AANP DIAGNOSTIC SLIDE SESSION 2016 CASE 2016-2

Katherine E. Schwetye, MD, PhD

Neuropathology Fellow

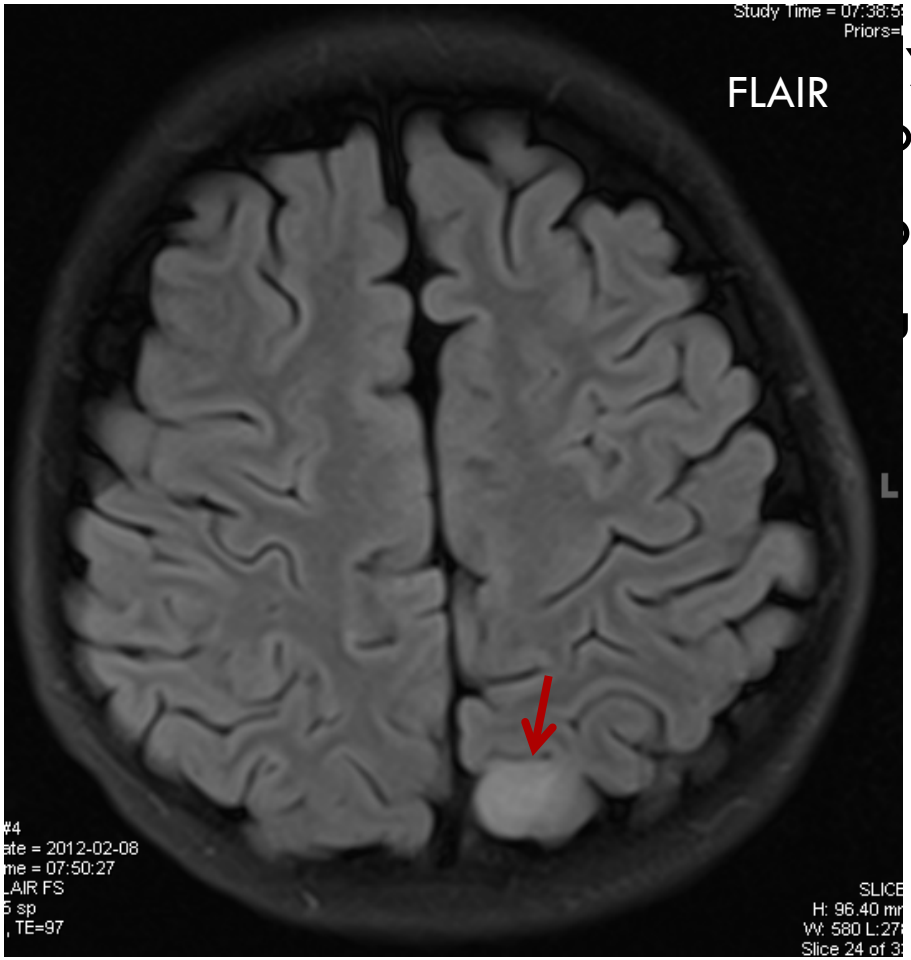
Robert E. Schmidt, MD, PhD

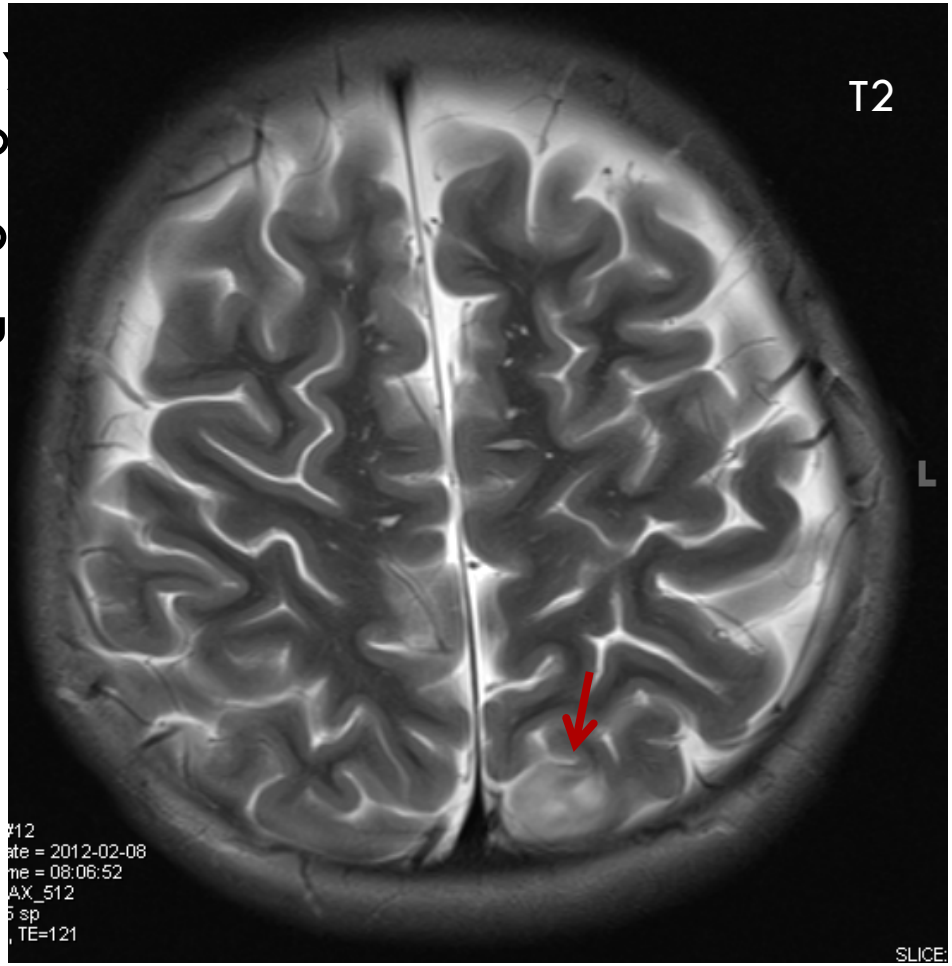
Professor and Division Head

Washington University in St. Louis
School of Medicine

No financial disclosures

Clinical history





Clinical history

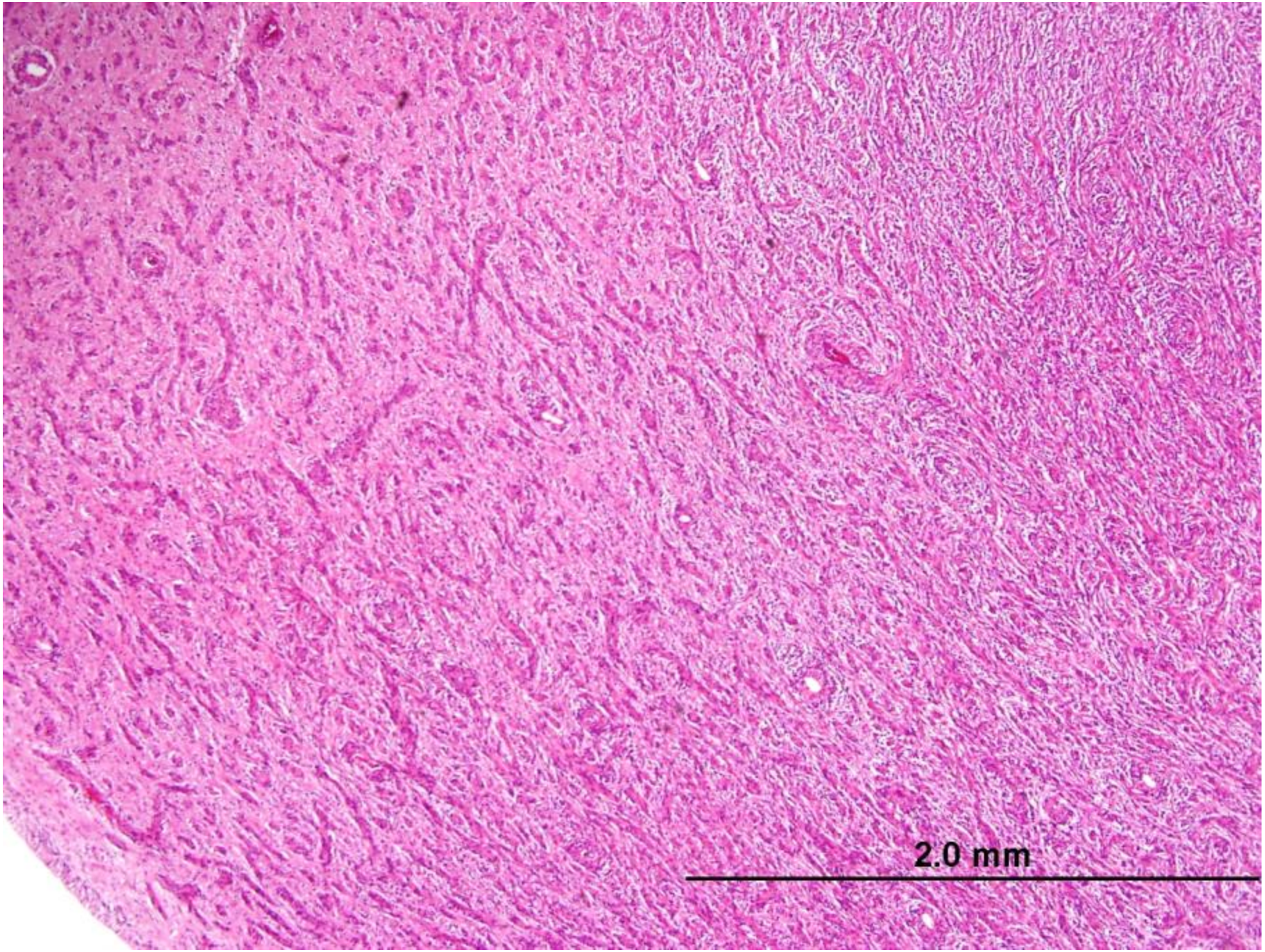
- Previous episodes of status epilepticus in November 2011, April 2014
- Meningococcal meningitis in January-February 2012

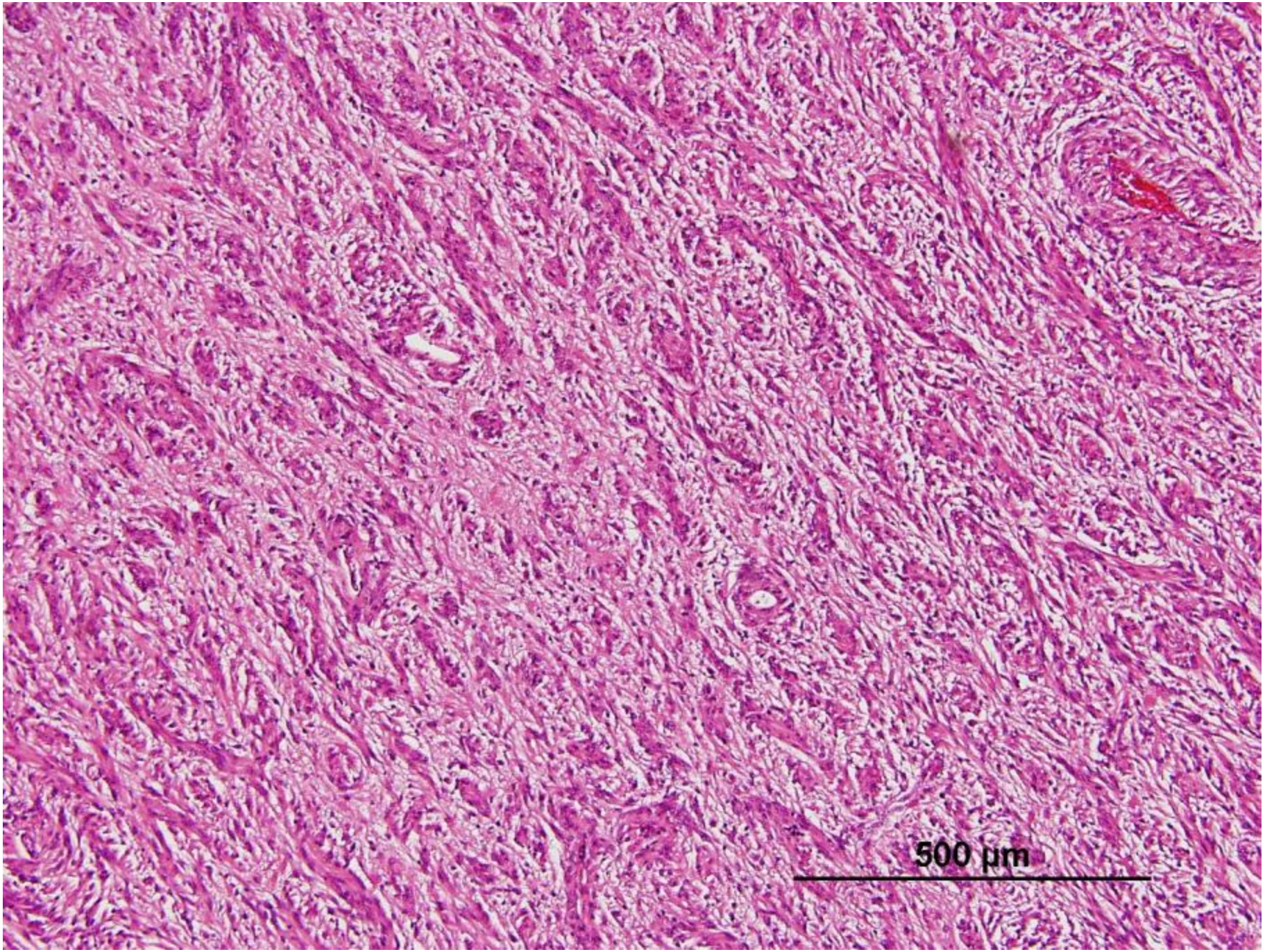
- In August 2014, the patient complained of his usual prodrome, which progressed to a generalized tonic-clonic seizure, bradycardia, and cardiac arrest

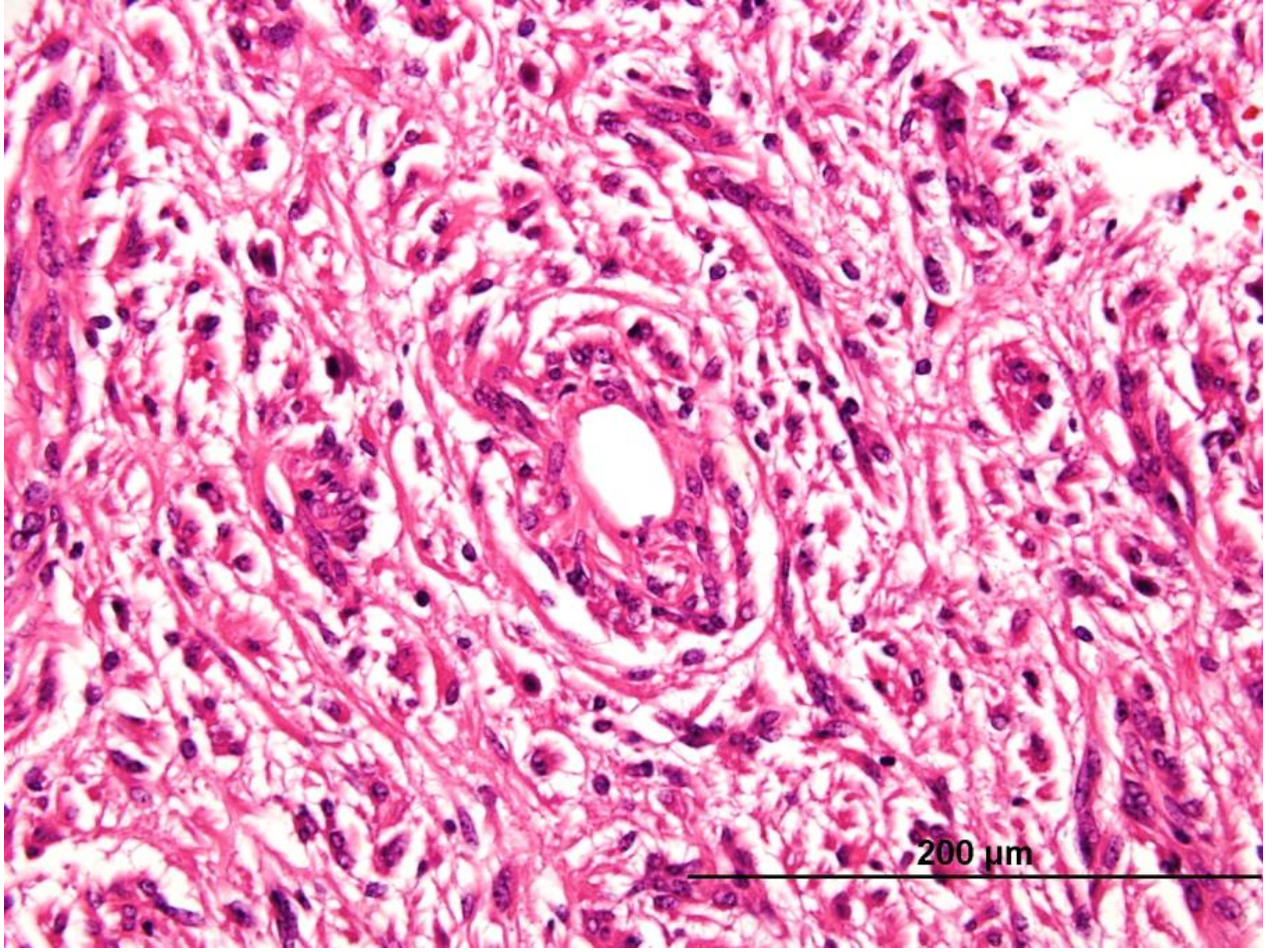
- Despite aggressive resuscitation, prognosis remained poor due to ongoing seizure activity, an aspiration event, fever up to 104° F, and development of disseminated intravascular coagulation complicated by bleeding from dislodged femoral arterial catheters

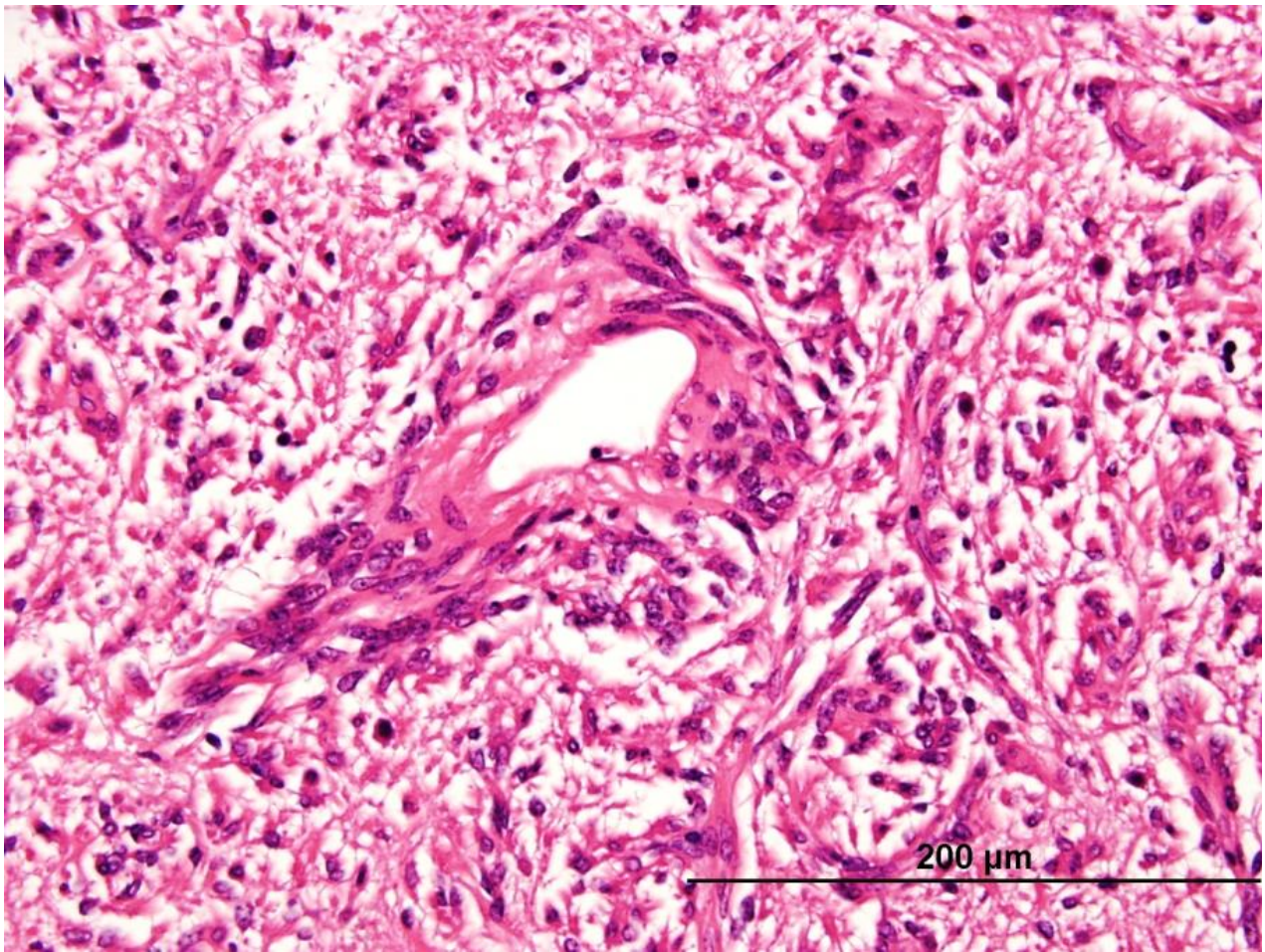
- His family elected to redirect care; death was pronounced approximately 18 hours after seizure onset

Left


2.0 mm

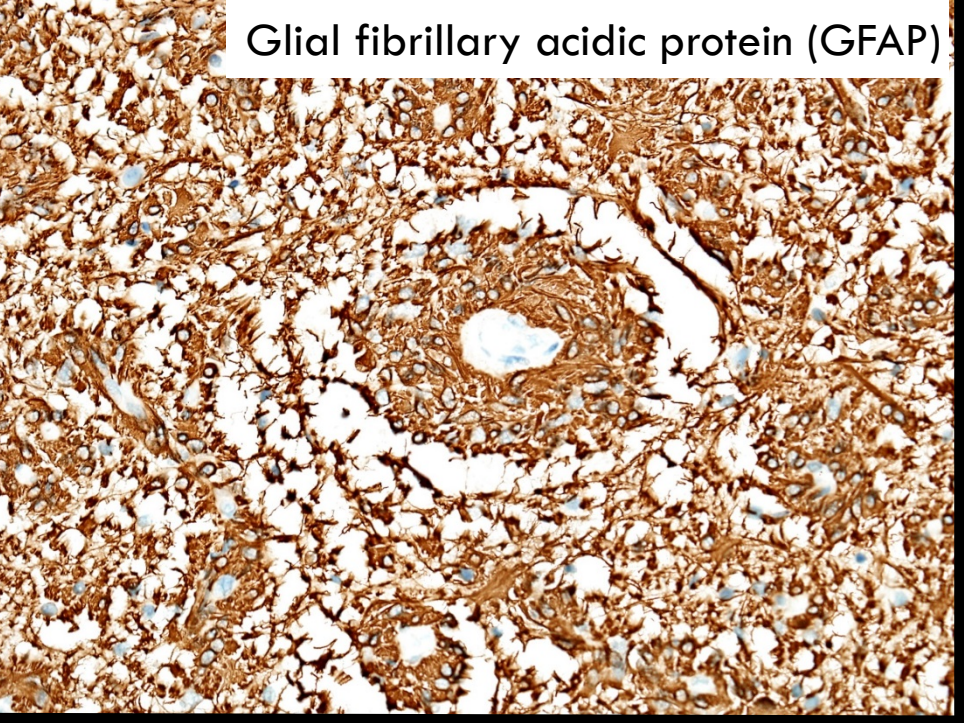

500 µm

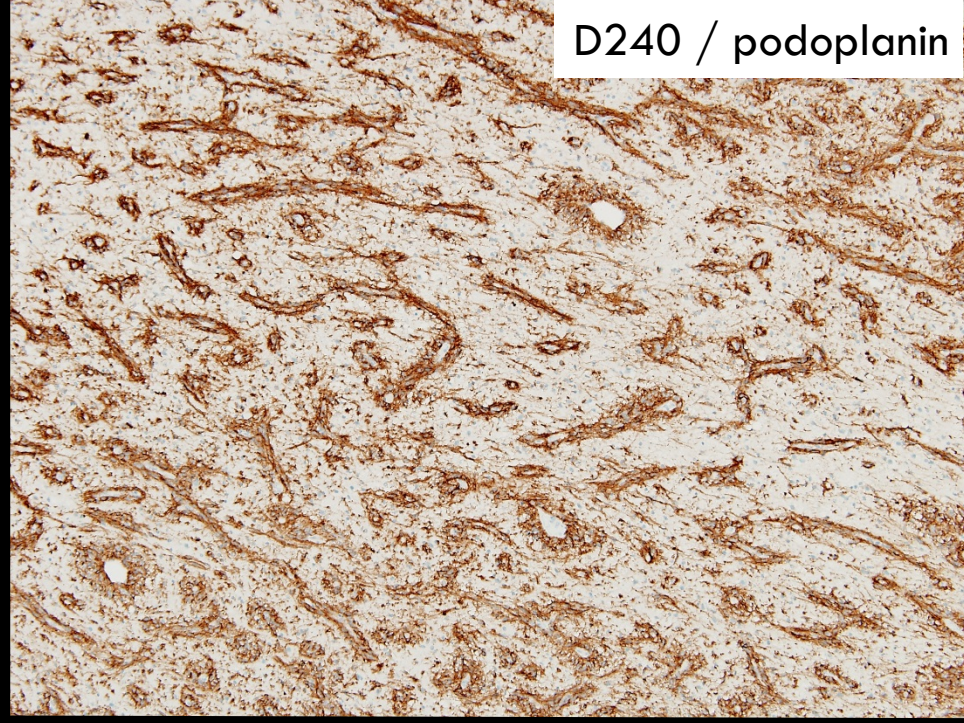

200 µm

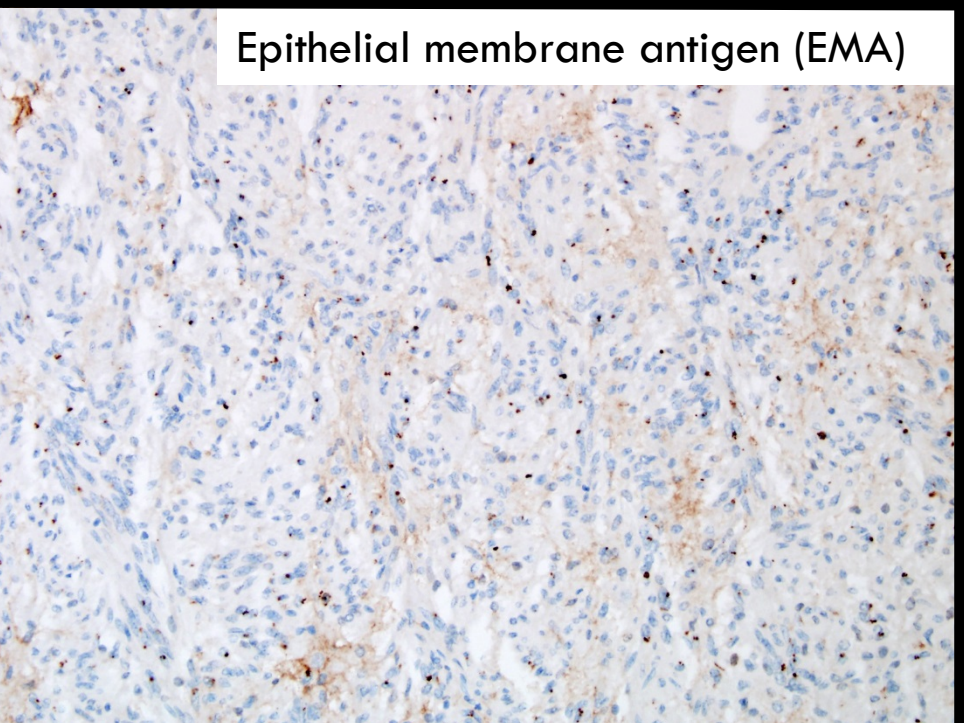

200 µm

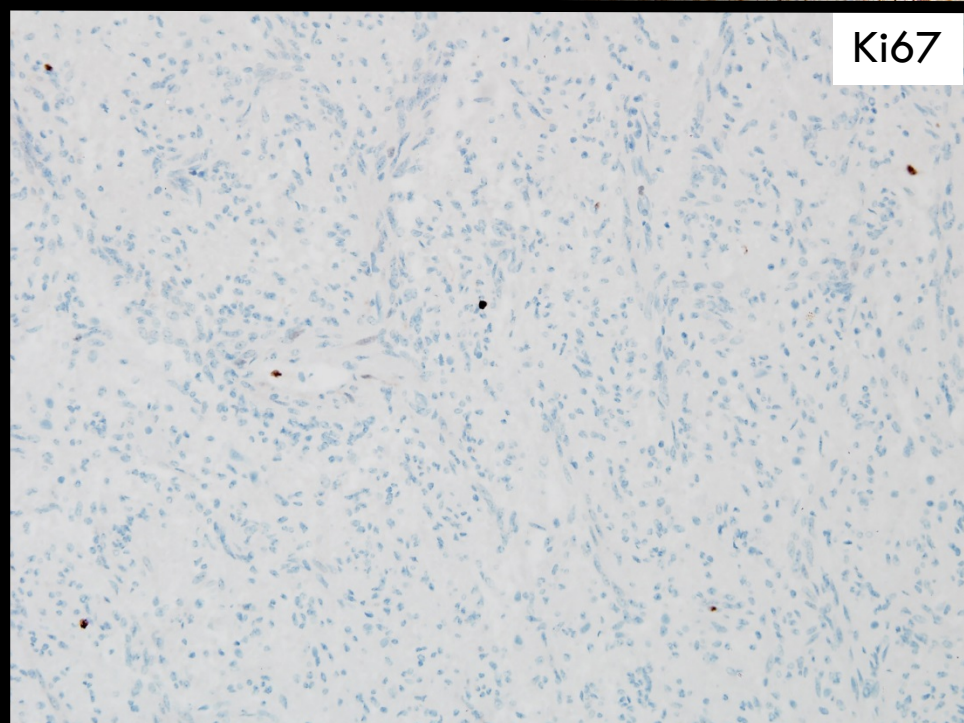
Audience comments?

Immunohistochemistry

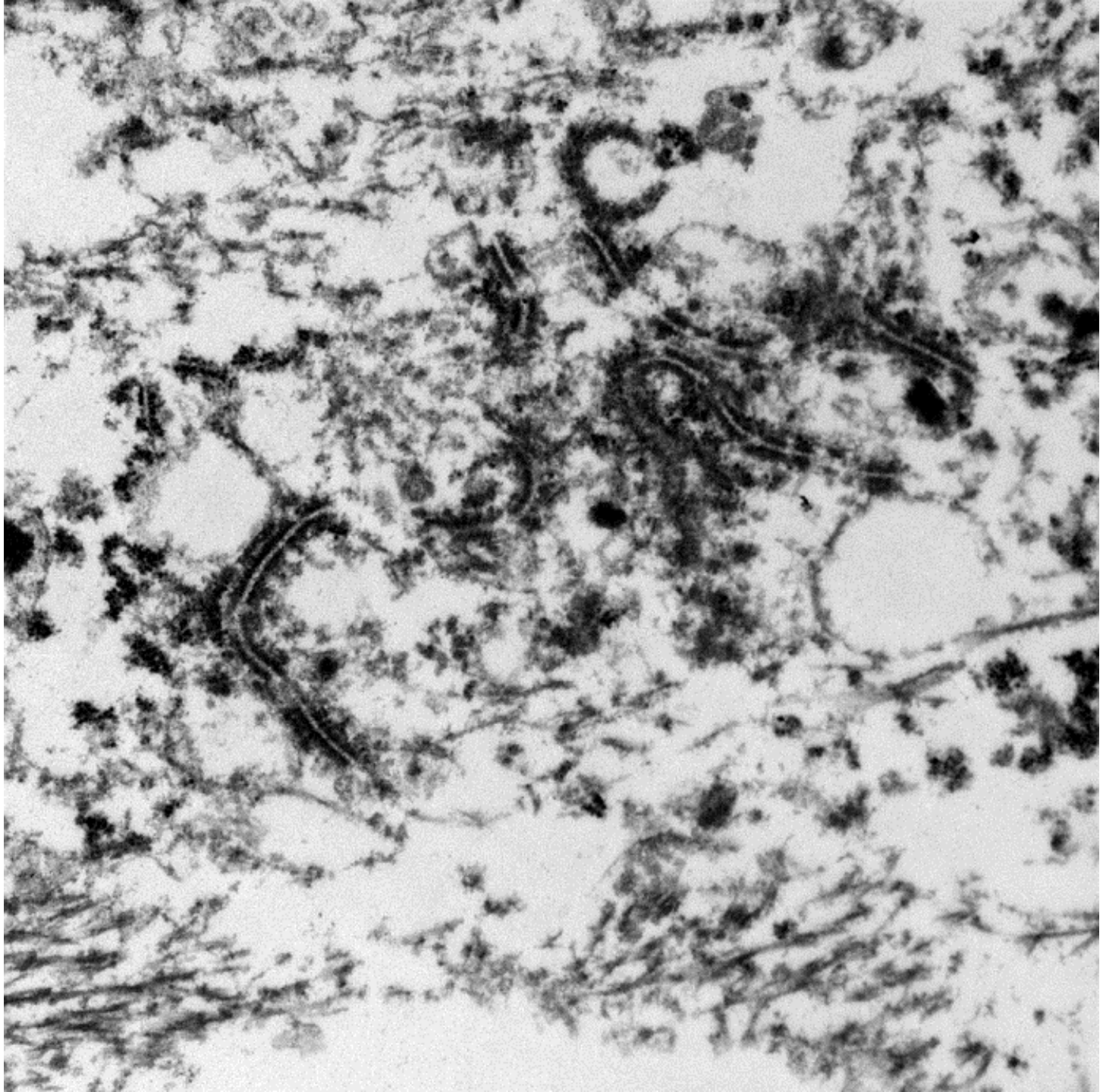

Glial fibrillary acidic protein (GFAP)


D240 / podoplanin


Epithelial membrane antigen (EMA)

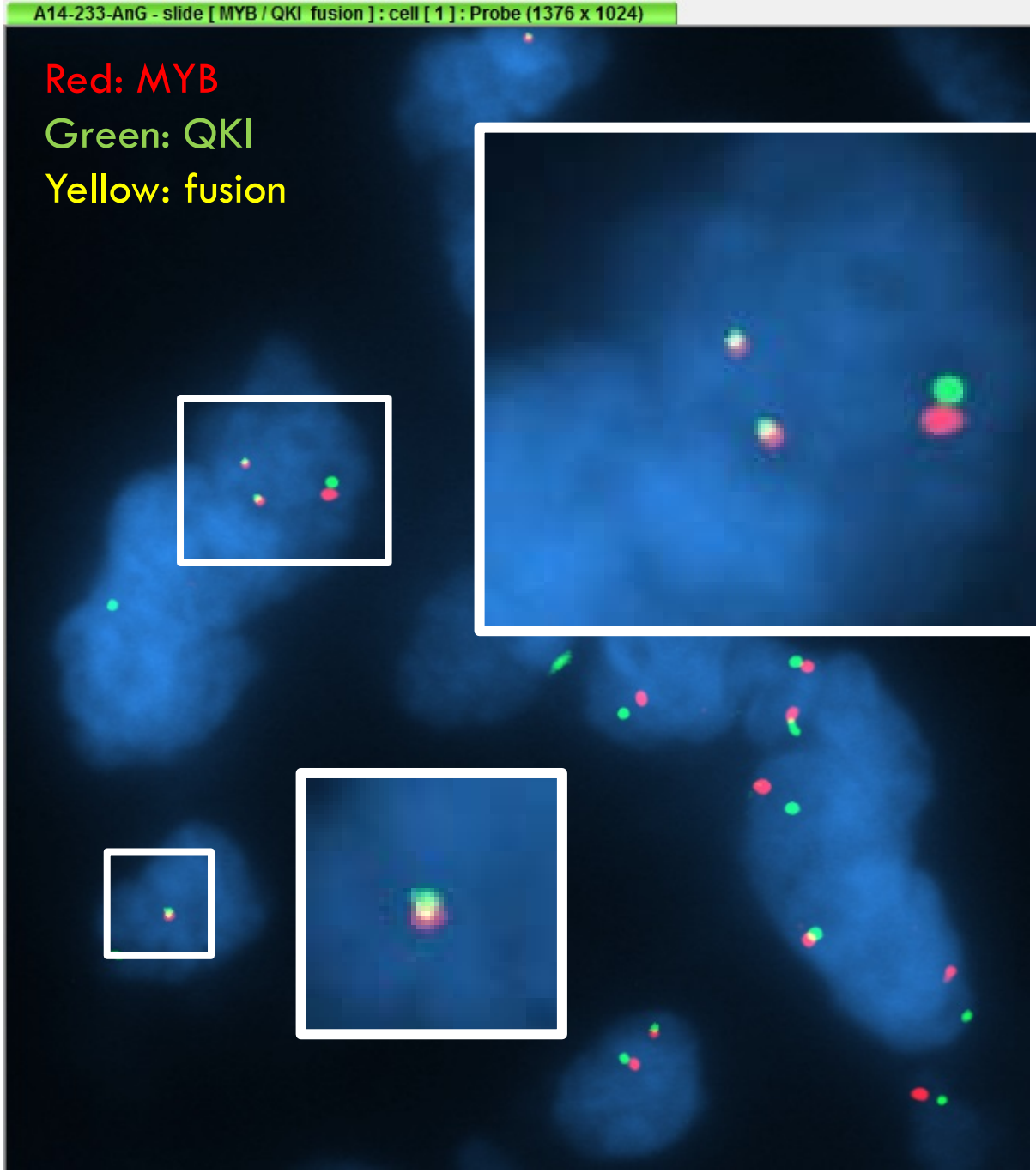

Ki67

Transmission electron microscopy



25000X

Fluorescence *in-situ* hybridization (FISH)



FISH analysis courtesy of Dr. David Ellison and Jim Dalton, St. Jude Children's Research Hospital

Diagnosis

- **ANGIOCENTRIC GLIOMA, WHO GRADE I**

Discussion

- Angiocentric glioma
  - Codified as a new brain tumor type in the 2007 WHO
    - First identified as such in 2005 (Wang M, et al. 2005; Lellouch-Tubiana A, et al. 2005)
    - Seizure is the most common presentation
    - Age range 2 - 79 y; mean of 16 y (Ampie L, et al. 2016)
      - ~50% present in the 1st decade of life
  - Slow-growing, supratentorial tumors
    - Temporal (39%), frontal (30%) cortex/subcortical white matter are most common sites (Ampie L et al., 2016; Cheng S et al, 2015)

Discussion

- Radiographic characteristics
  - Most are non-enhancing solid lesions associated with ill-defined hyperintensity on T2-weighted and FLAIR images
- Histological/immunohistochemical/ultrastructural features
  - H&E: proliferation of monomorphic, bipolar cells growing in a distinctive perivascular pattern, similar to the pseudorosettes of ependymoma and astroblastoma
  - IHC: variably immunoreactive for GFAP, dDotlike" or microlumenal EMA and D240 staining, low Ki-67
  - EM: Intracellular ciliated lumina with microvilli and intercellular "zipper" junctions

Discussion

- Recently, two independent groups reported recurrent genetic rearrangements involving the MYB and QKI genes (Bandopadhayay P et al., 2016; Qaddoumi I et al., 2016)
  - Unique to angiocentric gliomas

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ORIGINAL PAPER

Genetic alterations in uncommon low-grade neuroepithelial tumors: *BRAF*, *FGFR1*, and *MYB* mutations occur at high frequency and align with morphology

Ibrahim Qaddoumi[1] · Wilda Orisme[2] · Ji Wen[2] · Teresa Santiago[2] · Kirti Gupta[2] · James D. Dalton[2] · Bo Tang[2] · Kelly Haupfear[2] · Chandanamali Punchihewa[2] · John Easton[3] · Heather Mulder[3] · Kristy Boggs[3] · Ying Shao[3] · Michael Rusch[3] · Jared Becksfort[3] · Pankaj Gupta[3] · Shuoguo Wang[3] · Ryan P. Lee[2] · Daniel Brat[4] · V. Peter Collins[5] · Sonika Dahiya[6] · David George[7] · William Konomos[8] · Kathreena M. Kurian[9] · Kathryn McFadden[10] · Luciano Neder Serafini[11] · Hilary Nickols[12] · Arie Perry[13] · Sheila Shurtleff[2] · Amar Gajjar[1] · Fredrick A. Boop[14] · Paul D. Klimo Jr.[14] · Elaine R. Mardis[6] · Richard K. Wilson[6] · Suzanne J. Baker[15] · Jinghui Zhang[3] · Gang Wu[3] · James R. Downing[2] · Ruth G. Tatevossian[2] · David W. Ellison[2]

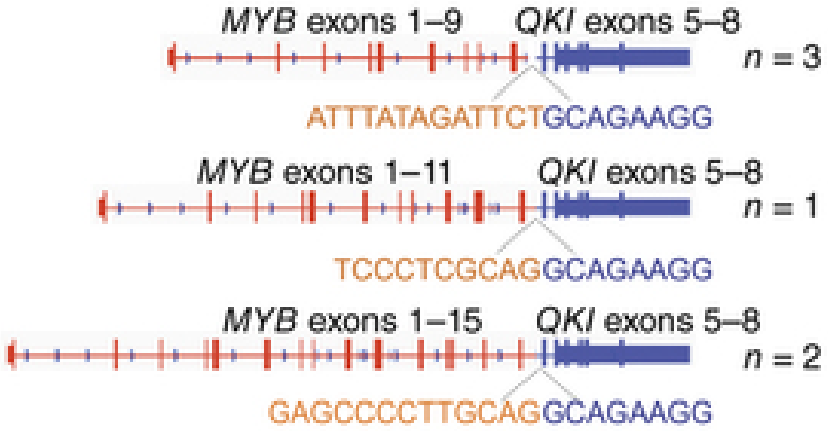
nature genetics

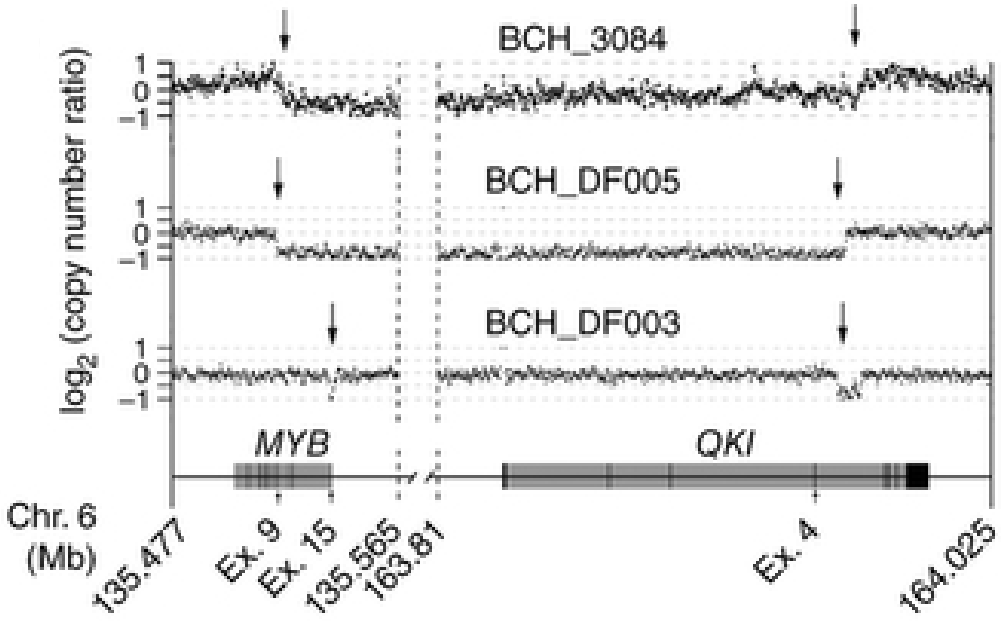
MYB-QKI rearrangements in angiocentric glioma drive tumorigenicity through a tripartite mechanism

Pratiti Bandopadhayay[1–4,50], Lori A Ramkissoon[5,50], Payal Jain[6–8,50], Guillaume Bergthold[1,9,50], Jeremiah Wala[1,3,4], Rhamy Zeid[4,5], Steven E Schumacher[1,3], Laura Urbanski[1], Ryan O'Rourke[1,3], William J Gibson[1,3,4], Kristine Pelton[5], Shakti H Ramkissoon[5,10–12], Harry J Han[6,7], Yuankun Zhu[6,7], Namrata Choudhari[6,7], Amanda Silva[5–7], Katie Boucher[6,7], Rosemary E Henn[6,7], Yun Jee Kang[5], David Knoff[5], Brenton R Paolella[1,3,4], Adrianne Gladden-Young[13], Pascale Varlet[14], Melanie Pages[14], Peleg M Horowitz[1,15], Alexander Federation[4,5], Hayley Malkin[2], Adam A Tracy[3], Sara Seepo[3], Matthew Ducar[10,16], Paul Van Hummelen[16], Mariarita Santi[17,18], Anna Maria Buccoliero[19], Mirko Scagnet[20], Daniel C Bowers[21], Caterina Giannini[22], Stephanie Puget[23], Cynthia Hawkins[24], Uri Tabori[25], Almos Klekner[26], Laszlo Bognar[26], Peter C Burger[27], Charles Eberhart[27], Fausto J Rodriguez[27], D Ashley Hill[28–30], Sabine Mueller[31–33], Daphne A Haas-Kogan[32,34,35], Joanna J Phillips[32,36], Sandro Santagata[1,10–12], Charles D Stiles[1], James E Bradner[3,5,37], Nada Jabado[38–40], Alon Goren[13], Jacques Grill[9], Azra H Ligon[41], Liliana Goumnerova[2,42,43], Angela J Waanders[44–46,48], Phillip B Storm[6,7,45,48], Mark W Kieran[2,4], Keith L Ligon[3,5,10–12,51], Rameen Beroukhim[1,3,5,37,49,51] & Adam C Resnick[6,7,45,47,48,51]

Tumors	*n*	*MYB-QKI*	Other *MYB*	No *MYB*
Angiocentric glioma	7	6	1	0
Non-angiocentric glioma	147	0	9	138

$P < 0.0001$





Bandopadhayay, P et al. Nat Genet. 2016 Mar;48(3):273-82

Discussion

- Most common rearrangement: MYB-QKI fusion event which truncates MYB

- Experimental models demonstrate the oncogenic potential of both the fusion transcript MYB-QKI and truncated MYB, recapitulate histomorphological features of the human tumor (Bandopadhayay P et al., 2016)

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6. Bandopadhayay, P et al. MYB-QKI rearrangements in angiocentric glioma drive tumorigenicity through a tripartite mechanism. Nat Genet. 2016 Mar;48(3):273-82.

7. Qaddoumi I, et al. Genetic alterations in uncommon low-grade neuroepithelial tumors: BRAF, FGFR1, and MYB mutations occur at high frequency and align with morphology. Acta Neuropathol. 2016 Jan 25.

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Thank you!


Institute of Health
at
Washington University
School of Medicine