O151
2-hour Oral Session
Emerging viruses: what about "Tick", "Chik" and "Zik"?

The increased expression of macrophage migration inhibitory factor in tick-borne encephalitis

Sambor S. Grygorczuk*[1], Anna Moniuszko[1], Renata Swierzbinska[1], Piotr Czupryna[1], Maciej Kondrusik[2], Slawomir Pancewicz[1]

[1]*Medical University of Bialystok, Department of Infectious Diseases and Neuroinfections, Bialystok, Poland*

[2]*Medical University in Białystok, Department of Infectious Diseases and Neuroinfections, Białystok, Poland*

Background: The host factors responsible for the variability of the clinical presentation of tick-borne encephalitis (TBE) are poorly known. The excessive inflammatory/immune response to TBE virus might have detrimental effect by 1) disruption of the blood/cerebrospinal fluid barrier facilitating virus entry into central nervous system (cns) and 2) cns tissue damage by a local inflammation/ immune response. Macrophage migration inhibitory factor (MIF) is a cytokine crucial for the initiation of the innate immune response, probably contributing to the immune-mediated pathology in bacterial meningitis and in infections with flaviviruses related to TBE virus, including West Nile virus. Tumor necrosis factor-□ (TNF□) is a pro-inflammatory cytokine induced by MIF, hypothesized to increase the blood/csf barrier permeability in West Nile encephalitis.

Material/methods: We have studied blood and cerebrospinal fluid (csf) samples obtained on admission to hospital from 36 patients with TBE virus infection (meningitis in 13, encephalomeningitis in 21, meningoencephalomyelitis in 2) and 7 patients with aseptic non-TBE meningitis. Control serum came from 6 healthy donors and control csf from 6 patients without cns infection. Concentrations of MIF and three major pro-inflammatory cytokines located downstream of MIF in the inflammatory cascade: TNF□, interleukin-1□ (IL-1□) and chemokine CXCL8 (IL-8) were measured in all samples with commercial ELISA kits. The csf pleocytosis, protein and albumin concentration were measured with standard techniques. The data were analyzed with non-parametric tests and $p < 0.05$ was considered significant.

Results: In TBE patients the median concentrations of cytokines were increased: MIF in serum and to a significantly lower level in csf, IL-1□ both in serum and csf while IL-8 in csf only. The concentration of TNF□ was not increased significantly. Serum IL-1□ concentration tended to be lower in patients with meningoencephalitis versus uncomplicated meningitis and in patients with altered mental status. Csf MIF correlated with csf albumin concentration and csf IL-1□ with csf neutrophil count. In non-TBEV meningitis the pattern of cytokine expression was similar, but some aspects of the response were more vivid: TNF□ in serum and csf was significantly upregulated and IL-8 intrathecal expression was significantly higher than in TBE group.

Conclusions: Expression of MIF and pro-inflammatory cytokines induced by MIF is upregulated in TBE. However, the response is moderate in comparison with non-TBE aseptic meningitis and does not increase with a clinical severity. The higher intrathecal expression of MIF is related to the increased permeability of blood/csf barrier, but without evident clinical consequences, while IL-1□ expression is related to csf pleocytosis and to milder clinical presentation, suggesting a protective effect. IL-8 is expressed intrathecally where it may contribute to leukocyte influx into csf. Overall, the observed

pattern of MIF, TNF□, IL-1□ and IL-8 expression does not reveal an immune-mediated pathology in human TBE virus infection.