P0133
Poster Session I
Basic science: pathogenesis

ROLE OF PMNS IN THE CONTROL OF MICROBIAL INFECTIONS IN MULTIPLE SCLEROSIS PATIENTS

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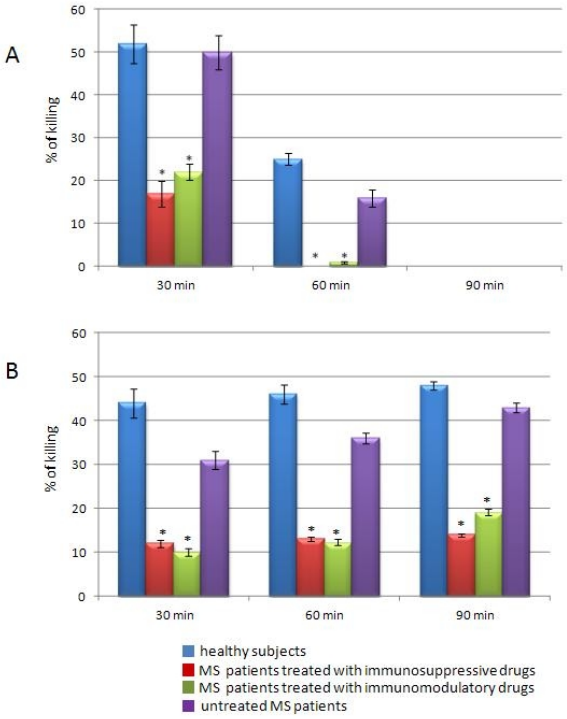
Figure 1. PMN intracellular killing activity (%) against *K. pneumoniae* (A) and *C. albicans* (B).



* $p<0.01$ significantly different from controls (HSs) and significantly different from untreated MS patients

Objectives. Recent literature data report that Multiple Sclerosis (MS) patients are at a noticeably raised risk of infections leading to hospital admission and infection-related mortality; immunotherapy may also influence this increasing risk. At present, data on the relationship among microbial factors, immunotherapies, and alterations of the innate immunity in MS patients are still lacking. In this interdisciplinary study, granted by ESCMID research grant 2012, neurologists, immunologists and microbiologists set the aims on the role of innate immune system in patients affected by MS in comparison with healthy subjects (HSs), used as controls.

Methods. The *in vitro* functional activity of polymorphonuclear cells (PMNs) harvested from 23 MS patients (with different disease duration, clinical classification and therapy) was compared with that of PMNs from 13 HSs against *Klebsiella pneumoniae,* as enteric Gram negative bacterium, and *Candida albicans*, as yeast, both pathogens responsible for frequent infections in MS patients. The PMN functional activity was determined by testing intracellular killing activity (by the evaluation of the survival index and the related killing percentage) and cytokine release profile (by ELISA). Statistical analysis was performed using the Graphpad Prism version 6.00 for Windows (Graphpad Software, San Diego, CA, USA) by one-way analysis of variance (ANOVA) followed by Tukey's multiple comparison test. P-values inferior to 0.01 were considered highly significant.

Results. Our findings provide a first evidence that even though in MS patients the number of PMNs is normal, their primary functions are significantly ($p<0.01$) altered: PMNs from MS patients displayed a reduced intracellular killing activity when compared to HSs within 90 minutes, in a way strongly related to the treatment but independent from MS status (Figure 1 A and B). Specifically, untreated MS PMNs showed a microbicidal activity similar to that observed for HS PMNs; on the contrary MS PMNs collected from MS patients treated, with either immunosuppressive or immunomodulatory drugs, displayed a significantly reduced intracellular killing activity if compared with HS PMNs and with untreated MS patients PMNs. In addition, during the incubation time, a gradual increased level of pro-inflammatory cytokines (IL-8, TNF-alpha and IL-1beta) was detected, even if statistically significant differences were not observed between MS patients and HSs.

Conclusions. The PMN functional impairment detected in MS patients could represent the cause of microbial infections; however the reduced PMN intracellular killing seems not dependent to the cytokine release pattern and could be related to other factors (respiratory burst, phagocytosis or apoptosis, etc). The validation of these results could help in identifying a subset of MS patients at high infection risk who could benefit from a closer follow-up or antibiotic prophylaxis.