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Multiple cytokines are involved in the early events leading to the Alzheimer's disease pathology

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Abstract

It is likely that neuroinflammation begins well before detectable cognitive impairment in Alzheimer's disease (AD) occurs. Clarifying the alterations occurring prior to the clinical manifestation of overt AD dementia may provide valuable insight into the early diagnosis and management of AD. Herein, to address the issue that neuroinflammation precedes development of AD pathology, we analyzed cytokine expression profiles of the brain, with focus on non-demented control patients with increasing AD pathology, referred to as high pathology control (HPC) cases, who provide an intermediate subset between AD and normal control cases referred to as low pathology control (LPC) cases. With a semi-quantitative analysis of cytokine mRNA, among 15 cytokines and their related molecules tested, we found the involvement of eight: interleukin-1(IL-1) receptor antagonist (IL-1ra), IL-1 converting enzyme (ICE), IL-2, IL-6, IL-8, tumor necrosis factor (TNF) α, macrophage-colony stimulating factor (M-CSF) and transforming growth factor (TGF) β1 during the development from LPC to HPC, while decreases in IL-1ra, IL-8, MCP-1 and TNFα, and an increase in TACE were implicated in the later development from HPC to AD. These findings indicate that neuroinflammation precedes the clinical manifestation of overt dementia, rather than being involved at the later stages of AD. *Tottori J. Clin. Res.* 1(2), 359-373, 2008

Key words: neuroinflammation, cytokines, Alzheimer's disease (AD), RT-PCR, AD pathology

Introduction

Determination of the biological and molecular alterations occurring prior to the clinical manifestation of overt AD dementia may provide valuable insight into the early diagnosis and management of AD[1)]. Recent gene ontology analyses have reveled that the significant group of differentially expressed genes between control and AD brains partly relate to genes involved in inflammation and immunological signaling, suggesting the involvement of immune cells and various inflammatory mediators in AD pathological process[1, 2)]. So our major focus was placed on clarifying the role of inflammation in AD pathogenesis, particularly prior to the manifestation of overt dementia. In fact, there have been increasing reports demonstrating