A CASE OF NATALIZUMAB-ASSOCIATED PML-IRIS: when early detection makes a difference

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Introduction:

Progressive multifocal leukoencephalopathy (PML) and Immune reconstitution inflammatory syndrome (IRIS) represent both serious and possibly fatal adverse reactions as consequence of treatment with Natalizumab (NTZ) in Multiple Sclerosis (MS).
More than 632 MS patients receiving long-term NTZ-treatment have been so far affected.

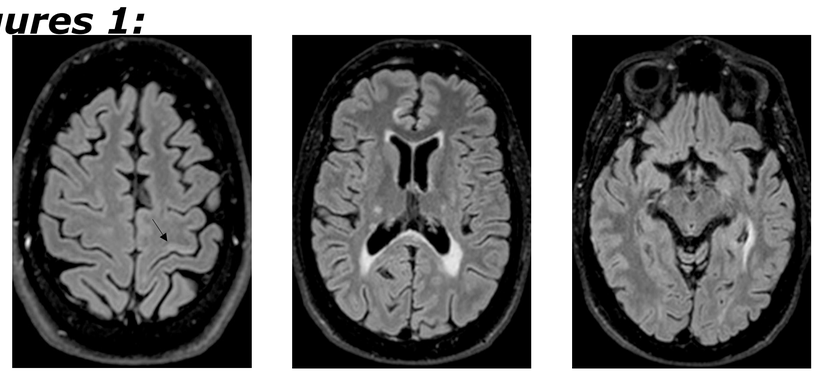
Case report:

- 32 years old man, suffering from MS since 2008.

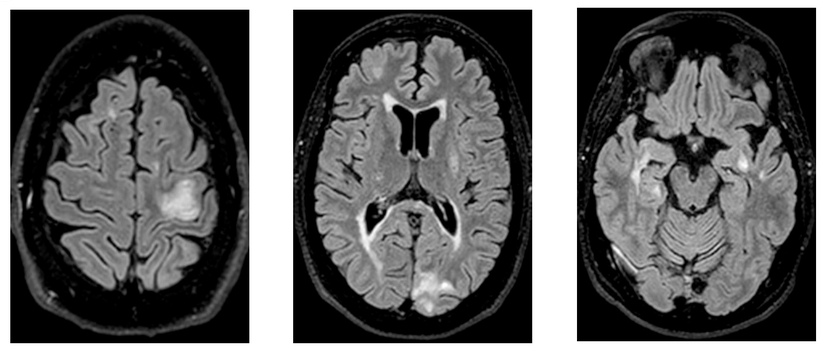
Disease modifying therapy: Copaxone for 3 years, Tysabri from 2011 until November 2015, overall 47 NTZ-infusions, initially monthly, since March 2015 bimonthly.
Test STRATIFY (11.09.2013): JCV positive, Index value 2,3.

- 23.12.2015 (scheduled date for NTZ-infusion): the patient reported a subjective light clumsiness of his right hand which has started at middle of November; his neurological examination resulted unchanged; instead, a revaluation of his brain-MRI previously performed (15.12.2015) showed a small lesion suspicious for PML in the left precentral gyrus (figures 1). NTZ was stopped immediately; no copy of the JCV genoma was found in the CSF.
- 11.01.2016: the patient demonstrated a significant strength reduction of his right arm (M3) and a right inferior quadrantanopia; brain-MRI of January 12 confirmed the suspicion of PML and demonstrated a multifocality of infection (figures 2). Diagnosis of PML was made even if no copy of the JCV genoma had yet been found in the CSF.
- Due to continuous worsening of symptoms and brain-MRI findings (26.01.2016) (figures 3), at the end of January the diagnosis of IRIS was made. Steroid treatment was started. Two weeks later improvement of symptoms and brain-MRI findings occurred (04.02.2016) (figures 4). No copy of the JVC genoma was detected in the latest CSF examination performed on January 28.
- While improving in the muscle strength, extrapyramidal hypertonus, myoclonus, and tremor in the right arm appeared. Seven months later (July 2016) the patient demonstrated a clinical relapse of MS, treated with methylprednisolone 1 gr iv for three days, with regression of symptoms. Current Karnofsky Score: 80. Current DMT: Copaxone 40 mg three time a week.
- PML TREATMENT: from January 28 methylprednisolone 1 gr iv for two days, followed by prednisone orally for six weeks.

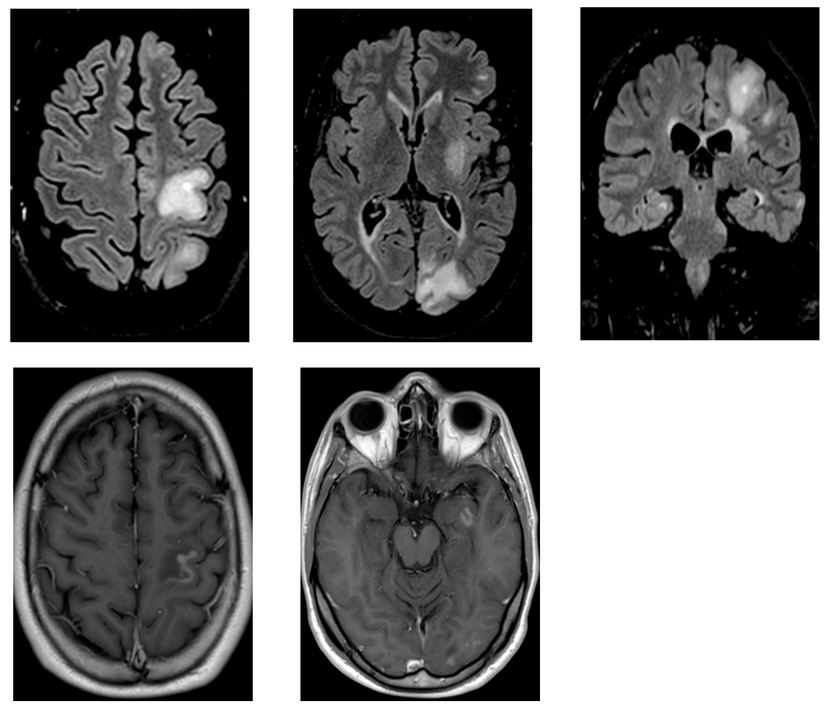
Figures 1:



Figures 2



Figures 3



Figures 4

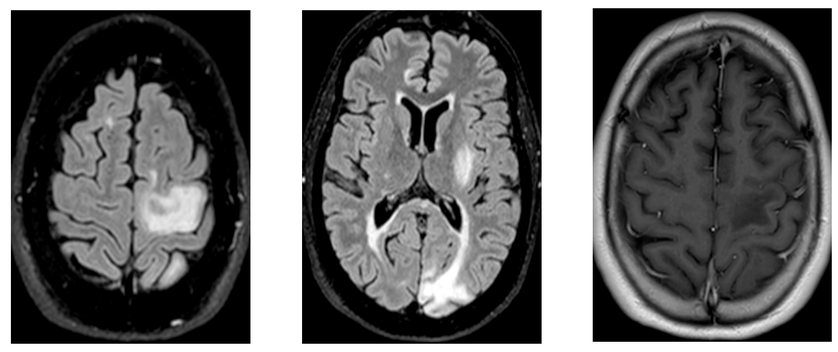


Fig. 1: small patchy area of hyperintensity in the juxtacortical white matter of the precentral gyrus.
Fig. 2: significant increase in size of the area of hyperintensity in the juxtacortical white matter of the precentral gyrus, new area of hyperintensity in the left calcarine area and in the region ventral from the left temporal horn. The area shows increased signal in the DWI, as well as in the ADC map.
Fig. 3: increased in size and number of the lesions with enhancement after GD application.
Fig. 4: decrease in number of the lesions and of the enhancement.

Conclusions:

The functional outcome is very much dependent on early detection, on the initial side where the JVC-infection can be found and on the low viral load: our patient had all three favorable elements, which results in mild sequelae.

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