A VARIANT OF GUILLAIN-BARRE' SYNDROME WITH ANTIBODIES AGAINST GANGLIOSIDES GM1 AND GD1B AND CENTRAL NERVOUS SYSTEM INVOLVEMENT- A CASE REPORT

F Gragnani[1], I.F. Pestalozza[1], F. Gilio[1], S. Rinalduzzi[1], S. Almonti[1], P. Galizia[1], G. Antonini[2], AM Cipriani[1].

- [1]Neurology and Neurophysiopathology Unit, Sandro Pertini Hospital, Rome, Italy
- [2]Department of Neuroscience, Mental Health and Sensory Organs, Faculty of Medicine and Psychology, Sapienza University of Rome, Italy

INTRODUCTION

Guillain-Barré syndrome (GBS) is an acute post-infectious demyelinating polyneuropathy with an acute onset characterised by generally fast progressive muscle weakness and paraesthesia. GBS is diagnosed by clinical, laboratory and neurophysiological findings. Anti-ganglioside antibodies in patient serum support the diagnosis (1).

GBS and its variant, Miller Fisher syndrome (MFS) have several subtypes, together forming a continuous spectrum of discrete and overlapping syndromes. The clinical presentation of GBS-related disorders is heterogeneous and the diagnosis may not be obvious at first (2).

We report a case of acute polyneuropathy associated with antibodies to gangliosides GM1 and GD1b, with central nervous system involvement.

CASE REPORT

A 35 year-old-man, affected by psychiatric disorder receiving neuroleptic and valproic acid, was admitted in April 2016 because of severe muscular pain of the lower limbs started about five days before, with progressive difficulty walking and mild distal upper limb sensory disturbance.

There were neither recent immunization nor infection.

THE FIRST MEDICAL EVALUATION revealed that he was conscious and quite cooperative. The patient complained pain in the legs and had an unbalanced gait as well as paresthesia in the hands. Muscle strength was 4/5 in proximal muscles of the lower limbs, normal in other muscles. Deep tendon reflexes and plantar reflex were normal. Sphincter control was intact. Autonomic functions were normal as well as sensory modalities.

In the acute-phase hyponatriemia (124 mEq/L) and elevation of creatine kinase (CK 1214 U/L) were identified, other biochemical and haematological tests were normal.

THE DAY AFTER ADMISSION to the Hospital, he complained of diarrhea and fever with mild drowsiness; CTscan of the brain was normal.

AFTER THREE DAYS, progressively he developed ophtalmoparesis, which worsened to a complete ophthalmoplegia, bilateral facial weakness, severe tetraparesis, areflexia and progressive brainstem dysfunction requiring artificial ventilation.

Laboratory exams showed persistent hyponatriemia (122 mEq/L) and marked elevation of creatine kinase (CK >10.000 U/L) with rapid improvement in values after hydration.

Cerebrospinal fluid, on the 5th illness day, showed high protein content (200 mg/dl) and increased lymphocyties cells (417 cells/µL)

Contrast enhanced Magnetic Resonance Imaging did not reveal any pathology of the brain and brain stem.

Electromyography (EMG) revealed decreased amplitude of sensory potentials of sural, median and ulnar nerves and reduced motor nerve conduction velocities and compound muscle action potential (CMAP) of peroneal and tibial nerves, together with conduction block in right peroneal nerve.

F waves were absent in left ulnar, left median and both peroneal and tibial nerves.

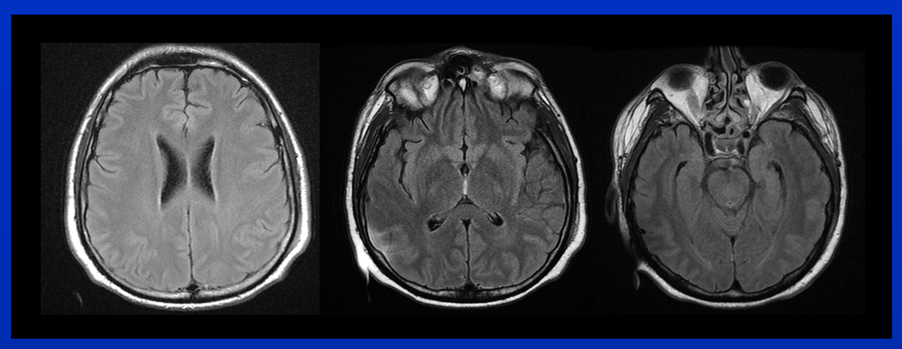
The serologic tests were performed for differential diagnosis. Campylobacter jejuni was negative. Serological tests were negative for H. Influenzae type B, S. Pneumoniae, N.meningitidis; PCR was negative for HIV, Herpes virus, Epstein-Barr virus, Cytomegalovirus, Enteroviruses, Respiratory viruses. Tests for the detection of bacterial infections were negative.

Serum obtained from the patient during the second week of disease contained a mild elevated level of **anti-GM1** IgG (104) and **anti-GD1b** (135) IgG antibodies. Serum IgM and IgG antibodies to GQ1b was normal.

The treatment started with intravenous gammaglobulin infusion (0.4 g/Kg/day) for 5 days, antibiotics and antiviral therapies were given, but neurological symptoms remained unchanged. Methylprednisolone was administered without clinical improvement. Twenty days later he underwent to a course of plasma-exchange with progressive improvement of symptoms.

One month after plasmapheresis he recovered from respiratory failure and ophthalmoplegia; he continued to have mild bilateral facial weakness, mild proximal and distal weakness in upper limbs (4 on the MRC scale) and moderate weakness in the lower limbs (3 on the MRC scale). All tendon reflexes were absent. He complained distal paraesthesia of glove-and-sock type. Then he started rehabilitation with global clinical improvement during following months.

RM imaging T1, T2, Flair and DWI imaging, with and without enhancement, detected no abnormalities in the brainstem and brain

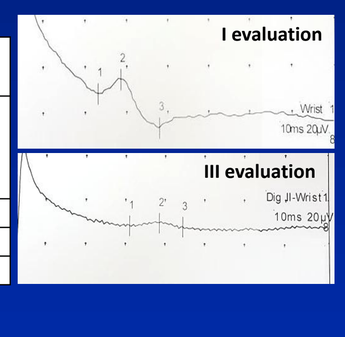


ELECTROPHYSIOLOGICAL ENMG FINDINGS

SENSITIVE NERVE CONDUCTION (SNC)

	I evaluation Day 3		II evaluation Day 10		III evaluation Day 30	
	Amplitude uV	Velocity m/s	Amplitude uV	Velocity m/s	Amplitude uV	Velocity m/s
S Median	16	52	4	42	1,8	41
S Ulnar	6	53	2,4	35	1,7	32
D Sural	9	53	6	42	3	28

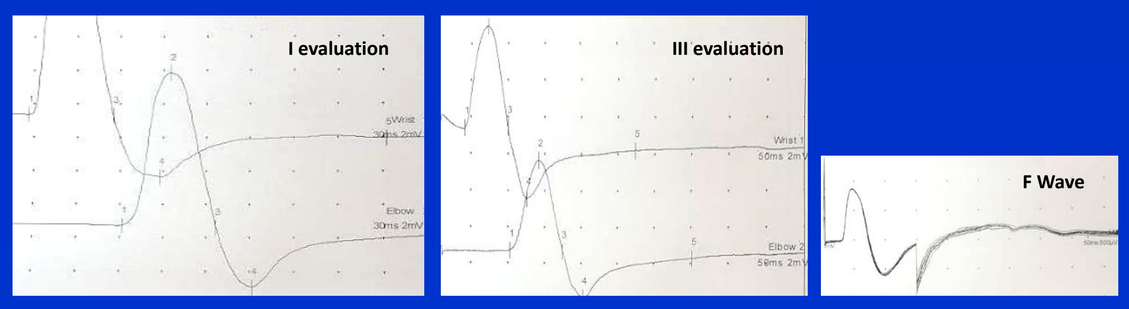
Sn Median Nerve



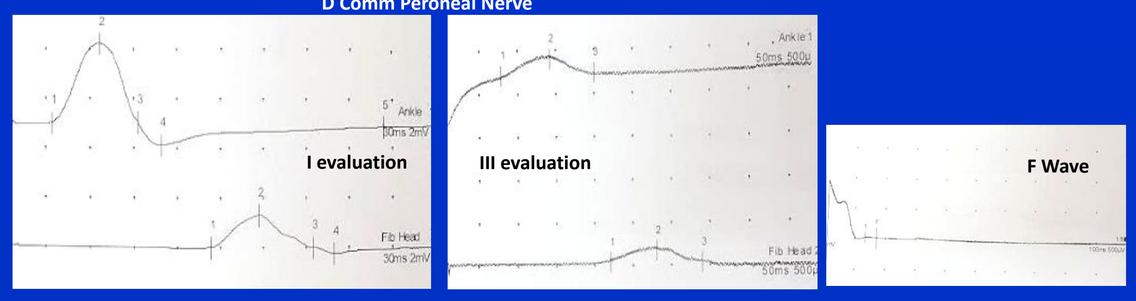
MOTOR NERVE CONDUCTION (MNC)

	I evaluation Day 3			III evaluation Day 30		
	Latency ms	Amplitude mV	Velocity m/s	Latency ms	Amplitude mV	Velocity m/s
Median						
Wrist	2.55	10.9		4.15	5.6	
Elbow	8.85	9.2	42.9	10.35	4.9	35.5
Ulnar						
Wrist	1.3	8.8		3.1	5.4	
Elbow	8.2	6.8	43.5	10.2	5.2	38.0
Comm Peroneal						
Ankle	3.3	3.3		7.9	0.3	
Fib Head	13.85	1.3	33.2	22.05	0.1	23.3

Sn Median Nerve

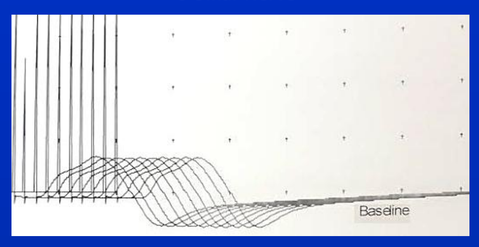


D Comm Peroneal Nerve



REPETITIVE NERVE STIMULATION

S Ulnar Nerve



DISCUSSION

The case we presented was characterized by central and peripheral symptoms, with ophtalmoplegia, ataxia and disturbance of consciousness associated with marked elevation of CK and demyelinating sensorimotor polyradiculoneuropathy (GBS). The case oriented us to the diagnosis of Bickerstaff's brainstem encephalitis with overlapping GBS, despite the negativity of GQ1b antibodies and the presence of anti-GM1 and anti-GD1b antibodies, which always supports the diagnosis of GBS (3,4, 5,6).

Mild to modest raised levels of CK have been documented in early stages of GBS, the cause of which is uncertain. The possible mechanism proposed in the literature is rapid extensive denervation due to severe axonal degeneration of motor nerve terminals can result in the release of muscle enzymes (10). Acute rhabdomyolysis leading to severe elevated CK levels in GBS is extremely rare (11)

In our patient we detected marked elevated levels of CK. Psychiatric drugs or a post-viral immune-mediated damage to muscle cells may be the possible etiology in our case of GBS.

Usually in GBS there is an increase in CSF protein concentration (80% of patients), with the mononuclear cell count being either normal (albuminocytologic dissociation) or <50 cells/µL.

The presence of severe pleocytosis in CSF induced us to consider also the possibility of a brainstem encephalitis associated to an acute demyelinating sensorimotor polyradiculoneuropathy and muscular involvement.

To our knowledge, there are few cases of GBS associated with encephalitis. Some authors reported a case of C.jejuni infection that caused both an acute polyradiculoneuropathy with combined encephalomyelitis (7). It has been reported a case of severe hepatitis E virus (HEV) infection associated GBS and encephalitis/encephalopathy in a 64-year-old male (8). GBS secondary to Japanese encephalitis virus (JEV) infection has been reported only in India and in one case in China. Furthermore, there is a case reported with Mycoplasma pneumonia infection associated with rhabdomyolysis and the GBS (9)

In our case, serological tests as well as Campylobacter jejuni colture were negative, in spite of fever and diarrhea during the first week.

In conclusion, GBS and its variants have several subtypes, which present in various ways and can be difficult to diagnose at first. In literature few cases characterized by GBS associated with encephalitis are described. In our patient the diagnosis remain uncertain, considering this case as a form of BBE-GBS with GQ1b negative and severe pleocytosis, as well as a case of GBS associated with encephalitis, in spite of normality of serological and CSF findings.

REFERENCES

1. Van Doorn PA, Ruts L, Jacobs BC. Clinical features, pathogenesis, and treatment of Guillain-Barré syndrome. Lancet Neurol 2008; 7: 939-50
2. Wakerley BR, Yuki N. Mimics and chameleons in Guillain-Barré and Miller Fisher syndromes. Pract Neurol. 2015;15:90-99.
3. Odaka M, Yuki Nyamada M, Koga M, Takemi T, Hirata K and Kuwabara S. Bickerstaff's brainstem encephalitis: clinical features of 62 cases and subgroup associated with Guillain-Barré syndrome. Brain, 2003; 126,2279-2290
4. Notturno F, Luciani M, Caporale CM, Ciarelli A, Uncini A. Antibodies to ganglioside complexes in Guillain-Barré syndrome: clinical correlates, fine specificity and complement activation. Int J Immunopathol Pharmacol. 2009;22 (2):437-45
5. Kusunoki S, Kaida K. Antibodies against gangliosides complexes in Guillain-Barré syndrome and related disorders. J Neurochem 201; 116: 828-832
6. Yuki N, Yoshino H, Sato S, Ohno T, Miyatake T. An acute axonal form of Guillain-Barré syndrome with antibodies against gangliosides GM1 and GD1b- a case report. Rinsho Shinkeigaku, 1990 Sep;30(9):989-93
7. Kamm CP, Keserue B, Humpert S, Wiest R, Nedeltchev K, Hess CW, Arnold M. Campylobacter jejuni abscess, encephalomyelytis, and acute polyradiculoneuropathy. Muscle Nerve, 2009; 40 (5): 875-9
8. Wu X, Liu K, Zhang H-L. Guillain-Barré syndrome and encephalitis/encephalopathy associated with acute severe hepatitis E infection. Neurol Sci 2015; 36: 165-166
9. Gupta R, Gupta A, Goyal V, Guleria R, Kumar A. Mycoplasma pneumonia associated with rhabdomyolysis and the Guillain-Barré syndrome. Indian J Chest Dis Allied Sci. 2005; 47(4): 305-8
10. Satoh J, Okada K, Kishi T, Nagayama S, Kuroda Y. Cramping pain and prolonged elevation of serum creatine kinase levels in a patient with Guillain-Barré syndrome following Campylobacter jejuni enteritis. Eur J Neurol. 2000 Jan;7(1):107-9.
11. Scott AJ, Ducan R, Henderson L, Jamal GA, Kennedy PG. Acute rhabdomyolysis associated with atypical Guillain-Barré syndrome. Postgrad Med J. 1991; 67:73-4.