A Case Report of Herpes Simplex Virus Encephalitis during Natalizumab Treatment for Relapsing Remitting Multiple Sclerosis

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Background
- Natalizumab is indicated as monotherapy for the treatment of patients with relapsing remitting multiple sclerosis (MS).
- Natalizumab inhibits migration of lymphocytes into the central nervous system (CNS), which potentially impairs immune surveillance for CNS infections.
- Natalizumab-associated reactivation of John Cunningham (JC) virus, causing progressive multifocal leukoencephalopathy (PML), is well documented.
- Natalizumab treatment for MS is less clearly linked to increased risk of other viral infections.
- Recent case series by Fine et al² reported 20 natalizumab-treated MS patients who developed CNS herpes simplex virus (HSV) infections.
- Potential role of prior immunosuppressant (IS) exposure in enhancing the risk of CNS HSV infection could not be determined.¹

Objective
- To describe a non-fatal case of herpes simplex virus encephalitis (HSE) in a patient with fulminating MS treated with natalizumab without prior IS or disease modifying therapy (DMT) exposure.

Case Report
- 38 year-old man with fulminating MS [Figure 1] was treated with natalizumab as initial therapy with first infusion on June 07, 2013.
- On September 24, 2013, after 4 months treatments with natalizumab, patient was found unresponsive following a seizure.
- MRI Brain showed a new T2/FLAIR hyperintense lesion in the left temporal lobe with associated foci edema and restricted diffusion [Figure 2].
- HSV type 1 DNA was detected in cerebrospinal fluid (CSF) by PCR; CSF JC virus PCR was negative.
- Overall, patient responded well to 6 weeks of IV acyclovir therapy that was started on day of HSE onset, followed by 4 out of 6 planned months of oral valacyclovir thus far.
- Subsequent MRI Brain 2 weeks after ictus showed interval development of petechial blood products in the left temporal lobe and insular region [Figure 3].

Results

April 29, 2013
- Figure 1: Baseline MRI Brain before initiation of natalizumab.
- Extensive T2/FLAIR lesion burden throughout the bilateral cerebral hemispheres and posterior fossa, characteristic of MS (A-C). No evidence of restricted diffusion on DWI sequences (D).

September 24, 2013
- Figure 2: MRI Brain at the time of HSE onset.
- Confluent T2/FLAIR hyperintensity throughout the left temporal lobe with diffuse edema and enlargement of the left amygdala and hippocampal formation (A-C). New restricted diffusion on DWI in the left temporal lobe (D).

October 08, 2013
- Figure 3: MRI Brain during HSE, after 2 weeks of IV acyclovir.
- Interval development of more confluent T2/FLAIR Hyperintensity (A-B) with associated petechial Blood products in the left medial temporal lobe and insula on SWI images (C). Interval resolution of restricted diffusion on DWI sequences (D).

March 24, 2014
- Figure 4: MRI Brain after acute HSE.
- Interval development of encephalomalacia in the left anterior temporal lobe, as illustrated on axial and sagittal FLAIR (A-B) and T1-weighted sequences (C). No restricted diffusion on DWI sequences (D).

Case Report (cont.)
- Repeat CSF studies after completion of 6 weeks of IV antiviral therapy showed no detectable HSV DNA.
- Patient has demonstrated residual neuropsychiatric disturbances since ictal event with otherwise near normal neurological examination.
- Neuropsychiatric symptoms included severe anterograde amnesia and impaired executive functioning.
- Repeat MRI Brain 6 months after HSE onset showed extensive encephalomalacia in the left temporal lobe [Figure 4] with otherwise radiographically stable MS lesion load.
- Re-starting DMT was favored in light of previous fulminating disease and risk of reactivation since stopping natalizumab.
- Patient and his family remain hesitant to re-start therapy, and he is currently being closely monitored off of DMT.

Conclusions
- Our case and previously reported cases¹-² suggest there is increased risk of CNS HSV infection with natalizumab therapy, even without prior IS exposure.
- Natalizumab label was recently changed to include a black box warning about CNS herpes infections.³
- Reported cases demonstrated good response with early detection and appropriate treatment with antiviral agents.
- Prolonged neuropsychiatric changes have been described in a previous case of HSE during natalizumab treatment for MS.²
- In addition to monitoring for PML, providers caring for MS patients treated with natalizumab should remain vigilant for other CNS infections.

References

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