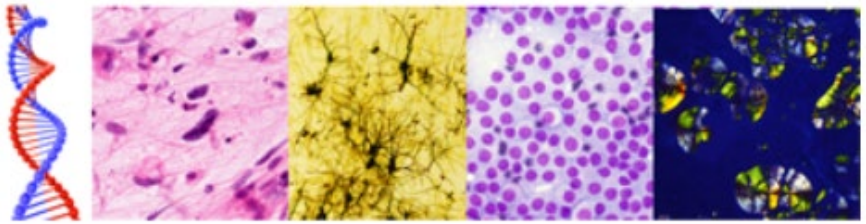
AMERICAN ASSOCIATION OF NEUROPATHOLOGISTS



Case # 6

Diagnostic Slide Seminar 2022

SickKids®

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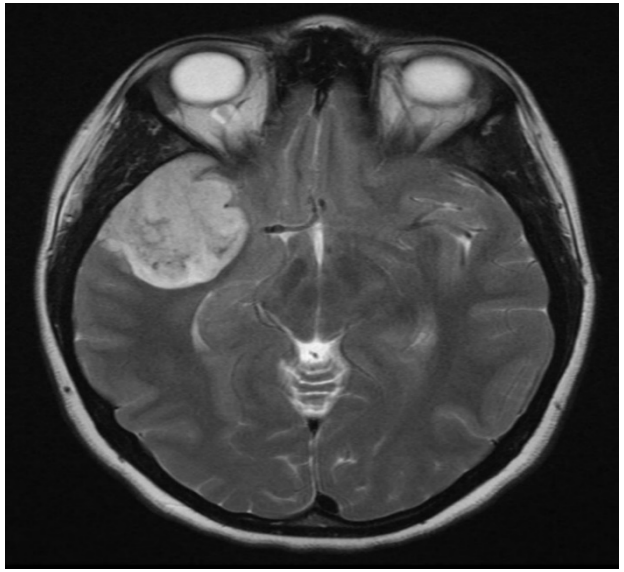
Clinical history

A 38-year-old woman originally presented at age of 23, with a 3-week history of diffuse headache between her eyes.
The MRI showed a well-defined lobulated mass within the right temporal lobe, with stippled enhancement and multiple small foci of calcification.
The patient underwent a partial resection of the lesion

T2



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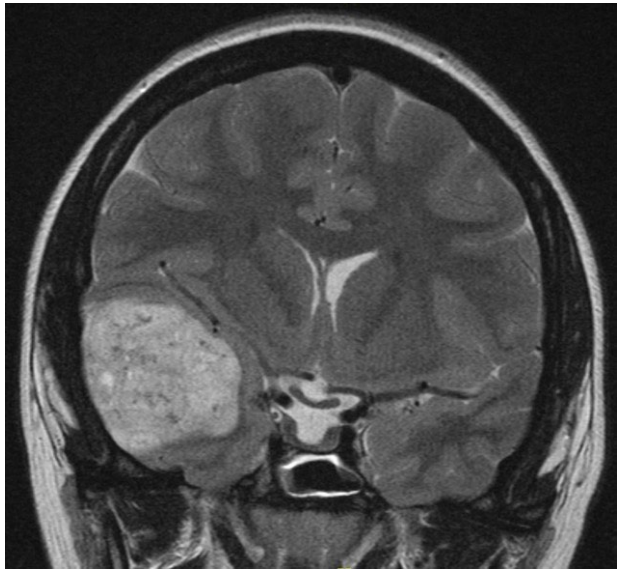
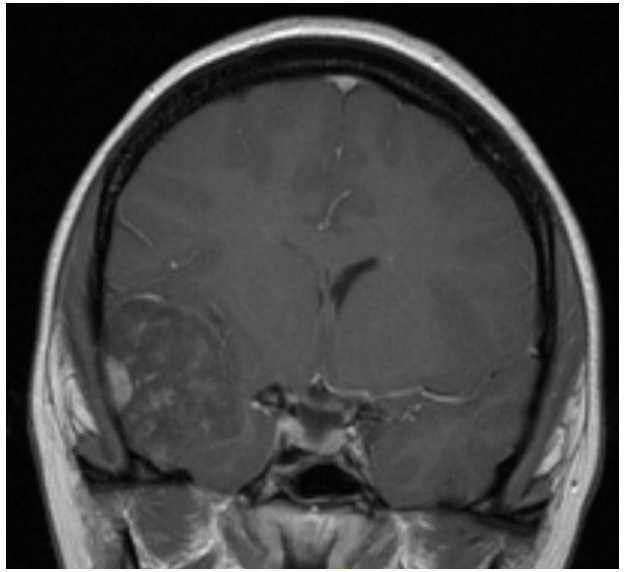
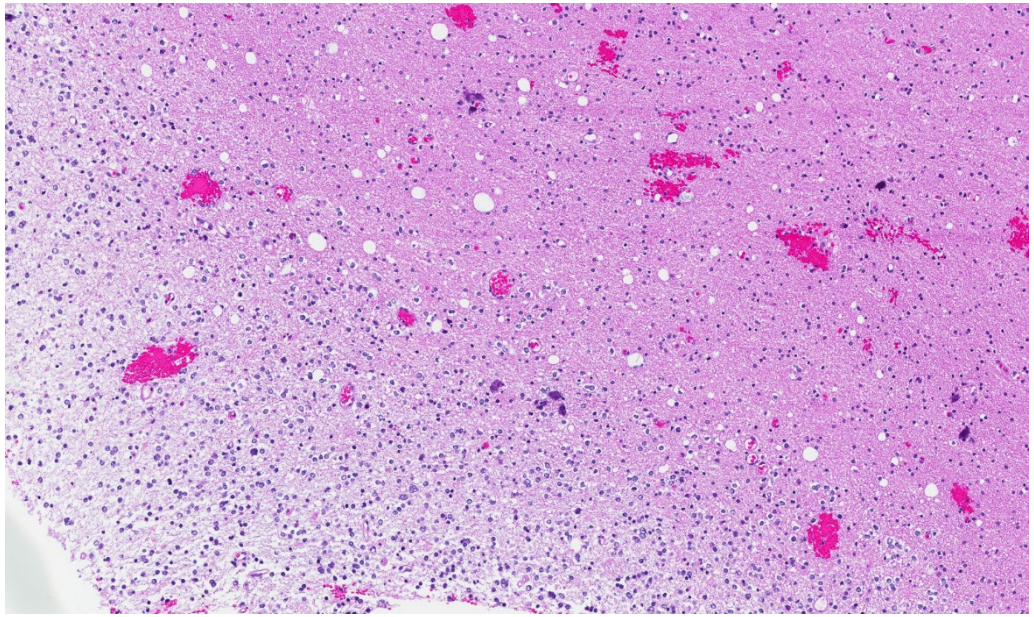
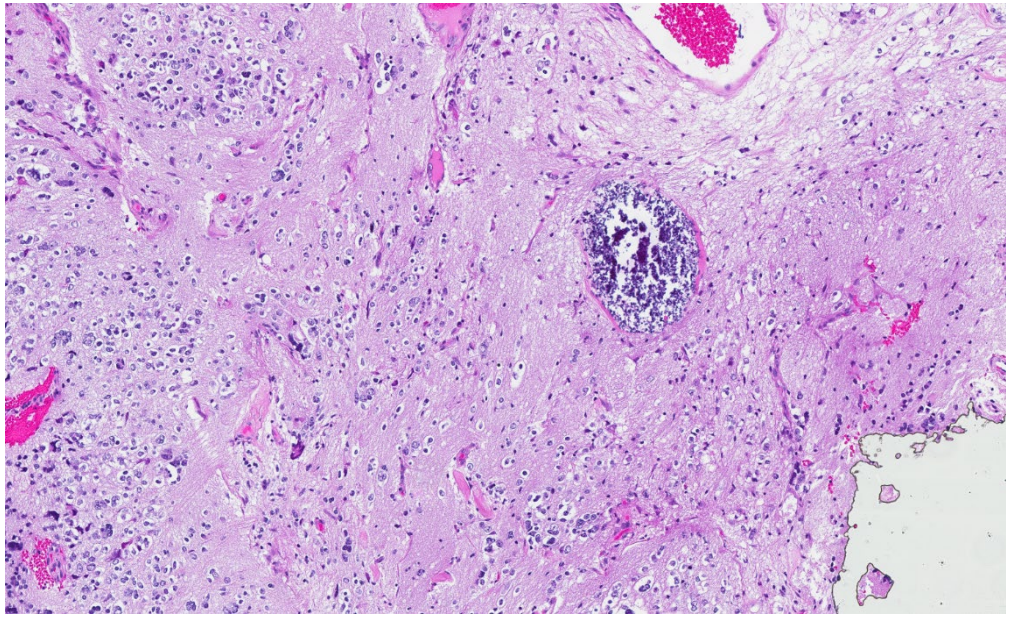


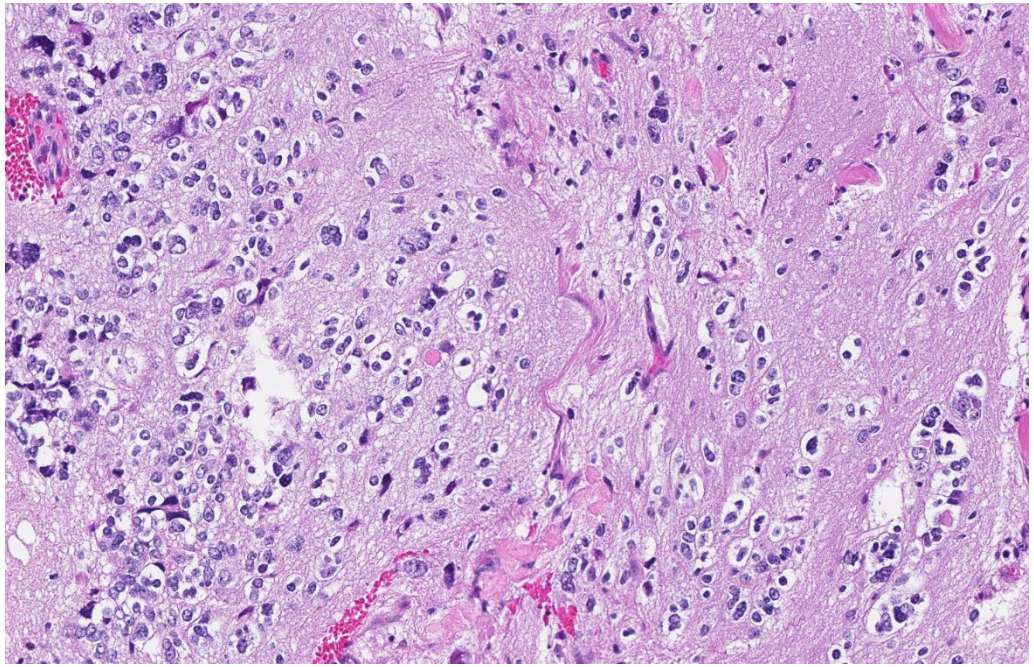
Gadolinium

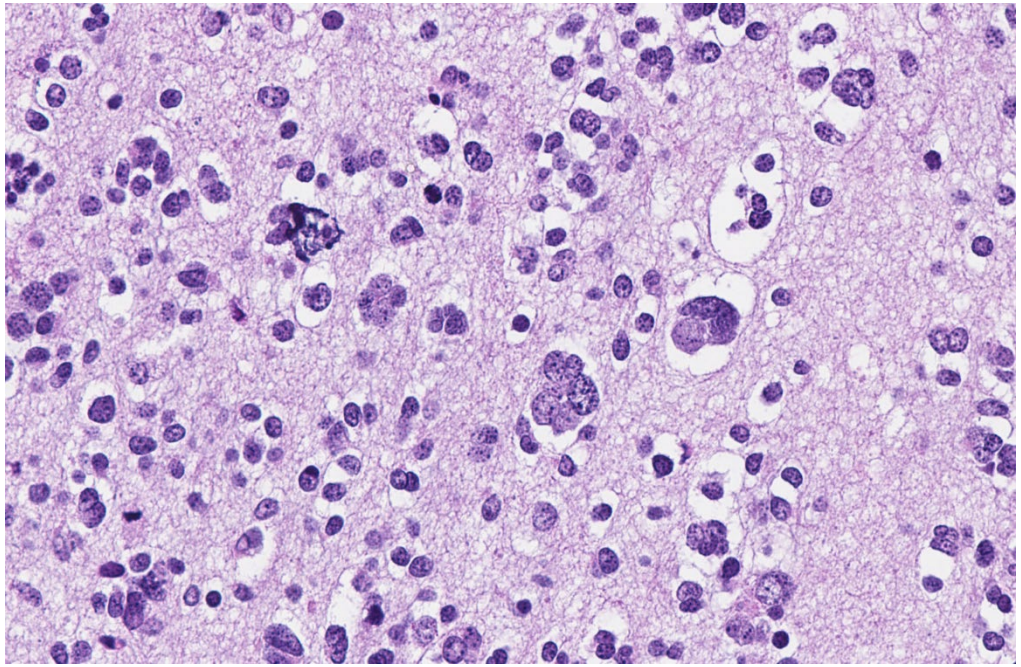


Histologic findings (Diagnosis at that time: Oligodendroglioma)



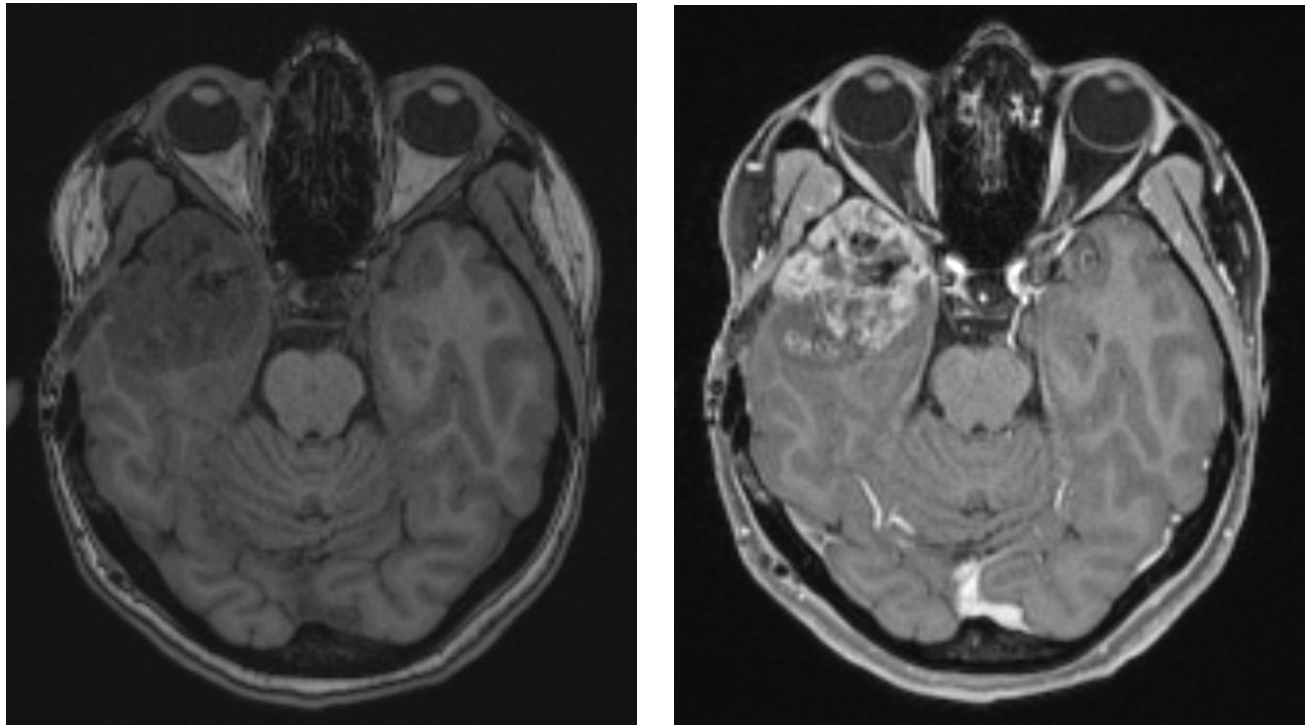




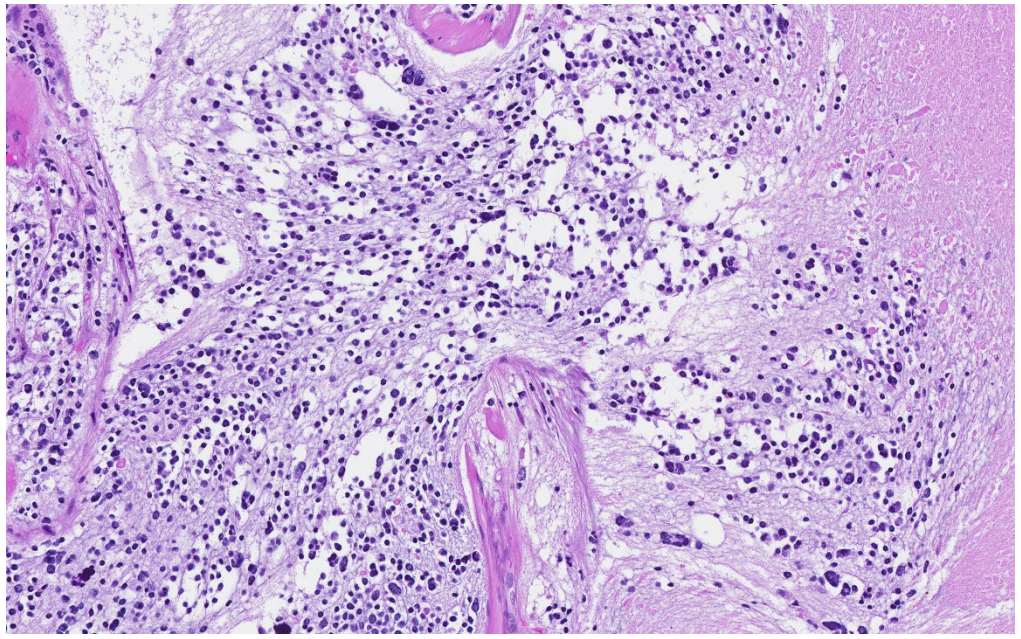


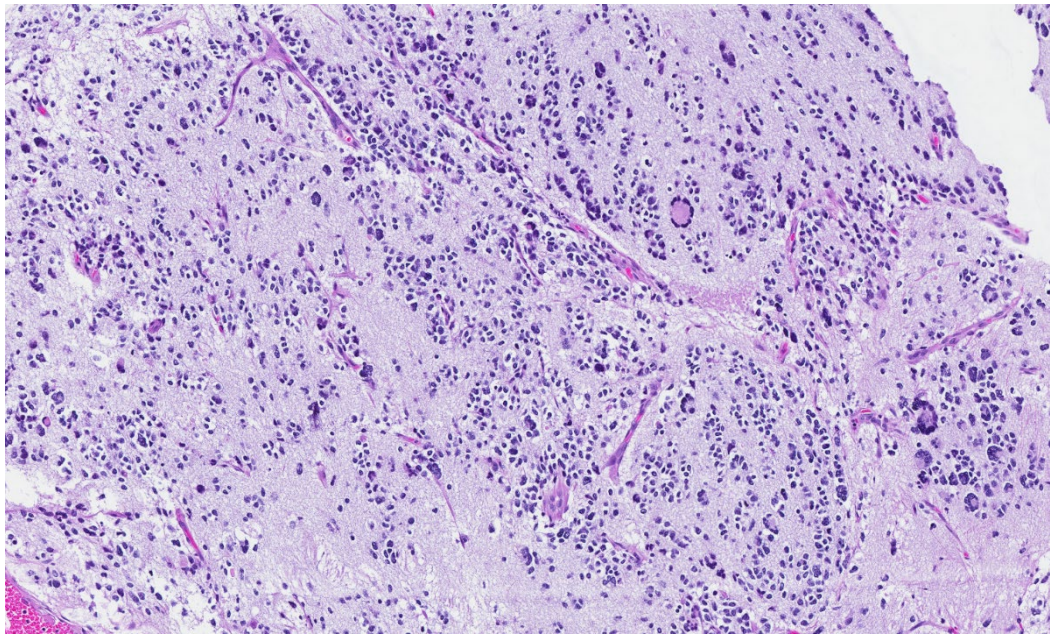
Follow-up

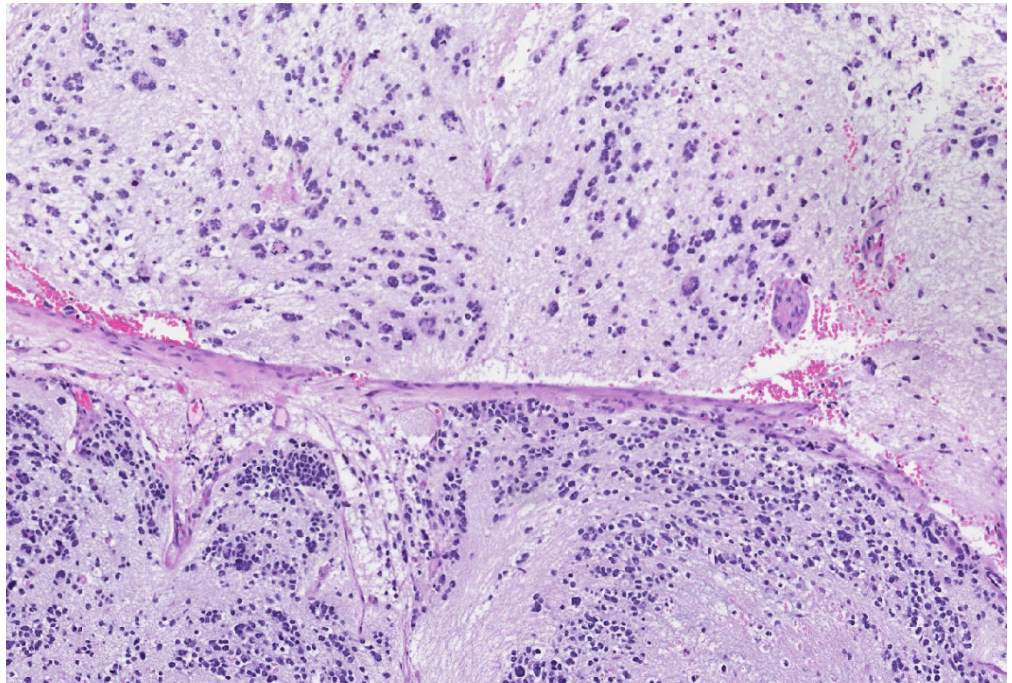
She had a stable clinical course + neuroimaging, without any chemo-radiation therapy
After 15 years, she started having a progressive headache.
The MRI showed an increase of the residual lesion (4.6 cm) with peripheral enhancement and coarse foci of calcification.
The patient underwent a second resection

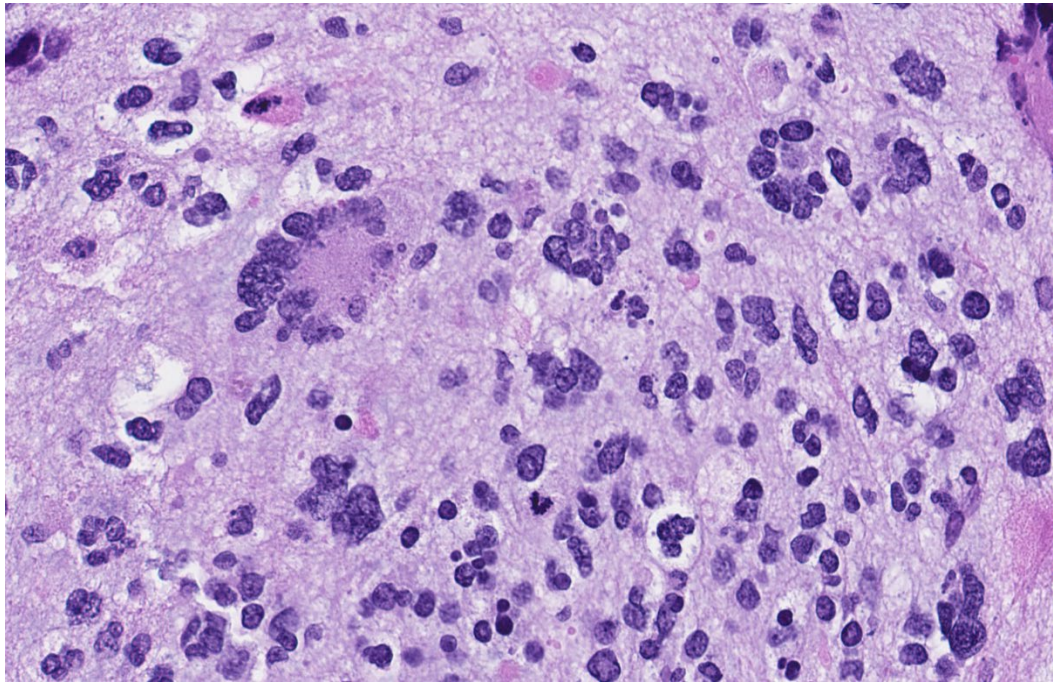


Histologic findings









Diagnosis?

Summary

SIMILAR HISTOLOGICAL FEATURES IN BOTH RESECTIONS

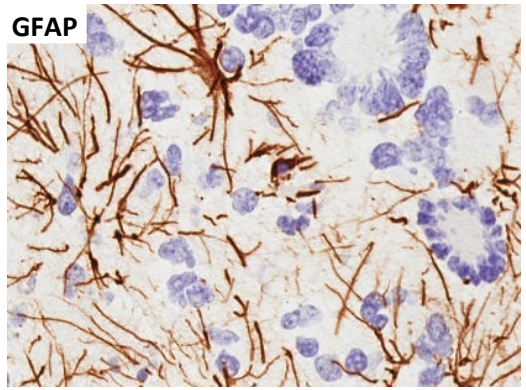
- Variable cellularity
- Tumor cells with small to medium-size round nuclei and clear perinuclear haloes
- Nuclear cluster with large pleomorphic nuclei
- Multinucleated cells
- Neuropil-like island
- Microcalcifications and larger confluent calcifications
- The recurrence shows a higher mitotic activity, a higher proliferation index and foci of necrosis

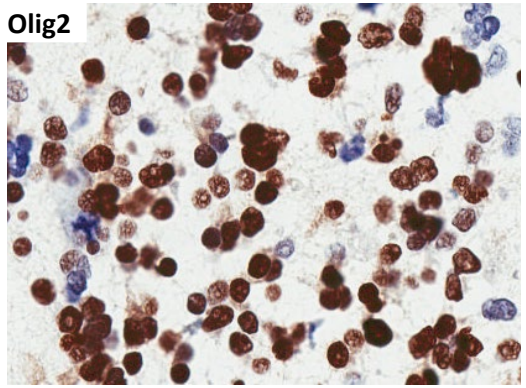
DIFFERENTIAL DIAGNOSIS:

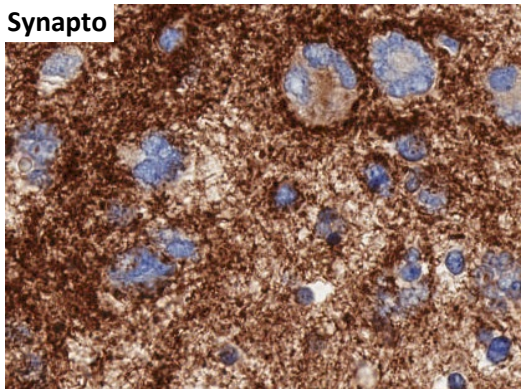
- Adult-type diffuse gliomas
  Astrocytoma, IDH-mutant
  Oligodendroglioma, IDH-mutant and 1p/19q-codeleted
  Glioblastoma, IDH-wildtype
- Glioneuronal tumor

Diagnostic Workup

Immunohistochemical panel	
GFAP	Negative
Olig2	Positive (variable)
Synaptophysin	Positive (variable)
Neu-N	Negative
IDH1	Negative
ATRX	Retained
MMR proteins	Retained
p53	Wild type pattern
BRAF V600E	Negative



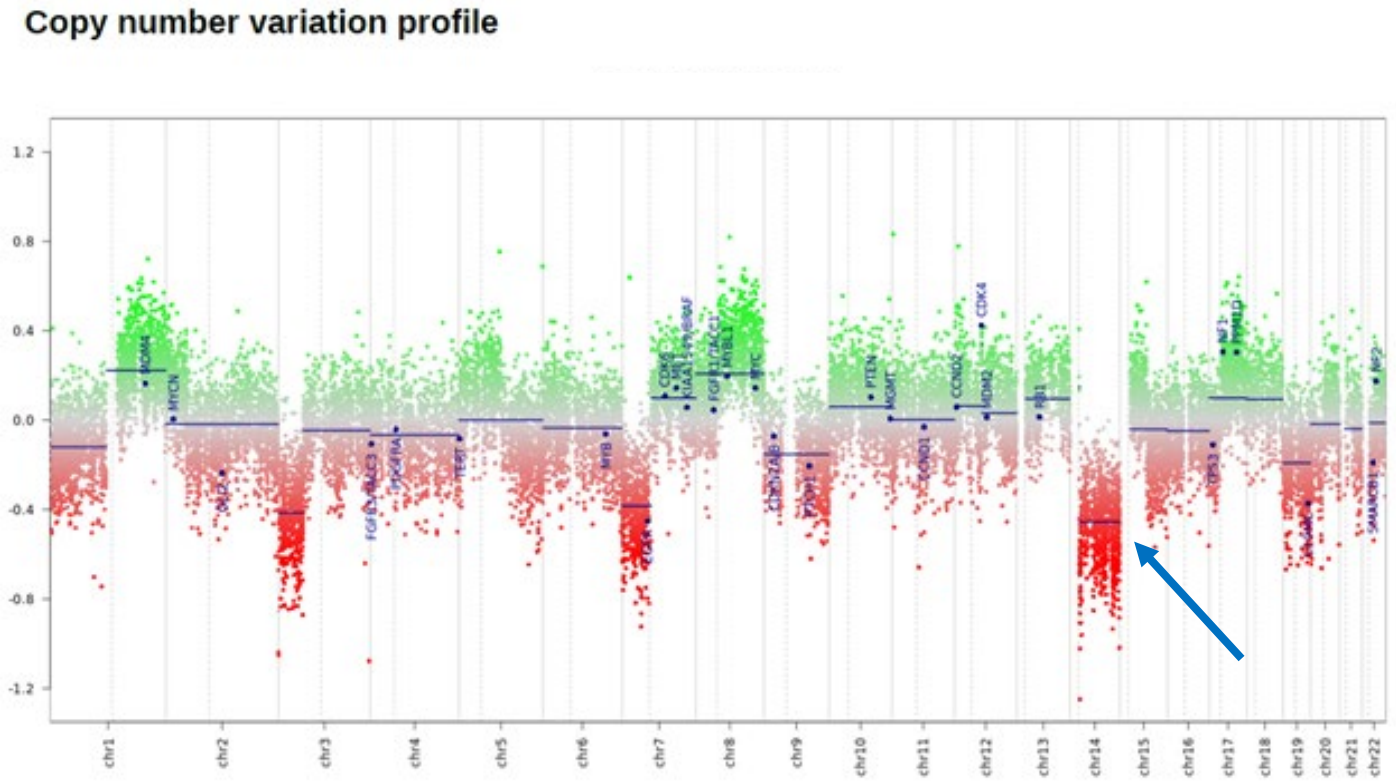




RNA sequencing analysis
No pathogenic SNVs/fusions identified

Methylation profile

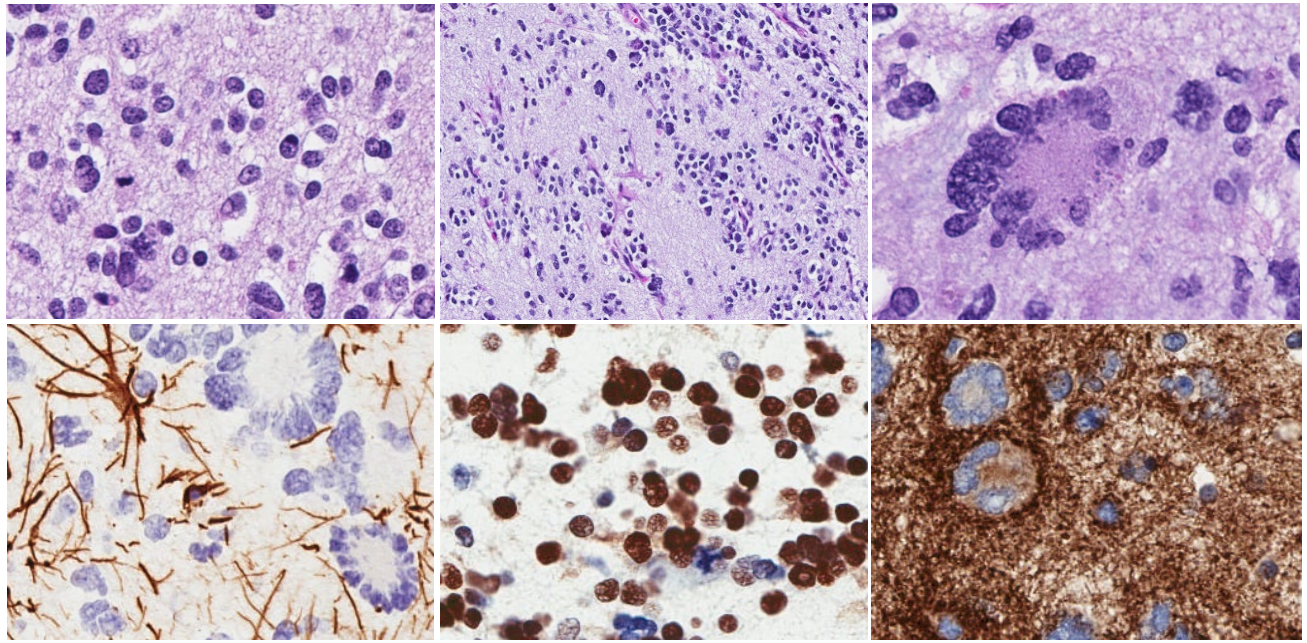
- **“Diffuse glioneuronal tumour with oligodendroglioma-like features and nuclear clusters” (DGONC)"** and the Copy Number Profile generated by the methylation analysis showed the characteristic monosomy of chromosome 14



DGONC

- Novel entity provisionally designated “diffuse glioneuronal CNS tumour with oligodendroglioma-like features and nuclear clusters” (DGONC)
- Predominantly occurs in pediatric patients (median: 9 years), located in the cerebral hemispheres, preferentially in the temporal lobes
- Histological and immunohistochemical profile overlaps with other CNS tumor entities:

- Isomorphic, round nuclei with oligodendroglioma-like perinuclear haloes, diffuse infiltration, neuropil-like islands, nuclear clusters
- GFAP-negativity, Olig2 and synaptophysin-positivity



DGONC

- Unknown oncogenic events or mechanisms leading to the occurrence of this tumor
  - RNA negative sequencing in our case

- It is **methylation-defined** glioneuronal CNS tumor class; **monosomy 14 (~100%)** is a hallmark - variable gain of 1q (26%), 17q (58%), and loss of 19q (35%)

- The literature on prognosis of this entity is limited: favourable clinical course despite many of the original histological diagnoses were of high-grade lesions
  - 5-year OS: 86%, median OS of 2.2 years (range 3 months – 8 years) →based on 12 cases

- Our case has the longest reported FU (15-year) and supports a long-term indolent behavior , even with no chemo or radiotherapy → outcome , currently under careful FU, with no therapy

Take home messages

- It is important to recognize DGONC – main dd from adult-type diffuse glioma- because of its good clinical behavior, long survival without therapy

- Despite it being a methylation-based diagnosis, its characteristic morphology and immunophenotype should make one think of this diagnosis and suggests a specific diagnostic workup

Thank you

References

- Deng et al. ”Diffuse glioneuronal tumour with oligodendroglioma-like features and nuclear clusters (DGONC) – a molecularly defined glioneuronal CNS tumour class displaying recurrent monosomy 14”

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- Pickles et al. “A case series of Diffuse Glioneuronal Tumours with Oligodendroglioma-like features and Nuclear Clusters (DGONC)”

  Neuropathol Appl Neurobiol. 2021 Apr;47(3):464-467)

- Capper et al. “DNA methylation-based classification of central nervous system tumours”

  Nature. 2018 Mar 22; 555(7697): 469–474