


A Rare Case of Guillain-Barré Syndrome With Severe Pandysautonomia

Journal of Investigative Medicine High
Impact Case Reports
Volume 9: 1–5
© 2021 American Federation for
Medical Research
DOI: 10.1177/23247096211019558
journals.sagepub.com/home/hic


Eneti Tagalao, BS¹, Frederick Venter, MD¹ , Li Liang, BS¹,
Jasbir Bhaika, MD¹, David Aguirre, MD¹, Janushe Patel, MD¹,
and Faisal Nasrawi, BS¹ 

Abstract

Acute pandysautonomia is a rare disorder characterized by autonomic failure affecting sympathetic, parasympathetic, and enteric functions. We present a case of acute inflammatory demyelinating polyneuropathy (AIDP) with severe pandysautonomia in a young, otherwise healthy, female who presented with gastrointestinal symptoms and sensory demyelinating polyneuropathy, which progressively worsened and subsequently developed bladder dysfunction and orthostatic hypotension. We discuss the challenges with diagnostic workup as well as the challenges we encountered as part of the management.

Keywords

pandysautonomia, Guillain-Barré, demyelinating polyneuropathy, gastroparesis, nephrology, neurology, IVIG, orthostatic hypotension

Introduction

Acute pandysautonomia is a rare complication of Guillain-Barré syndrome (GBS). Several publications delineate variants of GBS, the most common of which is acute inflammatory demyelinating polyneuropathy (AIDP).^{1–3} In the documented cases, patients who are symptomatic usually present with diarrhea, hyponatremia, cardiac symptoms, and/or urinary retention.⁴ Currently, there is little literature documenting GBS with severe acute pandysautonomia. We present a rare case of acute severe pandysautonomia in an otherwise healthy Hispanic female who presented with orthostatic hypotension, gastrointestinal symptoms, and bladder dysfunction in an atypical clinical course.

Case Presentation

A previously healthy 21-year-old Hispanic female initially presented to the emergency department with abdominal pain, anorexia, nausea, vomiting, diarrhea, urinary strain, and paresthesia with associated weakness in all 4 extremities for 9 days. Patient's lower extremity weakness initially started at the level of her toes bilaterally and slowly progressed to the mid-thigh level over the course of 2 months, accompanied by a complete loss of sensation in bilateral distal extremities. Similarly, and simultaneously, her upper extremity weakness started at the level of her fingers bilaterally and progressed up to the level of the elbow with a similar time course. She was unaware of any triggers and had no history of prior

surgeries or recent illness. Her social history was significant for smoking tetrahydrocannabinol (THC) e-cigarettes obtained from the street as well as recent history of hiking in the Tehachapi mountain range in California, days prior to the onset of her neurological symptom.

On presentation, vital signs were within normal limits. Her physical examination was significant for dry oral mucosa, 2/5 strength in distal lower and upper extremities and 4/5 strength in proximal lower extremities and upper extremities. Deep tendon reflexes and proprioception were reduced in all extremities, with a greater reduction in bilateral lower extremities. Passive range of motion was maintained. Furthermore, an isolated large 8 cm × 4 cm round targetoid skin lesion with central clearing was noted over the right scapula, which put Lyme disease higher on the differential (Figure 1).

Initial laboratory findings were significant for normocytic anemia (hemoglobin of 8.6 g/dL), erythrocyte sedimentation rate 14, and vitamin B₁₂ of 175 pg/mL. A lumbar puncture revealed cerebrospinal fluid protein of 58 mg/dL,

¹Kern Medical Center, Bakersfield, CA, USA

Received February 17, 2021. Revised April 27, 2021. Accepted April 29, 2021.

Corresponding Author:

Eneti Tagalao, BS, Department of Internal Medicine, Kern Medical Center, 1700 Mount Vernon Avenue, Bakersfield, CA 93305, USA.
Email: enetitagalao@mail.rossmed.edu





Figure 1. Skin lesion found over the right scapula.

glucose of 68 mg/dL, and white blood cell (WBC) of $1/\mu\text{L}$. *Campylobacter*, influenza, Lyme antibodies, cytomegalovirus, Zika, and HIV testing were all normal. Magnetic resonance imaging of the brain, cervical, thoracic, and lumbar regions as well as a magnetic resonance angiography of the head and neck revealed no acute abnormalities and were normal apart from mild degeneration of L4-L5 without canal or foraminal stenosis.

With the working diagnosis of GBS, the patient was initially started on intravenous immunoglobulin (IVIG) daily infusions and showed no noticeable improvement in her neurological symptoms after 5 days of therapy. Subsequently, she received 6 sessions of plasmapheresis with a slight transient improvement in strength that was soon followed by relapse of weakness and worsening of her symptoms, notably her autonomic symptoms.

The patient's hospital course was complicated by persistent severe nausea, vomiting, and diarrhea throughout the admission. An esophagogastroduodenoscopy (EGD) was performed and was consistent with reflux esophagitis and gastroparesis. The gastric body and fundus contained solid food with the last reported meal approximately 14 hours prior. The gastric antrum was normal. Biopsies showed no evidence for *Helicobacter pylori* and no changes to suggest vitamin B₁₂ deficiency. The lipase levels, as well as an abdominal ultrasound, were normal. However, an abdominal X-ray revealed gas-filled loops of small and large bowel. HIDA (hepatobiliary iminodiacetic acid) scan was consistent with acalculous chronic cholecystitis with reduced cholecystic ejection fraction. She subsequently underwent a laparoscopic cholecystectomy after 1 month of admission, but this yielded no further improvement in symptoms.

Additionally, she had progression of neurologic symptoms. She had loss of sensation to light touch and pinprick

from toes to mid-thighs bilaterally. Mild incoordination and jerking movements with dysmetria and dysdiadochokinesia were also noted without nystagmus or strabismus. Deep tendon reflexes and proprioception were absent in bilateral lower extremities and reduced in bilateral upper extremities. Concurrently, she had mild left-sided facial weakness, particularly in the CN VII distribution with decreased sensation (most consistent with peripheral etiology). Initial cobalamin level was 175 pg/mL, and methylmalonic acid was not measured. Cobalamin was repleted by 2 intramuscular injections and 1 oral dose of 1000 μg . This did not result in any improvement, complete blood count still exhibited normocytic anemia, and repeat B12 levels were not taken.

Another cycle of plasmapheresis was completed (6 sessions), after which the patient showed moderate improvement of her neurological symptoms. One-hour electroencephalogram showed mild diffuse encephalopathy and no seizures or epileptiform abnormalities. Electromyography done 1 month after admission was normal for muscles tested; however, nerve conduction studies showed severe sensory neuropathy and diffuse demyelinating neuropathy in bilateral lower extremities with normal nerve conduction studies in upper extremities (Figure 2).

During her 2-month hospitalization, she had 10-lb unintentional weight loss, along with diarrhea, severe nausea with vomiting refractory to multiple treatment and medication regimens. Patient also endorsed myalgia in her thighs, upper arms, and lower back, as well as episodes of weakness that limited her mobility and ambulation. Total creatinine kinase remained in the normal range despite subjective symptoms. For most of the patient's hospitalization, she was bedbound due to lightheadedness that was triggered on standing.

The hospital course was further complicated by urinary retention. She subsequently developed a urinary tract infection (UTI). Urinalysis showed WBC >50 with positivity for both leukocyte esterase and nitrites. Urine culture eventually grew methicillin-resistant *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Escherichia coli*. Toward the latter half of her 2-month hospitalization, more autonomic symptoms presented with persistent and severe orthostatic hypotension despite presenting vital signs in normal ranges. Comparative vital signs now show orthostatic vitals of blood pressure (BP) of 117/83 and heart rate (HR) of 90 while supine; BP of 89/59 and HR of 122 while sitting; and BP of 66/49 and HR of 152 while standing.

Initially, based on history as well as physical examination and laboratory findings, GBS was the highest in the differential. However, no clear trigger was established considering that the patient did not have any recent illness prior to the onset of neurological symptoms. She also had no recent history of vaccination. Though unlikely, one could argue that her UTI could have been the trigger; however, the patient did not have any previous UTI symptoms and the UTI might have developed after the onset of neurological symptoms due to bladder involvement.

SNC						
Nerve / Sites	Rec. Site	Peak Lat ms	Amplitude μ V	Segments	Distance cm	Temp. $^{\circ}$ C
R Median - Digit II (Antidromic)						
Wrist	Dig II	3.28	24.6	Wrist - Dig II	14	31.6
R Ulnar - Digit V (Antidromic)						
Wrist	Dig V	3.39	34.1	Wrist - Dig V	14	31.5
Ref.		≤ 3.80	≥ 9.0	Ref.		
R Median, Radial - Thumb comparison						
Median Wrist	Thumb	2.86	14.9	Median Wrist - Thumb	10	31.6
Ref.		≤ 3.00	≥ 9.0	Ref.		
Radial Wrist	Thumb	2.76	22.1	Radial Wrist - Thumb	10	31.6
Ref.		≤ 3.00	≥ 4.0	Ref.		
				Median Wrist - Radial Wrist		31.6
L Superficial peroneal - Ankle						
Lat leg	Ankle	NR	NR	Lat leg - Ankle	14	24.3
Ref.		≤ 4.40	≥ 4.0	Ref.		
L Sural - Ankle (Calf)						
Calf	Ankle	NR	NR	Calf - Ankle	14	26.4
Ref.		≤ 4.40	≥ 4.0	Ref.		
R Superficial peroneal - Ankle						
Lat leg	Ankle	NR	NR	Lat leg - Ankle	14	26.7
Ref.		≤ 4.40	≥ 4.0	Ref.		
R Sural - Ankle (Calf)						
Calf	Ankle	NR	NR	Calf - Ankle	14	28.7
Ref.		≤ 4.40	≥ 4.0	Ref.		

F Wave				
Nerve	F Lat ms	Ref. ms	M Lat ms	F-M Lat ms
R Median - APB	24.8	≤ 32.0	3.1	21.7
R Ulnar - ADM	25.0	≤ 32.0	2.2	22.8
R Peroneal - EDB	67.7	≤ 60.0	7.8	59.9
R Tibial - AH	82.0	≤ 60.0	8.6	73.4
L Tibial - AH	75.3	≤ 60.0	9.1	66.1
L Peroneal - EDB	61.1	≤ 60.0	6.7	54.4

Figure 2. Electromyography showed severe sensory neuropathy and diffuse demyelinating neuropathy in bilateral superficial peroneal nerves and sural nerves, with normal nerve conduction studies in upper extremities. Also note the skin temperatures in extremities, which may associate with autonomic vascular compromise despite use of an α -adrenergic agonist. F waves also show significant latencies in conduction, bilateral tibial nerves greater than peroneal nerves.

What made this case more interesting is the presence of the targetoid back lesion and the fact that she developed her symptoms soon after hiking. During the investigation, Lyme disease corresponds with her hiking history but resulted in

negative screen of Lyme antibodies (<0.90), and western blot was not collected. *Campylobacter* enteritis is also a consideration, given her initial gastrointestinal complaints without a prior viral illness or recent vaccination. *Campylobacter* is a

known trigger, resulting in molecular mimicry against axons, leading to the main working diagnosis of GBS or its variant Miller Fisher (cranial polyneuropathy) due to her facial weakness and sensory paresthesia. There may exist a possibility that in the post-convalescent period, our patient was no longer a fecal carrier at the time of sampling. Therefore, the sample was unable to capture the organism for its characteristic vibrioid morphology by direct microscopy. An additional consideration that may bear mentioning is the media used failed in sensitivity to the broad array of *Campylobacter* spp, but its failure to detect does not rule out its presence to cause disease. Another confounder is the negative results for anti-ganglioside antibodies (<1:100), specifically available for our laboratory testing was GQ1B Ab IgG, which associates glycolipid mimicry with *Campylobacter* and increased titers is diagnostic of Miller-Fisher syndrome variant of AIDP. While a negative test does not rule out GBS infection, a larger center with laboratory access to an anti-ganglioside antibodies panel should be considered.

Other infectious etiologies such as Brucellosis, Babesiosis, and West Nile Virus were considered, but were all eventually ruled out by laboratory findings. Furthermore, considering the recent use of THC e-cigarettes from unverified sources raised the suspicion for heavy metal toxicity, but testing for that returned normal.

Other etiologies that were considered but were ruled out included systemic lupus erythematosus, Sjogren's syndrome, rheumatoid arthritis, hepatitis, HIV, Cryptococcus, syphilis, and porphyria. Epstein-Barr virus interestingly shows no acute infection but rather a rise in antibodies from past infection (VCA Ab IgM: negative, but positive VCA Ab IgG and EBNA Ab IgG, 162.00 U/mL and 223.00 U/mL, respectively. The laboratory finding has a negative result <18 U/mL). All differential diagnoses were excluded due to negative laboratory workup leaving GBS as the diagnosis by exclusion. This was also supported by the albuminocytologic dissociation.

Uniquely, our patient suffered more pronounced autonomic dysfunction, specifically orthostatic hypotension and tachycardia, which failed conservative measures and necessitated uptitrations of midodrine 10 mg PO (by mouth) TID (thrice a day) and fludrocortisone 0.1 mg PO BID (twice a day) in order to tolerate standing. Her myalgia was refractory to tramadol, acetaminophen, pregabalin and only responded to morphine 2 mg IV Q4H (every hour) PRN (when necessary) and gabapentin 600 mg PO TID.

The persistent diarrhea, nausea, and vomiting throughout her admission were refractory to cholecystectomy (this occurred after initiation of IVIG and plasmapheresis treatment), ondansetron, metoclopramide, promethazine, dicyclomine, erythromycin, scopolamine, diphenhydramine, pantoprazole, famotidine, and aluminum-magnesium hydroxide-simethicone. Failed management with the aforementioned medications led to a trial of pyridostigmine 30 mg PO TID.

At the end of her admission, she was able to ambulate with assistance, tolerate oral intake, and started having bowel movements and control over her bladder. Unfortunately, due to the lack of insurance coverage and potential out of pocket expenses, the patient never followed-up with her outpatient appointments, and thus, her prognosis beyond the hospital admission remains unknown.

Discussion

Dysautonomia in GBS is associated with increased mortality and worse functional outcomes.⁵ Prevalence or incidence of pandysautonomia is currently difficult to assess as literature does not describe clinical variants of GBS in isolation.^{5,6} Prevalence of GBS in some literature review state seasonal variation with increased incidence in colder months associated with influenza vaccinations,⁷ but this is conflicting as other literature state no correlation.⁸ The overall incidence of GBS in North America and Europe have similar rates between 1.1/100 000 per year and 1.8/100 000 per year. Incidence increases with age after 50 years from 1.7/100 000 per year to 3.3/100 000 per year.⁹ Several variants of GBS are delineated, of which AIDP is the most common.^{1,10,11} In the documented cases, patients with AIDP usually present with diarrhea, hyponatremia, cardiac symptoms, and/or urinary retention.⁴ One retrospective review of GBS cases assesses the spectrum of dysautonomia with ileus, hypertension, and hypotension as the most common features.⁵ However, our patient presented with encephalopathy, sympathetic and parasympathetic symptoms concomitantly complicating management, and the clinical course.

Our initial course of treatment followed typical GBS treatment.¹² Treatment with IVIG has been suggested to treat acute pandysautonomia¹³; yet in our case, this therapy was not efficacious. Our patient presented with atypical symptoms in which GBS alone could not elucidate the patient's course considering the severe autonomic dysfunction evidenced by postural orthostatic hypotension/tachycardia, gastroparesis, bladder dysfunction, and the predominance of sensory neuropathy over the more common motor deficits of typical GBS.¹⁴ Failed management of gastrointestinal symptoms with more standard medications led to a trial of oral pyridostigmine 30 mg 3 times daily. This led to significant improvement in all gastrointestinal symptoms, tachycardia, orthostasis as well as motor strength that further confirmed suspicion of gastroparesis as a result of severe pandysautonomia secondary to GBS.

The development of orthostatic dysfunction was not discovered earlier in the patient's course due to inability to tolerate sitting/standing secondary to anorexia and neurological weakness. The factors may or may not be confounding. Weakness could be secondary to intractable nausea, vomiting, and anorexia. Weakness and paresthesia could also be secondary to vitamin B₁₂ deficiency occurring simultaneously with AIDP. However, this seems less likely due to the

normocytic anemia, EGD findings nonsuggestive of vitamin B₁₂ deficiency changes, and lack of improvement despite repletion of vitamin B₁₂. Patient's muscle atrophy after 2 months of being bed bound led to significant weakness and slow progress with physical therapy. Another confounding factor was the necessity of completing 2 rounds of plasmapheresis before enough motor strength returned to attempt orthostatic vitals.

Conclusion

Acute pandysautonomia is an uncommon clinical variant of GBS with an unclear etiology that requires more research. More evidence and trials are needed, given low density of literature and diagnosis. Encephalopathy, seizure-like activity, mood changes, sympathetic, and parasympathetic involvement are components of atypical GBS presentation and should warrant an investigation to GBS subtypes. Laboratory access to an anti-ganglioside antibodies panel should be considered to narrow the differential of subtypes.

Plasmapheresis is an effective treatment as evident in other literature when refractory to IVIG. The consideration of additional agents may be necessary when other autonomic symptoms arise and not amenable to plasmapheresis therapy alone such as midodrine and fludrocortisone for orthostatic hypotension. In our experience, pyridostigmine showed the most improvement when it came to the gastrointestinal and motor weakness manifestations of this condition.

Acknowledgments

We thank Dr Everardo Cobos (Chair-Elect, Western Section Council) and the American Federation for Medical Research for the opportunity of presenting our abstract at the Western Regional Research Conference earlier this year. Venter F (January 29-30, 2021). A rare case of pandysautonomia [Conference presentation abstract]. Western Regional Research Conference, Carmel, CA, USA.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethics Approval


Ethical approval to report this case was obtained from Kern Medical Institutional Review Board (ID # 19103).

Informed Consent

Written informed consent was obtained from the patient for their anonymized information to be published in this article.

ORCID iDs

Frederick Venter  <https://orcid.org/0000-0003-4301-0762>

Faisal Nasrawi  <https://orcid.org/0000-0002-6792-7666>

References

1. Newswanger DL, Warren CR. Guillain-Barré syndrome. *Am Fam Physician*. 2004;69:2405-2410.
2. Hahn AF. Guillain-Barré syndrome. *Lancet*. 1998;352:635-641.
3. Zochodne DW. Autonomic involvement in Guillain-Barré syndrome: a review. *Muscle Nerve*. 1994;17:1145-1155.
4. Anandan C, Khuder SA, Koffman BM. Prevalence of autonomic dysfunction in hospitalized patients with Guillain-Barré syndrome. *Muscle Nerve*. 2017;56:331-333.
5. Chakraborty T, Kramer CL, Wijdicks EFM, Rabinstein AA. Dysautonomia in Guillain-Barré syndrome: prevalence, clinical spectrum, and outcomes. *Neurocrit Care*. 2020;32:113-120. doi:10.1007/s12028-019-00781-w
6. Winer JB. Guillain-Barré syndrome. *Mol Pathol*. 2001;54:381-385.
7. Salmon DA, Proschan M, Forshee R, et al. Association between Guillain-Barré syndrome and influenza A (H1N1) 2009 monovalent inactivated vaccines in the USA: a meta-analysis. *Lancet*. 2013;381:1461-1468.
8. Kawai AT, Li L, Kuldorff M, et al. Absence of associations between influenza vaccines and increased risks of seizures, Guillain-Barré syndrome, encephalitis, or anaphylaxis in the 2012-2013 season. *Pharmacoepidemiol Drug Saf*. 2014;23:548-553.
9. McGrogan A, Madle GC, Seaman HE, de Vries CS. The epidemiology of Guillain-Barré syndrome worldwide. A systematic literature review. *Neuroepidemiology*. 2009;32:150-163.
10. Zhang G, Li Q, Zhang R, Wei X, Wang J, Qin X. Subtypes and prognosis of Guillain-Barré syndrome in Southwest China. *PLoS One*. 2015;10:e0133520. doi:10.1371/journal.pone.0133520
11. Kalita J, Misra UK, Goyal G, Das M. Guillain-Barré syndrome: subtypes and predictors of outcome from India. *J Peripher Nerv Syst*. 2014;19:36-43. doi:10.1111/jns5.12050
12. Verboon C, Doets AY, Galassi G, et al. Current treatment practice of Guillain-Barré syndrome. *Neurology*. 2019;93:e59-e76. doi:10.1212/wnl.0000000000007719
13. Mericle RA, Triggs WJ. Treatment of acute pandysautonomia with intravenous immunoglobulin. *J Neurol Neurosurg Psychiatry*. 1997;62:529-531.
14. Dimachkie MM, Barohn RJ. Guillain-Barré syndrome and variants. *Neurol Clin*. 2013;31:491-510.