Suspected HHV-6 related post-viral encephalitis: A case of treatment resistant catatonia

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BACKGROUND

Catatonia is a syndrome characterized by motor and behavioral abnormalities, associated with various psychiatric and medical conditions. Autoimmune encephalitis (AE) is increasingly recognized as a cause of catatonia [1] and may be diagnosed clinically regardless of the presence of detectable autoantibodies [2]. Human herpesvirus-6 (HHV-6), acquired almost universally in early childhood, has been associated with post-viral autoimmune encephalitis [3]. We describe a unique case of treatment-resistant catatonia, which was ultimately suspected to be due to HHV-6 related AE in an immunocompetent patient with no evidence of malignancy or active viral infection.

CASE PRESENTATION

A 73-year-old female with history of bipolar I disorder was admitted to the psychiatric unit for acute management of a mixed episode with psychotic features, treated with risperidone and divalproex. On hospital day (HD) #14, she was transferred to the medical floor for IV antibiotics in setting of urosepsis with tachycardia to 120s and leukocytosis with white blood cell (WBC) count elevated to 13.9K/uL, poor oral intake, and concern of delirium.

On initial evaluation by the C-L team, patient was nonverbal but able to point and shake her head in response to questions. Risperidone was continued for psychosis. On HD #16, she appeared stuporous, with significant muscular rigidity, waxy flexibility, catalepsy, staring, and autonomic instability. Lorazepam 1mg IV was administered for suspected catatonia:

	Vitals	Bush Francis
Before lorazepam	HR 123, BP 198/102	19
After lorazepam	HR 94, BP 103/65	7

Psychotropic medications were held out of concern for malignant catatonia vs neuroleptic malignant syndrome (NMS). Symptoms of catatonia did not significantly improve despite trials of lorazepam, zolpidem, memantine, bromocriptine, and several sessions of electroconvulsive therapy (ECT). Vitals remained labile and Bush Francis scores ranged 15-22.

CASE PRESENTATION (CONTINUED)

MEDICAL/ NEUROLOGICAL WORKUP

EEG: mild diffuse slowing; no epileptiform activity

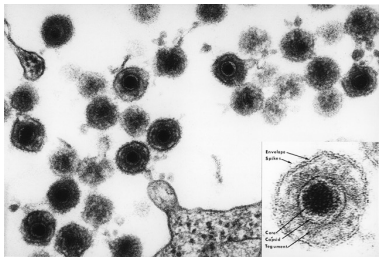
MRI brain w/o contrast: large ventricular system consistent with cerebral volume loss

Lumbar puncture (HD #23):

- CSF total nucleated cell count elevated at 9/uL with neutrophilic predominance (87%), elevated protein count of 116 mg/dL
- Negative paraneoplastic, autoimmune, and infectious panels

Additional studies:

- Serum HHV-6 IgG **positive**
- HIV, hepatitis A/B/C, syphilis, and Cryptococcus (serum) negative



HHV-6 viewed through an electron microscope
https://en.wikipedia.org/wiki/Human_herpesvirus_6

HD #25: methylprednisolone 1g IV daily started due to concern for autoimmune process, stopped after 3 days due to negative CSF studies

HD #35: Started on 5 day course of IV immune globulin (IVIG) 0.4g/kg daily for possible limbic encephalitis 2/2 HHV-6 infection. After 2 doses of IVIG, our patient demonstrated resolution of muscle rigidity with improved oral intake and spontaneous speech production. She demonstrated notable irritability, disorganization, and delusional thought content. On HD #45, she was transferred back to psychiatric unit for continued management of mania and psychosis. ECT was continued for a total of 16 inpatient sessions.

On the psychiatric unit, our patient continued to demonstrate remission of catatonia. Symptoms of psychosis and mania also improved, and she was safely discharged home on divalproex 500mg BID, lorazepam 0.5mg BID, memantine 10mg daily, quetiapine 50mg qhs.

DISCUSSION

Whereas our patient demonstrated minimal improvement with typical treatments for catatonia [4], she rapidly improved following administration of IVIG. This presentation, combined with neutrophilic pleocytosis in the CSF raised suspicion for post-infectious AE. This case contributes to a growing body of literature describing AE as a cause of catatonia, and there is emerging evidence connecting HHV-6 infection with the development of neuropsychiatric conditions across the lifespan, like multiple sclerosis, epilepsy, and Alzheimer's disease [3, 5]. More research is warranted regarding a possible connection among HHV-6, AE, and catatonia in immunocompetent individuals.

CONCLUSION

- Catatonia is not well-understood at this time and has many potential causes
- Consider autoimmune and/or infectious cause of treatment-resistant catatonia
- HHV-6 is commonly acquired early in life, but has been documented cause of autoimmune encephalitis and now associated catatonia in adults
- Completing a thorough medical/neurological workup is crucial

REFERENCES

1. Rogers, J. P., Pollak, T. A., Blackman, G., & David, A. S. (2019). Catatonia and the immune system: A review. *Lancet Psychiatry*, *6*, 620-630.
2. Pradhan, S. Das, A., Das, A., & Mulmuley, M. (2019). Antibody negative autoimmune encephalitis- Does it differ from definite one?. *Annals of Indian Academy of Neurology*, *22*(4), 401-408.
3. Harald, P. (2017). Postviral autoimmune encephalitis: Manifestations in children and adults. *Current Opinion in Neurology*, *30*(3), 327-333.
4. Mormando, C., & Francis, A. (2020). Catatonia reviewed: A unique syndrome updated. *International Review of Psychiatry*, *32*, 403-411.
5. Santpere, G., Telford, M., Andres-Benito, P., Navarro, A., & Ferrer, I. (2020). The presence of human herpesvirus 6 in the brain in health and disease. *Biomolecules*, *10*(11), 1520.