Movement Disorders
CLINICAL PRACTICE

CASE SERIES

Spectrum and Evolution of Movement Disorder Phenomenology in a Pediatric Powassan Encephalitis Case Series

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Abstract: Background: The Powassan virus is a rare neurotropic, tick-borne arbovirus associated with meningoencephalitis. Despite the virus's known predilection for the basal ganglia, there are no reports detailing the spectrum of movement disorders in children with Powassan meningoencephalitis.

Cases: We present 3 cases of pediatric Powassan encephalitis, highlighting the diverse and evolving movement disorders associated with this disease. We observed subcortical myoclonus and progressive generalized dystonia (patient 1), transient dyskinesias and refractory focal dystonia (patient 2), and generalized dystonia evolving into chorea and lingual dyskinesias (patient 3). One patient exhibited multifocal vasculitis on magnetic resonance imaging angiography, a novel finding.

Conclusions: Movement disorders were a primary source of the morbidity experienced by pediatric Powassan encephalitis patients throughout their disease course, underscoring the importance of regular monitoring and adaptable treatment strategies in this condition. Larger, prospective studies are necessary to fully delineate the spectrum of associated movement disorders in this rare and severe disease.

Powassan virus is a neurotropic, tick-borne arbovirus of the flavivirus genus transmitted by various tick species, including *Ixodes scapularis* (deer tick) and *Ixodes cookei* (groundhog tick).[1] The first reported case dates back to 1958 in a child who presented with fatal encephalitis in the town of Powassan, Ontario, Canada.[2] Since then, the number of reported cases in the United States has steadily increased, with cases primarily reported in the country's northeastern regions with a mortality rate of up to 7.1% in the pediatric population.[3,4] Powassan virus has an incubation of 1 to 5 weeks and a strong tropism for the basal ganglia, thalamus, cerebellum, and brainstem.[1,5] At present, no vaccine or specific treatments exist for Powassan virus infections.

In children, acute Powassan meningoencephalitis has been associated with various neurologic symptoms, including headache, seizures, and coma. In the adult population, complex movement disorders, including multifocal myoclonus, opsoclonus myoclonus, cogwheel rigidity, and ataxia, have been described, albeit with limited detail.[6–8] The spectrum of movement disorders associated with Powassan meningoencephalitis in children has not been described. Here, we present 3 cases and delineate the movement disorders spectrum and associated patterns of basal ganglia injury.

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Case Series

Key clinical features are summarized in Table 1.

Case 1

Patient 1 is a 2-year-old, previously healthy, developmentally typical, and fully immunized girl who presented with high fever, encephalopathy, dystonia, and status epilepticus after a deer tick bite while camping in New Hampshire. Initial magnetic resonance imaging (MRI) revealed bilateral T2 hyperintensities in the basal ganglia with evidence of vasogenic and cytotoxic edema (Fig. 1). Cerebrospinal fluid (CSF) studies eventually returned positive for Powassan virus immunoglobulin M (IgM) and polymerase chain reaction. Treatment included intravenous immunoglobulin (IVIG) 1 g/kg daily for 2 days and high-dose methylprednisolone 30 mg/kg for 5 days followed by a corticosteroid taper. Throughout her initial course, the patient exhibited axial hypotonia and weakness with notably poor head control. Additionally, she experienced episodes of severe generalized

TABLE 1 *Summary of demographic data and clinical manifestations in a series of 3 children with Powassan meningoencephalitis*

Clinical picture			
Background	**Patient 1**	**Patient 2**	**Patient 3**
Location	New Hampshire	Massachusetts	New York
Sex	Female	Female	Female
Age of initial presentation	2 yr	14 mo	5 yr
Age at last clinic appointment (yr)	3	2	10
Incubation period (weeks)	3	4	2
CSF studies at presentation			
WBC (0–7/mm^3)	62	221	119
Neutrophils (%)	43	28	22
Lymphocytes (%)	55	56	51
RBC (0–50/mm^3)	2	2	47
Protein (15–45 mg/dL)	62	34	45
Glucose (60–80 mg/dL)	56	56	56
Movement disorder phenotypes			
Dystonia	+	+	+
Chorea		+	+
Myoclonus	+		+
Admission for status dystonicus	+	+	
Other neurological manifestations			
Seizures	+		+
Encephalopathy	+	+	+
Hypotonia		+	
Spasticity		+	
Neuropsychiatric manifestations			+
Headache			+
Medications			
Corticosteroids in the acute period	+	+	+
IVIG in the acute period	+	+	
Number of anti-seizure medications	2		1
Number of dystonia-directed therapies	3	2	2

Abbreviations: CSF, cerebrospinal fluid; WBC, white blood cell; RBC, red blood cell; IVIG, intravenous immunoglobulin.

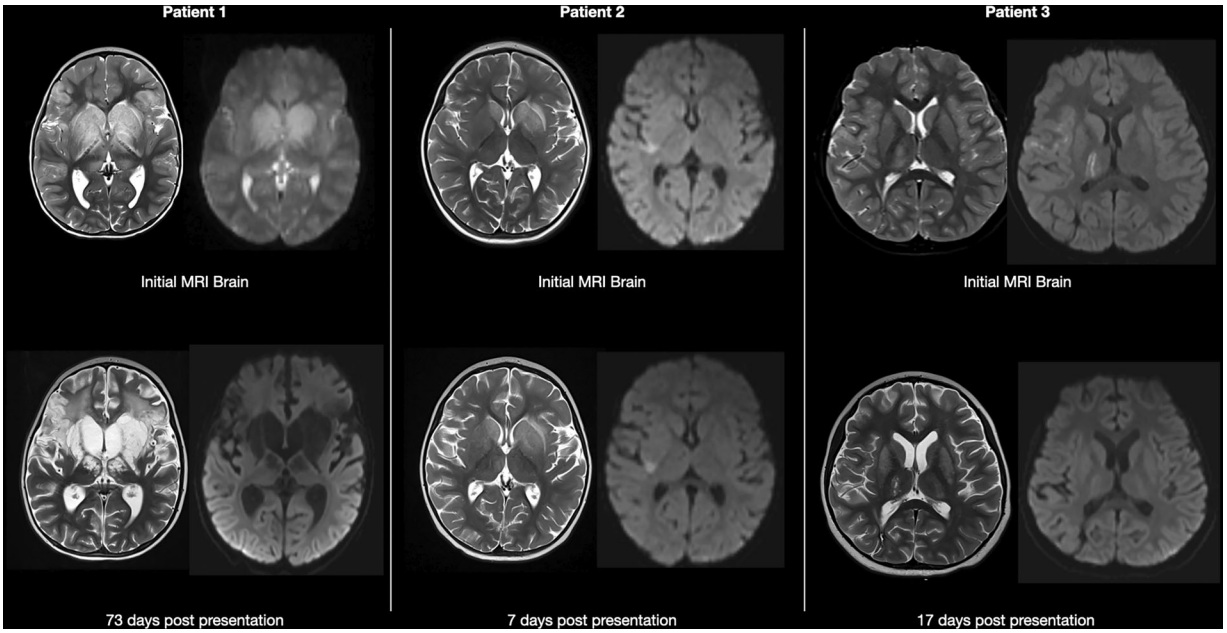


FIG. 1. Brain MRI (magnetic resonance imaging) with representative axial T2 and diffusion-weighted imaging (DWI) images. Patient 1: initial brain MRI showed bilaterally symmetric T2 hyperintensities with severe vasogenic and cytotoxic edema of the basal ganglia, posterior limb of the internal capsule, and midbrain. Additional T2 hyperintense signal and diffusion restriction were observed in the bilateral frontal lobes, corpus callosum, left temporal lobe, and left anterior pons. Follow-up MRI demonstrated evolution to cortical encephalomalacia and cavitation in the basal ganglia and brainstem, with Wallerian degeneration in the frontal white matter and mild to moderate ventriculomegaly. Patient 2: initial brain MRI revealed T2 hyperintensities predominantly in the left more than the right caudate head, left putamen, and left external capsule, along with diffuse leptomeningeal enhancement (not shown) and scattered diffusion restriction in the right posterior opercular cortex, right frontotemporal lobes, posterior limb of the right internal capsule, body and tail of the right caudate, and bilateral thalami. Follow-up neuroimaging 1 week after presentation revealed similar findings. Patient 3: initial brain MRI showed multifocal diffusion restriction in the right thalamus and right frontal lobe as well as T2 hyperintensity in the bilateral basal ganglia and left basal forebrain with diffuse leptomeningeal enhancement (not shown). Follow-up imaging showed expected evolution of infarcts in the right thalamus, right lateral frontal lobe, parasagittal right frontal lobe, and right parietal lobe.

dystonia characterized by arm and leg posturing, with the right hemibody being more involved than the left, accompanied by fist clenching and teeth grinding.

Approximately 1 month after initial presentation, she was readmitted for severe left hemibody nonepileptic myoclonus and an exaggerated startle reaction, described as shock-like, nonrhythmic, and nonsuppressible. These episodes were primarily triggered by loud sounds, occurring every minute while awake and disappearing during sleep. One month later, she presented with frequent, brief, startle-provoked tonic seizures captured on electroencephalogram (EEG). At this time, her medication regimen included clobazam, diazepam, levetiracetam, clonidine, gabapentin, and valproic acid (for both seizures and subcortical myoclonus). Follow-up neuroimaging revealed evolution to multifocal encephalomalacia (Fig. 1). Her clinical course stabilized allowing for de-escalation of care until 9 months after her initial presentation when she experienced an acute exacerbation in the context of a viral illness, ultimately leading to status dystonicus (Dystonia Severity Scale [DSS] 4) with an elevated creatine kinase (CK) of 1576 units/L.[9] She was consequently restarted on clonidine and diazepam.

At last follow-up, the patient remained globally developmentally delayed, nonverbal, and nonambulatory (Gross Motor Function Classification System [GMFCS] 5). She continued to experience frequent paroxysmal dystonic episodes triggered by discomfort and coughing (Video 1). This is compounded by significant axial and appendicular hypotonia, as well as lower-extremity spasticity with pyramidal signs.

Case 2

Patient 2 is a 14-month-old, previously healthy, developmentally typical girl who presented with a 4-day history of fever, cough, tachypnea, lethargy, and encephalopathy after a tick bite in the backyard of her home located in Newton, MA. On initial presentation, she exhibited axial and appendicular hypotonia with pyramidal signs. By day 3 of admission, she developed right hemibody dystonia and intermittent dyskinesias. Blood and CSF analyses were positive for Powassan virus IgM. Initial brain MRI showed T2 hyperintensities in the basal ganglia bilaterally, diffuse leptomeningeal enhancement, and scattered diffusion restriction (Fig. 1). EEG was normal, with no clinical concerns for seizures throughout her course.

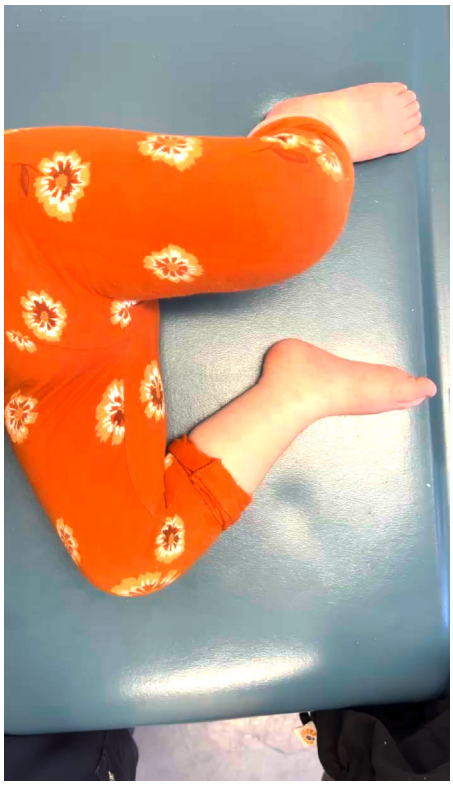
Video 1. Case 1. Video taken at last clinic appointment ~1 year after initial presentation. Patient is lying in her mother's lap with notable axial hypotonia. Frequent episodes of generalized dystonia characterized by flexion of bilateral arms and extension of lower limbs are observed, mostly triggered by stimuli such as coughing or loud noises. During examination of tone on the exam table, there is dystonia of her upper and lower extremities, with frequent exaggerated startle responses consistent with myoclonus.
Video content can be viewed at https://onlinelibrary.wiley.com/doi/10.1002/mdc3.14245

The child was readmitted 1 month later from an inpatient rehabilitation facility with severe dysautonomia and worsening dystonia (DSS 3), characterized by generalized dystonia involving the trunk, neck, and right lower extremity with opisthotonic posturing as well as an elevated CK of 389 units/L. Treatment included clonidine, diazepam, gabapentin, and phenobarbital (initiated for difficulties maintaining sleep as well as dystonia). She received IVIG 1 g/kg daily for 2 days and high-dose methylprednisone 30 mg/kg for 5 days followed by a taper.

Eight months after her initial injury, she exhibited persistent delays in expressive speech while maintaining preserved receptive language. She was able to cruise but not walk independently (GMFCS 3). Examination was significant for left lower-limb spasticity with clonus and bilateral Babinski sign. Dystonic posturing of the right ankle was present at rest and while walking, for which trihexyphenidyl was recently initiated (Video 2).

Case 3

Patient 3 is a 5-year-old previously healthy, developmentally typical girl who presented with high fever, headache, and lethargy, which evolved to coma requiring ventilatory support for 5 days after a tick exposure while camping in Rochester, NY. She began to develop progressive dystonia, initially manifesting as intermittent extensor posturing with subsequent generalization and prominent opisthotonic posturing (DSS 3). Initial MRI revealed T2 hyperintensities in the bilateral basal ganglia, multifocal infarcts, and diffuse leptomeningeal enhancement (Fig. 1). Notably, on MR angiography, the bilateral A2 and proximal right M2 segments were irregular, with enhancement of M1 (Fig. 2). A repeat MRI 3 days later showed an interval development of new areas of infarct, in keeping with multifocal vasculitis. She was eventually found to be positive for the Powassan virus. There were no clinical concerns for seizures,



Video 2. Case 2. Video taken at last clinic appointment ~1 year after initial presentation. Examination is notable for action-induced focal dystonia of the child's right ankle, characterized by intermittent foot inversion and toe walking on gait assessment.
Video content can be viewed at https://onlinelibrary.wiley.com/doi/10.1002/mdc3.14245

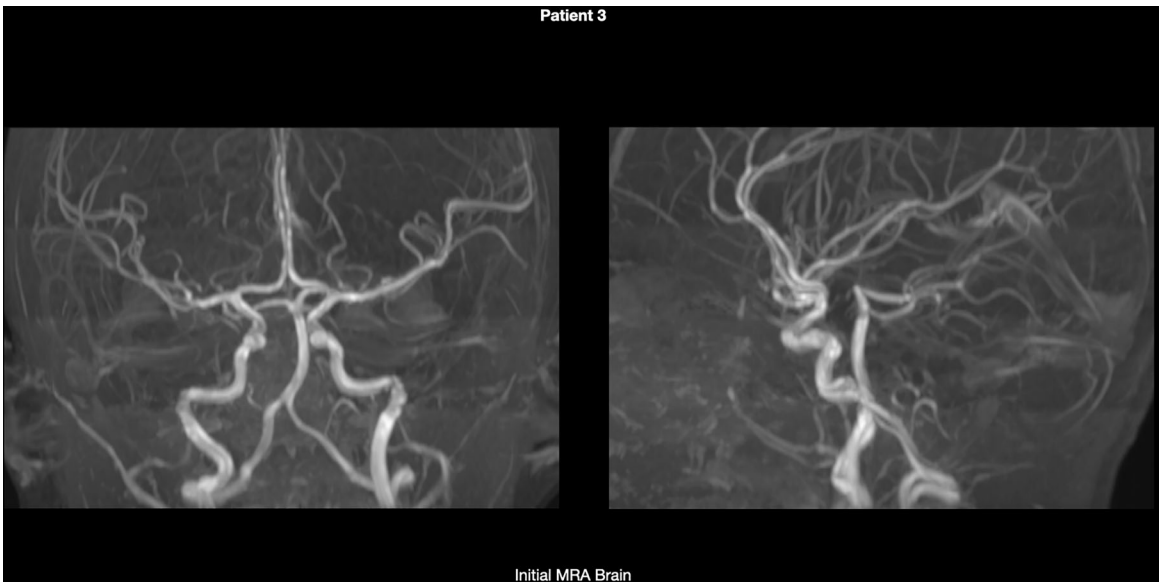


FIG. 2. Brain MR (magnetic resonance) angiography for patient 3: time-of-flight MR angiography demonstrates mild irregularity of bilateral A2 and proximal right M2 segments as well as mild enhancement surrounding the right M1 segment (not shown here), suggestive of multifocal vasculitis.

Video 3. Case 3. Video taken at initial presentation to hospital and at last appointment, just over 2 years later. Initial video demonstrates patient lying in bed with generalized dystonia characterized by sustained flexion of her upper and lower extremities, particularly notable in her right wrist and bilateral lower limbs. Striatal toe is visible in her right toe, and a dystonia tremor is noted in her left hand. Intermittent myoclonic jerks involving her shoulder are observed. At her follow-up visit 5 years later, physical exam was significant for generalized choreiform movements with postural tasks and gait assessment. Action-induced dystonia is also seen mostly in her right arm and foot.
Video content can be viewed at https://onlinelibrary.wiley.com/doi/10.1002/mdc3.14245

although a continuous EEG showed epileptiform discharges. She was initially treated with IVIG 1 g/kg daily for 2 days and high-dose methylprednisolone 30 mg/kg for 5 days followed by a taper.

Over time, the generalized dystonia evolved into chorea of the upper and lower extremities, causing injuries and impeding her ability to participate in rehabilitation. Her presentation was also significant for neuropsychiatric changes, including disinhibition, mood lability, anxiety, and perseveration, likely secondary to frontal-striatal dysfunction. Medication regimen included tetrabenazine, baclofen, diazepam, clonidine, gabapentin, and methylphenidate. At her last clinic visit, the patient could walk independently (GMFCS 1) but demonstrated ongoing generalized chorea, accompanied by lingual dyskinesias and right hemibody dystonia (Video 3).

Discussion

The spectrum of movement disorders in pediatric Powassan encephalitis has not been described and is likely underreported. This case series delineates the type and evolution of movement disorders in children, aligning with the virus's known predilection for basal ganglia injury.[5] The leading phenomenologies in our cohort included subcortical myoclonus and progressive generalized dystonia (patient 1), transient dyskinesias and refractory focal dystonia (patient 2), and generalized dystonia with evolution into chorea and lingual dyskinesias (patient 3). Two patients required admission for management of worsening dystonia after their acute presentation. All patients required multiple treatments for dystonia and chorea, highlighting the refractory nature throughout their disease course. This underscores the importance

of regular monitoring and adaptable treatment strategies in the management of movement disorders, which account for significant disease burden in pediatric Powassan encephalitis.

By better characterizing the phenotype of this rare disease, we hope to facilitate an early diagnosis in regions where this virus is endemic, as this may have treatment implications. All patients received high-dose corticosteroids, with 2 also receiving IVIG, interventions that have been suggested to promote clinical improvement.[4] There has also been a recent focus on testing small-molecule drugs and immunotherapies primarily for the inhibition of tick-borne encephalitis virus[10]; however, these therapies are not yet available for Powassan virus. Further investigation into the efficacy and safety of various treatment modalities is warranted.

A noteworthy finding in our case series was patient 3's MRI angiography demonstrating multifocal vasculitis. To the best of our knowledge, this finding has not been reported, although many previous cases have demonstrated multifocal infarcts in keeping with a micro-ischemic process.[4,5] Therefore, vascular imaging should be considered in cases of suspected Powassan encephalitis.

This report has several limitations: (1) the description of movement disorder phenomenologies in the acute phase may have lacked detail given that treatment focused on other acute complications, (2) the small cohort size with variable duration of follow-up, and (3) the lack of longitudinal MRI imaging beyond the acute phase in 2 patients.

In summary, this case series describes pediatric Powassan encephalitis with a focus on associated movement disorders, highlighting a complex and evolving pattern of hyperkinetic movement disorders with significant motor impairment and disability. Prospective studies in larger cohorts are needed to fully delineate the spectrum of movement disorders and associated disability in this rare and severe disease.

Author Roles

(1) Research project: A. Conception, B. Organization, C. Execution; (2) Statistical analysis: A. Design, B. Execution, C. Review and critique; (3) Manuscript: A. Writing of the first draft, B. Review and critique.

K.Y.: 1A, 1C, 2A, 3A
R.L.: 1B, 1C, 2B, 3A
V.Q.: 2C, 3B
R.S.: 2C, 3B
D.E.-F.: 1A, 2A, 3B

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Disclosures

Ethical Compliance Statement: We thank the patients and their families who supported this study. Written consent, including for videos, was obtained. This study was approved by the Institutional Review Board at Boston Children's Hospital (IRB-P00043928). We confirm that we have read the journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

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Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request. ■

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