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Case report

The utility of sural-sparing pattern in the electrodiagnosis of regional subtypes of Guillain-Barré Syndrome

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ABSTRACT

Objective: We present an exemplar patient, illustrating utility of the sural-sparing pattern in diagnosis of Guillain-Barré Syndrome (GBS). We then present data that sheds light on the pathophysiology of sural-sparing.

Method and results: We describe a case of complex ophthalmoplegia that exemplifies the challenge of diagnosing regional subtypes of Guillain-Barré Syndrome, and the value of scrutinizing sensory nerve action potentials for the sural-sparing pattern. We also demonstrate, in a series of GBS patients, how serial nerve conduction studies can reveal "covert" sural-sparing in patients without sural-sparing on the initial study. Finally, by studying the median and radial sensory nerve action potentials at digit I in GBS patients, we demonstrate that the likely pathology of sural-sparing is related to the predilection of median nerve for subclinical entrapment; where the blood-nerve barrier is deficient and therefore more exposed to the immunopathology of GBS.

Conclusion: Incorporating sural-sparing would improve the specificity of GBS electrodiagnosis; especially in difficult to diagnose regional subtypes of GBS.

We, and others, have previously reported the utility of sural-sparing pattern in aiding the electrodiagnosis of Guillain-Barré Syndrome (GBS), including non-demyelinating subtypes such as Miller-Fisher Syndrome (FS) (Albers and Kelly, 1989, Bromberg and Albers, 1993, Al-Shekhlee et al., 2005, Derksen et al., 2014, Umapathi et al., 2015). We have also highlighted that relative sural-sparing may be covert in the initial study and become apparent on follow-up (Umapathi et al, 2012, 2013). We describe an illustrative case. We then present data that, we believe, sheds light on the pathophysiology behind sural-sparing.

A 44-year old man presented with a few-day history of ptosis and diplopia from diffuse weakness of all extraocular muscles. He had prominent fatigability of the lids, Cogan lid-twitch and lid-hopping signs. Pupils were unremarkable. The initial diagnosis was ocular myasthenia gravis. However, on further interrogation the patient reported tingling in bilateral median nerve innervated fingers, contemporaneous to development of ocular symptoms. He had no limb weakness, objective sensory loss or ataxia. All deep tendon reflexes were normal. Spinal fluid was normal. Nevertheless, we considered acute ophthalmoparesis variant of FS a differential diagnosis. Nerve conduction studies (NCS) done on day 6 of illness, in particular the antidromically recorded sensory nerve action potentials (SNAPs), were within normal limits when compared with age and height-matched controls. However, careful scrutiny revealed the median SNAP of 20 μV was at the lower limit of normal for patient's age and height (our laboratory's normal >20 μV). In contrast, the sural SNAP of 14 μV was clearly in the normal range (our laboratory's normal >10 μV). There was no prolongation of median distal motor or sensory latencies (3.5 and 3.0 ms respectively) that suggests pre-existing carpal tunnel syndrome to explain his acral symptoms. This and the absence of significant decremental response on 3 Hz repetitive stimulation of proximal nerves prompted us to test serum anti-GQ1b Ig G. It was significantly raised (optical density 10 times more than upper limit of normal). Anti-acetylcholine receptor antibody was negative. A repeat NCS about 1 week later showed the extent of initial covert sural-sparing. The median nerve SNAP increased to 46 μV (latency unchanged at 3.0 ms) whilst the sural SNAP remained similar at 13 μV (Fig. 1). The ulnar SNAP on the first study was within normal range of 20 μV (our laboratory's normal >15 μV) but had increased to 35 μV on second study (latency 2.7 and 2.8 ms respectively). The rest of NCS, including tibial H and F reflexes, was normal. The patient made an uneventful recovery over the next few weeks. He did not receive intravenous immunoglobulin.

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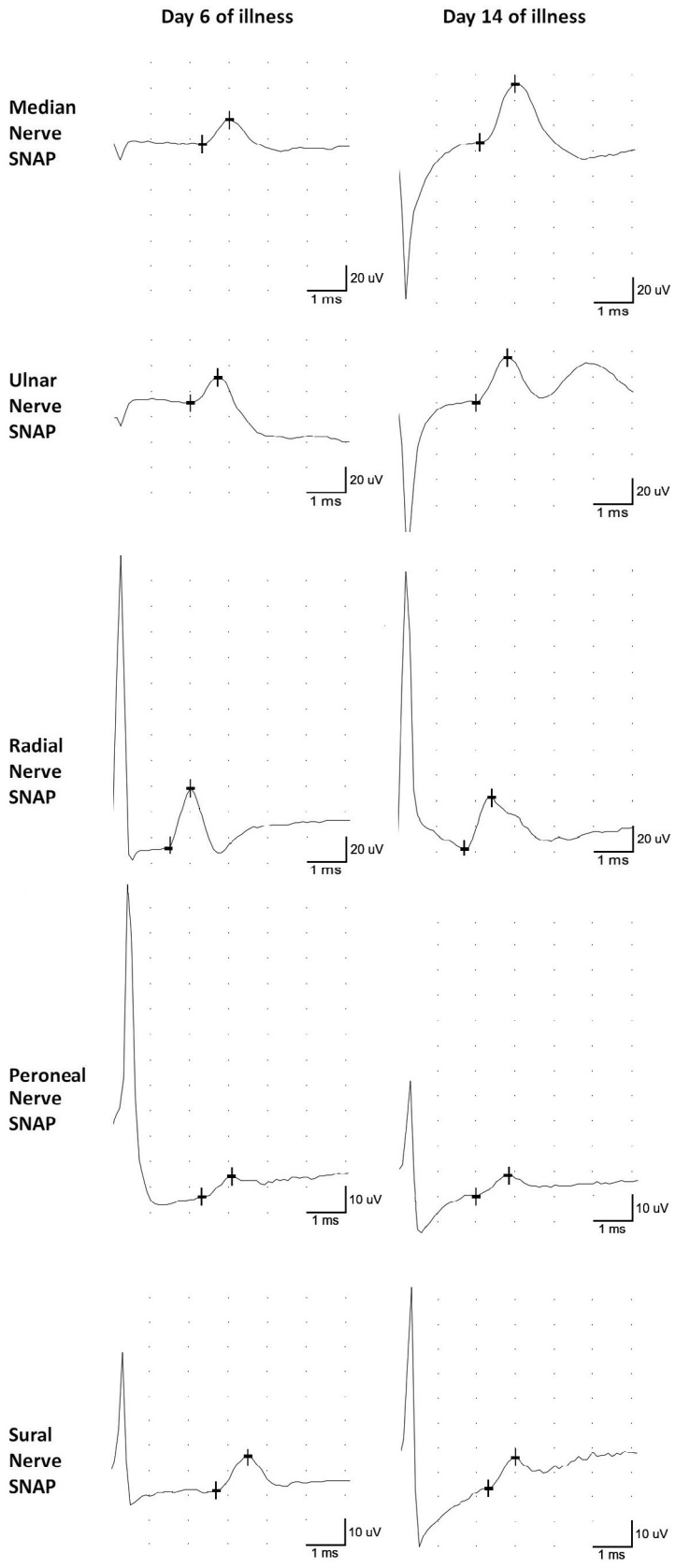

Fig. 1. Comparison of patient's median, ulnar, radial, peroneal and sural nerve SNAPs on Day 6 and Day 14 of illness.

This case illustrates the challenges in diagnosing regional subtypes of GBS, and the diagnostic value of scrutinizing upper limb SNAPs in relation to that of sural. To better understand the phenomenon of *covert* sural-sparing, we reviewed NCS of 125 patients prospectively enrolled into our institution's GBS database between 2007 and 2017 and selected those with serial NCS. We excluded

those with pre-existing neuropathy. The institution's review board approved the study. The methodology of the nerve conduction studies and the database has been described previously (Umapathi et al., 2012). GBS subtypes were diagnosed using a combination of clinical features, serial NCS and anti-ganglioside antibody profile. Sensory studies were antidromic and normal age and height-adjusted normal values were obtained from 245 controls (Umapathi et al., 2012). We delineated relative sural-sparing on first NCS as follows (Umapathi et al., 2015):[(Normal Median or Ulnar SNAP – Patient's Median or Ulnar SNAP)/(Normal Median or Ulnar SNAP)] > [(Normal Sural SNAP – Patient's Sural SNAP)/(Normal Sural SNAP)].

Serial NCS of those who did not show sural-sparing initially were studied for a greater change in convalescent median or ulnar SNAP compared to that of sural. Such covert sural-sparing can occur in two patterns: 1) As in the case illustrated above, seemingly normal upper limb SNAP amplitude increases significantly on follow-up NCS while the sural SNAP remains the same. 2) Normal upper limb SNAP amplitude, in a relatively early NCS, decrease significantly in serial NCS and that of sural SNAP does not. Serial SNAP amplitudes changes were considered significant if they were changed beyond the threshold validated by Capasso et al. (2011); namely median $\geq$44%, ulnar $\geq$47%, sural $\geq$58%. Eighty-six patients were analysed. Median duration from symptom onset to initial NCS was 22 days. Fifty-six patients (65.1%) demonstrated sural-sparing pattern on initial NCS. Nine were AIDP, 11 AMAN/AMSAN, 28 FS and 8 unclassified. Of the remaining 30 patients without sural-sparing pattern on first NCS, 4 had covert sural-sparing in follow-up studies; 1 AIDP, 2 AMAN/AMSAN and 1 FS.

Two hypotheses have been offered to explain sural-sparing (Bromberg and Albers, 1993, Umapathi et al., 2015). The immunological injury in GBS is maximum at areas with disrupted blood nerve barrier, likely to be present sub-clinically in common entrapment syndromes such as carpal tunnel syndrome. The sural nerve, not affected by entrapment, is hence spared. The alternative hypothesis is based on immunopathology at the distal end of nerves, where the blood-nerve barrier is also weak (Bromberg and Albers, 1993). Conventional NCS of median and ulnar nerves are recorded from their distal-most ends, at digits II and V respectively. The sural nerve is recorded near the lateral malleolus, some distance proximal to its terminal end, and therefore it could be spared. To explore these hypotheses, we studied the median and radial nerve SNAPs recorded at digit I in 37 GBS and FS patients. Both these nerves are studied at the terminal segments but the median nerve is more prone to entrapment compared to radial. Median and radial nerve digit 1 SNAPs were compared with the median age and height-matched values derived from 72 healthy controls. Twenty-one patients had sural-sparing; of which the majority, 18, had preferential decrease of median over radial SNAP. None had isolated radial SNAP abnormality. The remaining 3 patients had preferential decrease of radial over median SNAP. In contrast, in the cases without the sural-sparing pattern median nerve digit 1 SNAP was preferentially affected over radial digit 1 SNAP in slightly over half, 9 of the 16 cases ($p = 0.046$). The predilection for median nerve SNAP to be affected over radial SNAP at digit I suggests the disruption of blood nerve barrier at entrapment sites, rather than distal nerve endings, underlies the pathophysiology of the sural-sparing in GBS.

In summary, sural-sparing is an electrodiagnostic footprint of GBS and is seen, overtly or covertly, in half (Albers and Kelly, 1989, Al-Shekhlee et al., 2005) to two-thirds of patients. It is present in both axonal and demyelinating subtypes (Umapathi et al., 2015). It is most likely related to the predilection of median and ulnar nerves for subclinical entrapment, where the blood-nerve barrier is deficient. Incorporating sural-sparing would improve the specificity of GBS electrodiagnosis (Umapathi et al., 2019), especially in difficult to diagnose regional subtypes of GBS.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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