A case of HSV encephalitis in a patient treated with fingolimod

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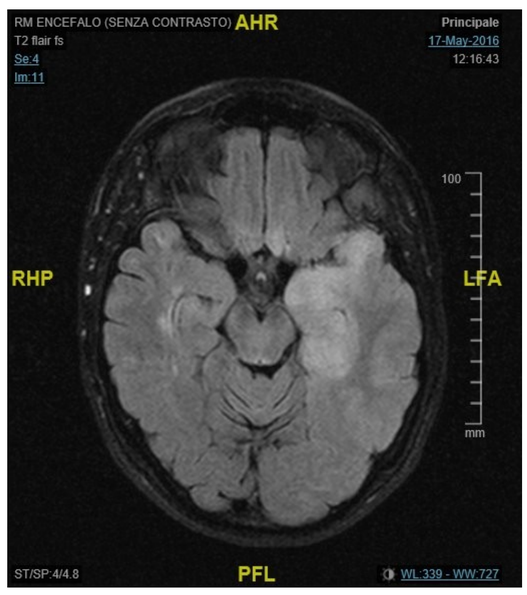
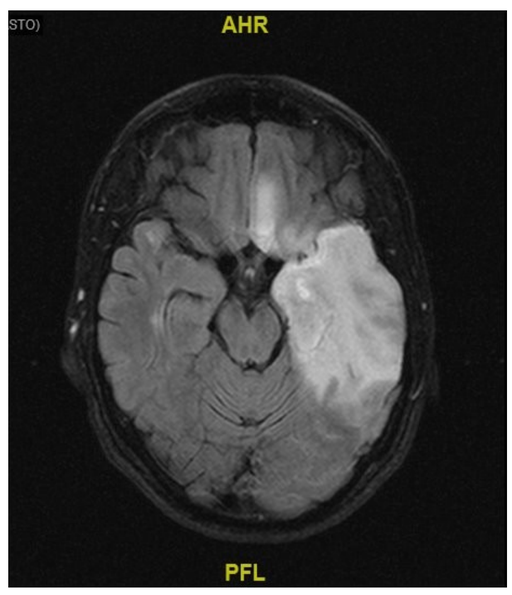
Case Report

We present a case of herpetic encephalitis in a 43 years-old woman with multiple sclerosis (MS), in treatment with fingolimod.

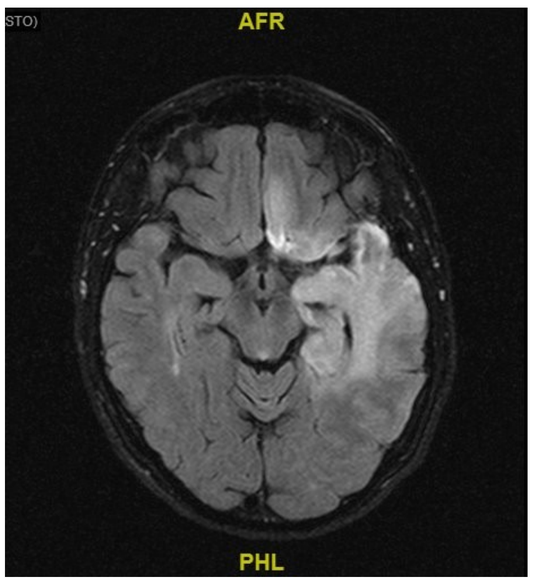
- Following diagnosis of MS at the age of 31 the patient initiated treatment with Glatiramer acetate, which was suspended 5 years later because of side effects at the injection site.
- At the age of 37 yo, in June 2010, she presented with diffused paresthesias, associated with right hemisphere MRI changes, compatible with active lesions. Azathioprine, 100 mg per day, was immediately prescribed and the treatment carried out for one year. She eventually started Fingolimod in February 2014.
- The treatment with Fingolimid was carried out until May 2016, when she was admitted to the neurology ward because of acute onset of headache, fever and generalized epileptic seizures. At admission she had fluent aphasia and showed mild signs of meningeal irritation.
- Left temporal hyperintensity in MRI FLAIR and DWI sequences presented mild enhancement after gadolinium injection.
- EEG presented electrical alterations in fronto-centro-temporal areas bilaterally, with prevalence in the left hemisphere, occasionally spreading to the whole brain, together with a globally slowed background pattern.
- CSF analysis revealed 20 leukocytes/µl (86% lymphocytes, 7% neutrophils, 7% other) and increased protein level (78.60 mg/dl). Herpes Simplex Virus (HSV) type 1 was identified in CSF.
- Serology for HSV was negative at baseline. She repeated the exam at 14 days (IgM: negative; IgG: 43,20) and at 21 days (IgM: negative; IgG: 62,20).



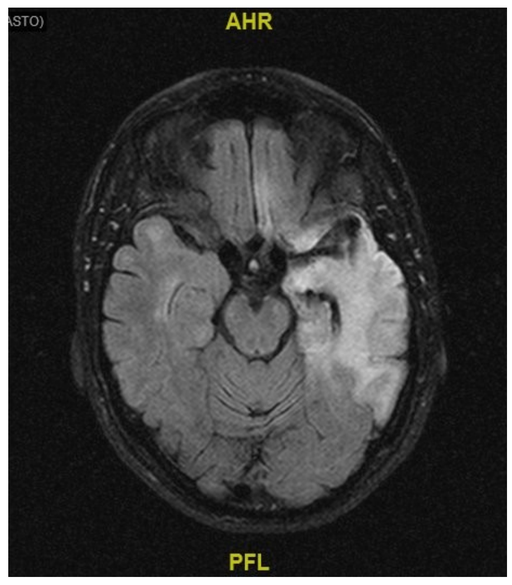
1st day of i.v. treatment



7th day of i.v. treatment



18th day of i.v. treatment



30th day of oral treatment

Clinical Outcomes and Follow Up

- She was treated with intravenous acyclovir 750 mg tid for 21 days, with benefits on symptoms. She continued therapy with oral acyclovir 800 mg five times a day for 30 days.
- A lumbar puncture, performed after intravenous treatment, showed 23 cells (100% lymphocytes), proteins: 84 mg/dl.
- MMSE (Mini Mental State Examination) was administered after the end of intravenous therapy: the score was 23/30. It wasn't possible to perform a complete neuropsychological assessment before because of the poor health condition of the patient.
- She underwent a brain MRI at the end of the oral treatment, which showed cortical laminar necrosis in the affected areas.
- She also underwent a thorough neuropsychological examination at the end of the oral treatment: MMSE was 28/30. She showed impaired verbal memory and a moderate aphasia.

Discussion and Conclusions

Fingolimod is an oral drug efficacious for treatment of MS. By modulating sphingosine 1-phosphate (S1P) receptors on lymphocytes, fingolimod inhibits egress of naïve and central memory lymphocytes from lymph nodes. The relative increase in effector memory T cells in blood is thought to ameliorate the immunopathologic response of the brain, by means of a still not thoroughly defined mechanism. However, a direct effect of fingolimod on the central nervous system (CNS) is not excluded.

The reported case raises concern about the potential role of fingolimod in increasing the risk for virus infection or reactivation. This report adds to few similar cases of encephalitis in patients treated with fingolimod reported in the literature. As our knowledge of the immunomodulatory/immunosuppressive mechanisms of the available treatments for MS continue to increase, we need to remain alert to previously unrecognized complications that may be related to them.

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-Chun J, Hartung HP. Mechanism of action of oral fingolimod (FTY720) in multiple sclerosis. Clin Neuropharmacol. 2010 Mar-Apr;33(2):91-101.
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