ORIGINAL ARTICLE

Neurodiagnostic Evaluation of a Child with First Complex Febrile Seizure

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Abstract:

Background: Febrile seizure is the most common type of childhood seizure and complex febrile seizure has been associated with the risk of epilepsy. The neurodiagnostic evaluation of a child with first CFS is still unclear. *Aim & Objective:* To assess the clinical characteristics and diagnostic evaluation of children aged 1 month to 5 years presenting with first Complex Febrile Seizure (CFS) and to determine the utility of various investigations in a case of first CFS. *Material and Methods*: A prospective study was conducted in the pediatric department of a tertiary hospital. Forty-nine children aged 1 month-5 years with first CFS fulfilling the inclusion criteria were enrolled in the study over duration of 8-months. All the cases were evaluated with complete blood count, serum calcium, serum electrolytes, Electroencephalography (EEG), CT/MRI and lumbar puncture. *Results:* The investigation results were analyzed with respect to different CFS parameter like type of seizure (focal or generalized) and duration of seizure(less than or more than 15 minutes). Upper respiratory tract infection is the main cause of febrile seizure. The duration of CFS did not vary according to the underlying cause. Serum calcium levels are found to be lower in children with complex febrile seizure. All children with CFS, whether focal or multiple generalized, whether of long or short duration, had a normal EEG. Children who had prolonged focal and multiple generalized seizures had abnormal neuroimaging but it was not statistically significant. *Conclusion:* We conclude from our study that a child with first CFS may not need EEG and neuroimaging as a diagnostic evaluation test. Hypocalcemia can be identified in these children and can be corrected to stop the seizure. Further studies are needed on a large series of children with first CFS to form guidelines for their neurodiagnostic evaluation.

Keywords: Complex, Febrile Seizure, EEG, MRI, CT

Introduction:

Febrile Seizure (FS) is the most common type of childhood seizure and one of the most prevalent causes of emergency hospital admission in children [1]. Between 2-5% of children in USA experience at least one febrile seizure before the age of 5 years, being more common in boys [2, 3]. Incidence of 10.3 % has been reported in a study from South India [4]. The prevalence of FS in India was found to be 2.27 per 1,000 populations in a North Indian study [5], while it was 3.28–5.71/1,000 in South India [6]. Between 9 and 35% of all first febrile seizures are complex [3].

A Complex Febrile Seizure (CFS) has been associated with an increased risk of epilepsy [7]. The incidence of an abnormal neuroimaging in a child less than 33 months with fever and focal seizure (a component of CFS) is 33% [8]. The possibility of a CFS as a sole marker for meningitis in clinical practice is a dilemma [9].

The American Academy of Pediatrics have laid down clear cut guidelines for the evaluation and management of a case of simple febrile seizure, which states that the focus should be on identifying the source of fever in a case of simple febrile seizure rather than doing a routine work up of a seizure like electroencephalogram, neuroimaging

and lumbar puncture [10]. While guidelines are available for simple febrile seizure, management of CFS is individualized. An expert committee on pediatric epilepsy in India in its consensus meeting in the year 2006 laid down certain guidelines for the diagnosis and management of childhood epilepsy, which states that CFS may need investigation like EEG, Neuroimaging and continuous use of anti-epileptic drugs [11]. Italian League against epilepsy 2009 recommends an early EEG, CT/MRI and lumbar puncture (with suspected CNS infection) in all cases with first complex febrile seizure [12].

Individual studies have been done which have questioned the role of EEG and CT scan in evaluation of first CFS. Hardasmalani and Saber conducted a study on the yield of diagnostic studies in children with complex febrile seizures, and they found that a majority of them do not need a detailed seizure workup routinely [13]. A study by Amir *et al* focusing on the need of neuroimaging to detect intracranial pathology in a case of CFS in the absence of other signs and symptoms of it proved that very few indeed have a lesion in the brain [14]. CFS remains one of the definite risk factor for development of epilepsy further in childhood. Whether to do EEG in all patients of CFS or only a subsection of it depending on the clinical features is a dilemma. Joshi and Wawrykow [15] in their study pointed towards the need of using clinical clues in requesting an EEG in a child with CFS, and they found that a family history of febrile seizure was associated with a normal EEG, suggesting a benign nature of illness. Fletcher [16] performed a study to know the necessity of lumbar puncture in patients with new onset CFSs, and concluded that acute bacterial meningitis is rare in patients with first CFS. Hence we proposed to do this study to determine the yield of diagnostic studies in the evaluation of children presenting with first CFS.

Material and Methods:

Study design:

Prospective Cohort Study

Place of the study:

Paediatric wards and paediatric intensive care unit, Lokmanya Tilak Muncipal Medical College and General Hospital, Sion, Mumbai- 400022.

Duration of the study:

October 2013 to May 2014

Inclusion criteria:

All children aged one month to 5 years with first CFS. Complex febrile seizure is defined as febrile seizure with one or more of following criteria i.e. Focal in nature, duration > 15 minutes, new events may reoccur within the next 24 hours. Focal nature of the seizure may be clonic and/ or tonic movements, loss of tone, head or eye deviation to one side, seizure activity followed by transient unilateral paralysis.

Exclusion criteria:

Children with underlying chronic neurological disorder like cerebral palsy, mental retardation, hydrocephalus, congenital central nervous system malformation.

Methodology:

All paediatric patients who fulfilled the inclusion criteria were enrolled after written informed consent obtained from parents/guardian. Detailed history of the patient was taken and entered in preformed study proforma. Following clinical details about the seizure i.e. type of seizure: focal or generalized, duration of seizure: less than 15 minutes or more than 15 minutes, type of focal seizure: clonic/tonic/atonic, head and/or eye deviation, seizure followed by transient unilateral

paralysis were recorded. Data regarding the investigations such as complete blood count, serum calcium, serum electrolytes, lumbar puncture, EEG (done within a week of the seizure), CT/MRI were recorded. Patients were reassessed at 48 hours and at discharge to record additional clinical details. The yield of these investigations were analysed to determine the incidence of intracranial pathology and the percentage of abnormal EEG in children with first CFS. The study protocol was approved by the hospital scientific and ethics committee.

Statistical Analysis:

All the data was collected using a pre-formed interview schedule and entered in Microsoft Excel sheet 2013. The data was then transferred and analyzed using SPSS software version 17. All the qualitative data was presented as frequency and percentages and were compared using Pearson's chi-square test while quantitative data was presented as mean and standard deviation. Confidence limit of 95% was taken and p-value of < 0.05 was considered as significant.

Results:

Forty nine children with a clinical diagnosis of first CFS were enrolled consecutively from October 2013 to May 2014. In the 49 patients we studied, 17 were from 1 to 12 months, 29 were in the age group of 13 to 36 months and 3 were from 37 to 60 months. Of these, 30 patients were male and 19 patients were female. (Table 1) Family history of febrile seizure was found in 6.12% of patients and 2.04% patients had epilepsy in family members. 75.51% of patients had convulsion at the onset of fever, and 24.49% had after a few hours of fever. Of these, 46.94% of patients had received antipyretics at home before convulsion and remaining 53.06% had not received any antipyretics. 48.98% of patients had Upper Respiratory Tract Infection (URTI) as the cause of fever, 34.69% were viral fevers, 12.24% were Acute Gastroenteritis (AGE) and 4.08% had Otitis Media (OM) (Table 2). 28.57% of children had a serum calcium level below 8.8 mg/dl and the mean value was 8.73mg/dl. In the age group of 1 to 12 months, 5 patients had focal and 12 had generalised seizure. In the age group of 13-36 months, 11 patients had focal and 18 had generalised convulsion. In the age group of 37-60 months 1 had focal and 2 were generalised seizures. Focal seizures were there in 34.7% and 65.3% had generalised seizures. Among the Focal Group, Head and Eye (FHE) deviation was there in 52.9%, Focal Clonic (FC) in 17.6%, Focal Tonic (FT) in 17.6%, 5.9% had Focal Atonic (FA) seizure and 5.9% had post Ictal Paralysis (FP). 42.9 % of cases had a prolonged duration (>15 minutes) and remainder 57.1% had a seizure of less than 15 minutes duration (Table 3). A total of 2 cases (4.08%) had abnormal neuroimaging findings. Out of these 2 children, one had tuberculoma on CT and had prolonged focal convulsions and second child had focal cerebral oedema and had multiple episodes of generalised convulsions. There is no statistical significance of neuroimaging findings with type and duration of convulsion. All 49 patients whether with prolonged or short duration seizures, whether focal or generalized had a normal EEG. When comparing the number of complex features present, it was observed that there was no statistical significance between the number of complex features present and the age and sex distribution.

Table 1: Demographic Data

Age	Male N (Percent)	Female N (Percent)	Total N (Percent)
1-12	9(18.36)	8(16.34)	17(34.69)
13-36	19(38.77)	10(20.40)	29(59.18)
37-60	2(04.08)	1(02.04)	3(06.12)
Total	30(61.21)	19(38.78)	49 (100.0)

Table 2: Cause of Fever

Causes of Fever	N (Percent)
Acute Gastroenteritis	06 (12.24)
Otitis Media	02 (04.08)
Upper Respiratory Tract Infection	24 (48.98)
Viral	17 (34.69)
Total	49(100.0)

Table 3: Type of Convulsion Vs Age in Months

Variables		1-12 months N (Percent)	13–36 months N(Percent)	37–60 months N(Percent)	Total N(Percent)
Type of Convulsion	**Focal**	05(29.41)	11(37.93)	01(33.33)	17(100)
Focal (N=17)	**Focal Atonic (FA)**	0	01(3.44)	0	01(5.88)
	Focal Clonic (FC)	0	02(6.89)	01(33.33)	03(17.64)
	Focal Head & Eye Deviation (FHE)	03(17.64)	06(20.68)	0	09(52.94)
	Focal with Todds Paralysis (FP)	0	01(3.44)	0	01(5.88)
	Focal Tonic (FT)	02(11.76)	01(3.44)	0	03(17.64)
Generalized (N=32)	**Generalized**	12(70.58)	18(62.06)	02(66.66)	32(100.0)
Total		17(100.0)	29(100.0)	03(100.0)	

Table 4: Cause, Underlying Duration and Age

Cause		Age			
		1-12 months (Percent)	13–36 months (Percent)	37–60 months (Percent)	Total
Acute Gastroenteritis	**> 15 Min**	03(75.0)	01(50.0)	0	04(66.7)
	< 15 Min	01(25.0)	01(50.0)	0	02(33.3)
	Total	04(100.0)	02(100.0)	0	06(100.0)
Otitis Media	**> 15 Min**	0	01(50.0)	0	01(50.0)
	< 15 Min	0	01(50.0)	0	01(50.0)
	Total	0	02(100.0)	0	02(100.0)
Upper Respiratory Tract Infection	**> 15 Min**	03(50.0)	04(22.3)	0	07(29.16)
	< 15 Min	03(50.0)	14(77.7)	0	17(70.84)
	Total	06(100.0)	18(100.0)	0	24(100.0)
Viral	**> 15 Min**	02(28.57)	04(57.14)	03(100.0)	09(52.95)
	< 15 Min	05(71.43)	03(42.86)	0	08(47.05)
	Total	07(100.0)	07(100.0)	03(100.0)	17(100.0)

Discussion:

In our study maximum numbers of children who presented with first complex febrile seizure have been in the age group of 13 to 36 months, which is the peak age of febrile seizures. Winkler *et al* [17] in their study also have shown that 56.8% of children with febrile seizure have been in the age group of 13 to 36 months.

Family history of febrile seizure is not significant in our study as we have included only complex febrile seizure episodes. In other studies in which all the febrile seizures (both simple and complex) have been included, family history has been significant. Winkler *et al* [17] have shown that 11.1% patients had a family history of febrile seizure and 9% have had a history of epilepsy, 0.5% patients had both. Salehi *et al* [18] have shown that 25.7% patients had a positive family history for febrile seizure.

In our study, maximum numbers of children have convulsions at the onset of fever and 46% of children have a seizure in spite of receiving antipyretics at home. Dubé *et al* [19] have shown that cytokines released during the febrile illness are responsible for the seizure and not the presence of fever at the time of seizure. Berg *et al* [20] have also shown that maximum number of children (57%) have had seizures after 1 to 24 hours of fever.

The most common cause of fever in our study has been URTI followed by viral fever, AGE and otitis media. Esmaili *et al* [21], Mahyar *et al* [22] and

Kolahi *et al* [23], all of them have shown that URTI is the most common cause of febrile seizure. Khodapanahande [24] in his survey has found nonspecific viral disease as the main cause of febrile seizure. The cause of complex febrile seizure varied according to the age. AGE, URTI and OM were the underlying causes in children below 3 years of age whereas viral fevers lead to CFS in all age groups.

In our study hypocalcemia i.e. serum calcium level below 8.8 mg% has been found in 28% of cases, hence serum calcium levels should be done and treatment should be given if the levels are low. Akbayram *et al* [25] have noticed calcium to be lower in patients with febrile seizures whereas Amouian *et al* [26] have not found any correlation and have concluded that the test is not necessary in a case of febrile seizure.

In our study we have correlated underlying cause, neuroimaging and EEG findings with the type and duration of convulsion. 21 out of the 49 children had CFS of longer duration and 28 had CFS of shorter duration. There was no significant difference in the duration of CFS according to the underlying cause. Only 2 cases have had positive intracranial pathology. Kimia *et al* [14] in his study on neuroimaging in CFS have got positive intracranial pathology in 4 cases of 526(0.8%). Out of these 4 cases, 2 have had intracranial haemorrhage, one due to acute disseminated encephalomyelitis and the other due to focal cerebral edema. Teng *et al* [27] have not found any significant neuroimaging findings in the 71 patients he studied. Hardasmalani and saber [13] studied 71 patients and only 1 patient has been with abnormal CT scan finding of viral meningoencephalitis.

Among all the 49 cases we studied we have noticed that none of them had an abnormal EEG recording. Maytal *et al* [28] also have found no abnormality on EEG in the 24 patients of complex febrile seizure they studied. Yucel *et al* [29] have got 22.5% abnormal EEG within 6 days of CFS.

While comparing the investigation results with number of complex features present, we have found no statistical significance. Hence whether a CFS was focal in nature, prolonged duration i.e. more than 15 minutes, multiple episodes within 24 hours or had 2 or more of the above features, the diagnostic evaluation will remain the same.

Conclusion:

CFSs are common in the age group of 13 to 36 months. Family history is not significant in our study but it can be attributed to the small number of study subjects. Antipyretics which were taken for fever did not affect the chance of a seizure. Upper respiratory tract infection is the main cause of febrile seizure. The duration of CFS did not vary according to the underlying cause. Serum calcium levels are found to be lower in children with CFS. Children with prolonged focal and multiple generalised seizure had abnormal neuroimaging but it was not statistically significant. EEG findings are normal in all children with CFS. Hence we conclude from our study that a child with first CFS may not need EEG and neuroimaging as a diagnostic evaluation test. Also in a child with first CFS, hypocalcemia can be identified and corrected appropriately to stop the seizure. We would recommend to further study the risk of recurrent febrile seizures and chances of subsequent epilepsy in children with first CFS. We would also like to study the association of the above recurrences with single or multiple complex features. Further studies are needed on a large series of children with first CFS which will help to form guidelines for the diagnostic evaluation of children with first CFS.

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