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Brain & Development 28 (2006) 19–23

BRAIN & DEVELOPMENT
Official Journal of the Japanese Society of Child Neurology

www.elsevier.com/locate/braindev

Original article

Cerebrospinal fluid interleukin-6 levels in patients with west syndrome

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Received 13 January 2004; received in revised form 25 November 2004; accepted 23 March 2005

Abstract

Elevated cytokine response has been reported in patients with epileptic seizures. The objective of this study was to investigate the possible role of interleukin-6 (IL-6) in the pathogenesis of infantile spasms in West syndrome (WS). We measured IL-6 levels in cerebrospinal fluid (CSF) obtained from the newly diagnosed patients with WS. Twelve patients with WS (Group I) were classified as symptomatic WS (Group IA) in eight and as cryptogenic WS (Group IB) in four. The results were compared with control groups including patients with tonic–clonic seizures associated with two different kind of inflammation of central nervous system; Group IIA (infection): bacterial meningitis/encephalitis and Group IIB (trauma): post-traumatic seizures. There was no statistically significant difference between the mean values of CSF IL-6 levels in patients with WS (2.95 ± 2.31 pg/ml) and those of subgroups of WS (Group IA: 2.26 ± 2.01 pg/ml and Group IB: 4.33 ± 2.52 pg/ml). Both control groups had highly increased IL-6 levels in CSF (Group IIA: 193.05 ± 185.52 pg/ml and Group IIB: 112.74 ± 167.44 pg/ml) than those of the patients with WS. Elevated IL-6 response in patients with tonic–clonic seizures associated with inflammation of central nervous system might be due to the seizures themselves or related to the underling etiology (infection or trauma). However, no elevated IL-6 response was found in patients with infantile spasms.

Keywords: West syndrome; Infantile spasm; Interleukin-6; Cytokines

1. Introduction

West syndrome (WS) is an age-related specific epileptic syndrome of infancy characterized by the combination of clusters of epileptic spasms and a peculiar interictal EEG patterns of hypsarrhythmia. The pathophysiology of infantile spasms in this specific epilepsy syndrome still remains unknown [1].

Cytokines are a heterogeneous group of polypeptide mediators associated classically with activation of the immune system and inflammatory responses. A growing amount of experimental and clinical evidence suggests that certain cytokines are involved in epilepsy as disease-modifying molecules [2]. Interleukin 1-beta (IL-1β) prolongs the duration of kainic acid-induced seizures and seems to promote neuronal damage, whereas its effects are blocked by IL-1 receptor antagonist. Elevated concentrations of IL-6 in cerebrospinal fluid (CSF) and plasma have been reported in patients after tonic–clonic seizures [3,4]. It is reported that increased IL-6 production might be a consequence of neuronal electrical activity associated with seizures and may reflect neuronal injury. Neuron specific enolase (NSE) is a brain-specific protein that may serve as a marker for neuronal injury in various neurologic disorders [5,6]. NSE levels in CSF were found to increase following status epilepticus and various types of seizures in adult and pediatric population [7–11].

In this study we have hypothesized that an elevated IL-6 response is associated with the inflammatory pathogenesis of infantile spasms in patients with WS. In addition, we examined simultaneously IL-6 and NSE levels in CSF to evaluate the magnitude of neuronal injury in children with WS.

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doi:10.1016/j.braindev.2005.03.007

2. Patients and methods

2.1. Patients

From January 1998 to May 2000, 12 patients with West syndrome were consecutively included in the study (Group I). Age at the onset of seizures was between 1 and 48 months (mean; 10.7 months). Eight patients were classified as symptomatic WS (Group IA) and four were as cryptogenic WS (Group IB) according to the previously described criteria [11]. All were well-documented patients with a characteristic triad of WS: typical epileptic spasms, mental deterioration, and EEG changes (hypsarrhythmia or modified hypsarrhythmia). In EEG recording, seven infants had hypsarrhthmia and five infants had modified hypsarrhythmia. The infantile spasms were classified as flexor in six infants, extensor in two infants and mixed type in four infants. Prior to the medical treatment of infantile spasms, CSF was obtained within 1–6 h of post-cluster period of seizures for IL-6 and NSE analysis.

2.2. Controls

A healthy control group was not conducted because of ethical problems of obtaining CSF from these children. Two disease control groups were designed with tonic–clonic seizures associated with two different kinds of inflammation of central nervous system: Group IIA (infection); 12 patients with bacterial meningitis/encephalitis and Group IIB (trauma); five patients with post-traumatic seizures. All patients in both groups of controls had generalized or partial tonic–clonic seizures. Controls were randomly selected from a population of an ongoing research including the patients with CNS inflammation. CSF samples were obtained within 1–6 h of post-convulsive period. Informed consents were obtained from parents. CSF samples contaminated with blood were not included in the analysis.

2.3. Interleukin-6

IL-6 was determined using a highly sensitive and specific enzyme-linked immunosorbent assay (Biotrak-Amersham, cellular communication assay, interleukin-6 human, ELISA system code RPN 2754, UK). The minimum detectable concentration for IL-6 was 0.1 pg/ml. The assay had no cross reactivity with the other cytokines. Inter- or intra-assay variabilities were less than 10%.

2.4. Neuron specific enolase

NSE was measured using an enzyme-immunological test for the quantitative determination of NSE (Enzyme-Test NSE) introduced by Boehringer Mannheim Immunodiagnostics. The method measures concentrations in the range 0–150 μg/L. The lower detection limit is 0.5 μg/L.

2.5. Statistics

Spearman's rank correlation coefficient was used for assessing the correlation between CSF IL-6 and NSE levels. The Mann–Whitney *U* test was used to compare CSF IL-6 and NSE levels among the groups.

Table 1
Demographic features of the patients with West syndrome (WS)

Pt.no Gender	Age onset (month)	Spasms	Developmental history	MRI	Etiology	EEG
Symptomatic WS						
1.M	4	E	Delayed	Fronto-temporal atrophy	HIE	H
2.M	10	F	Delayed	Cortical atrophy	HIE	H
3.M	3	F	Delayed	Right hemispheric atrophy	ICH	MH
4.M	6	F	Delayed	Cerebral atrophy	ICH	MH
5.M	24	F, E	Delayed	Cortical atrophy	HIE	H
6.F	3	E	Delayed	Cerebral atrophy	Leigh syndrome	H
7.M	4	F	Delayed	Fronto-temporal atrophy, PVL	HIE	MH
8.M	8	F	Delayed	Diffuse periventricular hyperintensity	Metachromatic leukodystrophy	H
Cryptogenic WS						
9.M	48	F	Normal	Normal	–	MH
10.M	21	F, E	Normal	Normal	–	MH
11.M	6	F	Normal	Normal	–	H
12.F	16	F	Normal	Normal	–	H

HIE, hypoxic ischemic encephalopathy; ICH, intracranial hemorrhage; PVL, periventricular leucomalasia; F, flexor; E, extensor, H, hypsarrhythmia; MH, modified hypsarrhythmia.