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Original article

Delirious behavior in influenza is associated with a reversible splenial lesion ☆

Jun-ichi Takanashi [a,*], Hiroko Tada [a,b], Haruo Kuroki [c], A. James Barkovich [d]

[a] *Department of Pediatrics, Kameda Medical Center, Kamogawa, 929 Higashi-cho, Kamogawa-shi, Chiba 296-8602, Japan*
[b] *Segawa Neurological Clinic for Children, Tokyo, Japan*
[c] *Sotobo Children's Clinic, Isumi, Japan*
[d] *Department of Radiology, University of California San Francisco, CA, USA*

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Abstract

Delirious behavior is one of the main clinical features in patients with clinically mild encephalitis/encephalopathy with a reversible splenial lesion. On the other hand, it has been reported that more than 10% of patients with influenza in Japan develop delirious behavior. Magnetic resonance imaging (MRI) studies in patients with influenza-associated delirious behavior were examined to determine how often a reversible splenial lesion is associated with this symptom. All patients who presented to Kameda Medical Center between November 2007 and March 2008 with delirious behavior associated with influenza were studied using MRI and EEG. Of the 370 patients with influenza, 11 had delirious behavior, lasting for less than 12 h. MRI revealed a reversible splenial lesion with homogenously reduced diffusion in 5 patients. Transient EEG abnormalities (occipital slow waves during wakefulness) were observed in 4 of the 9 patients examined. A reversible splenial lesion with reduced diffusion should be considered as an underlying condition in patients with delirious behavior associated with influenza.

Keywords: Influenza; Delirium; Encephalopathy; Splenium; Diffusion; Reversible

1. Introduction

Infection or fever is known to be a common cause of delirious behavior among children. It has been reported that more than 10% of patients with influenza (299/2846) in Japan develop delirious behavior during the course of illness [1,2]. Simple febrile delirium is usually reversible and benign; however, delirious behavior associated with influenza recently attracted attention when several pediatric patients jumped from significant heights and were injured or died [3].

A magnetic resonance imaging (MRI) of a reversible splenial lesion with transient reduced diffusion has been reported in patients with epilepsy taking antiepileptic drugs, most often when reducing them rapidly [4], and those with high altitude cerebral edema [5]. The MR finding is unusual but has also been reported in patients with clinically mild encephalitis or encephalopathy, leading to a new clinical-radiological syndrome, called clinically mild encephalitis/encephalopathy with a reversible splenial lesion (MERS) [6–8]. The reason for the transiently reduced diffusion within the lesions is unknown; possibilities that have been postulated include intramyelinic edema, interstitial edema in tightly packed fibers, and a transient inflammatory infiltrate [6,8].

Delirious behavior is one of the main clinical features in patients with MERS [6,7,9]. To investigate the relationship, MRI studies in a group of patients with influ-

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* Corresponding author. Tel.: +81 470 92 2211; fax: +81 470 99 1198.
E-mail address: jtaka@kameda.jp (J. Takanashi).

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enza-associated delirious behavior were examined to determine how often the splenial lesion is associated with this symptom.

2. Patients and methods

All patients who presented to Kameda Medical Center between November 2007 and March 2008 with delirious behavior associated with influenza were studied using MRI and EEG as soon as possible after presentation. The diagnosis of influenza was established by rapid antigen-detection assay from a nasopharyngeal swab. The number of patients with influenza was looked up by the information system of Kameda Medical Center. The diagnosis of encephalopathy is defined as acute onset of brain dysfunction such as seizures and disorders of consciousness, lasting for more than 12 h, with no evidence of inflammatory changes, such as pleocytosis of cerebrospinal fluid [6,10]. Delirious behavior is divided into the following components: visual hallucination; sensory misperceptions other than visual ones (such as auditory hallucination); emotional changes (such as laughter and fear); incoherent speech; purposeless movement; and impulsive behavior. When a splenial lesion was recognized on the initial MRI, a follow-up MRI was scheduled. The EEG was recorded during wakefulness, or wakefulness and sleep. A follow-up EEG was performed if the initial EEG was abnormal.

3. Results

Of the 370 patients with influenza seen during this period, 11 had delirious behavior (8 boys and 3 girls, aged from 3 to 10 years, mean age at 7.2). Clinical data are summarized in the Table 1. Delirious behavior was observed within 3 days of the onset of influenza, and lasted for less than 12 h. Therefore, a diagnosis of MERS was not given for the 11 patients, because a diagnosis of encephalopathy needs consciousness disturbance for more than 12 h [10]. All 11 patients had complete clinical recovery. Mild hyponatremia (Na<135mEq/l) was observed in 1/5 patient with a splenial lesion, and 2/5 patients without a splenial lesion. Blood examination showed no other abnormal data. No MRI or EEG could be performed during delirious behavior. MRI was performed within a day of delirious behavior in 10 of the 11 patients, revealing a splenial lesion with homogenously reduced diffusion in 5 patients (Fig. 1). One patient (patient 4) had lesions in the both the callosal splenium and the genu. No lesion outside of the corpus callosum was identified. All callosal lesions resolved by the time of the follow-up study, performed within 2 weeks of the initial MRI. EEG abnormalities (occipital slow waves during wakefulness) were observed in 4 of the 9 patients examined; 2 of these patients had

Table 1
Data for influenza patients with delirious behavior

Pt.	Age/sex	Pathogen	Premed	Na	Delirious behavior	Onset, duration	Other neurological symptoms	Initial EEG	Follow-up EEG	Lesion on initial MRI	Lesion in follow-up MRI
1	6/M	Influenza A	None	135	Emotinal change (fear, laughter)	D2, 4H		NE	NE	Splenium (D3)	None (D6)
2	5/F	Influenza B	Oseltamivir phosphate	135	Visual hallucination, misperception	D2, 7H	Seizure (D2)	Slow in O (D2)	Normal (D9)	Splenium (D2)	None (D12)
3	9/F	Influenza A	None	138	Emotinal change (laughter)	D2, 3H		Normal (D3)	NE	Splenium (D3)	None (D7)
4	10/M	Influenza A	Zanamivir hydrate	139	Incoherent speech	D3, 6H		Slow in O (D4)	Normal (D30)	Splenium, genu (D3)	None (D10)
5	3/M	Influenza B	None	134	Visual hallucination, incoherent speech	D3, 12H		Normal (D5)	NE	Splenium (D4)	None (D15)
6	8/M	Influenza A	Oseltamivir phosphate	NE	Visual hallucination, emotional change (fear)	D2, 10H		Normal (D7)	NE	None (D7)	NE
7	7/F	Influenza A	Zanamivir hydrate	141	Incoherent speech, emotinal change (laughter)	D2, 3H	Seizure (D2)	Normal (D5)	NE	None (D3)	NE
8	8/M	Influenza A	None	133	Visual hallucination, incoherent speech	D1, 5H		NE	NE	None (D2)	NE
9	7/M	Influenza A	None	136	Incoherent speech, emotinal change (fear)	D1, 6H		Normal (D2)	NE	None (D2)	NE
10	7/M	Influenza A	None	133	Visual hallucination, emotinal change (laughter)	D2, 3H		Slow in O (D3)	Normal (D32)	None (D3)	NE
11	9/M	Influenza A	None	139	Visual hallucination	D2, 3H		Slow in O (D2)	Normal (D26)	None (D2)	NE

Pt., patient; M, male; F, female; Premed, premedication; Na, serum sodium level; D, day; H, hour; O, occipital; NE, not examined.