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AANP Diagnostic Slide Session 2020 Case #11

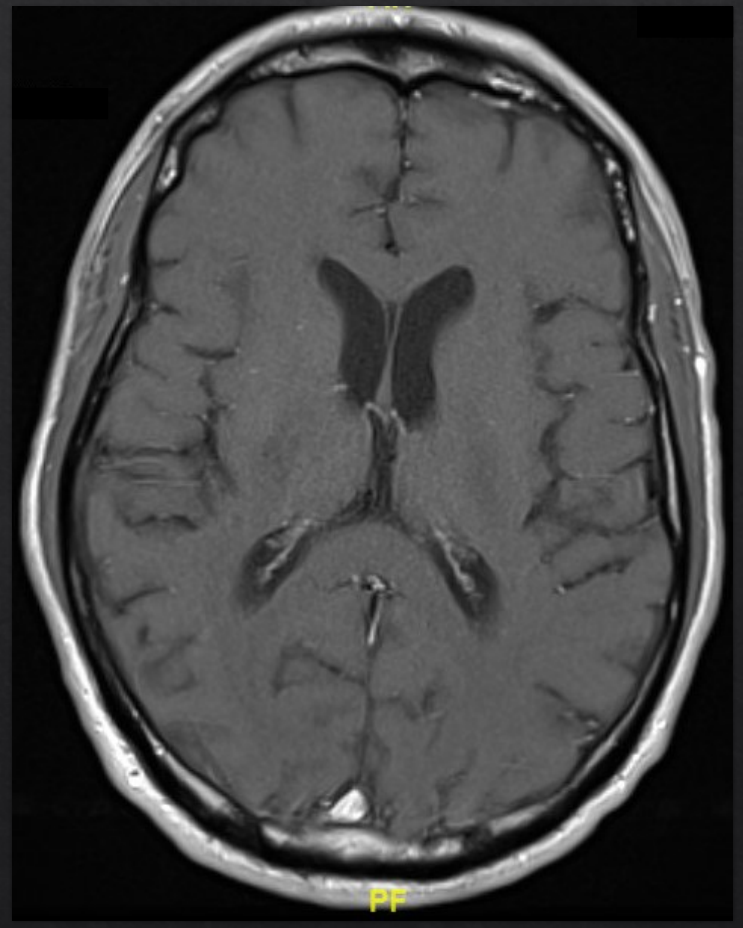
Disclosure

- The authors have no relevant conflicts to disclose.

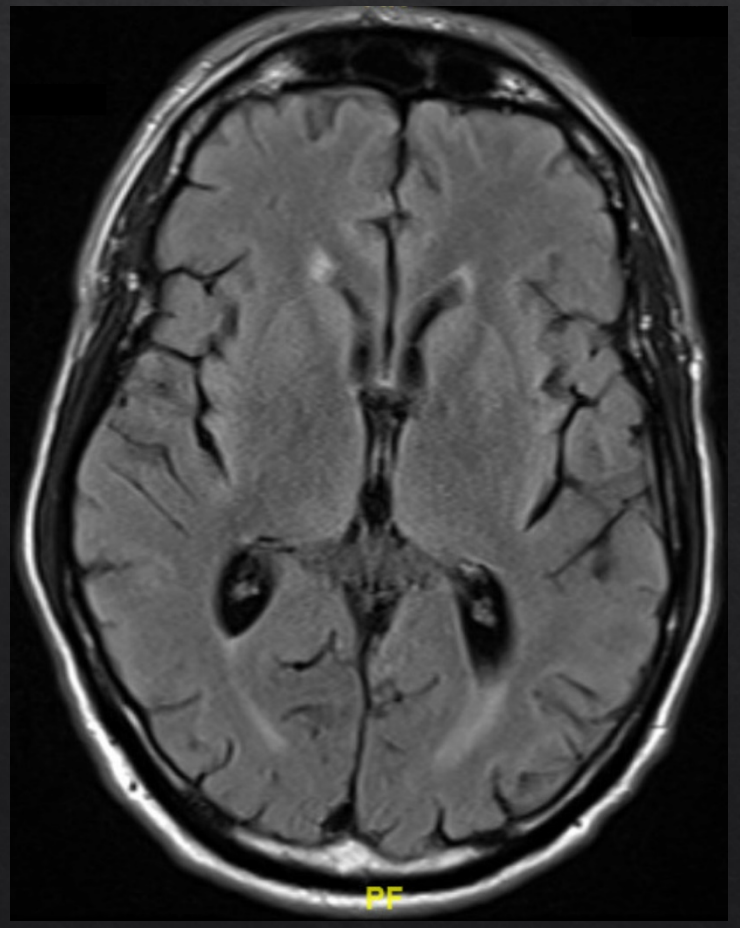
Clinical History

- 56-year-old male with PMH of mantle cell lymphoma presented with confusion.
- 10 months prior he had presented to his PCP with fatigue, joint pains, and weight loss.
- Over the ensuing months he developed worsening insomnia, cognitive difficulty, slow speech, memory impairment, disorientation, masked facies, and psychomotor slowing.
- Vital signs, basic laboratories, MRI, and EEG were unrevealing.
- Lumbar puncture revealed lymphocytic pleocytosis, elevated total protein, and minimally elevated glucose, with negative cytology and flow cytometry. RT-QuIC testing was negative.
- Empiric solumedrol and IVIG did not improve his symptoms.
- He continued to decline and eventually developed decorticate posturing and loss of responsiveness, expiring 10 weeks after presentation.

Imaging

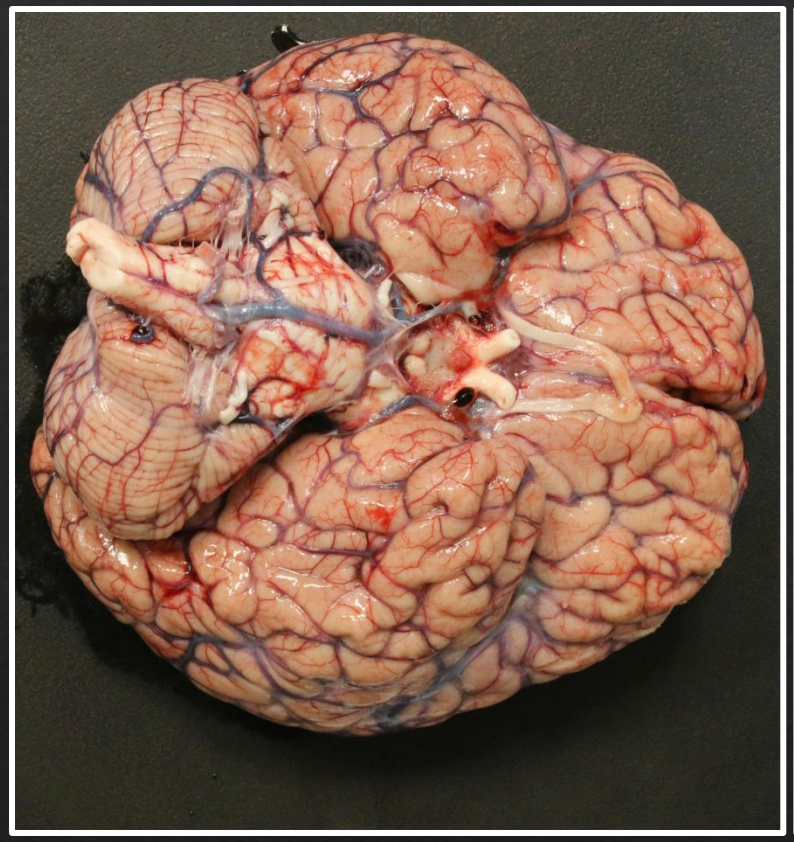


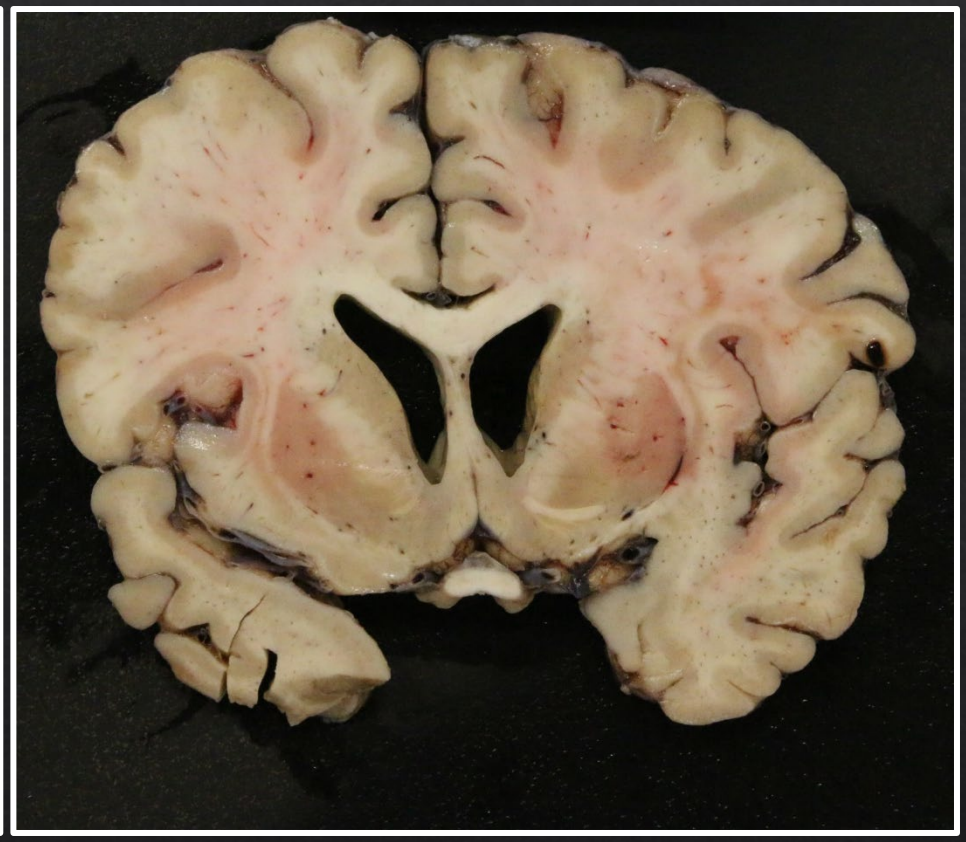
T1-Post



T2 FLAIR

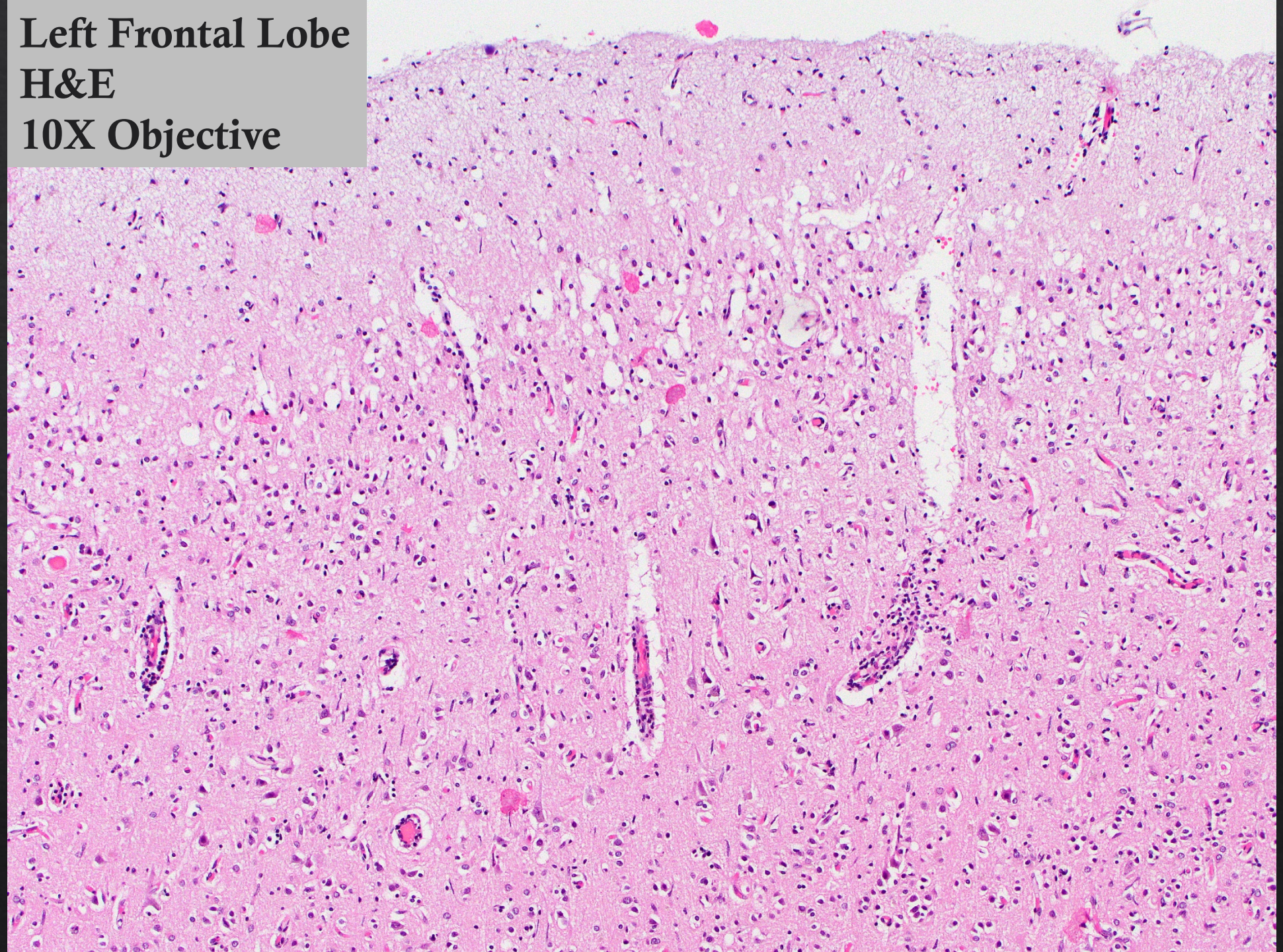
Autopsy



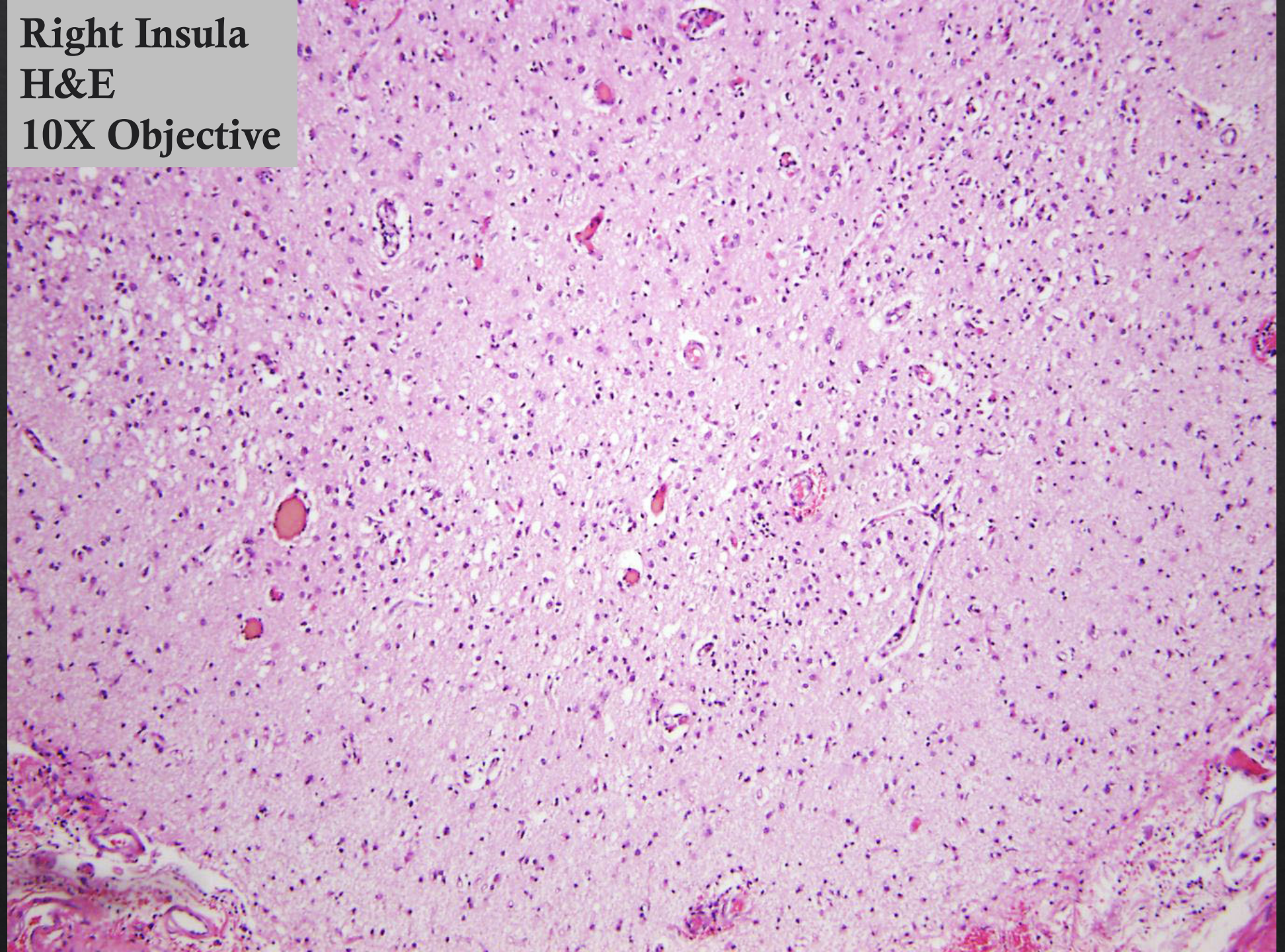


Brain Weight: 1240g

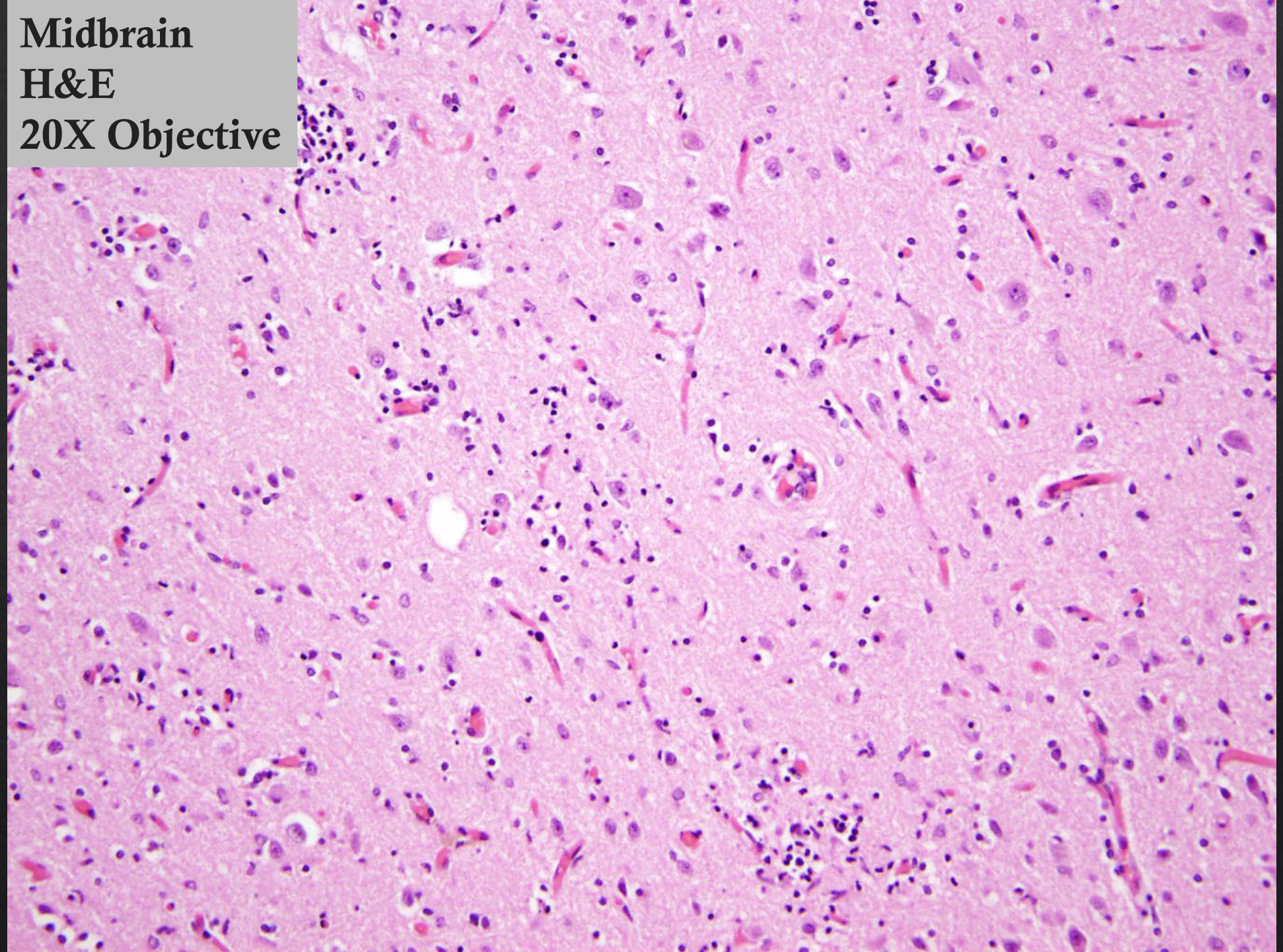
Left Frontal Lobe
H&E
10X Objective



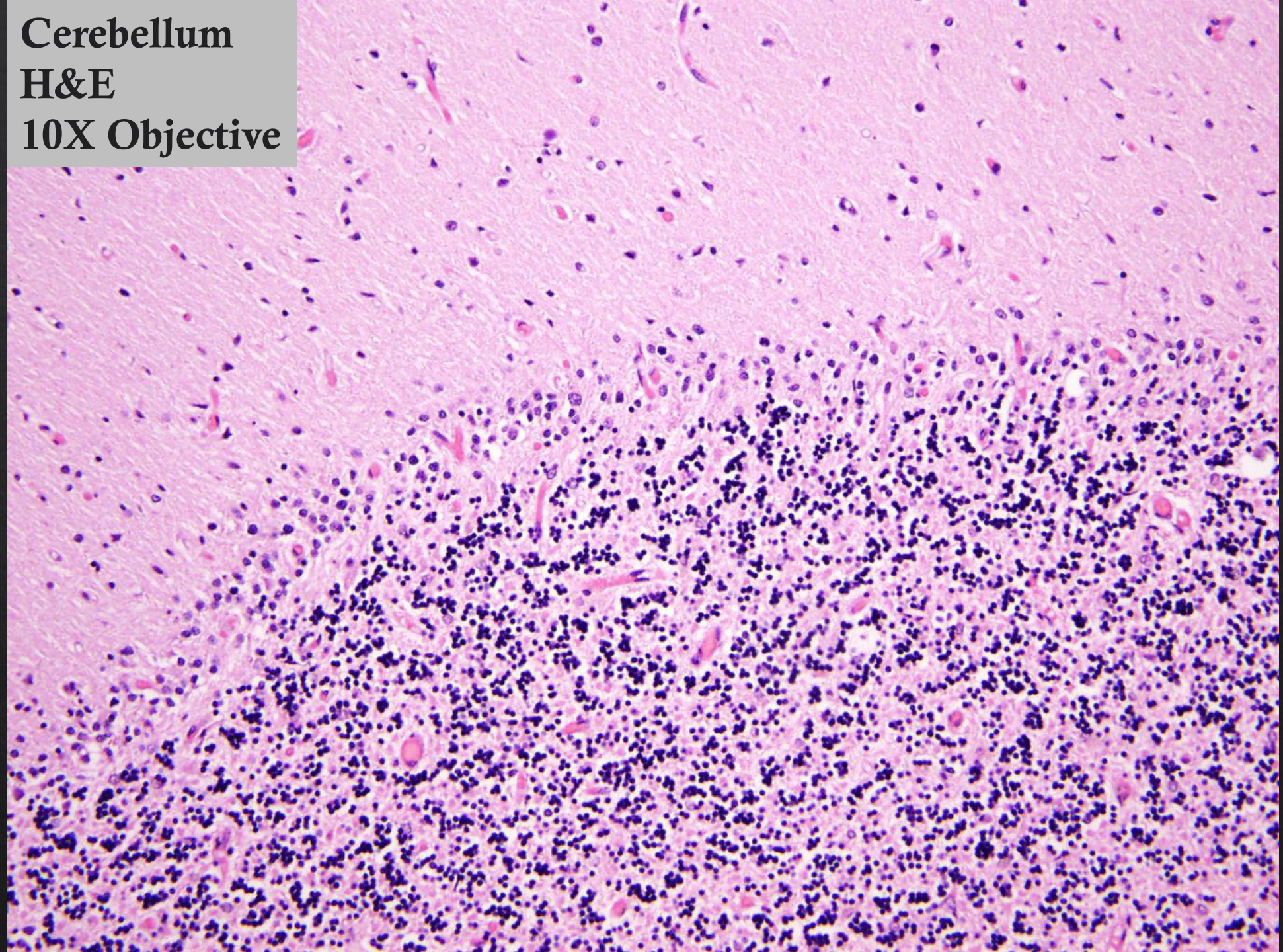
Right Insula
H&E
10X Objective



Midbrain
H&E
20X Objective

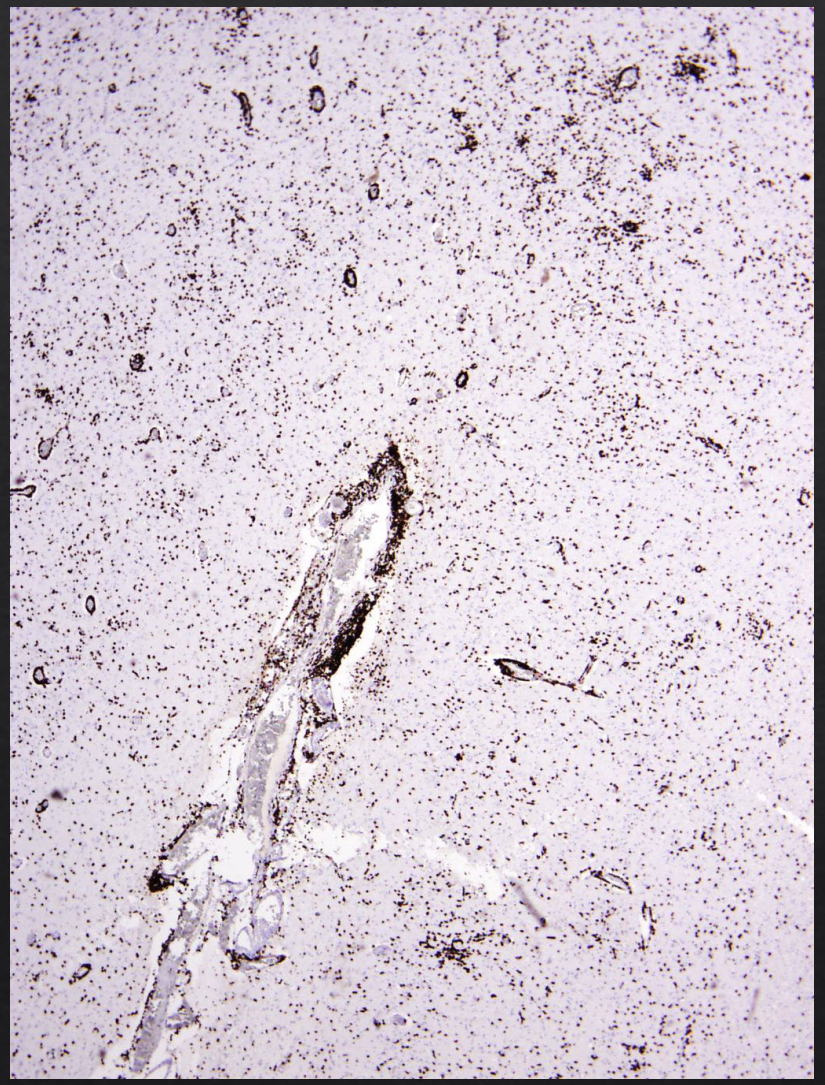


Cerebellum
H&E
10X Objective

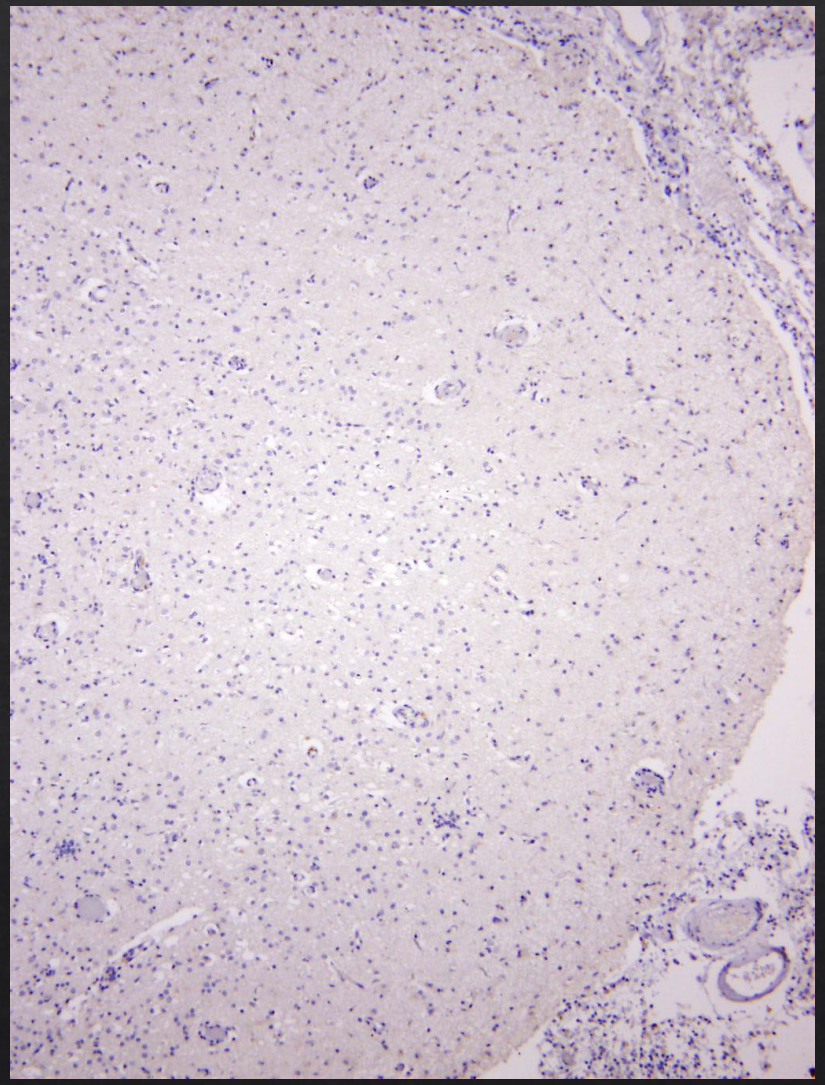


Diagnosis?

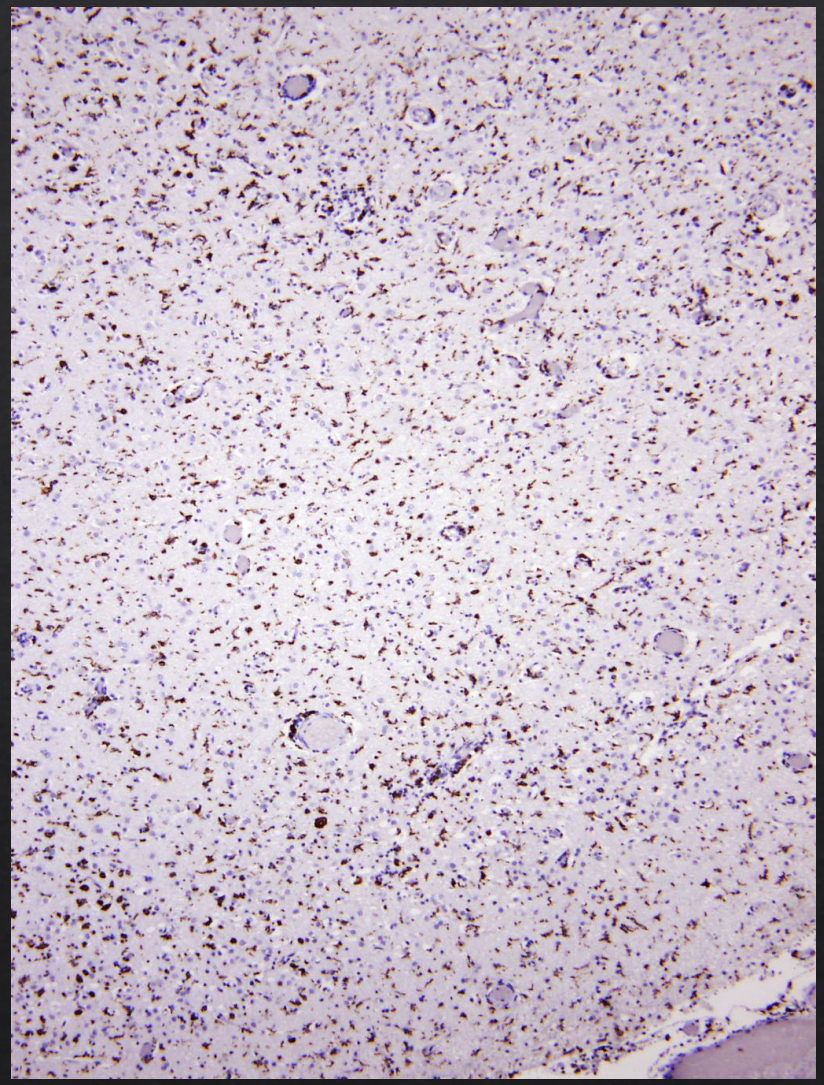
Right Insula (10X)



CD3



BSAP/PAX5



CD68

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Metagenomic next-generation sequencing

LABORATORY PHYSICIAN INTERPRETATION:

Organism Type:

DNA Viruses:
Not Detected

RNA Viruses:
California encephalitis virus**

Bacteria:
Not Detected

Fungi:
Not Detected

Parasites:
Not Detected

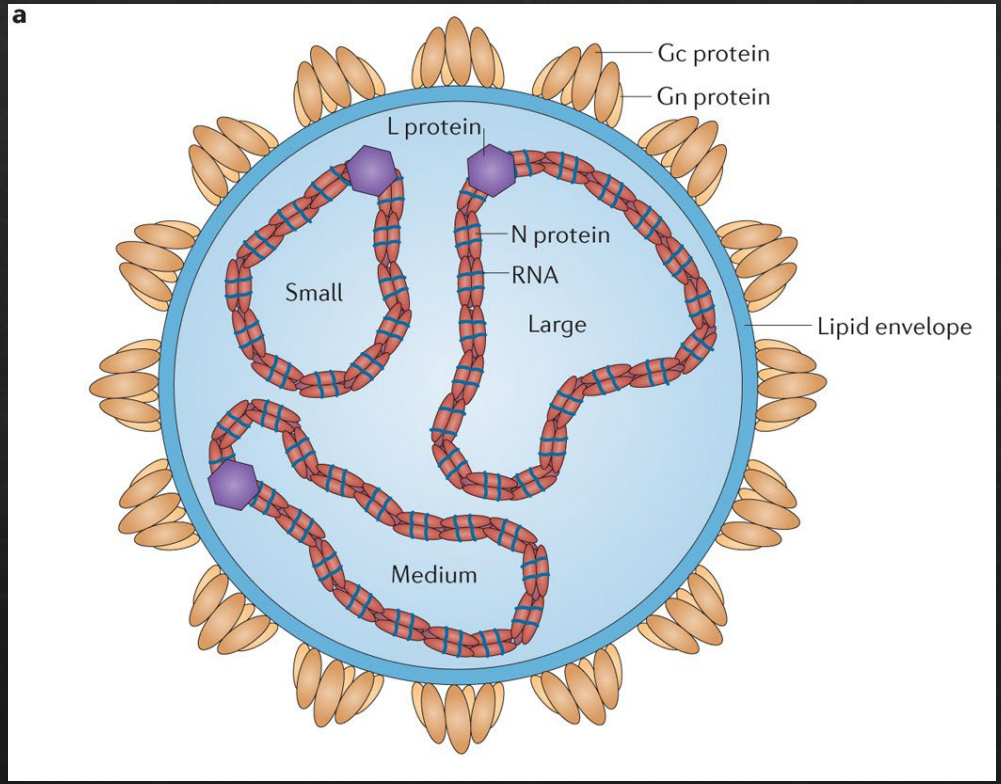
**This is a mosquito-borne arbovirus in the California serogroup of orthobunyaviruses that causes an acute febrile illness, meningitis, and/or meningoencephalitis (Pastula, et al., American Journal of Tropical Medicine and Hygience 93(2): 384-389). Viral sequences most closely match Jamestown Canyon virus, and detected reads map to 2 of the 3 segments of the viral genome.

FINAL NEUROPATHOLOGIC DIAGNOSIS:

ADULT BRAIN (Weight: 1240 grams, reference range 1250-1400g) with:

JAMESTOWN CANYON VIRUS ENCEPHALITIS

Jamestown Canyon Virus is an orthobunyavirus with a segmented single-strand negative-sense RNA genome. The primary reservoir is thought to be white-tailed deer, and the virus may be transmitted by multiple species of mosquito.



Elliott R. Orthobunyaviruses: recent genetic and structural insights. Nature Reviews Microbiology. 2014. 12:673–685.

Jamestown Canyon Virus encephalitis is typically characterized by microglial activation and nodularity, T-cell infiltration, leptomeningeal inflammation, and loss of cerebellar Purkinje neurons with associated gliosis.

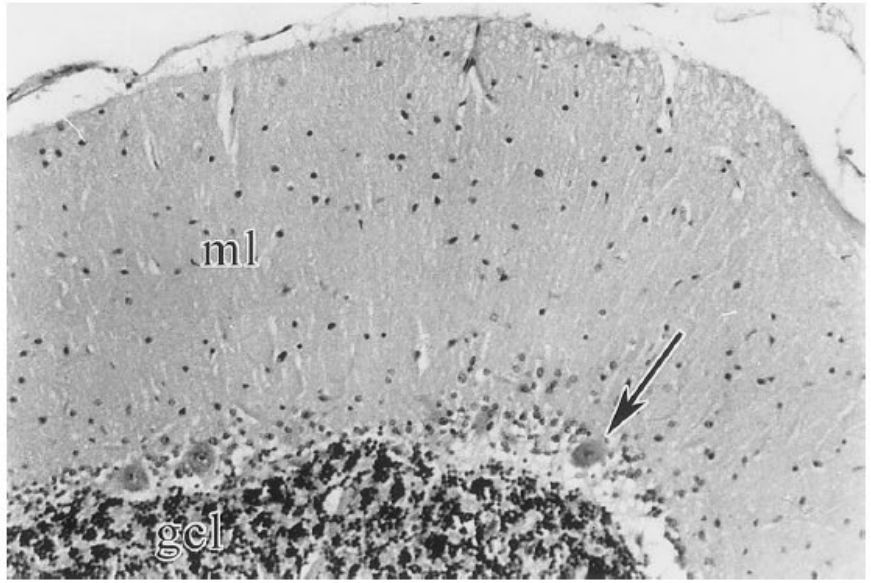


Figure 1. Cross-section of the cerebellum of a normal adult, showing the outer eosinophilic molecular layer (ml), Purkinje cell (indicated by the arrow), and densely granular cellular layer (gcl). Hematoxylin-eosin stain; magnification, ×100.

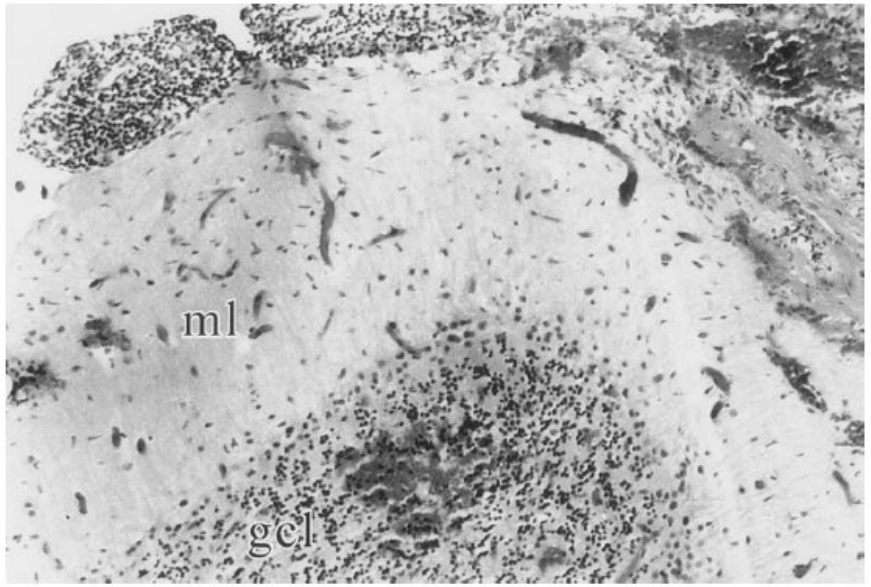


Figure 2. Cross-section of the cerebellum of the index patient, with inflammatory cell infiltrate in the leptomeninges with lymphocytes and macrophages, diffuse and focal microglial infiltrate in the molecular layer (ml), and Purkinje cell loss and severe cell loss in granular cellular layer (gcl). Hematoxylin-eosin stain; magnification, ×100.

Huang *et al.* Diagnosis of Jamestown Canyon encephalitis by polymerase chain reaction. 1999. Clin Infect Dis. 28(6):1294-7.

Jamestown Canyon Virus infections are more common in summer months and frequently involve the central nervous system, but only rarely lead to death of the patient.

TABLE 1. Number and percentage of reported cases of West Nile virus and other arboviral diseases, by virus type and selected patient characteristics — United States, 2017

Characteristic	Virus no. (%)					
	West Nile* (N = 2,097)	Jamestown Canyon (N = 75)	La Crosse (N = 63)	Powassan (N = 34)	St. Louis encephalitis* (N = 11)	Eastern equine encephalitis (N = 5)
Age group (yrs)						
<18	50 (2)	4 (5)	54 (86)	5 (15)	0 (0)	0 (0)
18–59	1,020 (49)	36 (48)	6 (10)	10 (29)	5 (45)	5 (100)
≥60	1,027 (49)	35 (47)	3 (5)	19 (56)	6 (55)	0 (0)
Sex						
Male	1,301 (62)	46 (61)	34 (54)	28 (82)	8 (73)	2 (40)
Female	796 (38)	29 (39)	29 (46)	6 (18)	3 (27)	3 (60)
Period of illness onset						
January–March	7 (<1)	1 (1)	1 (2)	0 (0)	1 (9)	0 (0)
April–June	87 (4)	25 (33)	4 (6)	21 (62)	0 (0)	0 (0)
July–September	1,814 (87)	45 (60)	53 (84)	7 (21)	8 (73)	1 (20)
October–December	185 (9)	4 (5)	5 (8)	6 (18)	1 (9)	4 (80)
Clinical syndrome						
Nonneuroinvasive	672 (32)	17 (23)	0 (0)	1 (3)	5 (45)	0 (0)
Neuroinvasive						
Encephalitis	714 (34)	29 (39)	53 (84)	22 (65)	2 (18)	3 (60)
Meningitis	530 (25)	5 (7)	10 (16)	7 (21)	3 (27)	0 (0)
AFP	89 (4)	4 (5)	0 (0)	2 (6)	1 (9)	0 (0)
Other	92 (4)	20 (27)	0 (0)	2 (6)	0 (0)	2 (40)
Outcome						
Hospitalization	1,545 (74)	46 (61)	63 (100)	33 (97)	6 (55)	5 (100)
Death	146 (7)	2 (3)	0 (0)	2 (6)	0 (0)	2 (40)

Abbreviation: AFP = acute flaccid paralysis.
* Date of illness onset missing for four cases of West Nile virus and one case of St. Louis encephalitis virus.

Curren EJ, *et al.* West Nile Virus and Other Nationally Notifiable Arboviral Diseases – United States, 2017. Morbidity and Mortality Weekly Report. October 2018. 67:41

References

- Curren EJ, *et al.* West Nile Virus and Other Nationally Notifiable Arboviral Diseases – United States, 2017. Morbidity and Mortality Weekly Report. October 2018. 67:41
- Elliott R. Orthobunyaviruses: recent genetic and structural insights. Nature Reviews Microbiology. 2014. 12:673–685.
- Huang *et al.* (1999) Diagnosis of Jamestown Canyon encephalitis by polymerase chain reaction. Clin Infect Dis. 28(6):1294-7.
- Pastula et al. (2015) Jamestown Canyon Virus Disease in the United States-2000-2013. Am J Trop Med Hyg. 93(2):384-9.

Questions?

Thank You!