

Diagnostic Slide Session Case 2017-7

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Disclosures

- No relevant financial relationships to disclose.

Clinical History

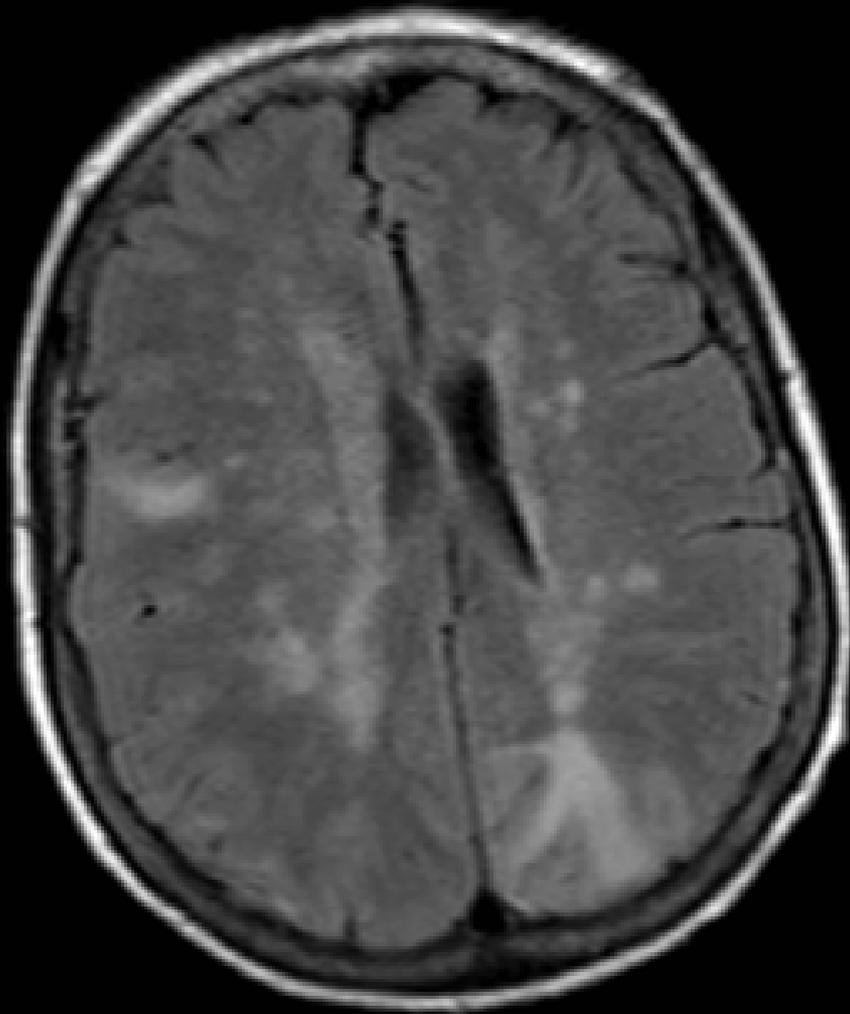
- 71-year-old female
- Past medical history
 - Fibromyalgia
 - Gastrointestinal bleeds
 - Hypertension
 - Migraines
- Social history
 - 50-pack-year of tobacco use
- Initial Presentation
 - Confusion
 - Generalized weakness
 - Headaches
 - Lethargy

Imaging and Laboratory Findings

- Initial CT imaging
 - Right temporal intraparenchymal hemorrhage with surrounding edema and mild mass effect
- Subsequent studies
 - Also numerous foci of microhemorrhages clustered in the right middle cerebral and left posterior cerebral artery distributions
- No prior anticoagulant or antiplatelet medications
- Unremarkable laboratory studies
- Platelet count 258,000/ μ L
- INR 1.0



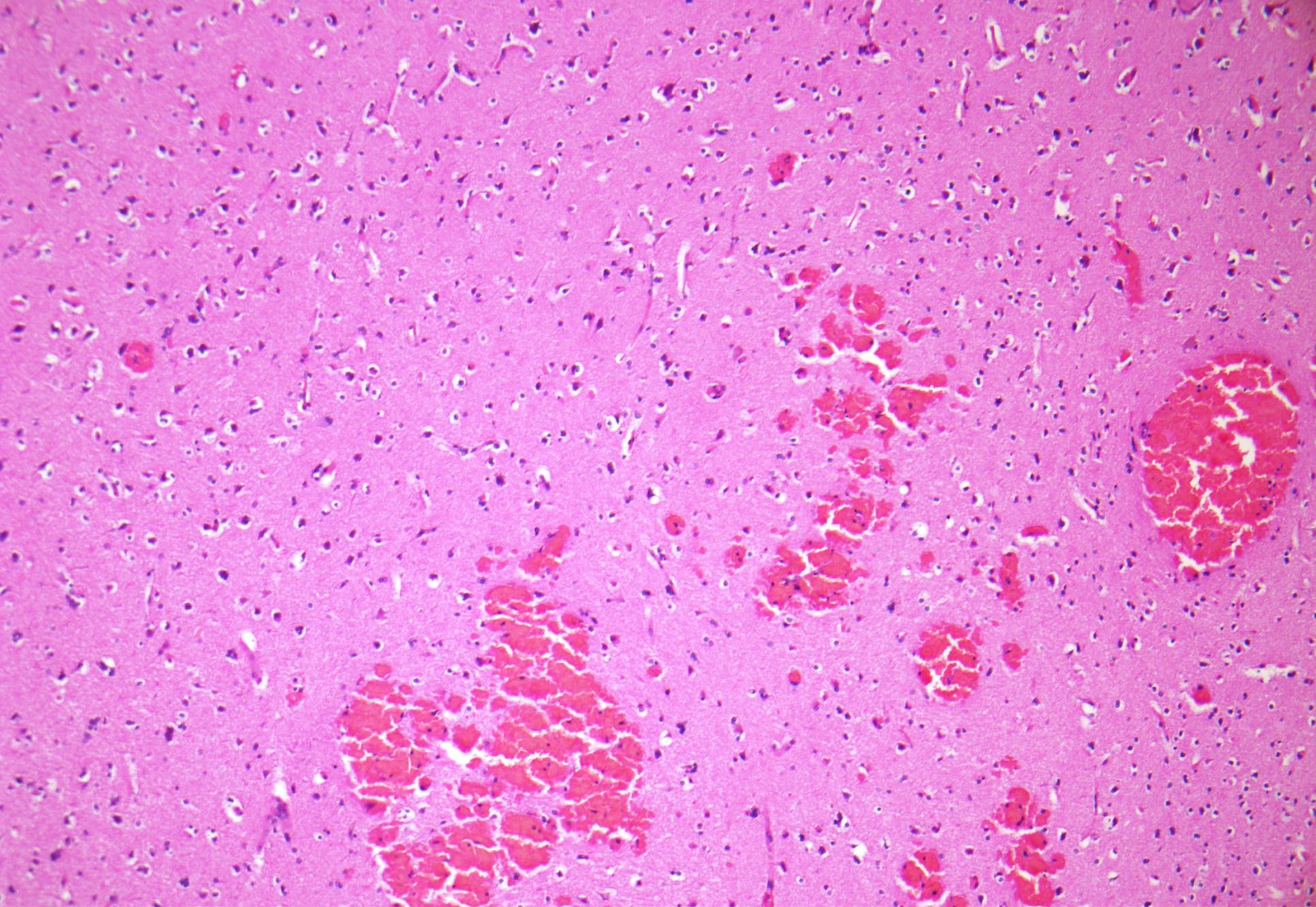
Axial Non-Contrast CT



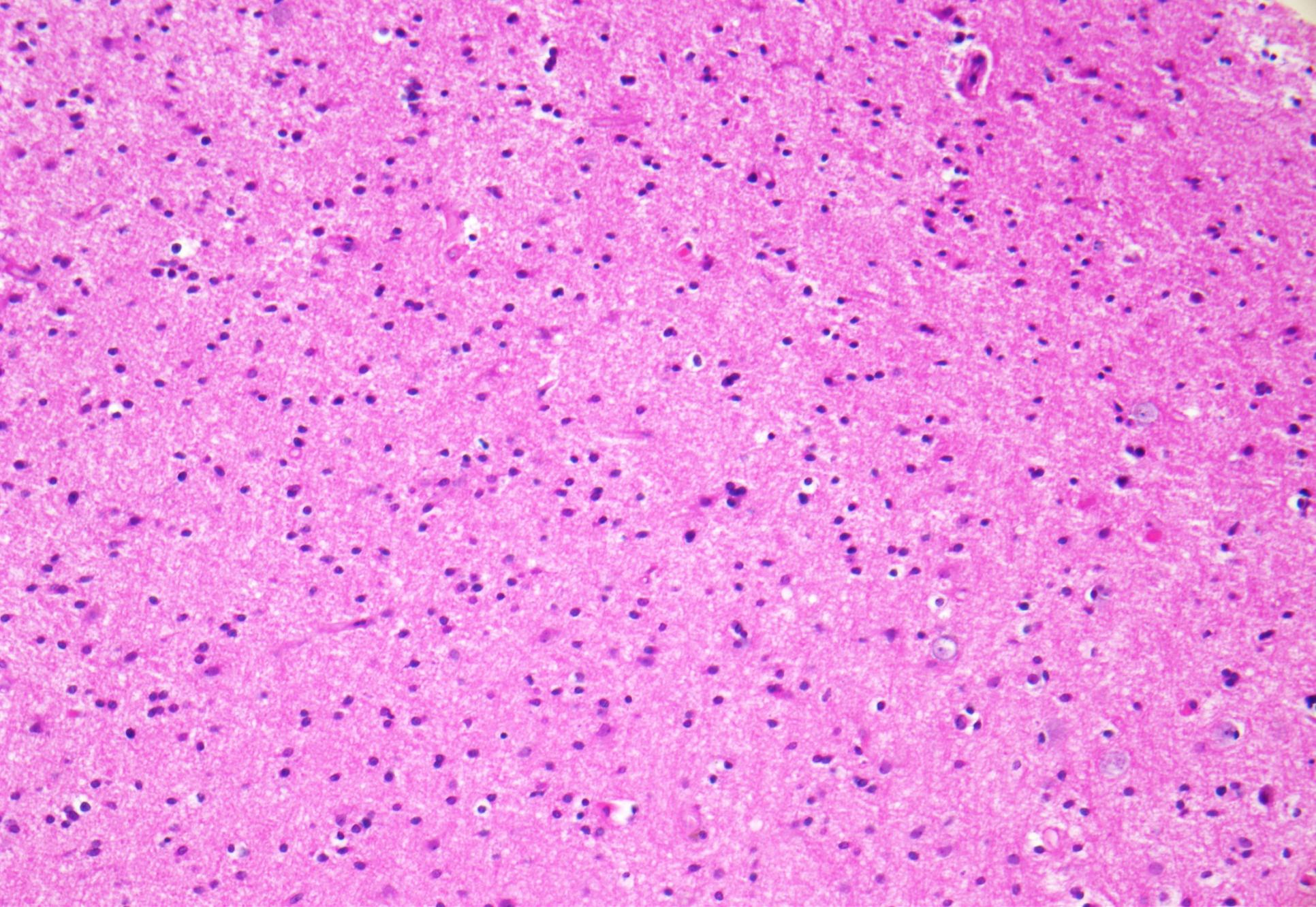
Axial MRI

Brain Biopsy Histopathology

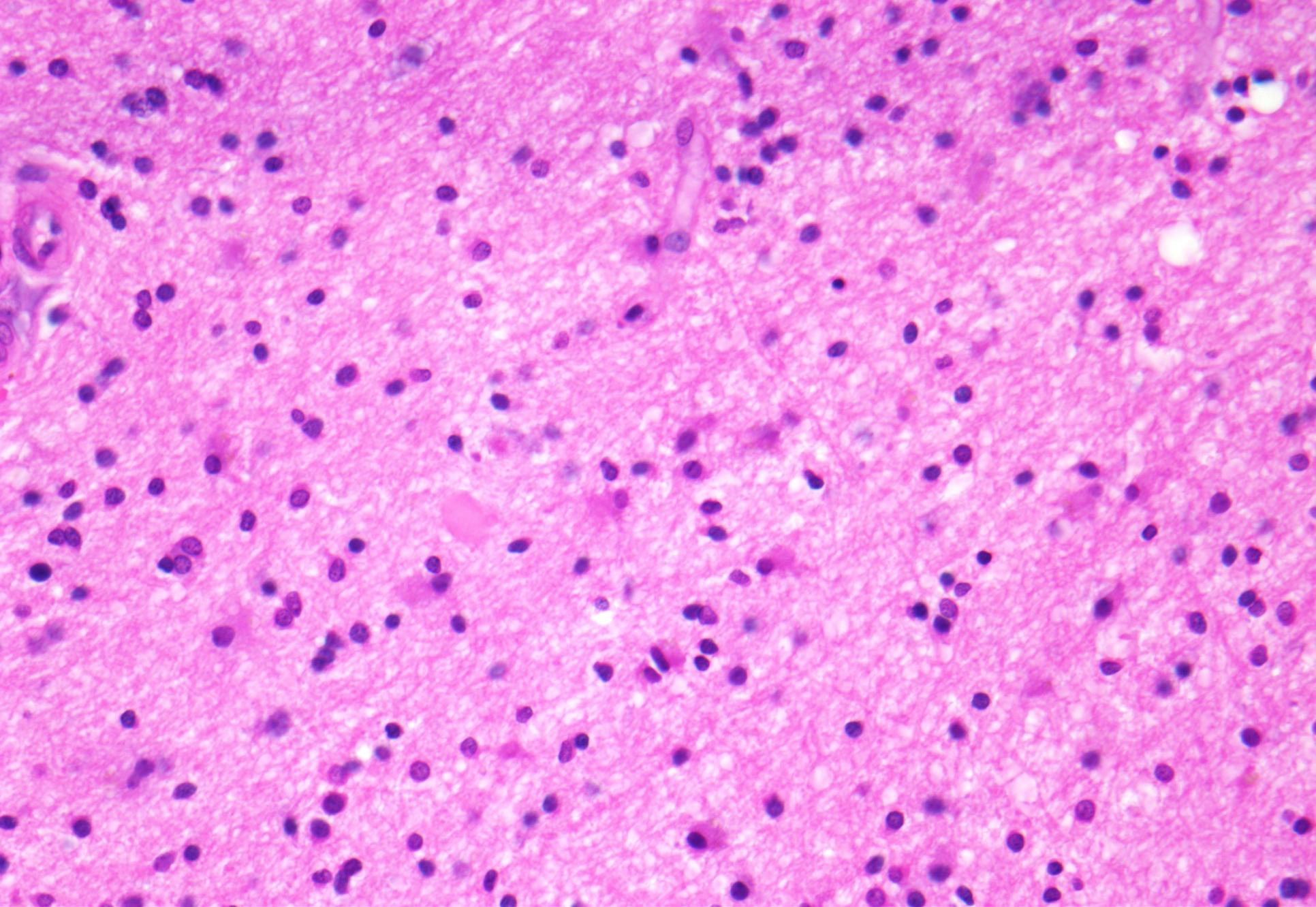
- Foci of intraparenchymal blood
- Moderately hypercellular brain parenchyma
- Infiltration by cells with mildly enlarged hyperchromatic nuclei
- Gemistocytic forms
- Conspicuous mitotic activity
- No vascular proliferation or necrosis
- Vessels with mural thickening
- Mild perivascular inflammation and pigment deposition



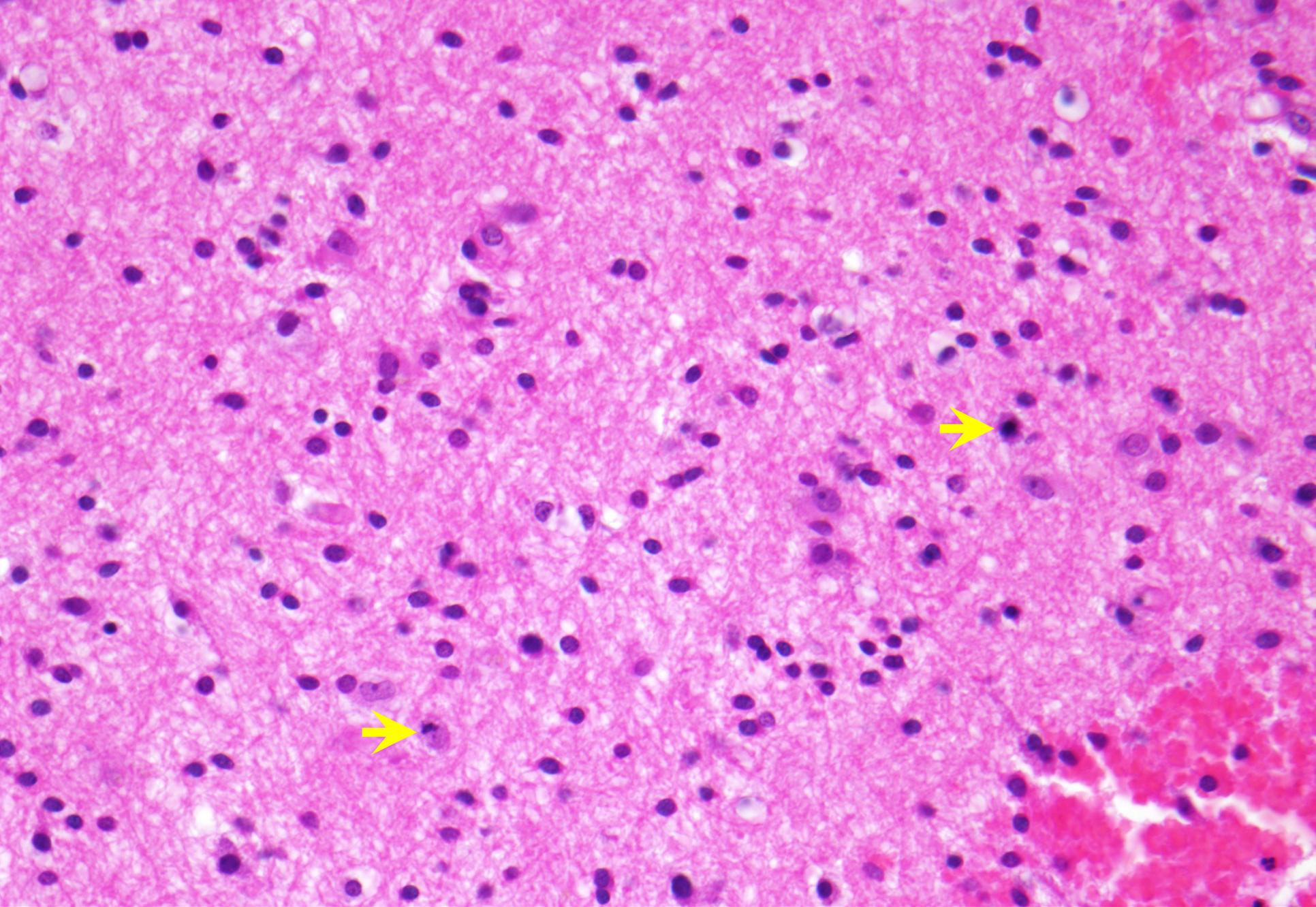
H&E, 10X Objective



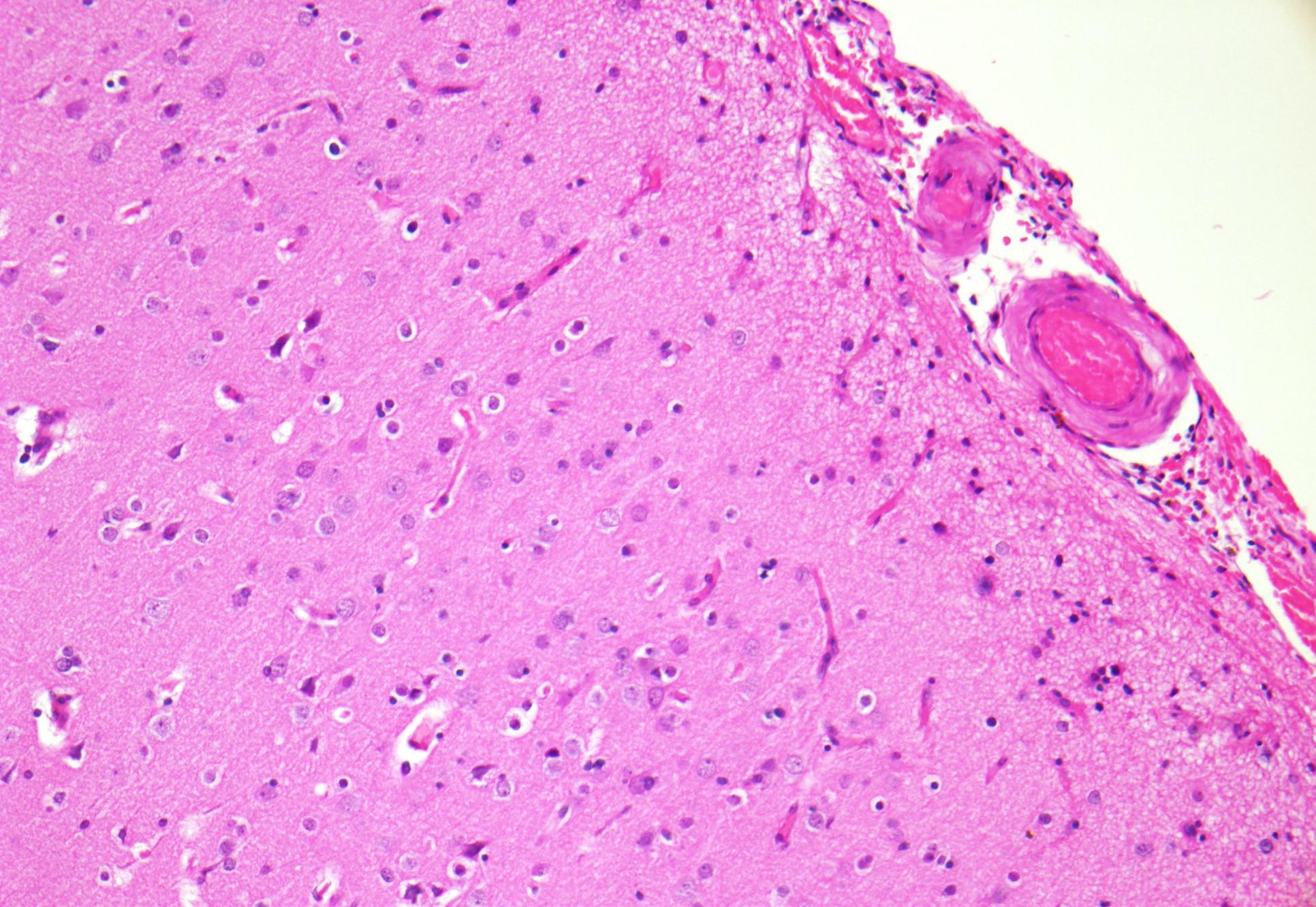
H&E, 20X Objective



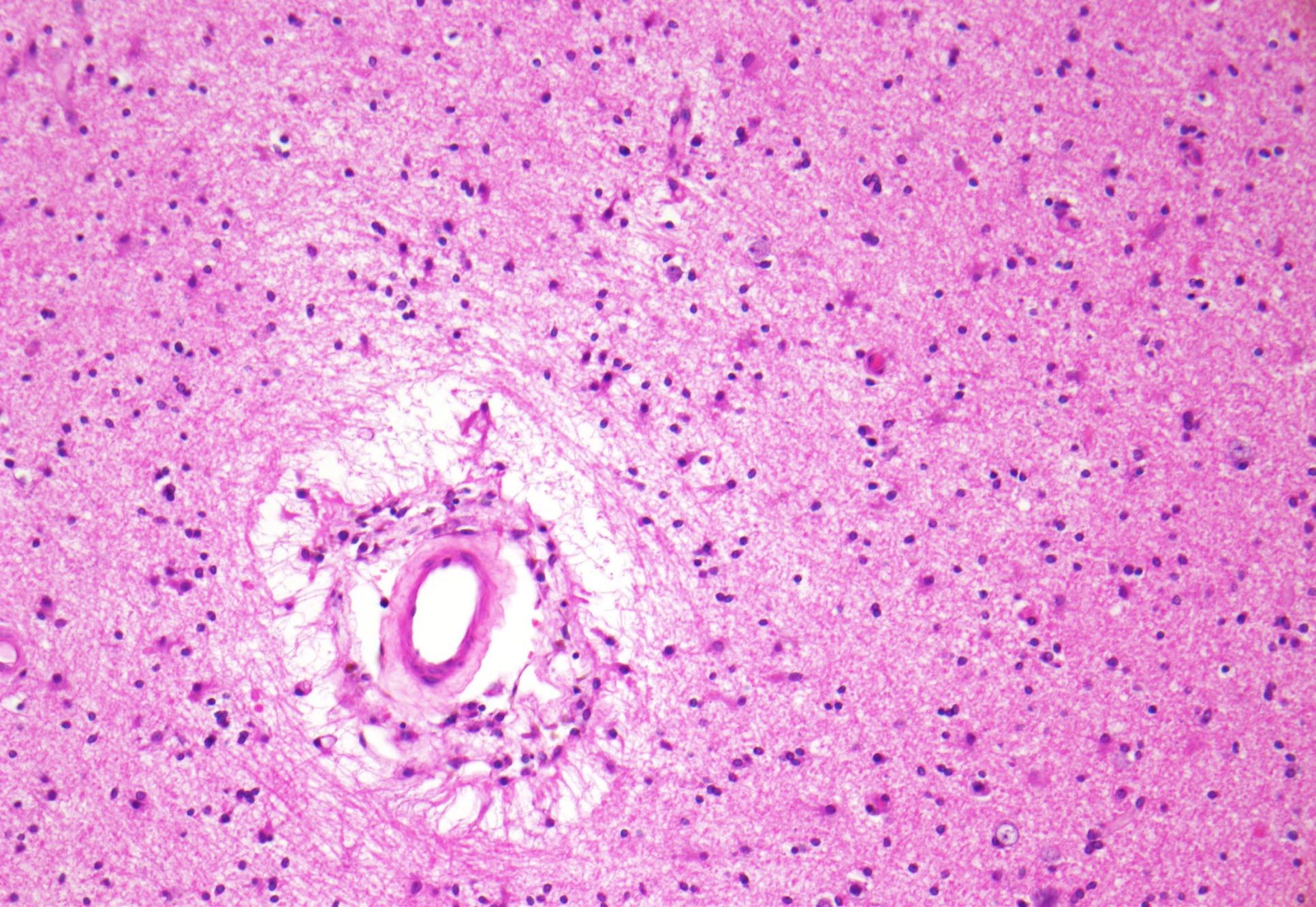
H&E, 40X Objective



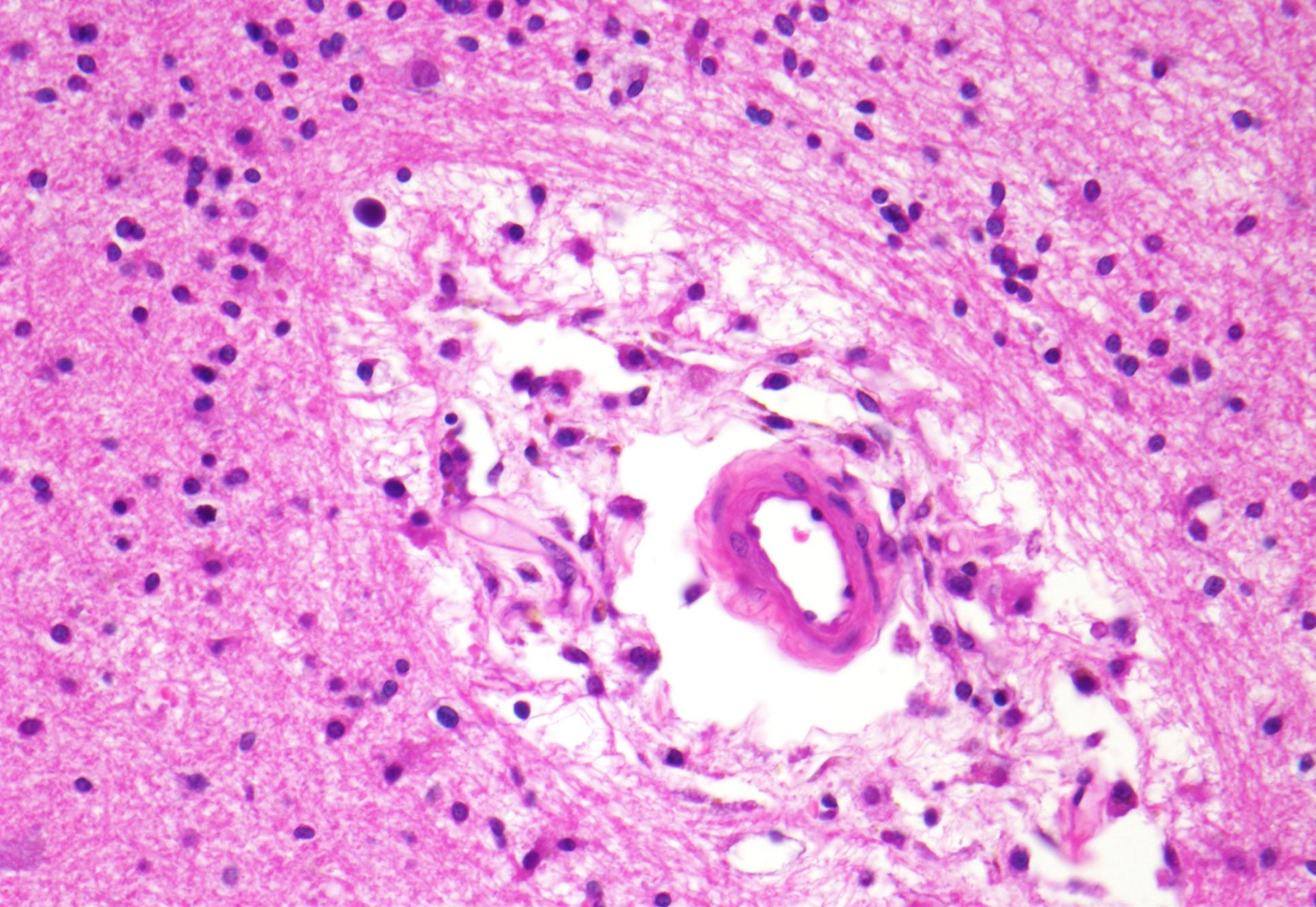
H&E, 40X Objective



H&E, 20X Objective



H&E, 20X Objective



H&E, 40X Objective

Audience Discussion

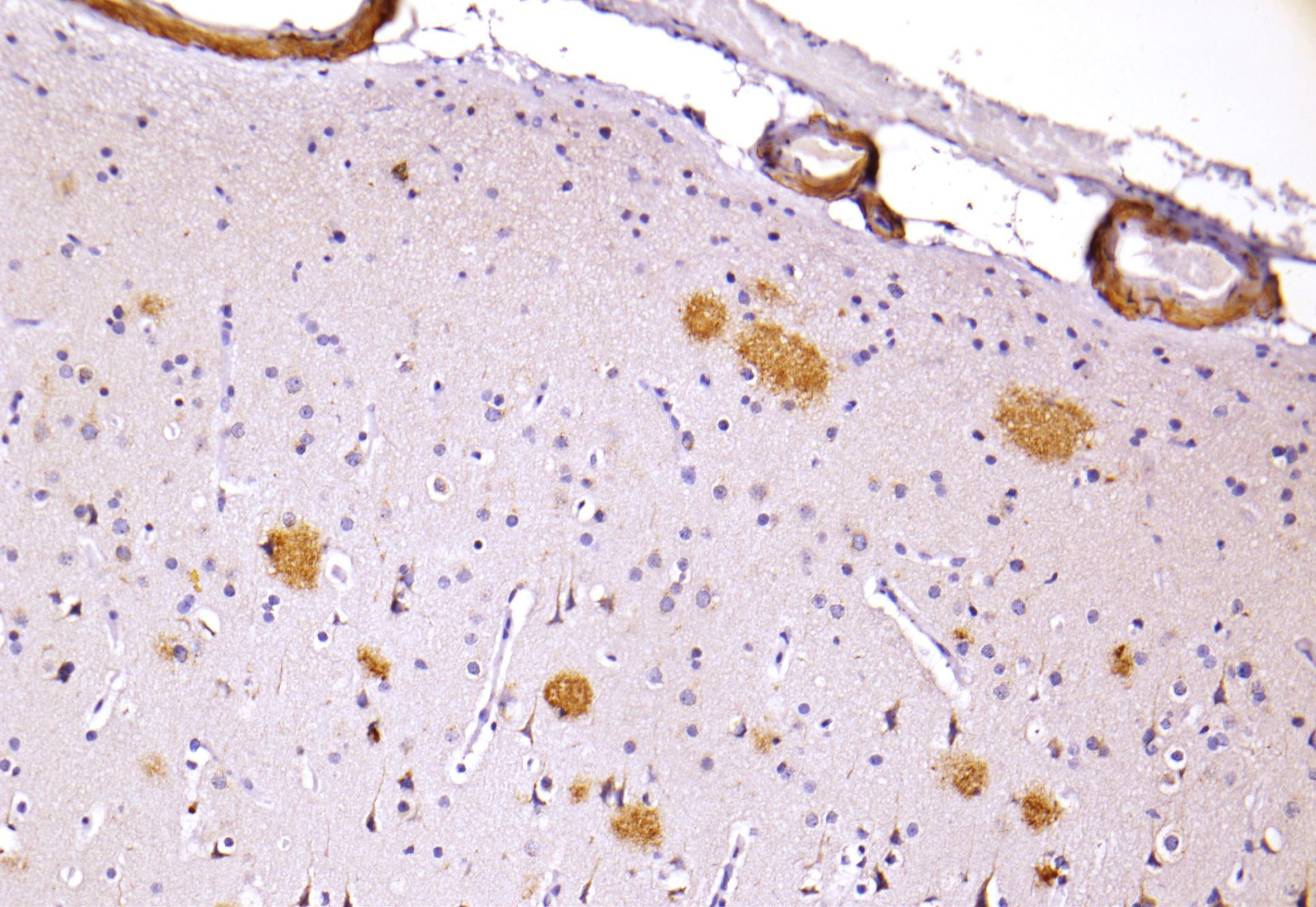
Immunohistochemistry

Molecular findings

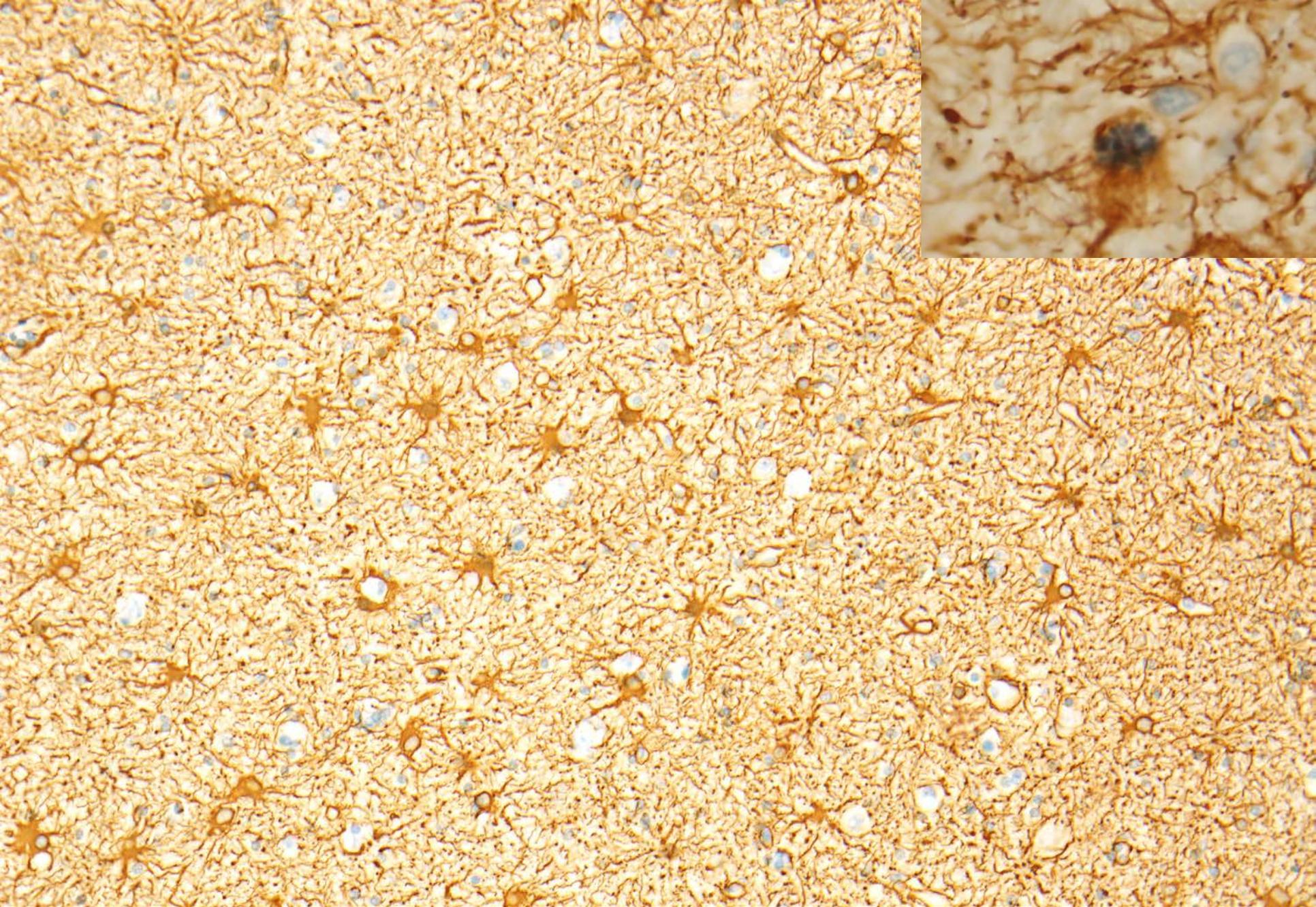
- Congophilic deposits in predominantly leptomeningeal and cortical vessels
- Diffuse amyloid plaques
- High Ki-67 proliferative index relative to cellularity
- Abundant CD68-immunoreactive cells (not shown)
- No evidence of an *IDH* mutation by immunohistochemistry and multiplex PCR



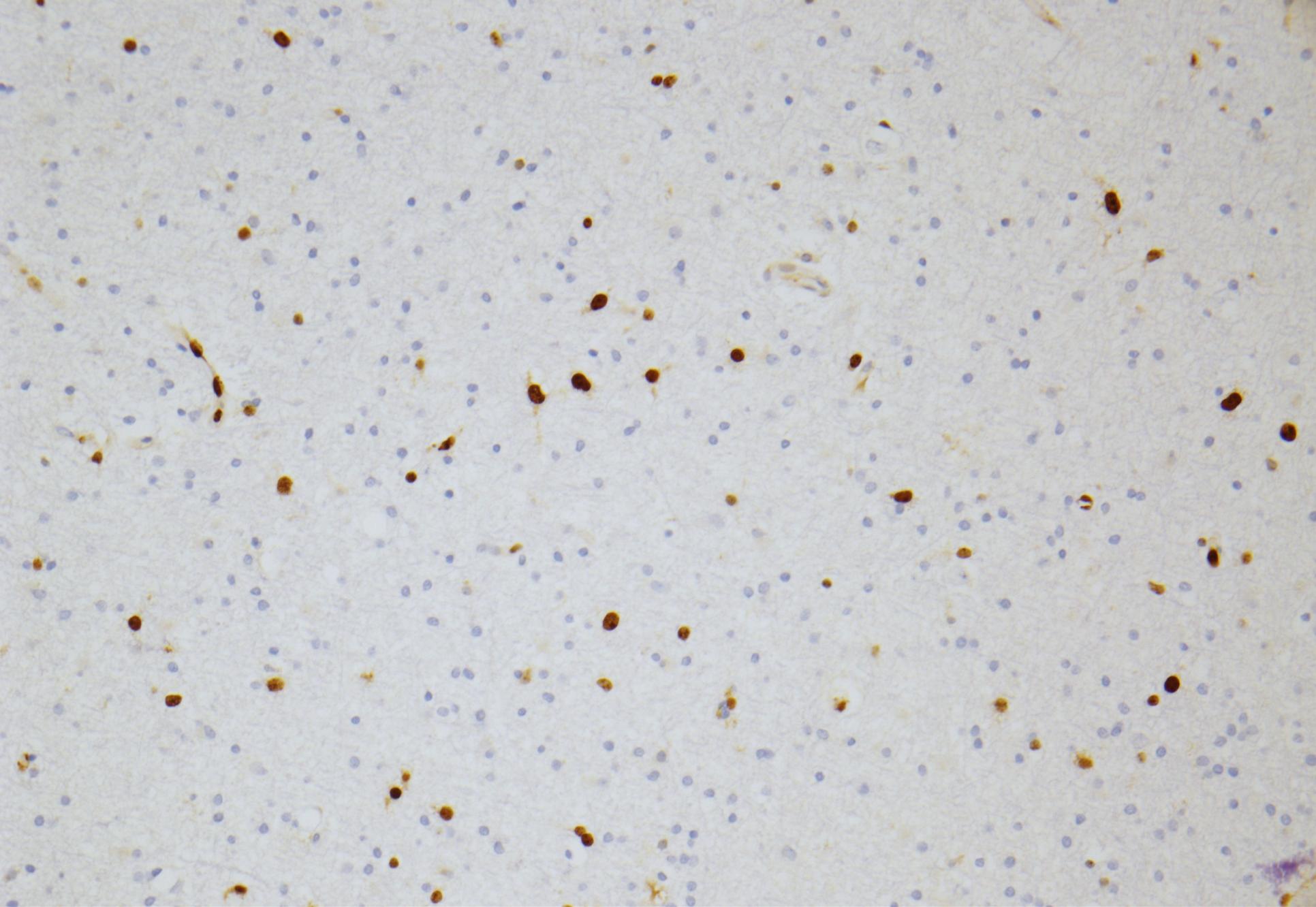
Congo Red, 20X Objective



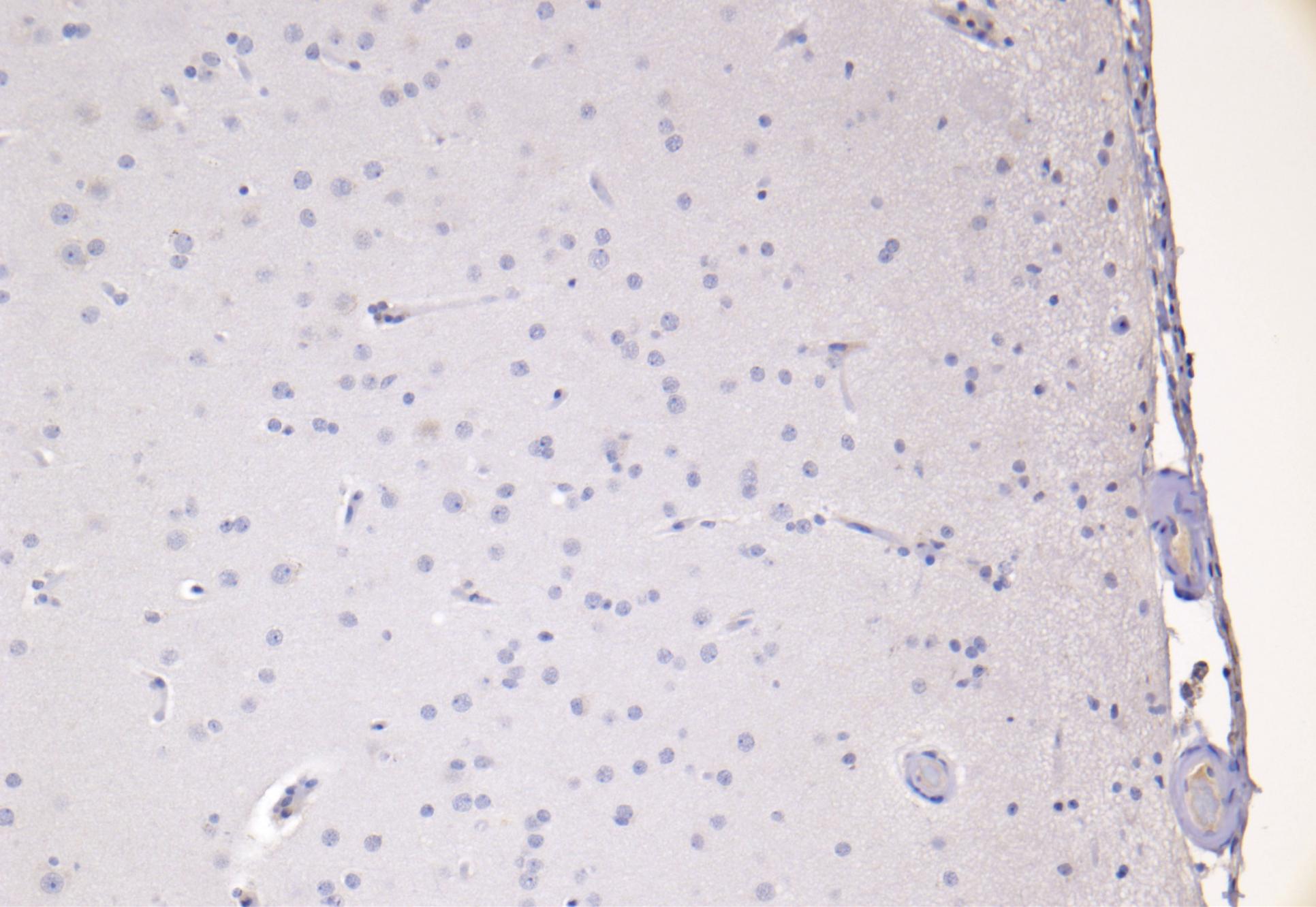
Beta-Amyloid, 20X Objective



GFAP, 20X Objective



Ki-67, 20X Objective



IDH-1 (R132H), 20X Objective

Final Diagnoses

- Cerebral amyloid angiopathy (CAA)
- Infiltrative proliferative process
 - Neoplastic versus reactive
 - Initially favored to be neoplastic

Clinical Follow-Up

- Fairly rapid and dramatic response to steroid treatment
- Patient homozygous for apolipoprotein E $\epsilon 4$
- Serial imaging over the next two years
 - No evidence of progression

Conclusion

- Clinically considered cerebral amyloid angiopathy-related inflammation (CAARI or CAA-I)
- No clinical support of an underlying neoplastic process given the lack of progression
- Case also subsequently reviewed about 1 year after presentation at the Mayo Clinic by Dr. Caterina Giannini

CAARI

Clinical and Imaging Findings

- Recently recognized entity
- Infrequently seen in a subset of patients with cerebral amyloid angiopathy (CAA)
- Thought to represent immune response to amyloid deposits
- Slightly younger age at onset than non-inflammatory CAA
- Clinically characterized by progressive cognitive decline, headaches, and seizures
- Cortical and subcortical microhemorrhages on imaging
- Large lobar hemorrhages uncommon
- Overrepresentation of apolipoprotein E ϵ 4 allele and ϵ 4 homozygosity

CAARI

Histopathology

- Congophilic amyloid- β mural depositions in cortical and leptomeningeal vessels (similar to CAA)
- Concomitant non-destructive perivascular inflammatory infiltrates
- Multinucleated giant cells often present

CAARI

Relationship with CAA and ABRA

- Amyloid- β vascular deposits seen in CAA without inflammation, CAARI, and amyloid- β -related angiitis (ABRA)
- ABRA
 - Characterized by a more destructive inflammatory process
 - Frequent demonstration of fully formed granulomas
- Recognized that ABRA and CAARI are most likely part of the same pathologic spectrum

References

- Eng JA, Frosch MP, Choi K, Rebeck GW, Greenberg SM. Clinical manifestations of cerebral amyloid angiopathy-related inflammation. *Ann Neurol*. 2004 Feb;55(2):250-6.
- Martucci M, Sarria S, Toledo M, Coscojuela P, Vert C, Siurana S, Auger C, Rovira A. Cerebral amyloid angiopathy-related inflammation: imaging findings and clinical outcome. *Neuroradiology*. 2014 Apr;56(4):283-9.
- Salvarani C, Hunder GG, Morris JM, Brown RD Jr, Christianson T, Giannini C. A β -related angiitis: comparison with CAA without inflammation and primary CNS vasculitis. *Neurology*. 2013 Oct 29;81(18):1596-603.
- Salvarani C, Brown RD Jr, Christianson T, Miller DV, Giannini C, Huston J 3rd, Hunder GG. An update of the Mayo Clinic cohort of patients with adult primary central nervous system vasculitis: description of 163 patients. *Medicine (Baltimore)*. 2015 May;94(21):e738.