Case report

A treatable cause of fasciculations with upper motor signs

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Sri Lanka Journal of Neurology, 2019, **6**, 21-24

Index words: lewis sumner syndrome, late onset conduction block, central and peripheral demyelination, plexus hypertrophy

Introduction

Patients with a lower motor neuron (LMN) syndrome characterized by weakness, wasting, diminished reflexes, fasciculations, cramps and minimal sensory involvement have a broad differential diagnosis. These include anterior horn cell disease (AHCD), Chronic inflammatory demyelinating polyneuropathy (CIDP), Multifocal Motor Neuropathy (MMN), Multifocal Acquired Demyelinating Sensory and Motor neuropathy (MADSAM) or Lewis Sumner Syndrome (LSS). Therefore an extensive electrophysiological search for inflammatory neuropathies is imperative to diagnose potentially treatable conditions.

LSS is a neuropathy characterized by asymmetric multifocal motor and sensory loss and conduction blocks (CB). Rarely peripheral nerve demyelinating diseases may be accompanied by CNS demyelination causing diagnostic confusion. The following case highlights the differential diagnosis and diagnostic pitfalls in diagnosing this rare electro-clinical syndrome that is highly treatable.

Case report

A 45-year-old man presented with a 3 weeks history of pain and weakness of the right arm. He complained of difficulty in lifting his arm, doing his buttons and persistent muscle twitching and cramps on the right. He was also unsteady on his feet. He was evaluated for a numb right foot two years ago and investigations with nerve conduction studies (NCS) revealed a diagnosis of 'length-dependent asymmetric sensory neuropathy'. Investigations for cause of neuropathy were normal.

Neurological examination revealed profuse fasciculation around right shoulder girdle and forearm muscles. There was hypertrophy of the biceps and distal wasting of forearm. Tone was normal. There was a 3-4 MRC grade weakness of deltoid, biceps, infraspinatus, finger extensors and finger flexors. No winging of scapula was detected. Reflexes were depressed on the right. There was no demonstrable sensory loss in the upper limbs. Localised tenderness over the right supra-clavicular area was noted without any lumps or lymph nodes. The right plantar had an extensor response on lower limb examination. The rest of the lower limbs, allowing for some patchy distal right sensory impairment were normal. The cranial nerves were normal. He was not ataxic but demonstrated impaired tandem gait.

The NCS of the lower limbs showed: absent sural (bilaterally) and superficial peroneal SNAPs on the right, normal lower limb motor responses and prolonged tibial F waves of 68ms. Upper limb nerve conduction velocity, F waves and SNAPs were normal. A partial motor Conduction Block (CB) in the upper limb (median nerve) was demonstrated when the study was repeated for the third time after 8 weeks. Compound muscle action potential (CMAP) was very low (0.2MV) and the distal motor latency (DML) was prolonged (10.8ms) over the right deltoid when stimulating over Erb's point. The needle EMG showed fasciculations (3+), in the right upper limb muscles and a few in the right tibialis anterior. No changes of acute denervation (fibs/ Positive Sharp Waves) were detected. The CSF showed elevated proteins (630mg/dl). The following results were normal; renal functions, blood count, ESR, CRP, liver functions, B12, folate, ANA, ANCA, HBA1C, protein electrophoresis, GM1 antibodies and cryoglobulins.

MRI cervical-spine showed no evidence of compressive radiculopathy. However there was focal high signal in the spinal cord at the level of C4. MRI of the brachial plexus showed thickened non-enhancing right C5/6 nerve roots. This abnormality extended through the brachial plexus further distally. No fat atrophy of shoulder girdle muscles was noted.

A trial of immunoglobulins made a significant improvement in disability within two weeks. However his arm became very weak after 4 months prompting a second course which resulted in a dramatic improvement in upper limb power to MRC 4+/5 within a week. The fasciculations of the arm and biceps hypertrophy had also resolved by this time.

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	DML (msec)	Amp (mV)	PML (msec)	Amp (mV)	CV (mmsec)	SNA (μV)	CV (mmsec)
1st study	4.1	4.5	9.9	4.0	46	5.6	58
2nd study	4.1	6.8	10.25	4.2	47	2.2	42
3rd study	3.4	4.2	9.35	2.1	47	-	-

PML – Proximal Motor Latency

AMP – Amplitude

CV – Conduction Velocity

SNAP – Sensory Nerve Action Potential

Figure 1. Electrophysiology parameters in consecutive studies of the right median nerve. The last study was done 8 weeks after the first. Arrows demonstrate partial CB.

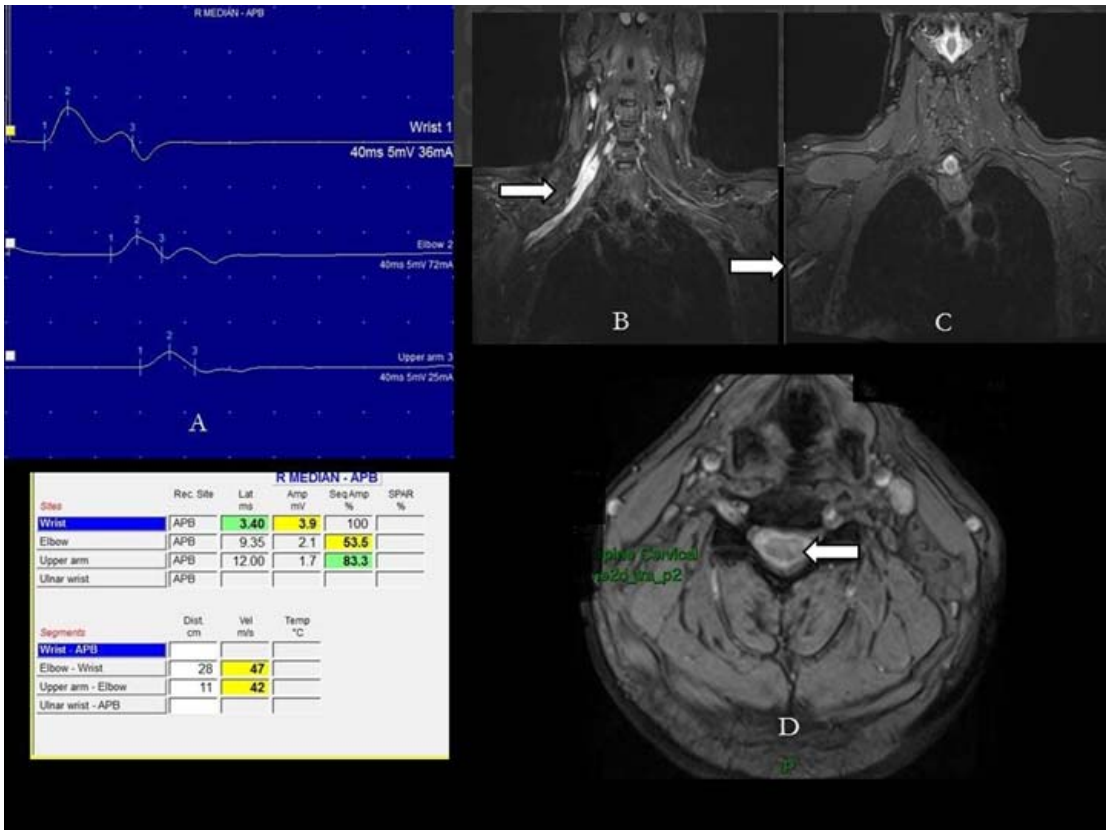

Figure 2.

A – Nerve conduction study demonstrating motor nerve conduction block over the elbow.

B – MRI STIR image demonstrating root hypertrophy involving C5, 6 and 7. MRI STIR image also shows hypertrophy of the right axillary nerve.

C – Spinal MRI – sagittal and axial sections showing focal demyelination a C4/C5 segment.

Discussion

AHCD, idiopathic brachial neuritis and mononeuritis multiplex (MNM) were considered initially in this patient. Needle EMG showed fasciculation's giving the impression of AHCD, however absence of denervation (ie:- fibs/ PSW) was against this diagnosis.

Acute shoulder pain with monoparesis is a common presentation for idiopathic brachial neuritis. EMG findings, notably absence of denervation potentials after 4 weeks makes brachial neuritis less likely in this patient. MNM is a painful, asymmetrical, sensory and motor peripheral neuropathy involving at least 2 nerves. However the presence of partial CB, prolonged F waves and the absence of NCS/ EMG features of asymmetric axonal neuropathy excludes MNM.

Our patient had slowly progressive markedly asymmetric multifocal neuropathy (lower limb prolonged F waves; absent SNAPs) with features of CB on NCS, elevated CSF protein absent anti-GM1 antibody (present in MMN) and thickened roots/plexus on MRI. These features strongly suggest a diagnosis of LSS. In chronic acquired demyelinating polyneuropathy, it is important to differentiate LSS from CIDP and MMN. In LSS, MMN, and CIDP, the NCS show features of demyelination, such as conduction block, temporal dispersion, prolonged distal motor latencies, slow conduction velocities, and absent or prolonged F-wave latencies in one or more motor nerves. LSS is different from MMN due to sensory nerve involvement and different from CIDP due to marked asymmetric multiple nerve involvement.

A series which compared LSS with MMN suggested that initial involvement was more frequent in upper limbs in MMN than LSS.[1] Motor weakness in the distribution of individual nerves was not different except for the median nerve, which was more frequently involved in LSS. F-waves were prolonged in the same proportion of patients with MMN as for LSS patients, but these abnormalities were more widespread in LSS. Sensory abnormalities were always absent with MMN and present in LSS. Our patient had initial lower limb involvement, F wave abnormalities, sensory findings and median nerve involvement which lent further support to the diagnosis.

It is unusual for LLS to present with focal muscular hypertrophy (FMH) which resolved along with fasciculations after treatment. It was postulated that severe fasciculations caused the muscle hypertrophy. This has been described previously.

Partial CB in this patient was diagnosed in the median nerve as CMAP amplitude and area decreased by 50% on proximal compared with distal stimulation, and CMAP duration increased by 30%. This is compliant with electro-diagnostic criteria. However caveats for the above, needs to be considered and include: over/under stimulation during the test and variations in anatomy of the median nerve (the first two NCS tests did not show any abnormality of the said nerve). The CB of the above patient was detected late in the course of the disease thus delaying the diagnosis. The delay is usually due to either less extensive electrophysiology or due to late onset CB. Lack of abnormal demyelinating findings in the distal limbs below the axilla or knee suggest that demyelination might have begun in the brachial or lumbar plexus in the early stage which might result in normal NCS of the peripheral nerves. CB found for the first time by stimulation at Erb's point has been described previously. In our case the CMAP of the deltoid was very low (<10% of expected normal) with significantly prolonged DML on stimulating Erb's point. However needle EMG did not demonstrate denervation changes; which suggests that this abnormality was due to proximal CB. Late onset CB with only F-waves being absent has been previously reported in LSS. Therefore it is suggested that repeated NCS should be undertaken to correctly diagnose LSS when it is suspected based on clinical symptoms with abnormal F-waves alone.

A confounder for the above diagnosis was an extensor plantar response suggesting an upper motor neuron (UMN) syndrome. Thus imaging of the CNS was performed in which we found an area of spinal cord demyelination. In a series which retrospectively investigated clinically and with MRI a cohort of patients with definite CIDP found 2 out of 12 patients with a clear clinical spinal cord syndrome and radiological findings compatible with spinal cord demyelination[2]. The neurophysiological profile of one patient was strongly suggestive of LSS. In both cases, clinical CNS dysfunction consisted of extensor plantar response. Our case showed only extensor plantar response which may reflect the restricted extent of the spinal lesion causing minimal dysfunction. The absence of exaggerated reflexes may have been due to concurrent neuropathy.

The MRI (T2 STIR sequence) also revealed a thickened right brachial plexus which has been reported in CIDP, MMN, hereditary neuropathy with liability to pressure palsies, hereditary demyelinating motor and sensory neuropathy, and neoplastic peripheral nerve infiltration. Enlargement of nerve roots/ plexus and hyperintensity demonstrates the local inflammatory process and oedema. Thus neuroimaging has become an increasingly useful tool in the diagnostic process of typical and atypical inflammatory neuropathy including LSS, CIDP and MMN especially when the electrophysiology is indeterminate.

This case emphasises importance of electrophysiology in diagnosing a very treatable inflammatory neuropathy with focus on extensive search for motor CB. Distal NCS may be normal during the initial course of the disease thus stressing the importance of stimulating proximally to improve sensitivity. When clinical suspicion is high repeated NCS testing is of value in detecting late onset CB, especially when considering the slow progression of the condition (it has been reported that the average time to diagnosis in LSS is 4.8 years). The presence of UMN signs in a patient with suspected LSS suggests concurrent CNS demyelination thus its presence should not preclude the diagnosis.

Key points:

- LSS is a highly treatable condition with LMN signs characterized by weakness, wasting, diminished reflexes, fasciculations cramps and minimal sensory signs.
- The presence of UMN signs in LSS suggests concurrent CNS demyelination.
- T2 STIR MRI imaging improves diagnostic yield of LSS.
- Distal electrophysiology may be normal during the initial course of LSS, stressing importance of stimulating proximally to improve sensitivity.
- Slow progression and late onset CB may delay diagnosis of LSS, emphasizing importance of repeated testing when clinical suspicion is high.

References

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