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Original article

Laboratory characteristics of acute encephalopathy with multiple organ dysfunctions

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Abstract

To clarify the laboratory characteristics and deduce the pathogenesis of acute encephalopathy associated with multiple organ dysfunctions in Japan. We measured cytokine levels [tumor necrosis factor alpha (TNF-α), soluble tumor necrosis factor-receptor 1 (sTNF-R1), and interleukin-6 (IL-6)] in serum and cerebrospinal fluid (CSF) as well as general laboratory examinations in 27 patients with acute encephalopathy. Urea nitrogen (UN), creatinine (Cr), aspartate aminotransferase (AST), lactic dehydrogenase (LDH), and C-reactive protein (CRP) levels in blood, and CSF protein levels at the initial stage were significantly higher in patients with an unfavorable outcome. TNF-α, sTNF-R1, and IL-6 levels at the initial stage were higher in the serum than in the CSF of patients with acute encephalopathy. Serum cytokine levels correlated well with patient outcome. The high CSF protein level and the high UN, Cr, AST, LDH, and CRP levels in the blood represent the severity of vascular leakage through the blood–brain barrier and multiple organ dysfunctions, respectively, and thus suggest an unfavorable prognosis. The high serum inflammatory cytokine levels at the initial stage and the good correlation of those levels with the outcome suggest that intravascular inflammation has a significant role in vascular leakage and multiple organ dysfunctions in acute encephalopathy.

Keywords: Acute encephalopathy; Multiple organ dysfunctions; Cytokines

1. Introduction

Central nervous system (CNS) manifestations follow various viral infections in children. Reye's syndrome is a well-known CNS complication associated with viral infections such as influenza and varicella. Recent investigations [1,2] demonstrated that the primary cause is mitochondrial permeability transition causing hepatocellular dysfunction, which, in turn, induces hypoglycemia and hyperammonemia. Recently, the high incidence and mortality of acute encephalopathy with multiple organ failure has become a serious health problem in Japan [3,4]. This type of encephalopathy is often associated with influenza and occasionally with other viral infections, and is usually combined with liver, renal, coagulative, and hematopoietic dysfunctions, but rarely with hypoglycemia and hyperammonemia. Therefore, this illness seems to be distinct from Reye's syndrome, although pathologic examination is needed to deny Reye's syndrome. Serum and CSF concentrations of several proinflammatory cytokines and cytokine receptor, such as interleukin (IL)-6, IL-1β, and soluble tumor necrosis factor-receptor 1 (sTNF-R1), are elevated in influenza-associated encephalopathy [5–7]. This suggests inflammation in blood vessels and/or in central nervous system (CNS) may contribute to the progression of the illness. The pathogenesis of the encephalitis, however, remains unclear. The laboratory characteristics of acute encephalopathy with multiple organ dysfunctions have not been fully described. And, the laboratory predictors of outcome at an initial stage might provide a clue to the pathogenesis of acute encephalopathy. We measured cytokine concentrations in serum and cerebrospinal fluid (CSF) samples collected simultaneously at the initial stage,

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Table 1
Summary of 27 patients with acute encephalopathy

Group	Outcome	Gender	Age	Onset	CT firdings	Pathogen	Method for identification	Organ dysfunction			
								Liver	Renal	Coagulative	Hematopoietic
A-1	Dead	F	1Y11M	97.03.03	Whole CE	Unknown		+	+	+	+
	Dead	M	4Y9M	98.02.23	Whole CE	Influenza AH3	Isolation	+	+	+	+
	Dead	M	0Y9M	99.01.31	Whole CE	Adenovirus 3	Isolation	+	+	NT	−
	Dead	M	8Y0M	99.02.05	Whole CE	Influenza AH3	Isolation	+	+	NT	+
	Dead	M	3Y5M	01.03.20	Whole CE	Influenza AH3	Isolation	+	+	+	+
	Dead	M	2Y1M	01.07.03	Whole CE+brain stem LD	Unknown		+	+	+	+
	Dead	F	7Y5M	01.11.12	Whole CE	Unknown		+	+	−	−
	Dead	F	7Y5M	01.12.31	Whole CE	Unknown		+	+	+	+
	Dead	F	3Y4M	02.01.05	Whole CE	Unknown		+	+	+	+
	Dead	F	7Y0M	02.02.19	Whole CE+brain stem LD	Influenza AH3	Isolation	+	+	+	+
	Dead	M	3Y10M	02.03.03	Whole CE	Influenza A	Antigen detection	+	−	−	+
A-2	Alive with severe sequela	F	2Y10M	97.05.10	Whole CE+bilateral talami LD	Influenza B	Isolation	+	−	−	−
	Alive with severe sequela	M	0Y11M	97.05.15	Left CE	HHV-6	Serology	+	−	−	−
	Alive with severe sequela	M	0Y7M	98.11.15	Whole CE	Unknown		+	−	+	−
	Alive with severe sequela	F	0Y9M	99.04.14	Right CE	HHV-6	Serology	+	−	+	−
	Alive with severe sequela	M	3Y10M	02.03.03	Whole CE	Influenza A	Antigen detection	+	−	+	+
A-3	Alive with mild sequela	F	5Y4M	98.03.02	Whole CE(sl)+ bilateral talami LD	Unknown		+	−	+	+
	Alive with mild sequela	M	0Y9M	98.04.28	Whole CE(sl)	Rotavirus	Antigen detection	+	−	−	+
	Alive without sequela	M	1Y3M	99.07.03	Bilateral talami LD	Unknown		+	−	−	+
	Alive without sequela	M	0Y11M	00.03.03	Right CE	Influenza AH3	Isolation	+	−	−	−
	Alive without sequela	F	0Y11M	00.06.08	Whole CE(sl)	Unknown		+	−	NT	+
	Alive without sequela	F	4Y0M	01.10.02	Whole CE(sl)	Unknown		−	−	−	−
	Alive without sequela	F	2Y4M	02.01.24	Whole CE(sl)	Influenza A	Antigen detection	−	−	−	−
	Alive without sequela	F	3Y3M	02.02.21	Whole CE(sl)	Influenza A	Antigen detection	−	−	NT	+
	Alive without sequela	M	9Y11M	02.02.27	Bilateral parietal CE	Unknown		−	−	−	−
	Alive without sequela	F	1Y2M	02.03.05	Whole CE(sl)	Influenza A	Antigen detection	−	−	−	−
	Alive with mild sequela	F	1Y11M	0.2.03.10	Right CE	Influenza AH3	Isolation	+	−	−	−

CE, cerebral edema; LD, low density; sl, slight; NT, not tested.