Case 2015-4

Abeer Tabbarah, M.D.
Barbara Crain, M.D. Ph.D.
Fausto Rodriguez, M.D.

Johns Hopkins University
Baltimore, M.D.
Disclosures

• None
Clinical history
Clinical history

• 73 year old black man
• 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)
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
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


Thank you!