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Two Cases of Guillain-Barré Syndrome Variants Presenting With Dysautonomia

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Abstract

We describe 2 pediatric cases presenting with posterior reversible encephalopathy syndrome secondary to autonomic dysfunction preceding the onset of motor symptoms in Guillain-Barré syndrome variants. Patient 1 presented acutely with encephalopathy, cerebellar signs, hypertension, lower limb weakness, and respiratory decompensation. Magnetic resonance imaging (MRI) brain showed occipital lesions consistent with posterior reversible encephalopathy syndrome. Nerve conduction studies were consistent with Miller-Fisher syndrome. After intravenous immunoglobulin and plasmapheresis, he improved clinically with radiological resolution. Patient 2 presented with headache, leg pain, seizures, and significant hypertension. Brain MRI was normal but spine MRI revealed enhancement of the cauda equina ventral nerve roots. She was areflexic with lower limb weakness a few days after intensive care unit admission and made a significant improvement after treatment with intravenous immunoglobulin. In children presenting with posterior reversible encephalopathy syndrome in the absent of other causes of primary hypertension, Guillain-Barré syndrome variants are an important differential etiology, presenting with autonomic dysfunction, even before signs of motor weakness become evident.

Keywords

Guillain-Barré syndrome, GBS variants, dysautonomia, posterior reversible encephalopathy syndrome

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Classical Guillain-Barré syndrome and its variant Miller Fisher syndrome represent a spectrum from discrete to overlapping syndromes variously affecting the cranial nerves and the limbs.[1] Although acute progressive weakness and areflexia are the hallmarks of Guillain-Barré syndrome, autonomic dysfunction has also been reported in around a third of patients diagnosed with Guillain-Barré syndrome variants.[2]

Posterior reversible encephalopathy syndrome is a clinical–radiological entity generally occurring in the setting of severe arterial hypertension and characterized by headache, decreased level of consciousness, visual disturbances, generalized seizures, and focal neurological signs. The association of posterior reversible encephalopathy syndrome with autoimmune-mediated inflammatory neuropathies such as Guillain-Barré syndrome is a rare and poorly understood phenomenon. Dysautonomia can also occur in the context of posterior reversible encephalopathy syndrome; however, to date, it has rarely been described as an initial manifestation of Guillain-Barré syndrome variants. In the context of Miller Fisher syndrome, it has been previously described as a coincidental finding or adverse event subsequent to treatment with intravenous immunoglobulin.

We report 2 children with Guillain-Barré syndrome variants, presenting with severe encephalopathy and autonomic

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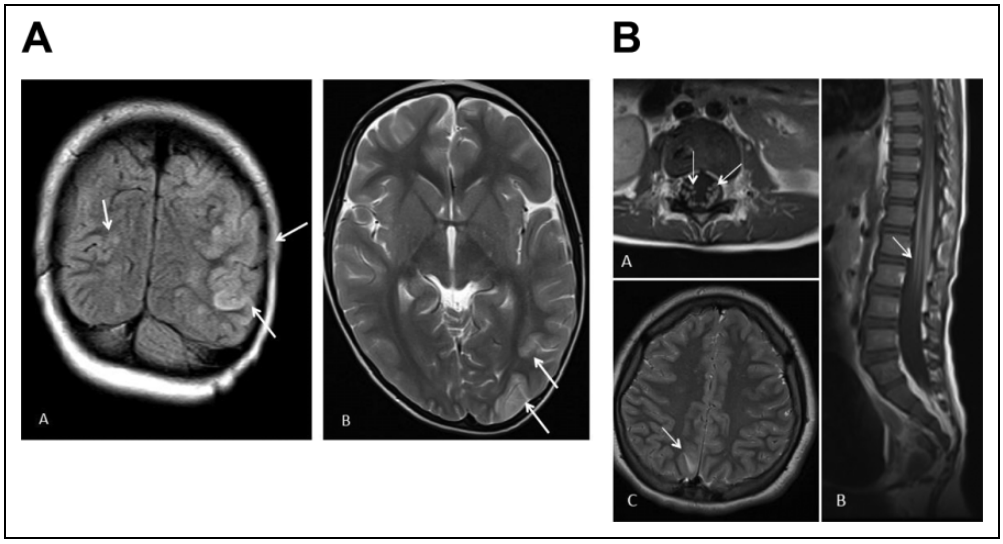

Figure 1. A, Patient 1: Magnetic resonance imaging (MRI) coronal FLAIR (A) at the level of the occipital lobes and axial T2-weighted images (B) shows multiple patchy areas of cortico–subcortical hyperintense signal (white arrows) in both posterior temporal and occipital lobes (more on the left). Radiological findings are consistent with posterior reversible encephalopathy syndrome (PRES). B, Magnetic resonance imaging (MRI) axial (A) and sagittal (B) postcontrast T1-weighted images in patient 1 shows diffuse enhancement and thickening of the cauda equina roots (white arrows in A and B); findings in keeping with Guillain-Barré syndrome (GBS). Axial T2-weighted images in patient 2 (C) show small right parietal subcortical area of hyperintense signal (arrow) in keeping with posterior reversible encephalopathy syndrome (PRES).

dysfunction. Written informed consent for the publication of the case descriptions was obtained for both patients.

Case Summaries

Patient 1

A 3-year-old boy presented following 4-day history of acute varicella infection with vomiting, neck pain, ataxia, slurred speech, and peripheral lower limb weakness. His previous medical history was only positive for recurrent febrile seizures. At admission, he was noted to be consistently hypertensive (systolic blood pressure up to 159 mm Hg), tachycardic (Heart Rate: 166), with a respiratory rate of 30 and oxygen saturations of 98%, and was initially started on empirical antimicrobials and acyclovir for presumed meningoencephalitis. The following day he had a respiratory decompensation requiring mechanical ventilation and generalized tonic–clonic seizures treated with phenytoin and midazolam infusion. Initial magnetic resonance imaging (MRI) brain on day 3 of illness showed bilateral and asymmetrical signal abnormalities of the parieto-occipital cortex consistent with posterior reversible encephalopathy syndrome (Figure 1a).

On day 2 of admission, he was also noted to have bilateral ophthalmoplegia, a left-sided Adie's tonic pupil, and lower limb areflexia. Arterial hypertension persisted, requiring treatment with hydralazine (up to 100 μg/kg/h) and clonidine (2 μg/kg/h) infusions. Repeat neuroimaging showed cranial nerve and cauda equina nerve root enhancement (Figure 1b), and nerve conduction studies on day 3 of admission (day 7 of illness) indicated a patchy neuropathic process affecting cranial nerves as well as peripheral nerves, consistent with Miller Fisher syndrome (Figure 2). Repeat nerve conduction studies on day 14 of admission were consistent with the previous findings, again with patchy demyelination and slowing of motor conduction. Cerebrospinal fluid on day 3 of admission was acellular and negative for culture and virology; protein count was not processed. Repeat cerebrospinal fluid 3 weeks into the illness was acellular with normal protein, negative Varicella Zoster Virus polymerase chain reaction, and the rest of the infective screen was unremarkable. Oligoclonal bands were negative in cerebrospinal fluid and serum. Treatment was escalated with 2 course of intravenous immunoglobulin (each course 2 g/kg) followed by plasmapheresis (7 cycles). His encephalopathy first resolved and he gradually regained power and reflexes in his lower limbs during the third week of admission, in addition to speech recovery, with marked clinical and radiological improvement (repeat MRI week 4 of illness). He was fully ambulant with normal lower limb power and reflexes at review 12 weeks after the initial illness.

Patient 2

A previously well 14-year-old girl presented with a 1-week history of frontal headaches, lower limb weakness, sensory abnormalities, and pain. She was noted on admission to have significant hypertension with arterial systolic blood pressure exceeding 170 mm Hg. Neurological examination showed no focal abnormalities, although lower limb reflexes were noted to be difficult to elicit at presentation. Two days after admission, she became unresponsive with multiple tonic–clonic seizures requiring intubation and ventilation for reduced conscious state. She received a loading dose of phenytoin and treated empirically for presumed encephalitis. Cerebrospinal fluid

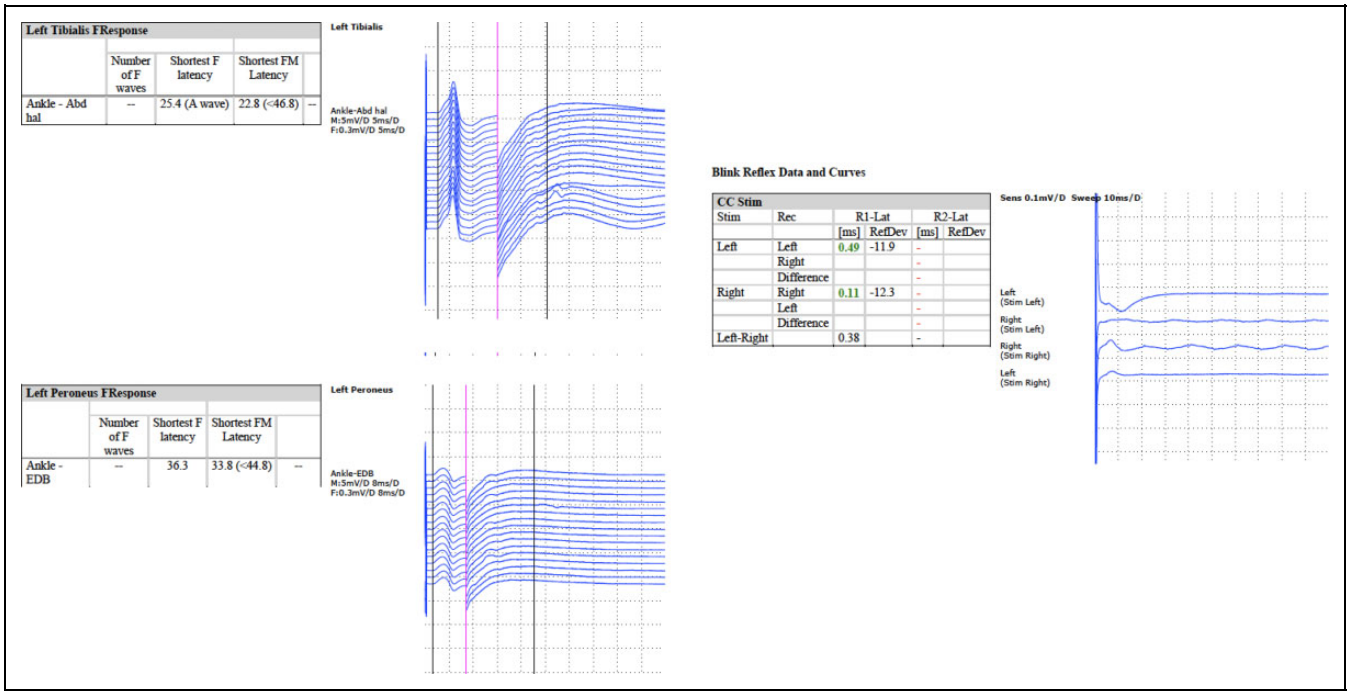

Figure 2. Nerve conduction studies demonstrating difficult to elicit F wave responses in the lower limbs. The blink reflex is also absent despite a demonstrable function in the facial nerve. This combination of findings supports a patchy neuropathic process affecting cranial nerves as well as peripheral nerves, compatible with the diagnosis of Miller Fisher syndrome.

analysis on day 3 of illness showed slightly raised protein (151 mg/dL), but infection and metabolic screenings were unremarkable. Initial computed tomography brain scan on day 4 of illness showed nonspecific edema and a right parietal lesion and MRI brain the following day confirmed this focal subcortical swelling consistent with posterior reversible encephalopathy syndrome. Due to marked liability of her systolic blood pressure (rising to 200 mm Hg at times), she required hydralazine (up to 70 µg/kg/h) and labetalol (up to 25 mg/h) infusions. Echocardiogram, abdominal and renal ultrasounds, and ophthalmological assessment excluded chronic causes of hypertension.

On her third day of admission (on intensive care unit), she was noted to have lower limb areflexia and nerve conduction studies on day 5 of illness demonstrated coincidental finding of a right peroneal nerve palsy, with no other signs of acute denervation. This was repeated on day 10 of illness with consistent findings of no signs of acute denervation, although the right peroneal nerve was not tested on this occasion. After initial extubation, she had a cardiac arrest requiring cardiorespiratory resuscitation and 2 further days of mechanical ventilation. Treatment with intravenous immunoglobulin (2 g/kg) led to clinical improvement with less marked weakness in lower limbs. Repeat MRI brain and spine 12 days after the initial computed tomography showed resolution of the right parietal lobe lesion (Figure 1b) and enhancement of the cauda equina ventral nerve roots, consistent with the presumptive diagnosis of Guillain-Barré syndrome variant, complicated by posterior reversible encephalopathy syndrome. At discharge, she was able to stand independently but had limited mobility due to proximal weakness. At follow-up 4 months after the initial presentation, she was able to walk and climb stairs independently with minimal support.

Discussion

We described 2 pediatric cases of Guillain-Barré syndrome variants with severe dysautonomia as a prominent presenting feature and secondary posterior reversible encephalopathy syndrome prior to the onset of motor symptoms. Most Guillain-Barré syndrome and Miller Fisher syndrome subtypes and variants share a number of common clinical features including a preceding infection, areflexia, distal paresthesia, and nerve conduction abnormalities.

Dysautonomia can occur acutely in Guillain-Barré syndrome and its variants, in addition to a number of other CNS diagnoses (Table 1). Chronic progressive causes include postganglionic cholinergic dysautonomia, familial dysautonomia, and neurodegenerative conditions (including Parkinson disease). A rare disorder, acute dysautonomia previously described in children may involve acute inflammatory neuropathy caused by an immune-mediated mechanism, similar to Guillain-Barré syndrome, and has been successfully treated with intravenous immunoglobulin[3]; this was also required in the management of both our patients.

A number of Guillain-Barré syndrome variants are characterized by localized involvement of autonomic nerves. In a retrospective review of a Chinese cohort of 43 children with

Table 1. Classification of Dysautonomia in Childhood (Disorders With Adult Onset Are Not Reported).

Cause of Dysautonomia		OMIM
Congenital dysautonomic syndromes	HSAN3—Familial dysautonomia *(Riley-Day syndrome)*	#223900
	HSAN1A[a]	#162400
	HSAN1B[a]	#600882
Dysautonomia associated with other congenital diseases	Rett syndrome	#312750
	Prader-Willi syndrome	#176270
	Fabry disease	#301500
	Congenital central hypoventilation syndrome	#209880
	Ehlers-Danlos syndrome	#130000
	Mitochondrial diseases	
Primary acquired dysautonomic syndromes	Postural orthostatic tachycardia syndrome	
	Neurally mediated (reflex) syncope	
	Neurocardiogenic syncope	
	Postviral dysautonomia	
	Postganglionic cholinergic dysautonomia	
Acquired dysautonomia associated with other disorders	Acquired neuropathies (infections, toxins, etc)	
	Celiac disease	
	Crohn disease/ulcerative colitis	
	Chiari malformation	
	Diabetes	
	Guillain-Barré syndrome/CIPD	
	Paraneoplastic syndrome	
	Rheumatological/autoimmune disorders (eg, SLE, APS, Sjögren disease)	
	Sarcoidosis	
	Vitamin deficiencies (eg, B6, B12, thiamine, niacin)	

Abbreviations: APS, antiphospholipid syndrome; CIPD, chronic inflammatory demyelinating polyneuropathy; HSAN, hereditary sensory and autonomic neuropathies; SLE, systemic lupus erythematosus.
[a]Only minimal autonomic features reported.

Guillain-Barré syndrome and its variants, cranial nerve involvement occurred in 17 (40%) children and autonomic dysfunction in 11 (26%) cases. Interestingly, children in the variants group were more likely to manifest cranial nerve involvement than those with typical Guillain-Barré syndrome[2] as seen in patient 1 who demonstrated cranial nerve enhancement on neuroimaging and Adie's tonic pupil.

A retrospective cohort of 11 adult patients with Miller Fisher syndrome suggested that bulbar palsy and dysautonomia might predict a relatively poor prognosis.[4] The mean duration of hospitalization was 16.8 days, and the longest hospital stay was noted in the one patient who developed bulbar palsy and autonomic dysfunction. The aggressive nature of disease progression in both our patients requiring Paediatric Intensive Care Unit admission suggests that this may apply for children, although both cases made a significant recovery a few weeks after admission.

Sensory and motor nerve conduction studies in patient 2 showed evidence of right peroneal nerve axonal loss in isolation. Previous literature suggests that the common vulnerable sites of nerve involvement in patients with Guillain-Barré syndrome tend to be distal motor nerves, the proximal segments, and the sites prone to compression.[5] Indeed, although the electromyography did not point toward the diagnosis of a Guillain-Barré syndrome variant in this case, electrophysiological abnormalities are often mild or nonspecific early in the disease.

Posterior reversible encephalopathy syndrome normally occurs in the context of arterial hypertension, as in both our cases. Vasogenic edema secondary to cerebral vessel endothelial dysfunction and breakdown of cerebral autoregulation is commonly assumed to be the underlying pathogenesis. A number of adult case reports have described posterior reversible encephalopathy syndrome as an initial manifestation of Guillain-Barré syndrome and Miller Fisher syndrome or even as a rare complication during intravenous immunoglobulin treatment.[6] Posterior reversible encephalopathy syndrome may manifest acutely or subacutely with headache, reduced consciousness, visual disturbances, focal neurological signs, and tonic–clonic seizures. Both patients reported here had generalized tonic–clonic seizures as part of their early disease manifestations and their symptoms were initially progressive, with almost complete regression once appropriate treatment (including intravenous immunoglobulin and plasmapheresis) was initiated.

Magnetic resonance imaging findings described in posterior reversible encephalopathy syndrome are characterized by bilateral and symmetrical hyperintense lesions on T2-weighted and FLAIR sequences, with a predilection for parietal and occipital areas. Involvement of frontal lobes, the internal and external capsules, and cerebellum have been described in the literature.[7] Irreversible damage can occur if this diagnosis is missed and inappropriate management instigated. In both our cases, early neuroimaging demonstrated parietal and occipital lesions consistent with posterior reversible encephalopathy syndrome in the context of dysautonomia and severe hypertension.

In conclusion, our 2 cases illustrate that Guillain-Barré syndrome variants could constitute an important differential etiology in children presenting with hypertensive encephalopathy (secondary to posterior reversible encephalopathy syndrome) and seizures. In such cases, the diagnosis of Guillain-Barré syndrome variants can be delayed or missed because encephalopathy and seizures are not typically presenting features. In our 2 cases, after appropriate management of posterior reversible encephalopathy syndrome, both children first recovered from their encephalopathy and then gradually from their motor impairment and weakness.

Author Contributions

OA-M, LDA, SB, YH, and MK contributed to conception and design. OA-M contributed to acquisition, analysis, and interpretation. OA-M,

LDA, SB, YH, and MK drafted the manuscript. LDA, YH, and MK contributed to analysis and interpretation. MP and FDA contributed to conception. MP and FDA contributed to analysis. All authors critically revised manuscript, gave final approval, and agrees to be accountable for all aspects of work ensuring integrity and accuracy. All authors contributed to care of the patient as well as the writing and editing of this report.

Declaration of Conflicting Interests

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Ethical Approval

This article presents a case report and does not involve any studies of human or animal subjects performed by any of the authors.

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