

Familial Guillain-Barré syndrome: First Indian report

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Abstract

Guillain-Barré syndrome (GBS) is the commonest acute immune-mediated peripheral neuropathy. Specific human leukocyte antigen types have been found in patients with axonal and demyelinating subtypes of GBS suggesting genetic susceptibility in the generation of GBS. However, familial occurrence of GBS is rare and 42 patients from 20 families have been reported. Majority of them are from European countries and two families have been documented from Asian countries, while none have been reported from India. Electrophysiological characterization in familial GBS has been limited. We report the clinical and detailed electrophysiological findings in two affected brothers with familial GBS from India who had GBS five years apart. Both of them had mixed axonal and demyelinating features in nerve conduction studies and had complete clinical recovery. Our report documents the first Indian familial occurrence of GBS. Detailed genetic and epidemiological studies are required to find the true prevalence of familial GBS.

Key Words

Familial Guillain-Barré syndrome, motor conduction block, nerve conduction studies

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Introduction

Guillain-Barré syndrome (GBS) is the commonest immune-mediated acute neuropathy with several causative factors including *Campylobacter jejuni* and viral infections.^[1] Studies have demonstrated presence of higher incidence of specific human leukocyte antigen (HLA) antigens in GBS suggesting genetic predisposition contributing to the immunopathogenesis and manifestations.^[2] Despite large number of patients with GBS, familial occurrence is rare. Following the first report in 1965, few families with familial GBS have been reported.^[3-11]

Among the 150 GBS patients seen in the neurological services of the hospital over last ten years, two were from a single family. Their clinical and electrophysiological data are presented below.

Case Reports

Patient 1

A 20-year-old man, sixth sib of nonconsanguineous parentage,

was admitted in August 2005 with distal onset quadriparesis of four days without respiratory or autonomic dysfunction. This was preceded by fever and sore throat one week earlier. Cranial nerves were normal. Muscle power was normal in proximal upper limbs, 4/5 in distal upper limbs and proximal lower limbs; 3/5 at ankle and toes. Touch and pinprick sensations were reduced in hands and feet with sluggish muscle stretch reflexes. Blood counts and biochemistry were normal. Nerve conduction studies performed on the second hospital day revealed conduction blocks in both ulnar nerves with moderate reduction of distal motor amplitudes [Table 1]. F-waves were delayed in right median and right common peroneal nerves, absent in both ulnar and left posterior tibial nerves. Bilateral facial paralysis with worsening of limb weakness occurred by fifth day of admission, making him bedbound. Cerebrospinal fluid (CSF) was acellular with 197 mg/dl protein. He was given intravenous immunoglobulin over one week. He had static deficits for two weeks before gradual improvement to normal power over the next six months.

Patient 2

Eldest brother of the first patient was admitted in January 2010 at the age of 34 years with quadriparesis that began two weeks earlier and progressed over ten days. There was no impairment of sphincter, autonomic, or respiratory functions. He had no antecedent infections or inoculations. His mental functions and cranial nerves were normal. Power in shoulder, elbow, hip, and knees were 3/5, while the fingers and toes were severely weak. Sensations were normal with diffuse areflexia. CSF revealed 10 lymphocytes/mm³ and 111 mg/dl protein. Nerve

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Table 1: The nerve conduction findings in the two patients

Nerve	Stimulation	Patient 1			Patient 2		
		Latency (msec)	Amp.	Velocity (m/sec)	Latency (msec)	Amp.	Velocity (m/sec)
Motor conductions							
Rt. median	Wrist	5.50 (<4.2)	2.27 (>4.0)		4.60	1.00	
	Elbow	8.50	2.27	71.3 (>48.0)	9.25	0.58	47.3
	Mid arm	10.60	2.23	56.2	11.25	0.48	57.5
Rt. ulnar	Wrist	5.30 (<3.4)	4.39 (>3.8)		3.45	0.46	
	Below elbow	9.05	4.05	54.4 (>49.0)	7.35	0.09	58.5
	Above elbow		No recordable CMAP		9.50	0.08	52.1
Lt. median	Wrist	5.05 (<4.2)	4.10 (>4.0)		ND		
	Elbow	8.55	4.22	59.4 (>48.0)	ND		
	Mid arm	10.30	4.27	67.4	ND		
Lt. ulnar	Wrist	5.20 (<3.4)	1.93 (>3.8)		ND		
	Below elbow	8.90	1.83	57.3 (>49.0)	ND		
	Above elbow		No recordable CMAP		ND		
Rt. CP	Ankle	11.70 (<5.5)	0.65 (>2.0)		17.5	0.47	
	Fibular neck	17.85	0.65	46.8 (>40.0)	25.9	0.08	41.1
	Popliteal fossa	21.15	0.32	28.5	29.3	0.08	26.5
Rt. PT	Ankle	6.20 (<5.8)	5.18 (>4.0)	50.8 (>40.0)	11.2	0.81	
	Popliteal fossa	15.15	5.19	46.0	24.1	0.15	32.7
Lt. CP	Ankle	9.45 (<5.5)	2.00 (>2.0)		ND		
	Fibular neck	15.10	2.00	51.3 (>40.0)	ND		
	Popliteal fossa	18.30	1.76	30.6	ND		
Lt. PT	Ankle	5.30 (<5.8)	5.40 (>4.0)		ND		
	Popliteal fossa	13.55	5.40	50.7 (>40.0)	ND		
Sensory conductions							
Rt. median	Digit 2*	3.12	2.59 (>8.0)	55.1 (>48.0)	3.28	7.90	51.8
Rt. ulnar	Digit 5*	2.88	6.65 (>8.0)	47.9 (>48.0)	2.96	5.60	47.3
Lt. median	Digit 2*	3.30	3.24	51.5	ND		
Lt. ulnar	Digit 5*	3.12	3.30	45.5	ND		
Rt. SP	Midleg†	2.86	10.26 (>5.0)	51.7 (>42.0)	2.82	10.90	56.0
Rt. SP	Midleg†	2.68	8.37	53.0	2.40	8.60	55.0
Rt. sural	Midcalf†	3.22	11.61 (>5.0)	48.6 (>42.0)	3.24	10.50	46.3
Lt. sural	Midcalf†	3.48	9.42	43.1	2.76	11.20	42.8

Latencies are in milliseconds, amplitudes of compound muscle action potentials are shown in millivolts; amplitudes of sensory nerve action potentials in microvolts; and the velocities are in meters/sec. Normative data for the nerve conduction parameters are given in parenthesis; Amp = Amplitude, Rt. = Right, Lt. = left, ND = Not done, CP = Common peroneal, PT = Posterior tibial, SP = Superficial peroneal, * = Orthodromic stimulation, † = Antidromic stimulation

conduction studies revealed reduced motor amplitudes with dispersion and reduced velocities [Figures 1 and 2, Table 1]. F-waves were absent and the R-R variability was normal. He had progressive improvement in the muscle power and started walking six days after admission. He was discharged one week later when the power had increased by one grade and had recovered completely at follow-up five months after discharge.

The parents and unaffected siblings had no neuromuscular symptoms and had normal neurological examination. Nerve conduction studies in the unaffected siblings were normal.

Discussion

Familial occurrence of GBS is rare with few publications over the last 45 years since the first publication in 1965.^[3] Over these years, 42 patients of GBS belonging to 20 families have been reported.^[3-11] Some of these patients would not fulfill the present diagnostic criteria for GBS.^[12] In the majority of the families

published, two members from each family were affected,^[3,4,6-11] while two families had three affected patients each.^[5,10]

Among the familial GBS patients published till date, no gender predilection was seen (19 female and 23 male) with wide variation in age ranging from infancy to 76 years. The affected family members have been quite varied with siblings, parent-offspring, grandparent-grandchild, uncle-nephew/niece, and cousins being affected in the individual families.^[3-11] In the 25 patients among 12 families from Netherlands, a tendency for younger age in the subsequently affected family member was noted,^[10] with similar observation in some studies.^[3,4] However, in our two patients, the older sibling was affected five years after the younger one.

Antecedent events in these familial GBS patients have been different in the various reports including the Dutch report. Respiratory tract infections were the commonest (11 patients), followed by flu (six patients), diarrhea (six patients), and *C. jejuni* in six patients. Other uncommon prodromes noted

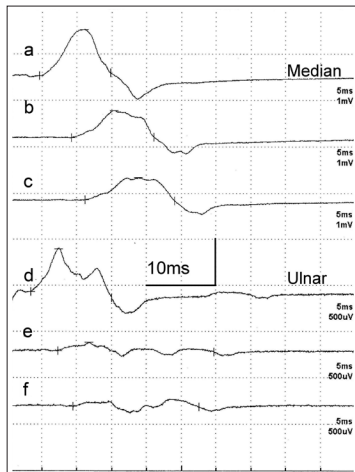


Figure 1: The motor nerve conduction in right upper limb revealing reduced amplitudes in median and ulnar nerves with temporal dispersion in ulnar nerve. Right median nerve was stimulated at wrist (a), elbow (b), and mid arm (c); ulnar nerve was stimulated at wrist (d), below elbow (e), and mid arm (f). Sensitivity 1 mV/d for median and 0.5mV/d for ulnar nerves

were cytomegalovirus infection, headache, nettle rash, and radicular pains, while three had no antecedent events.^[3-11] One of our patients had upper respiratory infection, while the second patient had no preceding illness. Both patients had clinical features consistent with GBS that was supported by the nerve conduction abnormalities and albuminocytological dissociation in CSF.^[12]

Published electrophysiological data in the familial GBS are limited and are suggestive of demyelinating neuropathy.^[6,7] In one family, daughter had acute motor axonal neuropathy (AMAN) following *Campylobacter* infection, while the father had acute inflammatory demyelinating polyneuropathy (AIDP).^[11] However, in other reports, details were not available to categorize to electrophysiological subtypes of GBS. Our two patients had combination of features of demyelination and axonopathy in motor nerve conduction, with more profound reduction of amplitudes in the second patient. The amplitudes of sensory nerve action potentials (SNAP) in upper limb were relatively reduced in comparison with the lower limbs in both patients. Reductions of SNAP amplitudes in median and ulnar nerves are encountered more frequently than in sural nerves in patients with AIDP, while the sensory nerve conduction abnormalities are uncommon in AMAN.^[13]

Increased incidence of GBS in siblings over the expected frequency in the population was noted in the study from Netherlands.^[10] Genetic evaluation has been done in few families with familial GBS. HLA typing in father and son revealed similarity in A2, A29, B5, B44, Bw4, Dr7, and Drw53 antigens.^[6] Mother and son shared HLA DR2 in another family.^[9] In contrast, HLA association was not seen in two Israeli patients, wherein father had chronic inflammatory demyelinating polyneuropathy (CIDP) and daughter had AIDP.^[7] A subsequent publication from this family reported another daughter developing CIDP and all these three patients had chromosomal deletion at 17p12 locus which is involved in hereditary neuropathy with liability for pressure palsies.^[14]

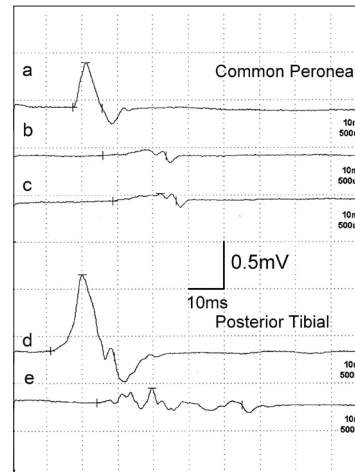


Figure 2: Motor nerve conduction in right lower limb revealing increased distal latencies, reduced amplitudes with temporal dispersion, and partial conduction block. Common peroneal nerve was stimulated at ankle (a), below fibular neck (b), and popliteal fossa (c); posterior tibial nerve was stimulated at ankle (d) and popliteal fossa (e)

A recent report from Sri Lanka documented an affected father with AIDP and daughter with AMAN sharing HLA types DR12, DQ6, and DQ7.^[11]

A study from China revealed different HLA epitopes involved in increased susceptibility and protection from AIDP. Similar association was not seen for AMAN suggesting a different pathogenic mechanism.^[2] Pandey and Vedeler demonstrated increased frequency of KM3 homozygotes in patients with GBS, suggesting the role of genetic markers of the constant region of kappa chain in the pathogenesis of GBS.^[15] These findings probably indicate why only few of the subjects with the antecedent infections from *C. jejuni* develop GBS. The genetic predisposition may increase the susceptibility of the patient exposed to the infections known to precipitate GBS. However, further detailed genetic studies are required in patients with familial GBS to assess contribution of the genetic factors.

Literature survey did not reveal an earlier report of familial GBS from India and we believe that this is the first report from India. Detailed genetic studies in our patients and the unaffected siblings probably could have provided information on the genetic susceptibility. Epidemiological and genetic studies may ascertain the true prevalence of familial GBS.

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