Mass General Brigham

American Association of Neuropathologists (AANP) 2024 Annual Diagnostic Slide Session Case 10

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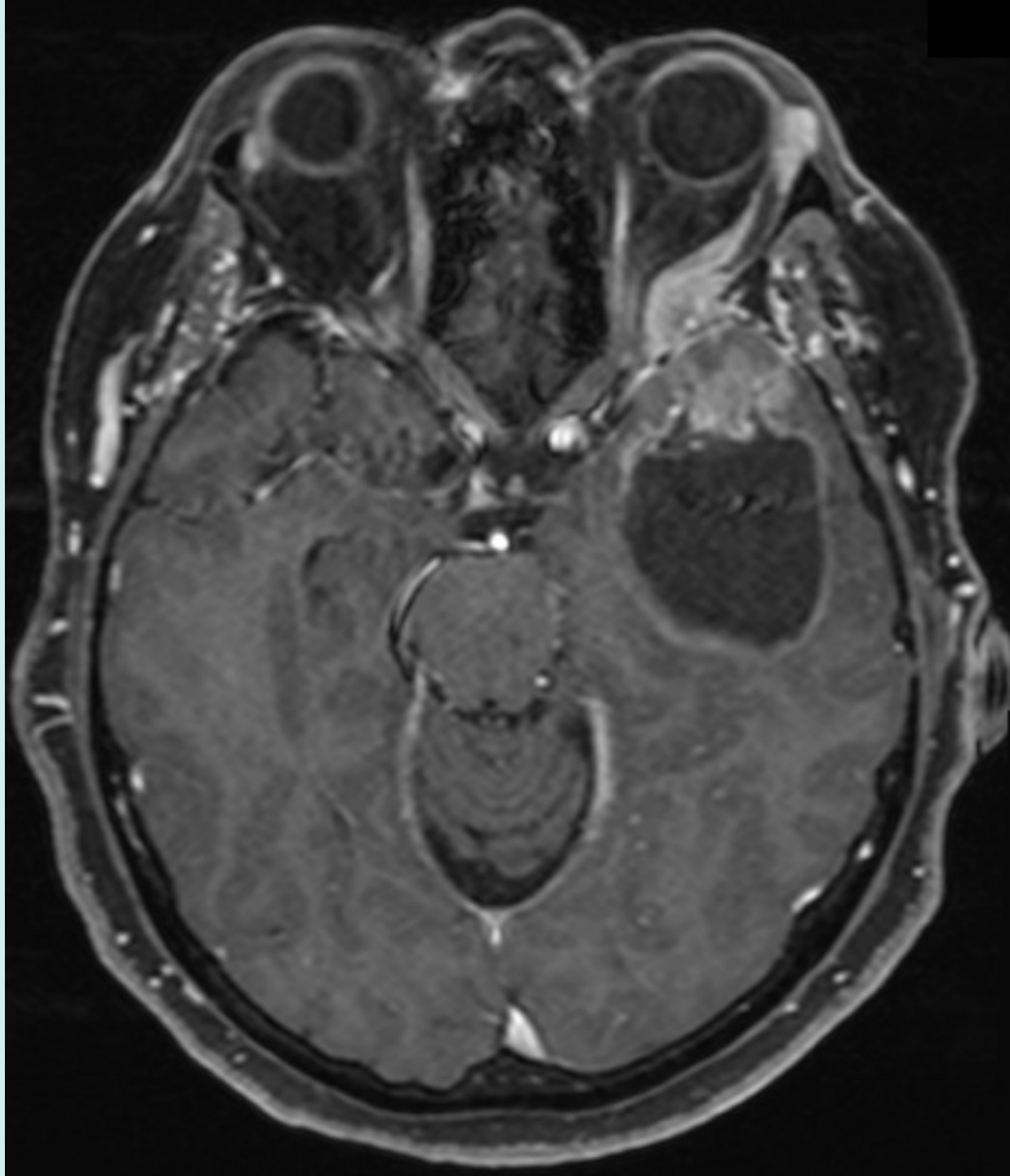
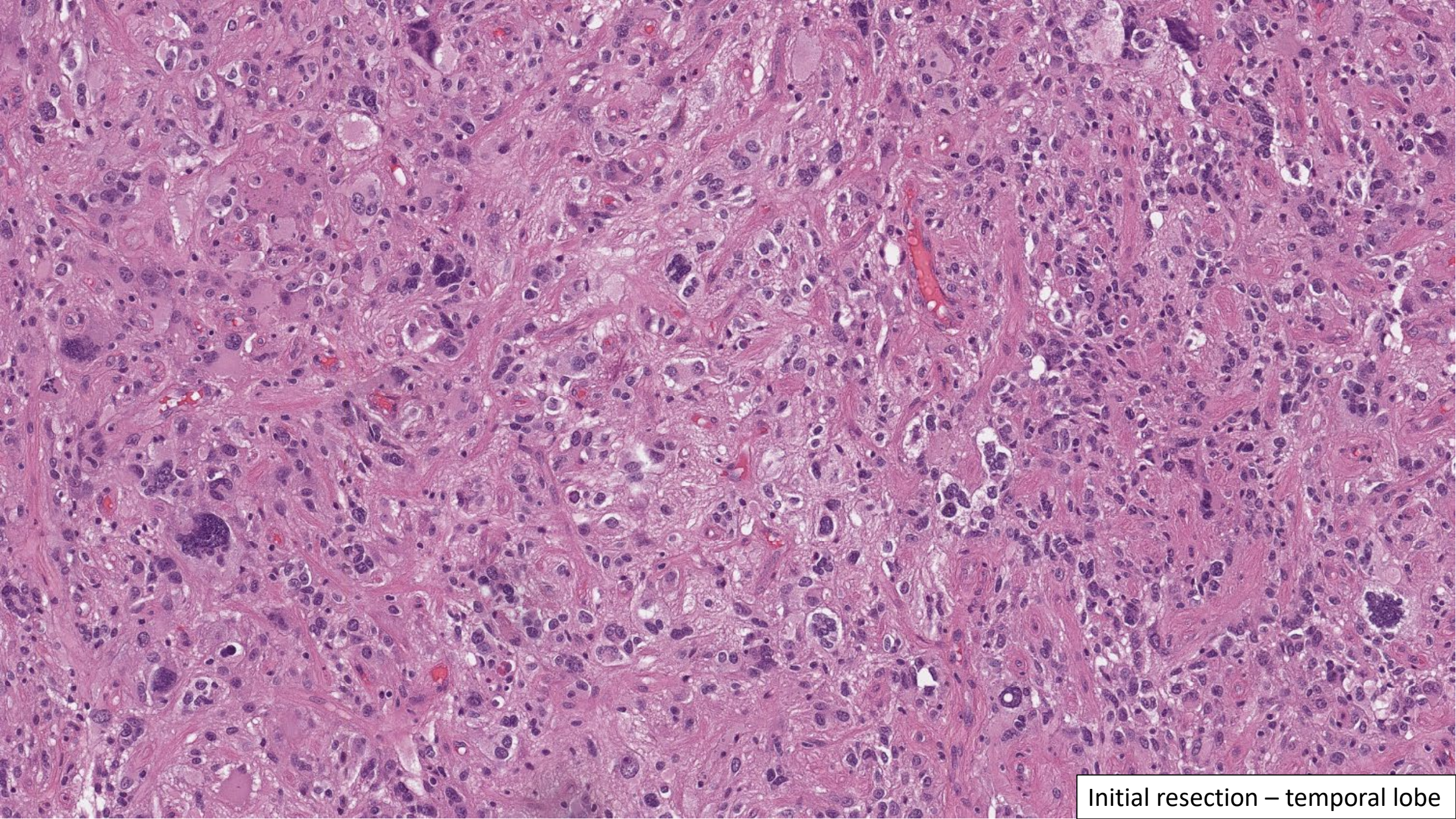
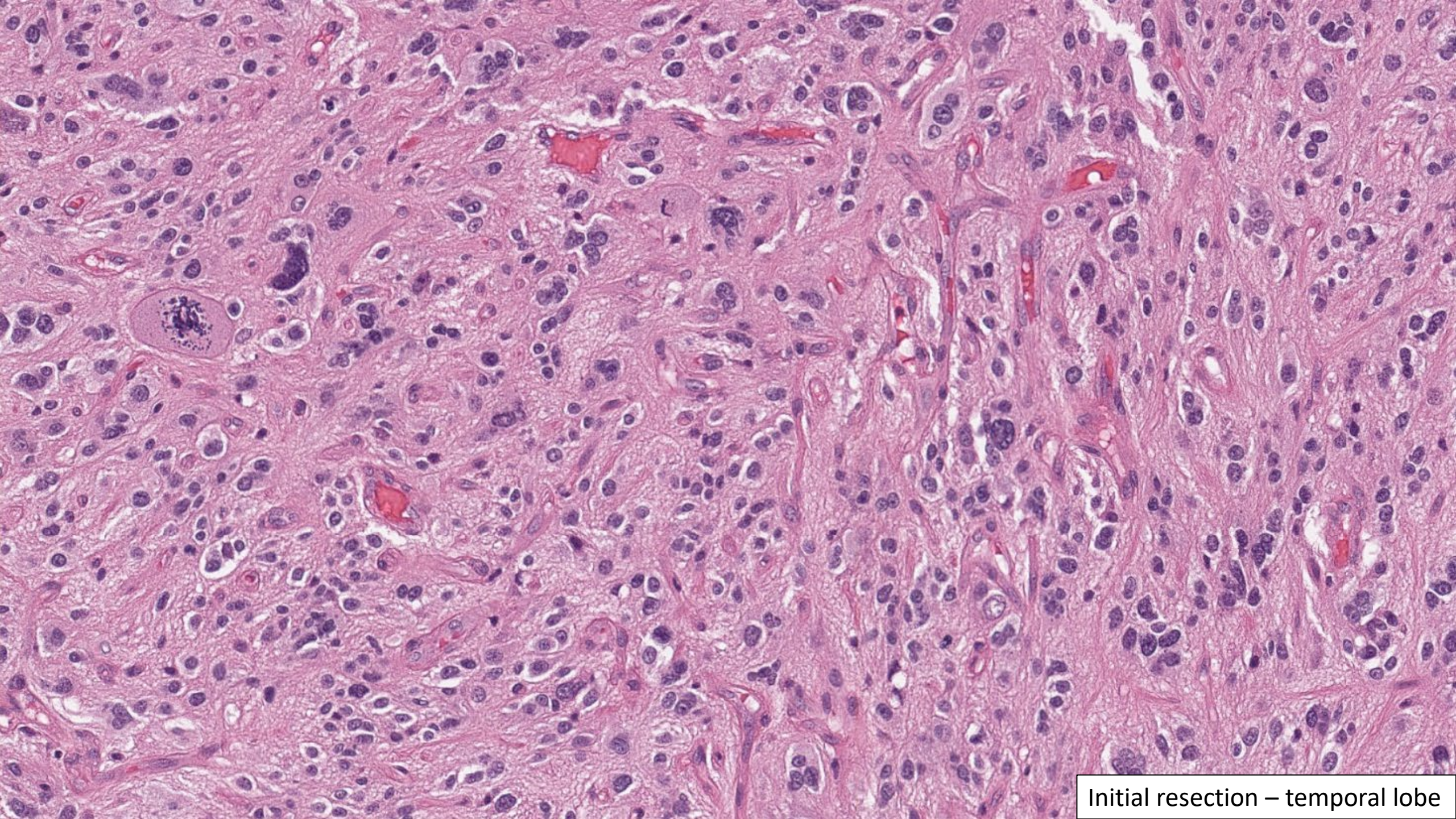
Clinical History

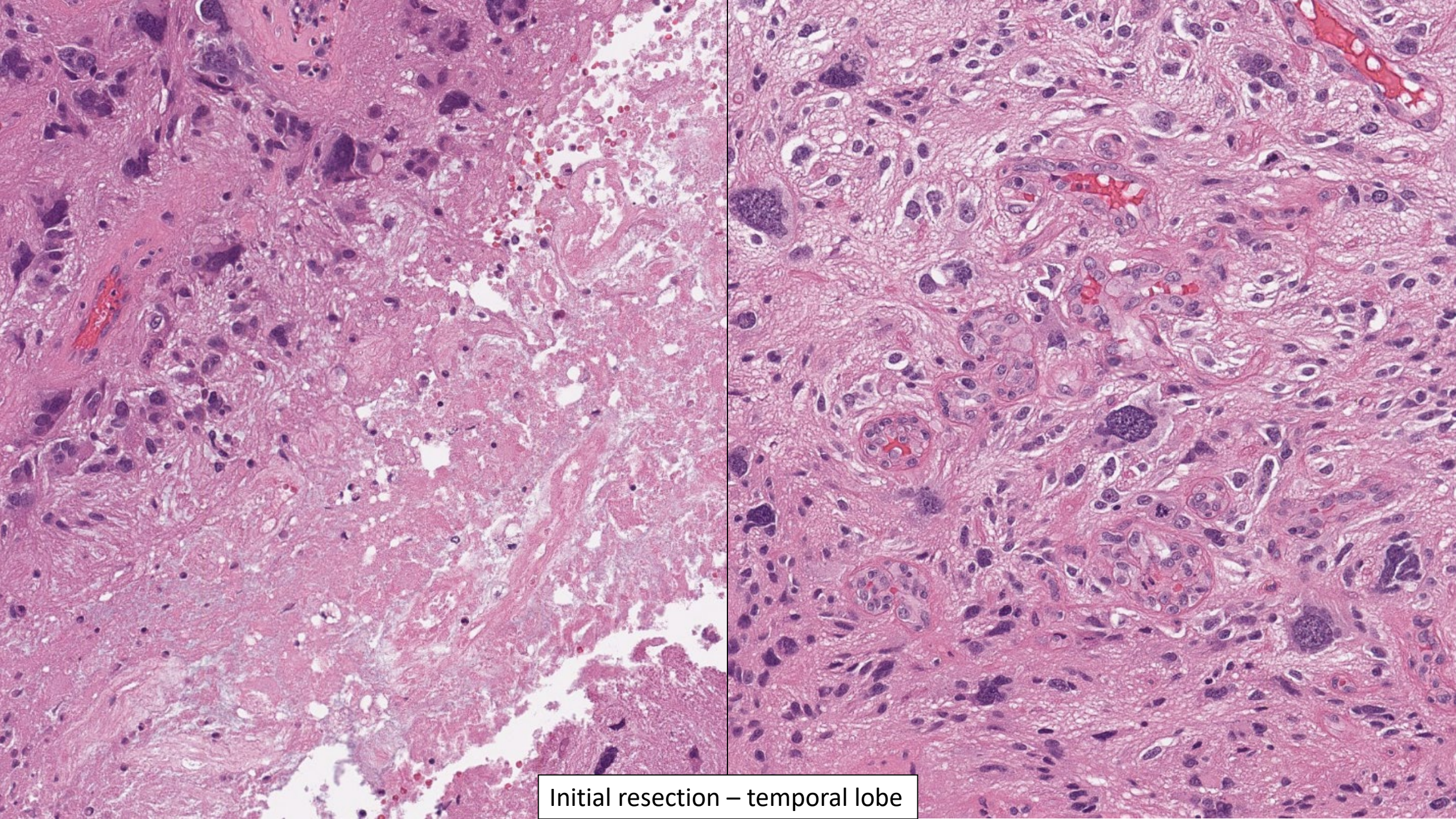
55-year-old woman presented with severe headache and one month of progressive memory decline with word-finding difficulties.

Found to have a large irregularly enhancing mass in the left temporal lobe with extension into the left orbit.

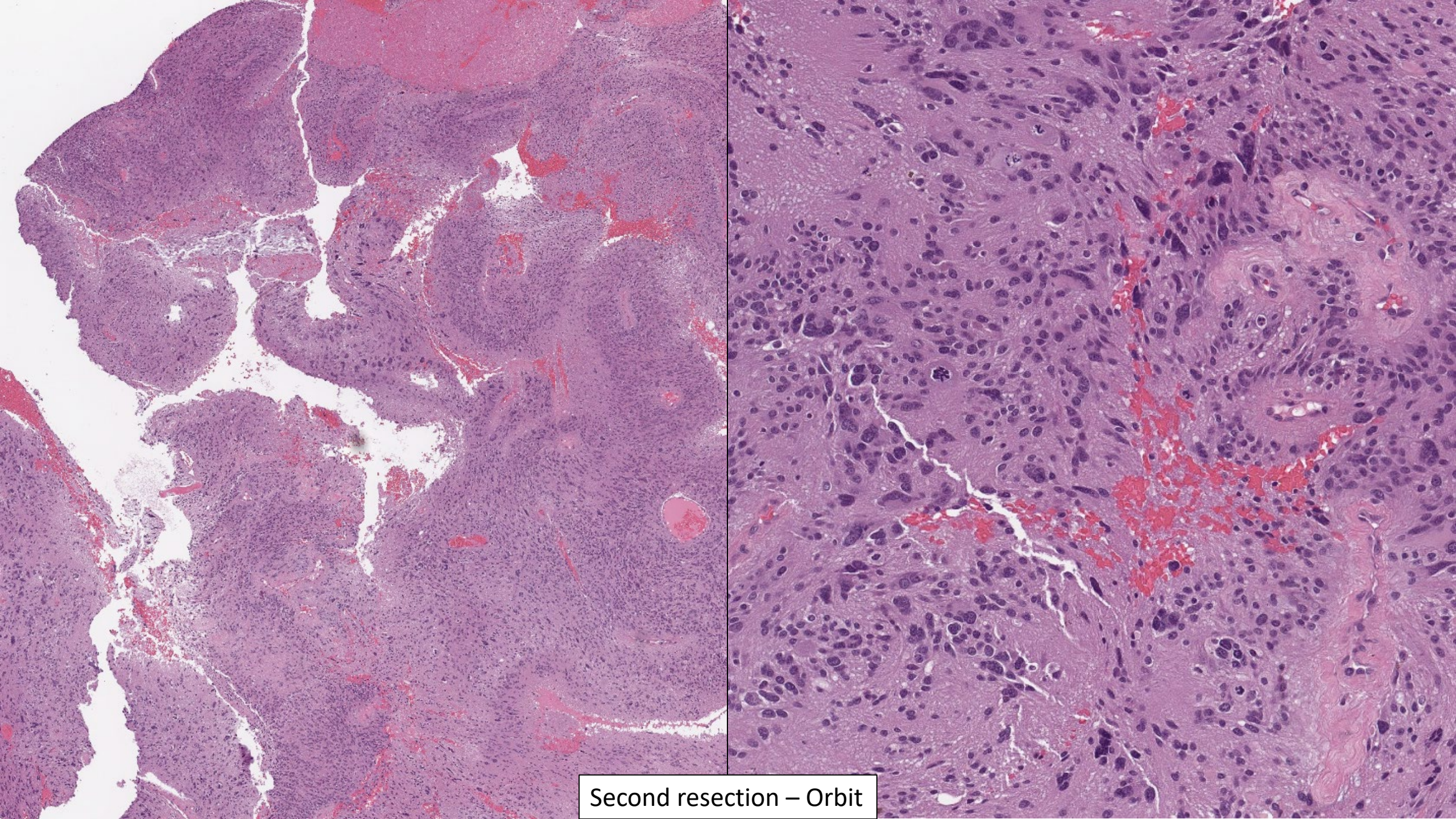



Initial resection – temporal lobe


Initial resection – temporal lobe



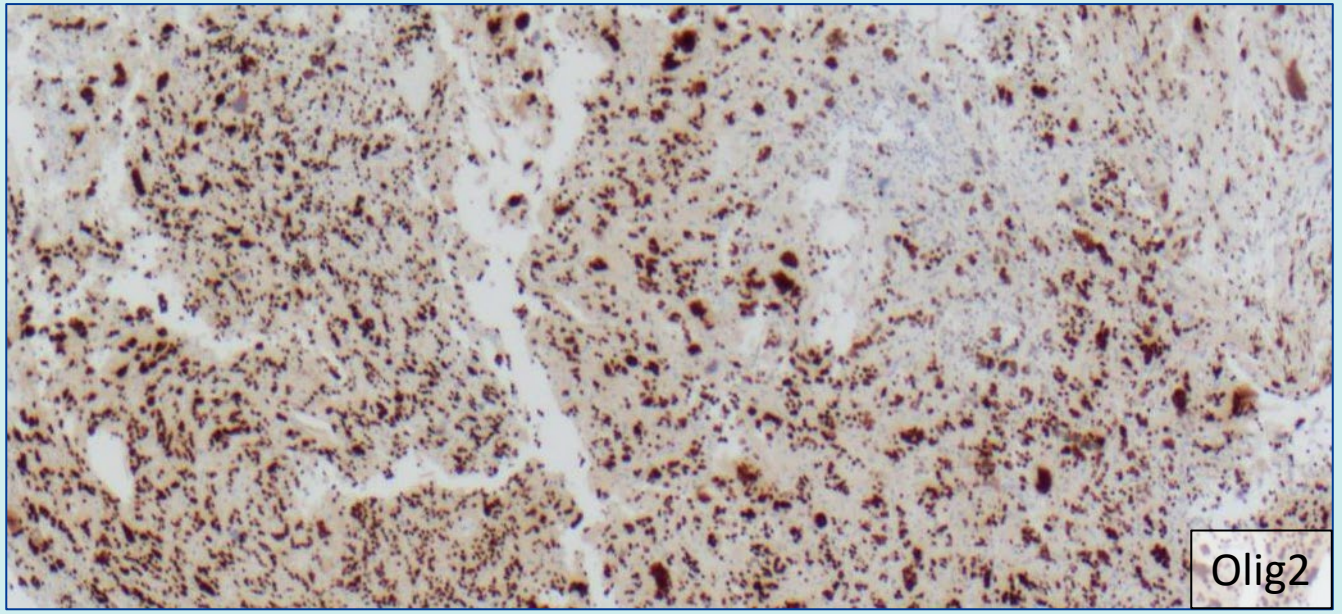
Initial resection – temporal lobe

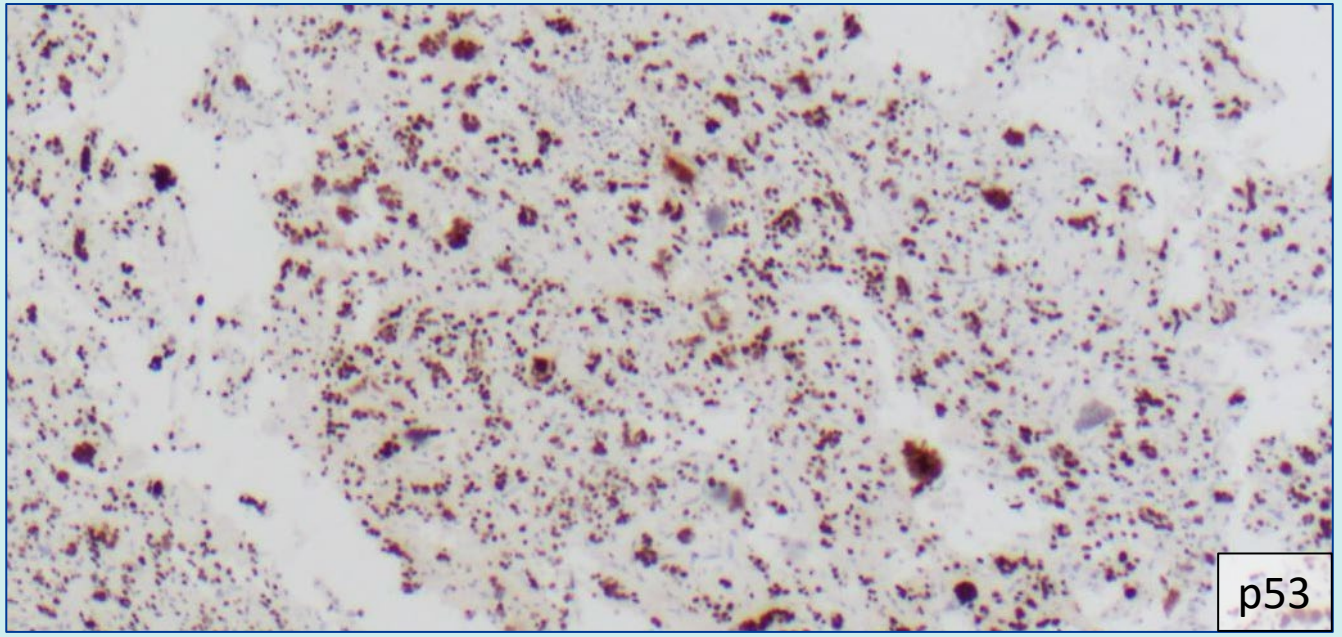


Second resection – Orbit

DIAGNOSIS?

Immunohistochemical staining	
Olig2	Positive
p53	Strong positivity
GFAP	Negative
NeuN	
CD34	
MelanA	
BRAF V600E	
IDH1 R132H	
ATRX	Retained
Reticulin	No increased deposition





Initial resection

Molecular Studies

SNVs: TP53 p.Arg248Trp; MLH1 p.Met359Thr; PIK3R1 p.Thr576del

CNVs: ERBB2 loss, NF2 loss, RNF43 loss

Fusions: NEGATIVE for reportable fusions

Final Diagnosis: Glioblastoma with giant cells, IDH-wildtype, CNS WHO grade 4

DNA METHYLATION-BASED TUMOR CLASSIFICATION	
Methylation Class:	no match

Second resection (2 years later)

DNA METHYLATION-BASED TUMOR CLASSIFICATION	
Molecular Information	prior specimen positive for mutations in TP53, MLH1, and PIK3R1, losses in chromosomes 13 and 17.
Consensus Methylation Profiling Class	High grade glioma with pleomorphic and pseudopapillary features (HPAP) (suggestive scores on both the current and prior specimen for this class)

HIGH-GRADE GLIOMA MATCHING TO METHYLATION CLASS "HIGH-GRADE GLIOMA WITH PLEOMORPHIC AND PSEUDOPAPILLARY FEATURES (HPAP)".

High-grade glioma with pleomorphic and pseudopapillary features (HPAP)

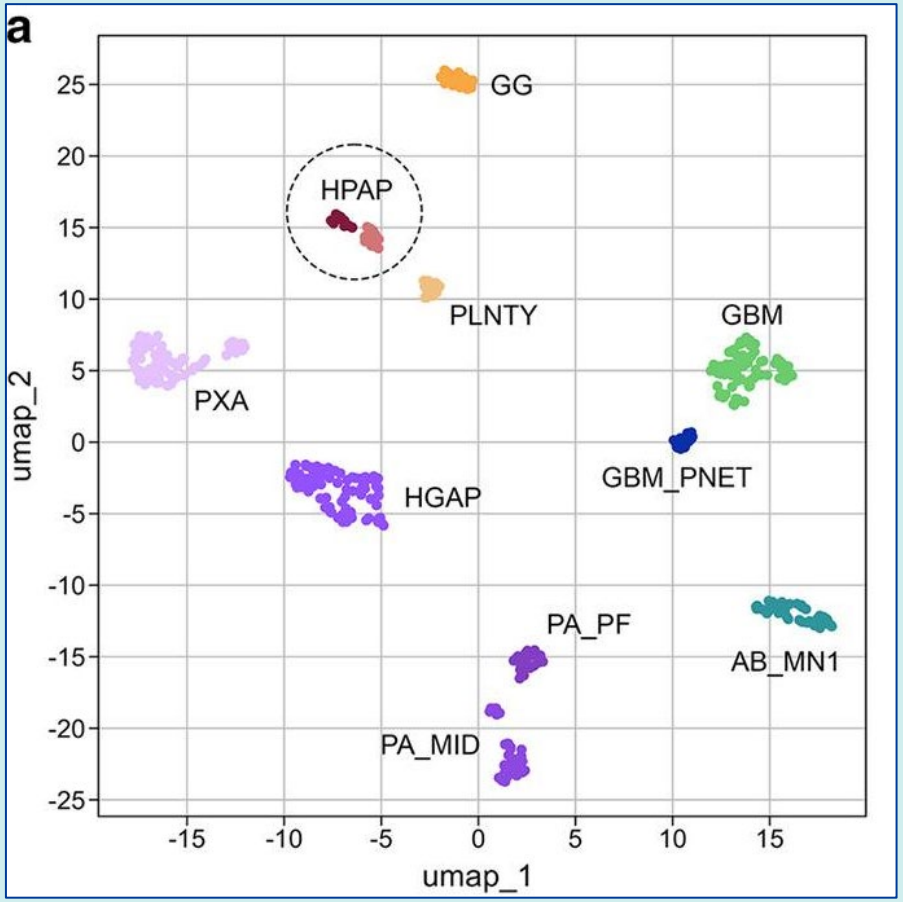
ORIGINAL PAPER

Check for updates

High-grade glioma with pleomorphic and pseudopapillary features (HPAP): a proposed type of circumscribed glioma in adults harboring frequent *TP53* mutations and recurrent monosomy 13

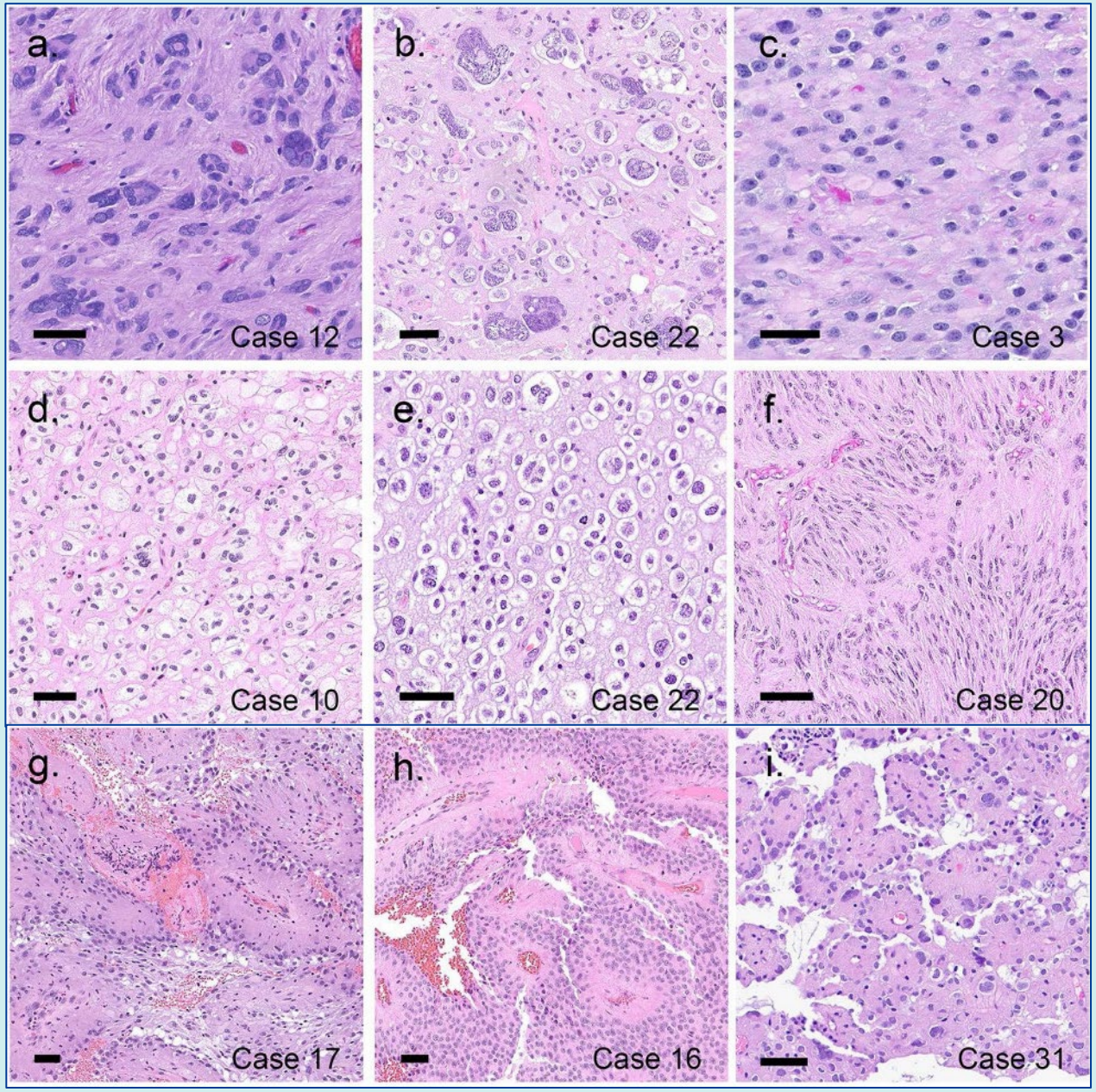
Drew Pratt[1] · Zied Abdullaev[1] · Antonios Papanicolau-Sengos[1] · Courtney Ketchum[1] · Pavalan Panneer Selvam[1] · Hye-Jung Chung[1] · Ina Lee[1] · Mark Raffeld[1] · Mark R. Gilbert[2] · Terri S. Armstrong[2] · Peter Pytel[3] · Ewa Borys[4] · Joshua M. Klonoski[5] · Matthew McCord[6] · Craig Horbinski[6] · Daniel Brat[6] · Arie Perry[7] · David Solomon[7] · Charles Eberhart[8] · Caterina Giannini[9] · Martha Quezado[1] · Kenneth Aldape[1]

Identified a previously uncharacterized glioma type using unsupervised clustering of DNA methylation data



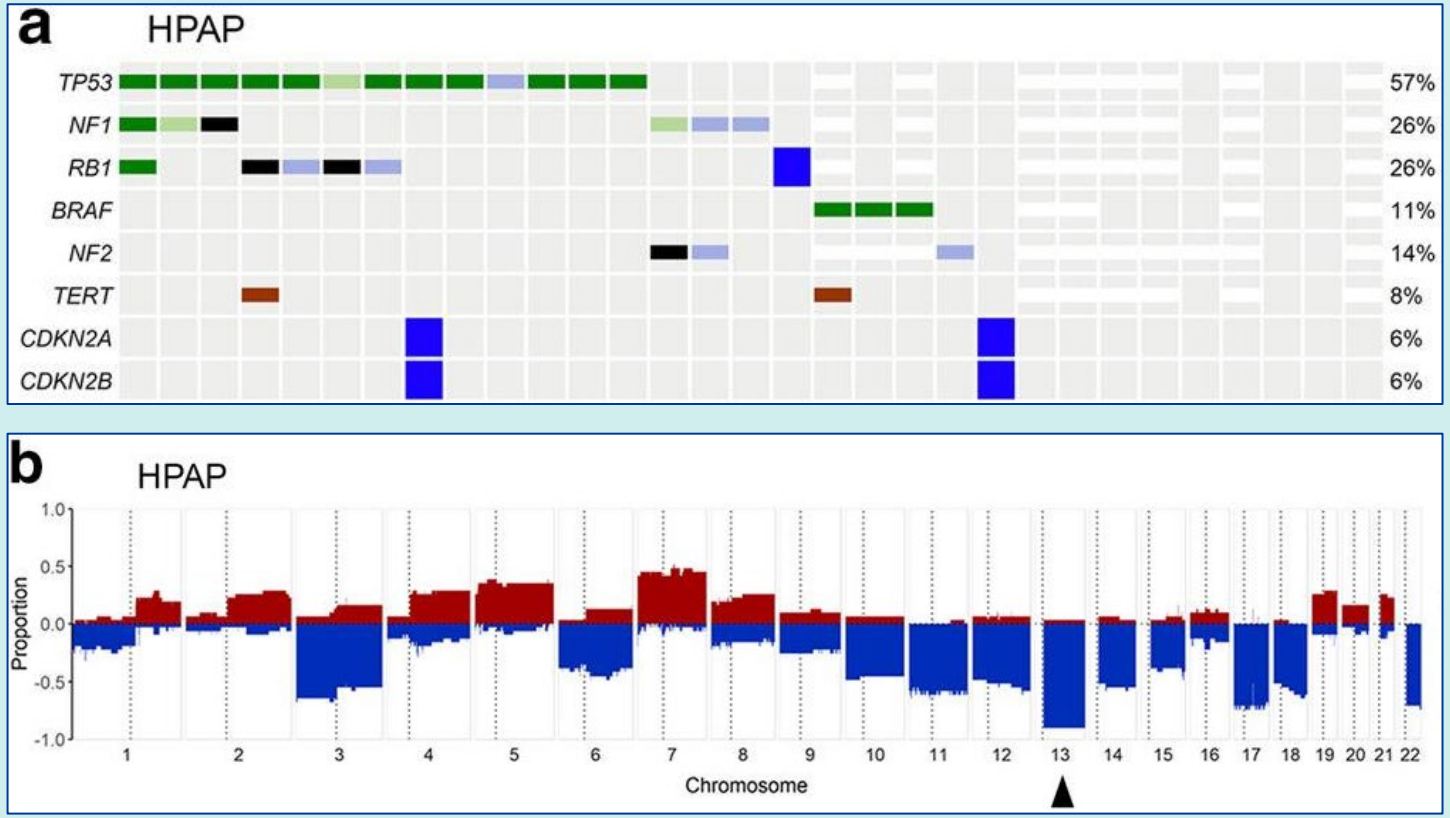
Histologic features

- Broad morphologic features
- Generally characterized by marked pleomorphism, giant cell morphology, and multinucleation.
- Occasional bland to oligodendroglial-like morphology, perivascular pseudorosettes, loss of cellular cohesion leading to pseudopapillary structures
- Predominantly non-infiltrative appearance



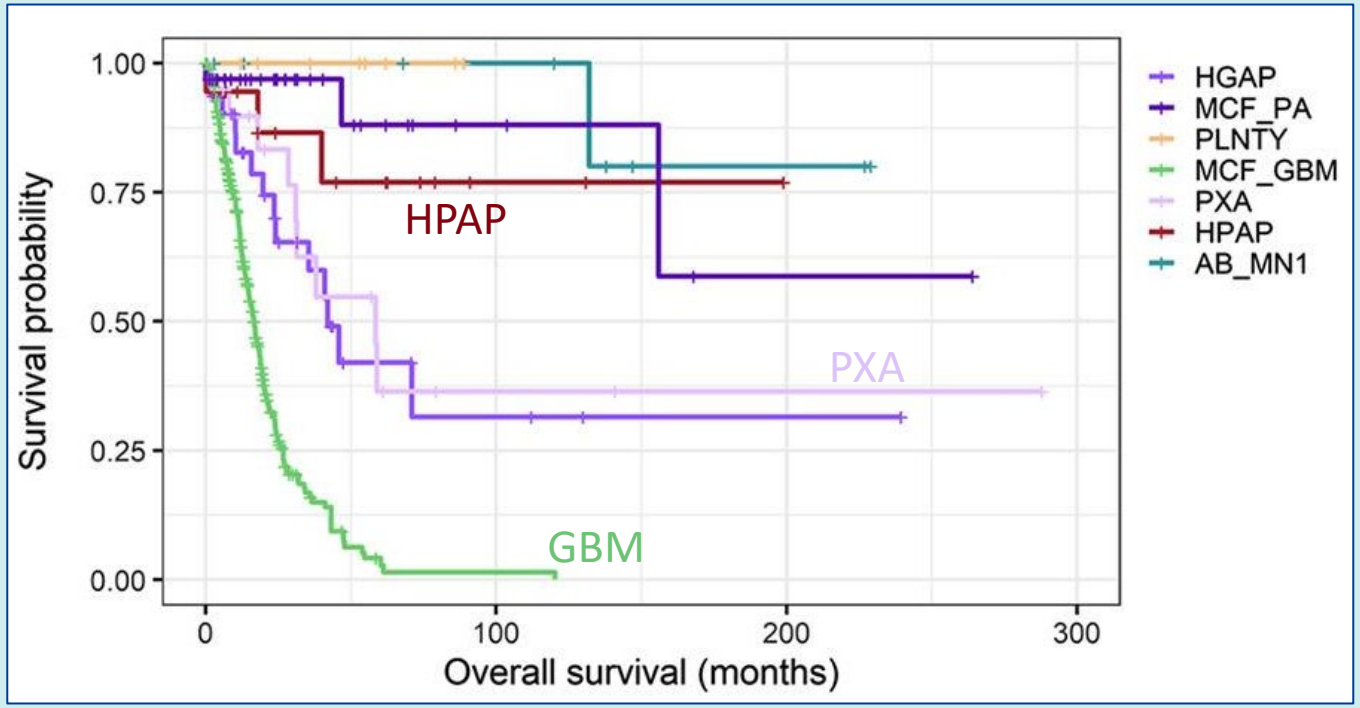
Molecular alterations

- Recurrent alterations in TP53 (13/23 cases; 57%), RB1 (6/23, 26%), NF1 (6/23, 26%), NF2 (3/21, 14%), BRAF V600E (3/25; 12%)
- Most cases showed monosomy 13 (28/31) and loss of chr 17
- Frequent losses of chr 3, 6, 10-15, 18, and 22.
- Generally, do not show CDKN2A/B loss or TERT promoter mutation



Diagnostic notes

- The initial tumor was diagnosed as a Glioblastoma with giant cell morphology.
  - Due to the poor prognosis associated with this diagnosis, the patient was not deemed to be a candidate for orbital exenteration.
- The diagnosis of HPAP led to changes in prognosis for the patient which altered management.



References

1. Pratt D, Abdullaev Z, Papanicolau-Sengos A, Ketchum C, Panneer Selvam P, Chung HJ, Lee I, Raffeld M, Gilbert MR, Armstrong TS, Pytel P, Borys E, Klonoski JM, McCord M, Horbinski C, Brat D, Perry A, Solomon D, Eberhart C, Giannini C, Quezado M, Aldape K. High-grade glioma with pleomorphic and pseudopapillary features (HPAP): a proposed type of circumscribed glioma in adults harboring frequent TP53 mutations and recurrent monosomy 13. Acta Neuropathol. 2022 Mar;143(3):403-414. PMID: 35103816.

2. Gubbiotti MA, Weinberg JS, Weathers SP, Dasgupta P, Tom MC, Aldape K, Quezado M, Abdullaev Z, Huse JT, Ballester LY. An incidental finding of a high-grade glioma with pleomorphic and pseudopapillary features (HPAP) with PBRM1 mutation. J Neuropathol Exp Neurol. 2024 Jan 19;83(2):139-141. PMID: 38164987.

Acknowledgements

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