Case Report
DOI: http://dx.doi.org/10.47746/FMCR.2022.3305

Guillain–Barré Syndrome with MFS and AMSAN Variants: A Rare Case

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Received: 20 April 2022; **Accepted:** 10 May 2022

ABSTRACT

Background: The immunologically mediated polyneuropathies Guillain–Barré syndrome (GBS) and Guillain–Barré syndrome (GBS) are important clinically. It is assumed to have a hereditary component, although no genetic risk locus has been identified. It's thought to be autoimmune, but the causes are unknown. It might be generated by molecular mimicry, such as from pathogens and vaccines, but hosting factor and co-founding host reactions would undoubtedly alter disease incidence and course. Case Presentation: A 57 year old female, three weeks after influenza vaccination she started complaining of double vision, left eye ptosis, dizziness, and bilateral symmetric upper and lower extremities weakness which described as “feeling sleepy”, both proximal and distal muscles are equally affected. The patient sought medical advice, ophthalmology examination and radiological imaging were free. Conclusion: AMSAN is recently identified GBS variant characterized by sensory symptoms, loss of deep tendon reflexes, and distant weakness with immediate onset.

Keywords: *Guillain–Barré, Immune Response, Axonal Neuropathy, Polyradiculoneuropathy*

Introduction

Guillain–Barré syndrome (GBS) is an inflammatory disease of the PNS and is the most common cause of acute flaccid paralysis, with an annual global incidence of approximately 1–2 per 100,000 person-years (Sejvar *et al*., 2011). GBS occurs more frequently in males than in females and the incidence increases with age, although all age groups can be affected (Sejvar *et al*., 2011). Although the clinical manifestations of GBS is variable and various discrete clinical forms occur, patients with GBS often appear with weakness and sensory symptoms in the legs that proceed to the arms and cranial muscles. The patient's medical history, as well as neurological, electrophysiological, and cerebrospinal fluid (CSF) investigations, are used to diagnose GBS (Asbury, 1978; Asbury and Cornblath, 1990; Sejvar *et al*., 2011). Other illnesses with a clinical presentation similar to GBS should be checked out (Sejvar *et al*., 2011). Acute inflammatory demyelinating polyradiculoneuropathy (AIDP), acute motor axonal neuropathy (AMAN), and acute motor sensory axonal neuropathy are the three subgroups of GBS that

electrophysiological tests may identify (AMSAN) (Hadden *et al*., 1998).

Although the pathophysiology of GBS is unknown, it is believed to be caused by an abnormal immune response to an infection that leads in peripheral nerve injury. Serum antibodies against gangliosides, which are abundant in the axolemma and other peripheral nerve components, are identified in a subset of GBS patients (Yuki, 2001). Complement activation, macrophage infiltration, and oedema are common features of damaged nerve roots and peripheral nerves in GBS patients (Yuki, 2001). Various methods have been used to record results in GBS clinical studies all around the world. In the majority of studies, improvement in GBS disability rating scale is the key predictive factor. The Rasch-built Overall Disability Score (RODS), Overall Neuropathy Restrictions Scale (ONLS), and Weariness Severity Scale (FSS) were created as clinical trial outcome measures and are used to assess disability, activity limitations, and fatigue in patients with GBS, respectively. These tools, however, were created in HIC cohorts of GBS patients, and the questions may not be culturally suitable in LMIC.

Case Presentation

A 57 year old female, presented to the neurology department complaints of diplopia, left eye ptosis, dizziness, and bilateral symmetric upper and lower extremities weakness which is described as “feeling sleepy”, both proximal and distal muscles are equally affected. She get a flu vaccine three weeks prior to her complaints with unremarkable immunological state before vaccination. She had diarrhea for three days two weeks prior to her admission. There was no history of sensory impairment or sphincter dysfunction. Her family and social history were unremarkable. On examination she was conscious and full alert. She had ptosis on both sides and her eyeballs were frozen. The power of lower and upper limbs showed weakness in joints flexion and extension. During her hospitalization she developed respiratory failure admitted her to ICU. Lumbar puncture was done, shows cytoalbuminic dissociation (protein in CSF 55, upper limit 45). She started treatment with intravenous immunoglobulin (IVIG) at 0.4 g/kg/day, take five doses totally, this improve her weakness from nearly bedridden to mild limb weakness, but diplopia persisted so gave her eye patch. On the medical discharge take advice to start medications at home with;

Gel 30g.
Acid 600 mg.
DeeDense 2000.
Amicor 5 mg.
Clopidogrel 75 mg.
Famotidine 40 mg.
Fexofenadine HCl 180 mg.

She was readmitted on the next day with weakness of the face, droop mouth, and distal upper and lower limbs weakness which were more prominent on the left side. Her new complaint was associated with difficulty swallowing for both solids and liquids, and changing in the tone of her voice. A neurological examination revealed similar findings with variable sensory loss to fine touch, crude touch, vibration and proprioception, absent tendon reflexes in the upper and lower limbs, the power of lower limbs showed weakness in hip flexion, extension and knee flexion and extension (MRC score: 4/5 bilaterally), upper limbs examination showed weakness in shoulder flexion (MRC score: 3/5 in the right upper limb and 4/5 in the left upper limb).

At this stage, further workup was performed, whole spinal magnetic resonance imaging (MRI) scan shows diffuse posterior bulges at the level of L2/L3, L3/L4 and L4/L5 with degenerative changes at L4/L5 level (Fig. 1), brain magnetic resonance imaging (MRI) findings suggest benign increased intracranial pressure (Fig. 2). The nerve conduction study demonstrated prolonged distal latency and reduced amplitude at motor and sensory nerves, these findings consistent with acute motor and sensory axonal neuropathy (Table 1).

She received another one dose of IVIG, there was no improvement as expected, and her symptoms persisted. According to this, she began treatment with plasmapheresis. She completed 8 courses within two weeks, her neurological symptoms improved, no more weakness noted on the examination and discharged with a good general condition

Table 1: Nerve Conduction Studies.

Motor Nerve Results:

	Latency		Amplitude		F-Lat
Site	**(ms)**	**Norm**	**(mV)**	**Norm**	**(ms)**
Right Median (APB)					
Wrist	6.6	<4.2	0.56	>5.0	32.6
Left Ulnar (ADM)					
Wrist	26.4	<4.2	0.24	>3.0	
Right Ulnar (ADM)					
Wrist	3.3	<4.2	6.9	>3.0	29.6
Bel Elbow	8.2	-	5.4	-	
Left Tibial (AHB)					
Ankle	6.1	<6.1	0.92	>4.4	
Right Tibial (AHB)					
Ankle	7.1	<6.1	2.2	>4.4	58.7

Sensory Nerve Results:

	Latency (Peak)		Amplitude (P-P)	
Site	**(ms)**	**Norm**	**(mV)**	**Norm**
Right Ulnar				
Wrist-Dig V	3.6	<3.7	7	>15
Right Radial				
Forearm-Wrist	2.9	<3.1	9	-

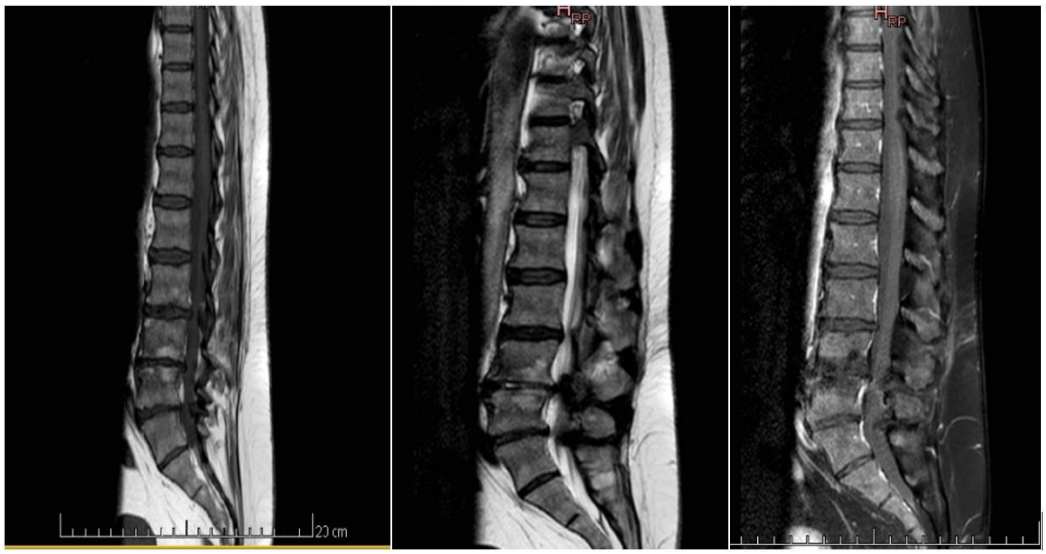

Figure 1: Spinal magnetic resonance imaging (MRI) scan.

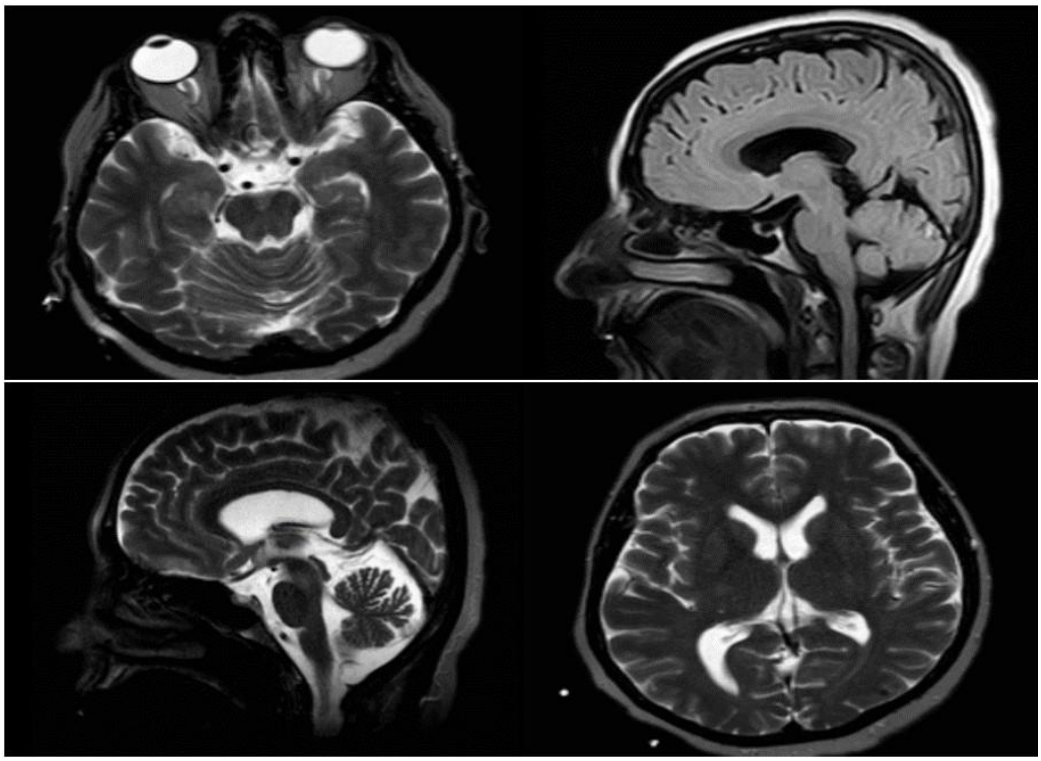

Figure 2: Brain magnetic resonance imaging (MRI).

Discussion and Conclusion

AMSAN is a newly described variant of GBS characterized by the combination sensory manifestations, deep tendon reflexes loss and distal weakness with acute onset (Vucic *et al*., 2009). We diagnosed the AMSAN associated with another variant Miller Fischer subtype. Miller-Fisher syndrome is combined of three characteristics opthalmoplegia, ataxia, and loss of reflexes (Yepishin *et al*., 2016).

The pathophysiology of AMSAN is quite different, as the macrophages attack the space between schwann cells and the axon, leaving the myelin sheath intact (Vucic *et al*., 2009). The AMSAN patients tend to have slow recovery with sensory involvement (Yuki *et al*., 1999). AMSAN usually has a fatal course. AMSAN is usually distinguished with the inexcitability of the nerves, associated with widespread muscular fibrillation. All of this is accounted by the axonal degeneration. These cases differ from GBS with different features, first of all severe symptoms peak earlier than usual for cases of GBS. In addition, AMSAN is usually more severe, some reports indicated that 60% of the patients will end with ventillatory support. On the pathological level, AMSAN usually lacks primary demyelination (Feasby *et al*., 1986). The main aspect of pathological findings were Wallerian degeneration varying in severity between nerves with minimal lymphocytic infiltration, absent inflammation, no demyelination (Jacobs *et al*., 1995). Electrophysiological studies are the main diagnostic tool with no defined criteria till now. Features are loss of excitability, with reduced SNAP amplitude by 80 % lower than the lower limit, with motor abnormalities. Additionally, antiganglioside antibodies may aid in the diagnosis (Kuwabara *et al*., 2000; Chowdhury and Arora, 2001). Differential diagnosis of AMSAN would include acute polio, critical care polyneuropathy, toxic neuropathy, porphyria and alcohol axonal neuropathy (Chowdhury and Arora, 2001).

Miller Fischer syndrome presentation is special in different aspects. Firstly, it is usually preceded by respiratory symptoms in contrast to GBs. In addition, part of patients has GI symptoms (Yuki, 1997). It is worth noting that MFS usually affect oculomotor and trochlear nerves. Different explanations hide behind that, but specifically it relies that GQ1b, a ganglioside found abundantly within these nerves. It is known that MFS is characterized by the presence of anti-GQ1b antibodies (Yuki, 1997). MFS diagnosis relies basically on clinical diagnosis, with the typical triad. The first appearing symptom usually is the bilateral ophthalmplegia with rapid onset. The clinical onset help to rule out other possibilities like myasthenia gravis and thyroid diseases (Bukhari and Taboada, 2017). It usually has a progressive course, until it reaches a point where the recovery starts at this nadir (Anthony *et al*., 2012).

Differential diagnosis of MFS include, Bickerstaff's brainstem encephalitis, botulism, stroke in brainstem, myasthenic syndromes and thiamine deficiency- Wernicke's encephalopathy. MFS has special

course of symptoms, as it usually has rapid onset of symptoms compared to other diseases. Ataxia in MFS lacks lateralization and this make it differentiated from other causes of ataxia, mainly cerebellar lesions (Gupta *et al*., 2016). GBS patients usually have normal white blood cells counts within the CSF. Testing anti-GQ1-b is highly recommended to affirm the diagnosis of MFS. It is worthy to note, that these antibodies are also found in other variants of GBS (Jacobs *et al*., 1995; Gupta *et al*., 2016; Chiba *et al*., 1997). Anti GQ1-b has a sensitivity of 95% to MFS, with a specificity higher than 90% (Kuijf *et al*., 2009).

GBS generally is treated with plasmaphresis and IV immunoglobulins (Yepishin *et al*., 2016). For AMSAN it seems that patients with anti GM1 antibodies and defined C.Jejuni infection are less susceptible to treatment with IVIG (Chowdhury and Arora, 2001; Visser *et al*., 1995; Jacobs *et al*., 1996). MFS course is self-resolving and follows benign course with recovery. MFS usually takes one to three months resolve, while full recovery takes six months (Mori *et al*., 2001). MFS usually responds well to IVIG and plasmaphresis (Overell and Willison, 2005).

Statements: Non-author contributors that should be included in the Acknowledgement section.

Statement of Ethics: Consent to publish statement: Informed consent was taken from the patient.

Conflict of Interest Statement: No Conflict of Interest.

Funding Sources: No Funding Sources.

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