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CASE REPORT

Systemic inflammatory response syndrome and prolonged hypoperfusion lesions in an infant with respiratory syncytial virus encephalopathy

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Abstract Respiratory syncytial virus (RSV) is a cause of neurological complications in infants. We report a rare case of RSV encephalopathy in an infant who presented with poor sucking and hypothermia at 17 days of age after suffering from rhinorrhea and a cough for several days. After hospitalization, the patient presented with stupor and hypotonia lasting for at least 24 h, and was intubated, sedated, and ventilated for treatment of pneumonia. These symptoms led to diagnosis of pediatric systemic inflammatory response syndrome (SIRS) caused by RSV infection. High-dose steroid therapy was combined with artificial ventilation because the initial ventilation therapy was ineffective. Interleukin (IL)-6 levels in spinal fluid were markedly increased upon admission, and serum IL-6 and IL-8 levels showed even greater elevation. The patient was diagnosed with RSV encephalopathy. On day 5, high signal intensity in the bilateral hippocampus was observed on diffusion-weighted magnetic resonance imaging (MRI). On day 14, the patient presented with delayed partial seizure and an electroencephalogram showed occasional unilateral spikes in the parietal area, but the hippocampal abnormality had improved to normal on MRI. ^{99m}Tc-labeled ethylcysteinate dimer single-photon emission computed tomography (SPECT) on day 18 showed hypoperfusion of the bilateral frontal and parietal regions and the unilateral temporal region. SPECT at 3 months after onset still showed hypoperfusion of the bilateral frontal region and unilateral temporal region, but hypoperfusion of the bilateral parietal region had improved. The patient has no neurological deficit at 6 months. These findings suggest that RSV encephalopathy with cytokine storm induces several symptoms and complications, including SIRS and prolonged brain hypoperfusion on SPECT.

Keywords Respiratory syncytial virus · Encephalopathy · Cytokine · Infant · Single-photon emission computed tomography

Introduction

Infection with respiratory syncytial virus (RSV) causes bronchitis, bronchiolitis, and pneumonia, and leads to neurological complications in 1.8 % of cases [1]. These neurological complications include RSV encephalopathy [2, 3], the cause of which remains unclear. Kawashima et al. [4] defined three pathogenic types of RSV encephalopathy characterized by metabolic error, excitotoxicity, and cytokine storm. Here, we describe a rare case of a neonate with RSV encephalopathy of the cytokine storm type, which involved development of pediatric systemic inflammatory response syndrome (SIRS) and prolonged hypoperfusion lesions on brain single-photon emission computed tomography (SPECT) without neurological sequelae.

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Case report

The patient was a male infant born at 39 weeks gestation (birth weight, 3,562 g). At this time, his brother and cousin both had a cold, and the patient presented with rhinorrhea and cough after several days. At 17 days of age, his parents brought him to the emergency department because of poor sucking for more than half a day and hypothermia (33.0 °C). The patient was in a continuous stupor with hypotonia and did not respond to pain. He presented with cyanosis, and percutaneous oxygen saturation was 86 %. The desaturation was reversed by oxygenation. After hospitalization, a physical examination showed wheezes and hepatomegaly. Respiratory therapy with nasal continuous positive airway pressure was started, but apnea persisted.

Laboratory findings upon admission showed increased aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactase dehydrogenase (LDH), creatine phosphokinase (CPK), and carbon dioxide ($PaCO_2$) (Table 1). AST, ALT, LDH, and CPK levels in serum increased progressively until day 2. RSV antigen was detected in a nasopharyngeal swab. The results of several cultures were negative. Chest radiography and computed tomography scans showed bilateral pulmonary infiltrative shadow, atelectasis, and severe air trapping. A diagnosis of pediatric SIRS caused by RSV infection was made based on the published criteria for this condition [5].

The patient was intubated and ventilated immediately. Profound sedation was used because high-pressure mechanical ventilation was required. Immunomodulatory therapy with high-dose steroids (methylprednisolone 30 mg/kg/day for 3 days) was also initiated because the respiratory therapies were ineffective. On day 5, there were no significant abnormalities on T_1-weighted, T_2-weighted, and fluid-attenuated inversion recovery magnetic resonance imaging (MRI), but the bilateral hippocampus showed a high signal intensity in diffusion-weighted imaging (DWI) MRI with reduction of the apparent diffusion coefficient (ADC) (Fig. 1 a, b). An electroencephalogram (EEG) was normal on day 5. The patient was extubated on day 7.

On day 14, the hippocampal abnormality and ADC were improved on DWI MRI. However, on the same day, the

Table 1 Laboratory data at admission

Peripheral blood		Arterial blood gas analysis (FiO_2 0.30–0.45)	
WBC	20,200/μl	pH	7.228
Nt	31 %	$PaCO_2$	69.4 Torr
Ly	47 %	PaO_2	72.7 Torr
Mo	10 %	HCO_3^-	27.9 mmol/l
Eo	2 %	BE	−0.1 mEq/l
Ba	0 %	Serology	
RBC	305×10^4/μl	CRP	3.87 mg/dl
Hb	10.1 g/dl	Procalcitonin	0.77 ng/ml
Ht	32.4 %	IgG	853 mg/dl
Plt	52.7×10^4/μl	IgM	32 mg/dl
Biochemistry		IgA	5 mg/dl
TP	6.7 g/dl	Ferritin	8163 ng/ml
Alb	4.1 g/dl	IL-6 (<4 pg/ml)[a]	304 pg/ml
AST	192 U/l	Serology during hospitalization	
ALT	160 U/l	IL-1β (<10 pg/ml)[a]	<200 pg/ml
T-bil	1.3 mg/dl	IL-8 (<2 pg/ml)[a]	115 pg/ml
LDH	1359 U/l	IL-10 (<5 pg/ml)[a]	<20 pg/ml
CK	439 U/l	MCP-1 (200–722 pg/ml)[a]	<625 pg/ml
BUN	12 mg/dl	TNF-α (0.6–2.8 pg/ml)[a]	<5 pg/ml
Cre	0.24 mg/dl	Cerebral spinal fluid	
Na	122 mEq/l	IL-6 (<0.4 pg/ml)[a]	102 pg/ml
K	5.8 mEq/l	Viral culture	(–)
Cl	89 mEq/l	Protein	88 mg/dl
Glucose	55 g/dl	Cell count	2/μl
Culture		–	–
Blood	(–)	–	–
Spinal fluid	(–)	–	–
Nasal	*Haemophilus influenzae*	–	–

[a] Normal value or range. IL-6 was measured using Human IL-6 CLEIA (Fujirebio, Japan). IL-1β, IL-8, and IL-10 were measured using BIOSOURCE IL-1β, IL-8, and IL-10 ELISA kits (BioSource Europe, Nivelles, Belgium). MCP-1 and TNF-α were measured using Human MCP-1 and TNF-α Immunoassay kits (R&D Systems, Minneapolis, MN, USA)