An "Unforgettable" Case of Patchy Memory Loss Due to Human Herpesvirus-6 Encephalitis after Stem Cell Transplant for Acute Myeloid Leukemia Keck School of Medicine of USC

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Background

- Human herpesvirus-6 (HHV-6) reactivation following stem cell transplantation (SCT) for acute myelogenous leukemia (AML) is common and often clinically insignificant ¹.
- When symptoms do occur, they can include acute limbic encephalitis (amnesia, seizures, confusion, lethargy), fever, photophobia, focal neurologic deficits, hyponatremia, hallucinations. Can be fatal ¹.
- While CT of the brain is often normal, MRI shows abnormality of temporal lobes ².
- We present a rare case of patchy memory loss, initially hypothesized to be functional neurologic disorder (FND), later diagnosed as HHV-6 encephalitis.

Case

A 36yoF with AML is admitted for SCT and subsequent monitoring:

- Neutropenic fevers, thrombocytopenia, elevated LFTs, diarrhea attributed to Graft-versus-Host Disease → tacrolimus up-titrated
- Hallucinations, photophobia, tremor attributed to posterior reversible encephalopathy syndrome (PRES) from tacrolimus toxicity

Twenty-four days after SCT, she develops amnesia:

- Episodic memory loss, varies day to day and improves with cuing
- Retrograde amnesia inconsistent (e.g. remembers 1 year but not 10 years back)
- Excluded metabolic, endocrine, electrolyte, vascular abnormalities, hypoxia, and seizures as cause of encephalopathy

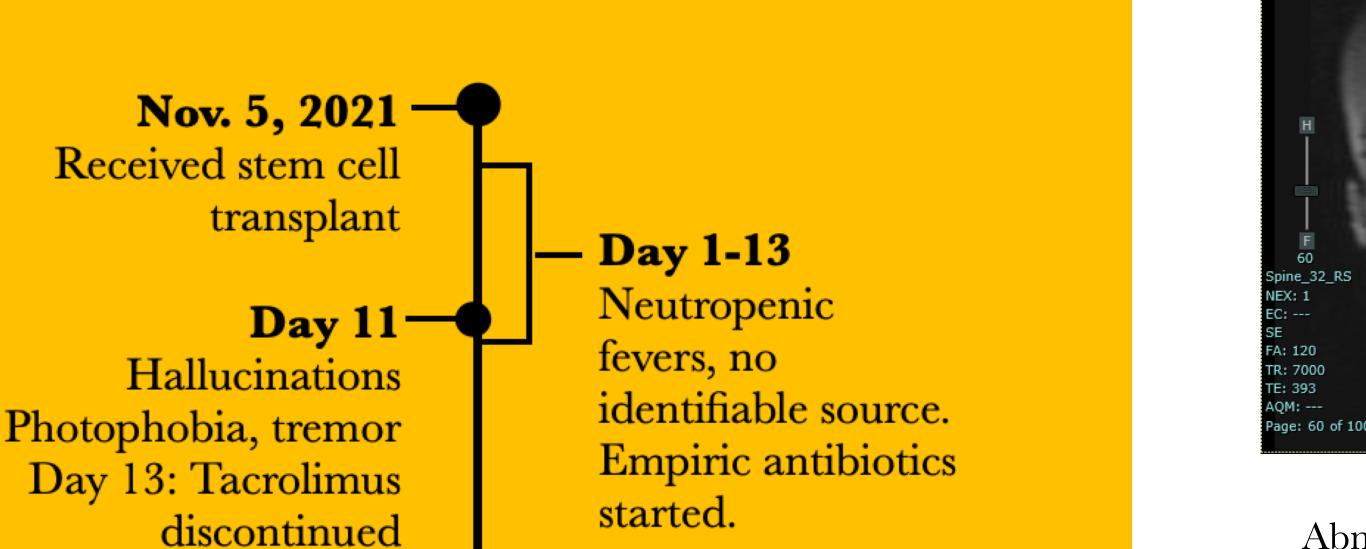
Improves with treatment for HHV-6 Encephalitis:

• MOCA 24/30 (12/6/21) \rightarrow MOCA 29/30 (7/13/22)

Workup Performed

Negative Findings	Positive Findings
Focal neurologic deficits	Elevated LFTs
Thyroid studies	Vit D and Calcium low
Vitamin B1, B6, B12, Folate	Intermittent hyponatremia
Ammonia	Brain MRI
HIV, RPR, Serum HHV6	CSF HHV6 (Qualitative)
Heavy metals (lead, mercury, arsenic)	CSF HHV6 (Quantitative)
Tacrolimus levels	CSF CMV
Blood culture, Urinalysis and Urine Chemistry	
Head CT	
EEG (except diffuse slowing)	
CSF (Cryptococcus, Enterovirus, E. coli, Haemophilus, Herpes Simplex Virus 1/2, Human parechovirus, Listeria, N. meningitidis, S. agalactiae, S. pneumoniae, Varicella-Zoster)	

Timeline MRI Findings



Day 24 consulted, dx: migraines Disorientation,

memory loss, speech Day 27 latency Concerns noted Tremor, myoclonus, regarding patient's bilateral ankle clonus memory loss being AMS workup started. patchy and inconsistent Day 25: LP performed

Day 28 — **Day 28**

Psychiatry consulted to CSF HHV6 + rule out "pseudo (qualitative) dementia" or functional Head MRI performed neurological disorder Foscarnet started (empiric tx)

Day 29

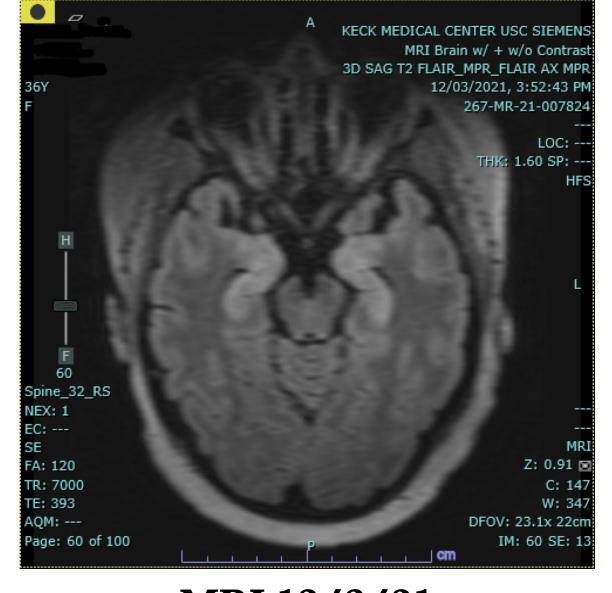
Day 14: Neurology

ID consulted, noted her — AMS was intermittent. Maintained reservation about accuracy of HHV6 diagnosis based on qualitative test only.

Day 38 — Repeat LP Quantitative HHV6 1690

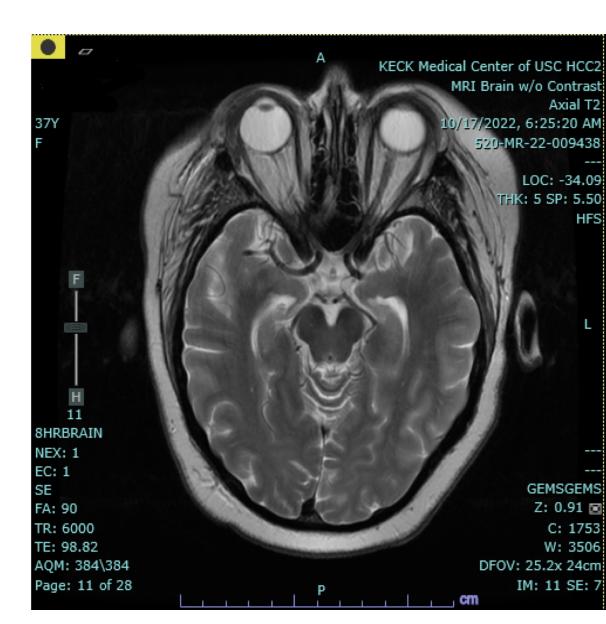
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Day 32 MRI confirmed HHV6 encephalitis diagnosis. Treatment continued. Symptoms gradually improved.



MRI 12/3/21 Abnormal symmetric diffusion signal abnormality involving bilateral hippocampus and

amygdala



MRI 10/17/22 Repeat MRI after treatment

Discussion

- While HHV-6 presented within the typical timeframe of symptom onset and with amnesia^{1,2}, timely diagnosis presented several challenges.
- HHV-6 encephalitis was eventually diagnosed according to lab and imaging findings. However, patchy memory loss without other neuropsychiatric symptoms was attributed to FND and delayed treatment.
- Minimal studies have described HHV-6 encephalitis presenting with patchy memory loss for personal events, rather than typical anterograde/retrograde amnesia³.
- Permanent cognitive deficits in memory and executive functioning can result.
- Further research is needed to better describe memory loss phenotypes resulting from HHV-6 encephalitis.

References

¹Frey, J. W., Cherabie, J. N., & Assi, M. A. (2017). Human herpesvirus-6 encephalitis following chemotherapy induction for acute myelogenous leukemia. Transplant infectious disease: an official journal of the Transplantation Society, 19(6).

²Zerr D. M. (2006). Human herpesvirus 6 and central nervous system disease in hematopoietic cell transplantation. Journal of clinical virology: the official publication of the Pan American Society for Clinical Virology, 37 Suppl 1, S52–S56.

³Kapur, N., & Brooks, D. J. (1999). Temporally-specific retrograde amnesia in two cases of discrete bilateral hippocampal pathology. Hippocampus, 9(3), 247–254.