Serum Neurofilament Light Chain Levels Increase at the Onset of PML in Natalizumab Treated MS Patients

G Dalla Costa[1], R Furlan[2], A Finardi[2], F Sangalli[1], B Colombo[1], L Moiola[1], P Cinque[3], E Kolb[4], A Haghikia[4], R Gold[4], G Comi[1], V Martinelli[1]

[1] Department of Neurology, San Raffaele Hospital, Milan, Italy
[2] Neuroimmunology Research Unit, San Raffaele Hospital, Milan, Italy
[3] Infectious Diseases Research Unit, San Raffaele Hospital, Milan, Italy
[4] Department of Neurology, Ruhr-University Bochum and St Josef-Hospital, Bochum, Germany.

Introduction: The monoclonal antibody natalizumab is a highly effective treatment for patients with multiple sclerosis (MS). However, the drug is associated with increased risk of progressive multifocal leukoencephalopathy (PML), a severe infection of the CNS caused by the reactivation of JC virus. Huge efforts have been made to improve risk stratification algorithms and to facilitate early disease recognition, but no serum biomarker is currently available for the condition.
The aim of this study was to assess whether serum neurofilaments light chains (Nfl) are a reliable biomarker for the early recognition of PML during natalizumab treatment.

Methods: Patients were recruited from 2 European MS cohorts. Of 213 patients with MS, 102 had been treated with natalizumab (9–84 months), 37 received other immune-modulatory treatments, and 74 were untreated. 12 healthy controls (HC) were also enrolled. We had access to samples from 25 natalizumab PML patients. Serum NfL concentration was assessed using an ECL immunoassay.

Results: NFL levels were higher in treated (18.0 ± 11.8 pg/ml) or untreated (22.7 ± 17.5 pg/ml) MS patients than in HC (10.8 ± 6.9 pg/ml) (p 0.05 and 0.04 respectively), and were associated with the presence of recent clinical relapses or enhancing lesions at MRI (p 0.01). Natalizumab treated patients had Nfl levels similar to those of other MS patients (17.0 ± 10.4 pg/ml and 20.1 ± 13.4 pg/ml respectively). At the onset of PML, serum Nfl levels were highly increased (346.1 ± 95.9 pg/ml, $p < 0.001$), and they continued to grow till the onset of immune reconstitution inflammatory syndrome (710.5 ± 468.5).

Conclusions: If replicated in future studies, serum NfL may represent a reliable and easily accessible biomarker of early PML detection in natalizumab treated MS patients.