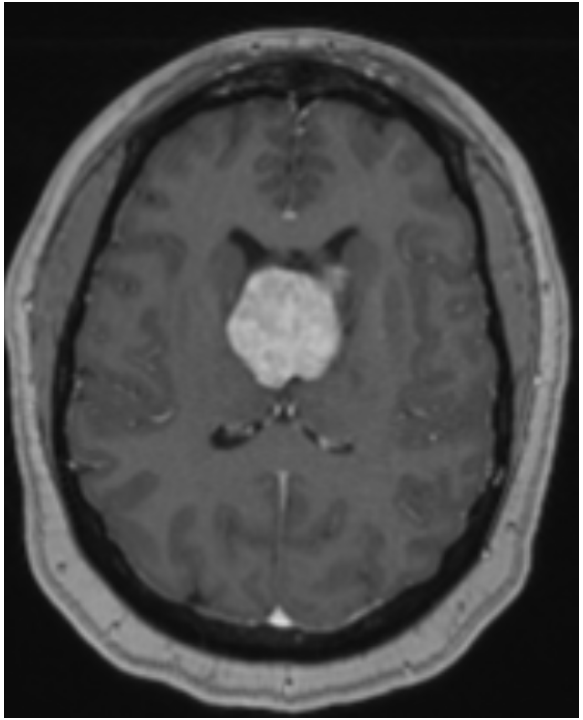
History and Physical Examination

- The patient is a 32-year-old female with 1-year-duration of:
  - Gradual and progressive headaches
  - Cognitive dysfunction (poor concentration and difficulty with memory)
  - Fatigue
  - Difficulty with performing daily activities
  - Bilateral blurred vision
- Physical examination: BMI of 45. Neurological exam unremarkable.

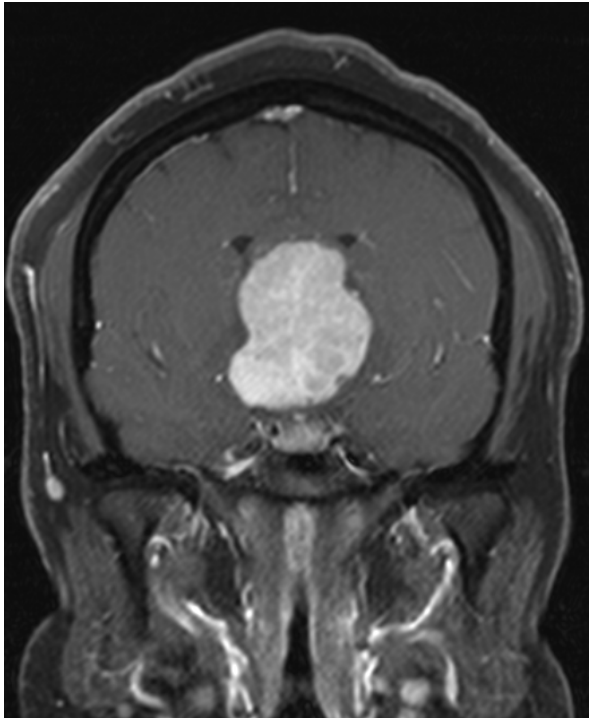
Imaging



MRI (T1 + C) Axial

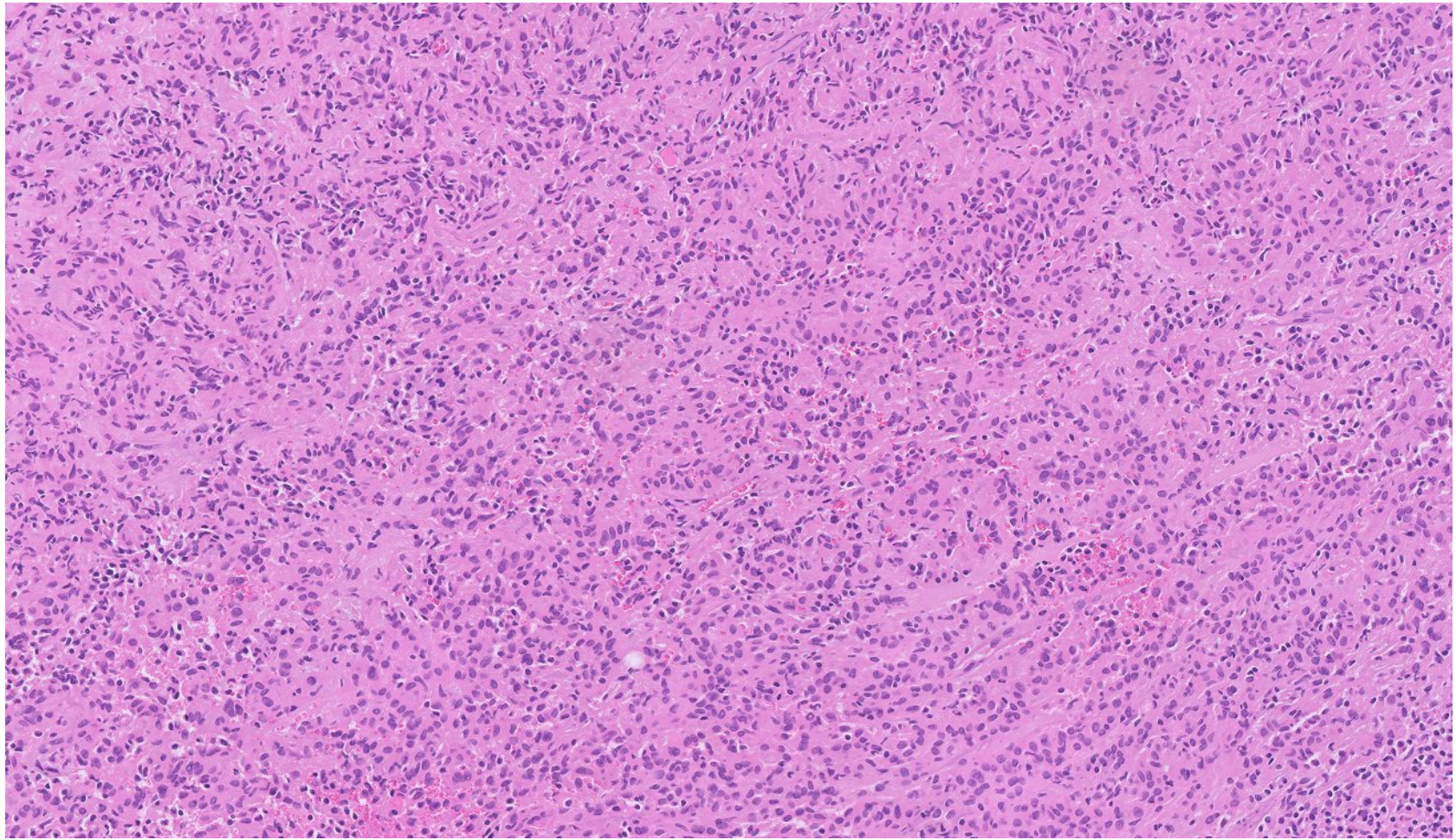


MRI (T1 + C) Axial

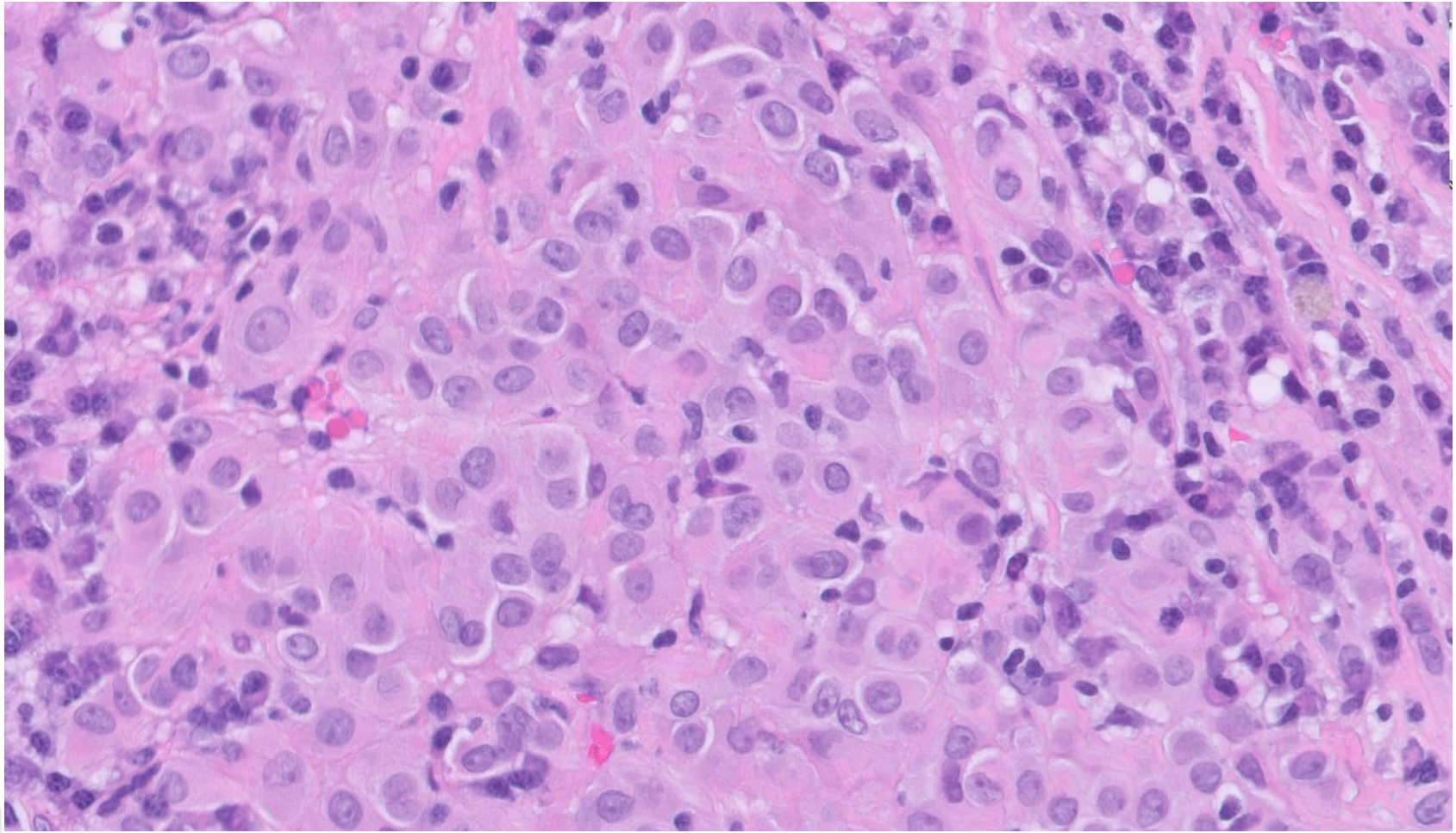


MRI (T1 + C) Coronal

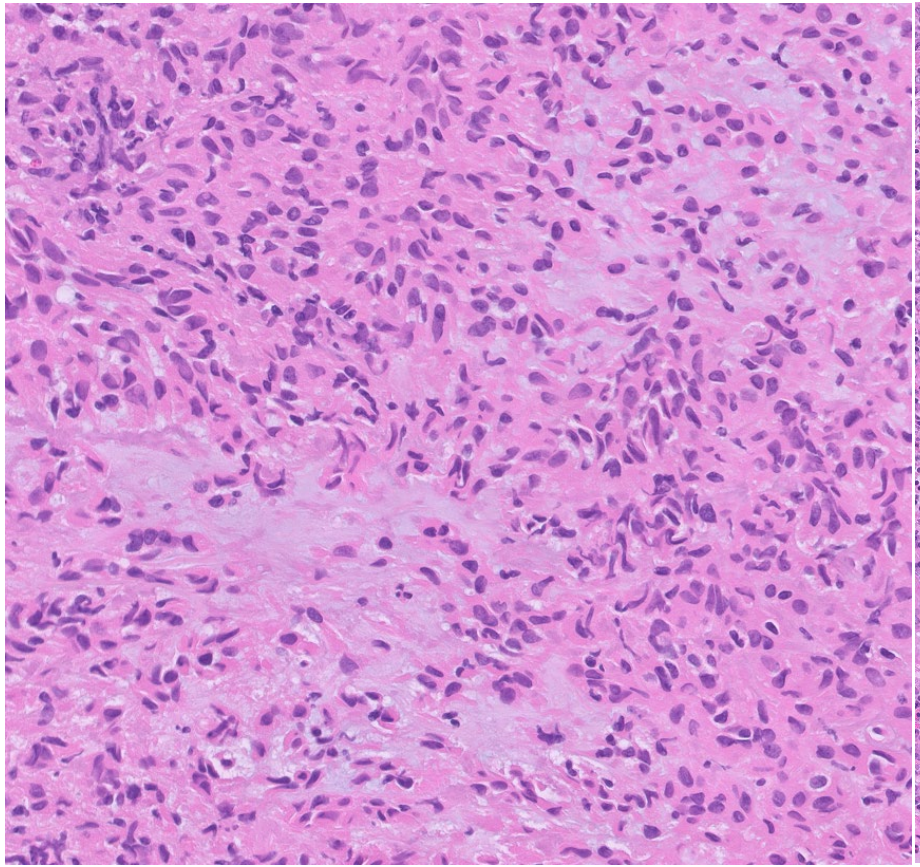
Histology

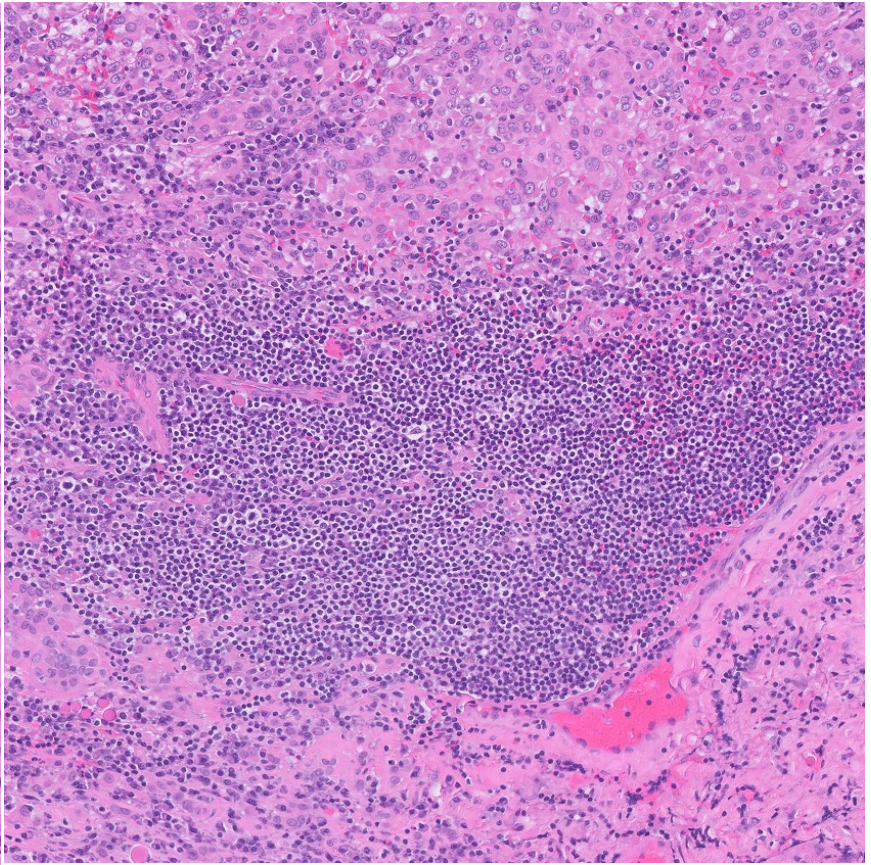


Histology



Histology



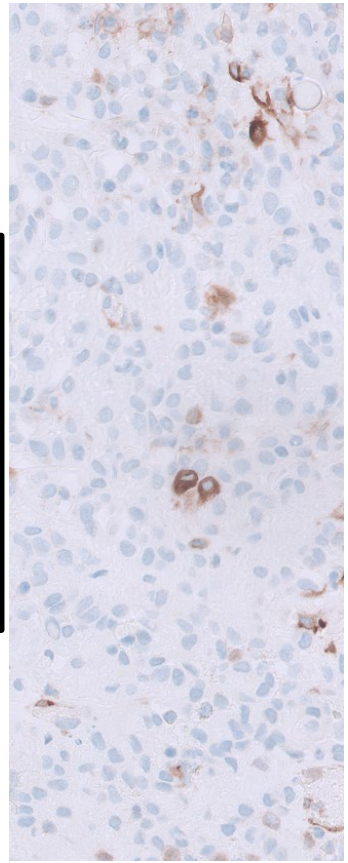


Diagnosis??

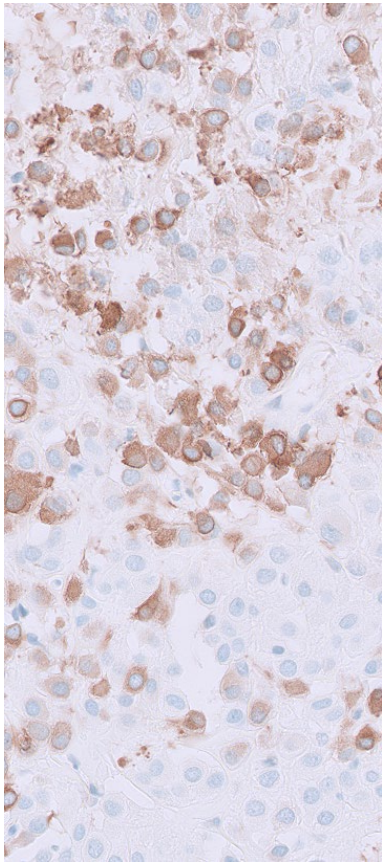
Radiologic differential diagnosis

- Meningioma
- Suprasellar craniopharyngioma
- Germinoma/germ cell tumor
- Granulomatous inflammatory process
- Choroid plexus tumor, ependymoma, hypothalamic glial neoplasm and central neurocytoma are less likely

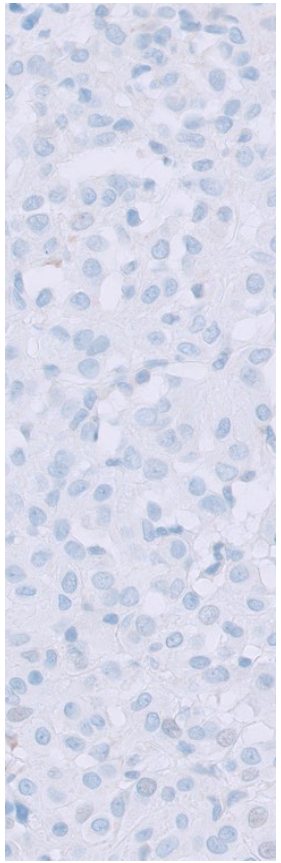
IHC



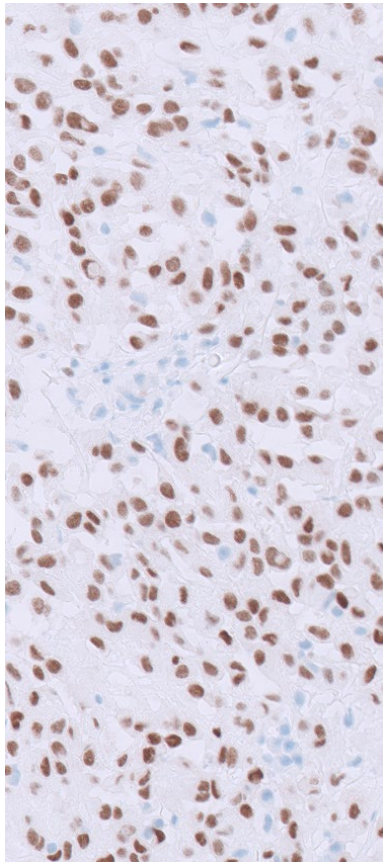
SSTR2A



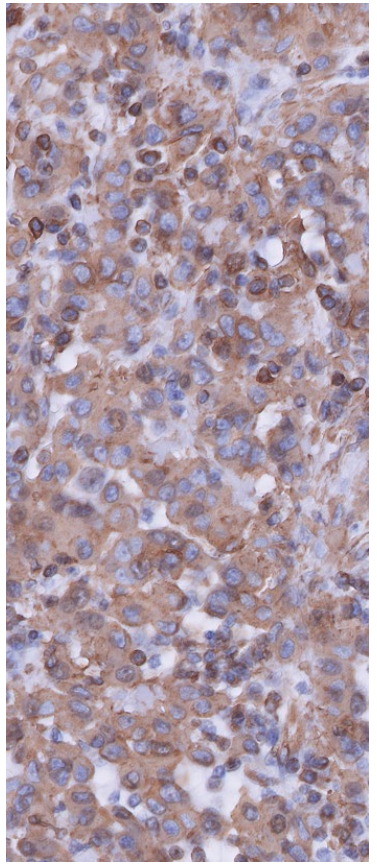
GFAP



Olig2

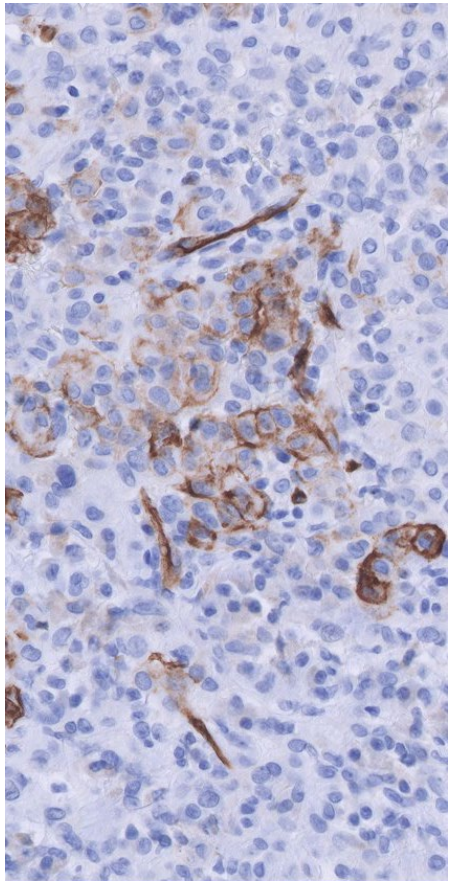


TTF-1

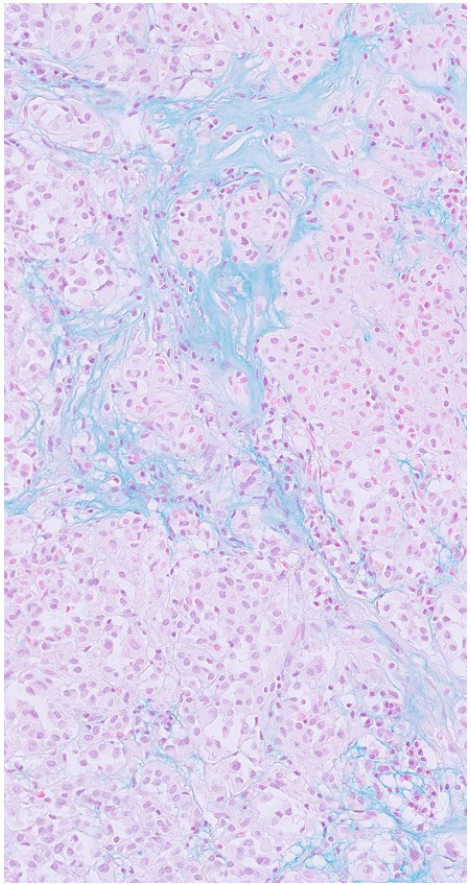


Vimentin

IHC



CD34



Alcian Blue

EMA: Patchy positive
S100: Patchy positive

PR: Negative
STAT6: Negative

Ki67: 2-3%

Molecular Studies

- A pathogenic P.D463H mutation was detected in the PRKCA gene by DNA sequencing.

Final Integrated Diagnosis

Chordoid glioma, CNS WHO grade 2.

PRKCA gene mutation detected p.D463H (Seq)

Journal of Neuropathology and Experimental Neurology

Vol. 57, No. 3
March, 1998
pp. 283–290

Third Ventricular Chordoid Glioma: A Distinct Clinicopathologic Entity

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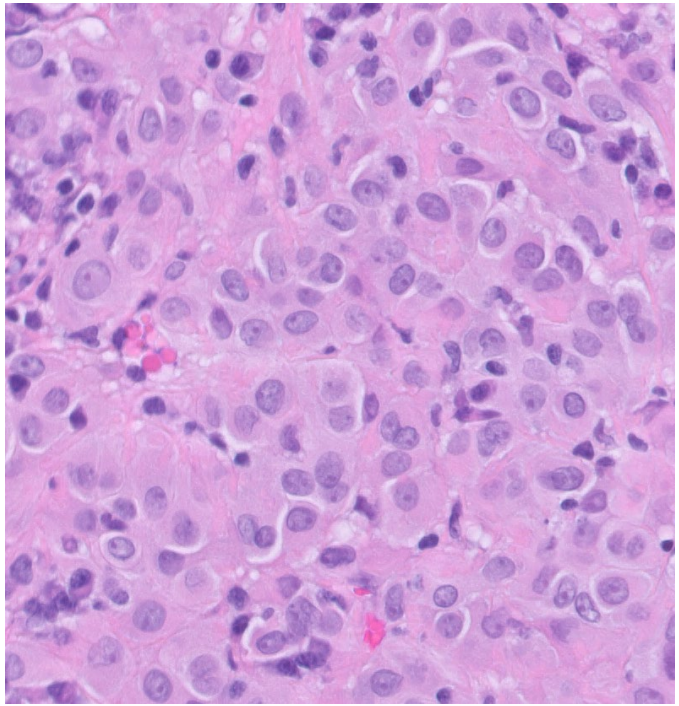
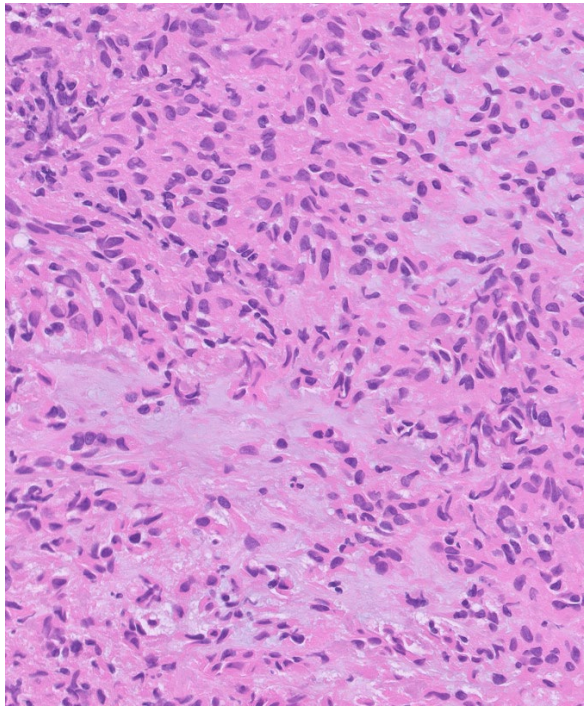
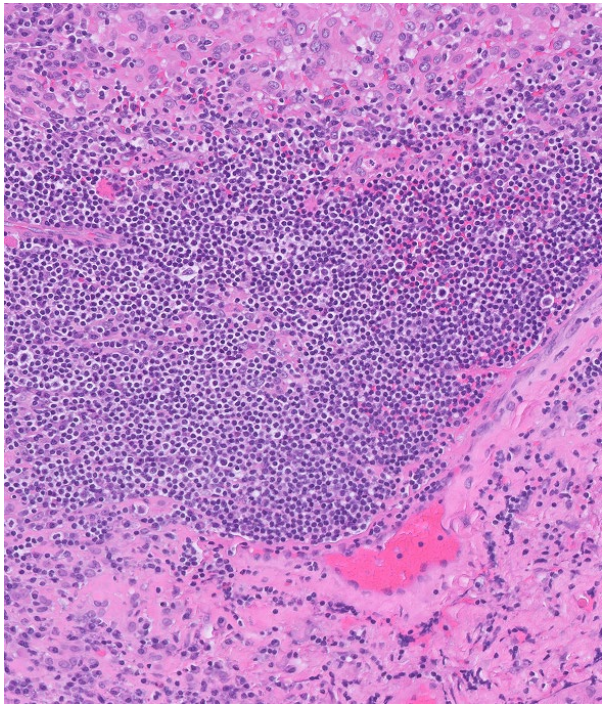
Abstract. We have encountered a series of 8 third ventricular neoplasms with a distinctive chordoid appearance that appear to represent a clinicopathologic entity. The tumors occurred in 7 females and 1 male, ranging in age from 31 to 70 years. In all cases, imaging studies showed a large well-circumscribed third ventricular mass; a cystic component was noted in 2. The tumors consisted of cords and clusters of cohesive, oval-to-polygonal epithelioid cells with abundant eosinophilic cytoplasm, relatively uniform round-to-oval nuclei, and inconspicuous nucleoli. Mitotic activity was absent. The stroma consisted of scant, coarse fibrillar processes, as well as prominent, slightly basophilic, extracellular mucin resembling that in chordomas. Throughout the tumor, and surrounding its well-defined borders, were infiltrates of mature lymphocytes and plasma cells. Russell bodies were prominent in the latter. Adjacent brain tissue showed reactive changes with gliosis and numerous Rosenthal fibers.

Immunohistochemically, tumor cells were strongly reactive for GFAP and vimentin, but negative or only weakly staining for EMA. The MIB-1 labeling index was approximately 1%. Ultrastructural examination of 4 cases revealed focal microvilli, scattered "intermediate" junctions, and focal basal lamina formation. Neither desmosomes nor cilia were seen. Total resections were achieved in 2 cases; only subtotal removals were achieved in 6. Subsequent tumor enlargement was noted in 3 of the 6 patients with incomplete resection, and of these, two died at post-operative intervals of 8 months and 3 years. The other patient survives 4 years post-operatively with stable residual disease. Of the 2 patients with total resection, 1 was lost to follow-up; the other, during a brief follow-up period, did well without evidence of recurrence.

Histology







Diagnostic criteria for chordoid glioma (CNS WHO, 2021)

Essential:
A glial neoplasm with chordoid features located in the anterior third ventricle
Desirable:
Nuclear thyroid transcription factor 1 (TTF1) immunopositivity
PRKCA p.D463H mutation or DNA methylation profile aligning with chordoid glioma

Differential Diagnoses of Chordoid Glioma

	Chordoid glioma	Chordoma	Meningioma (chordoid or lymphoplasmacytic)
Location	Anterior portion of the third ventricle.	Axial skeleton (skull base and the sacrococcygeal region) .	Usually supratentorial.
Histology	Clusters and cords of epithelioid cells within a variably mucinous stroma. Lymphoplasmacytic infiltrate.	Cords or ribbons separated by a myxoid matrix. Physaliphorous cells.	Small foci of whorl formation and psammoma bodies.
IHC	GFAP ++ TTF1 ++ CD34++ Vimentin ++ EMA variable S100 Variable	Brachyury ++ Cytokeratins ++ GFAP – CD34 –	SSTR2A ++ EMA ++ GFAP – CD34 – TTF1 –

(Brat et al, 1998)

(Sangoi et al, 2009)

Diagnostic Molecular Pathology

ARTICLE

DOI: 10.1038/s41467-018-02826-8 OPEN

A recurrent kinase domain mutation in *PRKCA* defines chordoid glioma of the third ventricle

Benjamin Goode[1], Gourish Mondal[1], Michael Hyun[1], Diego Garrido Ruiz[2], Yu-Hsiu Lin[3], Jessica Van Ziffle[1,4], Nancy M. Joseph[1,4], Courtney Onodera[4], Eric Talevich[4], James P. Grenert[1,4], Iman H. Hewedi[5], Matija Snuderl[6], Daniel J. Brat[7], Bette K. Kleinschmidt-DeMasters[8], Fausto J. Rodriguez[9], David N. Louis[10], William H. Yong[11], M. Beatriz Lopes[12], Marc K. Rosenblum[13], Nicholas Butowski[14], Tarik Tihan[1], Andrew W. Bollen[1], Joanna J. Phillips[1,14], Arun P. Wiita[2,3], Iwei Yeh[1,4], Matthew P. Jacobson[2], Boris C. Bastian[1,4], Arie Perry[1,14] & David A. Solomon[1,4]

ARTICLE

DOI: 10.1038/s41467-018-04622-w OPEN

A recurrent point mutation in *PRKCA* is a hallmark of chordoid gliomas

Shai Rosenberg[1,2], Iva Simeonova[1], Franck Bielle[1,3], Maite Verreault[1], Bertille Bance[1], Isabelle Le Roux[1], Mailys Daniau[1], Arun Nadaradjane[1], Vincent Gleize[1], Sophie Paris[1], Yannick Marie[1,4], Marine Giry[1], Marc Polivka[5], Dominique Figarella-Branger[6], Marie-Hélène Aubriot-Lorton[7], Chiara Villa[8], Alexandre Vasiljevic[9], Emmanuèle Lechapt-Zalcman[10], Michel Kalamarides[1,11], Ariane Sharif[12], Karima Mokhtari[1,3], Stefano Maria Pagnotta[13,14], Antonio Iavarone[14,15], Anna Lasorella[14,16], Emmanuelle Huillard[1] & Marc Sanson[1,4,17,18]

The p.D463H missense mutation in the *PRKCA* gene is nearly ubiquitous in chordoid glioma, having been found in 28 of 29 tumors studied to date.

The *PRKCA* p.D463H mutation is a diagnostic hallmark for chordoid glioma.

Acknowledgments

- Robert Bell, MD, MHS (Indiana University/Neuropathology)
- Kathy Newell, MD (Indiana University/Neuropathology)
- Chunhai Hao, MD, PhD (Indiana University/Neuropathology)
- Devon Jackson, MD (Indiana University/Neuropathology)
- Aaron Cohen-Gadol, MD (Indiana University/Neurosurgery)
- Edward Dropcho, MD (Indiana University/Neuro-oncology)
- Diane Donegan, MD (Indiana University/Endocrinology)
- Alexander Vortmeyer, MD, PhD (University of Mississippi/Neuropathology)
- Philip Boyer, MD, PhD (East Carolina University/Neuropathology)

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