

55th annual diagnostic slide session

Case 2014-4

Submitted by
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Geoffrey Murdoch M.D.

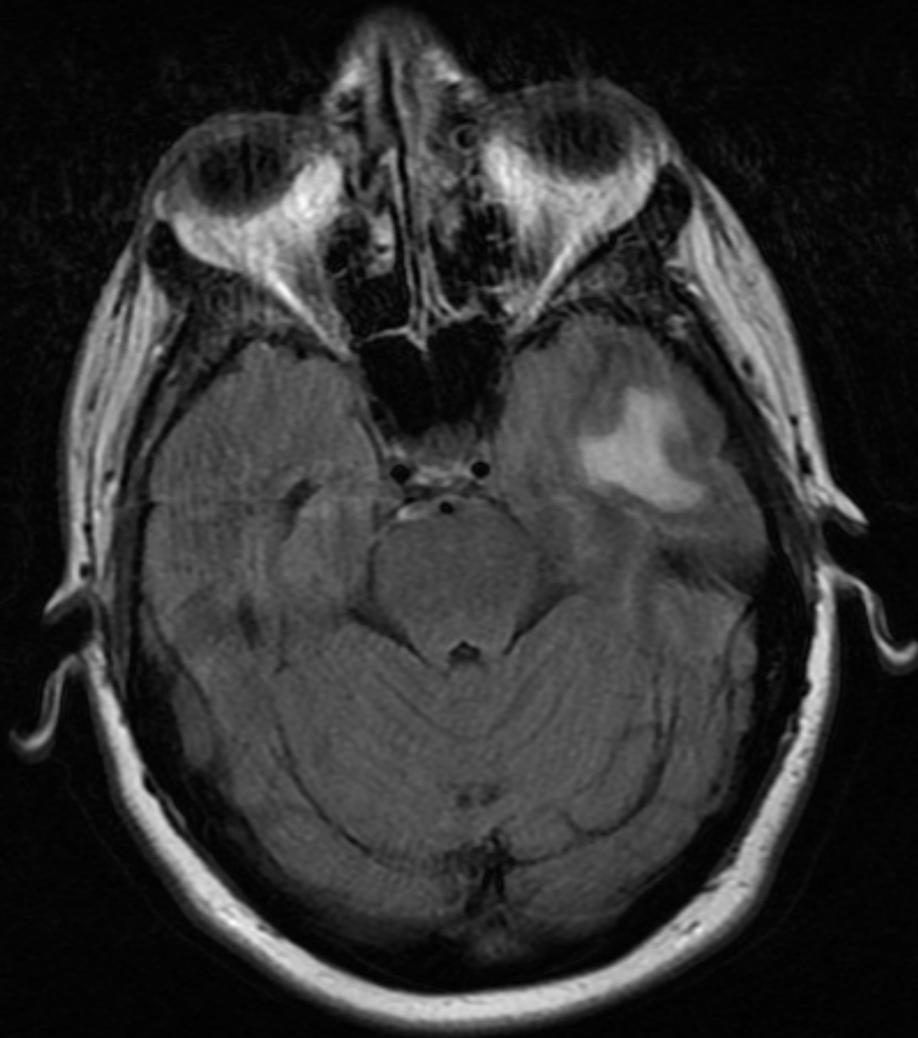
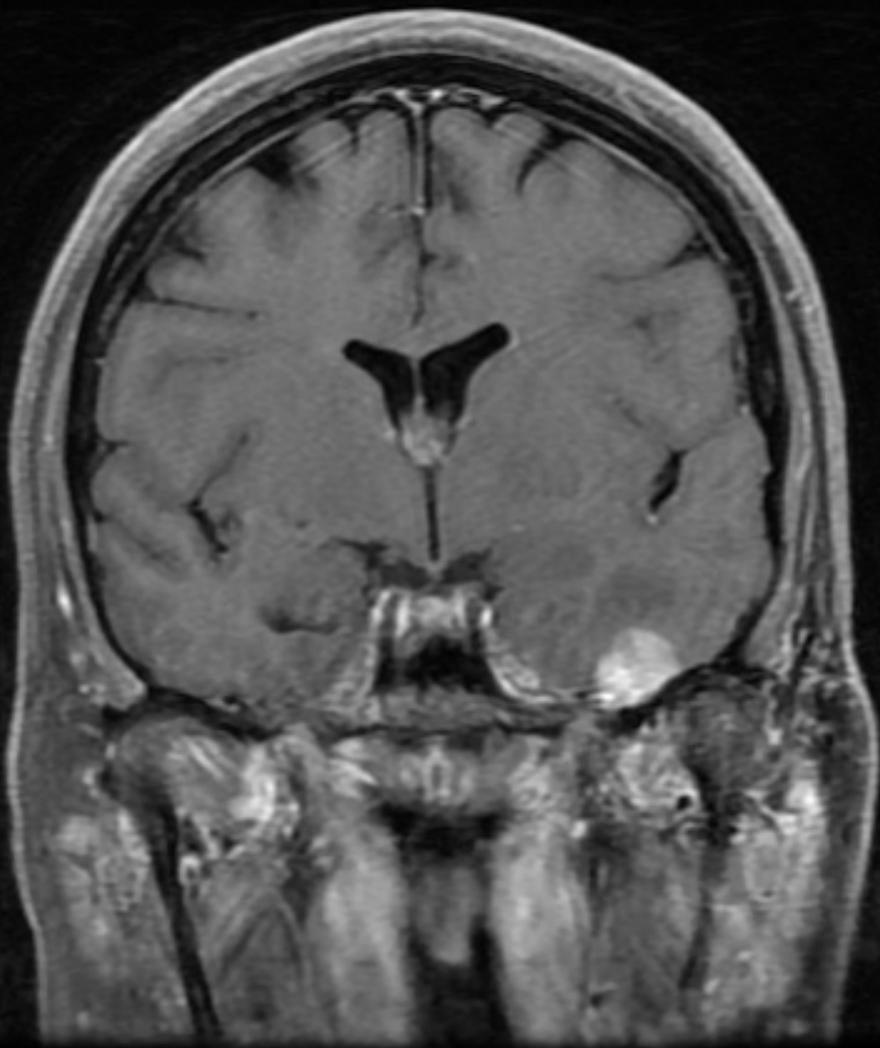
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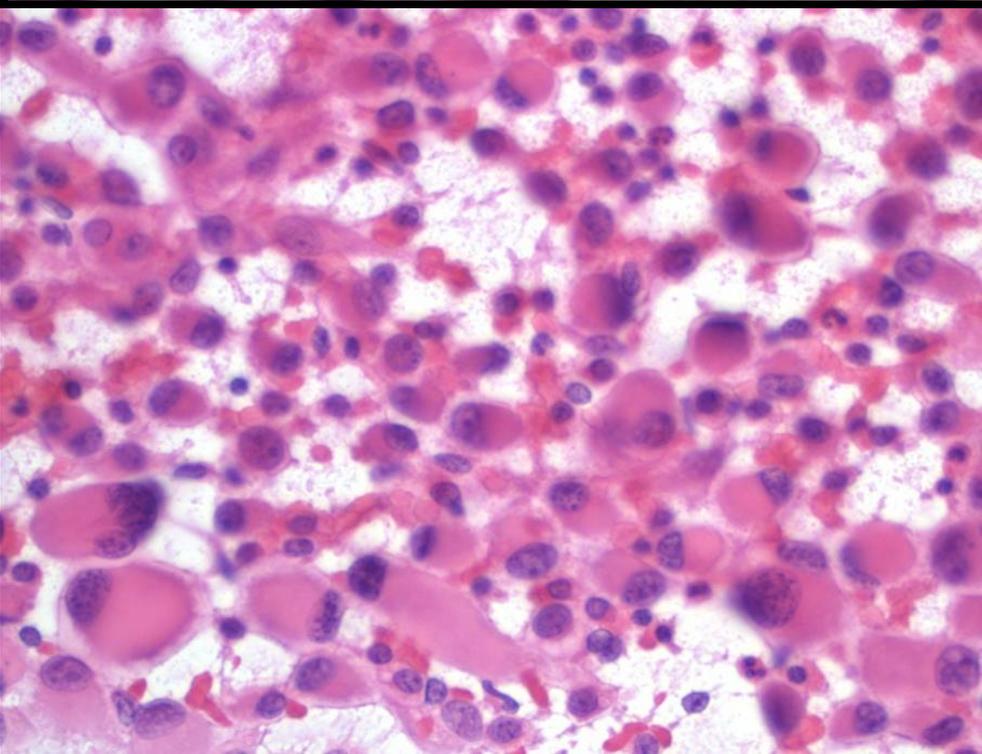
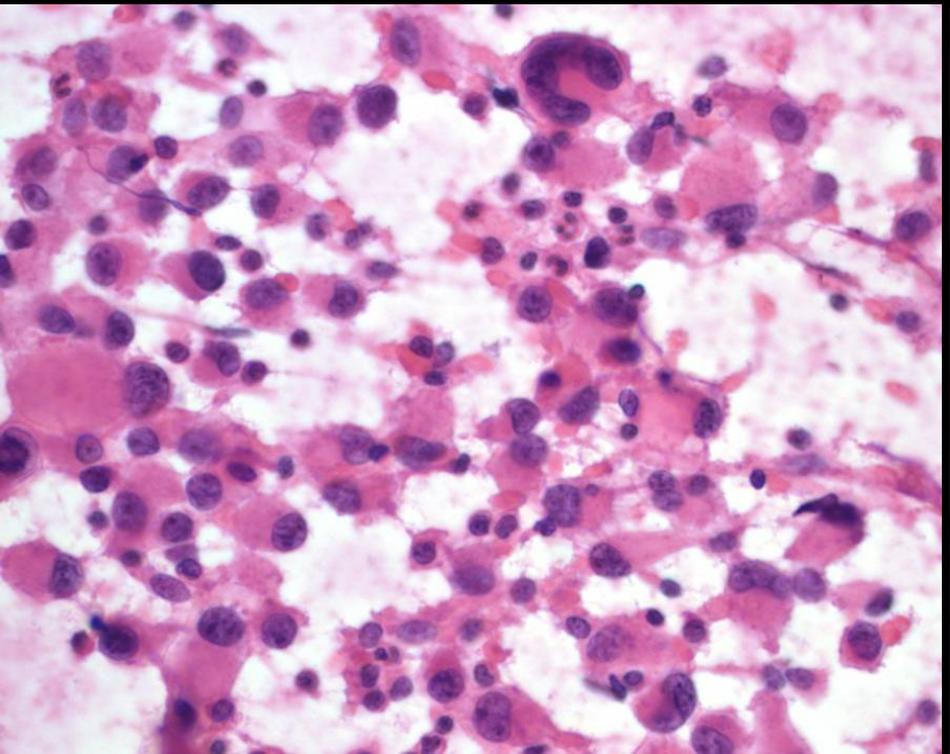
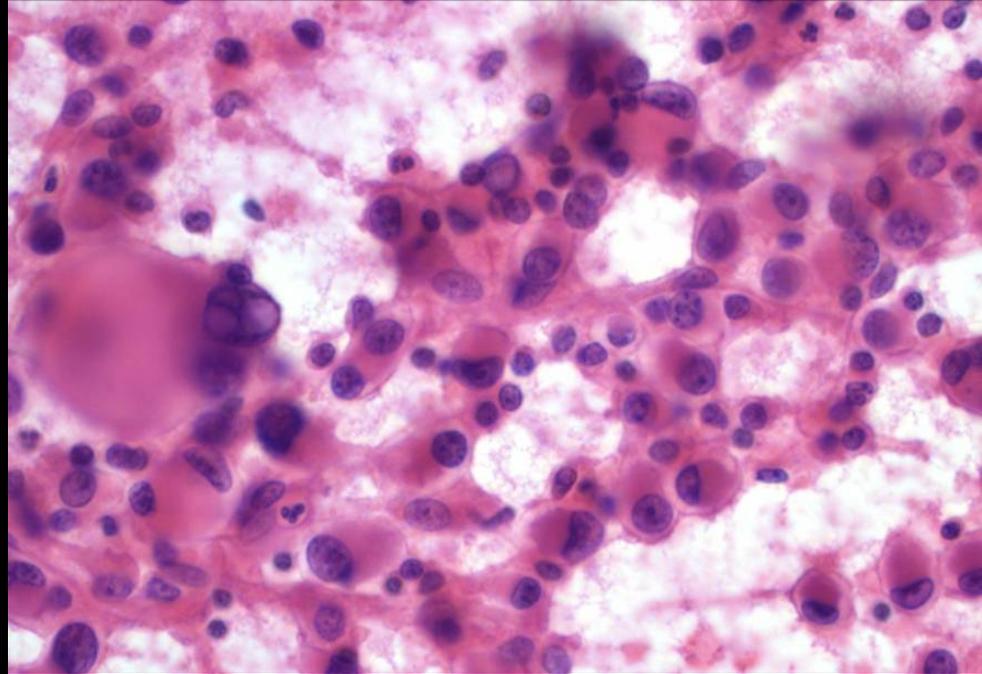
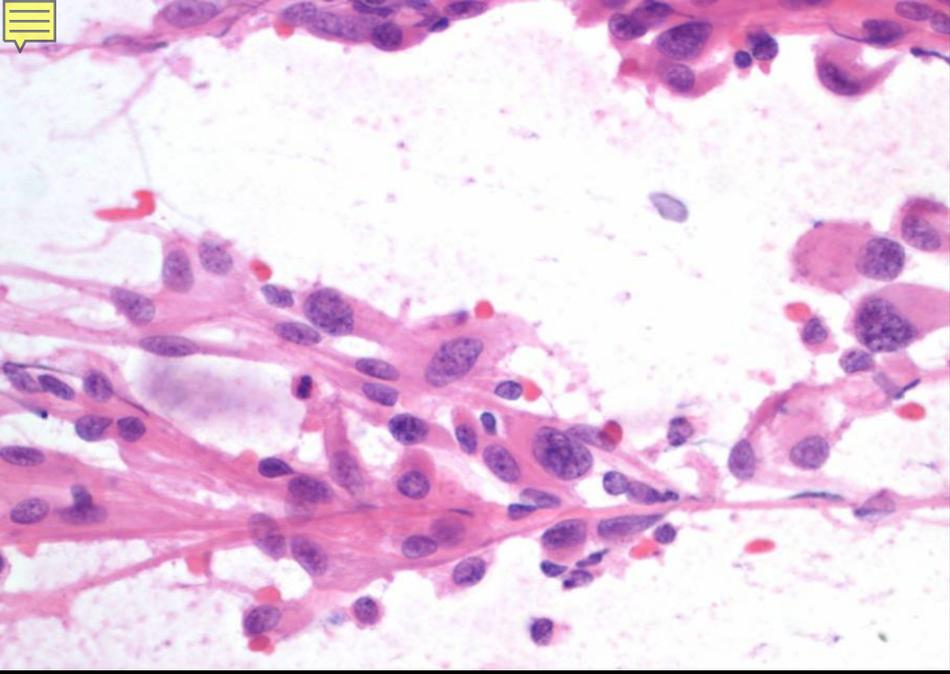
I have no disclosures

Clinical history – Dec 2012

- 39 year-old female suffered a seizure while doing Christmas shopping

MRI

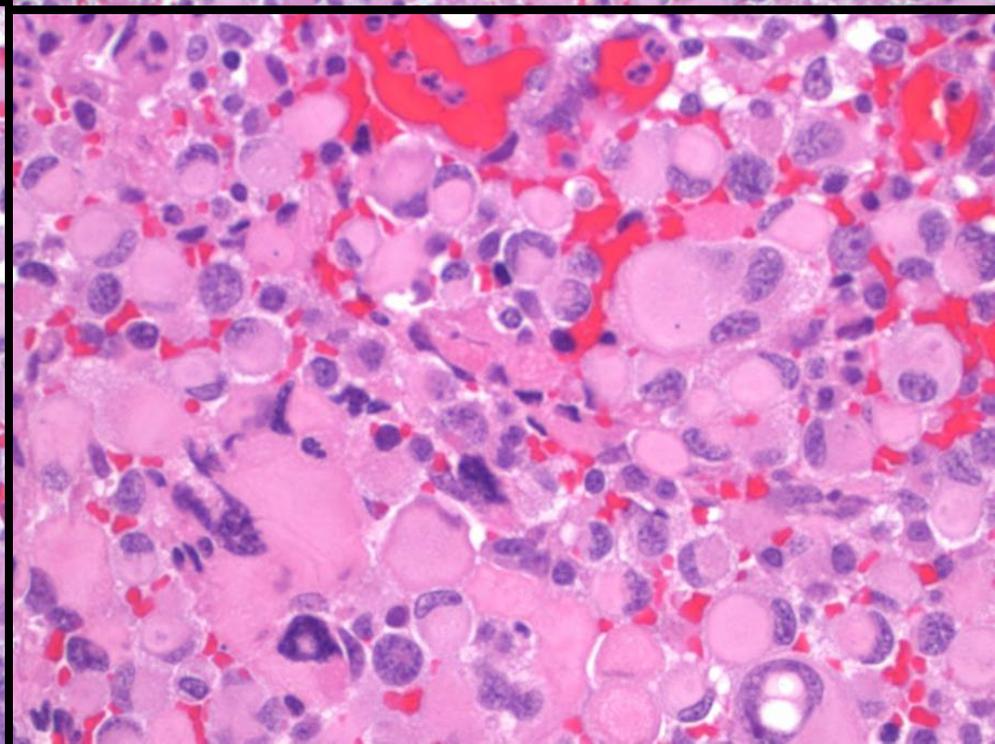
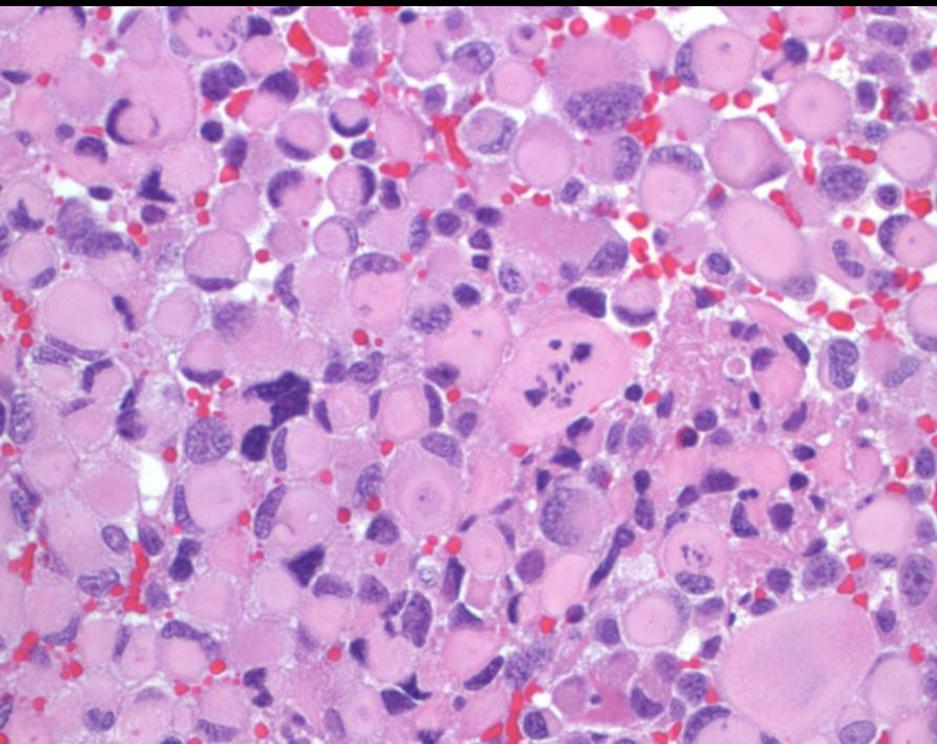
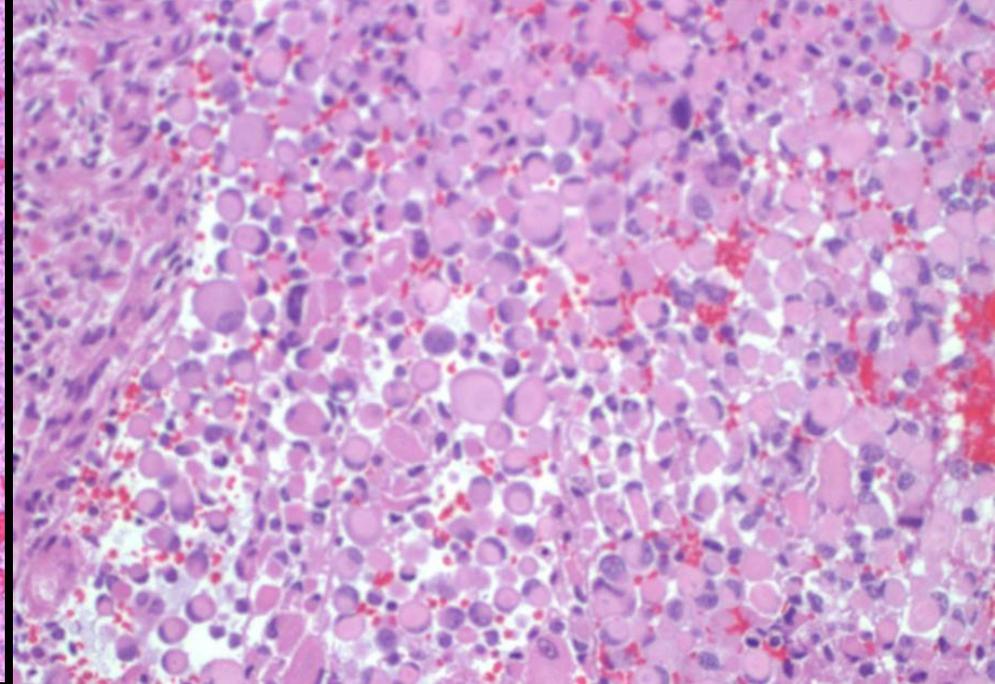
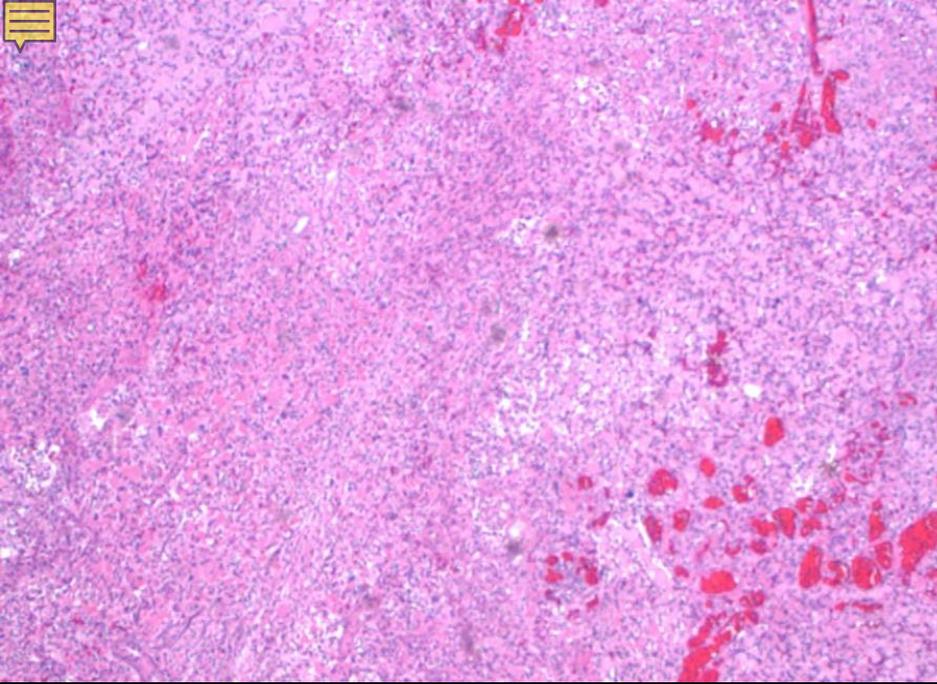


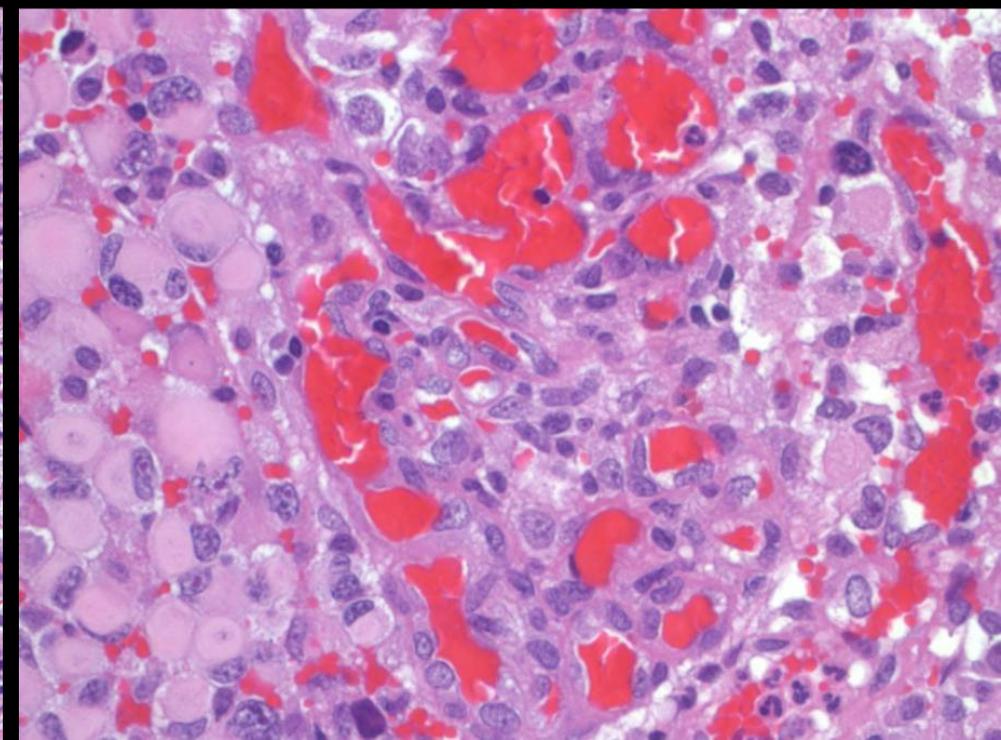
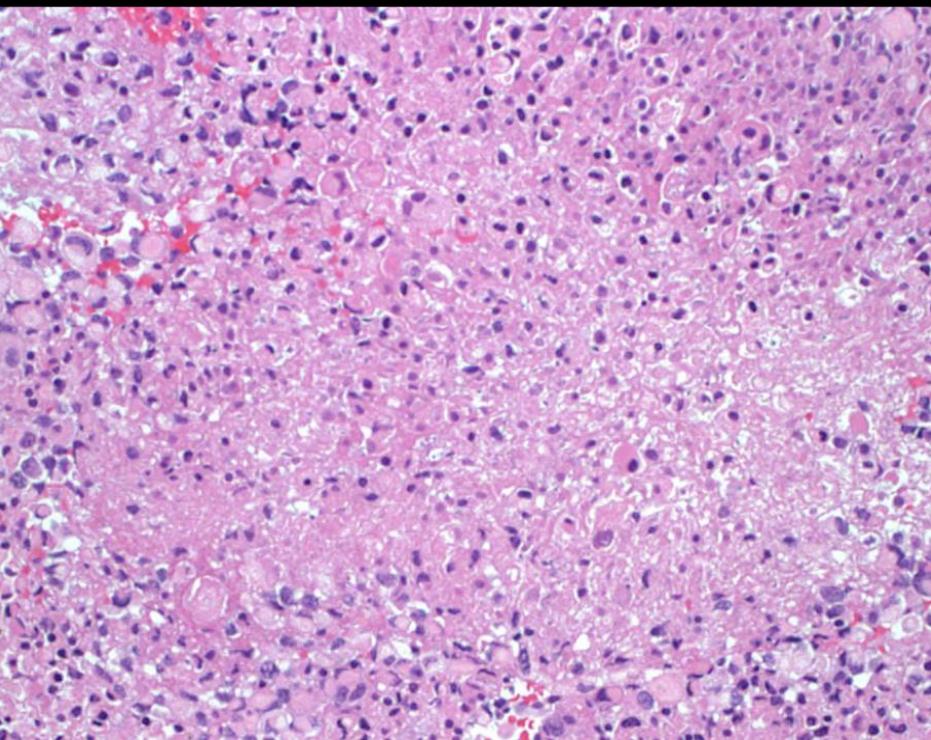
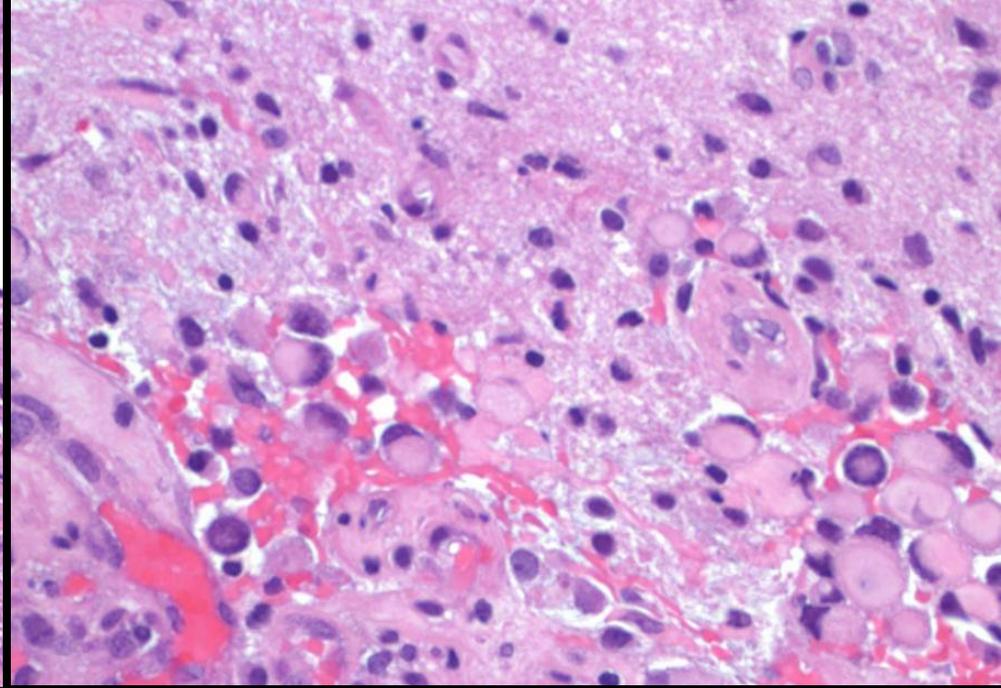
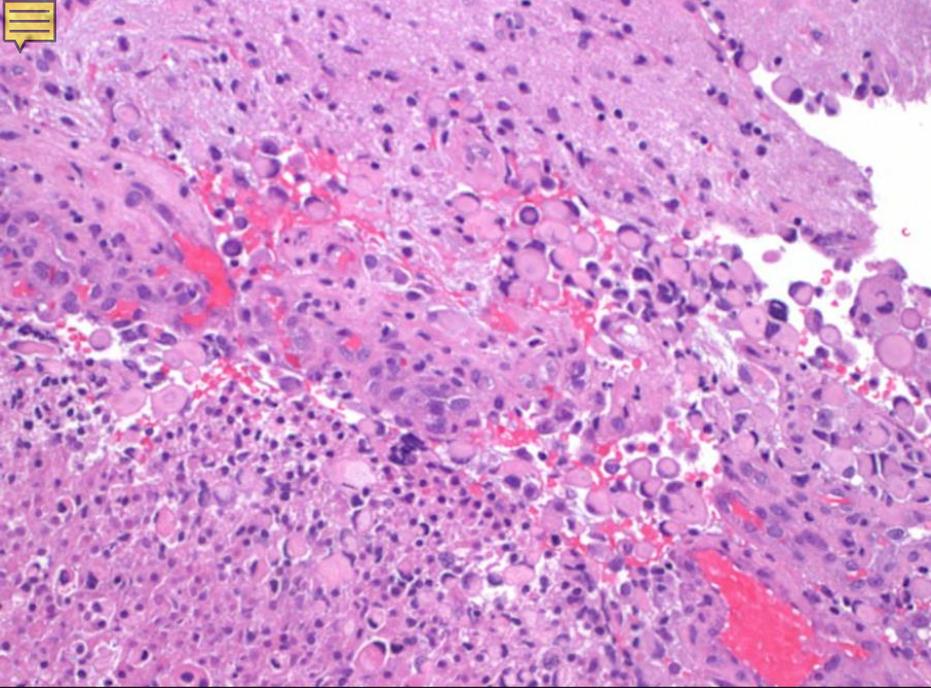




Intraoperative diagnosis

- Malignant neoplasm with rhabdoid features

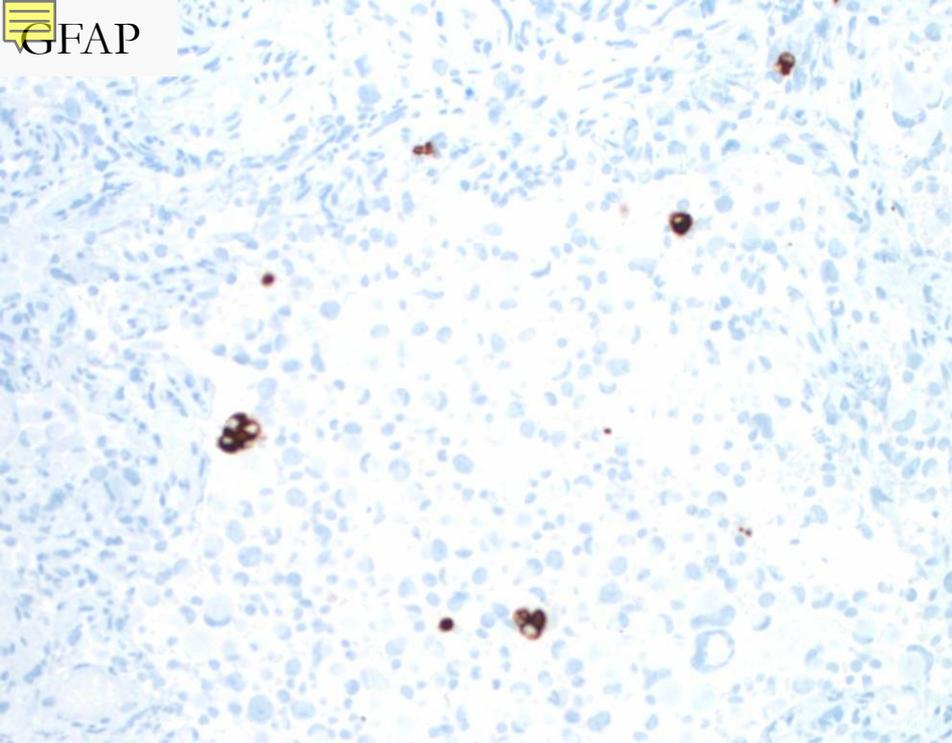




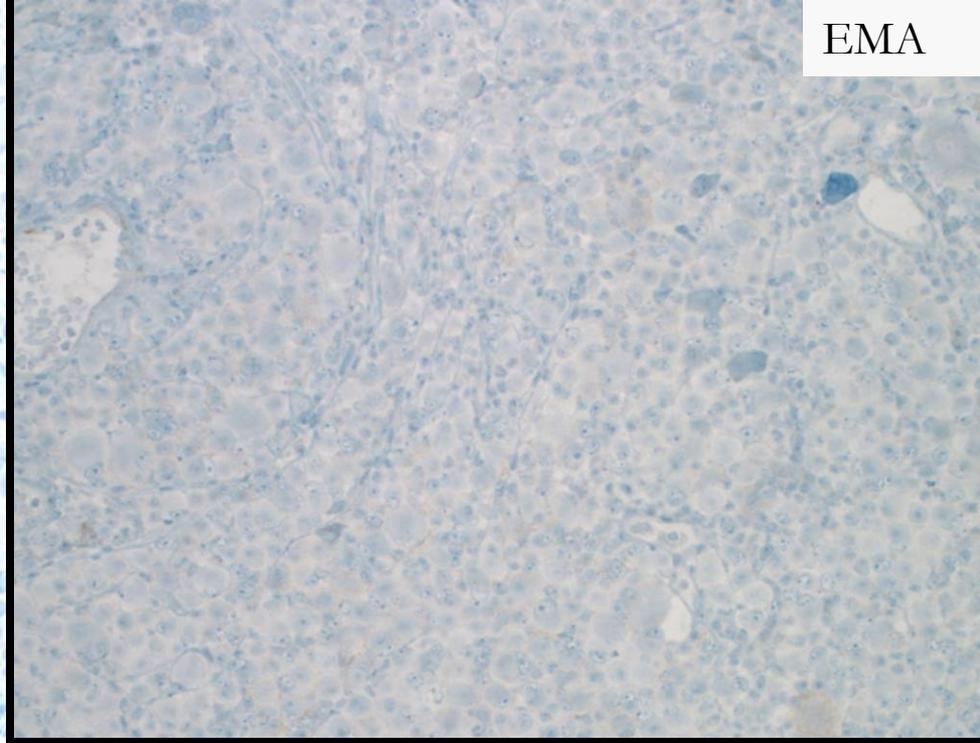


Differential diagnosis?

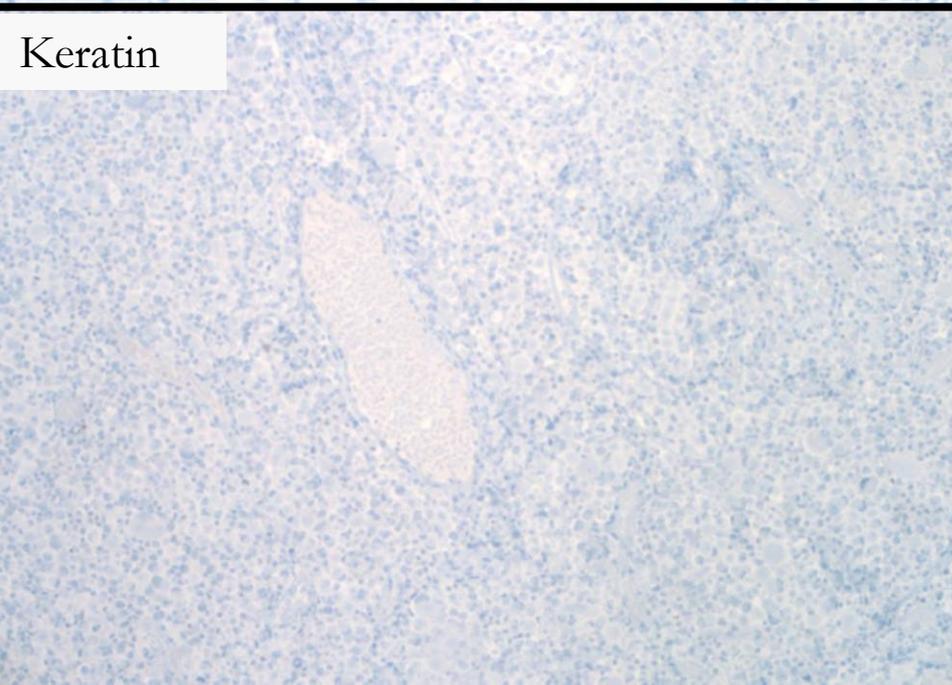
GFAP



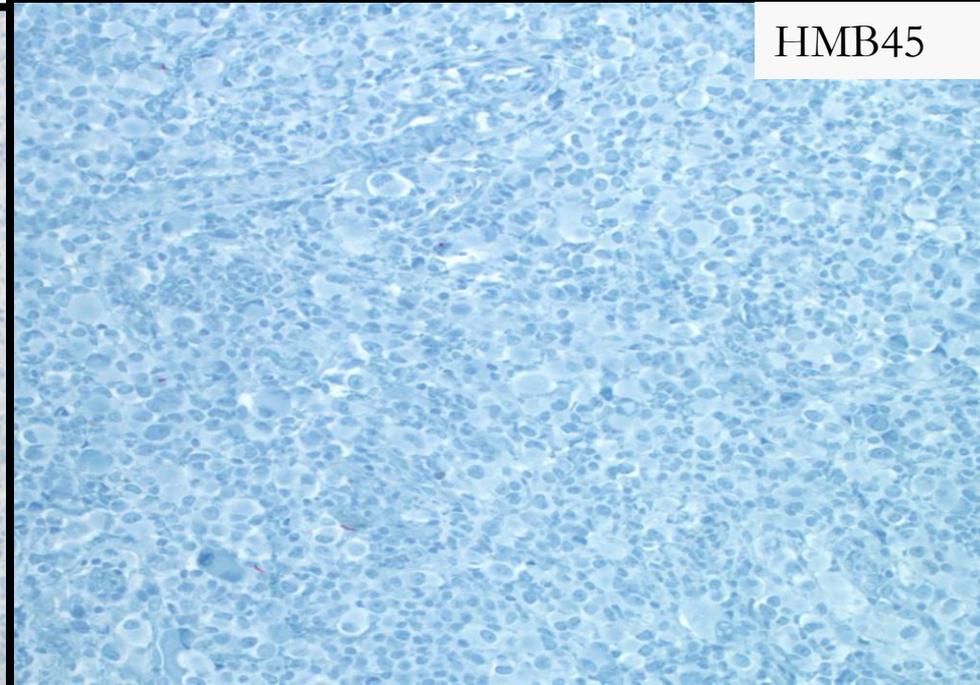
EMA

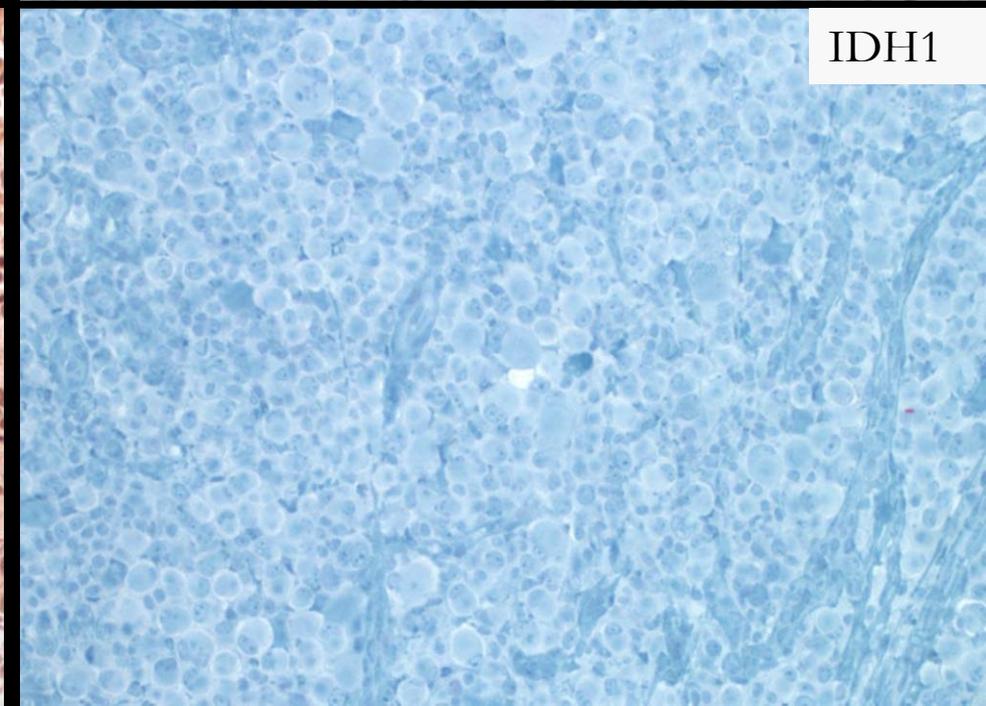
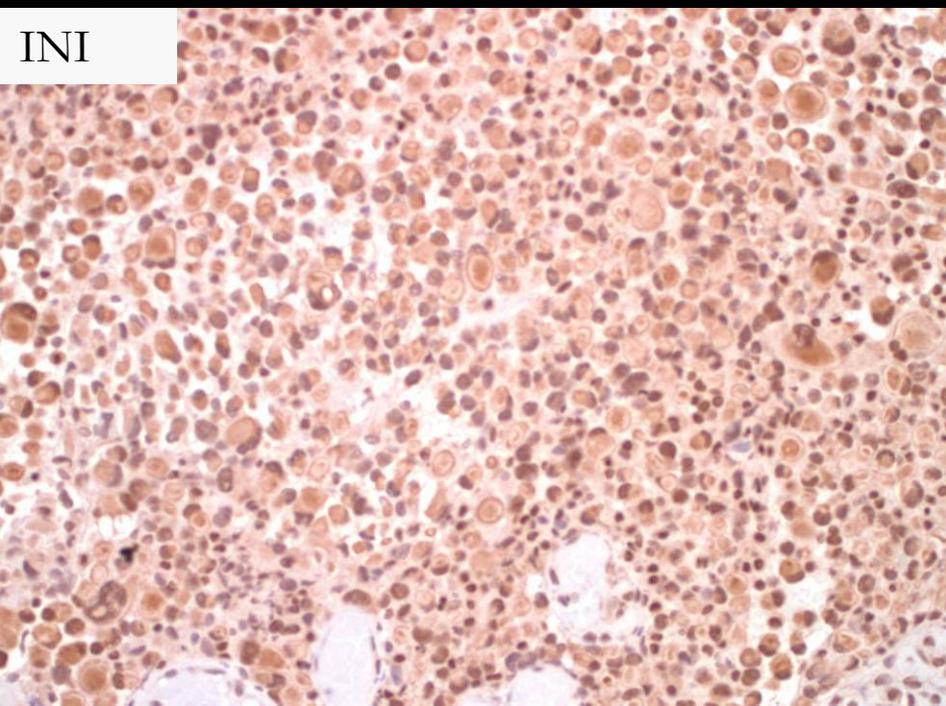
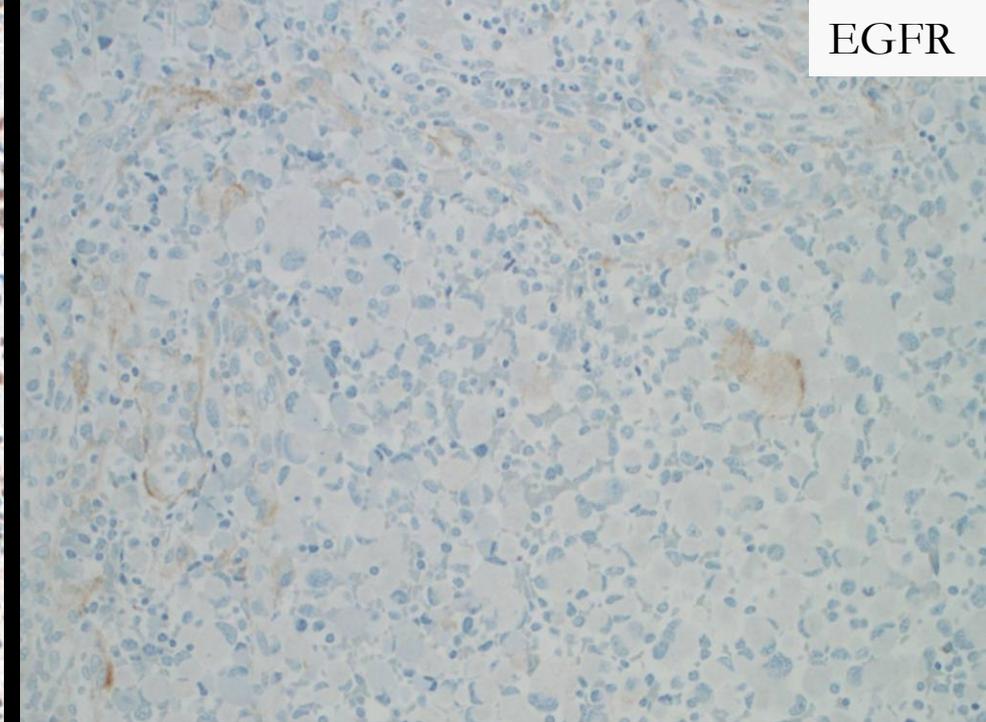
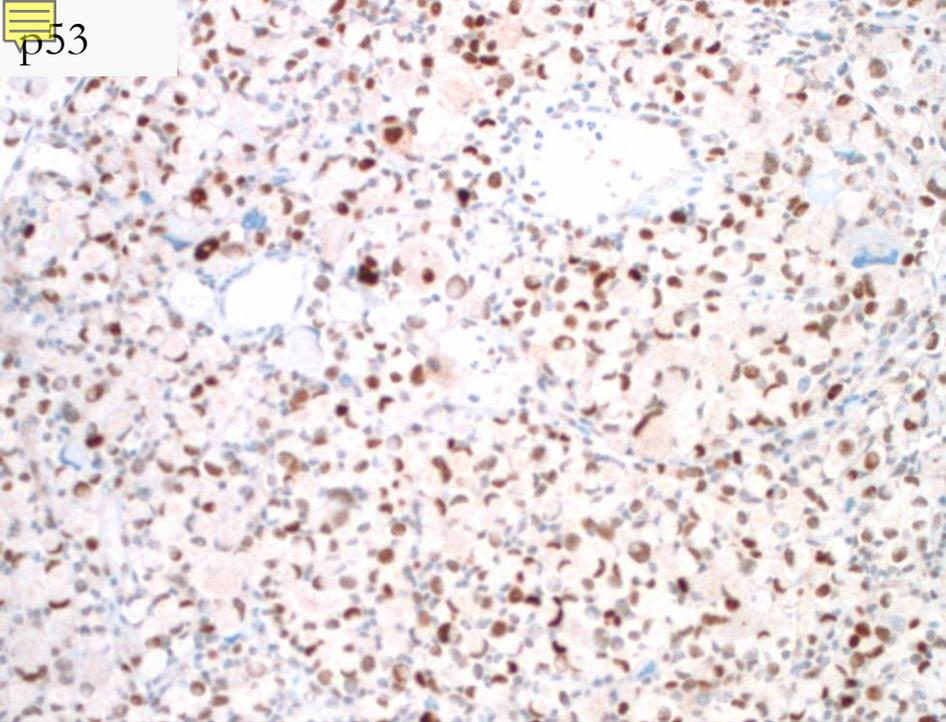


Keratin

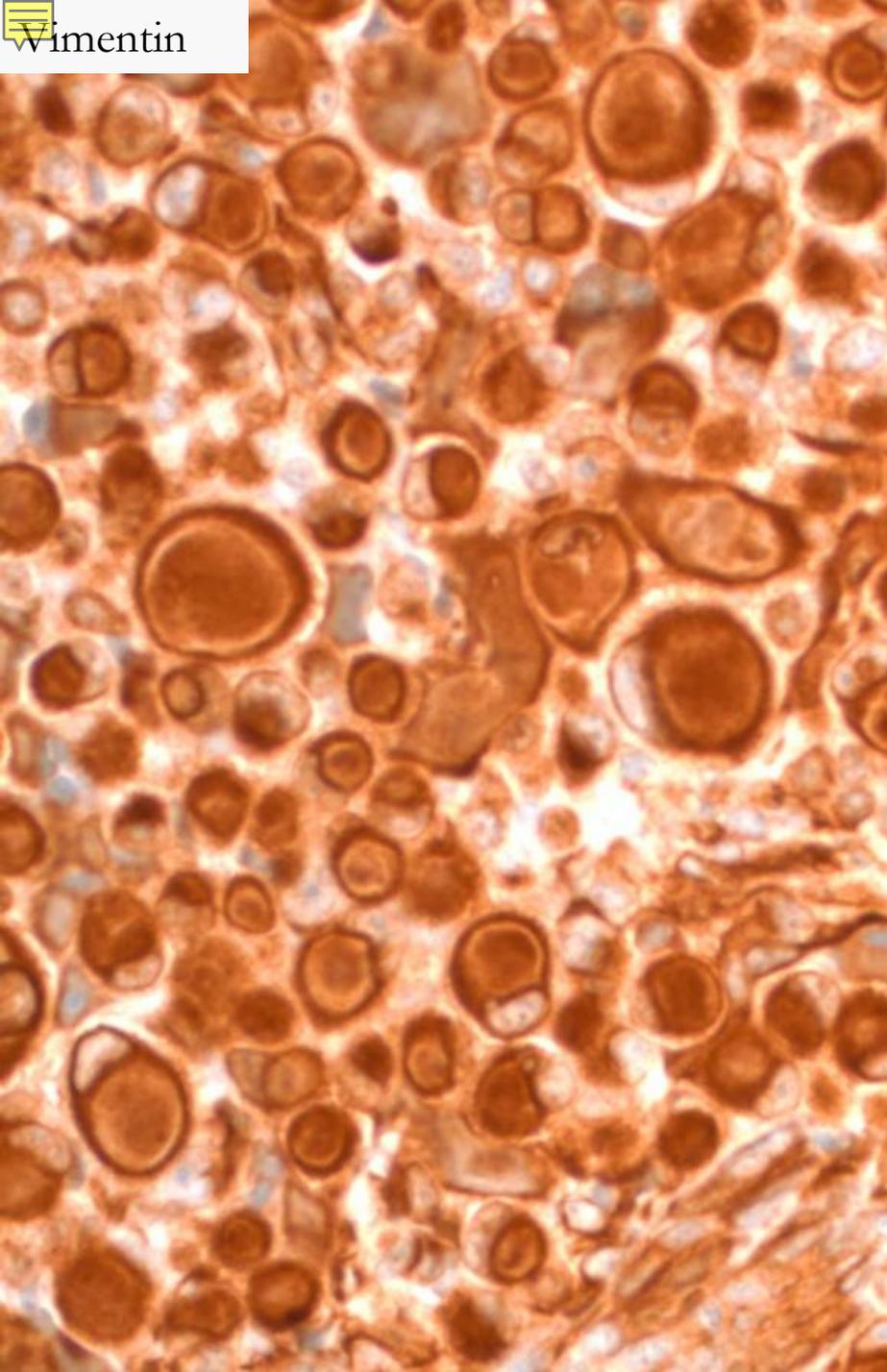


HMB45

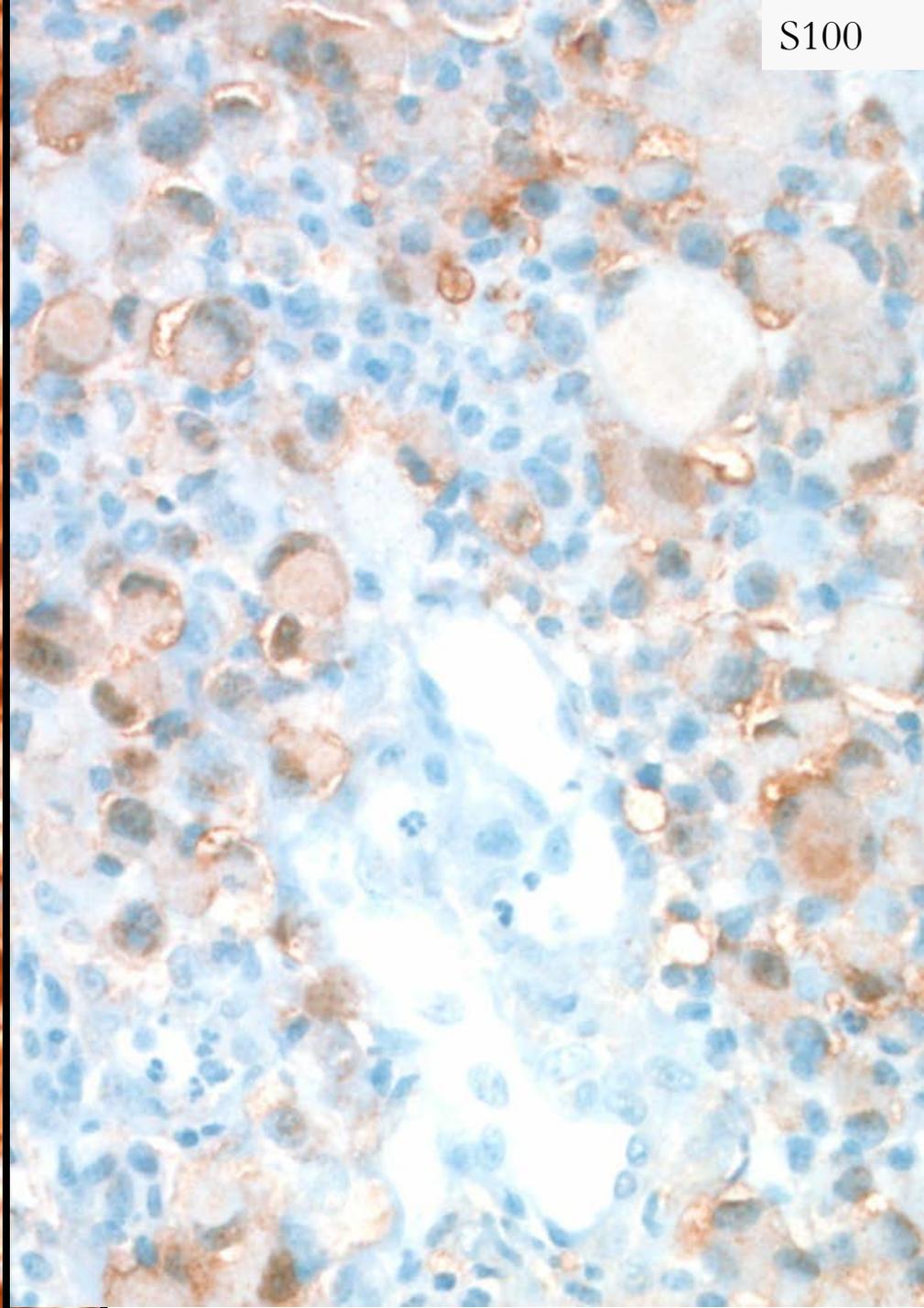


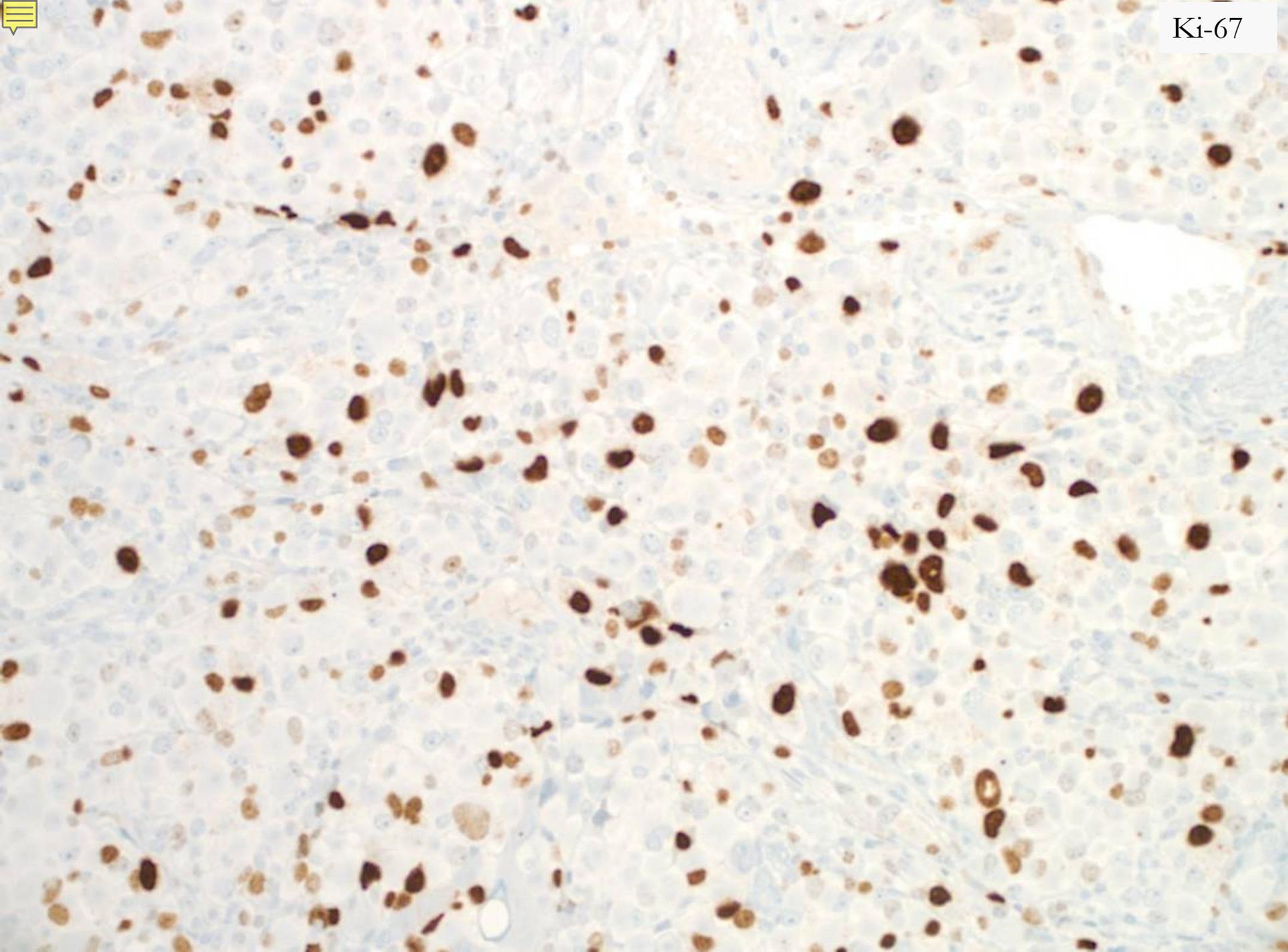


Wimentin

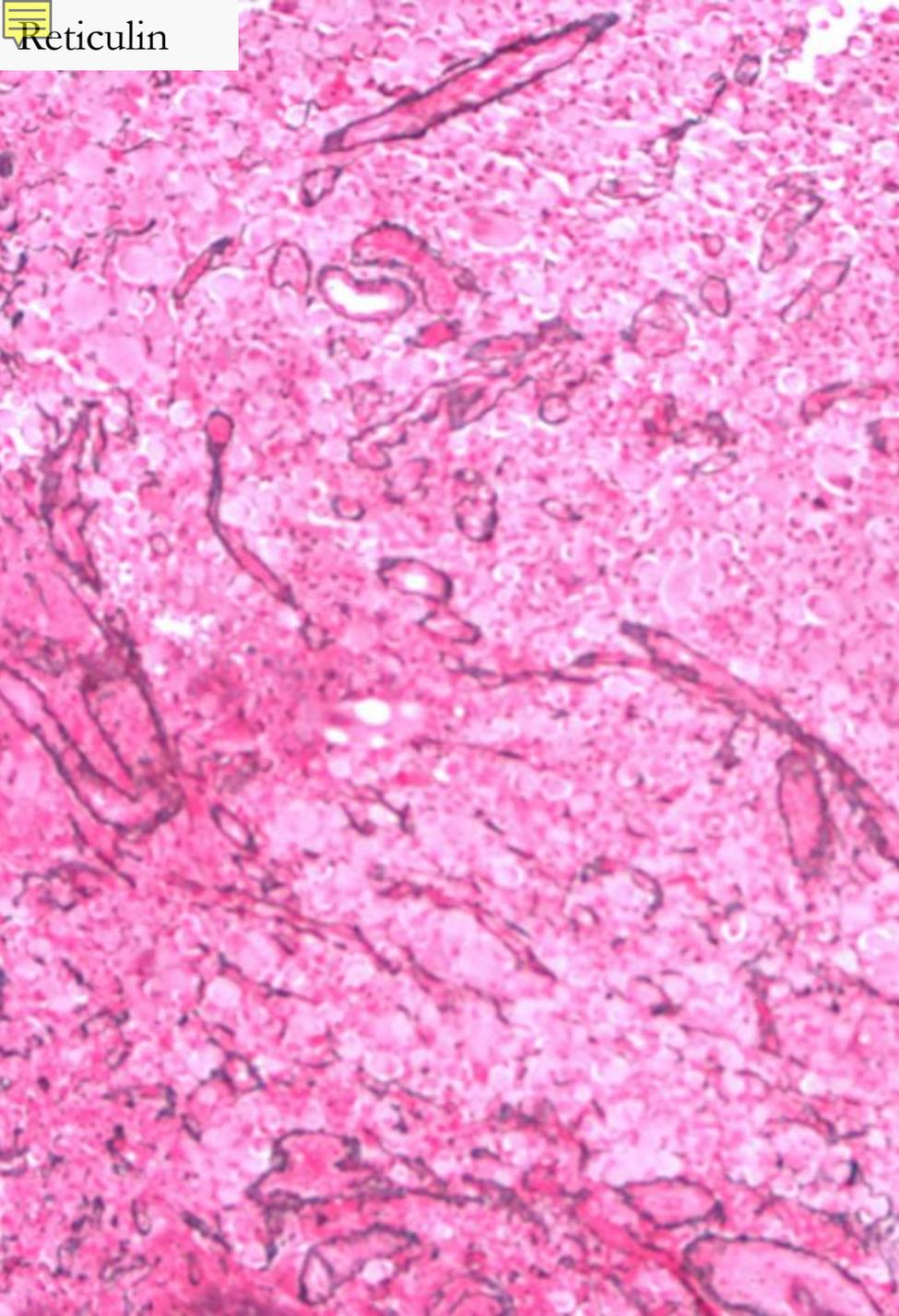


S100

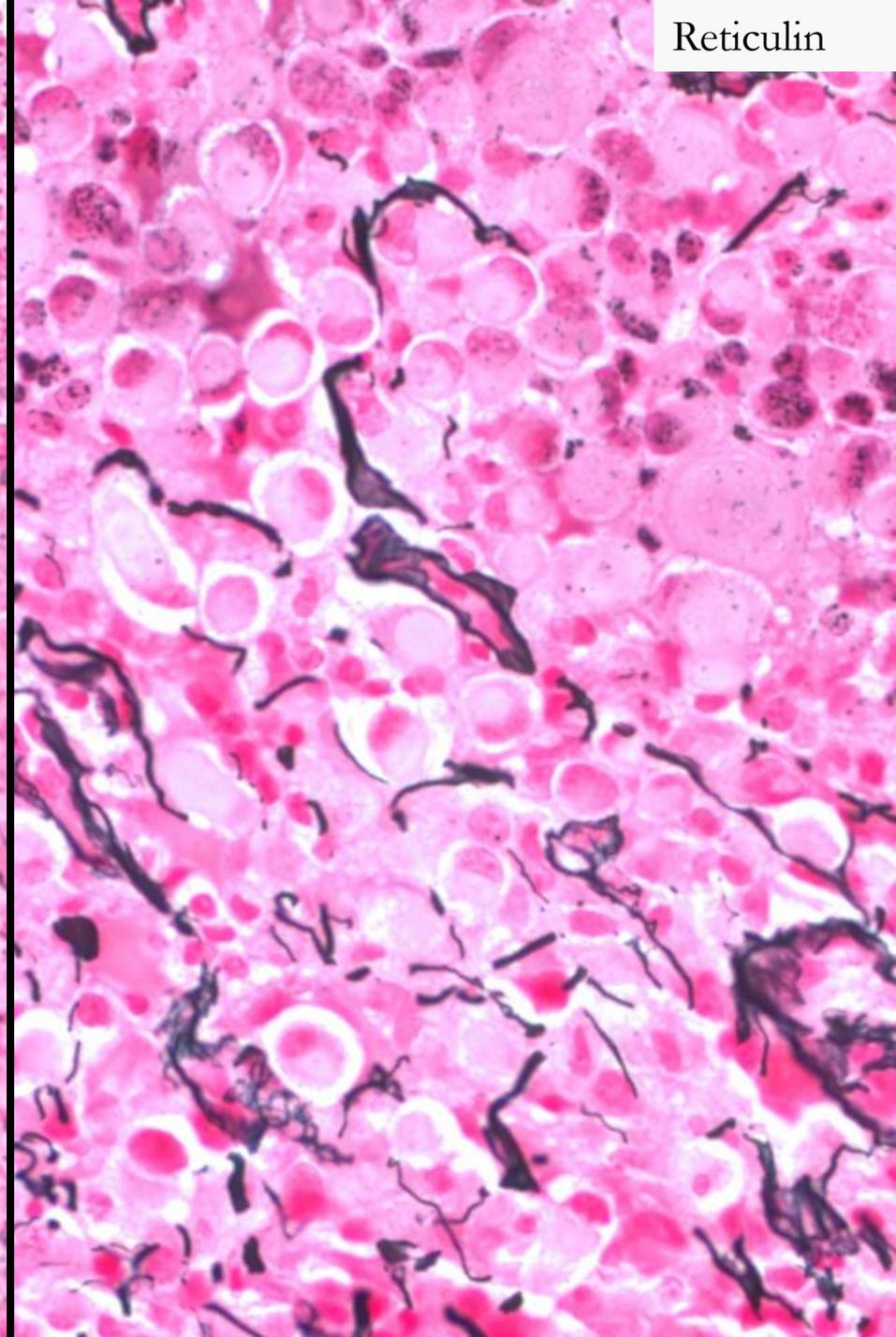




Reticulin



Reticulin





FISH

- EGFR
 - Overall NOT amplified (ratio = 1.53)
 - Amplified in FEW cells
- P16
 - 11.7% homozygous deletion
- 1p and 19q
 - No deletions



Molecular anatomic pathology testing

- *IDH1* and *IDH2*
 - NOT identified
- *MGMT* promoter methylation
 - NOT identified



Final diagnosis – Dec 2012

- Glioblastoma, WHO grade IV
 - Rhabdoid/epithelioid morphology

Epithelioid Versus Rhabdoid Glioblastomas Are Distinguished by Monosomy 22 and Immunohistochemical Expression of INI-1 but not Claudin 6

Bette Kay Kleinschmidt-DeMasters, MD,†‡ Ali H. Alassiri, MD,§ Diane K. Birks, MS,‡||
Kathy L. Newell, MD, GR,¶|| Wayne Moore, MD,§ and Kevin O. Lillehei, MD‡*

- E-GBM: superficial, supratentorial tumors, monomorphic cells
- R-GBM: rhabdoid cells in an otherwise “classic” GBM



Results

- 8 E-GBM and 2 R-GBM
- R-GBMs show focal loss of INI and show monosomy 22
- E-GBMs do not

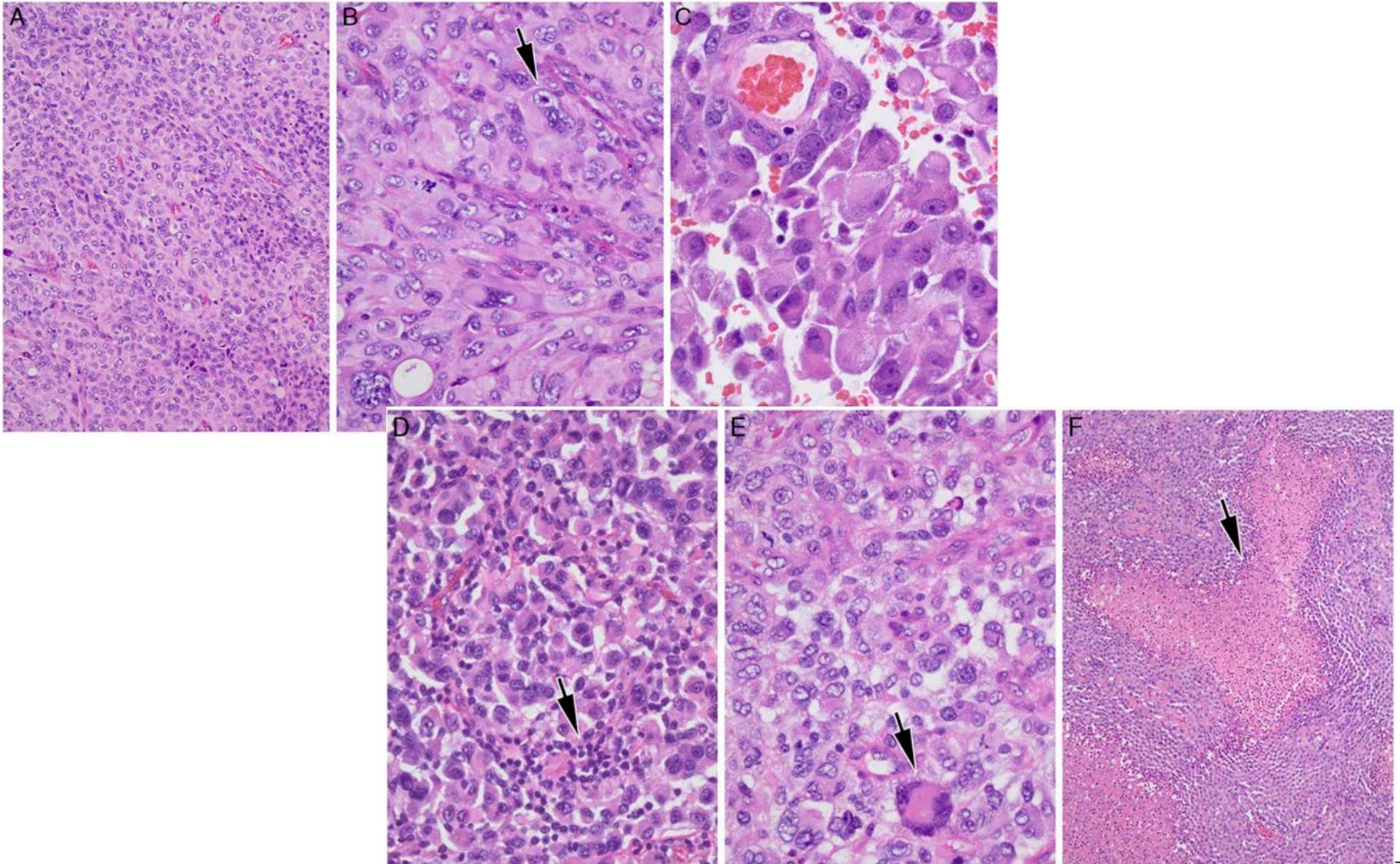
Epithelioid GBMs Show a High Percentage of *BRAF* V600E Mutation

Bette Kay Kleinschmidt-DeMasters, MD,†‡ Dara L. Aisner, MD, PhD,* Diane K. Birks, MS,†§
and Nicholas K. Foreman, MD§*

RESULTS

Tumor Type	Cases	BRAF V600E	INI IHC
E-GBM	13	7/13	No loss
GC-GBM	9	0/9	Not done
R-GBM	2	0/2	Focal loss

E-GBM histology



Clinical, radiological, histological and molecular characteristics of paediatric epithelioid glioblastoma

A. Broniscer*§, R. G. Tatevossian†, N. D. Sabin‡, P. Klimo Jr¶**, J. Dalton†, R. Leet, A. Gajjar*§ and D. W. Ellison†

*Departments of *Oncology, †Pathology and ‡Radiological Sciences, St. Jude Children's Research Hospital, Department of §Pediatrics and ¶Neurosurgery, University of Tennessee Health Science Center, and **Semmes-Murphey Neurologic and Spine Institute, Memphis, TN, USA*

- 6 patients
- Median age: 7.6 years
- 3/6 (50%) harbored *BRAF* V600E mutation



Final diagnosis

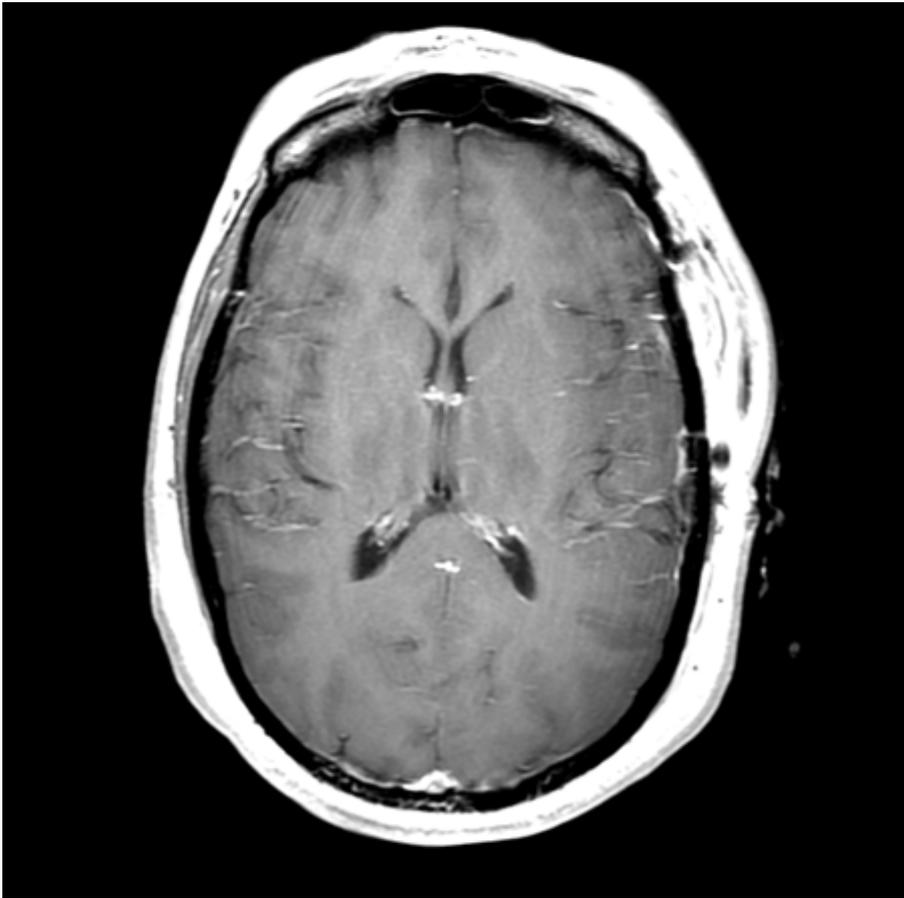
- POSITIVE for BRAF V600E mutation
- Epithelioid glioblastoma, WHO grade IV



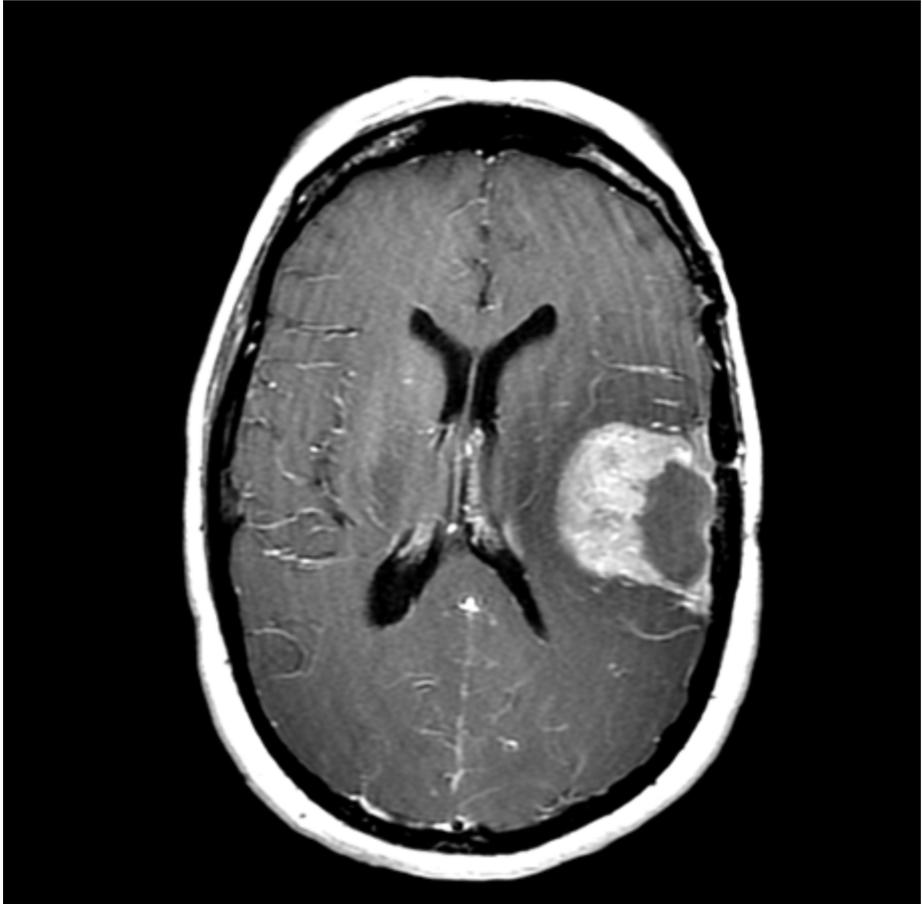
Clinical course

- 1/13
 - Temozolomide and radiation therapy
- 3/13 – First recurrence
 - Cyberknife treatment to new temporal lobe lesion
- 6/13 – Second recurrence
 - Multifocal enhancing disease progression.
 - Patient begins Avastin therapy
- 11/13 – Maximally symptomatic
 - Discussions for hospice care

Dec 2012

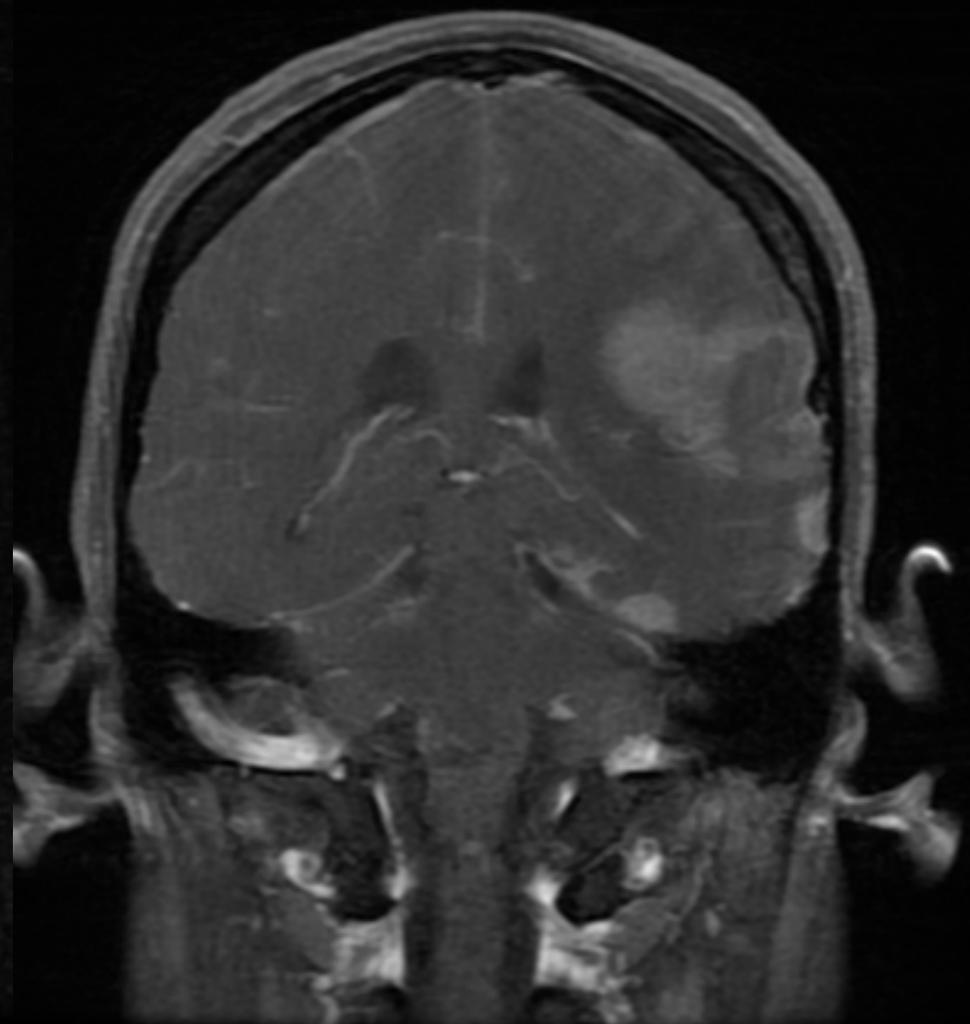
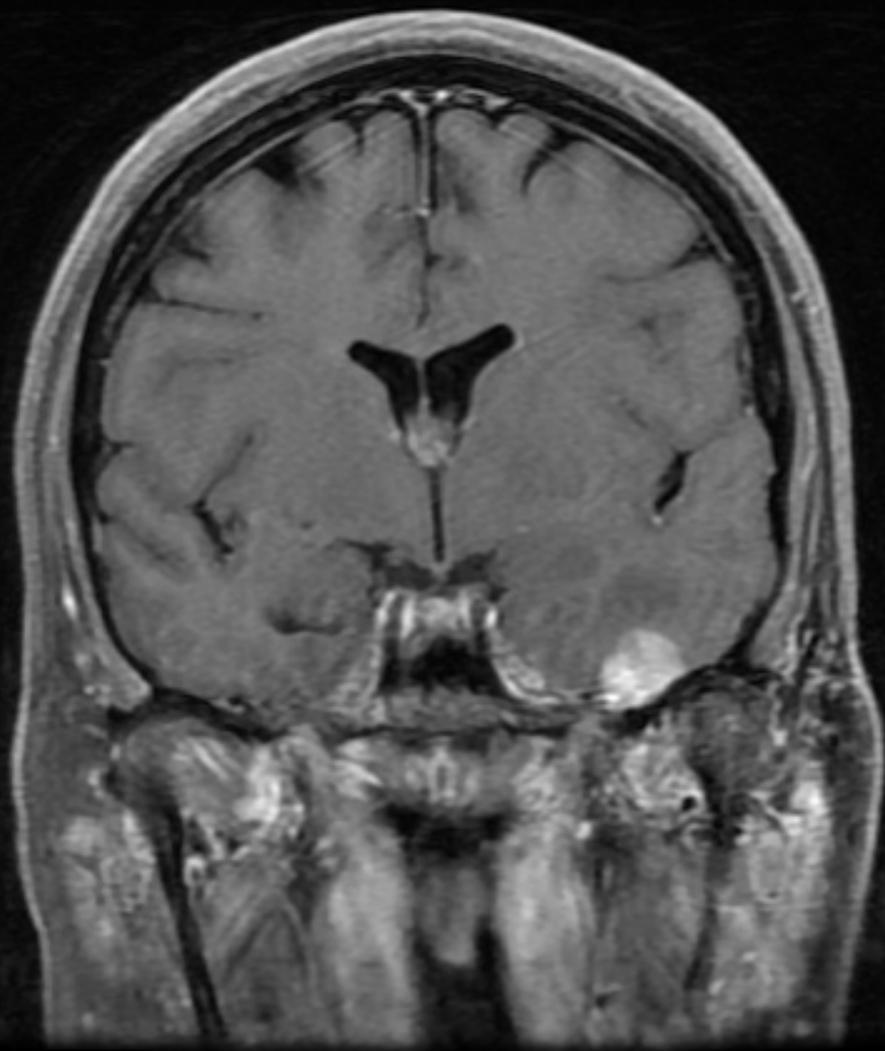


Nov 2013



Dec 2012

Nov 2013



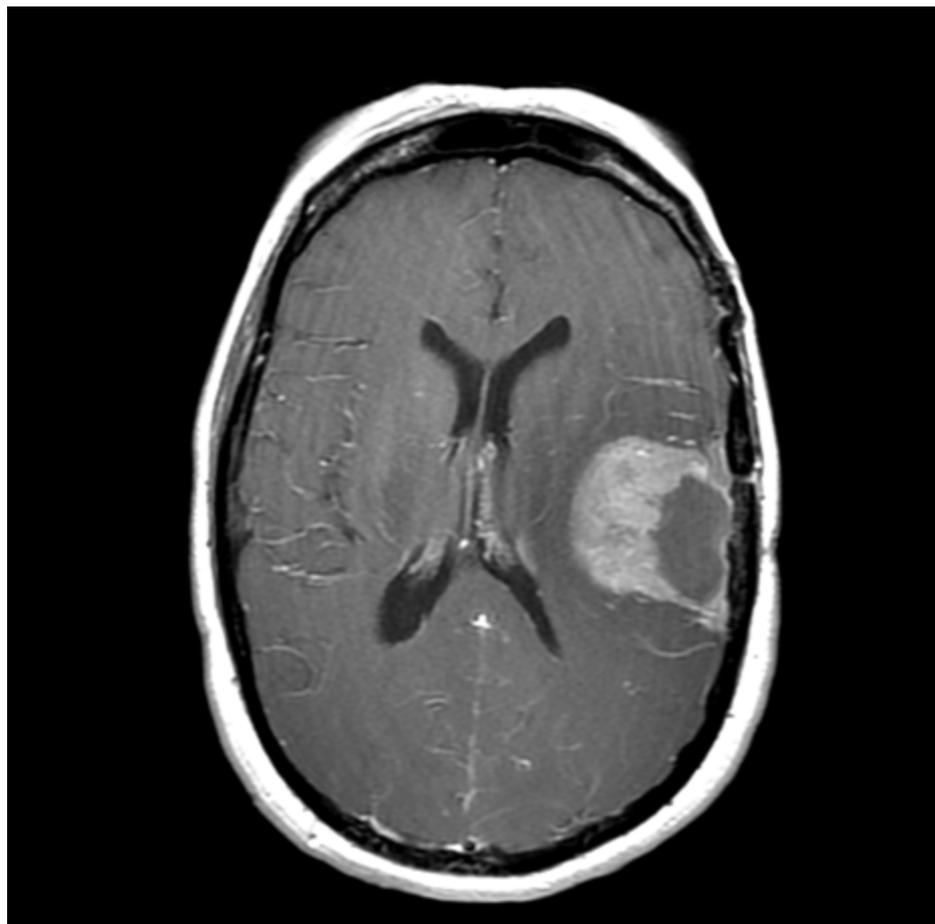
December 2013

- Patient is finally approved for vemurafenib (Zelboraf), a BRAF inhibitor.

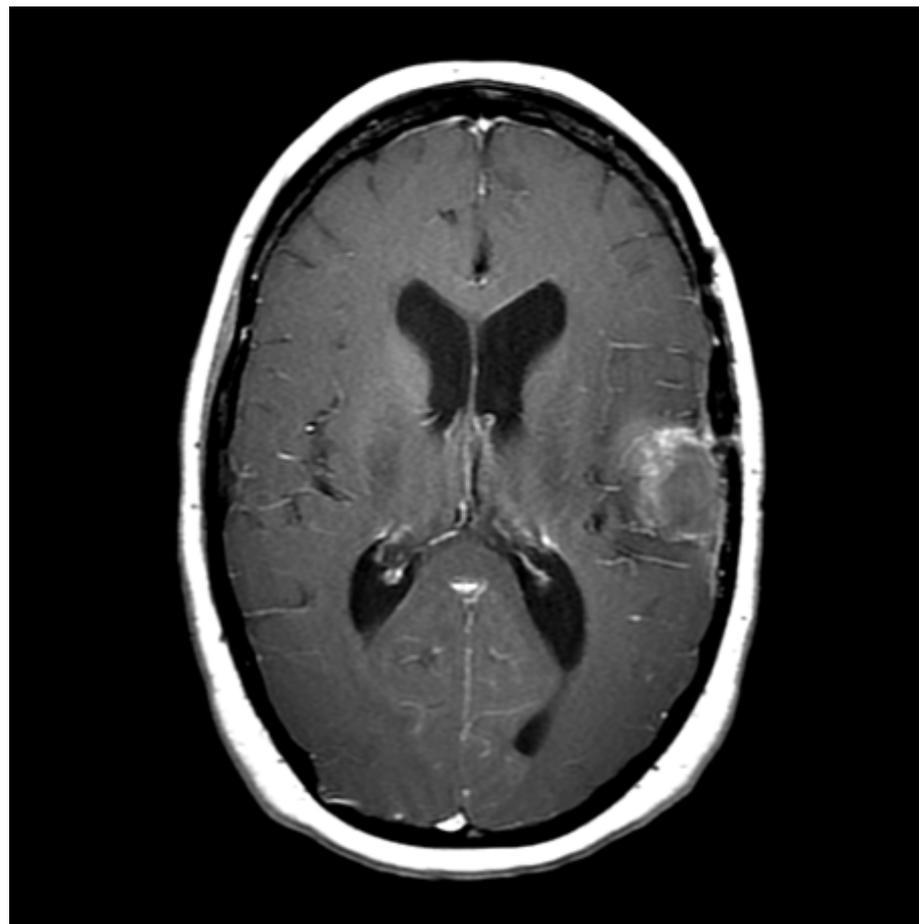
December 2013

- Within two weeks, she reports resolution of headaches, improvement of speech and memory.
- She celebrates Christmas with her husband and two kids.

Nov 2013



Jan 2014



CASE REPORT

Open Access

Complete clinical regression of a BRAF V600E-mutant pediatric glioblastoma multiforme after BRAF inhibitor therapy

Giles W Robinson^{1*}, Brent A Orr² and Amar Gajjar¹

Conclusion

- Epithelioid GBM with *BRAF* V600E mutation in an adult that responded dramatically to a BRAF inhibitor (vemurafenib)

Thank you!