Síndrome de Guillain-Barré: experiência de uma Unidade de Cuidados Intensivos e revisão da literatura

Guillain-Barré Syndrome: Experience of an Intensive Care Unit and literature review

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Resumo

Introdução e objectivo: A Síndrome de Guillain-Barré (SGB) é uma entidade que historicamente foi sempre bem definida, contudo, com o avanço do conhecimento científico revelou-se uma síndrome heterogénea, apresentando variantes com características clínicas distintas e fisiopatologia específica. Exceptuando a variante de Miller-Fisher o SGB caracteriza-se por ausência dos reflexos osteotendinosos (ROT) e paralisia muscular ascendente, flácida, de magnitude variável, podendo cursar com insuficiência respiratória por paralisia dos músculos respiratórios. Analiticamente o achado característico é a dissociação albumino-citológica. O electromiograma auxilia o diagnóstico, sendo contudo mais útil na identificação da variante. Os autores apresentam os casos de SGB com necessidade de internamento na Unidade de Cuidados Intensivos Polivalentes (UCIP) do Hospital de São Teotónio (HST). O objectivo deste estudo foi avaliar as características demográficas, evolução clínica da doença, tipos de variantes e resposta à terapêutica. Foram também analisadas as complicações e tempos de internamento e sua relação com a variante da doença.

Material e métodos: Estudo retrospectivo dos casos diagnosticados nos últimos 10 anos, com necessidade de internamento na UCIP (entre 31 de Janeiro de 2001 e 31 de Janeiro de 2011), através da análise dos respectivos processos clínicos.

Resultados: Dos vinte e um doentes com o diagnóstico de SGB, sete doentes necessitaram de internamento na UCIP, todos por falência respiratória; cinco homens e duas mulheres. A idade média foi de 50,8 anos. Foi identificado um evento precipitante em dois doentes. Quatro doentes apresentaram evolução rápida da doença (menos de 5 dias até ao internamento) e todos apresentavam formas axonais. Surgiram sinais de disfunção autonómica em 43% dos doentes. Todos apresentaram dissociação albumino-citológica. O tempo médio de ventilação mecânica (VM) foi de 24,4 dias, sendo este mais elevado nas formas axonais. O tempo médio de internamento na UCIP e hospitalar foram, respectivamente, 29,7 dias e 93,4 dias, sendo mais elevados nas formas axonais. Todos os doentes foram medicados com imunoglobulina humana endovenosa, não havendo complicações associadas ao tratamento.

Conclusão: As formas axonais estão associadas a evolução clínica mais rápida e de maior gravidade neurológica, o que se reflecte nos maiores tempo de VM e internamento. Associam-se também a taxas de recuperação menores e, como tal, maior morbilidade e mortalidade. O tratamento foi dirigido no sentido de modificar o curso da doença, e neste aspecto tanto a plasmaferese como a imunoglobulina humana endovenosa apresentam eficácia semelhante. O tratamento de suporte, nomeadamente ventilatório e da disfunção autonómica é de extrema importância no sentido de evitar complicações potencialmente fatais.

Palavras-chave: síndrome de Guillain-Barré, polineuropatia inflamatória desmielinizante aguda, neuropatia axonal, sindrome de Miller-Fisher, imunoglobulina endovenosa, plasmaferese.

Abstract

Introduction and objective: Guillain-Barré syndrome (GBS) is a historically well defined entity, however, the advance of scientific knowledge has proven to be a heterogeneous syndrome, with multiple variants, each one with distinct clinical features and specific pathophysiology. Except for the Miller-Fisher variant of GBS, it is characterized by the absence of osteotendinous reflexes and ascending flaccid muscle paralysis of variable magnitude, which may progress to respiratory failure by paralysis of respiratory muscles. Analytically, the main characteristic finding is the cerebro-spinal-fluid albumin-cytologic dissociation. The electromyogram helps the diagnosis, but it's more useful in identifying the clinical variant. The authors present the cases of GBS requiring hospitalization in the Intensive Care Unit (ICU) in our hospital. The aim of this study was to evaluate the demographic, clinical disease, type of variant and response to therapy. We also analyzed the complications and hospitalization time and its relation to the clinical variant of the disease.

Material and Methods: A retrospective study of GBS cases diagnosed in the last 10 years, requiring hospitalization in the Intensive Care Unit (from the 31st January 2001 to the 31st January 2011), through the analysis of their clinical files.

Results: Of the twenty-one patients diagnosed with GBS in the selected period, seven patients required admission to the ICU, all due to respiratory failure. It were five men and two women. The mean age was 50.8 years. A precipitating event was identified in two patients. Four patients evolved rapidly (less than 5 days to hospitalization in ICU) and all of these had axonal variants. There were signs of autonomic dysfunction in 43% of patients. All had albumin-cytologic dissociation. The mean duration of mechanical ventilation (MV) was 24.4 days, and this was higher in axonal forms. The average time of stay in ICU and hospital were, respectively, 29.7 days and 93.4 days, being higher in axonal forms. All patients received intravenous immunoglobulin. There were no complications associated with treatment.

Conclusion: Axonal variants are associated with a quicker disease progression and severe neurological deficits, which are reflected in prolonged time of MV and hospitalization. These are also associated with lower recovery rates and increased morbidity and mortality. Treatment was directed towards modifying the course of the disease, and in this respect both plasmapheresis and intravenous human immunoglobulin have similar efficacy. Supportive care, including respiratory care and treatment of autonomic dysfunction are extremely important to avoid potentially fatal complications.

Key words: Guillain-Barré syndrome, acute inflammatory demyelinating polyneuropathy, axonal neuropathy, Miller-Fisher syndrome, intravenous immunoglobulin, plasmapheresis.

INTRODUCTION AND OBJECTIVE

The authors present a retrospective descriptive study with the objective of characterizing inpatients of Multipurpose Intensive Care Unit (UCIP) of Hospital de São Teotónio with a diagnosis of Guillain-Barré Syndrome (GBS).

MATERIAL AND METHODS

This is a retrospective study, where the authors have assessed the cases with a GBS diagnosis in the last 10 years, with a need of admission in the multipurpose intensive care unit (from the 31st January 2001 to the 31st January 2011).

Data were collected from the individual consultation of ICU admission files and the individual hospital file of each patient. A data base was set up with different variable to be evaluated: gender, age, precipitating agent, triggering event time related with symptomatology onset, variant, implemented therapy, tests carried out, mechanic ventilation time (MV), need for tracheostomy, admission time in ICU and hospital and progression after hospital discharge. Such data were then assessed and compared with data from other series, namely those published in Portugal.

RESULTS AND DISCUSSION

In the period of time considered there were 259.377 admissions in the HST, 21 of which with a GBS diagnosis, what considering the population in the area of hospital influence, is equivalent to an incidence of 0.81 patients per 100,000 inhabitants per year. However, it is important to refer that the Emergency Service in our hospital does not have a daily support in Neurology specialty, reason why GBS patients might have been transferred for other health care institution, therefore the actual incidence may be slightly higher than the presented one.

From the 21 patients admitted due to GBS there was a need for ICU admission of 7 patients (33.3%), all due to respiratory failure with a need for mechanical ventilation, a percentage which complies with the need described of mechanical ventilation, of around 30%.[1]

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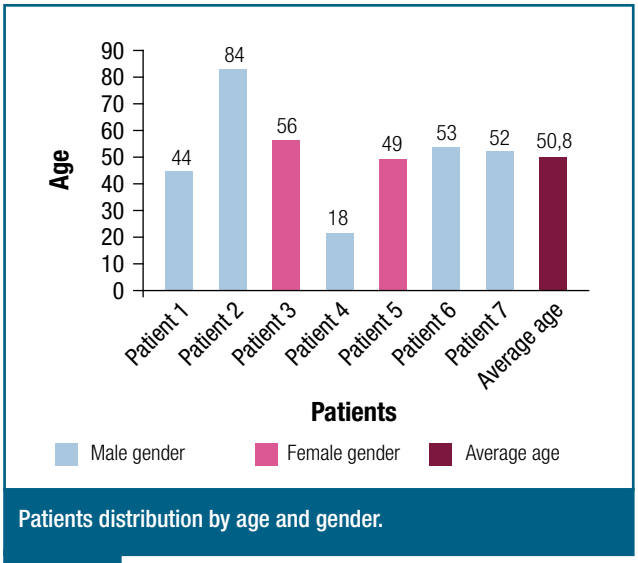


Patients distribution by age and gender.

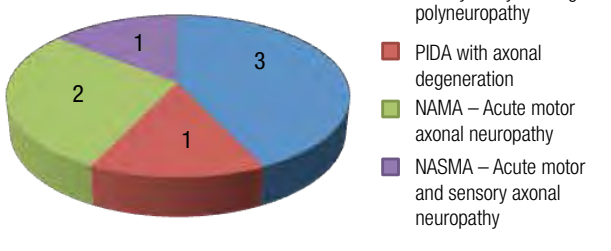
FIG. 1

The ICU inpatients average age was of 50.8 years old. Five patients were men and two women. Female patients average age was 52.5 years old and male 50.2 years old. In our series it was seen that GBS occurred preferentially in individuals rather young, being an important cause of morbidity and mortality in these patients. (*Figure 1*)

It was possible to identify a triggering event in two patients; one of them has shown a gastroenteritis condition and another respiratory infection of the upper airways. The first had an acute inflammatory demyelinating polyneuropathy and the second an acute motor and sensory axonal neuropathy. No antibody measurements were carried out.

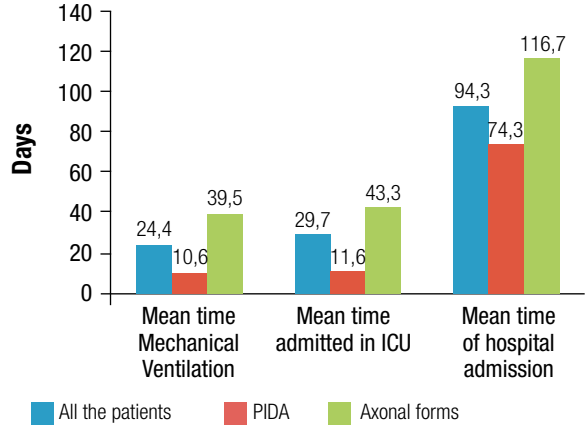
The objective exam on ICU admission of all patients was a flaccid tetraparesis with reduced or absent osteotendinous reflexes; five patients presented bilateral facial paresis and three patients with signs of reaching other cranial nerves.

Regarding the timeframe, symptoms have evolved until ICU admission, it was verified that four patients had a period of time lower than five days, and from these, three patients presented axonal forms and a patient an acute inflammatory demyelinating polyneuropathy with axonal degeneration. Three patients had a clinical condition evolving for a fortnight or more, and all these had an acute inflammatory demyelinating polyneuropathy. Therefore, we can ascer-



Distribution of the disease variants.

FIG. 2



Mechanical ventilation and hospitalization period according to the variant

FIG. 3

tain that in, our series, the axonal forms presented a quicker evolution for respiratory failure with a need for mechanical ventilation.

Signs of autonomic dysfunction were present in three patients, what is equivalent to 43%, and expressed themselves by tachycardia, hypertension, long QT interval, atrial fibrillation again and sphincter incontinence.

Lumbar puncture has revealed a albumin-cytological dissociation in all patients, with an average value of CSF proteins of 124 mg/dL. Electromyography has enabled to determine the variables: four cases of acute inflammatory demyelinating polyneuropathy, being than in one of them there was a secondary axonal degeneration, two cases of acute motor axonal neuropathy and a case of acute motor and sensory axonal neuropathy. (*Figure* 2)

All patients were treated with endovenous immunoglobulin in a 0.4g/Kg dosage, with an average length of treatment of 5.4 days (a maximum of 8 days, and a minimum of 5 days). There were no complications during the treatment.

There was the need for mechanical ventilation in all patients, with an average time of mechanical ventilation of 24.4 days. In the demyelinating variants the average mechanical ventilation was 10.6 days, while in the axonal forms this was of 39.5 days. The tracheostomy was carried out in three patients and performed in average in the eleventh day of mechanical ventilation.

The average time of admission in the ICU was of 29.7 days, in the acute inflammatory demyelinating polyneuropathy was 11.6 days and in the axonal variants of 43.3 days; the mean time of hospitalization was of 93.4 days (74.3 days in average for acute inflammatory demyelinating polyneuropathy and 116.7 days in average in axonal variants). Figure 3 relates the need of mechanical ventilation and admission times in the ICU with the variant.

Two patients died one year after the GBS diagnosis; one of them in the same admission episode (but already after ICU discharge) and in another new admission after a fortnight. The cause of death was nosocomial pneumonia in two patients and both presented a sensitive axonal variant.

Figure I shows the main characteristics of patients in our series.

CONCLUSION

The data presented are in accordance with those described in some series published,2 reflecting the need of mechanical ventilation in around 20-30% of patients and a more aggressive character and a delayed recovery pattern of axonal forms.[2,3]

In the work by Fonseca T. et al,[3] thirteen of the fifteen patients admitted by GBS had a favorable evolution, with a less favorable progressin in two who presented conditions of acute motor axonal neuropathy and acute motor and sensory axonal neuropathy. The need for mechanical ventilation and admission in intensive care was lower than in our series (around 13%), and more frequent in axonal variants. Periods of admission were similar.

In the remaining endpoints we can refer that, in a general way, our series is closer of those published in the literature, both in epidemiology, clinical evolution, variants found and respective severity and treatment, whether with endovenous or support immunoglobulin.[4,5]

LITERATURE REVIEW: GUILLAIN-BARRE SYNDROME

History

GBS history started to be drawn in 1859, year when Jean Baptiste Octave Landry de Thézillat describes 10 cases of ascending paralysis, among them an obituary by "asphyxia". Surprisingly, the patient's *post mortem* did not show any changes and this new syndrome would become known as Landry's ascending paralysis.[6]

In 1916, during World War II, Georges Guillain, Jean-Alexandre Barré and André Strohl, at the time young physicians on military service, observed two French soldiers with lower limbs partial paralysis and areflexia of osteotendinous reflexes, with one only change in the tests carried out and that was an albuminocytologic dissociation of the cerebrospinal fluid. They published the case (*Fig. 4*) and due to the similarity with the Landry's ascending paralysis condition, some advocate that it is the same clinical entity.[6]

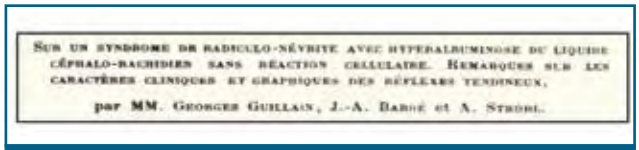
As time went on this new syndrome acquires a role of its own in the spectrum of neurologic diseases, being accepted the eponymous of Guillain-Barré, used for the first time in 1927 by Dragonescu and Claudian. However, history ends up forgetting unfairly, the name of Strohl, equally important in its initial definition.[6]

In 1956, the Canadian neurologist Charles Miller-Fisher describes three patients with ophtalmoplegia, ataxia and areflexia and, due to the similarity of the condition with some GBS patients' reports, it was presumed to be a *GBS-like syndrome*.[7]

More recently, in the 80ties, epidemic axonal variants are described in China country side, particularly in children and later its association with *Campylobacter jejuni* infection and a direct axonal lesion as a main pathogenic mechanism.[8]

Clinical variants

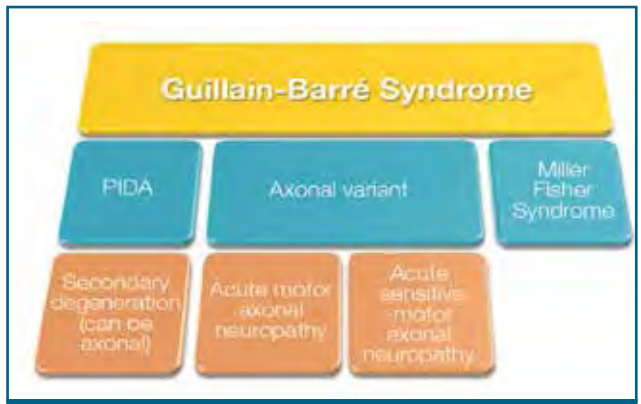
In spite of in the clinical practice to refer to this entity


Sur un syndrome de radiculo-névrite avec hyperalbuminose du liquide céphalo-rachidien sans réaction cellulaire. Remarques sur les caractères cliniques et graphiques des réflexes tendineux,

par MM. Georges Guillain, J.-A. Barré et A. Strohl.

Heading of the original article of the GBS initial description.

FIG. 4



Esquematização das variantes do SGB.

FIG. 5

as *Guillain-Barré Syndrome*, as already mentioned, this includes an heterogeneous syndrome, with multiple variants, namely an acute inflammatory demyelinating polyneuropathy, a variant or Miller-Fisher syndrome, an acute motor axonal neuropathy and an acute motor and sensory axonal neuropathy.[9] These present pathophysiological mechanisms, with distinct presentation and evolution, reason why its identification is important approaching GBS patients.[9] *Fig. 5* shows a chart of the GBS main variants.

Acute inflammatory demyelinating polyneuropathy includes 85 to 90% of GBS cases and it is characterized by progressive muscular weakness, symmetrical, with hyporeflexia or areflexia of osteotendinous reflexes. It is characterized by a multifocal demyelination, in plaques, of all peripheral nerves, mediated by auto-antibodies against the myelin sheath in the Schwann cells. The severity peak is reached on the third and fourth week of the disease and the re-myelination occurs during weeks or months. However, some patients present a delayed or incomplete recovery, mainly in those with a secondary axonal degeneration.[9]

TABLE I

Acute sensitive-motor axonal neuropathy

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Gender	Male	Male	Female	Male	Female	Male	Male
Age	44 years	84 years	56 years	18 years	49 years	53 years	52 years
Triggering event	NI	NI	NI	NI	NI	Acute gastroenteritis	Respiratory infection
Time of symptoms-ICU admission	3 weeks	3 days	5 days	It was not determined	5 days	2 weeks	2 days
Clinical exam at entrance	Flacid tetraparesis	Flacid tetraparesis	Flacid tetraparesis; bilateral facial paresis	Flacid tetraparesis, dysphagia	Flacid tetraparesis, dysphonia, dysphagia	Flacid tetraparesis, areflexia,	Flacid tetraparesis, areflexia
Autonomic signs	Tachycardia/ bradicardia	Bradicardia/QT long	Hypertension/ sphyncters incontinence / hyperhydrosis/ atrial fibrilation	No	No	No	No
Variant	acute inflammatory demyelinating polyneuropathy	acute motor axonal neuropathy	acute inflammatory demyelinating polyneuropathy (degen. axonal)	acute inflammatory demyelinating polyneuropathy	acute motor axonal neuropathy	acute inflammatory demyelinating polyneuropathy	acute motor and sensory axonal neuropathy
Treatment	ENDOVENOUS IMMUNOGLOBULIN						
MV period	10 days	19 days	39 days	16 days	10 days	6 days	90 days
ICU admission time	10 days	17 days	17 days	15 days	12 days	10 days	127 days
Intercurrences during admissio	Nosocomial pneumonia by Escherichia coli	Pneumonia by Acinectobacter baumannii	None	None	None	None	PAV and MSSA and Haemophilus influenzae; iatrogenic pneumothorax and pneumomedaystin

Subtitle: NI: non identified; endovenous immunoglobulin; PAV: pneumonia associated to the ventilator; MSSA: methicillin sensitive staphylococcus aureus

Miller Fisher Syndrome represents around 5% of GBS cases and is typically described by the coexistence of ophthalmoplegia with ataxia and areflexia. Around 25% of patients show muscular weakness in the extremities and in more rare cases can evolve with cerebellar ataxia and hyporreflexia.[10] It is known at present that in 90% of cases the Miller Fisher Syndrome there are circulating auto-antibodies anti -GQ1b, linking to the GQ1b epitope of the cranial nerves accounting for ocular motricity.[11]

Acute motor axonal neuropathy is the most common GBS form in China and Japan affecting mainly young individuals. In most cases it is associated to the recent infection by *Campylobacter jejuni*. It presents a similar symptomatology and prognosis similar to acute inflammatory demyelinating polyneuropathy, with a selective involvement of motor fibers and direct axonal lesion and not by demyelinating processes.[12]

Acute motor and sensory axonal neuropathy is a more aggressive form of acute motor axonal neuropathy compromising motor and sensitive fibers. It is characterized by a marked axonal degeneration and it is associated mainly to auto-antibodies anti-GM1, whose production is induced by a previous *Campylobacter jejuni* infection. By mechanisms of molecular mimicry (GM1 ganglioside present in the axonal membrane is antigenically very similar to the GM1--like polysaccharide of *Campylobacter jejuni* cellular wall), there is a neuronal lesion by auto-antibodies production.[13]

The recent infection by Haemophilus influenza is the second cause more often implied in the development of acute motor and sensory axonal neuropathy and it is associated to a quicker and complete recovery.[14]

There are rarer forms of GBS presentation. The pharynx-cervical-brachial variant evolves with muscular weakness in the upper limbs, dysphagia and facial paresis, being preserved the muscular strength in the lower limbs. Acute pandysautonomy is a very rare variant characterized by the exuberance of dysautonomy signs (diarrhea, vomiting, vertigo, abdominal pain, ileus, orthostatic hypotension, urinary retention, changes of the cardiac rhythm and hypohidrosis). Bickerstaff's encephalitis is characterized by ophthalmoplegia and ataxia (establishing a differential with Miller Fisher Syndrome), however it co-exists in general with hypereflexia. Finally there can be a limited involvement of the lower limbs – paraparesis variant or with a selective involvement of sensitive fibers and ataxia – BGS sensitive and pure.[15]

Epidemiology and etiology

GBS presents a world distribution with an incidence of 1 to 2 cases per each 100.000 inhabitants per year. It affects all the age groups, but mainly the young adult and the elderly. In about 60% of cases there is a history of respiratory or gastrointestinal infection (viral or bacterial). The general mortality rate is around 4%.[16]

Regarding GBS etiology there are several agents/triggering events, namely infections by *Campylobacter jejuni, Haemophilus influenzae, Mycoplasma pneumoniae, cytomegalovirus, Epstein-Barr virus,* varicella-zoster and human immunodeficiency virus.[17]

Case reports were also referred associating GBS development after the following events: infection by A, B and C hepatitis virus, post-surgical period of several surgeries, bone marrow post-transplant, isotretinoin medication, Hodgkin's disease, systemic lupus erythematosus, sarcoidosis and medication with TNF-alpha antagonists[9,18,19] what can indicate that there are other pathophysiological mechanisms for the disease development.

Clinical presentation and diagnosis

GBS cardinal sign is the muscular weakness, progressive, ascending and symmetric with absent or very reduced osteotendinous reflexes. Muscular weakness evolves throughout days to weeks since the symptoms onset and it is variable in intensity, changing from discreet gait unease to the paralysis of respiratory muscles. Four weeks after the symptomatology onset, around 90% of patients have already reached the disease peak.[9] The need for mechanical ventilation occurs in around 30% of patients.[1] It can also evolve with facial paresis (in around half of patients) and with paresis of oropharynx muscles. The eye extrinsic muscles paresis occurs in 15% of patients. There is a development of paresthesia in the hands and feet on over 80% of patients and are usually mild; a great part of patients also refers moderate to intense lumbar pain.[9]

It is important the early detection of disautonomy signs, as this is an important cause of mortality in this group of patients. It is characterized by tachycardia (the most common sign), orthostatic hypotension, changes in the cardiac rhythm, ileus, hypohidrosis and urinary retention. In some patients can happen hypertension periods alternating with hypotension and bradicardia.[20]

GBS diagnosis is essentially clinical and its diagnostic criteria are described in *Table II*.

As differential diagnosis it is important to mention a chronic demyelinating polyradiculopathy, with a clinical evolution, on the contrary of acute inflammatory demyelinating polyneuropathy, dragging for over 8 weeks and in crescendo, only rarely is associated to an identifiable triggering event involving less frequently the cranial nerves.[21] Other polyneuropathies should be considered, namely those related with arsenic poisoning, n-hexane inhalation, hypophosphatemia, hypokalemia, vasculitis (namely Churg-Strauss syndrome), Lyme's disease and acute

porphyria.[21]

Regarding the medullar pathology it should be considered myelopathy by compression of the spinal cord and acute transverse myelitis. In this context it is relevant the role of nuclear magnetic resonance, and regarding the pathology of the neuromuscular junction it is important to exclude botulism and myasthenia gravis.[22]

Regarding the muscular pathology we consider acute polymyositis and critical disease myopathy, with the first affecting predominantly the proximal muscles and the second is, from the start excluded during the anamnesis in most patients.[23]

Diagnosis additional tests

As mentioned previously, GBS diagnosis is clinical. As mentioned, the GBS diagnosis is clinical. Diagnosis additional tests help in cases where the diagnosis is doubtful, or for a better definition and characterization of the variant and exclusion of eventual associated lesions.

TABLE II

GBS diagnostic criteria.[42]

Necessary to the diagnostic	Progressive muscular weakness of more than one limb, variable severity, from paresthesia to muscular paralysis of all members, trunk, facial muscles and bulbar and/or internuclear ophthalmoplegia;
	Areflexia of osteotendinous reflexes. Distal areflexia is practically universal; in the more proximal tendons there can be hyporeflexia;
Supporting the diagnosis	Progression of the signs and symptoms throughout days up to 4 weeks;
	Relative symmetry;
	Light sensitive signs and symptoms;
	Involvement of cranial nerves specially bilateral facial paresis;
	Recovery after 2-4 weeks after reaching the disease peak;
	Without evidence of fever;
	Increase on CSF proteins with a normal leukocytes count;
	Changes in the neurophysiological studies consistent with GBS;

Adapted from: Criteria for diagnosis of Guillain-Barré syndrome. Ann Neurol 1978; 3:565

Lumbar puncture is important in GBS suspicion, as the presence of albumin-cytological dissemination (increase of proteins in the CSF with normal levels of leukocytes) strongly supports the diagnosis. It is present in around 90% of GBS to the 6-7 days of evolution after the symptoms onset.[24]

The electromyogram reveals a polyneuropathy pattern with predominating characteristics of demyelinating in acute inflammatory demyelinating polyneuropathy and of diffuse axonal lesion in acute motor axonal neuropathy and acute motor and sensory axonal neuropathy.[9]

The determination of auto-antibodies is not done routinely, but can be considered in cases where there are doubts about the diagnosis or determining the variant. Therefore, anti-GQ1b antibodies are positive in 85-90% cases of Miller-Fisher Syndrome with anti--GM1 and anti-GD1b antibodies are more associated to axonal variants.[23]

Imageology tests, particularly NMR can help excluding bone marrow lesions.[22]

Treatment

GBS treatment, regardless of the variant, is based in two pillars: directed treatment, immunomodulator, in the attempt to modify the disease progression and support treatment.[9]

Both plasmapheresis as endovenous immunoglobulin are authorized and revealed to be effective in GBS treatment. Plasmapheresis consists in the removal of circulating antibodies, complement fractions and cytokines. There is evidence proving plasmapheresis superiority and support care versus support care isolately, in what refers to an early improvement of muscle strength and a reduction on the mechanic ventilation time.[24] It is more effective if started in the first 7 days of the disease, although it is licit to start plasmapheresis up to 30 days after the disease onset, as there is still evidence of benefit.[25] The scheme set out is the filtration of 200 to 250 mL/kg of plasma weight for 10 to 14 days, in 5 or 6 procedures, using albumin 5% as a replacement fluid. (25) There are some case reports suggesting that plasmapheresis can be more effective than endovenous immunoglobulin in axonal variants, however, all clinical trials and meta-analysis testify the quality of the efficacy in both procedures.[26]

TABLE III

Recommendations of the American Academy of Neurology for GBS treatment[43]

1	The choice between endovenous immunoglobulin and plasmapheresis depends on the hospital availability, the patient´s risk factors and contraindications and the physician´s preferences;
2	The treatment with endovenous immunoglobulin or plasmapheresis speeds up the recovery or reduces the likelihood of complications;
3	The combination of two treatments is not recommended;
4	Corticotherapy has not interest in the treatment;
5	Plasmapheresis should be started in the first 4 weeks after the disease onset, ideally in the first 7 days;
6	Endovenous immunoglobulin should be started in the first 4 weeks, ideally in the first 2 weeks;
7	The treatment scheme with endovenous immunoglobulin is of 0.4g/Kg during 5 to 6 days and the main secondary effect are an acute renal failure, rash, aseptic meningitis, hyperviscosity and thrombotic phenomena;
8	Plasmapheresis should be based in 4 to 6 sessions throughout the course of 8-10 days (total 200-250 mL/Kg) and the main problems to anticipate, serious infections/sepsis and problems with venous access;

Adapted from: Hughes RA, et al. Practice parameter: immunotherapy for Guillain-Barré syndrome: report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2003;61(6):736-740.

The endovenous immunoglobulin is the most often used scheme due to its universal use and ease of administration. It is known that patients with a more serious disease can benefit in a longer treatment duration (6 days), in a usual dosage of 0.4g/kg.[27] The combination of two therapeutic modes is not recommended, as it does not provide an additional improvement regarding each one isolately.[28]

Corticosteroids drugs do not present any benefit in the GBS treatment therefore are not recommended. In a recent meta-analysis with over 500 patients, corticosteroids did not reveal any benefit in terms of a quicker improvement or the need for mechanical ventilation, regarding endovenous immunoglobulin or plasmapheresis.[29]

There has been a growing interest by the hypothetic role and theoretically beneficial of Beta interferon in such patients, however the studies carried out so far, do not show additional benefits and, as such, the therapy is not recommended.[30]

Other therapeutic modes are the tripterygium polyglucoside, an herbal medicine, used empirically in GBS treatment in certain oriental cultures, it is not recommended as it does not show to be beneficial31 and the cerebrospinal fluid filtration, which did not reveal a statistically significant benefit regarding the therapy with plasmapheresis and therefore is not recommended.[32]

Table III makes a summary of the current recommendations for the GBS immunomodulation treatment.

Other aspect equally important while approaching a GBS patient is a support treatment that often leads to intensive care hospitalization. In such context, it is important to refer the ventilatory support, the autonomic dysfunction, cardiovascular, gastrointestinal and urinary support, psychological support, effective control of pain and recovery.

Respiratory failure with a need for invasive mechanic ventilation occurs in around 30% of patients and can evolve quickly reason why it is important a tight surveillance.1 Recommendations for orotracheal intubation and mechanical ventilation, a forced vital capacity lower than 20 mL/kg, a maximum inspiratory pressure lower than 30 cmH2O and a maximum expiratory pressure lower than 40 cmH_2O.[33] On the other hand, the bulb dysfunction and the subsequent difficulty on swallowing and elimination of secretions can be on its own an indication for orotracheal intubation.[33]

Some predictive aspects of the need for mechanical ventilation in the early stages of the disease are described, namely a quick evolution (in less than 7 days) for breathing difficulty, unable of coughing and eliminating secretions, unable to keep orthostatism, unable to mobilize and lift the upper limbs above the elbows, unable to raise the head and transaminases increase. It was demonstrated that patients presenting at least four of the previous criteria have an 85% probability of needing mechanical ventilation.[34]

The ventilator weaning should be gradual and based on the muscular strength and adaptation of ventilatory modes less controlled by the ventilator. The incapacity to flex the foot and a blockade of the

nervous conduction in the sciatic nerve by the end of the modifying disease therapy was associated to a need of more prolonged mechanical ventilation (over a fortnight), what can imply to carry out an early tracheostomy.[35] This should be made at two weeks of mechanical ventilation, if a significant improvement of the pulmonary volumes is not verified.[36]

The two factors which predict success in extubation, with a 82% sensitivity and a 90% positive predictive value are the lower inspiratory pressure (lower than 50 cm H2O) on the day of extubation and an increase of over 4 mL/kg in the current volume, regarding the orotracheal intubation and the beginning of mechanical ventilation.[37] Again such endpoints help identifying patients with a possibility of an early extubation or referring for an early tracheostomy.[37]

Autonomic dysfunction occurs in around 70% of patients is the main cause of mortality in patients admitted in a context of intensive care, where the ventilation is secured.[20] The probability of autonomic dysfunction is proportionally higher to the severity. It is manifested by tachycardia, arterial hypertensions or orthostatic hypotension, often bradycardia, urinary retention, ileus and hyposudoresis.[20] In this context, it is important a continuous monitoring of the arterial pressure, heart beat and electrocardiography and keeping the hydro-electrolytic and acid-base balance.

Regarding the cardiovascular support whose need is related with the autonomic dysfunction, orthostatic hypotension must be avoided, particularly important while lifting a quadriplegic patient, keeping an adequate blood volume, mainly in ventilated patients with positive pressure and avoiding hypotensive drugs, and paying attention to arrhythmias during secretion aspirations are more frequent in GBS and autonomic dysfunction patients.[36]

The abdomen daily exam with an auscultation of the abdominal sounds is important before a suspicion of adynamic ileus and administration of opioid drugs should be very strict. Erythromycin and neostigmine can be beneficial to the treatment of ileus.[36]

Neuropathy pain occurs in around half of GBS patients always in need of treatment.[38] Gabapentin and carbamazepine are the most effective drugs in the acute stage. Opioids are effective, but the side effects are frequent and can worsen the autonomic dysfunction.[38] As a maintenance therapy can be used tricyclic antidepressant drugs, gabapentin and pregabaline.[39]

Around 80% of patients present anxiety signs and panic attacks and reactive psychosis occurring in respectively 67% and 25%.40 Psychotic episodes are associated more to severe tetraparesis, affecting cranial nerves and the need for mechanical ventilation. It is therefore of value a psychological evaluation in a more stable disease stage.[40]

The recovery is the end stage of an epopee almost always long and of great morbidity, where it is highlighted mainly the importance of individual programs of isometric, isotonic and isokinetic exercise where the patient needs to relearn postures.41 Such exercise should be regular and in a long term approach a multidisciplinary team, in the attempt of avoiding persisting fatigue, that often emerges in such patients, even after the initial neurologic pathology is under control.[41] ■

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