

Diagnostic Slide Session 2017

Case 2017-4

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Disclosures

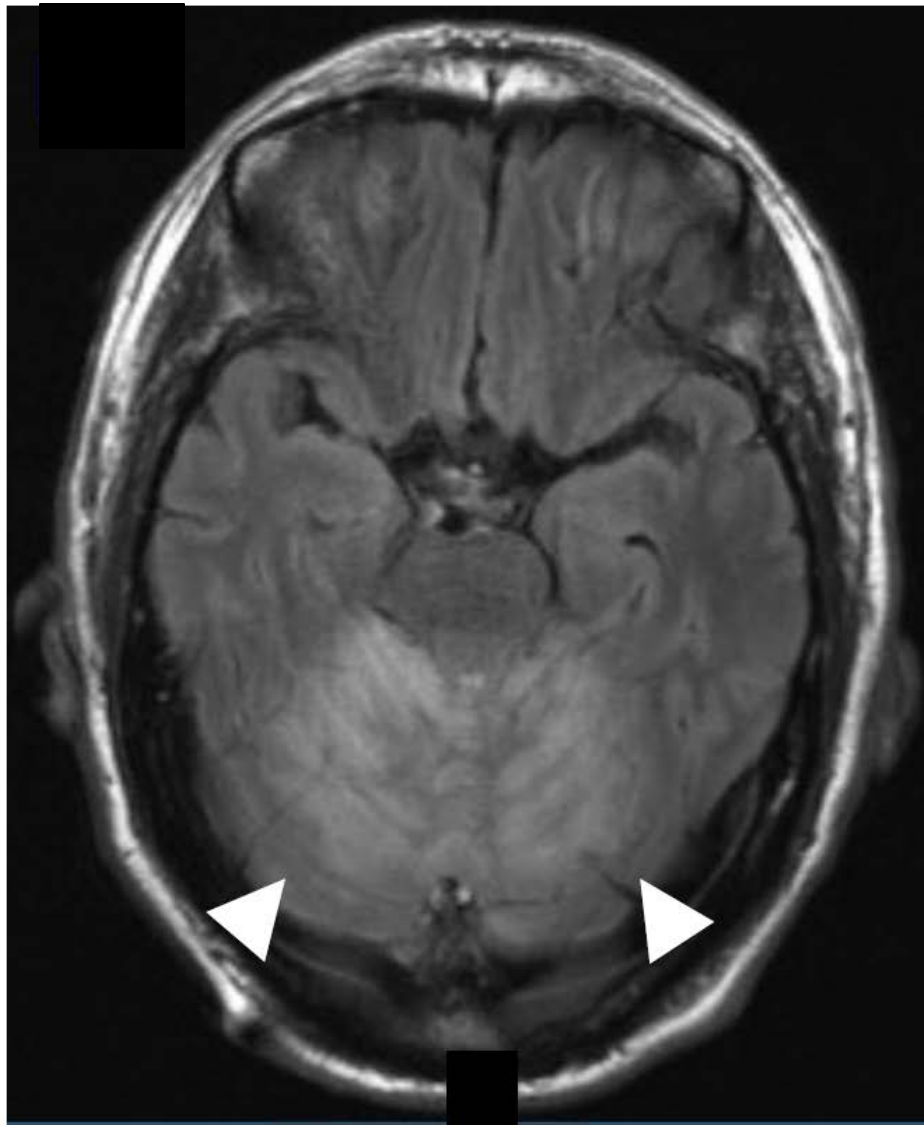
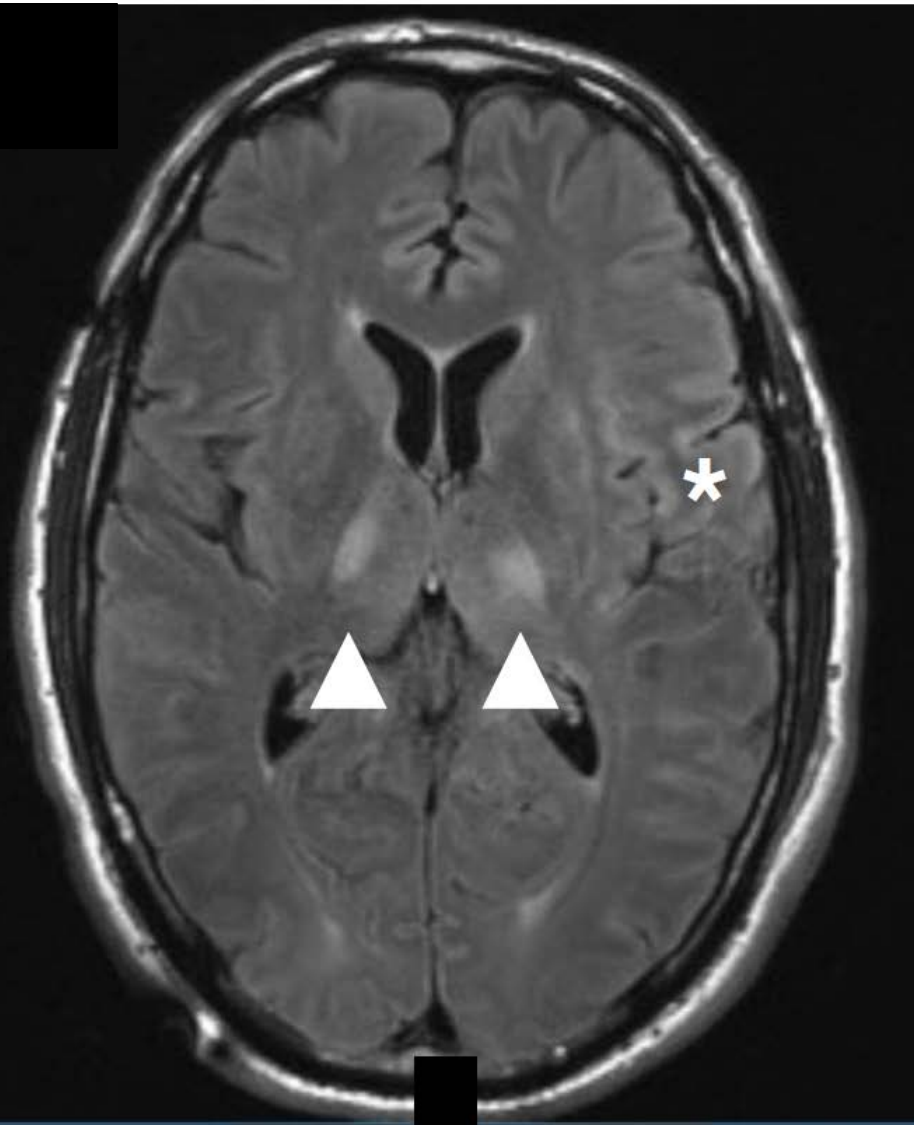
- **No conflicts of interest to report.**

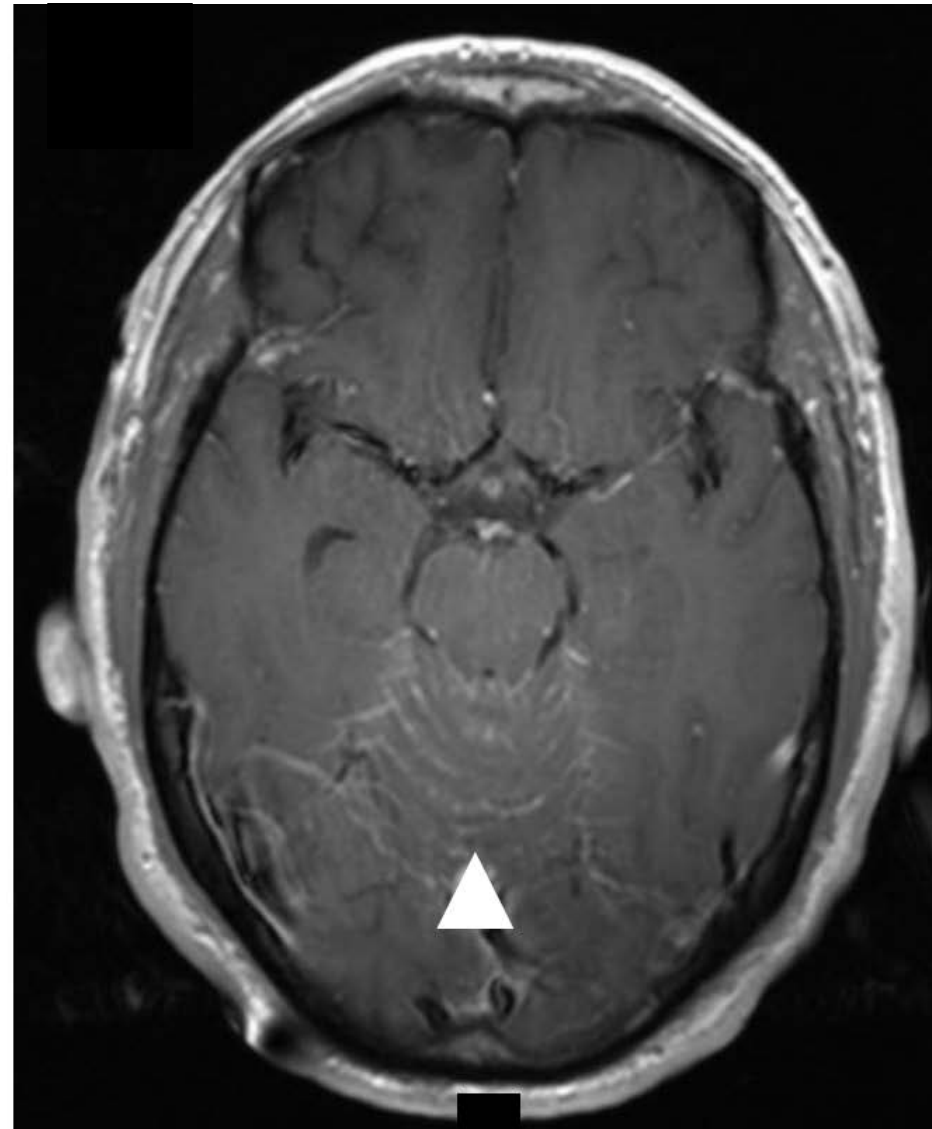
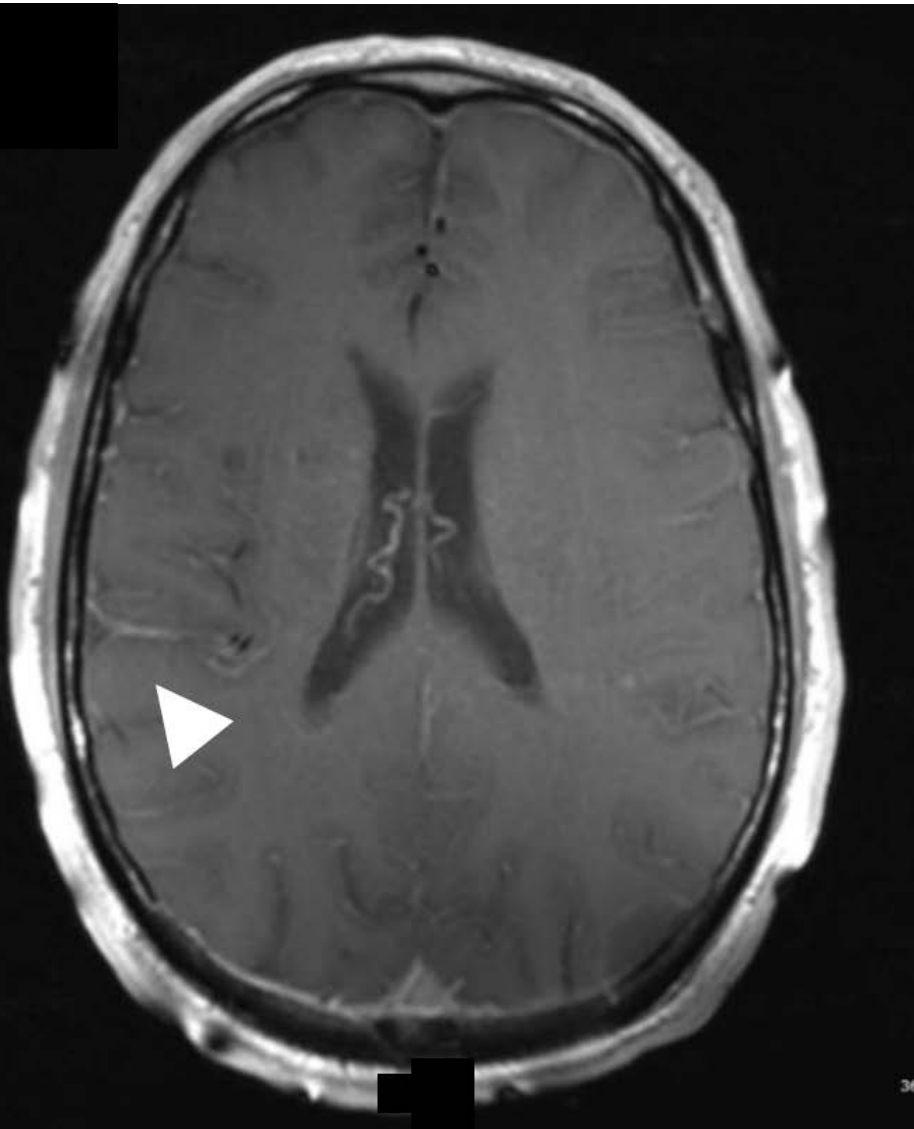


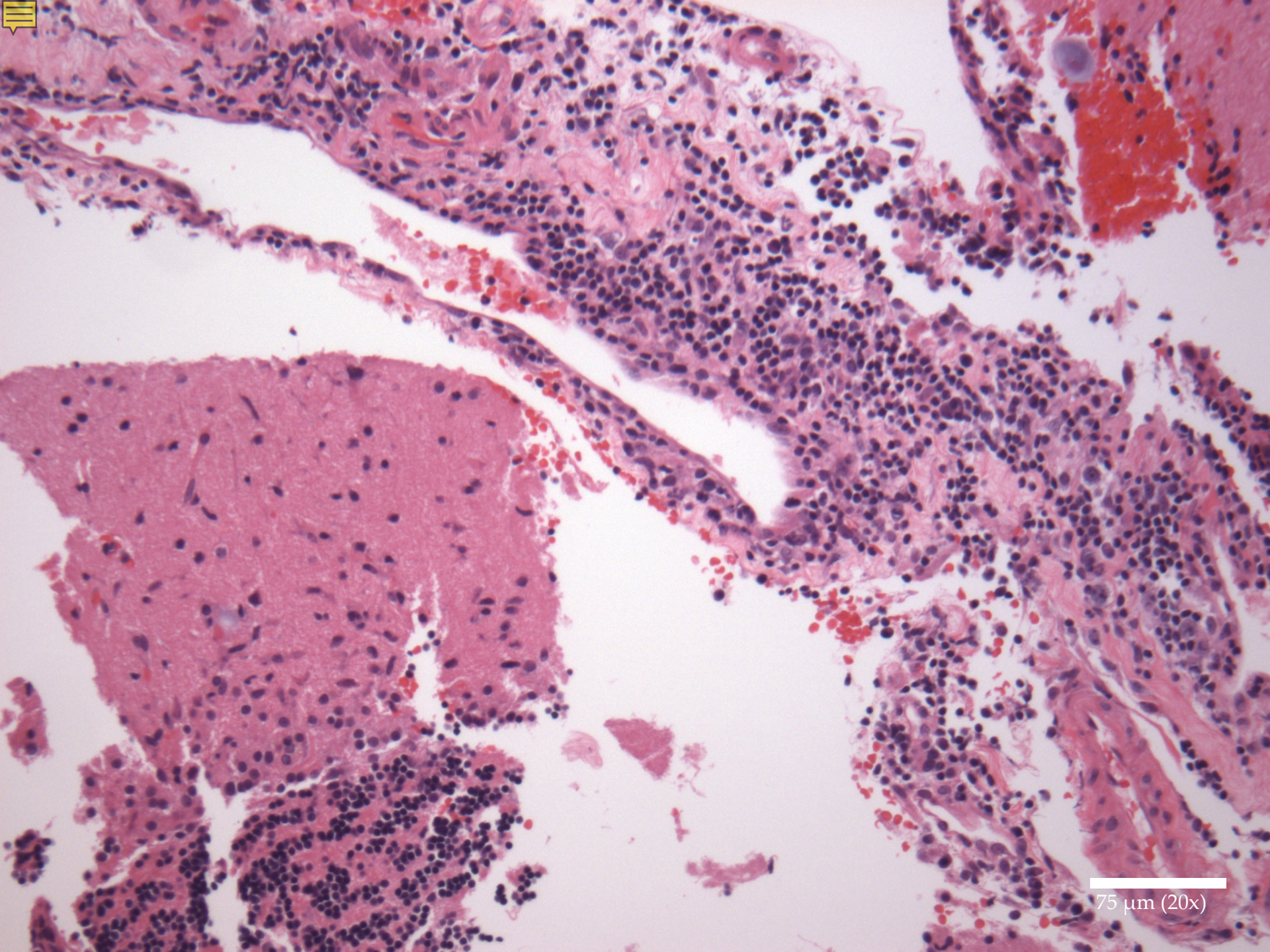
Clinical history

- 61 year-old man with multiple recent tick bites presented with 3 day history of headache, gait instability, lethargy and confusion
- Symptoms worsened rapidly requiring endotracheal intubation and failing to open his eyes to stimulation or follow commands despite minimal sedation
- LP showed lymphocytic pleocytosis
 - 430 leukocytes (96% lymphocytes and 4% monocytes) and 5 red blood cells per cubic millimeter, protein of 133 mg per deciliter, and glucose of 43 mg per deciliter
- Past HX: Crohn's disease (Rx: adalimumab)

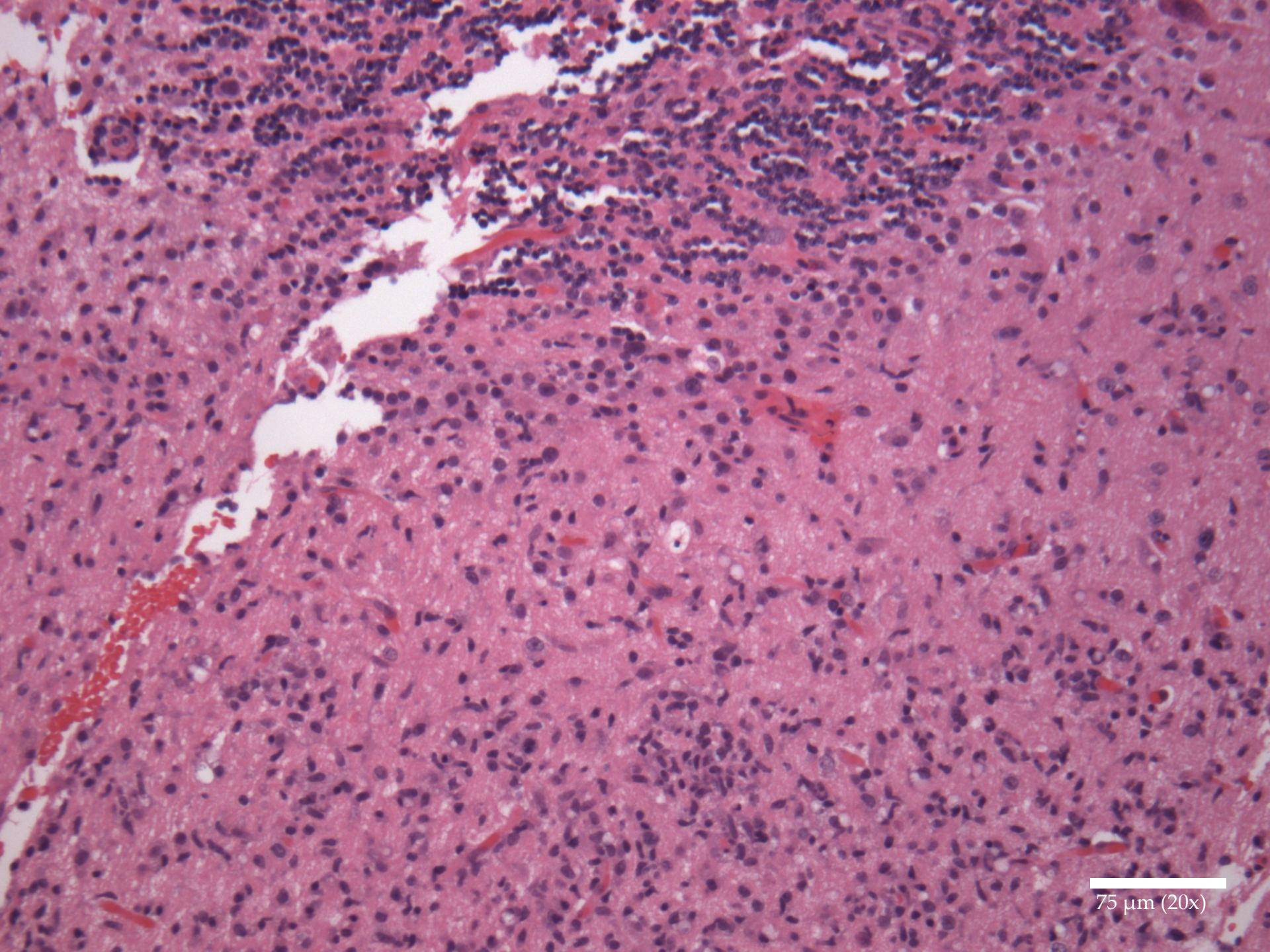




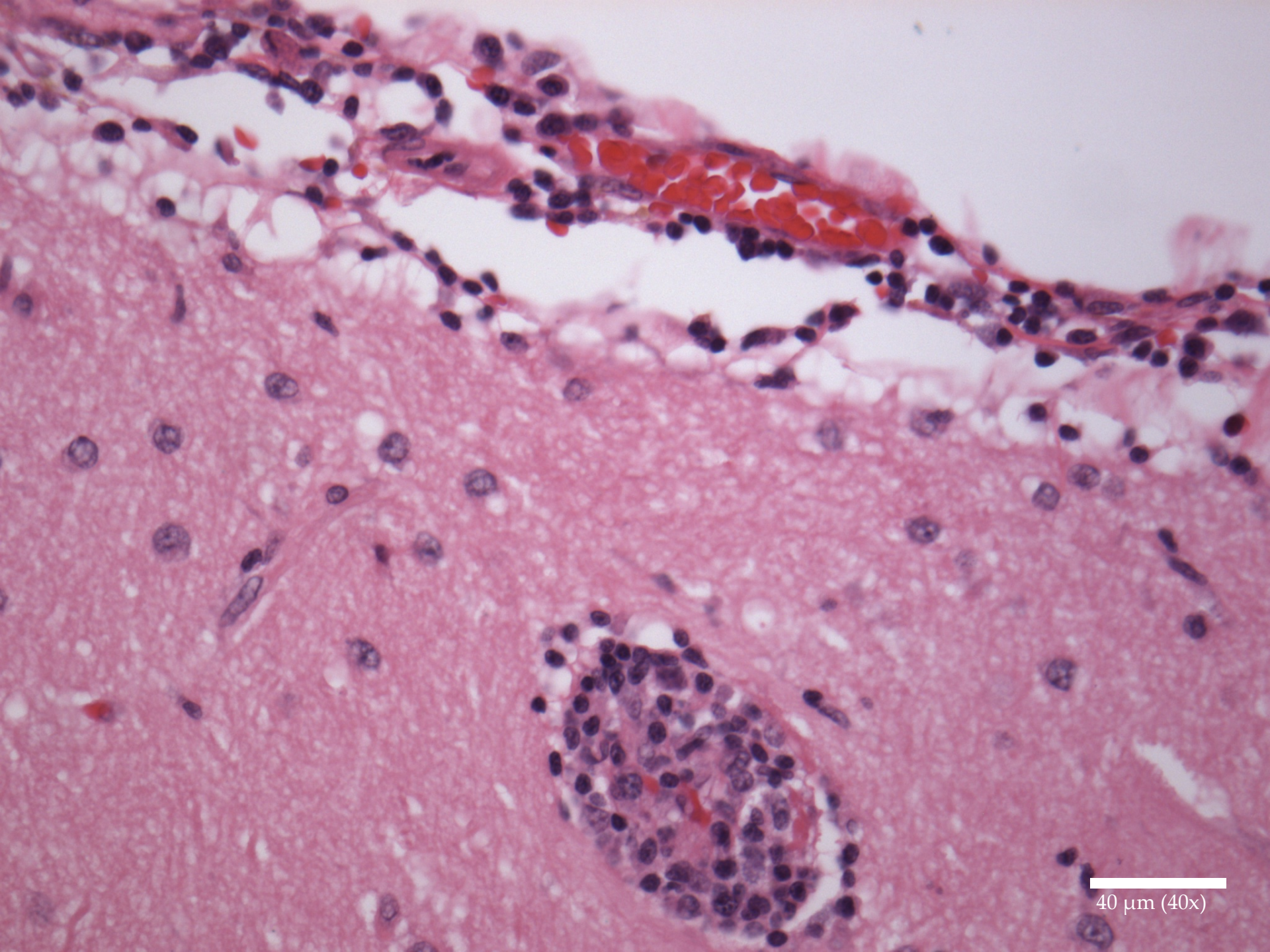




75 μm (20x)



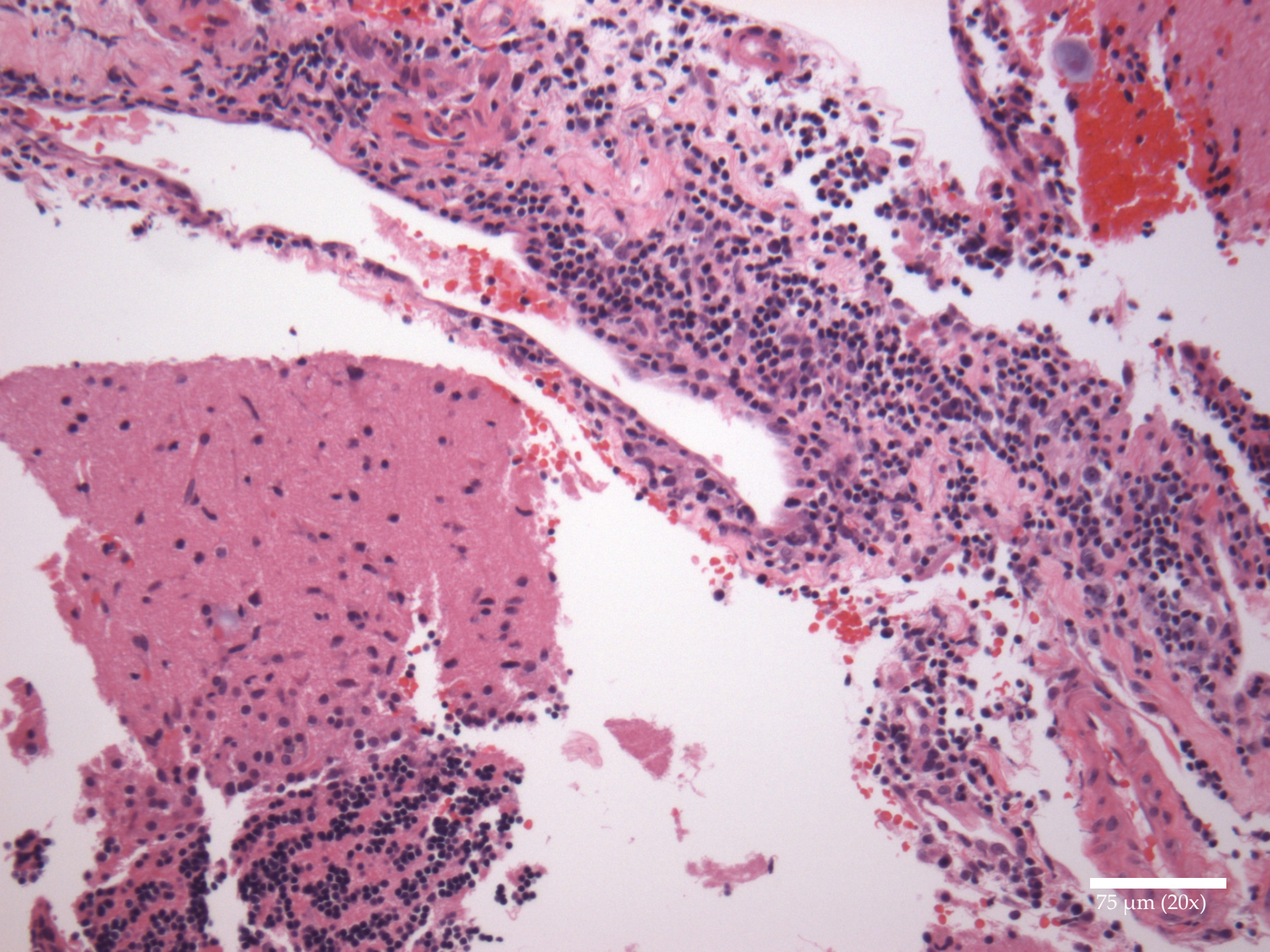
75 μ m (20x)



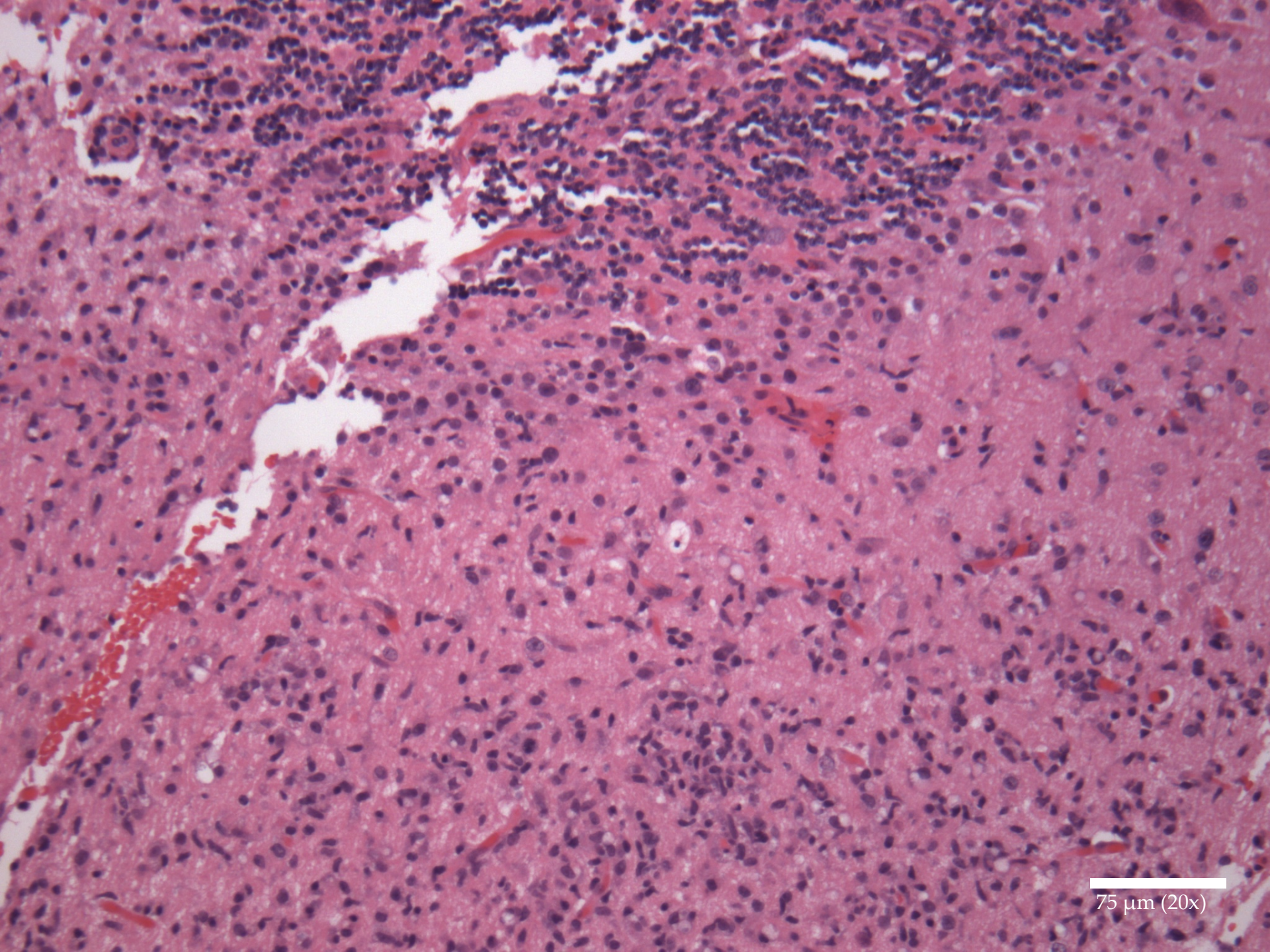
40 μ m (40x)

Audience discussion

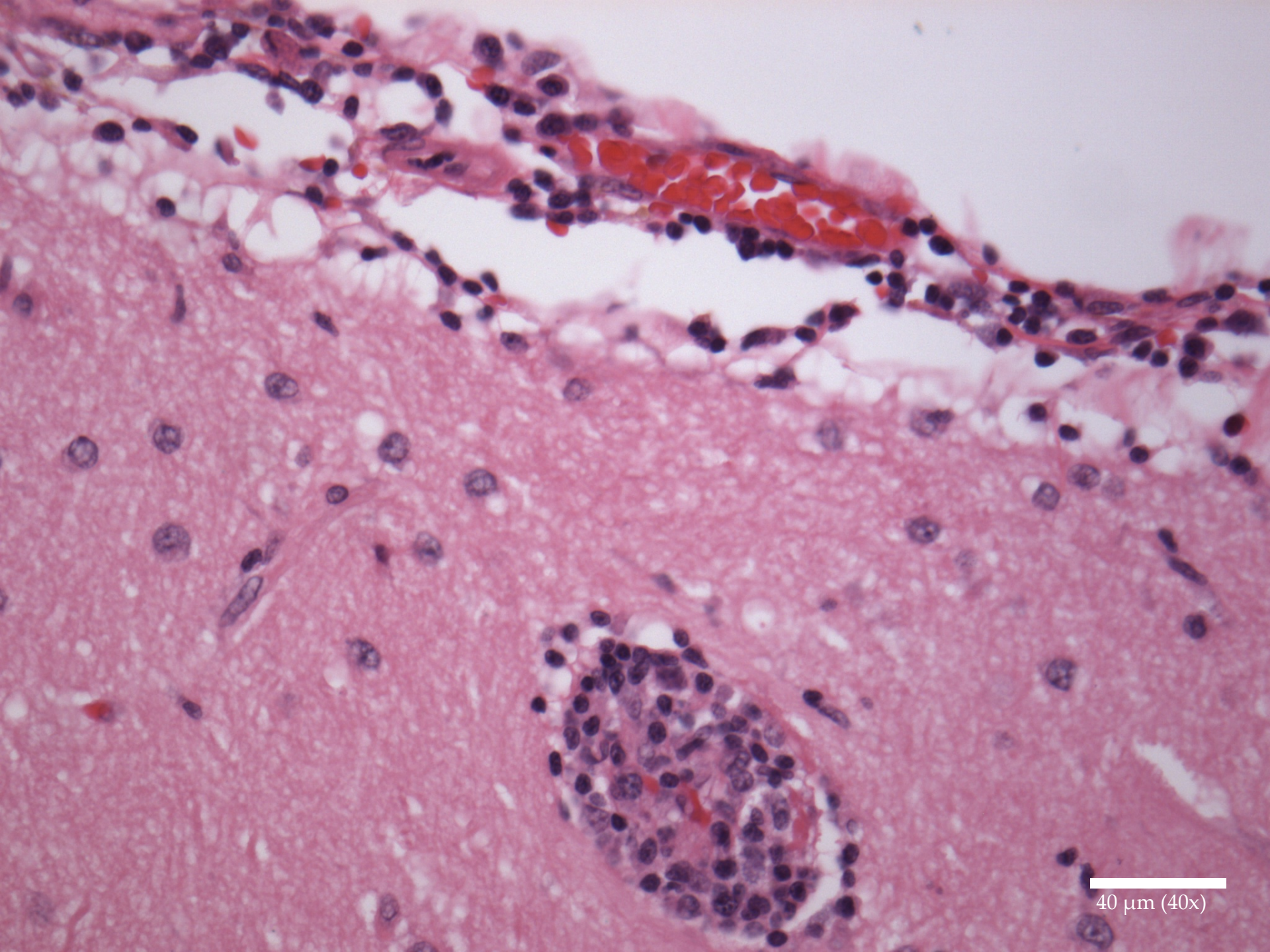




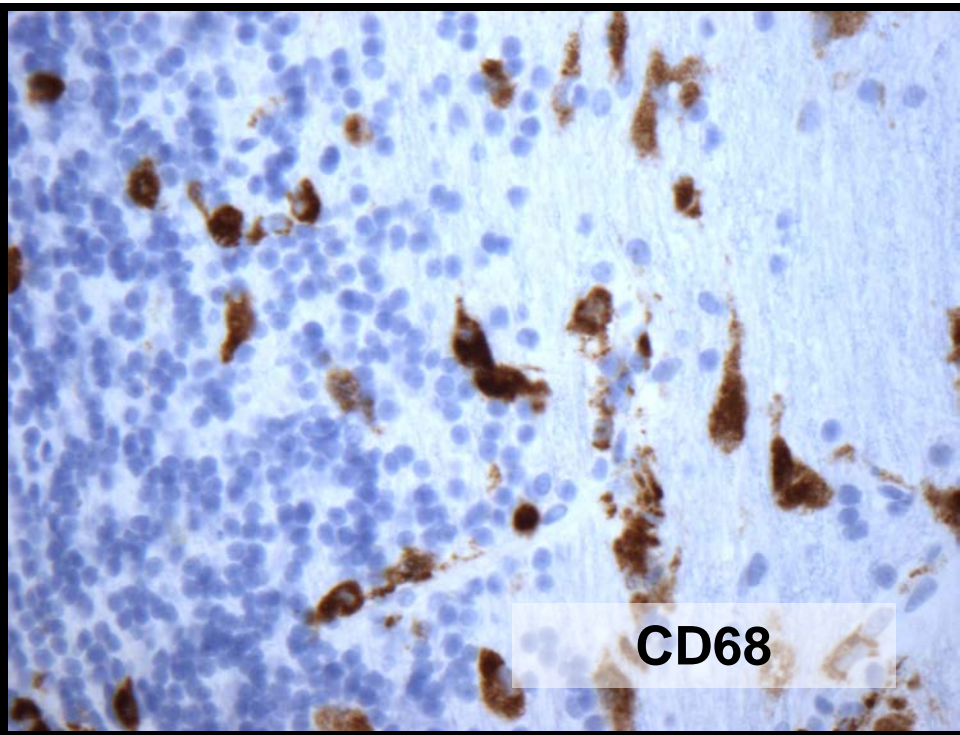
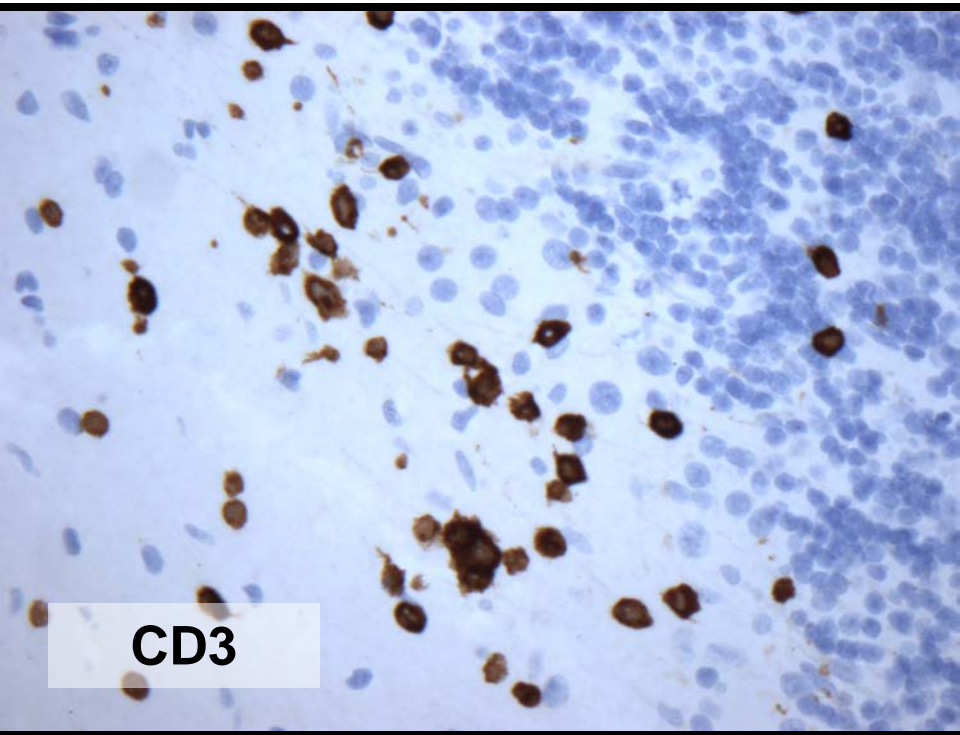
75 μm (20x)



75 μ m (20x)



40 μ m (40x)



Timeline of diagnostic tests

- Wide range of testing performed initially
- Day 8: patient enrolled in research protocol for deep sequencing of CSF sample
- Day 11: Brain biopsy performed
- Day 12: Powassan virus sequences detected in CSF sample. With permission of IRB, information reported to clinical team
- CDC received tissue block, IHC equivocal
- Day 40: Serology testing positive at CDC



Research study

- Metagenomic sequencing was performed for rapid and unbiased pathogen detection
- Among 2.4 million total sequencing reads, ten reads belonged to Powassan virus
- Partial Powassan virus genome was assembled from CSF representing 19% of the genome
- Powassan virus not detected in patient's plasma (7.3 million reads) or whole blood (9.3 million reads)
- Metagenomic sequencing from brain biopsy performed later also detected Powassan virus, and assembled another partial genome (22%)
- These partial genomes were highly similar, and both belonged to Powassan lineage II



| Location | Date | Source | GenBank ID |
|-------------|------|--------------------------|------------|
| New England | 2016 | Human CSF | |
| New England | 2016 | Human brain | |
| Connecticut | 2010 | <i>Ixodes scapularis</i> | KU886216 |

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| Connecticut | 2010 | <i>Ixodes scapularis</i> | KU886216 |
| Nantucket | 1996 | <i>Ixodes scapularis</i> | HM440559 |
| Connecticut | 1995 | Ixodid tick | AF311056 |
| New York | 2013 | <i>Ixodes scapularis</i> | KJ746872 |
| Wisconsin | 2008 | <i>Ixodes scapularis</i> | HM440560 |
| Wisconsin | 2008 | <i>Ixodes scapularis</i> | HM440561 |



Final diagnosis

Powassan virus encephalitis

- Revealed by metagenomic CSF testing
- Confirmed by serology testing at CDC
- All other studies negative



Protect yourself from infected ticks carrying life-threatening Powassan virus

 **USA TODAY NETWORK** Ashley May , USA TODAY Published 1:50 p.m. ET May 3, 2017 | Updated 5:52 a.m. ET May 4, 2017


CBS NEWS / May 5, 2017, 2:23 PM

Experts warn of deadly tick-borne Powassan virus

Powassan Virus Is the Scary New Reason to Avoid Ticks

Amanda MacMillan
May 04, 2017



 For more, visit [TIME Health](#).

Rare, tick-borne Powassan virus worries some experts about possible spread

 Linda Carroll
TODAY

May 1, 2017 at 10:24 AM



Powassan virus

- Emerging flavivirus transmitted by *Ixodes* ticks
- Presenting symptoms include fever, headache, nausea, confusion, weakness
- CSF: usually normal glucose, elevated protein, and pleocytosis of 100 to 400 leukocytes per cubic millimeter
- Brain MRI: T₂-weighted/FLAIR hyperintensities within the basal ganglia and thalamus
- Unlike other *Ixodes*-borne pathogens, Powassan virus can be transmitted within just 15 minutes of tick attachment



Conclusion

- We describe a patient with severe encephalitis secondary to Powassan virus, identified by rapid metagenomic sequencing four weeks earlier than by standard serologic testing
- Rapid, unbiased, sensitive diagnostic testing
- Powassan encephalitis virus confers high morbidity & mortality even in immunocompetent patients; supportive care only
- This patient:
 - Minimal neurological recovery, with a tracheostomy and percutaneous endoscopic gastrostomy tube
 - Discharged to SNF on hospital day 30.
 - Four months after discharge, he was able to nod his head to questions but remained quadriplegic



References

- Piantadosi A, et al. Rapid detection of Powassan virus in a patient with encephalitis by metagenomic sequencing, submitted, 2017.
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- Hicar, M, Edwards, K, Bloch, K. "Powassan Virus Infection Presenting as Acute Disseminated Encephalomyelitis In Tennessee". *The pediatric infectious disease journal*. 2011; 30: 86–88.
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