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Albuminocytological dissociation in different electrophysiological gbs variants

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ALBUMINOCYTOLOGICAL DISSOCIATION IN DIFFERENT ELECTROPHYSIOLOGICAL GBS VARIANTS

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ABSTRACT

Objectives: The objective of our study was to determine the distribution of different electrophysiological variants of GBS and its relationship with albuminocytological dissociation (ACD). The rationale of the study was to determine whether presence or absence of albuminocytological dissociation has any association with NCS findings and whether can be relied upon as an indirect predictor of axonal variant which warrants poor patient outcomes versus demyelinating.

Materials and Methods: A consecutive series of 76 patients who presented at PIMS over a 12 month period with GBS were included. Nerve Conduction studies (NCS) and Electromyographic (EMG) findings with CSF characterization for albuminocytological dissociation were recorded. P value < 0.05 was taken significant. Results: NCS revealed AIDP as the most common variant (44; 57.8%) followed by AMAN (19; 25%) and AMSAN (7; 9.2%). For 5(6.5%) patients with normal NCS, EMG revealed early neuropathic changes in 4 (80% of normal NCS; 5.2% of total) (suggesting axonal degeneration). Total axonal degenerative type accounted for (AMAN + AMSAN + axonal neuropathy on EMG=30) 39.4% while demyelinating (AIDP + prolonged/absent F-wave=45) 59.2%. ACD was found in 60 (78.9%) patients. There was no signification association between ACD and NCS variants (p>0.05). Conclusion: AIDP is the most prevalent (58%) GBS variant in our population, at least in the vicinity of Islamabad. There is high prevalence of axonal variants (≈40% of total) as compared to Western countries. There is no correlation between ACD and NCS variants. ACD cannot be used as an independent predictor of NCS variant. Presence or absence of ACD has no definite predilection for axonal variant which itself warrants poor patient outcomes versus demyelinating type.

Key Words: Gullain-Barré Syndrome; variants; nerve conduction studies; electromyography; albuminocytological dissociation; cerebrospinal fluid, association.

INTRODUCTION

Acute flaccid paralysis (AFP) has a wide spectrum of etiologies. One such common preventable cause is poliomyelitis which is still being reported in Pakistan. With marked decline in the incidence of polio, Guillain-Barré syndrome is now a common cause of acute flaccid paralysis. Two-thirds of GBS patients develop the neurologic symptoms 2-4 weeks after respiratory or gastrointestinal infection. The initial symptoms are sublepalesthesias in the toes and fingertips, followed by lower extremity weakness that may ascend over hours to days to involve the arms, cranial nerves, and in severe cases the muscles of respiration. Respiratory muscle weakness is a poor prognostic sign. At some point during their illness, up to 10 percent of patients require mechanical ventilation. GBS has several electro physiological manifestations and variants namely AIDP (Acute Inflammatory Demyelinating Polyneuropathy), AMAN (Acute Motor Axonal Neuropathy), AMSAN (Acute Motor Sensory Axonal Neuropathy) or normal. Each has its own diagnostic and prognostic significance and guides management at least to some extent on individual basis. CSF is characteristically acellular. Protein levels may be normal during the first week of the illness, but the majority will have an increase in protein if measured 2 or 3 weeks later, called albuminocytological dissociation (raised protein concentration without pleocytosis). Since the knowledge about novel presentations of GBS is currently evolving, one must remain abreast not only with the worldwide spectrum of GBS but of its local variants, both clinical and electrophysiological. Meanwhile, the importance of albumino cytological dissociation cannot be denied both diagnostically and prognostically. The rationale of the study was to determine whether presence or absence of albuminocytological dissociation has any association with NCS findings and whether can be relied upon as an indirect predictor of axonal variant which warrants poor patient outcomes versus demyelinating.

MATERIALS AND METHODS

This study was a single-center, observational, descriptive
At some point during their illness, up to 10 percent of AMAN (Acute Motor Axonal Neuropathy), AMSAN (Acute Motor Sensory Axonal Neuropathy) or normal. The nerve conduction study (NCS) was carried out using Caddwell Sierra II Wedge NCS EMG machine by a neurologist. Electrophysiological tests were performed in all patients and data was recorded. Lumbar puncture was done for CSF R/E (cerebrospinal fluid routine examination) in all patients consenting. CSF protein estimation with albuminocytological dissociation was calculated. Albuminocytological dissociation was defined as CSF with raised protein (>45mg/dl; lab reference at our centre) and total cell count of ≤ 10/mm³.

Patients with alcoholism, any trauma affecting muscles or nerves, renal or metabolic dysfunctions, peripheral vascular diseases, myopathy, motor neuron disorders, any genetic or other disorders affecting nerve and muscles, CIDP (Chronic Inflammatory Demyelinating Polyneuropathy), diabetic peripheral neuropathy were excluded. Electrophysiologically, based on NCS, the following variants were defined: AIDP (Acute Inflammatory Demyelinating Polyneuropathy), AMAN (Acute Motor Axonal Neuropathy), AMSAN (Acute Motor Sensory Axonal Neuropathy) or normal. The nerve conduction studies were performed within 24-72 h of hospitalization in all cases. Needle EMG was also performed. At least one motor and one sensory nerve were tested on the upper and lower limbs. F-wave responses were recorded in all the extremities. Additionally, routine motor conduction studies were performed on the median, ulnar, peroneal and tibial nerves using conventional procedures. Sensory nerve studies were performed on the median, ulnar and sural nerves. The amplitude of the negative phase was measured for compound muscle action potentials and sensory nerve action potentials. Patients were classified into AIDP or AMAN based on the existing electrodiagnostic criteria. AMSAN was defined as the presence of AMAN pattern in motor nerve studies with sensory nerve action potential amplitude reduction more than 50% of the normal in two or more sensory nerves. Miller-Fischer Syndrome (MFS) was defined as triad of ataxia, ophthalmoplegia and areflexia without other possible causes. Polynuertis cranialis was defined as that only involving multiple cranial nerves while paraparetic as that only involving legs. People were offered plasma exchange (PE), Intravenous Immunoglobulin (IVIG), PE followed by IVIG or none accordingly. The data was analyzed using SPSS version 17.0. Mean and standard deviation were calculated for numerical variables. Descriptive statistics were used to determine frequency and percentages for categorical variables and results were expressed either graphically or tabulated. Chi-square (x²) test was used and p values were calculated. P value < 0.05 was taken significant.

RESULTS

Mean age was 34.7 ± 18.0 years ranging from 12-75 years. Gender distribution revealed male preponderance; 59 (77.6%) males and 17 (22.4%) females; 3.5:1. Mean duration of illness before presentation to hospital was 9.7 ± 7.6 ranging from 4 to 21 days. Most common clinical presentation was quadriparesis variety (73 out of 76; 96.1%). Other variants included one (1.3%) Miller-Fischer, one (1.3%) polyneuritis cranialis and one (1.3%) paraparetic variant. NCS revealed AIDP as the most common variant (44; 57.8%) followed by AMAN (19; 25%) and AMSAN (7; 9.2%); axonal (AMAN + AMSAN=26, 34.2%)(Figure 1).
Polyneuropathy), AMAN (Acute Motor Axonal Neuropathy),
AMSAN (Acute Motor Sensory Axonal Neuropathy).

For 5 (6.5%) patients with normal NCS, EMG revealed
early neuropathic changes in 4 (80% of normal NCS; 5.2%
of total) (suggesting axonal degeneration) while one (20% of
normal NCS; 1.3% of total) proved to be Miller-Fischer
Syndrome. The remaining one (1.3% of total) only had the
finding of prolonged/absent F-wave markers as the sole
sign of proximal demyelination. Total axonal degenerative
type accounted for (AMAN + AMSAN + axonal neuropathy
on EMG=30) 39.4% while demyelinating (AIDP +
prolonged/absent F-wave=45) 59.2% (Figure 2).

Figure 2: NCS and EMG based differentiation of variants
of Gullain-Barré Syndrome.

ACD was found in 60 (78.9%) patients. Mean CSF protein
was 131.1 ± 110 mg/dl ranging from 19 to 467 mg/dl (for
all patients with CSF reports whether ACD or not).
However, there was no correlation between ACD and
NCS/EMG variants (p>0.05) (Table 1).

Table 1: Relationship of Nerve Conduction Study variants
with Cerebro Spinal Fluid protein

<table>
<thead>
<tr>
<th>Electrophysiological variant</th>
<th>Albuminocytological dissociation in CSF</th>
<th>Statistical significance p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCS defined variant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AIDP</td>
<td>37 (61.7)</td>
<td>7 (43.7)</td>
</tr>
<tr>
<td>AMAN</td>
<td>15 (25)</td>
<td>4 (25)</td>
</tr>
<tr>
<td>AMSAN</td>
<td>4 (6.7)</td>
<td>3 (18.7)</td>
</tr>
<tr>
<td>Normal</td>
<td>3 (5.0)</td>
<td>2 (12.5)</td>
</tr>
<tr>
<td>Only H A F-wave</td>
<td>1 (1.7)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Total</td>
<td>60 (100)</td>
<td>16 (100)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NCS plus EMG differentiation</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Demyelinating</td>
<td>38 (63.3)</td>
<td>7 (43.7)</td>
</tr>
<tr>
<td>Axonal</td>
<td>22 (36.7)</td>
<td>8 (50)</td>
</tr>
<tr>
<td>Normal</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Total</td>
<td>60 (100)</td>
<td>16 (100)</td>
</tr>
</tbody>
</table>

Table 1: Relationship of Nerve Conduction Study variants
with Cerebro Spinal Fluid protein. AIDP (Acute
Inflammatory Demyelinating Polyneuropathy), AMAN
(Acute Motor Axonal Neuropathy), AMSAN (Acute Motor
Sensory Axonal Neuropathy), P=prolonged, A=absent.

DISCUSSION

GBS is a common cause of acute flaccid paralysis.
Distinguishing patients with different variants of GBS from
one another can be of great prognostic value. Prognosis
depends on the time of presentation and delay in treatment.
Despite all improvements in treatment and supportive care, the
dead rate is still around 5%, even in the best intensive care units.6
Worldwide, the death rate runs slightly higher, mostly from a lack of availability of
life-support equipment during the lengthy plateau lasting
to six weeks and in some cases up to one year, when
a ventilator is needed in the worst cases.6 Poor prognostic
factors include age over 40 years, duration of active
disease, high CSF protein content, rapid progression of
motor weakness, preceding diarrheal illness, marked
disability at presentation, electrophysiological signs of
axonal neuropathy, requirement of ventilatory support, high
anti-GM1 titer and poor upper-limb muscle strength.1, 2, 6
Incidence of GBS, according to a rough estimate is much
higher in South-Asia as compared to Europe and America
and axonal variants account for a much larger proportion.12
An epidemiologic study reported an 8-13% mortality
rate despite ICU management in GBS, although the rate
may be less than 5% in tertiary care centers with a team
of medical professionals who are familiar with GBS
management.6 The most prevalent clinical variant, to our
observation, wasthe quadripareticvariety in which all four
limbs were involved usually in ascending manner.NCS
revealed AIDP as the most common variant (44; 57.8%)
followed by AMAN (19; 25%) and AMSAN (7; 9.2%);
axonal (AMAN + AMSAN=26, 34.2%) (Figure 1).Upon
review of data from local literature, Zaheer et al. in 2005
commented on a set of 25 patients from Lahore region
that the break down of different patterns of neuropathy
was 36% demyelinating, 12% axonal and 52% of mixed
variety having both demyelinating and axonal components.
11 They concluded that the pattern of neuropathy in GBS
is nearly the same as reported in most European and local
studies except Chinese endemic cases where axonal form
is more frequent. However, other authors like Khan et al.
did not concur with their findings.12 They suggested that
axonal variants constitute 40% of GBS. The variants,
according to them were distributed as AIDP-60%,
AMAN-30% and AMSAN-10% i.e., axonal-40%. Their data
set consisted of 40 patients from vicinity of Rawalpindi
region and their results were much similar to ours when
reported in 2010.They concluded that a high frequency of
the axonal variants persists in Pakistan.12 Siddiqui and
colleagues in 2013 studied a group of 29 GBS patients
having AIDP-62%, AMAN-27.5% and AMSAN-10.3%(≈
axonal-38%) and concluded likewise.\textsuperscript{(13)} A study by
Yadegan et al. from Tehran, Iran done over a period of 11
years on 121 GBS patients concluded in 2007 a
distribution pattern of 63%, 23% and 14% of AIDP, AMAN
and AMSAN respectively (axonal-37%).\textsuperscript{(14)} Meta-analysis
reports from Europe and the United States state that
60–80% of people with GBS have demyelinating subtype
(AIDP) and AMAN affects only a small number (6–7%). These reports suggest that in Asia and Central and
South America, the proportion of axonal GBS is significantly higher (30–65%).\textsuperscript{(18)} Our findings of
demyelinating variant (AIDP + prolonged/absent
F-wave=45) being ≈ 59% and axonal (AMAN + AMSAN
+ axonal neuropathy on EMG=30) ≈ 40% is in
agreement with these international reports suggesting a
relatively poor overall prognosis of GBS in our population
(Figure 2). Our findings support the dictum that there is
high prevalence of axonal variants (≈40% of total) in our
population (Asians) as compared to Western countries.\textsuperscript{(6)}
We found that 6.5% NCS were normal and EMG had to be
done in order to reveal early neuropathic changes of axonal
degeneration in 4 (66.7% of normal NCS; 5.2% of total).
This highlights the fact that when NCS does not reveal
overt demyelination or axonopathy, EMG is mandatory and
most of the time reveals neuropathic changes even earlier
in the course of disease suggesting axonal degeneration.
A paper by Shabbir et al. published in 2012 identified that
out of a set of 18 patients with axonal GBS, 12 showed
fibrillation potentials, positive sharp waves and increased
insertional activity within 4-12 days of symptoms onset
and 6 beyond that period.\textsuperscript{(15)} Active denervation in the form
of fibrillation potentials and positive sharp waves were
noted frequently and decreased interference pattern in
almost all patients. On the basis of their observations of
finding fibrillation potentials, positive sharp waves and
decreased interference pattern early in the course of
disease i-e-, before two weeks of symptom onset, they
raised the query for a possible new hyperacute or
fulminant variant of GBS.\textsuperscript{(15)} The 4 of our patients with
normal NCS revealed similar earlier changes of axonal
neuropathy (all NCS/EMG done within 24-72 hours and
symptom onset in all of these 4 patients being 3-4 days
only) supporting their idea but needs further confirmation.
It also suggests that when clinically indicated, NCS should
be combined by detailed EMG study especially if NCS turns
out to be normal. In a study by Akbayram et al. done in 36
children in 2010-11, 51.4% showed albuminocytological
dissociation on cerebrospinal fluid examination.\textsuperscript{(6)}
According to Yadegari and colleagues, higher levels of CSF
protein are more frequent in AIDP subtype. They
commented that although the rise in CSF protein is more
frequent in demyelinating variant, it may not have enough
sensitivity to discriminate AIDP from axonal subtypes.

Hence, the diagnosis of GBS and defining its subtypes
should not be made based on a single finding.\textsuperscript{(14)} We found
ACD in 60 (78.9%) patients with mean CSF protein of
131.1 ± 110 mg/dl ranging from 19 to 467 mg/dl.
However, there was no correlation between ACD and
NCS/EMG variants (p>0.05) (Table 1). Our findings
therefore concur with that of Yadegari et al.,\textsuperscript{(13)} and further
augments their findings signifying that NCS/EMG are not
only essential diagnostic tools but prognostic as well by
helping differentiate between axonal and demyelinating
types irrespective of whether ACD is present or not (Table
1). Classifying patients on the basis of nerve conduction
studies and electromyography can be helpful in guiding the
prognosis of GBS in addition to being diagnostically
pertinent. It helps stratify patients at beginning and thus
help modify management plans accordingly with the hope
of better patient outcomes. However, this classification
should be based on a comprehensive and compact
agreement between clinical presentation, CSF findings
and detailed electrophysiological studies and not on a
single factor. While high CSF is suggested by some to be a
marker of poor patient outcomes, ACD per se does not
differ among different NSC variants and mere presence or
absence of ACD cannot predict axonal or demyelinating
neuropathy which themselves are independent predictors
of outcome.

CONCLUSION

AIDP is the most prevalent (58%) GBS variant in our
population, at least in the vicinity of Islamabad. There is
high prevalence of axonal variants (≈40% of total) as
compared to Western countries. There is no correlation
between ACD and NCS variants. ACD cannot be used as
an independent predictor of NCS variant Presence or
absence of ACD has no definite predilection for axonal
variant which itself warrants poor patient outcomes versus
demyelinating type.

CONFLICT OF INTEREST

The authors declare that they do not have any competing
interests.

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