Arq Neuropsiquiatr 2005;63(3-B):772-775

GUILLAIN-BARRÉ SYNDROME IN THE ELDERLY

Clinical, electrophysiological, therapeutic and outcome features

Marcondes C. França Jr[1a], Leonardo Deus-Silva[1a], Rafael de Castro[1a], Solange G. Garibaldi[1b], Beatriz H.M. Pfeilsticker[1b], Anamarli Nucci[1b], José F.C. Marques Jr[2]

ABSTRACT - There are few papers devoted to geriatric Guillain-Barré (GBS) and many related issues remain unanswered. *Objective:* To describe clinical, electrophysiological and therapeutic features in this age. *Method:* Clinico-epidemiological data and therapy of GBS patients older than 60 years were reviewed. Hughes scores were used to quantify neurological deficit and define outcome. *Results:* Among 18 patients (mean age 64.8 years), 9 had evident prodrome and 80% noticed initially sensory-motor deficit. Demyelinating GBS was found in 8 and axonal in 6 subjects. There was one Miller-Fisher and 3 unclassified cases. Plasmapheresis (PFX) was single therapy in 12 patients and intravenous immunoglobulin (IVIg) in 2. Disability scores just before therapy were similar in both groups, so as short and long term outcome. *Conclusion:* Axonal GBS seems to be more frequent in the elderly and this may have prognostic implications. PFX and IVIg were suitable options, but complications were noticed with PFX. Prospective studies are needed to better understand and manage GBS in the elderly.

KEY WORDS: Guillain-Barré syndrome, plasmapheresis, intravenous immunoglobulin, elderly.

Síndrome de Guillain-Barré no idoso: aspectos clínico-eletrofisiológicos, terapêutico e prognóstico

RESUMO - Publicações sobre a síndrome de Guillain-Barré (SGB) no idoso são escassas e várias questões sobre o tema estão abertas. *Objetivo:* Descrever aspectos clínico-eletrofisiológicos, terapêuticos e prognóstico no idoso. *Método:* Revisamos os prontuários de pacientes acima de 60 anos com SGB. A escala de Hughes foi usada para quantificar os déficits iniciais e finais. *Resultados:* No total de 18 pacientes (média de idade 64,8 anos), 50% tiveram pródromo e 80% tiveram déficit sensitivo-motor no início. SGB desmielinizante foi encontrada em 8 pacientes, axonal em 6 e uma síndrome de Miller-Fisher. Três casos não puderam ser classificados. Plasmaférese (PFX) foi empregada isoladamente em 12 pacientes e imunoglobulina endovenosa (IVIg) em 2. A disfunção inicial nos dois grupos tratados era semelhante, assim como a evolução a curto e longo prazo. *Conclusão:* A forma axonal da SGB parece ser mais freqüente no idoso e isto pode ter implicações prognósticas. PFX e IVIg foram eficazes, mas complicações ocorreram apenas no grupo tratado com PFX. Estudos prospectivos são necessários para um melhor entendimento e manejo da SGB no idoso.

PALAVRAS-CHAVE: síndrome de Guillain-Barré, plasmaférese, imunoglobulina endovenosa, idosos.

Guillain-Barré syndrome (GBS) is an immune-mediated neuropathy characterized by the acute onset of symmetric weakness with areflexia and sensory deficits[1]. It has been described worldwide with similar annual incidence rates ranging from 0.4 to 4.0 per 100.000 inhabitants and slight male predominance[2]. In most countries, GBS is now the most frequent etiology of acute flaccid paralysis and still an important cause of severe disability, particularly among aged patients[2].

Research in late decades has greatly improved our knowledge about the immune mechanisms responsible for the condition. GBS is probably an autoimmune disease directed against peripheral myelin or axon triggered by a preceding infection[3]. In this scenario, immunomodulation has gained uni-

[1]Department of Neurology; [2]Hemotherapy Center, Faculty of Medical Sciences, Campinas State University, Campinas SP, Brazil (UNICAMP): [1a]MD; [1b]MD, PhD; [2]MD, PhD.

Received 26 January 2005, received in final form 28 April 2005. Accepted 28 May 2005

Dra. Anamarli Nucci - Departamento de Neurologia / Faculdade de Ciências Médicas (UNICAMP) - Caixa Postal 6111 - 13083-970 Campinas SP - Brasil. E-mail: anucci@ni.hc.unicamp.br

versal acceptance as a first line therapy and several trials have shown the effectiveness of plasmapheresis (PFX)[4-8] and intravenous immunoglobulin (IVIg)[9,10]. Both approaches have similar results[9,10]

Despite this, some management issues remain unanswered. There are few papers specifically addressing clinical features and therapy among elderly people[11-14]. Most available data do not take into account peculiarities of the geriatric group. In this setting, the present study was undertaken to evaluate the clinical findings of GBS and the treatment approaches among older patients.

METHOD

We retrospectively reviewed medical records of patients older than 60 years meeting standard diagnostic criteria for GBS[15] admitted to UNICAMP Hospital between 1990 and 2004. This unit is a tertiary university center in southern Brazil, which provides specialized neurological care for approximately 5000000 inhabitants. There were 18 cases, including 8 women and 10 men. They were followed at regular appointments after the onset of GBS (range 6 to 36 months).

We recorded epidemiological and laboratorial data, namely sex, age on onset, prodromal events, initial symptoms, cerebrospinal fluid (CSF) findings and electroneuromyographic studies (ENMG). In accordance with a previous report 16, patients were classified into four clinico-electrophysiologic subtypes of GBS: acute inflammatory demyelinating polyneuropathy (AIDP), axonal GBS, Miller Fisher syndrome (MFS), and unclassified cases (the ones without ENMG). MFS necessarily presented ataxia, areflexia and ophthalmoplegia.

Clinical features and neurological deficits were recorded during the course of the illness. A disability scale modified from Hughes et al.[17] was used to quantify the functional status of patients on admission, at nadir of deficits previously to institution of treatment, and at 7, 60 and 365 days after therapy. Median times to peak disability and duration of hospitalization were also identified.

PFX and IVIg were the usual therapeutic options. PFX was performed by the same apheresis team on automated machines with continuous flow. Normal saline 0.9% plus 5% albumin was the replacement solution. Approximately 30 ml/kg of plasma was cleared in each session and a central venous line was the usual vascular access. The number of procedures for each patient ranged from 1 to 5 on an alternate day schedule. IVIg in a total dose of 2g/Kg was infused along 5 consecutive days. Obvious contra-indications both for PFX (infected patients, hemodynamic instability, extremely low weight) and IVIg (eg, IgA deficiency) precluded their use. We recorded the time before onset of treatment and the frequency of complications.

Demographical and clinical features on admission were displayed as mean ± one standard deviation.

RESULTS

Mean age of the whole group was 64.8 years (range 60 to 79 years) with a slight male predominance. Half of the patients had a preceding event within the 4 weeks before onset of GBS, such as upper respiratory tract infection (6 cases) and acute gastroenteritis (3 cases). Limb sensory complaints and weakness were the initial symptoms in more than 80% of cases. Cranial nerve involvement was found in 8 subjects, 5 of which had facial diplegia. Gait and limb ataxia at examination were present in 2 patients. Autonomic failure, manifested by fluctuating blood pressure and cardiac rhythm, was noticed in 6 patients and one presented atonic ileus.

According to ENMG features, there were 8 patients presenting AIDP, 6 axonal GBS and one MFS. Three patients had no ENMG evaluation (unclassified cases). CSF analysis revealed mean white blood cell count of 2 cells/mm^3 and protein concentration of 138.9 mg/dL. Two patients presented initially normal CSF findings, but ENMG supported GBS diagnosis. Basic clinical data of patients are resumed in Table 1.

PFX and IVIg were the sole therapy in 12 and 2 patients, respectively. The MFS patient had both PFX and IVIg. Three patients were not treated with either option. This last group included two patients with mild forms of GBS, which first came for evaluation already in the recovery phase and one who had cardiac arrest and died in the 5th day of illness.

Mean age of patients in the PFX group was 64.1 years and in the IVIg 63.5. In the PFX group, there were 5 axonal GBS, 6 AIDP and one unclassified. In the IVIg group, there were one axonal GBS and one AIDP. Mean times before treatment onset in PFX was 6.1 days and in IVIg 11.5 days. Mean times from onset of symptoms to nadir of deficits in both groups were 8.6 and 15.5 days, respectively. On admission, nadir, 7, 60 and 365 days after treatment, disability scores are resumed in Table 2. Duration of hospitalization was also shown in this Table.

Adverse events of PFX included central venous catheter related complications (3 patients), electrolyte disturbance (1) and hypotension (2). In contrast, neither of the IVIg patients had any complication. In our series, overall mortality was 22%. One of these patients had a rapidly progressive course with severe disautonomia and early cardiac arrest, so that there was not enough time to start specific therapy. The remaining three cases that died had PFX, but only one death was possibly related to the procedure since infection of catheter was the source of bacteremia and sepsis.

Table 1. Basic clinical data of patients.

	AIDP (n = 8)	Axonal GBS (n = 6)	MFS (n = 1)	Unclassified (n = 3)
Mean age (years)	65.0 ± 6.4	66.0 ± 2.5	65	62.0 ± 2.0
Sex (Male/Female)	5/3	3/3	0/1	2/1
Preceding evens				
Upper respiratory tract infection	2	4	0	0
Acute gastroenteritis	2	1	0	0
Initial symptom				
Limb numbness	3	3	0	1
Limb weakness	4	3	0	1
Pain	1	0	0	1
Gait ataxia	0	0	1	0
Cranial nerve deficit n (%)	3 (37%)	2 (66%)	1 (100%)	2 (66%)
Respiratory failure n (%)	3 (37%)	3 (50%)	0 (0%)	2 (66%)
Autonomic dysfunction n (%)	3 (37%)	2 (33%)	0 (0%)	2 (66%)
CSF cell / mm3	1.8 ± 1.3	2.5 ± 1.7	2.0	1.3 ± 1.1
CSF proteins (mg/dL)	190 ± 89.8	70.4 ± 28.0	69.5	104 ± 55.1

AIDP, Acute inflamatory demyelimating polyneuriphathy; CBS, Guillain-Barré syndrome; MFS, Miller Fisher syndrome; CSF, cerebrospinal Fluid.

Table 2. Outcome of treated patients.

	PFX (n = 12)	IVIg (n = 2)	PFX + IVIg (n = 1)
Time to nadir (days)	8.6 ± 3.7	15.5 ± 6.3	10
Disability score on admission	4.0 ± 0.7	3.5 ± 0.7	3
Disability score at nadir	4.5 ± 0.5	4.5 ± 0.7	3
Disability score 7 days after therapy	4.1 ± 1.3	4.0 ± 1.4	3
Disability score 60 days after therapy	2.5 ± 2.1	3.0 ± 1.4	2
Disability score 365 days after therapy	2.1 ± 2.3	2.0 ± 1.4	1
Duration of hospitalization (days)	26.0 ± 13.2	37.5 ± 31.8	30

PFX, Plasmapheresis; IVIg, intravenous immunoglobulin.

DISCUSSION

Major clinical and epidemiological features in our patients, such as prodromal events, initial complaints, frequency of autonomic and respiratory compromise, were in accordance to previous reports[11,12]. Distinctly to Sridharan et al.[11], we found cranial nerves to be involved quite frequently. Although there is no separate geriatric unit in UNICAMP Hospital, we had only three individuals older than 70 years and none in the 80's. This finding is in accordance with a recent paper from São Paulo[18] and is best explained as we notice that people older than 80 years account for only 1% of the Brazilian population in striking contrast to most European countries.

In our survey, axonal GBS was identified in one third of cases, all of which had exclusive motor involvement. Similarly, Rana and Rana[14] found a high proportion of axonal GBS in older patients. Such forms supposedly have a worse outcome particularly among aged patients[19,20] and indeed three deceived patients were in this group.

Patients were eligible for treatment whenever their Hughes disability score was higher than two or deficits worsened fast. When obvious contraindications for PFX existed, IVIg was employed and vice-versa. Of these 18 patients, 10 were diagnosed before 1996, when IVIg first became available in our service. As PFX was already proven effective for GBS and easily performed at our Hemotherapy Unit, it was the usual option for most cases.

In both groups, disability scores at the different moments disclosed clear improvement. IVIg-treated individuals had a trend toward longer duration of hospitalization. However, adverse events were only recorded in PFX-treated cases. Hypotension has been already identified as a major problem in this age and is possibly related to decreased cardiovascular reserve[14]. Complications related to central venous access (local infection, pneumothorax and pleural effusion) were also hazardous in this series.

As a tertiary hospital-based series including only elderly people, we found a high mortality rate. In fact, one patient had early cardiac arrest. In the other 3 cases, deaths occurred after prolonged hospitalization due to sepsis. In two of these, nosocomial pneumonia was the source of infection and in the other *Staphylococcus aureus* was isolated (catheter infection). Besides, two patients presented significant co-morbidity (heart failure and diabetes mellitus), which further worsened their prognosis. These findings are in striking contrast with those reported in a Brazilian survey of GBS among children[21].

Our study was a retrospective one, therefore presenting clear limitations. Despite this, it may yield some meaningful insight into geriatric GBS. Frequency of axonal GBS seems to be higher in the elderly and this may have prognostic implications. Besides, PFX and IVIg were both suitable options in this age group, but complications were noticed with PFX. Further prospective studies are needed to better understand and manage GBS in the elderly.

REFERENCES

1. Kuwabara S. Guillain-Barré syndrome: epidemiology, pathophysiology and management. Drugs 2004;64:597-610.
2. Hughes RAC, Rees JH. Clinical and epidemiological features of Guillain-Barré syndrome. J Infect Dis 1997;176(Suppl 2):S92-S98.
3. Hartung HP, Willison HJ, Kieseier BC. Acute immunoinflammatory neuropathy: update on Guillain-Barré syndrome. Curr Opin Neurol 2002;15:571-577.
4. French Cooperative Group in Plasma Exchange in Guillain-Barré Syndrome. Efficiency of plasma exchange in Guillain-Barré syndrome: role of replacement fluids. Ann Neurol 1987;22:753-761.
5. Greenwood RJ, Newsom Davis JM, Hughes RAC, et al. Controlled trial of plasma exchange in acute inflammatory polyradiculoneuropathy. Lancet 1984;1:877-879.
6. Osterman PO, Lundemo G, Pirskanen R, et al. Beneficial effects of plasma exchange in acute inflammatory polyradiculoneuropathy. Lancet 1984;2:1296–1299.
7. The Guillain-Barré Syndrome Study Group. Plasmapheresis and acute Guillain-Barré syndrome. Neurology 1985;35:1096-1104.
8. French Cooperative Group on Plasma Exchange in Guillain-Barré Syndrome. Plasma exchange in Guillain-Barré syndrome: one-year follow-up. Ann Neurol 1992;32:94-97.
9. Van der Meché FGA, Schmitz PIM, Dutch Guillain-Barré Study Group. A randomized trial comparing intravenous immune globulin and plasma exchange in Guillain-Barré syndrome. N Engl J Med 1992;326:1123-1129.
10. Plasma Exchange/Sandoglobulin Guillain-Barré Syndrome Trial Group. Randomised trial of plasma exchange, intravenous immunoglobulin, and combined treatments in Guillain-Barré syndrome. Lancet 1997; 349:225-230.
11. Sridharan GV, Tallis RC, Gautam PC. Guillain-Barré syndrome in the elderly: a retrospective comparative study. Gerontology 1993;39:170-175.
12. Winner SJ, Evans JG. Guillain-Barré syndrome in Oxfordshire: clinical features in relation to age. Age Ageing 1993;22:164-170.
13. Yamashita S, Morinaga T, Matsumoto K, Sakamoto T, Kaku N, Matsukura S. Severe Guillain-Barré syndrome in aged patients: the effect of plasmapheresis. Intern Med 1992;31:1313-1316.
14. Rana SS, Rana S. Intravenous immunoglobulins versus plasmapheresis in older patients with Guillain-Barré syndrome. J Am Geriatr Soc 1999;47:1387-1388.
15. Asbury AK, Cornblath DR. Assessment of current diagnostic criteria for Guillain-Barré syndrome. Ann Neurol 1990;27(Suppl):S21-S24.
16. Seneviratne U. Guillain-Barré syndrome. Postgrad Med J 2000;76:774-82.
17. Hughes RAC, Newsom-Davis JM, Perkin GD, Pierce JM. Controlled trial of prednisolone in acute polyneuropathy. Lancet 1978;2:750-753.
18. Rocha MSG, Brucki SMD, Carvalho AAS, Lima UWP. Epidemiologic features of Guillain-Barre syndrome in São Paulo, Brazil. Arq Neuropsiquiatr 2004;62:33-37.
19. Van der Meche FG, Visser LH, Jacobs BC, Endtz HP, Meulstee J, van Doorn PA. Guillain-Barré syndrome: multifactorial mechanisms versus defined subgroups. J Infect Dis 1997;176 (Suppl 2):S99-S102.
20. Sheth RD, Riggs JE, Hobbs GR, Gutmann L. Age and Guillain-Barré syndrome severity. Muscle Nerve 1996;19:375-377.
21. Dias-Tosta E, Kuckelhaus CS. Guillain-Barre syndrome in a population less than 15 years old in Brazil. Arq Neuropsiquiatr 2002;60:367-373