

CELLULAR IMMUNE RESPONSE TO POLYOMAVIRUS JCV IN PATIENTS WITH MULTIPLE SCLEROSIS TREATED WITH NATALIZUMAB

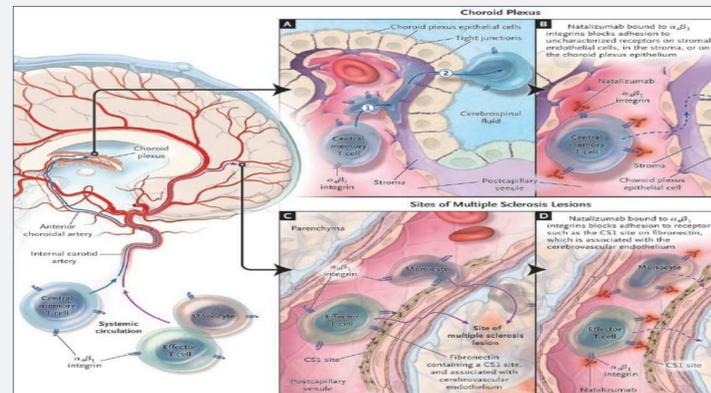


Di Nauta A., Sidoti F., Mantovani S., Piccighello A, Rittà M, *Cavalla P., *Masera S., Costa C., Cavallo R.

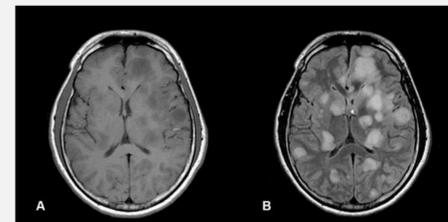
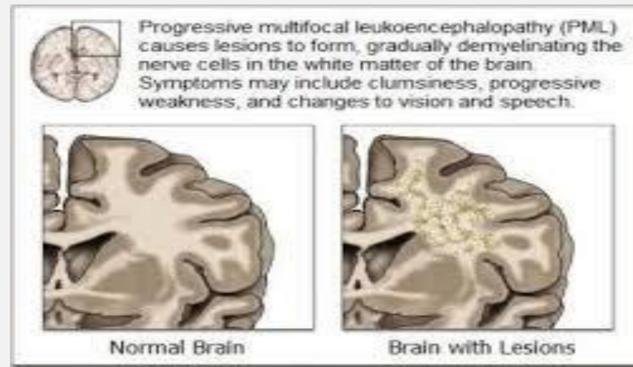
Microbiology and Virology Unit, Laboratory of Virology; *Multiple Sclerosis Center, Department of Neuroscience, University of Turin and Health and Science City of Turin Hospital, Via Santena 9 – 10126 Turin, Italy.

INTRODUCTION AND PURPOSE

In recent years, natalizumab, a selective monoclonal antibody that inhibits the migration of leukocytes into central nervous system, has been successfully used for the treatment of relapsing-remitting highly inflammatory multiple sclerosis (MS). However, its employment has been limited by the risk of reactivation of polyomavirus JCV in the central nervous system with development of progressive multifocal leukoencephalopathy (PML).



The pathogenic mechanisms of PML are poorly known; it is currently believed that cellular immune response can play a role in this context. Given the efficacy of natalizumab in this group of patients, the risk of viral reactivation and PML development should be carefully evaluated. Recently, an ELISA assay for the evaluation of antibody response to JCV has been developed. In this study, we evaluated the role of JCV-specific cellular immune response, the relation to humoral immune response and viral replication in a population of MS patients treated with natalizumab.

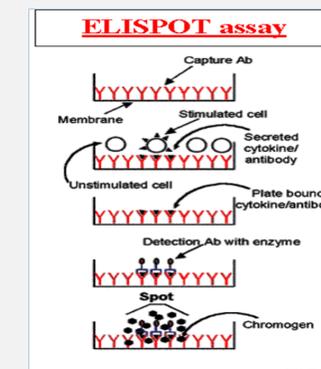


METHODS

All consecutive MS patients (33F/20M; mean age 29.1 years; mean duration of disease 121.2 months) treated with natalizumab for >1 month were included in the study. Viral reactivation was evaluated on serial serum specimens by quantification of JCV-DNA in real-time PCR; ELISpot assay was used to evaluate cellular immune response on concomitant whole blood specimens. JCV-specific humoral response was investigated in all the patients by ELISA, seronegative patients were re-tested after 1 year.

RESULTS

31/53 patients (58.5%) were JCV-seropositive. No difference was found between seronegative and seropositive patients in terms of demographic and clinical features (including duration of disease, type and duration of therapy before natalizumab administration). JCV-specific cellular immune response was evidenced in at least one time point in 70.9% of seropositive patients, although this response was never persistent. Moreover, the level of response (number of spot forming units/200000 peripheral blood mononuclear cells) was weak in most of the cases. All seronegative patients were non-responders (as expected), only two seronegative patients seroconverted at the subsequent serological evaluation at 1 year. No specimen resulted positive for JCV-DNA.



CONCLUSIONS

Natalizumab can impact of JCV-specific cellular immune response. In seropositive patients, although approximately 70% was responder in at least one case, virus-specific response was not persistent. Further studies are performed to understand the interplay between JCV and the host in this clinical context.

