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Cerebrospinal Fluid Cytokine and Chemokine Patterns in Central Nervous System Infections, Hemorrhage and Neoplasms

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ABSTRACT

Cytokines and chemokines are soluble proteins that act as regulators of cellular functions throughout the body. Cytokines and chemokines released in the setting of various CNS disorders appear in the CSF compartment where detection of levels they can provide insight into pathogenic processes such as neuroinflammation. We utilized the Multiplex Cytokine Kit from MillipLEX MAP to perform multiplex analysis of CSF samples from patients with various CNS disease processes. Cytokine/chemokine profiles were different in various CNS disease processes. CSF fluids from patients with meningitis were divided into five groups: bacterial, viral, tuberculosis, Neuroborreliosis, and pseudomeningocele (PC). Cytokine/chemokine profiles were associated with different etiologies of meningitis and may suggest a component of the inflammatory cascade. Cytokine/chemokine profiles may be useful in determining the nature of a pro-inflammatory case of unknown etiology?

INTRODUCTION

Because of its relationship to the critical structures of the central nervous system (CNS), the cerebrospinal fluid (CSF) compartment reflects the current state of the CNS, especially in neurological diseases. When pathogens invade the CNS, the inflammatory cascade hinges upon the expression of pro- and anti-inflammatory chemokines and cytokines, which become detectable in the CSF. Because various bacterial and viral pathogens utilize various mechanisms to elicit host response, the patterns of chemokines and cytokines released during these various infections are different. A variety of cells including microglia/macrophages play a role in initiating, coordinating, and regulating the innate response to infectious agents and other stimuli via expression of a variety of chemokines/ cytokines.

METHODS

We utilized the Milliplex HCYTOMAG Biotin assay/system to perform multiplex Elisa profiling of 42 different cytokines in the CSF of patients with a variety of CNS disease processes. We measured levels of pro-inflammatory, anti-inflammatory, or similar to control cytokines in the CSF of patients with a variety of CNS disease processes along with control (non-infectious, non-tumor, non-hemorrhagic) samples. We focused on the clinical cases with one, single disease process present. The cases reported include Lyme neuroborreliosis (Lyme), 13 year old male neuroborreliosis tuberculosis meningitis (TB) in an immunosuppressed patient on adalimumab therapy, Streptococcus milleri meningitis (SMM) in a 73 year old man following repair of a left subclavian pseudoaneurysm, West Nile Virus encephalitis (WNV) in 35 year old female, and subarachnoid hemorrhage (SAH) secondary to rupture of cerebral aneurysm and three controls that were negative for infectious organisms in non-CNS, non-neurological disease processes.

RESULTS

Chemokine/lymphotoxin levels (pg/ml) in a variety of disease processes are presented in the table.

CONCLUSIONS

1) Cytokine/chemokine profiles are different in various CNS disease processes. 2) Cytokine/chemokine profiles may be useful in determining the nature of the inflammatory process, especially in the setting of inconclusive microbiological tests. 3) In the context of a pro-inflammatory state, very low levels of MDC/CCL2 may suggest a distinct pro-inflammatory response, possibly related to deficient anti-inflammatory mechanisms. 4) With further studies, CSF cytokine/chemokine profiles will provide more information, including predictions regarding clinical course and disease outcome.