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Pediatric Rehabilitation Outcomes in Severe Neuroinvasive Powassan Virus Infection: A Case Series

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Abstract

Objective: This case series describes the presentation, clinical course, and functional outcomes of four pediatric patients with neuroinvasive Powassan virus infection who were admitted to inpatient rehabilitation with severe neurologic impairments.

Design/Methods: Retrospective case series.

Results: Inpatient rehabilitation treatment resulted in functional improvement across all patients with the most consistent gains noted in cognitive functions, including comprehension and social interaction. Younger age at time of infection was associated with delayed-onset seizure disorder, more severe impairment, and worse long-term outcomes. Older patients demonstrated a movement disorder predominant phenotype and faster return to community-based activities.

Conclusion: As cases of pediatric neuroinvasive Powassan virus cases rise, physiatrists in endemic areas should be prepared to recognize associated neurologic patterns and rehabilitation trajectories.

Keywords: Powassan virus, Case report, Pediatric encephalitis, Rehabilitation outcomes

Introduction

Powassan virus is a rare neuroinvasive arbovirus that is endemic to the Northeast and Great Lakes regions of the United States, as well as parts of Canada and eastern Russia [1]. Severe infections in adults are associated with seizures, cognitive impairment, and a 10% fatality rate [2]. Due to the rarity of infection, there are limited reports on pediatric cases, and to date, there are no detailed accounts of inpatient rehabilitation outcomes of this patient population, which limits clinicians' ability to guide prognosis and family counseling. Furthermore, increasing survivorship is resulting in more patients presenting for inpatient rehabilitation (IPR) treatment. Thus, there is a need to improve general awareness of the condition and expected medical complications, describe typical associated functional impairments, and detail long-term prognoses. In this case series, we describe the course of care of four Caucasian, non-Hispanic, previously healthy female children who completed IPR for neurologic impairments acquired following neuro-invasive Powassan virus infection (**Table 1**). Parental verbal consent was obtained for inclusion in this case series.

Table 1. Pediatric functional independence measure (WeeFIM) scores at inpatient rehabilitation facility admission (AD) and discharge (DC).

	Case 1		Case 2		Case 3		Case 4	
	AD	**DC**	**AD**	**DC**	**AD**	**DC**	**AD**	**DC**
Self-Care Subtotal	8	24	8	8	8	8	8	8
Eating	1	3	1	1	1	1	1	1
Grooming	1	2	1	1	1	1	1	1
Bathing	1	2	1	1	1	1	1	1
Upper body dressing	1	3	1	1	1	1	1	1
Lower body dressing	1	1	1	1	1	1	1	1
Toileting	1	2	1	1	1	1	1	1
Bladder	1	5	1	1	1	1	1	1
Bowel	1	6	1	1	1	1	1	1
Mobility Subtotal	5	17	5	5	5	5	5	5
Transfer: Chair	1	4	1	1	1	1	1	1
Transfer: Toilet	1	4	1	1	1	1	1	1
Transfer: Tub	1	3	1	1	1	1	1	1
Walk	1	4	1	1	1	1	1	1
Stairs	1	2	1	1	1	1	1	1
Cognition Subtotal	6	22	5	6	5	7	5	5
Comprehension	2	4	1	2	1	2	1	1
Expression	1	5	1	1	1	1	1	1
Social	1	4	1	1	1	2	1	1
Problem	1	4	1	1	1	1	1	1
Memory	1	5	1	1	1	1	1	1
Total Score	18	63	18	19	18	20	18	18

Case 1

An 11-year-old female presented with generalized tonic-clonic seizure after six days of fever and gastrointestinal symptoms. There were no known tick exposures. Lumbar puncture (LP) found pleocytosis and elevated opening pressure. Cerebrospinal fluid serologic testing confirmed Powassan virus infection. Vitamin 25OH-D level was low (22 ng/mL). Magnetic resonance imaging (MRI) of the brain showed abnormalities in bilateral basal ganglia, right thalamus, and bilateral parietal-temporal lobes. She was treated with 5-days of high dose methylprednisolone, 2 doses intravenous immunoglobulin (IVIG), and 4-week enteral steroid taper. Electroencephalography (EEG) studies found generalized attenuation of faster frequencies in the right hemisphere without breakthrough epileptiform activity. She was discharged to inpatient rehabilitation facility (IRF) after 15-day hospitalization.

At IRF admission, she was nonverbal with impairments in receptive communication, processing speed, memory, and problem solving. She was admitted on a regular texture diet. She required assistance in mobility and self-care activities, including eating, grooming, toileting, and bathing due to right-dominant hemiparesis. She had an abnormal, circumducted gait pattern limiting ambulation endurance. After a 16-day inpatient rehabilitation program, she had regained verbal communication, improved self-care function to supervision assistance, and was ambulating >1,500 feet in a single session. She completed her steroid taper and discontinued seizure prophylaxis. She transitioned to outpatient physical, occupational, and speech therapy at discharge.

At five-year-follow-up, she is doing well and excelling academically with support from an individualized education plan (IEP). Her post-hospitalization course is notable for ongoing difficulties with inattention for which she was trialed

on multiple agents. Her most recent exam was without focal deficits and neuropsychological evaluation found intellectual ability in low average range with weaknesses in attention, working memory, and processing speed.

Case 2

A five-year-old presented with three days of high fevers (Tmax 39.4°C), neck pain, gastrointestinal symptoms, and left hemiparesis. Parents reported tick bite approximately two weeks before presentation. Workup found elevated inflammatory markers including positive lupus anticoagulant, low protein C (also known as autoprothrombin IIA and blood coagulation factor XIV), and mild lymphocytic pleocytosis on lumbar puncture. Serum Powassan virus IgM and plaque reduction neutralization test (PRNT) were positive. Brain MRI showed bilateral asymmetric basal ganglia edema with multifocal regions of diffusion restriction affecting bilateral thalami, right amygdala, hippocampus, and splenium. EEG showed frequent right occipital discharges with clinical seizures; she completed 8 weeks of prophylactic levetiracetam. She was treated with 3-days of high dose methylprednisolone followed by 12-week enteral steroid taper and supplementation for vitamin D deficiency (level 25.7). Acute hospitalization was 42-days in duration.

At IRF admission, she exhibited neurologic impairments affecting cognition, communication, mobility, fine motor skills, and feeding. Cognitively, she was awake and could follow simple commands. She demonstrated profound oral-motor impairments that resulted in near mutism and required a nasogastric tube for nutritional supplementation. She had impairments in auditory comprehension, motor speech production, memory, attention, and problem solving. She was dependent for all self-care and mobility activities, including wheelchair skills. Additional rehabilitation concerns included severe focal dystonia affecting the left lower extremity, oral-facial dyskinetic movement disorder, and urinary retention. After 58-day IRF treatment, she regained verbal communication and oral feeding. Auditory comprehension also returned to age-appropriate function. She had persistent deficits in emotional regulation and inattention which were treated with clonidine and methylphenidate, respectively. She was ambulating up to 750 feet with contact guard assistance. Dystonia improved and diazepam was weaned. Oral-fascial dyskinesis was controlled with tetrabenazine. Urinary retention self-resolved. She continued with outpatient physical, occupational, and speech therapy at discharge.

At 4-year follow-up, she is doing well and returned to school with IEP supports. Her post-IRF course is notable for interval development of generalized chorea, anxiety disorder with panic attacks, and perseverative behaviors. She remains on dexmethylphenidate and clonidine for inattention and mood regulation.

Case 3

A 24-month-old presented following several weeks of daily fevers (Tmax 38.5°C), urinary retention, and language regression. She was intubated for acute decline in mentation. Lumbar puncture showed pleocytosis with hyperproteinorachia and serologic testing confirmed Powassan virus infection. Brain MRI found abnormalities affecting bilateral basal ganglia, thalami, midbrain, medial temporal lobes, and cerebellum. EEG showed global slowing without epileptiform activity, and she was started on levetiracetam for seizure prophylaxis. She was treated with 5-days methylprednisolone and 3-days IVIG. Her 77-day acute hospitalization was complicated by autonomic dysregulation with episodes of central fever, tachycardia, and diaphoresis; spastic dystonia treated with multiple enteral agents and botulinum toxin injections; and severe dysphagia with aspiration pneumonia for which she had gastrostomy placement.

At IRF admission, she presented in a disorder of consciousness state and severe spasticity affecting bilateral lower extremities. Chemodenervation procedure using 10 units per kilogram-body-weight of onabotulinumtoxinA 10 units/kg to bilateral ankle plantarflexors and knee flexors resulted in minimal improvements in functional passive range of motion and the knees and ankles. Approximately 40 days into the IRF course, she had clinically emerged from a minimally conscious state with improvements in state regulation, gross motor skills, and nonverbal communication.

During the IRF admission, she then developed episodes of horizontal gaze deviation with tonic limb movements which prompted transfer back to acute care. EEG found greater than 100 seizures/day with concern for a Lennox-Gastaut background. She was briefly stabilized and return to IRF, but was quickly readmitted to acute care for persistent breakthrough seizures and intermittent breath-holding spells with associated desaturations, and ultimately discharged to the community following medical stabilization.

At 2-year follow-up, steady functional gains have been achieved in gross and fine motor skills, receptive communication, nonverbal expressive communication, and feeding. She continues to undergo serial onabotulinumtoxinA chemodenervation procedures and she has been noted with post-procedure improvements in passive and active range of motion, decreased pain, and improved tolerance for bracing and supported-standing. She is using an eye-gaze augmentative communication device to express her wants and needs in full sentences. Current medical concerns include urinary retention requiring clean intermittent catheterization and treatment for recurrent urinary tract infections. She is also pending surgical fixation for interval development of neuromuscular scoliosis.

Case 4

A 30-month-old who presented with 3 days high-grade fevers (Tmax 41°C), dyscoordination, and somnolence. LP found lymphocytic pleocytosis and serologic testing confirmed Powassan virus infection. MRI Brain showed cytotoxic and vasogenic edema diffusely in the deep gray matter, bilateral cortex, brainstem, and cerebellum. EEG showed status epilepticus for which she was loaded with multiple antiepileptic agents followed by maintenance levetiracetam (60 mg/kg/day). She was treated with 5 days high-dose IV methylprednisolone, 2 doses IVIG, and 4-week enteral steroid taper. Her 36-day acute care course included neuroirritability, hypertonicity, and oropharyngeal dysphagia with nasogastric tube dependence.

At IPR, she was oriented to self but neuroirritability was functionally limiting and she was dependent in communication, swallow, mobility, and self-care. Following 31 days of IRF treatment, she returned to acute hospital for planned gastrostomy tube placement. Her post-operative course was complicated by new rhythmic movements and subsequent EEG found >600 tonic seizures/day. She had prolonged post-operative acute hospital course to achieve seizure stabilization.

Following prolonged post-operative acute hospitalization to achieve seizure control, she returned to complete an additional 28-day IRF treatment (59 days total). At IRF discharge to community, she remained dependent across all functional domains but had achieved improvements in arousal and state

Table 2. Summary of four pediatric patients with neuroinvasive Powassan virus infection who were admitted to inpatient rehabilitation.

	Age	Presentation	Key MRI Findings	IRF treatment	Follow-up outcome			
					Communication	Feeding	Mobility	Academics
Case 1	11 yrs	6-days of fever and gastrointestinal symptoms with generalized tonic-clonic seizure	Abnormalities in bilateral basal ganglia, right thalamus, and bilateral parietal-temporal lobes	16 days	Verbal	Full oral feeder	Independent ambulator	Returned to streamlined school with IEP
Case 2	5 yrs	3-days of fever, neck pain, gastrointestinal symptoms, and left hemiparesis	Bilateral basal ganglia edema with multifocal diffusion restriction affecting bilateral thalami, right amygdala, hippocampus, and splenium	58 days	Verbal	Full oral feeder	Independent ambulator	Returned to streamlined school with IEP
Case 3	2 yrs	Several weeks of daily fevers, urinary retention, and language regression	Abnormalities affecting bilateral basal ganglia, thalami, midbrain, medial temporal lobes, and cerebellum	40 days and readmitted to acute hospital for seizures	Nonverbal expression with eye-gaze AAC device	Limited oral tastes, otherwise GT dependent	Maximal assistance for short-distance ambulation, Dependent wheelchair user	School-based services with IEP
Case 4	2.5 yrs	3-days fevers, discoordination, and somnolence	Cytotoxic and vasogenic edema diffusely in the deep gray matter, bilateral cortex, brainstem, and cerebellum	59 days with prolonged interval acute hospitalization for GT placement and seizure management	Nonverbal expression choice communication board	2 puree meals daily with GT supplementation	Maximal assistance for standing, dependent wheelchair user	School-based services with IEP

regulation and was consistently tracking in both visual and auditory domains. She also achieved improvements in oral-motor skills and was participating in pureed solids trials. In motor skills, she was participating in hand-over-hand sensory play and participating in ambulation trials with 2-person assistance.

At 1-year following incident infectious illness, she experienced severe dystonic crisis, interval worsening of startle-induced myoclonic seizures, and significant functional decline for which she required repeated acute hospitalizations. Following multidisciplinary consultation with pediatric neuro-immunology and rheumatology, she was started on monthly maintenance IVIG infusions, which she has tolerated well, and has subsequently regained multiple functional skills.

At 2-year follow-up, she is using an augmentative communication device to express basic wants and needs, has replaced up to 2 tube feeds per day with meals by mouth, demonstrates increased functional use of upper extremities including hand-over-hand self-feeding, and is moving short-distances independently through crawling.

Discussion

The current report describes 4 previously neurotypical children who experienced significant neurologic and functional impairment due to neuroinvasive Powassan virus infection and were subsequently treated in an inpatient rehabilitation program. Overall, this group of patients is notable for its femaleness and bimodal distribution with respect to age, seizure disorder, and long-term outcomes.

This case series is notably female, particularly given that previous reports on adults with Powassan virus infection are predominantly male [3]. While a retrospective review of pediatric seronegative acute disseminated encephalomyelitis (ADEM) also reported higher rates in males, higher rates of neurologic complications including seizures and hemiparesis were noted among in female individuals [4]. Furthermore, studies on gender disparities in immunologic responses have found expression of inflammatory markers are higher in female children [5]. Therefore, while reported community rates of Powassan virus infection are higher in males, the preponderance of females in this case series of patients who required IRF admission for neuroinvasive Powassan virus infection may reflect gender differences related to inflammatory response.

In this cohort, younger age was associated with delayed presentation of a severe seizure disorder. Age effects on seizure risk are well described in animal studies in which structural brain immaturity is relatively proconvulsant, or more likely to seizure in response to trauma, fever, and infection [6]. Extensive cytotoxic injuries likely amplified seizure risk in these patients further increases future seizure risk. The delayed seizure disorder observed in the younger patients may reflect secondary brain injury, particularly affecting the hippocampus, incurred during the prolonged period of acute medical illness in younger patients. These findings also align with previous reports which find increased seizure burden is associated with less favorable outcomes in pediatric encephalitis [7]. The increased medical supervision provided in IPR may be especially beneficial for younger patients with viral encephalitis as timely diagnosis and intervention of delayed seizure conditions reduces secondary brain injury and maximize neurorehabilitative potential.

Older children showed faster motor recovery but persistent executive function deficits, echoing trends seen in pediatric traumatic brain injury [8] and viral encephalitis [9]. Conversely, younger patients not only experienced more severe acute disease but are also at higher risk of delayed-onset epilepsy and prolonged functional dependence. This aligns with a growing literature demonstrating early brain injury irreparably disrupts neuronal maturation [10], resulting in higher rates of intellectual disability and neurologic impairments among individuals who sustain significant brain injury at younger ages. As a result, early neuropsychological evaluation and IEP establishment are essential for these individuals to achieve school integration. Notably all four patients in this case series have returned to school with varying levels of support provided through an IEP.

Advancements in medical management have increased survival following previously fatal pediatric brain conditions, resulting in increasing pediatric survivors presenting for pediatric inpatient rehabilitation. Medical rehabilitation treatment for rare neurorehabilitation conditions, like neuroinvasive Powassan virus infection, is generally extrapolated from experiences established in pediatric severe traumatic brain injury and stroke. The current case series provides Powassan virus encephalitis specific considerations with respect to degree of neurologic impairments, rehabilitation outcomes, and medical complications. In particular, this case series demonstrates that for individuals with new functional impairments in the setting of Powassan virus infection, a course of inpatient rehabilitation is beneficial for: 1) decreasing neurologic impairment, 2) optimizing spasticity and dystonia management, 3) providing family education on long-term seizure vigilance, and 4) facilitating transition back to the community with in-home and outpatient rehabilitation resources.

Competing Interests

The authors have no conflicts of interest relevant to this article to disclose.

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