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Original article

Callosal lesions and delirious behavior during febrile illness

Akihisa Okumura [a,*], Fumio Hayakawa [b], Toru Kato [b], Motomasa Suzuki [b], Takeshi Tsuji [b], Yukiko Fukumoto [b], Tomohiko Nakata [b], Kazuyoshi Watanabe [c], Tsuneo Morishima [d]

[a] *Department of Pediatrics, Juntendo University School of Medicine, 2-1-1 Hongo, Bunkyo-ku, Tokyo 113-8421, Japan*
[b] *Department of Pediatrics, Okazaki City Hospital, Goshoai 3-1, Koryuji-cho, Okazaki, Aichi 444-8553, Japan*
[c] *Faculty of Medical Welfare, Aichi Shukutoku University, Sakuragaoka 23, Chikusa-ku, Nagoya, Aichi 464-8671, Japan*
[d] *Department of Pediatrics, Okayama University Graduate School of Medicine and Dentistry and Pharmaceutical Sciences, 2-5-1 Shikatacho, Okayama 700-8558, Japan*

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Abstract

We retrospectively reviewed electroencephalography and magnetic resonance imaging findings for 21 children exhibiting delirious behavior during febrile illness. Among these, five patients had transient callosal lesions with or without white matter lesions on diffusion-weighted images. We compared the clinical characteristics, duration, and components of delirious behavior, the duration and severity of reduced consciousness, and EEG findings among patients with or without callosal lesions. No significant differences were detected in these items according to the presence or absence of callosal lesions. Adding insight into the pathogenesis of this condition, our study revealed that callosal lesions are not uncommon in patients exhibiting delirious behavior during febrile illness.

Keywords: Delirious behavior; Febrile illness; Callosal lesion; Diffusion-weighted images

1. Introduction

Delirious behavior is an important symptom of acute encephalopathy. In 2001, the Annual Report of the National Research Committee on Influenza-associated Encephalopathy in Japan stated that abnormal behavior was observed during the early period of the disease in 30 of 70 children who died of influenza-associated encephalitis/encephalopathy. However, children may show delirious behavior in association with high-fever even without acute encephalopathy. Our previous studies showed focal slowing of electroencephalographic activity and slight increases in interleukin (IL)-6 levels in patients with delirious behavior [1,2]. However, few reports have been published regarding magnetic resonance imaging (MRI) abnormalities in patients with delirious behavior. Reversible callosal lesions are observed in patients with various diseases or conditions, including acute encephalopathy [3], epilepsy [4], cerebellitis [5], and convulsions with mild gastroenteritis [6]. We found that transient callosal lesions are observed in some children with delirious behavior. In this report, we describe another condition leading to transient callosal lesions.

2. Patients and methods

The subjects of this study were 21 consecutive children who fulfilled the following criteria: onset between January 2000 and September 2006, delirious behavior in association with febrile illness, and electroencephalography (EEG) and MRI within 72 h of the onset of

* Corresponding author. Tel.: +81 3 3813 3111; fax: +81 3 5800 1580.
E-mail address: okumura@med.juntendo.ac.jp (A. Okumura).

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neurological symptoms. Patients with bacterial meningitis or worsening of an underlying disease were excluded from the study. In Okazaki City Hospital, EEG was performed as soon as possible for children admitted who exhibited delirious behavior. MRI was performed when acute encephalopathy was suspected by attending pediatricians, although no patients were diagnosed with acute encephalopathy. To avoid unnecessary burden, MRI was not performed when the patient exhibited complete recovery of consciousness and a normal neurological examination within a few hours of the onset of delirious behavior.

Sixteen boys and five girls were examined, with a mean age of 6.6 years (range, 3.8–15 years). Convulsions were observed in three patients (14%). The causative pathogens of prodromal febrile illness were influenza in eight patients, mycoplasma in one patient, and mumps in one patient. The causative agent was not specified in the remaining 11 patients with non-specific febrile illness. All patients recovered without neurological sequelae.

Delirious behavior was diagnosed according to the diagnostic criteria of delirium in the Diagnostic and Statistical Manual of Mental Disorders [7]. Delirious behavior was noted under the following conditions: disturbance of consciousness with reduced ability to focus, sustain, or shift attention; a change in cognition or the development of perceptual disturbance; a disturbance developing over a short period of time (usually hours to days) and fluctuating throughout the day; and a disturbance unrelated to the direct physiological consequences of a general medical condition. We also investigated the presence or absence of the following components of delirious behavior in each event: visual hallucinations (e.g., "I see angels flying."), non-visual sensory misperceptions (e.g., "I wet my pants," without urinating), incoherent speech (e.g., meaningless answers to specific questions), emotional changes (e.g., crying loudly without reason), purposeless movements (e.g., pacing), impulsive behavior (e.g., suddenly running out the door or disobeying caregivers).

The severity of reduced consciousness upon admission was deemed mild when the patient remained awake, but seemed absent-minded or lacking in spontaneity, or moderate when the patient tended to sleep, but was arousable with verbal and/or tactile stimulation.

EEG was performed during both wakefulness and sleep, according to the 10–20 international methods. When a patient was not arousable, painful stimuli were applied to evaluate changes before and after stimuli. EEG findings during wakefulness or after painful stimuli were used to categorize patients into two groups: normal patients versus those showing focal slowing, which was defined as the insertion of high-voltage slow waves, primarily in the occipital regions, with relatively well preserved rhythmic alpha activities.

During MRI, conventional T1- and T2-weighted images, fluid-attenuated inversion recovery images, and diffusion-weighted images were obtained using a standard protocol. MRI findings were used to categorize patients into two groups: normal patients versus those showing callosal lesions, which were defined as abnormally high-intensity regions in the corpus callosum on T2- and/or diffusion-weighted images. Other types of MRI abnormalities were not observed in any patient.

Data were analyzed using the Mann–Whitney's *U*-test for numerical variables and the Fisher exact probability test for categorical variables. A p value of <0.05 was considered statistically significant.

3. Results

Callosal lesions were identified in 5 (24%) of 21 patients. Two patients showed additional white matter lesions, and the remaining three showed callosal lesions alone. Follow-up MRI was performed 4–12 days after admission, and all MRI were normal. The clinical course of two representative patients is briefly described below.

3.1. Patient 1

A previously healthy 8-year-old boy presented with unusual behavior and pyrexia beginning at the day before presentation. A nasal swab was positive for the influenza A antigen. The patient looked around restlessly and could not say his name or respond to questions in an appropriate manner. He had a brief generalized convulsion at 2 h post-admission. Although he was alert immediately after the convulsion, MRI was performed. High-intensity regions were observed in the genu and splenium of the corpus callosum on diffusion-weighted images (Fig. 1). Cerebrospinal fluid analysis and EEG showed no abnormal findings. After MRI, the patient showed further improvement in terms of consciousness, but then relapsed into delirious behavior 5 h later. He could not count his mother's fingers and repeatedly and continually uttered the word "no." In addition, his consciousness was mildly reduced. That night, he sat up every 10–15 min and uttered meaningless words or phrases. He did not seem to recognize his mother. The patient was treated with methylprednisolone pulse therapy. The following morning, the patient was alert and showed no delirious behavior, but he was unable to remember the events of the previous day. Delirious behavior did not recur. MRI performed 8 days after admission revealed no abnormal findings.

3.2. Patient 2

A previously healthy 7-year-old boy was admitted with a 2-day history of pyrexia, vomiting, and bilateral parotid swelling. Cerebrospinal fluid analysis showed cell counts of 84 cells/μl and 29 mg/dl protein. The