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Clinical features of benign infantile convulsions associated with mild gastroenteritis

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Abstract: Objective The aim of the study was to investigate the clinical features of benign infantile convulsions associated with mild gastroenteritis (BICE) and provide helpful information for the accurate diagnosis and effective management of BICE. **Methods** The patients, aged 3-36 months, with gastroenteritis accompanied with convulsions were clinically observed and followed up for more than 18 months. **Results** BICE was diagnosed in 12 cases with a peak onset age of (16.0 ± 6.5) months. Six (50%) of the cases occurred in winter. All seizures developed within the first 5 days of the course and 9 (75%) within the first 3 days. The cases presented with generalized or partial seizures. Early clustering seizure attacks were seen in 7 patients (58%). Seizures averaged 2.1 attacks per course. Interictal electroencephalogram (EEG), brain imaging, blood biochemical profile and cerebrospinal fluid (CSF) testing did not show abnormality in all cases. No antiepileptic medications were prescribed to the patients as the seizures had stopped. Three (25%) of the cases experienced relapses that usually did not happen more than twice. The longest course of BICE lasted 8 months. All cases demonstrated normal psychomotor development and had no individual or family history of febrile convulsion or epilepsy. **Conclusions** In this study BICE showed the following clinical features: It occurred at a peak age of 1 to 2 years old and was frequently seen in wintertime. The convulsions usually developed in early days of the course in generalized or partial and mostly in clustering patterns. There were no significant changes in blood biochemical profile, CSF, brain imaging and interictal EEG. The course usually lasted less than 12 months although a small portion of the patients relapsed. An anti-epileptic therapy may not be necessary after seizure cessation in children with BICE.

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Key words: Gastroenteritis; Seizures; Infant

轻度胃肠炎伴良性婴幼儿惊厥的临床研究

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[**摘　要**] **目的** 认识轻度胃肠炎伴良性婴幼儿惊厥(BICE)的临床特点,做到正确诊断和合理治疗。**方法** 对年龄在3~36个月的轻度胃肠炎伴惊厥的患儿进行临床观察和出院后18个月以上的随访。**结果** 12例诊断为BICE,发病年龄(16.0±6.5)个月,6例(50%)冬季发病,9例(75%)3 d内发生惊厥,为全身性或部分性发作,7例(58%)有早期频繁发作,一次病程中惊厥平均发作2.1次。发作间期EEG、脑影像学、血生化及脑脊液检查正常。惊厥停止后未行抗痫治疗,3例(25%)复发,复发≤2次,病程最长为8个月。所有病例精神运动发育正常。**结论** 本组BICE具有以下特点:1~2岁高发,冬季多发,无家族史;无热惊厥多出现于病程的早期,全身性或部分性发作,早期频繁发作多见;血电解质、血生化、脑脊液、脑影像学和发作间期脑电图正常;部分病例可复发,病程少于1年,预后好。惊厥停止后不推荐应用抗癫痫药。

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[**关　键　词**] 胃肠炎;惊厥;婴儿

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Benign infantile convulsions associated with mild gastroenteritis (BICE) was first described by Japanese authors in 1982[1]. Since then, the disease has been reported in other countries including China[2]. BICE is not uncommon in younger children. However, an incomplete understanding of the clinical process and pathogenesis of BICE results in difficulties in the diagnosis and management of the disease. In the current

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study, the clinical and laboratory data of BICE patients who were managed in Sino-Japan Friendship Hospital were analyzed and the recently published literatures related to BICE were reviewed. The purpose of the study was to improve the understanding of BICE in order to facilitate its diagnosis and management.

Subjects and methods

Subjects

The patients with mild gastroenteritis accompanied with convulsions, who were admitted into Sino-Japan Friendship Hospital between January 1999 and December 2003, were primarily selected for the research. Individual and family health histories of the patients were collected. All patients received routine physical examination and necessary laboratory tests including routine stool test, biochemical profile, cerebrospinal fluid (CSF) tests, neuroradiological imaging and interictal electroencephalogram (EEG). The patients who were consistent with the features of BICE (see below) were followed up. The BICE relapse and the evaluation of the psychomotor development of the patients ere recorded through outpatient inquiries in clinic visits or by telephone and mail.

Diagnosis of BICE

BICE is diagnosed based on the published data[1-4]. 1) The patients should be in the age group between 6 and 36 months old and have no significant disorders in the past medical history. 2) They might present with mild vomit and/or diarrhea and possible mild dehydration but have no acidosis and electrolytic imbalance. 3) Convulsions usually occur within the first five days of the course and with normal body temperature or low fever (below 38 ℃). They can be a single or multiple attacks. 4) There should be no abnormal changes in interictal EEG, brain CT and MR image and the blood levels of glucose, calcium and magnesium. The patients are usually positive for Rotaviral antigen in stool. 5) The clinical process of BICE is generally benign with low recurrent rate and no significant influence on the growth and development of children. Other causes resulting in convulsions should be excluded, including febrile seizure, brain injuries induced in prenatal period or by other causes, encephalitis, meningitis, encephalopathy and epilepsy with identified etiology.

Results

Incidence of BICE

A total of 23 hospitalized patients with mild gastroenteritis developed convulsions during the research. Eleven patients (6 with body temperatures above 38℃, 1 with hyponatremia, 2 with hypocalcemia and 2 with brain damage in prenatal period) were excluded from further research observation. The other 12 patients (7 boys and 5 girls) who were consistent with the diagnosis of BICE were finally included in the study, accounting for 8.7% (12/138) of the total hospitalized patients with gastroenteritis at the same period of time.

Season distribution

Six of the 12 patients (50%) presented with BICE in winter, one in November, three in December and two in January. Of the rest of the patients 3 were seen in October, 2 in August and 1 in May.

Age distribution

The mean age at the onset of BICE was 16 ± 6.5 months old (5 to 23 months old). Nine cases (75%) were aged between 13 and 23 months old.

Clinical features of convulsions

All 12 cases had their seizure attacks within the first 5 days of the course. Nine cases (75%) underwent the attacks within the first 3 days.

The frequency of the seizure attacks was variable during the course. Seven patients (58%) experienced two or more attacks. One of the patients had attacks 8 times within 24 hours, with complete consciousness between attacks and without signs of status epileptics. On average, seizure attacks occurred 2.1 times during each course.

Based on the medical observation and parents' description, the seizures in patients with BICE were categorized as generalized tonic-clonic (GTC) in 6 cases (50%), generalized tonic in 1 case (8%) and partial seizures in 5 cases (42%, characterized clinically by staring, motion arrest or head and/or eye deviation. Two cases had secondary generalized seizures). All seizure attacks lasted 1 to 3 minutes.

EEG recordings

A total of 17 interictal EEGs (both consciousness EEGs and sleep EEGs) were performed on the 12 cases of BICE within 3 days after seizure attacks. They all demonstrated normal background activity. In 6 cases, 7 sleep EEGs showed occasional single atypical middle or low amplitude sharp-slow waves or spike-slow waves in unilateral or bilateral frontal, central or parietal lobes.

Cerebral images

No abnormalities were found in 12 cerebral CT and 2 MR images.

Laboratory tests

Sodium concentration in blood was 137.0 ± 5.0 mmol/L, calcium 10.3 ± 1.3 mmol/L and glucose 5.3 ± 1.1 mmol/L. The stool specimens were grossly watery and yellow-green. Microscopically, 3 cases were normal, 3 were found with 1-3 leukocytes per high power field and 2 were found with fat globules. Two patients were lumber punctured, and their CSF tests were normal.

Past and family history

All cases had no past or family history of febrile seizures or epilepsy.

Management

Seven cases received intravenous injections of diazepam (0.3 - 0.5 mg/kg) or intramuscular injections of barbiphenyl sodium (5 - 8 mg/kg) at the onset of their first seizure attacks. The attacks ceased in 3 of them. Four cases with recurrent convulsions were repeatedly given anti-epileptics and 3 were finally controlled. One case experienced 8 attacks within 24 hours. A satisfactory control was not reached in this case even after being given enough doses of diazepam, barbiphenyl sodium and chloral hydrate, although no signs of status epilepticus were observed. In all 12 cases, no anti-epileptic medications were prescribed after the convulsions had stopped.

Follow-up

The patients were followed up for an average of 38.8 months (18 to 59 months), until the youngest patient was 40 months old. Three patients (25%) relapsed during the follow-up. Two cases had recurrent seizure attacks within 6 months while 1 case had an attack between 6 and 12 months after the first seizure attack. One of the 3 cases relapsed twice and 2 other cases only once. Two of the recurrent cases manifested with mild vomiting and diarrhea followed by afebrile seizures.

During the follow-up, almost all patients developed upper respiratory tract infection complicated with high fever (body temperature higher than 38.5°C) but no febrile convulsions were observed. All 12 patients had normal psychomotor development.

Discussion

There is a variable range of the reported incidence of BICE. It was 0.12% to 1.78% in Japan, Gaoxiong in Taiwan province and North China region[2, 5, 6]. The incidence of seizure attacks in the hospitalized children with Rotaviral gastroenteritis was reported as 2% to 6.4%[6,7]. This study showed an 8.7% incidence of BICE in the hospitalized patients, much higher than the reported rates. One of possible reasons was that most of the infants with mild gastroenteritis was treated as out-patients.

The etiology of BICE remains poorly understood. Researchers in Japan suggest that BICE might be just one patterns of benign infantile convulsion[5,8] because visual EEG (VEEG) monitoring demonstrated that the seizure started locally followed by a generalization. A similar domestic report suggested that diarrhea might be only an inducer for the convulsion[9]. It was also noted that the seasonal distribution of BICE appeared compatible with that of Rotaviral enteritis, suggesting that BICE may be a mild type of Rotavirus-related encephalitis. This was supported by the findings that the specimens from BICE patients, including CSF, blood, pharyngeal swab and stool, were positive for IgG antibody to Rotavirus or Rotaviral genome[10,11]. The authors from this study and other authors believe that BICE might be what is called situation-related seizures related to a lower threshold status for seizure in the young children with acute gastroenteritis associated with bacteremia or viremia [4,6,12].

BICE is most commonly seen in infants at the age of 1 to 3 years[2,4,6,12]. It was believed in the past that the seizure in BICE presented with a generalized tonic-clonic pattern[3]. However, it is known now that the

partial seizures do occur and may develop a secondary transformation of generalized form. The patients manifest clinically with staring, motion arrest, head or/and eye deviation, cyanosis and automatism[8,9]. The seizure attacks usually last no more than 5 minutes. They may come while children are playing or be induced by crying and pain[12]. In their early phase, the attacks may present with a clustered pattern. In the literatures, the average onset of the seizures in BICE was reported variably from 1.6 to 2.6 attacks per course[2,6,12], and was 2.1 in this study. There is no report thus far of BICE cases complicated with status epileptics. Epileptic discharges recorded by VEEG at seizure onset were focal or multi-focal in origin, followed by generalization in some cases[8,9,13].

Diagnosis of BICE is not a problem if one follows the features as mentioned above, but the differentials below should be considered. Afebrile convulsions in BICE must be distinguished from those induced by vomit/diarrhea-related biochemical disturbances such as hypoglycemia and electrolytic imbalances including hypernatremia, hyponatremia, hypocalcemia and hypomagnesemia. Severe myoclonic epilepsy in infancy, benign partial epilepsy in infancy with complex partial seizures and periodical vomiting should be also in the differentials. Sometimes frequent attacks of partial seizure in a short course in BICE should be separated from recently described migrating partial epilepsy in infancy. The latter usually shows refractory status epileptics and regression in psychomotor development. The convulsion with low fever in BICE needs to distinguish from febrile seizures (especially complex type), central nerve system infections and toxic encephalopathy.

The clustering seizure attacks in the early phase of the disease are not sensitive to the anti-epileptic medications, which is one of the features in BICE[12]. A recent retrospective report indicated that lidocaine showed an effective rate of 100% in controlling this type of early seizure attacks compared to 38% to 70% with diazepam, bromazepam or phenobabital[14].

There is no consistency regarding whether continuous anti-epileptics may still be required after seizure cessation in BICE. In practice, some of the BICE patients continued to receive anti-epileptic medications even after being discharged[5,9,15]. However, the therapeutic course is unclear. It has been reported that no anti-epileptics are required after seizure cessation since there is no or low recurrence in BICE[2,4,7,12]. In this study, 25% patients relapsed. The recurrent rate was higher than those reported. However, the authors from this study generally agree that it is not necessary to continue using anti-epileptics in patients after seizure arrest. It has been widely accepted that BICE has a better prognosis.

In conclusion, BICE in this study showed the following clinical features: It was commonly seen in infants with age between 1 and 2 years old and without family history. It occurred predominantly in wintertime. The convulsion mostly happened in the first 3 days of the course and presented with either generalized or partial patterns. The seizure in BICE was characteristic of early multiple attacks. No abnormal changes were noted in serum electrolytes, biochemical profile, CSF, brain imaging and interictal EEG. The convulsion might recur in some cases but usually no more than 2 attacks. The course lasted mostly less than one year with good prognosis.

The understanding of BICE clinical characteristics will be helpful for the early diagnosis and proper management of the disease. It will also assist to reduce unnecessary employment of laboratory examinations and medications, which will certainly relieve the financial and mental pressures on the families. In addition, the patients themselves may avoid suffering from many possible side effects caused by a long-term unnecessary use of the medications.

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·病例报告·

22 号环状染色体综合征 1 例报告

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[中图分类号] Q987.1 [文献标识码] E

男婴,3 个月,因咳嗽 5 d 入院。患儿为第 2 胎第 2 产,足月顺产,出生体重 2.5 kg,无窒息抢救史,生后至今哭声细弱,吸奶差,生长慢,对外界反应较差。其姐 3 岁,生长发育正常。父母健康,非近亲结婚,家族中无类似病例。体查:体重 3.8kg,头围 32 cm,颅骨重叠,神志清楚,哭声细弱,反应差,低位耳,双耳听力差,眼距增宽,内眦赘皮,鼻梁宽,硬腭高,全身肌张力低下,心脏听诊闻及柔和的收缩期杂音,彩色多谱勒示卵圆孔未闭、动脉导管未闭,胸部 X 线检查未见异常。疑诊猫叫综合征。染色体检查分析示:46,XY, -22, +r(22) (p12q13),确诊为 22 号环状染色体综合征。家长放弃治疗出院。

22 号环状染色体综合征是由第 22 号染色体突变所致的临床综合征,1977 年由 Hunter 等[1]首次报道。常见的特征有:中度的发育和智力障碍,不能读,不能写,小头,中指骨短,妇女多毛症,球形鼻,上腭发育不良,肌张力减退,运动失调性步态等。生存期一般无明显影响。有一家三代 5 人中带有 r(22) 的报道[2]。国外已有多例 22 号环状染色体综合征的报道,国内迄今报道女性 22 号环状染色体综合征 1 例伴有感音性耳聋[3]。本例病儿为男性,家系中无类似病人,遗憾的是未能作其家系染色体分析。

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