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Functional status of children with encephalitis in an inpatient rehabilitation setting: A case series

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Abstract

Introduction—Patterns and predictors of recovery from encephalitis are poorly understood.

Methods—This study examined functional status and reviewed charts of all children who presented to a pediatric inpatient rehabilitation facility with encephalitis between 1996 and 2010. Functional status at admission and discharge from inpatient rehabilitation was evaluated using the Functional Independence Measure for Children (WeeFIM) Self-care, Mobility, Cognitive, and Total Developmental Functional Quotient scores (DFQ, % of age-appropriate function). Charts were reviewed to characterize key clinical features and findings.

Results—Of the 13 children identified, the mean age was 9 years (range 5–16) with 54% males. Mean WeeFIM Total DFQ at admission was 37 (range: 15–90) and at discharge was 64 (range: 16–96). Average change in WeeFIM Total DFQ from admission to discharge was 26.7 (range 0–55, $p < 0.001$). WeeFIM domain scores improved between admission and discharge (Self-Care: $p < 0.001$, Cognition: $p < 0.01$, Mobility: $p < 0.001$). Eleven children displayed significant impairments in functional skills, defined as DFQ of ≤ 85 , at discharge. Key clinical features and findings were diverse and not related to functional outcome.

Conclusions—Results suggest that significant functional improvement in children with encephalitis occurs during inpatient rehabilitation. Further research is necessary to identify predictors of outcome in children with encephalitis.

Keywords

Encephalitis; children and adolescents; functional independence measure; outcome; rehabilitation

Introduction

Encephalitis is acute inflammation of the brain parenchyma due to infectious and non-infectious (e.g., autoimmune) etiologies. Common clinical signs and symptoms at presentation include fever, headaches, altered mental status, seizures, and/or focal neurologic signs. Laboratory and imaging tests are useful for confirming the diagnosis of encephalitis. Common findings include cerebrospinal fluid (CSF) containing more than 5 WBC/ μ L, diffuse slowing on electroencephalogram (EEG), and T2 hyperintensities on magnetic resonance imaging (MRI).[1–3] Additionally, in some cases, CSF polymerase chain reaction studies can identify a viral agent responsible for the encephalitis.[4]

Identifiable etiologies of encephalitis include bacterial etiologies such as *Mycoplasma pneumoniae*, viral etiologies such as herpes simplex virus (HSV), varicella zoster virus (VZV), cytomegalovirus (CMV), Japanese encephalitis, and West Nile Virus (WNV), and fungal etiologies. In addition, immune-mediated forms of encephalitis have been identified, such as encephalitis associated with antibodies against NR1–NR2 heteromers of the N-methyl-D-aspartate (NMDA) receptor.[5,6] While extensive testing for these identifiable causes of encephalitis has reduced the proportion of encephalitis due to unknown etiology, the percentage of individuals with encephalitis due to unknown causes remains higher than any other single cause of encephalitis.[7,8]

Overall rates of encephalitis are low. In the general population, 0.3 to 0.5 per 100,000 individuals in the United States per year are affected. However, encephalitis occurs more frequently in children than adults, with an annual incidence of 10.5 cases per 100,000 children per year.[9] Because encephalitis is rare and varies by region and time period examined, few studies have examined prognosis and functional outcome, especially in children.

The clinical course of specific types of encephalitis of a known etiology are better described in the literature, including the course for *Mycoplasma pneumoniae*,[2] Japanese Encephalitis,[10] Herpes Simplex Encephalitis,[11] and West Nile Encephalitis.[12] More recently, the clinical course and outcome of Anti-NMDA receptor encephalitis has received considerable attention.[13–15] However, little information describing the clinical course and functional outcomes of the relatively high percentage of cases in which no etiology is discovered is available. In a recent study of children and adults, including a large group of individuals with encephalitis of unknown etiology, 40% of patients experienced long-term disability; the most frequent problems were difficulty concentrating, behavioral concerns, speech disorders, and memory loss.[16] Additionally, in a recent multicenter examination of subjects within the UK, cluster analysis revealed distinct groups based on symptoms and diagnostic features, rather than etiology.[17] These results suggest that separating patients by etiology may not be necessary to understand outcomes.

Very few studies have examined functional outcome of children with encephalitis who require inpatient rehabilitation. In a study of five adults with West Nile Virus who received inpatient rehabilitation, all patients demonstrated functional improvements.[18] In a case series of 7 adults and 1 child with viral or presumed viral encephalitis who participated in inpatient rehabilitation, all individuals displayed functional improvement but rate of recovery was variable.[19] The one pediatric patient had a low FIM score at admission (<30), and compared to the adults, the pediatric patient showed the most drastic improvement in FIM scores. Recently, a case series reported on the rehabilitation of six children with Anti-NMDA receptor encephalitis. All of these children made progress during inpatient rehabilitation, but all demonstrated persistent functional deficits at the time of discharge.[14] To date, the functional outcome of pediatric patients receiving inpatient rehabilitation for encephalitis of varying etiologies has not been reported.

In the pediatric traumatic brain injury (TBI) literature, several variables are associated with functional outcome at discharge from inpatient rehabilitation. Longer length of stay (LOS) and time to admission (TTA) are associated with worse functional outcome.[20,21] Younger age at injury is also associated with worse outcomes after TBI and other childhood brain injuries, [22–24] although not all studies consistently report this finding.[25,26] In children with encephalitis, the association between these variables and functional outcome at discharge from inpatient rehabilitation has not yet been explored.

There is also limited literature describing the relationship between acute clinical and neuroimaging findings and later functional outcome in children with encephalitis. Some studies suggest that specific early illness features, such as altered mental status and focal neurological deficits at the time of admission, duration of illness, and presence of seizures, are associated with outcome.[10,17,27]

Given the paucity of literature examining rehabilitation outcome in children with encephalitis, the aims of this study are to: 1) describe the functional outcome of children with encephalitis who presented to an inpatient rehabilitation unit; 2) identify patient variables associated with functional independence at discharge from inpatient rehabilitation; and 3) examine the key clinical features and findings that may be associated with functional outcome at discharge from rehabilitation. Based on outcomes from previous studies, the authors hypothesize that there will be significant functional improvement over the course of inpatient rehabilitation. Longer TTA, LOS, and younger age at the time of illness are expected to be associated with greater impairments in functional skills.

Methods

Procedure

Data were collected as part of routine clinical care and selected variables were entered into a program evaluation database. The Johns Hopkins University School of Medicine's Institutional Review Board (IRB) granted exempt status approval for a separate research database to be created for this study that was stripped of all patient identifiers and protected health information. The IRB approval also granted access to medical records. Medical record review was conducted to characterize key clinical features and findings, including the

clinical presentation of the patients and important neuroimaging, EEG, and CSF findings, as well as key therapeutic interventions.

Participants

Medical records of patients who were admitted to an inpatient pediatric neurorehabilitation unit between April 1996 and December 2010 were reviewed for a diagnosis of encephalitis. Data were collected from children between the ages of 3–18 years who were diagnosed with encephalitis and who were admitted to inpatient rehabilitation following their acute care hospitalization. All children underwent extensive infectious disease and immunological work ups at academic medical centers in the acute care setting and antibiotics and antiviral agents were initiated while results of the etiologic evaluations were pending. All children were residing in suburban areas at the time they became ill. All but one child were living in the Mid-Atlantic area at the time of illness (Maryland, Virginia, North Carolina). The one child who did not reside in the Mid-Atlantic area at the time of illness had previously lived in Maryland, but had moved to the West Coast just prior to becoming ill. There were no clear outbreaks of encephalitis in the region where the children resided during the time periods when the included children developed encephalitis. Children were excluded from the analyses if they had premorbid neurologic or psychiatric disorders or were admitted to another facility for their first inpatient rehabilitation admission following illness. Data were analyzed from children (n=13) who met the above criteria.

During inpatient rehabilitation, all children participated in comprehensive physical, occupational, and speech language therapy tailored to each individual's need with regard to functional skills. All children received a total of three hours of therapy each weekday and a shortened therapy schedule on one weekend day. In addition, neurobehavioral status was closely monitored by neuropsychology. Medical management was frequently required for seizures, sleep difficulties, and dysregulated behavior. Behavioral psychology services were also used, as needed, to optimize sleep and behavior. When appropriate, based on the child's cognitive functioning and anticipated length of stay of at least three weeks, educational services were provided on weekdays.

Measures

Functional Independence Measure for Children – Second Edition (WeeFIM)—

Functional outcomes were quantified using the Functional Independence Measure for Children – Second Edition (WeeFIM II, Uniform Data System for Medical Rehabilitation, Buffalo, NY), an 18-item performance-based instrument that assesses mobility, self-care, and cognitive abilities.[28] The WeeFIM has been validated in children with typical development [29] as well as in children with developmental disabilities and acquired brain injury.[30,31] While the WeeFIM was initially designed to describe levels of independence across typically developing children aged 6 months through 7 years,[29] it has been validated for use in adolescents with cerebral palsy up to age 16 years [32] and is commonly used to evaluate older children and young adults with development disabilities up to 21 years of age.[20,33,34] As part of routine clinical care WeeFIM ratings were obtained by each child's primary therapists at admission and at discharge.

Given the wide age range of children evaluated in the current study, WeeFIM Developmental Functional Quotients (DFQs) were calculated to obtain age corrected scores. Each WeeFIM item is rated on a scale from 1–7. The WeeFIM manual provides age-based normative scores that are used to calculate the DFQ. DFQs are calculated by dividing the child's raw score by the age-based normative scores and multiplying that number by 100 to reflect percent of “normal” or “age-appropriate” functioning, allowing comparison across age groups. An age appropriate DFQ is 100, but DFQs can range from 14 (for a child who receives scores well below age-based expectations) to greater than 100 (for a child who performs above the age-based expectations). DFQs were obtained for total score and self-care, mobility, and cognition domain scores.

Time from injury to admission (TTA)—This variable was defined as the total number of days from the onset of symptoms to admission to inpatient rehabilitation. Onset of symptoms was obtained through medical record review. Because children are typically transferred to rehabilitation when medically stable and able to benefit from rehabilitation, TTA is thought to be reflective of the period of medical instability.

Length of rehabilitation stay (LOS)—Length of rehabilitation stay was defined as the total number of days that a patient was admitted to inpatient rehabilitation and was obtained from the performance evaluation database. If a patient was transferred to an acute medical facility (e.g., due to medical instability or to undergo a surgical procedure) and then re-admitted to the unit continue rehabilitation under the initial treatment plan, the days the child stayed in the acute care setting during the transfer were not included in LOS. Of the 13 children in this series, one child was transferred back to acute care for two days, 16 days into the 72-day rehabilitation admission, due to a prolonged seizure.

Key Clinical Features and Findings—All available records, including limited acute care records that accompanied patient to inpatient rehabilitation, were reviewed. Information abstracted included description of presenting symptoms and neuroimaging, EEG, and CSF findings. Information obtained regarding the acute care stay included the need for cardiorespiratory support (intubation and/or use of vasopressors), the use of immune-modulating therapies (i.e., steroids, plasmapheresis, or IVIG), and medically induced coma to induce burst suppression or the ketogenic diet (as markers of intractable seizures). Evidence of hypotension during acute care (documentation of hypotension, support with vasopressors, or documented need for fluid boluses) was also abstracted. Anti-epileptic medications prescribed at discharge from inpatient rehabilitation were also noted as marker of persisting seizures.

Statistical analysis

All statistical analyses were completed using SPSS 20.0 (www.spss.com), and alpha was set at $p < 0.05$ for all analyses. Descriptive statistics were calculated to examine demographic and rehabilitation variables. Paired t-tests were used to examine differences in WeeFIM scores between admission and discharge. Bivariate correlation analyses were conducted to investigate relationships between age at onset, TTA, LOS, and discharge WeeFIM Total DFQ scores.

Exploratory analyses were conducted to examine other factors potentially associated with outcome. Because there were several children with and without seizures as a presenting symptom and data regarding presenting symptoms were available for all children, an independent sample t-test was used to examine difference in outcome between children presenting with and without seizures. An independent sample t-test was also used to examine difference in outcome between children who were and were not intubated during their acute care admission. In this small sample, the other clinical features, findings, and interventions that may have been associated with outcome were not examined statistically. Instead, data were examined qualitatively for any associations with best or worst functional outcome.

Results

Demographics and Rehabilitation Variables

The 13 children included in the study ranged in age from 5 to 16 years at the time of injury, with a mean age of 9 years. Seven children were boys (54%). While a clinical diagnosis of encephalitis was made by the acute care facility in all cases, a definitive etiology for the encephalitis was not obtained for nine of the participants (69%). Mean TTA from symptom onset was 47.2 days (range 14–82 days), and rehabilitation LOS ranged from 11–91 days with mean of 47.7 days. Demographic characteristics of the patients included in the study sample are presented in Table 1.

Each child's WeeFim DFQs from admission and discharge for total score, as well as the domain subscores (self-care, mobility, and cognition) are provided in Table 2. WeeFIM total, mobility, and self care scores improved between admission and discharge for all but one child. For the cognitive domain, in addition to the one child that did not improve across all domains, another child displayed a decline in cognitive skills. Two children (15%) had discharge WeeFIM Total DFQ score at or above 85 (within the normal range), four children (31%) had discharge WeeFIM Total DFQ scores between 84 and 70 (below age expectations) and seven children (54%) had discharge WeeFIM Total DFQ scores below 70 (well below age expectations).

Recovery of Functional Skills

Paired t-tests revealed significant improvement in functional skills between admission and discharge based on total and all subscale WeeFIM DFQs. Figure 1 displays the WeeFIM DFQ scores at admission and discharge.

Correlations between demographic and rehabilitation variables and WeeFIM outcomes

WeeFIM total DFQs at admission were significantly correlated with total DFQs at discharge. Admission and discharge WeeFIM total DFQ scores were inversely correlated with length of stay, as children who were more functionally impaired had longer lengths of stay. TTA and age at admission were not significantly correlated with admission or discharge WeeFIM Total DFQ scores. Correlations are provided in Table 3.

Exploration of key clinical features and findings

Table 4 provides details about presenting symptoms, neuroimaging, EEG, and CSF findings, as well as key treatment interventions for all thirteen children. Seizures were a common presenting feature occurring in nine of thirteen patients. All but one child had altered mental status as a presenting symptom. Eleven of thirteen patients had abnormal neuroimaging at some point after onset of illness. Eleven of twelve patients had abnormalities on EEG; for one patient EEG data were not available. For seven patients there were clear elevations in CSF white blood cells; CSF data were not available for three children. Eight children required intubation during their acute care hospitalization. Two patients were placed in a medically induced coma to manage seizures. Only one child (subject #11) had evidence of hypotension. All but three children (subjects # 1, 2, 12) were taking anti-epileptic medication at the time of discharge and outcomes for the three children who were not prescribed anti-epileptic medication at discharge from rehabilitation were mid-range (DFQ=70, 59, 75 respectively).

Exploratory Analyses

Children with and without seizures at presentation to acute care displayed differences in outcome only for the cognitive subscale of the WeeFIM. Specifically, results revealed that children presenting with seizures had significantly lower cognitive DFQ scores at discharge than children without seizures [Children with seizures, $n = 9$, mean = 42.7 (sd = 18.7), Children without seizures, $n = 4$, mean = 75.3 (sd = 11.8), $t = 3.17$, $p < 0.01$].

There were no significant differences between children who were and were not intubated during acute care in functional outcome at discharge. Inspection of other key clinical features including presenting symptoms, neuroimaging, EEG, CSF, and other treatment interventions did not reveal any clear associations between these features and best or worst rehabilitation outcome.

Discussion

To sum, this study sought to describe the functional outcome of children with encephalitis who required inpatient rehabilitation. As hypothesized, children made significant gains in functional skills over the course of rehabilitation. The authors also attempted to identify patient variables associated with functioning at discharge. As expected, it was found that longer LOS was associated greater functional impairment at discharge. TTA and age at admission, however, were not associated with outcome.

Improvement in functional skills suggests that inpatient rehabilitation is appropriate for many children who have sustained functional declines after encephalitis. These findings are similar to the report by Houtrow and colleagues who examined functional outcome in six children with diagnosed Anti-NMDA receptor encephalitis (14). In their cohort, however, it appears that functional status at admission was very poor for all of their patients, whereas in the current study there was much more variability at admission. Despite that variability, most children in this cohort made significant functional gains over admission. Most, however, remained impaired (DFQ = 85) upon discharge.

In this study's cohort, two of the thirteen children did not display functional improvements between admission and discharge from inpatient rehabilitation. One child (subject #6) did not make any functional gains as measured by the WeeFIM. This child's WeeFIM scores were extremely low at admission. Low score at admission, however, did not necessarily translate to poor functional gains, as four other children were admitted with similar level of functional impairment and all of these children showed improvement in functioning by discharge of the magnitude captured by the WeeFIM. Another child (subject #4) had a decline in the cognitive domain between admission and discharge, but showed recovery in the other two domains. Qualitatively, as the child's motor skills improved, extreme impulsivity and perseveration was observed. He displayed aggression and attempted to escape therapy sessions. This extreme level of behavioral dysregulation impacted his scores on the cognitive domain of the WeeFIM, including his ability to problem solve and interact well with others.

As expected, greater LOS at the rehabilitation facility predicted poorer functional status at admission and discharge, as children with more functional impairments often require more time in rehabilitation. TTA, a marker for length of medical instability, however, was not associated with outcome. This finding differs from the results commonly found in children with TBI where TTA is associated with functional outcome.[20,21] It is unclear if the lack of a significant correlation is because TTA is not an important variable in children with encephalitis or if it is because of the limited power of this small sample. Additionally, collecting accurate TTA data for this population was challenging because symptoms are often present but unrecognized in the days, and sometimes weeks, prior to admission. Importantly, the one child who did not improve (subject #6) had the longest TTA and LOS.

Also, in contrast to the literature on pediatric brain injury,[22–24] age at the time of illness was not associated with functional outcome at discharge. This current dataset, however, is limited due to not only the small sample size, but also the restricted age range between 5 and 16 years. In some studies of pediatric TBI, younger age at injury is more likely to result in greater impairment when including children injured before school-age.[22] Further studies including children who develop encephalitis very early in life are needed to further explore the impact of age.

Exploratory analyses revealed that children with seizures at presentation had worse cognitive outcomes than children without seizures at presentation. This is consistent with previous reports suggesting that early seizures are associated with worse outcome in individuals with encephalitis.[27] Interestingly, children presenting with seizures were not significantly different in self-care and motor outcomes, suggesting that early seizures may impact outcome of cognitive skills more than motor and self-care skills. Use of anti-epileptic medication, a marker for persisting seizures, did not appear to be related to cognitive outcome across the entire group; however, the two children taking the most anti-epileptic medications at discharge from inpatient rehabilitation (three medications each) did have very low cognitive DFQ scores at discharge, suggesting that seizure severity and/or sedation effects of multiple anti-epileptic medications may have attenuated functional outcome.

Inspection of other key clinical features and findings, including presenting symptoms, neuroimaging, EEG, CSF, and other treatment interventions, did not reveal any clear associations between these features and rehabilitation outcome. Almost all children in our study had abnormalities on neuroimaging. Neuroimaging for subject #6 (the child who did not improve) revealed diffuse cerebral atrophy with relative sparing of the cerebellum and brainstem. Two other children, however, who made notable gains, also displayed global volume loss on imaging. The extent of volume loss is not clear from the records, and it is possible that subject #6 had more extensive atrophy. Similarly, EEG findings were not associated with outcome. In fact, the one child with a normal EEG had the worst outcomes. It is possible that the child had later EEGs that were abnormal, but no additional EEGs were described in the medical record.

The findings of this study need to be considered in the context of several limitations and should be considered preliminary. First, the sample size is small and the patient group heterogeneous, making it difficult to draw conclusions. Second, these data were collected retrospectively by chart review and the details of the acute care stay were limited. Specifically, important variables that might impact outcome such as altered mental status at presentation were not assessed in a consistent manner. Additionally, detailed records of the acute care status and interventions were not available. Also, several key features, such as ICU length of stay, which may be associated with outcome, were not available for all subjects. In addition, given that all children were admitted to one rehabilitation center, the results might not generalize to other facilities or regions of the country.

Conclusion

In conclusion, children with encephalitis who warrant inpatient rehabilitation show significant functional gains over admission, but the degree of recovery from encephalitis is variable across children. Despite recovery over admission, most children displayed significant impairment in functional outcome at discharge, highlighting the need for ongoing intervention after discharge. Few variables were found to be predictive of outcome. Further research with a larger group of children is necessary to more fully describe recovery following encephalitis in children and to identify predictors of functional outcome following childhood encephalitis. Additionally, with recent advances in diagnosis and treatment for encephalitis, functional outcomes should be re-examined in an updated cohort. Although preliminary, these analyses are nevertheless an important step towards understanding the recovery of children with encephalitis.

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Figure 1.
Mean WeeF IM DFQ Scores at Admission and Discharge (n = 13)
**p< 001, *p<01

Table 1

Patient Characteristics

Subject	Presumed Diagnosis	Age at Admit	Gender	TTA	LOS
1	<i>Unknown etiology</i>	9.46	Female	14	29
2	<i>Unknown etiology</i>	5.10	Female	29	56
3	<i>Unknown etiology</i>	8.74	Female	46	49
4	<i>Unknown etiology</i>	9.15	Male	61	29
5	<i>Unknown etiology</i>	8.74	Female	15	32
6	<i>Unknown etiology</i>	6.32	Female	82	91
7	<i>Unknown etiology</i>	15.90	Male	62	26
8	<i>Unknown etiology</i>	5.85	Male	28	32
9	<i>Influenza B</i>	14.17	Female	73	85
10	<i>Anti-NMDA receptor encephalitis</i>	7.84	Male	62	60
11	<i>Unknown etiology</i>	8.38	Male	54	72
12	<i>West Nile Virus</i>	5.96	Male	25	48
13	<i>Presumed Mycoplasma</i>	13.82	Male	63	11

Table 2

WeeFIM DFQ

Subject	Total		Self Care		Mobility		Cognition	
	admission	discharge	admission	discharge	admission	discharge	admission	discharge
1	15	70	14	71	14	77	17	60
2	17	59	16	57	14	60	21	63
3	16	67	14	77	20	80	14	37
4	56	64	57	73	57	77	51	37
5	79	90	82	96	97	97	54	71
6	16	16	17	18	14	14	16	15
7	63	76	66	73	66	89	54	69
8	35	71	35	77	49	82	21	48
9	26	65	27	71	20	57	31	63
10	18	34	23	34	14	49	15	21
11	22	51	18	55	37	60	14	34
12	34	75	23	63	47	91	36	76
13	90	96	95	96	91	100	91	96

Table 3

Correlations with functional status at discharge (n = 13)

	Admission WeeFIM Total DFQ	Discharge WeeFIM Total DFQ
Admission DFQ		.71 **
Age	-.30	.20
Time to admission	-.01	-.49
Length of stay	-.69 **	-.78 **

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Table 4

Key Clinical Features and Findings

Subject	Presenting symptoms	Key neuroimaging*	Key EEG	Key CSF (and other laboratory findings)**	Additional Intervention	Anti-Epileptic Medication at Rehab Discharge
1	Headache, then generalized seizure, altered mental status	2 days post-admission (MRI): Swollen gyri in the frontal and temporal lobes, T2 hyperintensities in bilateral basal ganglia, bilateral thalami, and left cerebral peduncle	2 days post-admission: Diffuse slowing	Admission: WBC 23	None	None
2	Fatigue, headache, emesis, then weakness and mental status changes	1 day post-admission (MRI): T2 hyperintensity of the cerebellum	Within first 2 weeks after admission: Diffuse slowing	Admission: WBC 1135, RBC 875; (Nasal swab: + metapneumovirus)	Solumedrol	None
3	Fever and emesis, then generalized seizure, altered mental status	Within 1 week post-admission (MRI): Inflammation mostly affecting the left temporal lobe with additional involvement in the right occipital, right temporal, and left frontal areas	Continuous EEG monitoring days 6-17 after admission: Left frontal spikes	CSF data unavailable; (Serum: + EBV IgG)	Intubated, Thiopental burst suppression, IVIG, Steroids	Phenobarital, Topamax, Keppra
4	Fever, vomiting, headache, abdominal pain, then generalized seizure, altered mental status	1 week post-admission (MRI): Edema in the amygdala and hippocampus consistent with findings of limbic encephalitis; 2 months post-admission: Bilateral hippocampal atrophy	Day of Admission: Diffuse slowing with frontal intermittent rhythmical delta activity (HirDA); 2 months after admission: Bilateral spikes and intermittent slowing	6 days post-admission: WBC 0	Intubated	Keppra, Depakote
5	Sore throat, fever, malaise, headache, then generalized seizure	5 days post-admission (MRI): Diffuse hyperemia of the cerebrum with multiple small foci of T2-prolongation	Within first week post-admission: Unilateral spikes, diffuse slowing	Day of admission: WBC 45, RBC 139, protein 79	Intubated	Tegretol
6	Generalized seizure, altered mental status	1 day post-admission (MRI): Diffuse atrophy of the cerebrum with relative sparing of the cerebellum and brainstem	Day of admission: Normal prolonged EEG	Day of admission: WBC 1	None	Keppra, Depakote
7	Focal seizure, altered mental status	2 months post-admission (MRI): No abnormalities noted	2 months post-admission: Diffuse slowing with intermittent focal slowing in the left frontotemporal area	2 weeks post-admission: WBC 12	Intubated, Methylprednisone (high dose)	Dilantin

Subject	Presenting symptoms	Key neuroimaging*	Key EEG	Key CSF (and other laboratory findings)**	Additional Intervention	Anti-Epileptic Medication at Rehab Discharge
8	Generalized seizure, altered mental status	3 weeks post-admission (MRI): No abnormalities noted	1 day post-admission: Focal slowing on the left; 10 days post-admission: Diffuse slowing	1 day post-admission: WBC 22	Solumedrol	Dilantin, Tegretol
9	Fever then generalized seizure, altered mental status	2 weeks post-admission (MRI): Generalized cerebral edema with mild enhancement of the hippocampi	2.5 months post-admission: Subtle bifrontal or diffuse slowing intermittently	Day of admission: WBC 1, RBC 1800	Plasmapheresis, IVIG, Intubated, Pentobarbital for burst suppression, Solumedrol, Ketogenic diet	Dilantin, Phenobarbital
10	Headache, then generalized seizure, then progressive agitation/aggression	1 month post-admission (MRI): Mild global volume loss	1 day post-admission: Right frontal slowing; 6 days post-admission: Right-sided spikes and slowing and secondary generalized seizure discharges	1 day post-admission: WBC 14	Intubated, Steroids, Plasmapheresis, IVIG	Kepra, Valium
11	Fever, then generalized seizure, altered mental status	1.5 months post-admission: Moderate global atrophy, symmetrical atrophy of hippocampal gyri but no sclerosis of the temporal lobes	Continuous EEG of first 3 weeks of admission: Consistent with seizure disorder of widespread origin (focal and generalized characteristics); 2 months post-admission: Rhythmic and semi-rhythmic bilateral, anterior maximal slow and sharp-and-slow waves, intermittent diffuse slowing	Day of admission: WBC 17, RBC 263	Intubated, Pentobarbital for burst suppression, Ketogenic diet, Solumedrol, vasopressor support	Topamax, Kepra, Phenobarbital
12	Rash and fever, then headache and vomiting, then fatigue/agitation	Day of admission (CT): Edema of medial right basal ganglia and anterior thalamus, right thalamic and 2 cerebellar lesions	none	Unknown	Intubated, Steroids	None
13	Cognitive/behavioral changes	Day of admission (MRI): Leptomeningeal enhancement over parietal cortex and posterior fossa	2 days post-admission: Diffuse slowing with intermittent 2-3 sec runs of sharp and slow waves predominant (asymmetrical)	Unknown	IVIG	Tegretol

* Earlier neuroimaging studies, if not commented on in this table, were normal

** Findings are CSF data, unless otherwise stated

WBC=CSF white blood cell count (per cubic millimeter)

RBC=CSF red blood cell count (per cubic millimeter)

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