Viral meningitis post-infectious cognitive dysfunction and associated neuropathology

Jesper Damsgaard¹, Henning Andersen², Simon Hjerrild³, Edvard Marinovskij⁴, Michael Christiansen⁵, Susanna Deutch⁶, Britta Tarp⁷, Lars Nielsen⁸, Alex Laursen¹, Katrine Schou¹, Lars Oestergaard¹, Peter Derek Christian Leutscher¹

¹ Department of Infectious Diseases, Aarhus University Hospital, Skejby, Denmark. ² Department of Neurology, Aarhus University Hospital, Aarhus NBG, Denmark. ³ Centre for Psychiatric Research, Aarhus University Hospital, Risskov, Denmark. ⁴ Department of Diagnostic Imaging, Aarhus University Hospital, Skejby, Denmark. ⁵ Department of Clinical Biochemistry and Immunology, the State Serum Institute, Copenhagen, Denmark. ⁶ Department of Internal Medicine, The Regional Hospital of Randers, Denmark. ⁷ Department of Internal Medicine/Infectious Diseases, The Region Hospital of Silkeborg, Denmark. ⁸ Department of Virology, the State Serum Institute, Copenhagen, Denmark.

Objective

Our aim was to examine cognitive dysfunction and associated clinical, neuroradiologcal and biochemical markers in adult patients with viral meningitis.

Background

Viral meningitis is a common infection in the central nervous system (CNS). Generally, the disease is considered self-limiting with a mild clinical course. However, recent studies have indicated that patients with viral meningitis may develop persisting cognitive impairment such as short-term memory loss and attention deficits⁽¹⁻²⁾. Patients with CNS infections are commonly hospitalized in a department of general internal medicine where therapy is primarily focused on the initial acute phase of the disease aiming at normalisation of infection parameters. Cognitive dysfunction may thus be overlooked.

Magnetic Resonance Imaging (MRI) using Diffusion Weighted Imaging (DWI) has provided more detailed and accurate imaging than standard sequences⁽³⁻⁵⁾. MRI spectroscopy indicates that variations in the concentrations of different substances can be used as surrogate markers for cerebral damage (gliosis and neuroinflammation)^(3-5,6). Brain-specific proteins in cerebrospinal fluid (CSF) for instance protein S-100B, glial fibrillary acidic protein (GFAP), myelin basic protein (MBP), neuron-specific enolase (NSE) and neopterin⁽⁷⁻⁸⁾ can be used as biomarkers of neuronal injury in meningitis. Similarly, serum cytokines can be used to monitor the inflammatory process.

Study Design: A prospective follow-up study. Lumbar puncture was used as an obligatory diagnostic test. Cognitive tests were carried out in order to study the cognitive function of the patients over time and to make a systematic assessment of depression using the Major Depression Inventory (MDI) and the Health-related Quality of Life (HQOL) SF-36 questionaires. The computerized cognitive testing system, CogState, was used five times from disease onset until follow-up (at three months). MRI was performed within 72 hours of admission. The CSF was tested for etiology, level of brain-specific proteins and detection of intrathecal antibody synthesis (IgG, intrathecal synthesis). Serum was analysed for level of cytokines (multiple xMAP lunimex), distribution of apo- ε 4 allel (risk factor for Alzheimer's disease and cardiovascular diseases) and detection of matched intrathecal IgG antibody synthesis (figure 1).

Figure 1: Examinations program of the patients at admission and follow-up



Hypotheses

 Viral meningitis, properly named viral meningo-encephalitis, results not only in meningeal irritation, but also in parenchymal lesions leading to adverse cognitive dysfunction.

 The degree of post-infectious cognitive dysfunction correlates with abnormalities visualised by MRI (particular DWI and spectroscopy) and changes in concentrations of brain-specific proteins in CSV and cytokines in serum.

Methods

Participants: A total of 35 patients with possible viral meningitis based on clinical evaluation. More over, 20 patients suffering from bacterial meningitis were included allowing comparison of parameters. Patients admitted to Aarhus University Hospital (Dept. of Infectious Diseases and Dept. of Neurology) as well as the Regional Hospitals of Randers and Silkeborg (Dept. of Internal Medicine) during a period of six months and fulfilling the inclusion and exclusion criteria were invited to participate in the study.



Results and perspective

Results are pending. We hope that the study will provide new insight into the prevalence and extent of neuropsychological adverse manifestations and associated prognostic indicators in patients with viral meningitis.

References

¹Schmidt H. et al. "Neuropshychological sequelae of bacterial and viral meningitis". Brain 2006;129:333-345. ²Sittinger H. et al. "Mild cognitive impairment after viral meningitis in adults". J Neurol 2002;249:554-560. ³Bulakbasi N. et al. "Central Nervous System Infections of Herpesvirus Family". Neuroimag Clin N Am 2008;18:53-84. ⁴Kastrup O. et al. "Neuroimaging of Infections of the Central Nervous System". Semin Neurol 2008;28:511-522. ⁵Gupta KR. et al. "Imaging of Nonspecific (Nonherpetis) Acute Viral Infections". Neuroimag Clin N Am 2008;18:41-52. ⁶Foerster BR. "Intracranial Infections: Clinical and Imaging Characteristics". Acta Radiologica 2007;8:875-893. ⁷Spinella PC. Et al. "Cereborspinal fluid levels of S-100B in children and its elevation in pediatric meningitis". Pediatr Crit Care 2004;5:53-57.

⁸Lamers KJB. Et al. "Protein S-100B, NSE, MBP and GFAP in CSF and blood of neurological patients". Brain Res Bulletin 2003;61:261-264.

Correspondence

Jesper Damsgaard, Research Year Student and Medical Student Dept. of Infectious Diseases, Research Unit Aarhus University Hospital, Skejby Brendstrupgaardsvej 100, 8200 Aarhus N, Denmark Phone: +45 3025 7499, e-mail: jesper.damsgaard@studmed.au.dk

Acknowledgements

Funded by The Danish Council for Independent Research | Medical Sciences (FSS).

