Cache Valley Virus Encephalitis presenting as Akinetic Mutism after Renal Transplantation

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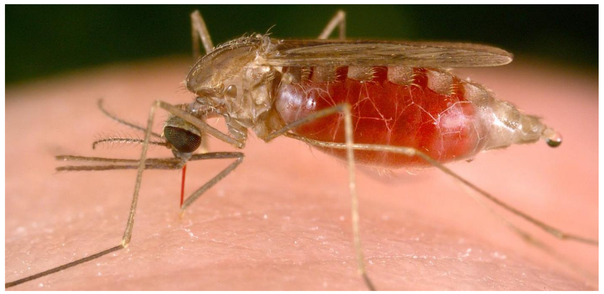
Background

Cache Valley Virus is a neuro-invasive mosquito-vector bunyavirus most commonly detected in North American mammals such as sheep and deer. The few reports of human disease describe meningoencephalitis, including cases in the setting of rituximab immunosuppression (Yang 2018) and X-linked agammaglobinemia (Wilson 2017). We describe a case of Cache Valley Virus encephalitis presenting as akinetic mutism after renal transplantation.

Vector: culicine and anopheline mosquitoes



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Hosts: ungulate mammals (sheep, deer > cattle, horses)

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Cache Valley Virus

- RNA Virus
- Family: *Bunyaviridae*
- Genus: *Orthobunyavirus*

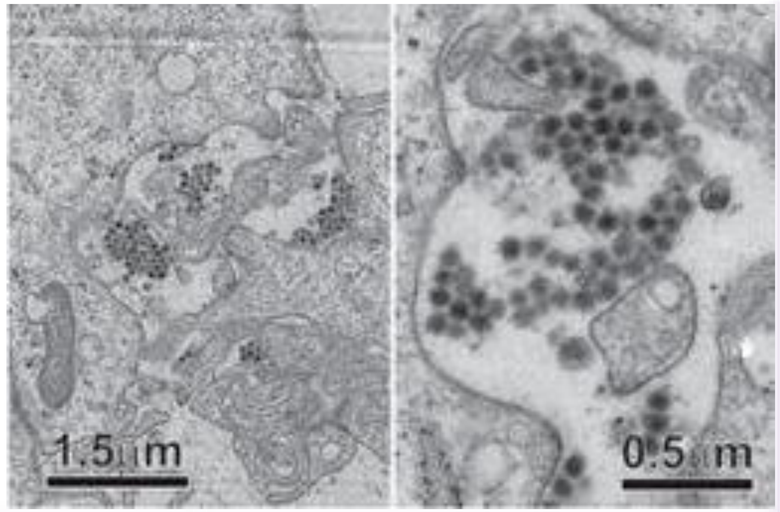

Figure 1. Electron microscopy visualizing Cache Valley Virus particles in membrane surrounded compartments within neurons after co-cultured with infected human frontal cortex from autopsy (Yang 2018)

Case

60-year-old female with sickle cell anemia and hypertension was hospitalized 1.5 months after kidney transplantation with altered mental status, malaise, chills, weight loss, and loose stools. She had another brief hospitalization after transplantation for vaso-occlusive crisis requiring blood transfusions. On current admission, UTI and C. difficile colitis were treated with antibiotics, though low-grade fever fluctuated throughout admission. Initial hypoactive delirium bordered on akinetic mutism but lacked unique behavioral features of catatonia. The patient demonstrated very limited command following and required tube feeds. CT Head, MRI Brain, and MRV brain were unremarkable. EEG demonstrated moderate encephalopathy and generalized periodic discharges/triphasic waves. Tacrolimus was transitioned to cyclosporine without mentation benefit and mycophenolate was continued.

Methylphenidate 20 mg twice daily mildly increased movement and prompted vacuous communication but was discontinued due to tachycardia. Serum autoimmune panel was unremarkable. CSF samples were obtained 3 times with negative cultures and negative EBV, AFB, Cryptococcus, VZV, CMV, HSV, Enterovirus, HHV6, VDRL, WNV, JC virus, BK virus, general meningitis panel, Mayo ENC2 paraneoplastic panel. By 2 months into admission, mental status had transitioned to completely nonverbal akinetic mutism with no command following despite eye tracking. CSF sample was sent to UCSF for metagenomic next-generation sequencing (mNGS), which confirmed Cache Valley Virus. Immunosuppression was discontinued, and the patient was started monthly IVIG. CDC investigation later confirmed that a transfusion the patient had received was the source of Cache Valley Virus.

Discussion

- Cache Valley Virus is an extremely rare etiology of encephalitis, though at least five cases have been confirmed.
- Relevant risk factors in this case were post-renal transplant immunosuppression and a history of significant blood transfusions.
- Hypoactive delirium is common in the medical course following transplantation, sustained presentations with akinetic mutism-like presentations may prompt consideration of possible immunosuppression enabled viral encephalitis.

Conclusions

In cases of prolonged hypoactive delirium deteriorating to akinetic mutism states after initiation of immunosuppression for transplantation, activation of viral encephalitis is relevant to consider in the differential diagnosis, especially in patients with a history of significant blood transfusions.

References

- Yang Y, et al. Fatal Cache Valley virus meningoencephalitis associated with rituximab maintenance therapy. Am J Hematol 2018; 93(4):590–594.
- Wilson, et al. A Novel Cause of Chronic Viral Meningitis: Cache Valley Virus. Ann Neurol 2017;82:105-114.
- Sexton D, et al. Life-Threatening Cache Valley Virus Infection. NEJM 1997;336:547-550.