

# **Herpes Simplex Virus Encephalitis as a Novel Manifestation of Common Variable Immunodeficiency: Two Case Reports and Review of the Literature.**

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# Case #1

- ▶ 25 year old male presents to the emergency room with fever and a 12 hour history of delirium with combative behavior. CT scan head negative.
- ▶ CSF: WBC-2060 (92% lymphs), RBC-240 (0-2), protein-123(12-40), glucose-53(40-70)
- ▶ HSV PCR positive.



## Past Medical History:

- Bacterial meningitis-2001
- Pneumonia-2002, 2003
- Sinusitis-innumerable

## Significant Labs:

- Total Protein-5.4 (6.0-8.5)
- Albumin-4.0
- IgG <33, IgA<6.7, IgM-57
- Secondary causes of hypogammaglobulinemia ruled out

# Case #2

HPI: 42 year old white male presents to emergency room with 1 day history of headache and new onset seizures. CT scan head negative.

- ▶ CSF studies: WBC-20(90% lymphs) , RBC-240 (0-2). protein 123 (12-40), glucose 53 (40-70)
- ▶ Enterovirus PCR negative, West Nile Virus PCR negative
- ▶ HSV PCR positive

## Past Medical History:

1. Sinusitis- innumerable
2. Pneumonia: 1995, 1996, 1998, 2000, 2000, 2003, 2003
3. Herpes zoster: 1976

## Significant Labs:

- IgG < 100 mg/dL, IgA 40 mg/dL, IgM 17 mg/dL.
- Secondary causes of hypogammaglobulinemia ruled out

# Immunologic Parameters

	Normal Range	Patient 1 24 yo male	Patient 2 42 yo male
Immunoglobulins			
IgG	654-1618	<33	<100
IgA	68-378	<6.7	40
IgM	60-263	57	<17
Lymphocyte (%)			
T cells	57-84	97 * (87)	79
B cells	5-24	1 * (13)	12
Absolute CD4+ T Cell Count	400-1100	586	520
CD4/CD8 T cells	0.9-4.6	1.18	1.42

\* repeat laboratory value 2 weeks later

# Methods

We searched OVID medline (1966-present), PubMed, Google and MD Consult with the terms herpes simplex virus, encephalitis, meningitis and common variable immunodeficiency in order to generate a list of all case reports on HSVE in CVID.

No case reports of HSVE in CVID were identified using this methodology.

# Reported Causes of Encephalitis/Meningitis in Patients with CVID and Agammaglobulinemia

## CVID

- H. influenzae
- S. pneumoniae
- P. aeruginosa
- Measles
- JC virus
- West Nile Virus
- CMV

## Agammaglobulinemia

- H. influenza
- S. Pneumoniae
- Coxsackie B3
- Echovirus
- Adenovirus
- Polio
- JC virus

# Discussion

- ▶ The development of HSVE in both of these patients was a consequence of delayed diagnosis as both patients experienced multiple atypical infections for their ages before being diagnosed with CVID
- ▶ combined B/T cell abnormalities in patients with advanced CVID may render these patients more susceptible to infections by HSV

# Discussion

- ▶ The lack of reported HSV encephalitis as a complication of CVID suggests that IVIG provides sufficient HSV specific IgG to prevent reactivation and dissemination of HSV
- ▶ Alternatively, the administration of IVIG may have immunoregulatory effects that lead to enhanced T cell immunity which helps suppress reactivation of HSV in these patients.

# Conclusions

- We believe that the development of HSVE in these two patients with CVID was a consequence of delayed recognition of their profound hypogammaglobulinemia
- The lack of HSV encephalitis case reports in the literature suggests that IVIG replacement provides enough anti-HSV IgG to prevent reactivation
- Early identification of humoral immunodeficiency in the setting of recurrent bacterial infections is imperative as IVIG has been shown to prevent HSVE