Clinical Characteristics and Risk Factors for a Complex First Febrile Convulsion

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ABSTRACT

Objectives: To determine the frequency of complex features in febrile convulsion, association of complex febrile convulsion with neurological findings and risk factors associated with complex febrile convulsion.

Methodology: Retrospective review of clinical records of 379 patients admitted for their first febrile convulsion over a two-year period.

Results: Complex features occurred in 37.2% patients. Focal seizures tended to be prolonged as well. There was also significant association between prolonged or focal seizures with presence of neurological abnormalities. The longer the duration of the seizure, the higher was the likelihood of neurological abnormalities. Risk factors associated with a complex first febrile convulsion were: 1) Age of 15 months or less, 2) Birth weight of 2 kg or less and 3) initial temperature of 38°C or less.

Conclusions: Any acute febrile convulsion should be abbreviated soonest possible as neurological abnormalities, which may be signs of cerebral insult become more likely with increasing duration of seizures. The risk factors found associated with complex febrile convulsion underline the propensity of the immature, developing brain to abnormal seizure discharges in response to a lower temperature threshold.

Keywords: complex febrile seizure, risk factors, neurological abnormalities

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INTRODUCTION

Febrile convulsions occur in approximately 2 - 5% of the population[1,2]. Among those who would develop febrile convulsion, up to 20 - 35% of them would have complex febrile convulsion[2,3]. A complex febrile convulsion is defined as a febrile seizure having one or more of the following: 15 minutes or more in duration, more than one seizure in 24 hours or focal features[1].

Complex febrile convulsion had been shown to be related to subsequent epilepsy[4]. In addition, earlier studies carried the notion that complex febrile convulsion was also associated with increased mortality[5] and long-term neurological deficits[6].

With these implications in mind, it is important to identify which children are at risk of complex febrile convulsion and how such convulsions are associated with neurological findings in the acute stage.

This study sets out to identify factors associated with a first febrile convulsion that is complex and to determine relationship between complex features and neurological abnormalities at presentation.

MATERIALS AND METHODS

This is a descriptive study of data obtained from the patient's clinical records. Admitted patients with a diagnosis of a first febrile convulsion over a two-year period between January 1993 to December 1994 were identified using the computer database from the Medical Records Office, University of Malaya Medical Centre, Kuala Lumpur, Malaysia. The individual patients' records were then retrieved and data on demographic, seizure and fever characteristics, along with birth and family histories were obtained.

A febrile convulsion is defined as a seizure that occurs in childhood after age one month, associated with a febrile illness not caused by an infection of the central nervous system, without previous neonatal seizures or previous unprovoked seizures and not meeting the criteria for other acute symptomatic seizures[7]. For the purpose of this study, children with pre-existing neurological deficits or developmental delay were excluded.

Complex febrile convulsions were with one or more of the following characteristics: 15 minutes or more in duration, multiple (more than one) seizure in 24 hours or focal features[1]. If seizures were multiple, the duration of the longest seizure was recorded. If the patient did not regain consciousness in between clinical seizures, he is considered to have a single seizure.

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Table I. Association of Complex Features in Febrile Convulsion with Presence of Neurological Abnormalities.

Seizure Characteristics	Presence of neurological abnormalities* Yes (%) (n=33)	No (%) (n=334)	Rate Ratio (95% CI†)
>=1 complex	15 (45%)	125 (37%)	0.6 (0.3 -1.3)
>=2 complex	6 (18%)	8 (2%)	9.2 (3 - 28)
Focal	4 (12%)	1 (0.3%)	48 (5 - 500)
Duration >=15 minutes	13 (39%)	34 (10%)	6.4 (3 - 14)
Duration >=30 minutes	8 (24%)	8 (2%)	14.3 (5 - 42)
Multiple (>1 episode)	7 (21%)	98 (28%)	1.5 (0.6 - 3.5)

* Data missing from two patients
† 95% confidence interval

Information on the earliest recorded per axilla temperature following seizure was obtained from clinical notes from the emergency department or letters written by referring doctors. In a separate study, it has been shown that 80% of parents were able to bring their child with febrile convulsion to the attention of doctors within 30 minutes (Ling SG, unpublished data). Therefore, the temperature recorded would relate closely to the temperature at the time of seizure. The interval from fever onset to the occurrence of seizure was also determined from the case notes. The neurological findings used in this study were the clinical features recorded during the initial examination on admission. Patients were regarded as having neurological abnormalities if one or more of the following were present: hypertonia, hyper-reflexia, ankle clonus, hypotonia and hemiparesis.

The data was then analysed using chi-square test or Fisher's exact test for univariate associations, using significance level of 0.05. Logistic regression was used for multivariate analyses. The data was also complemented by the utilisation of risk ratio with a 95% confidence interval. Three sets of analyses were performed. The first examined the association among seizure characteristics. The second analysis studied the relationship of complex features with neurological abnormalities while the third explored factors associated with a complex febrile convulsion.

RESULTS

Patient Population

There were a total of 379 patients admitted for their first febrile convulsion (case retrieval rate of 88%), made up of 232 (61.2%) boys and 147 (38.8%) girls. Their ages ranged from 1 - 68 months with a mean of 19 months and a median of 16 months. There were 204 (53.8%) Malays, 73 (19.3%) Chinese, 89 (23.5%) Indians and 13 (3.4%) from other ethnic groups.

From the 379 patients, 141 (37.2%) patients had complex febrile convulsion. 127 (33.5%) had one complex feature, 12 (3.5%) had two complex features and 2 (0.5%) patients had three complex features. 5 (1.3%) patients had focal seizure, 47 (12.4%) patients had prolonged seizure lasting 15 minutes or more while 106 (28.0%) patients had multiple (>1) seizure episodes within 24 hours.

Association among complex features in febrile convulsion

Four out of five patients with focal seizures also had prolonged seizures >=15 minutes. This was statistically significant ($p<0.001$). However, multiple (>1) seizures have not been found to be significantly associated with focal (p=0.l) or prolonged seizures (p=0.9).

Association between neurological findings and complex febrile convulsion

Neurological deficits were more likely if there were two or more complex features present. Neurological deficits were also more commonly found if seizures were focal or prolonged but there was no association between neurological deficits and multiplicity of seizures (Table I).

The risk of neurological deficits increased with increasing duration of the seizures. Those who had seizures lasting 15 minutes or more were 6.4 times more likely to develop neurological deficits compared to those with short-lasting seizures. This risk increased to 14 times if the seizure lasted for 30 minutes or more (Table I). The chi-square test for trend comparing presence of neurological abnormalities in three categories of seizure duration (<15 minutes, 15 - 29 minutes and >=30 minutes) also showed a significantly increased likelihood of neurological deficits with increasing duration of seizure ($p<0.0001$). The neurological deficits in all 33 affected patients were transient and resolved by the time the patients were discharged.

Risk factors for complex febrile convulsion

Using multivariate logistic regression analysis for each complex feature (Table II), significant risk factors found to be associated with complex features were 1) age of 15 months or less, 2) birth weight of 2 kg or less and 3) initial temperature of less than 38°C.

Children aged 15 months or less were significantly more likely to develop complex febrile convulsion with at least one complex feature and seizure duration of 30 minutes or more. Although these younger children were also likely to have focal, prolonged (>=15 minutes) or multiple seizures, these did not reach statistical significance.

Children with birth weight of 2 kg or less were also associated with complex febrile convulsion, particularly with focal seizure and prolonged seizure duration of 15 minutes or more.

Table II. Analysis of Risk Factors Associated with Complex Febrile Convulsion.

Risk factor	Number of patients† n=379	Seizure Characteristics					
		>=1 complex n=141	>=2 complex n=14	Focal n=5	Duration >=15 mins n=47	Duration >=30 mins n=16	Multiple> 1 episode n=106
Age, months							
<=15	176	76	8	3	27	12	56
>15	203	65	6	2	20	4	50
p value*		0.05	0.2	0.5	0.2	0.04	0.1
Gender							
Male	232	92	10	3	31	10	69
Female	147	49	4	2	16	6	37
p value*		0.3	0.5	0.8	0.8	0.9	0.2
Temperature, °C							
<38	120	42	10	3	17	7	34
>=38	257	97	4	2	28	8	72
p value*		0.7	0.002	0.2	0.3	0.2	0.7
Interval between fever and seizure onset, hours							
<=12	163	62	4	2	18	6	47
>12	207	77	10	3	28	10	58
p value*		0.6	0.3	0.9	0.6	0.6	0.7
Birth weight, kg							
<=2	9	7	2	1	4	0	4
>2	365	134	12	4	43	16	102
p value*		0.02	0.001	0.02	0.006	0.9	0.2
Family history of epilepsy First-degree relatives							
Yes	6	0	0	0	0	0	0
No	365	137	14	5	47	16	102
p value*		0.6	0.9	0.9	0.8	0.9	0.7
Family history of febrile convulsion First-degree relatives							
Yes	62	17	2	1	7	4	12
No	309	120	12	4	40	12	90
p value*		0.1	0.9	0.7	0.7	0.7	0.2

* Multivariate logistic regression analysis
† Total may not tally due to missing data

Children with initial temperature at presentation of less than 38°C were also more likely to develop complex febrile convulsion but this only reached statistical significance if two or more complex features were present.

DISCUSSION

From this study, 37.2% of patients admitted for their first febrile convulsion had complex features. This was consistent with most hospital-based studies, which quoted figures of between 32 to 35%[3,8]. Population-based studies tended to have a lower incidence of complex febrile convulsion, occurring in between 18 to 20% of patients[1,2].

However, what was striking in this study was the low incidence of focal seizure, occurring in only 1.3% of the patients. This was far less than that found in hospital-based studies elsewhere, which reported incidences of between 16 to 29%[3,9,10]. This apparent difference in incidence might be a true reflection of variation among different population groups or due to lack of uniformity in classification and assessment of focality of seizure[11].

The association between focal seizures and prolonged seizures had been documented in several other studies[3,10]. The apparent dissociation of these two complex features from multiplicity of seizures in all the analyses performed may indicate a different underlying aetiology or predisposing factors leading to these complex features.

The increased incidence of acute neurological deficits detected in children with complex febrile convulsion appeared to be more related to focality and duration of seizure rather than to multiplicity of seizures. Children with focal seizures were often associated with Todd's hemiparesis, explaining their higher propensity to neurological deficits. From this study, the risk of developing neurological deficits increased with increasing duration of seizure. Although all children with

neurological deficits made uneventful recoveries in this study, this finding indicated that prolonged duration of the seizure might be a more important factor in causing insult or injury to the brain compared to multiple but short seizures. It would seem logical then to abbreviate any seizure and prevent development of prolonged seizures.

Young age as a risk factor for complex febrile convulsion had been demonstrated in previous studies[3,9,10,12]. Besides complex febrile convulsion, young age at onset of febrile convulsion had also been shown to be related with recurrence[13]. In addition, for those with recurrence, complex features tended to repeat[3]. Therefore, younger children would be more likely to develop recurrent complex febrile convulsion.

The association of complex febrile convulsion with a relatively lower degree of pyrexia closest to the time of seizure occurrence had only been shown in one other study[3]. This finding might indicate a lower seizure threshold in response to fever in certain susceptible children. In contrast to this association, high grade fever was shown to be related to febrile convulsion occurrence[14] and also further recurrences[8,13]. This gave an indication that while high grade fever might bring on febrile convulsion, it did not influence the type of convulsion.

The association of low birth weight and complex febrile convulsion in this study had not been previously described. This relationship could be explained by the fact that low birth weight infants tended to be either premature infants or infants with intrauterine growth retardation, who were more likely to experience hypoxia or other adverse perinatal events. The relationship between birth asphyxia or prior neurodevelopmental abnormalities with complex features had been previously described[9,12]. However, one large study had not shown any association between neurodevelopmental abnormalities and complex features[3]. Furthermore, this present study had excluded children with prior neurodevelopmental deficits.

Gender, family histories of epilepsy or febrile convulsion and interval between fever onset and seizure occurrence had not been shown to increase risk of complex febrile convulsion in this study. Only one study showed a predominance of girls who developed complex features[15]. Family histories of seizures had generally not been shown to be associated with complex features in other studies[9,15,16]. Only a study by Verity[2] showed an association between family history and complex febrile convulsion. However, in his study, even second and third degree relatives were included, making the finding less reliable. A short interval between fever and seizure onset predisposed to recurrence of febrile convulsion[15] but probably not associated with complex features, was shown in this study.

In conclusion, 37.2% of febrile convulsion were complex. Focal seizure tended to be prolonged as well. Risk of acute neurological abnormality increased with increasing duration of seizure. The significant risk factors associated with complex febrile convulsion in this study might indicate the susceptibility of a young maturing brain to complex febrile convulsion in response to a lower temperature threshold.

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