Clinical Neurophysiology 126 (2015) 2376–2380

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Sural-sparing is seen in axonal as well as demyelinating forms of Guillain–Barré syndrome

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ARTICLE INFO

Article history:
Accepted 28 January 2015
Available online 9 February 2015

Keywords:
Guillain–Barré syndrome
Sural-sparing
Electrodiagnosis

HIGHLIGHTS

- Sural-sparing pattern is seen in axonal and demyelinating forms of Guillain–Barré syndrome (GBS).
- It reflects a pathological process that is common to both types of GBS.
- Question diagnosis of any GBS-subtype if sural is abnormal, whilst sparing median, ulnar sensory potentials.

ABSTRACT

Objective: The "sural-sparing pattern" of Guillain–Barré syndrome (GBS) is believed to reflect demyelinating pathology. We asked if it is present in non-demyelinating GBS-subtypes, namely acute motor axonal neuropathy (AMAN), acute motor-sensory axonal neuropathy (AMSAN) and Miller Fisher syndrome (MFS), in addition to acute inflammatory demyelinating polyneuropathy (AIDP).
Methods: We studied the occurrence of sural-sparing pattern in clinically defined GBS and MFS patients. Using serial electrodiagnostic studies, GBS patients were divided into AIDP, according to appearance of demyelination–remyelination and AMAN/AMSAN, if there were signs of reversible conduction failure or Wallerian-like degeneration. Equivocal cases were left unclassified. We defined sural-sparing as a greater decrease in median and or ulnar sensory nerve action potential than that of the sural, compared to age and height-matched normal controls.
Results: Twelve of 30 GBS and 7 of 20 MFS patients had sural-sparing. This pattern was seen in 4 of 8 AIDP, 5 of 13 AMAN/AMSAN and 3 of 9 unclassified cases. Sequential studies uncovered sural-sparing, initially covert, in additional 1 MFS, 1 unclassified, 1 AIDP and 1 AMAN/AMSAN patient.
Conclusions: Sural-sparing occurs in axonal and demyelinating GBS subtypes.
Significance: The sural-sparing pattern reflects a pathological process common to axonal and demyelinating GBS-subtypes alike.

1. Introduction

The relative sparing of the sural sensory nerve action potential (SNAP) in relation to median and ulnar SNAP, the sural-sparing pattern, is a useful electrodiagnostic tool in the evaluation of patients with suspected Guillain–Barré syndrome (GBS). Its diagnostic utility has been demonstrated in various studies (Albers and Kelly, 1989; Bromberg and Albers, 1993; Al-Shekhlee et al., 2007). A recent study showed its added value in distinguishing GBS from its clinical mimics (Derksen et al., 2014). The occurrence of sural-sparing in GBS has largely been attributed to its demyelinating pathology and well documented only in acute inflammatory demyelinating polyneuropathy (AIDP) (Albers and Kelly, 1989; Bromberg and Albers, 1993; Al-Shekhlee et al., 2007). There are few studies that have examined sural-sparing in non-demyelinating GBS subtypes. We observed sural-sparing in a significant proportion of patients when we studied reversible conduction failure (RCF) in Miller Fisher syndrome (MFS) (Umapathi et al.,

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http://dx.doi.org/10.1016/j.clinph.2015.01.016
1388-2457/

2012, 2014). Sekiguchi et al. found 22% and 27% of 47 MFS patients had reduction in median and ulnar SNAPs while sural SNAP was reduced in only 6% (Sekiguchi et al., 2013). Sural-sparing was present in some of the patients in a study that demonstrated sensory changes in acute motor axonal neuropathy (AMAN) (Capasso et al., 2011). We therefore wanted to systematically examine the occurrence of sural-sparing in various GBS-subtypes that were delineated using serial nerve conduction studies (NCS).

2. Methods

2.1. Subjects

We used standard clinical criteria to define GBS and MFS (Sejvar et al., 2011). The patients were previously enrolled in the institution's GBS database. We assayed serum anti-ganglioside IgG antibodies (Yuki et al., 1997).

2.2. Categorization into axonal and demyelinating forms using serial nerve conduction studies

We have described previously the electrodiagnostic protocol (Umapathi et al., 2012). Using serial NCS, GBS patients were divided into axonal and demyelinating forms (Uncini and Kuwabara, 2012; Tsang et al., 2013). By definition AMAN patients should not have any sensory complaints or findings. However, a previous study had shown, using serial nerve conduction studies, significant SNAPs abnormalities in AMAN patients (Capasso et al., 2011). We did not want to exclude these AMAN patients with no sensory symptoms or signs as that would reduce the power of the study considerably. On the other hand labeling these patients with sensory abnormalities, albeit only on electrophysiological studies, as having AMAN would be technically wrong. Hence, we grouped AMAN and acute motor sensory axonal neuropathy (AMSAN) patients under the combined term AMAN/AMSAN.

We used standard criteria to diagnose demyelinating and axonal features on initial NCS. On serial NCS, a diagnosis of AIDP would require changes occurring at a time interval consistent with demyelination or remyelination (Uncini and Kuwabara, 2012; Tsang et al., 2013). Specifically, a decrease in compound muscle action potential (CMAP) must resolve with signs of remyelination namely, prolonged distal motor latency, temporal dispersion and persistent or worsening conduction slowing. Conduction velocity (CV) should remain reduced or improve with associated signs of persistent demyelination or remyelination on the CMAP, such as prolonged distal motor latency or temporal dispersion.

For AMAN/AMSAN, sequential NCS must demonstrate RCF or axonal degeneration–regeneration (Uncini and Kuwabara, 2012; Tsang et al., 2013). RCF is defined as a reduction of CMAP amplitude or conduction block (CB) that resolves without development of demyelinating–remyelinating features described above. Likewise CV slowing should resolve in the second or third study without associated demyelinating–remyelinating changes. Length-dependent conduction failure, where the CB disappears by the progressive reduction of distal CMAP, is due to Wallerian-like degeneration and indicates AMAN. The changes should be seen in at least 2 nerves. Any case that did not satisfy the above criteria was labeled unclassified. Patients who initially presented as MFS but proceeded to GBS were labeled as MFS/AMAN or MFS/AIDP according to the serial NCS.

2.3. Definition of sural-sparing pattern

We defined sural-sparing as a greater decrease in the median and or ulnar SNAP compared to the decrease in sural SNAP. It was computed as follows:

$$\frac{\text{Normal median or Ulnar SNAP-patient's median or Ulnar SNAP}}{\text{Normal median or Ulnar SNAP}} > \frac{\text{Normal sural SNAP-patient's sural SNAP}}{\text{Normal sural SNAP}}$$

We used age-height matched normal values derived from 245 controls (Umapathi et al., 2012). We disregarded median SNAP changes attributable to carpal tunnel syndrome and excluded patients with pre-existent polyneuropathy. Institutional review board approved the study. Informed consent was obtained.

3. Results

3.1. Patients, anti-ganglioside antibodies and NCS

The median age of patients was 50 years (range, 13–79 years). All except 2 MFS patients had at least 2 serial NCS. The initial NCS was done at median 7 days (range, 1–18 days).

3.2. The sural-sparing pattern

Table 1 shows the age, gender, GBS sub-type, anti-ganglioside antibody results and serial sensory NCS of the patients with sural-sparing. The AMAN patients had raised anti-ganglioside antibodies. All except one MFS patients had increased anti-GQ1b Ig G antibody. Low-titre anti-GT1a antibody was present in one AIDP patient.

As can be seen in the percentage decrease in median, ulnar and sural SNAPs, eleven out of 30 GBS and 7 out of 20 MFS patients had the sural-sparing pattern on initial study (Table 1). *Patient* 3 with AIDP did not have sural sensory nerve conduction recordings on the initial study at the intensive care unit. The subsequent study at day 21 showed sural-sparing. Only 1 patient out of the cohort of 50 patients had an abnormal sural SNAP without reduced ulnar or median SNAP at presentation. With regards to GBS subtypes, sural-sparing was present in 4 of 8 AIDP patients, 5 of 13 AMAN (representative case shown in Fig. 1A and B respectively) and 3 of 9 unclassified cases. Fig. 1C shows the initial sensory NCS of *Patient* 21 with MFS.

Sequential studies uncovered sural-sparing in 4 other patients. Two patients (1 MFS, *Patient* 16; and 1 unclassified, *Patient* 14) had normal initial SNAPs based on age and height matched controls. Subsequently, their median and ulnar SNAPs increased by at least 50% whereas the sural SNAPs remained largely unchanged, indicating sural-sparing that was covert at presentation (Fig. 1D illustrates *Patient* 16's SNAPs). We did not measure test–retest variability of SNAPs in controls, and deemed a 50% increase in serial SNAPs as significant, based approximately on the least significant change in median, ulnar and sural SNAP of 45%, 49% and 60% respectively that was derived by Capasso et al. (2011). One AIDP patient, *Patient* 2, had unrecordable SNAPs initially, notwithstanding the ambient artifacts at intensive care unit that confounded the recording. *Patient* 10, with clinical features of MFS that progressed to severe GBS, had inexcitable nerves on day 5, 19 and 45. In follow-up NCS, the sural SNAPs of both patients showed better recovery than median and ulnar nerves, suggesting sural-sparing that was covert initially. Fig. 1E shows the SNAPs of *Patient* 10.

4. Discussion

We demonstrated sural-sparing pattern in axonal as well as demyelinating subtypes of GBS. Regardless of subtype, approximately one-third of GBS patients have sural-sparing. The similar proportion of cases having sural-sparing across the subtypes adds to the veracity of our findings. More useful for the electrodiagnostician is the observation that only 1 out of the 50