



# Case 2015-4

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# Disclosures

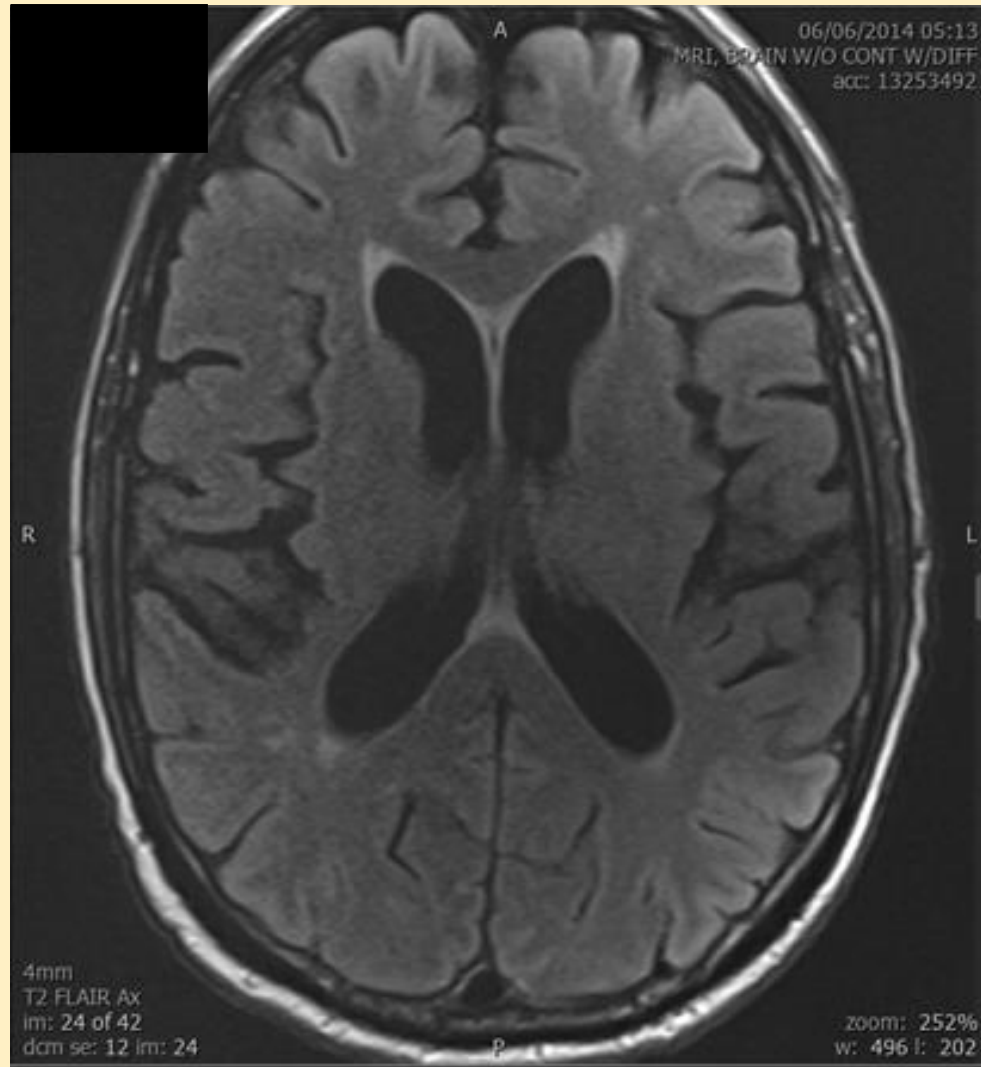
- None

Clinical history

# Clinical history

- 73 year old black man
- PMH: angioimmunoblastic T-cell lymphoma (2009) s/p chemotherapy with complete remission (2010)
- Treatment-related acute myeloid leukemia (2012)
- Non-myeloablative haploidentical bone marrow transplant (4/2014)
- Aphasia, gait imbalance, and altered mental status (6/2014)
- Generalized tonic-clonic seizure (6/2014)
- Abnormal EEG activity (6-7/2014)
- Aplastic bone marrow with failed graft
- Polymicrobial bacteremia and septic shock (7/2014)

# MRI T2 FLAIR



Autopsy findings

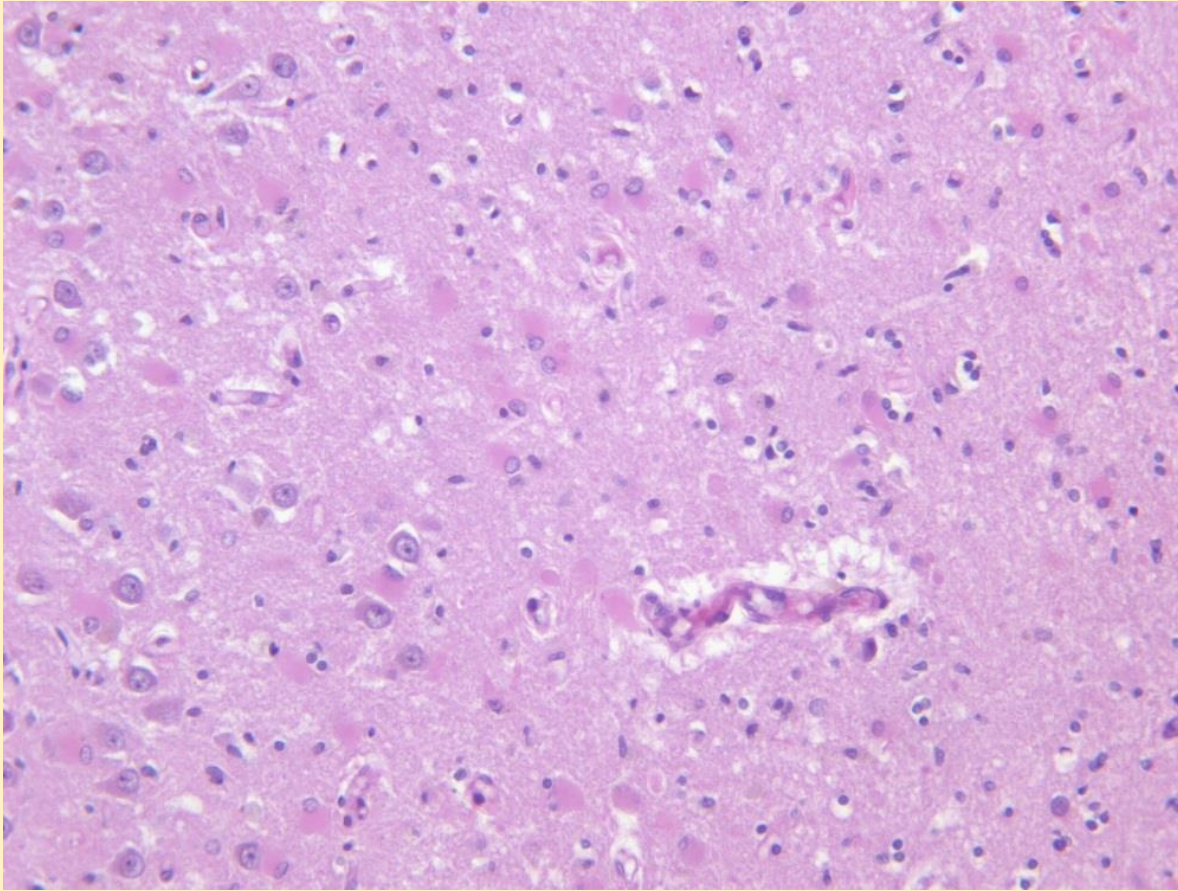
# Neuropathology

- Brain weight: 1530 g (ref 1100-1700 g)
- Moderately dilated ventricular system bilaterally
- Remote lacunar infarct, 3 mm, right putamen
- Atherosclerosis, multifocal, non-occlusive, circle of Willis and branches

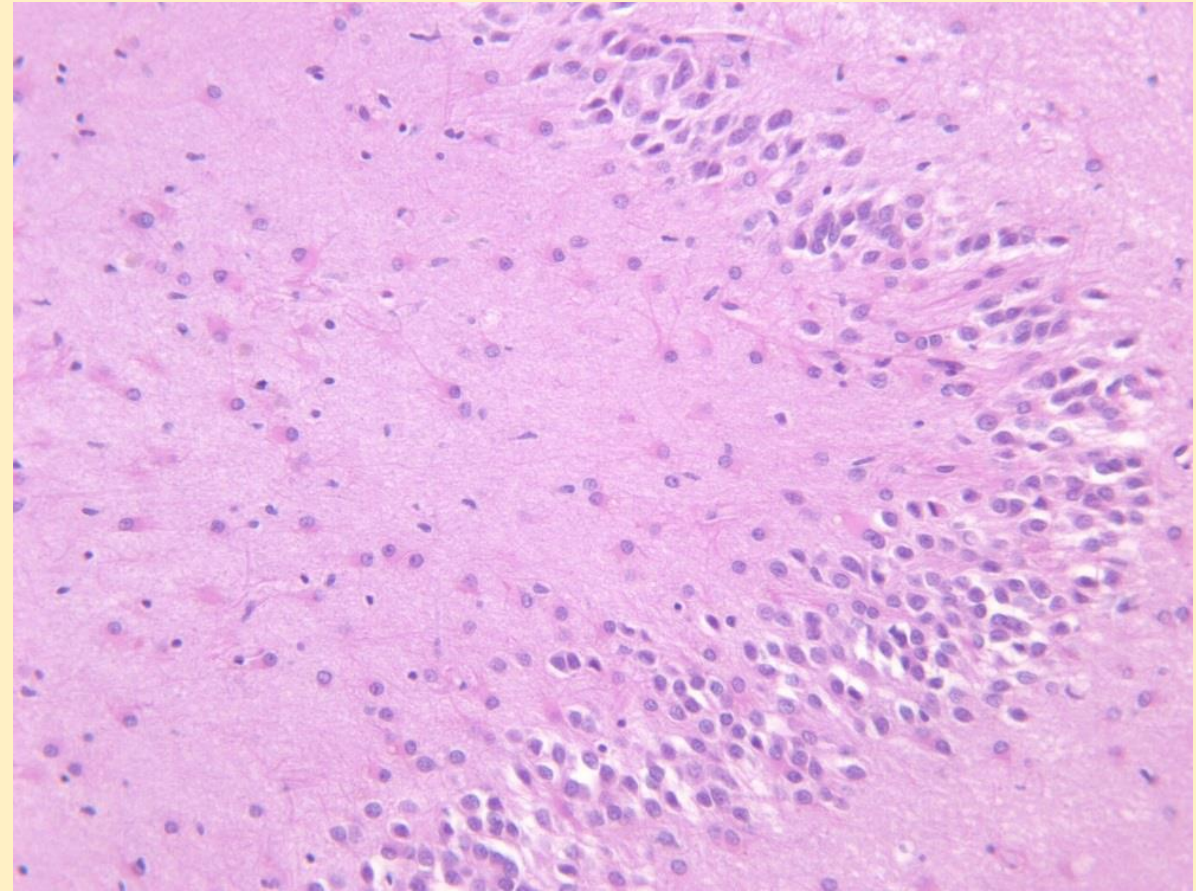


# Hippocampus

CA1

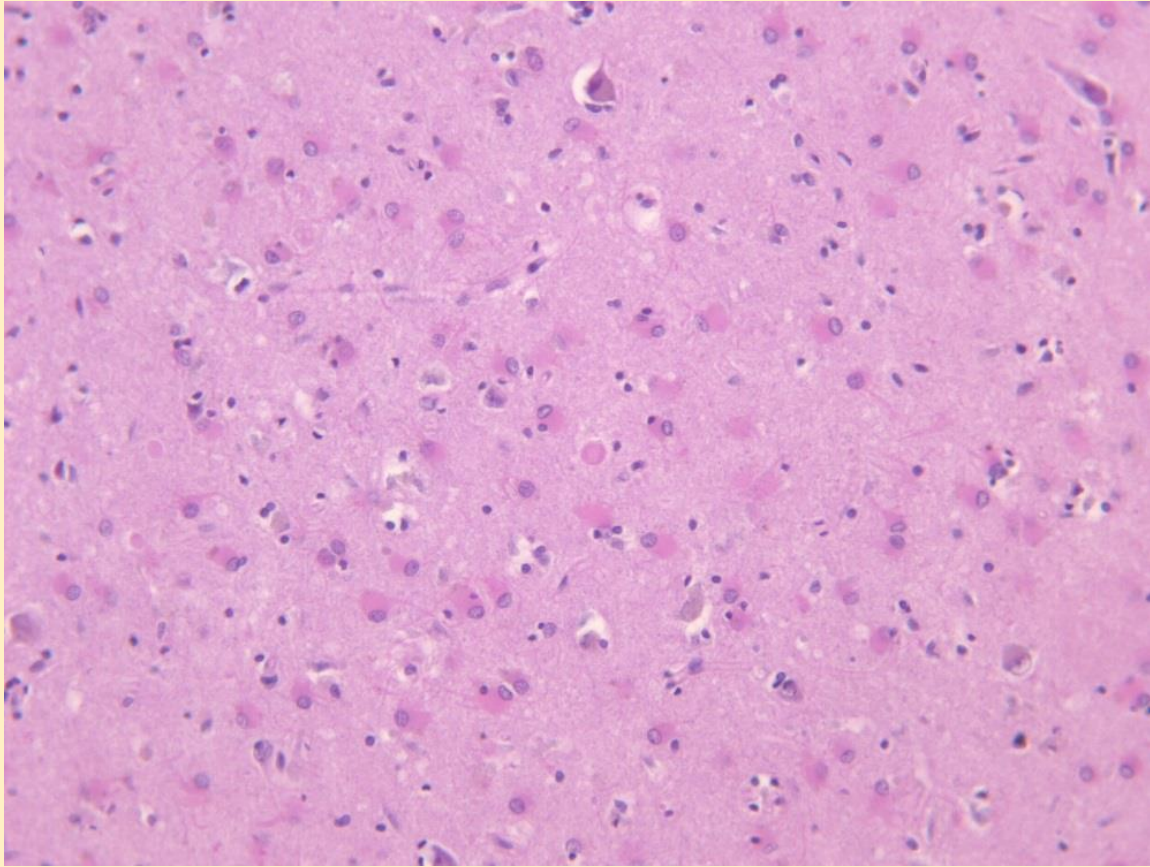


CA4

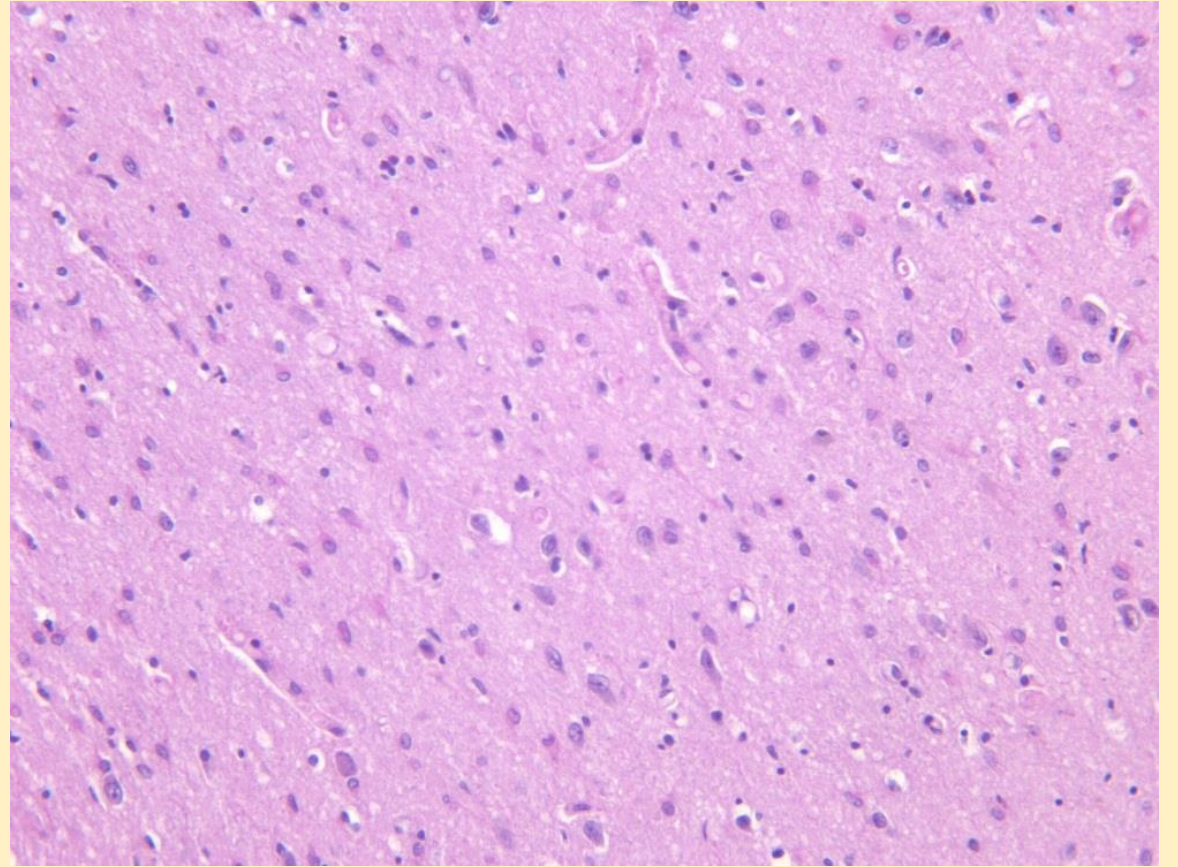




# Amygdala

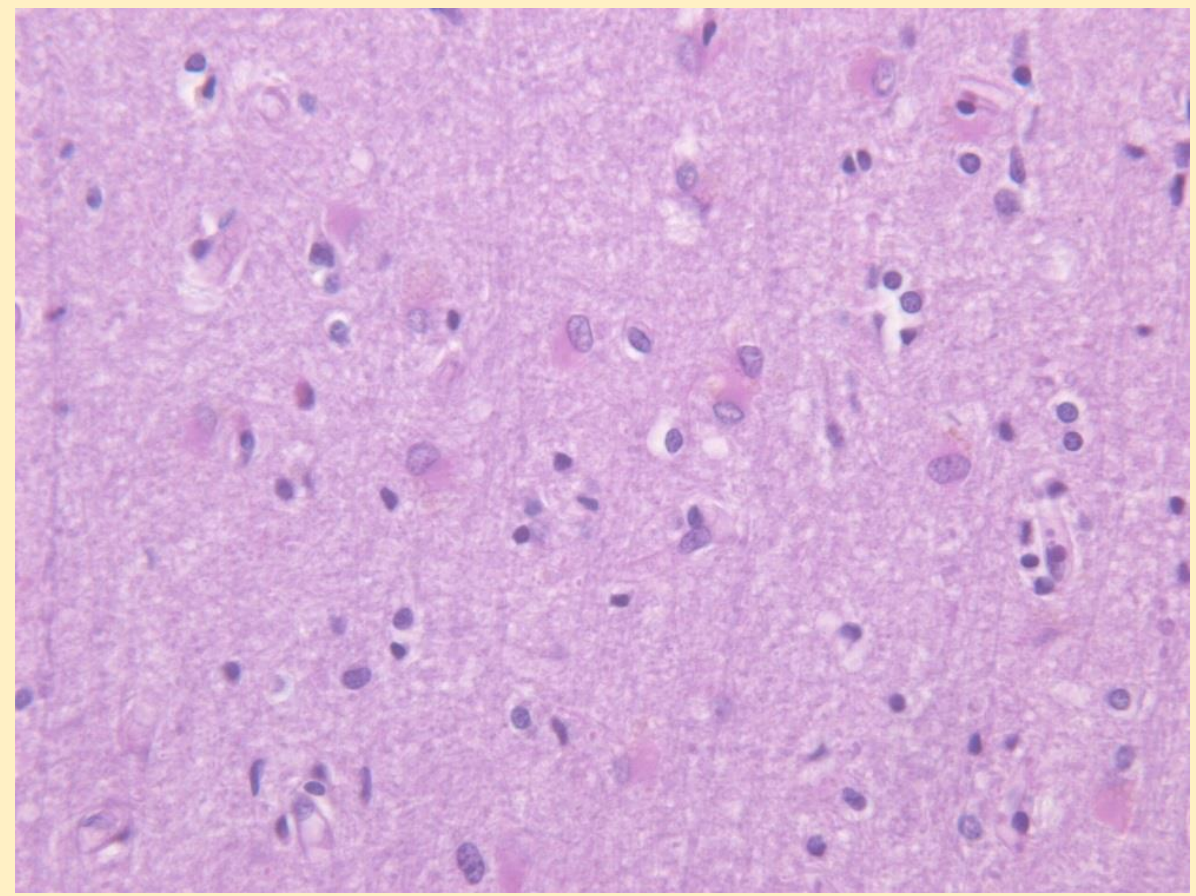
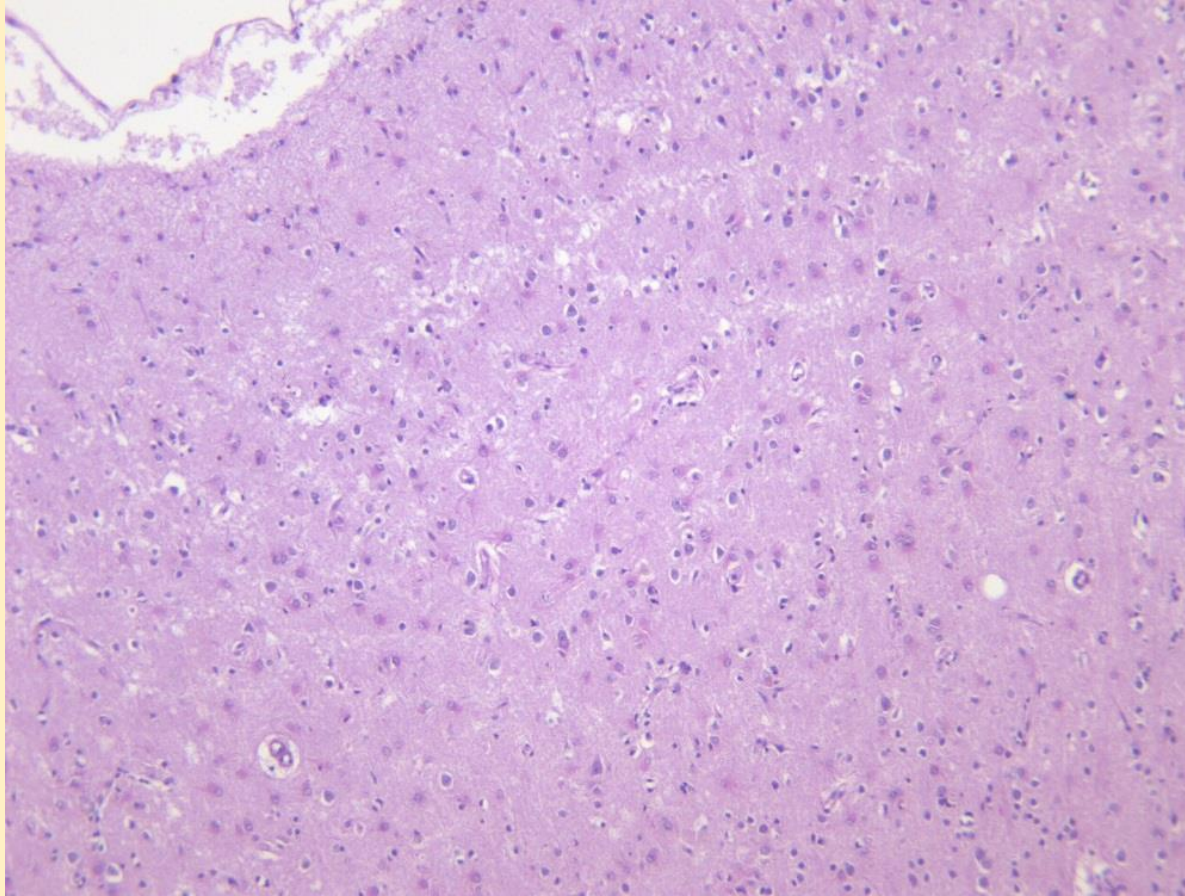


# Caudate





# Parietal cortex



# Neuropathology

- No active inflammation or viral inclusions
- Watershed areas, Purkinje cells not involved

# Discussion

# Lumbar puncture results

- CSF HHV6 PCR (6/2014) **positive**: 107240 copies/mL
- Treated with ganciclovir and foscarnet
- CSF HHV6 PCR (7/2014) **negative**: <500 copies/mL

# Additional testing

- Unstained sections of formalin fixed paraffin-embedded brain tissue sent to the CDC
- HHV6 A and B PCR: negative

# Diagnosis

- *Consistent with HHV-6 post-infectious sequelae*
- Hypoxic/ischemic change



# Post-transplant acute limbic encephalitis (PALE)

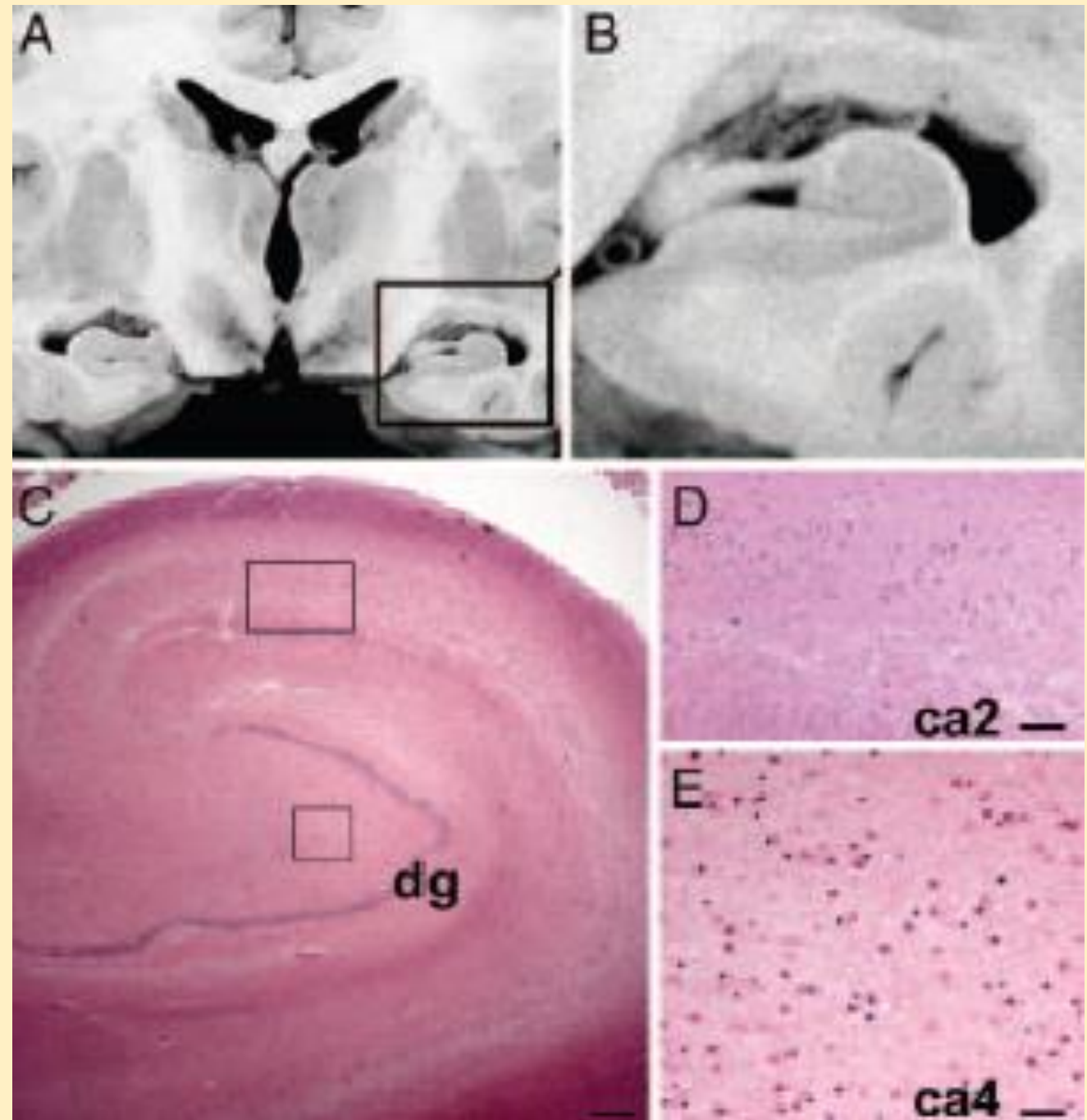
- Allogeneic hematopoietic stem cell transplantation (HSCT)
- 15-60 days post HSCT
- Clinical features:
  - Marked anterograde amnesia
  - Seizures or EEG abnormalities
  - Syndrome of inappropriate antidiuretic hormone (SIADH)
- All ages
- Men more vulnerable than women
- Mild CSF pleocytosis
- Bilateral T2/FLAIR hyperintensities within uncus, amygdala, and hippocampus, extending into the subiculum and entorhinal cortex

# Is PALE caused by HHV-6?

- CSF PCR detected HHV-6 in majority of cases
- Negative cases due to:
  - less sensitive assay
  - undetectable levels in CSF but detected in postmortem brain

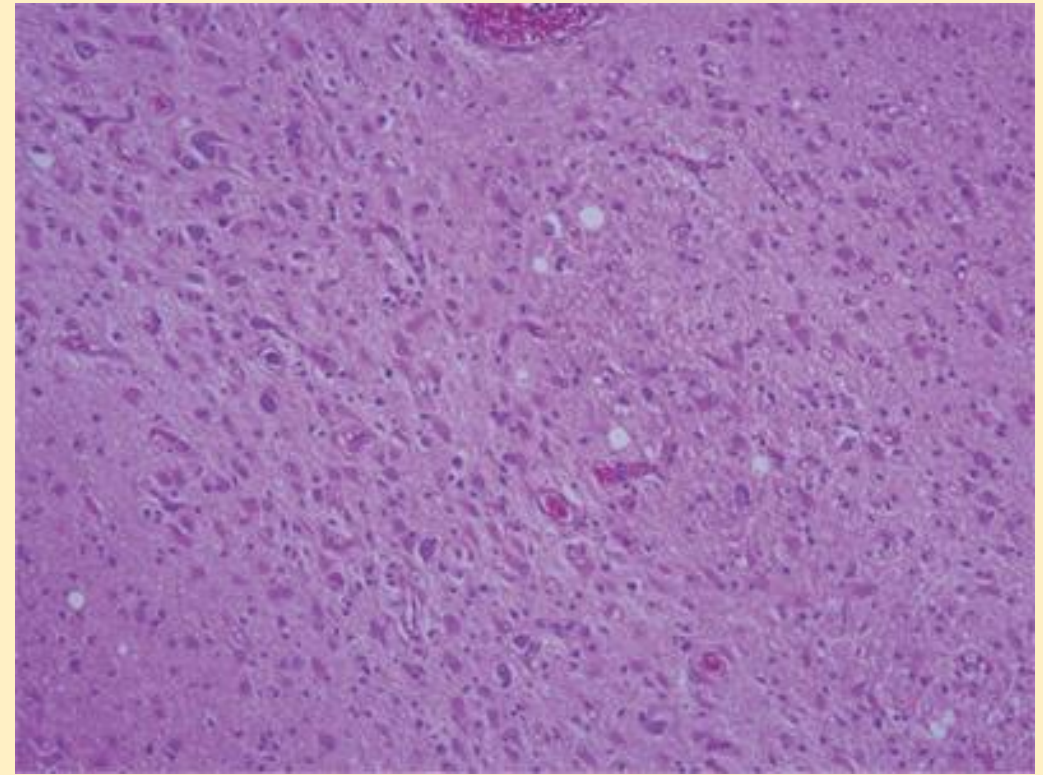
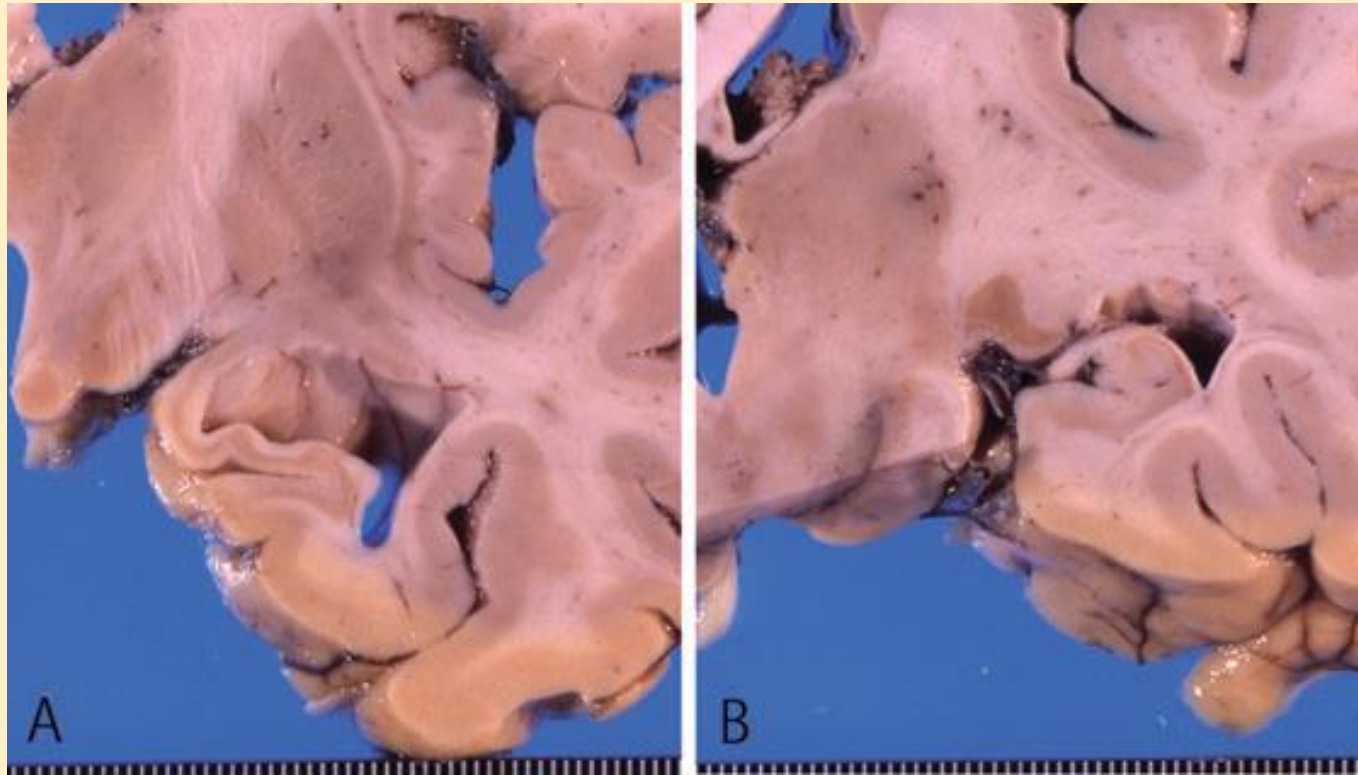
# Neuropathology

## Hippocampus



# Neuropathology

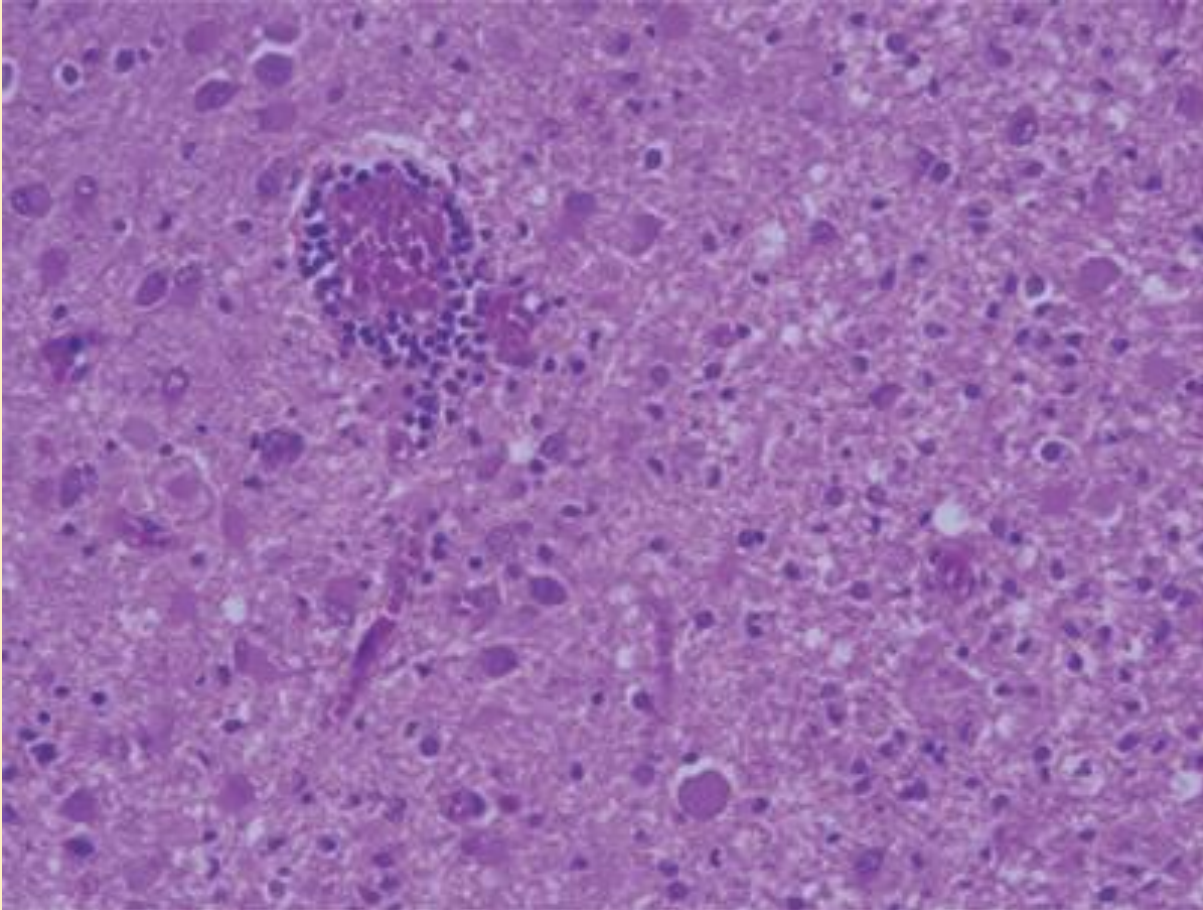
## Hippocampus



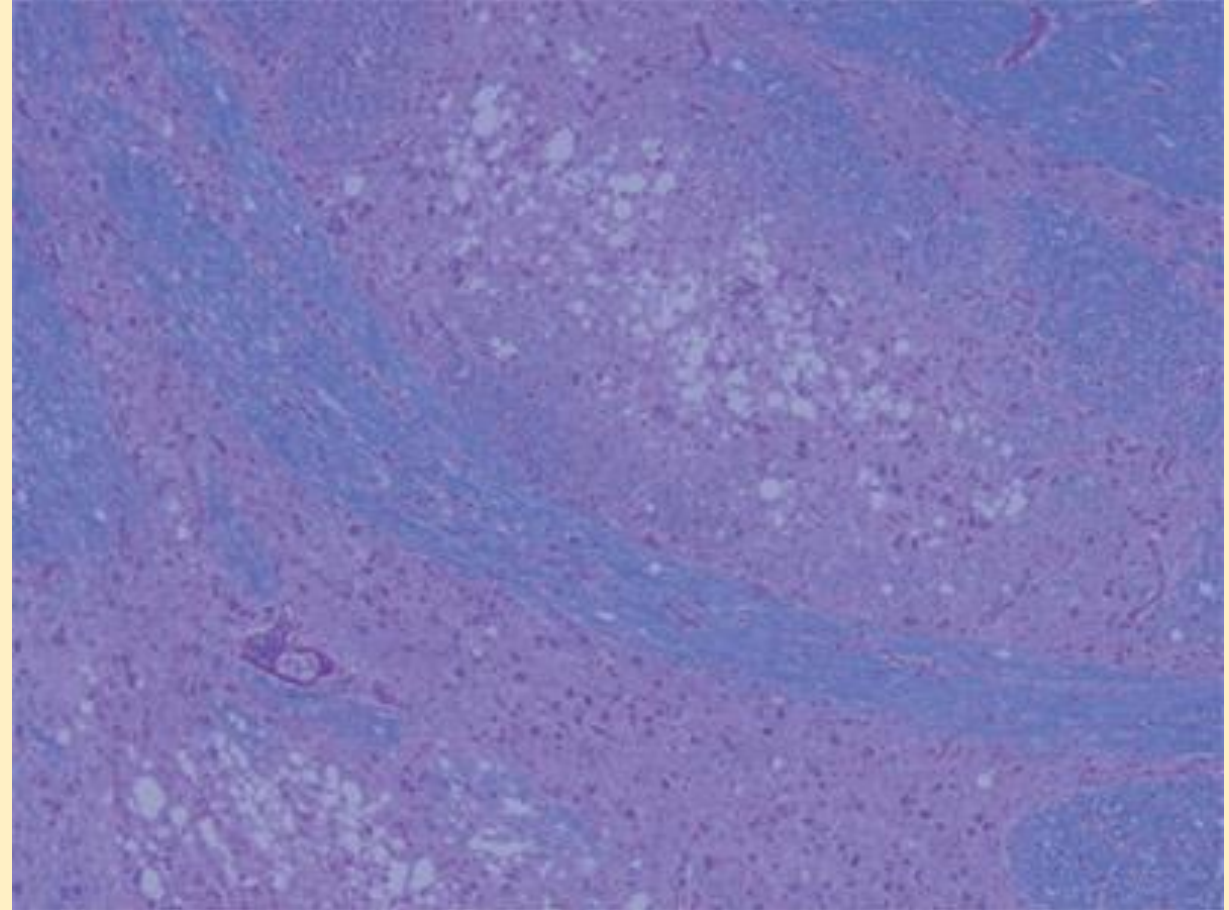


# Neuropathology

**Clastrum**



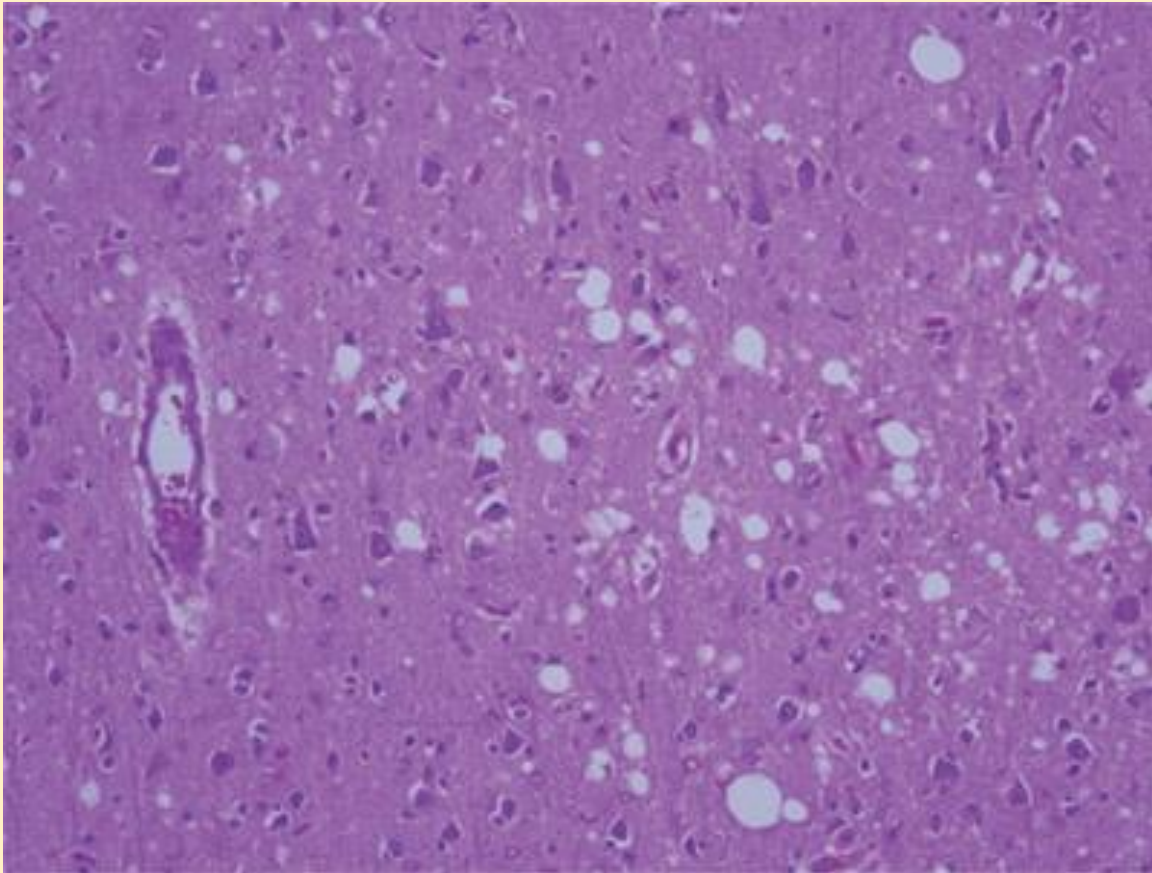
**Basis pontis**



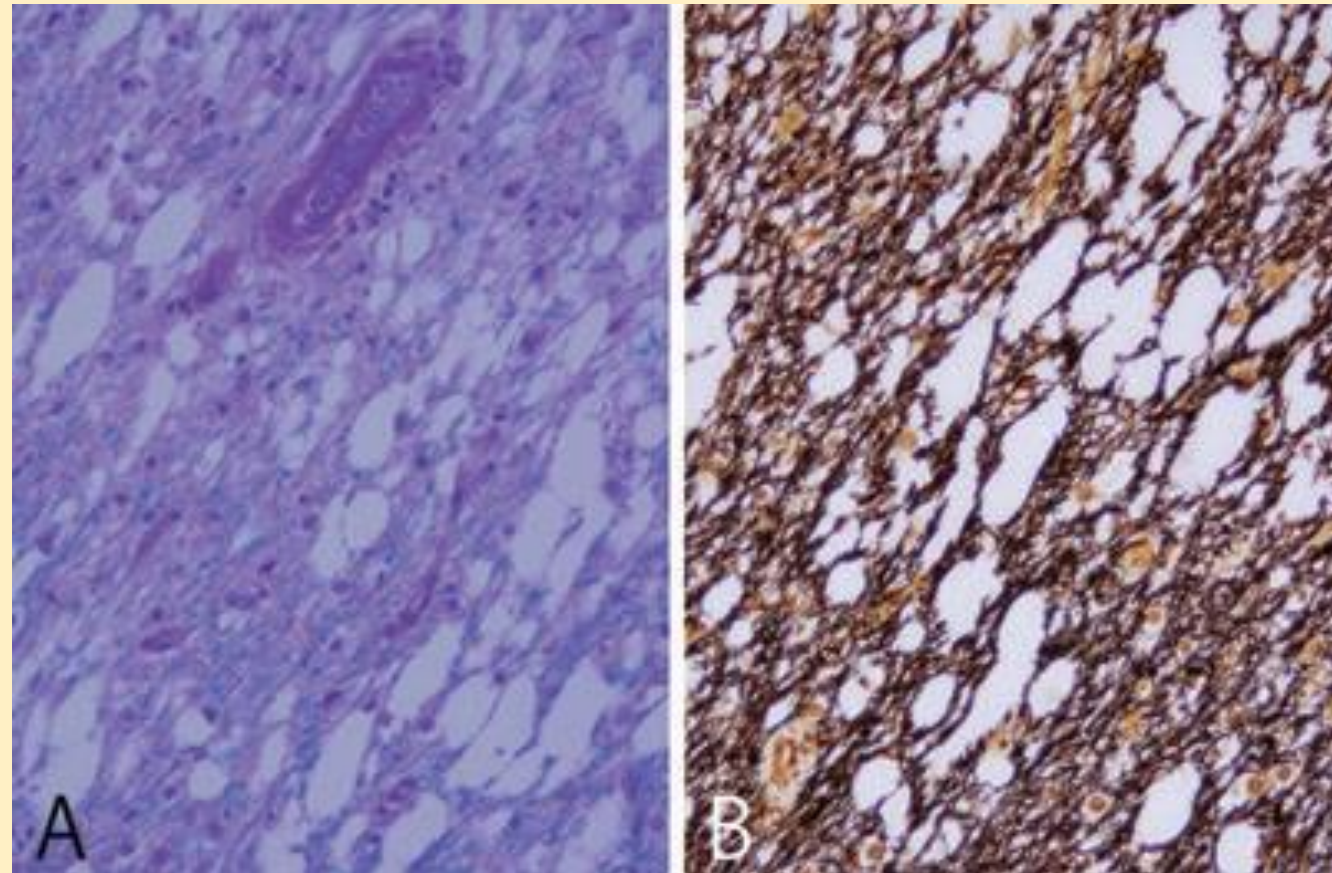


# Neuropathology

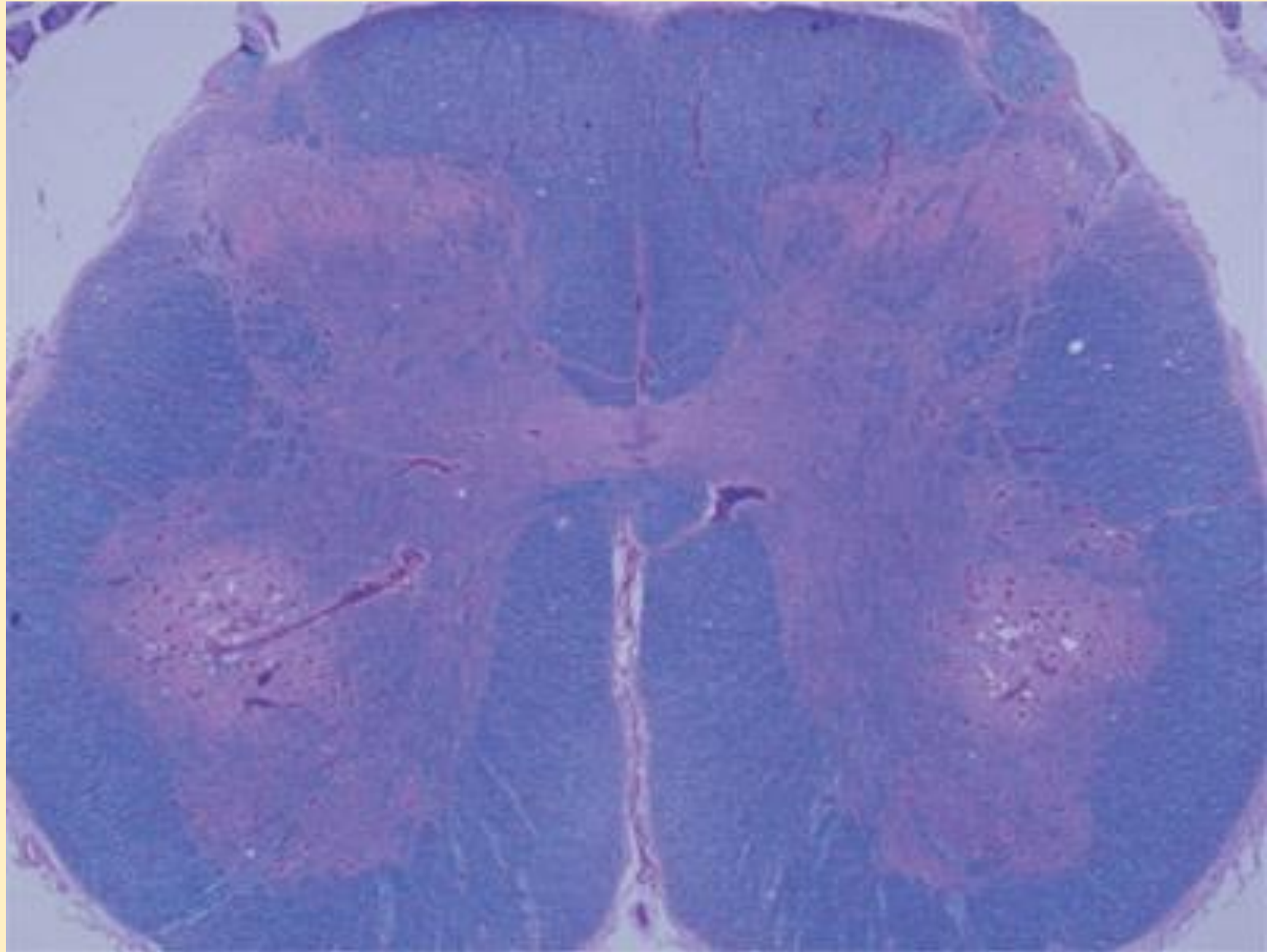
**Frontal lobe**



**Cerebellum**



Neuropathology  
**Lumbar spinal cord**





# Correlation between PCR in brain and CSF

- HHV-6 levels in CSF before death undetectable by quantitative PCR, positive by nested PCR
- HHV-6 DNA identified in brain, but not all regions
- Hippocampus consistently involved

# References

- Seeley et al. Post-transplant acute limbic encephalitis Clinical features and relationship to HHV6. *Neurology*. 2007 Jul 10;69(2):156-65.
- Shintaku et al. Human herpes virus 6 encephalomyelitis after bone marrow transplantation: Report of an autopsy case. *Neuropathology*. 2010 Feb 1;30(1):50-5. doi: 10.1111/j.1440-1789.2009.01020.x. Epub 2009 Apr 26
- Fotheringham et al. Detection of active human herpesvirus-6 infection in the brain: Correlation with polymerase chain reaction detection in cerebrospinal fluid. *J Infect Dis*. 2007 Feb 1;195(3):450-4. Epub 2006 Dec 27
- Drobyski et al. Brief Report: Fatal encephalitis due to variant human herpesvirus-6 infection in a bone marrow-transplant recipient. *Engl J Med*. 1994 May 12;330(19):1356-60.

Thank you!

