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Cerebrospinal Fluid Findings in Children with Fever-Associated Status Epilepticus; Results of the Febrile Status Epilepticus (FEBSTAT) Study

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Abstract

This prospective multicenter study of 200 patients with fever-associated status epilepticus (FSE) patients of whom 136 had nontraumatic lumbar punctures confirms that FSE rarely causes cerebrospinal fluid (CSF) pleocytosis. CSF glucose and protein were unremarkable. Temperature, age, seizure focality, and seizure duration did not affect results. CSF pleocytosis should not be attributed to FSE.

Children with simple febrile seizures and fever-associated status epilepticus (FSE) are encountered commonly in pediatric practice and emergency medicine. Whereas conditions for performance of lumbar puncture and expected normal cerebrospinal fluid (CSF) findings are clear for simple febrile seizures, there are fewer data for CSF findings in FSE. We assessed CSF findings of children enrolled in a multicenter study of FSE [1] to clarify expectations for those in whom no CNS infection or other pathology was identified.

METHODS

In a prospective multicenter study examining the long term consequences of febrile status epilepticus (FEBSTAT), 200 children were enrolled at five participating centers (Montefiore Medical Center, Bronx; Children's Memorial Hospital, Chicago; Duke University Medical Center, Durham: Virginia Commonwealth University, Richmond and Eastern Virginia Medical School/Children's Hospital of The King's Daughters, Norfolk). Details of the recruitment, methodology, and the clinical features of the cohort have been published previously [1]. FSE was defined as a single seizure or a series of seizures without interim recovery lasting ≥30 minutes that otherwise met the definition of a febrile seizure (2,3) as defined as a provoked seizure where the sole identifiable acute provocation was fever

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(temperature >38.4°C, 101.0° F). The procedures were approved by the Institutional Review Boards for the Protection of Human Subjects at all participating institutions.

RESULTS

An LP was performed in 154 (77%) of the children at the discretion of the attending physicians. One hundred and thirty-six children had a non-traumatic LP (<1000 RBC), 116 (96.2%) of whom had 3 or fewer WBCs/ mm^3 (Figure).

Although mean temperature was not indicative, age, prior febrile seizures, duration of FSE, and focality were statistically significantly associated with the likelihood of receiving an LP in the emergency department (Table). Children who had an LP performed were younger than children who did not have an LP ($p<0.0001$), were less likely to have had a prior febrile seizure ($p=0.033$), and had a longer median duration of FSE ($p<0.001$). Focal FSE accounted for a higher proportion of LPs performed than generalized FSE ($p=0.03$). Furthermore, a higher proportion of children whose episode of FSE was definitely recognized as status epilepticus by the clinicians in the emergency department received an LP ($p=0.04$).

Mean CSF protein levels among 131 (96.3%) of the 136 children with a non-traumatic LP was 22 mg/dL, with values ranging from 8 mg/dL to 137 mg/dL. Twenty-nine percent of these children had protein levels of ≤15 mg/dL, 51.1% with ≤19 mg/dL, and 75.6% with ≤24 mg/dL. Only 3 (2.3%) children had CSF protein of >60mg/dL. There was insufficient evidence to suggest a statistically significant correlation between protein levels and seizure duration ($r = -0.017$, $p = 0.84$). Even after exclusion of one child with a seizure duration greater than 700 minutes and another child with a protein level of 137, the correlation, although slightly positive, did not reach statistical significance ($r = 0.09$, $p = 0.30$). Furthermore, we did not observe a statistically significant association between age at FSE (≤ 1 year vs. >1 year) and mean protein levels ($p=0.50$). The mean glucose level among 132 (97.1%) of the 136 children with nontraumatic LPs was 89.6 mg/dL with values ranging between 46 mg/dL and 201 mg/dL. Noteworthy was one 5 month old child who presented with suspected FSE and was subsequently excluded due to a positive CSF bacterial culture (admission CSF: 1 WBC/ mm^3, 0 RBC/ mm^3, glucose 93mg/dL, protein 17mg/dL).

DISCUSSION

CSF results from this large group of prolonged febrile seizure patients (FEBSTAT) were usually normal (96% had 5 or fewer WBC/ mm^3). The American Academy of Neurology practice parameter on the diagnostic evaluation of the child with status epilepticus supports the diagnostic utility of the LP (4). These data do not contradict the current approach to LP in the child with a simple febrile seizure and the emerging consensus that children with apparent simple febrile seizures, who otherwise appear well, are at low risk for serious infection (5,6,7). There is a growing consensus (7,8,9,10) that unexplained CSF pleocytosis after seizures in children should prompt a careful search for other possible medical explanations than simply being attributed to a ictal phenomena, a position clearly supported by our findings. Specific reports of CSF pleocytosis in children with SE of nonselective origin , both complex febrile seizures and status epilepticus, and children with simple febrile seizures (5,9,11) all support the impression that excess numbers of WBC in the CSF should not be dismissed as an ictal phenomena. In young infants, a higher degree of clinical suspicion may be needed even in the absence of a clear pleocytosis because they are recognized to be at greater risk for presentation with CNS infection showing minimal signs (5,8,10). This is also reflected in the American Academy of Pediatrics practice parameter for

the diagnostic evaluation of the child with a simple febrile seizure, which specifically excludes children under 6 months of age (6).

In a published "Clinical Prediction Rule" (10), the authors approached this topic from the perspective of abnormal CSF results and concluded that the occurrence of seizures with an abnormal CSF (10 or more WBC/mm^3) increased the risk for meningitis in children.

Fever associated SE is a medical emergency with potentially severe consequences. We confirm that CSF finding are usually normal in children with FSE. Abnormal CSF results should prompt close clinical scrutiny and additional tests and treatment as indicated. Normal CSF cell counts and chemistries, although expected and reassuring, do not eliminate the possibility of CNS infection, especially in the youngest patients.

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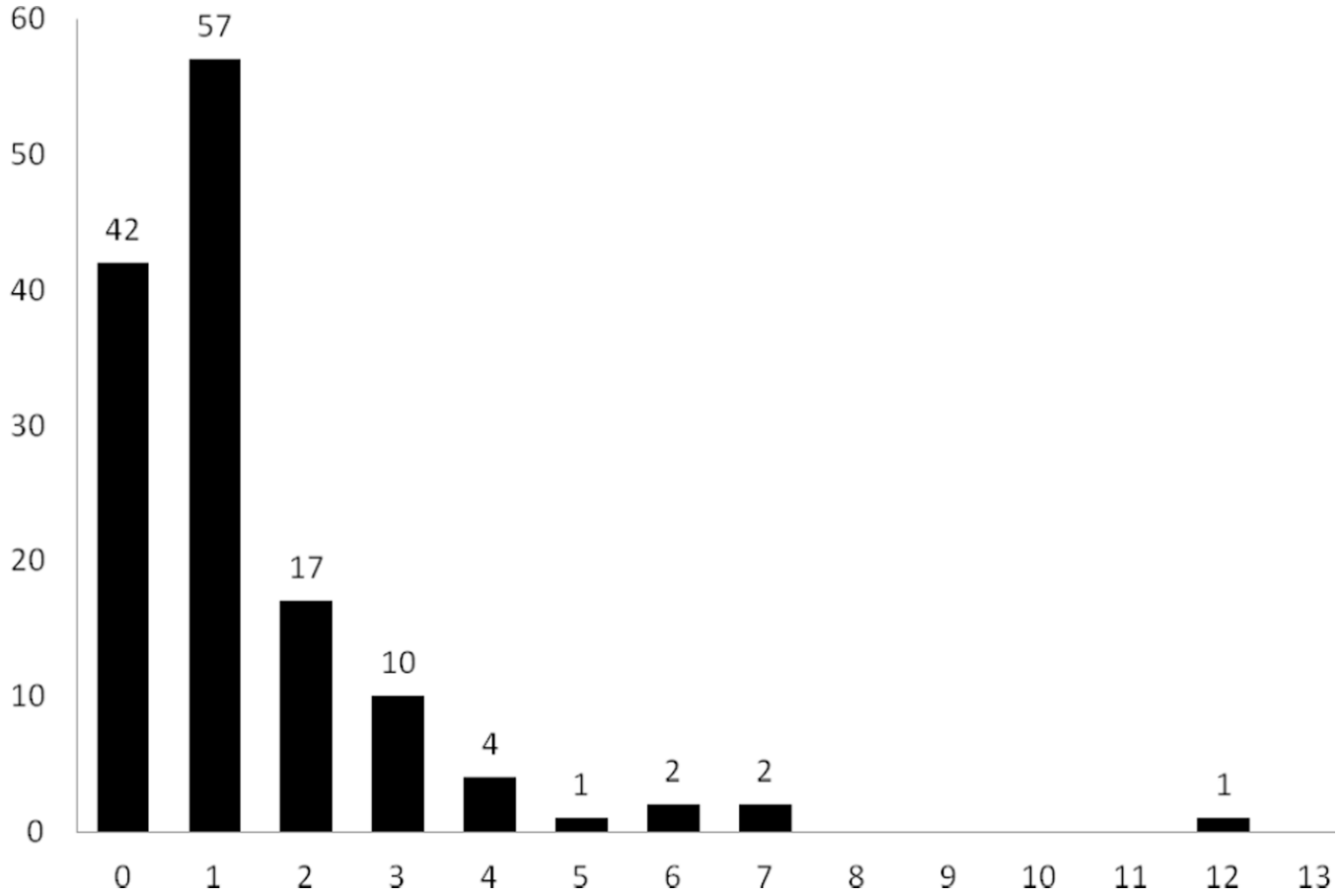

Figure.
Number of CSF WBCs/ mm^3 in 136 children with (FSE) with a nontraumatic lumbar puncture (<1000 RBC/ mm^3).
x axis = number of WBC/ mm^3, y axis = number of children

Table 1

Attributes of febrile status epilepticus (FSE) cases with and without a lumbar puncture (LP) at baseline

Variable	With LP (N=154)	Without LP (N=46)	Total (N=200)	p-value
Age at FSE				
Median age (months)	15 (IQR=11.0–21.0)	22.5 (IQR=16.0–35.0)	16 (IQE=12.0–24.0)	<0.0001
Age ≥ 18 months	55 (35.7%)	33 (71.7%)	88 (44.9%)	<0.0001
Prior febrile seizures	25 (16.6%)	14 (30.4%)	39 (19.5%)	0.033
Definite prior FSE	4 (2.6%)	3 (6.5%)	7 (3.5%)	
Possible prior FSE	3 (2%)	3 (6.5%)	6 (3%)	
Duration of FSE				
Median seizure duration (minutes)	79.5 (IQR=50.0–120.0)	53.5 (IQR=45.0–70.0)	70 (IQR 47.0–107.5)	<0.001
Duration ≥60 minutes	99 (64.3%)	20 (43.5%)	119 (59.5%)	0.012
Focal FSE				
Definitely	80 (52%)	22 (47.8%)	102 (51%)	0.03
Probably	28 (18.2%)	6 (13%)	34 (17%)	
Possibly	17 (11%)	1 (2.2%)	18 (9%)	
Definitely Generalized	29 (18.8%)	17 (37.1%)	46 (23%)	
Cerebral lateralization				
Definite	48 (31.2%)	13 (28.3%)	61 (30.5%)	0.71
FSE type				
Continuous	88 (57.1%)	27 (58.7%)	115 (57.5%)	0.45
Intermittent without recovery in between	46 (29.9%)	16 (34.8%)	62 (31%)	
Intermittent due to drug administration	20 (13%)	3 (6.5%)	23 (11.5%)	
FSE recognized by non-study clinicians				
Yes	109 (70.8%)	25 (54.4%)	134 (67%)	0.04
No	45 (29.2%)	21 (45.7%)	66 (33%)	
Temperature in the ED				
Mean temperature (°F)[1]	102.3 ± 1.8	101.8 ± 1.7	102.2 ± 1.8	0.16

Data are median (IQR), frequency (%), or mean ± SD.

[1]Missing information for 1 child.