A Diagnosis Made by ‘Facilitation’

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Abstract
Lambert Eaton myasthenic syndrome is a presynaptic neuromuscular junction disorder, which has unique features on electrodiagnostic testing. Here we describe a middle aged lady with symmetric, progressive, areflexic weakness in lower limbs, who had the typical electrodiagnostic findings of diffuse attenuation of motor amplitudes, and increase in these amplitudes after brief exercise of the muscle sampled.

Case Report
A 44 year old lady presented with a 2 year history of ill-defined, progressively increasing pain in both legs, and weakness in the form of difficulty in standing from sitting position. Pain in the legs was dull, aching, ill-localised and present at rest and movement, without any sensory loss or paraesthesiae. The weakness initially affected left lower limb, then right lower limb after 3 months. At onset, she was able to grip her footwear, but had gradually lost this function over past 8 months. For the past 6 months, she had been unable to stand or walk without support. At presentation to us, she could not maintain sitting position, forcing her to remain supine. She had no weakness of upper limbs, or ocular/facial/neck or respiratory muscle weakness, and no diurnal variation.

She also complained of dryness of mouth and difficulty in swallowing solid food for 6 months, with no regurgitation. She had noticed decreased appetite since 1 year, with a weight loss of 10 Kgs over 2 yrs. Constipation was present, but there was no postural dizziness, visual blurring, dryness of skin, or urinary problems. Her periods had been regular, and she had no gynaecological, gastrointestinal or respiratory complaints.

General examination was normal except for mild pallor and a dry tongue. Skin and joint examination showed no evidence of any auto-immune pathology.

Pulse was 100/min regular, BP was 130/80 mm hg supine, 126/70 mm Hg standing, and RR was 18/min.

HMF and speech were normal.

Pupils were 3-4 mm reacting to light and accommodation. All cranial nerves were normal. Extraocular and palatal movements were normal and gag was intact. Neck flexion and extension were normal.

Tone was decreased in both lower limbs. Tibialis anterior, gastrocnemii, and vasti were bilaterally wasted with no fasciculations. Hammer-toes and a high arch of the feet was seen bilaterally. Power in upper limbs was uniformly Gd 5, and in lower limbs was symmetrically Gd 3 for all movements at hips and knees, Gd 4 at ankles, and Gd 0 at toes. Upper limb deep tendon reflexes were normal, but knee and ankle jerks were symmetrically absent. Superficial reflexes were normal and plantars flexor. Sensory examination was normal. No clinical evidence of fatiguing was present in ocular or limb muscles, and the absent tendon reflexes in lower limbs did not emerge after exercising the muscles.

Autonomic examination showed normally reacting pupils and no significant postural BP drop (10/8 mm Hg). RR variation on ECG on standing and slow breathing was maintained and rise in diastolic BP on sustained hand grip was 10 mm Hg. Dryness of tongue was the only remarkable feature.

Clinical differential diagnosis included a polynueropathy (CIDP, inherited motor polyneuropathy) or a Neuromuscular Junction disorder (Pre / post-synaptic).

Complete hemogram, blood sugars, renal and liver functions, infective markers (HIV, HBsAg, HCV, VDRL), and TFT were normal. S. CPK was 66 U/L.

NCS showed diffusely attenuated compound muscle action potentials (CMAP’s) in upper and lower limbs, with preserved sensory potentials (Figures 1 and 2). Slow rate RNS showed 12% decrement from 1st-4th CMAP. Post-exercise facilitation of over 500% in all the muscles tested confirmed the diagnosis of pre-synaptic pathology (Figures 1 and 2). EMG showed short duration, low amplitude polyphasic motor unit potentials in all the muscles sampled (Figure 3).

A search for underlying autoimmune pathology or neoplasia was undertaken. CSF examination was normal, serum protein electrophoresis was normal, and ANA, Anti-Ro and Anti-La antibodies were negative. VGCC antibody titer is awaited. Search for a primary neoplasm included CECT chest, craniospinal MRI and whole body PET scan. These were unremarkable except for a 1 cm sized L adrenal adenoma, which appeared benign on contrast CT as well as CT-PET.

With a diagnosis of Eaton-Lambert syndrome (with no associated neoplasm or auto-immune pathology detected), plasmapheresis was initiated. Patient developed dysautonomic symptoms in the form of bradycardia and hypotension during 1st exchange and procedure had to be terminated. IV IgG (2 gm/kg total) was given over 5 days, and she was started on T. Prednisolone 1 mg/Kg, T. Azathioprine 50 mg OD, raised to BD dose after 2 weeks and T. Pyridostigmine 60 mg qd.

Patient’s generalised fatigue improved gradually, and she could stand and walk with minimal support at discharge 8 weeks later. At 8 months follow-up, she is symptom-free on azathioprine, pyridostigmine, and low-dose steroids. She has been advised regular follow up for assessment of need for any further immunotherapy.

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and regular screening for malignancy.

**Discussion**

LEMS is a diagnosis made on NCS studies, as in our patient. The peculiar finding of diffusely attenuated CMAPs with preserved sensory responses, should prompt a study for LEMS, a presynaptic NMJ disorder associated with P/Q VGCC antibodies. This pattern may also be seen in anterior horn cell disorders (MND or polio), diffuse polyradiculopathies, pure motor axonopathies, other presynaptic neuromuscular junction disorders (Botulism) and end-stage myopathies. Assessing CMAP after brief exercise in suspected LEMS is as accurate as doing rapid RNS, and has the advantage of being less painful, along with ease of performance on many motor nerves. NCS findings in LEMS include attenuated CMAPs, decrement on slow RNS, 60-100% facilitation on rapid RNS or after brief exercise, and a pseudomyopathic EMG pattern if NM blockade is severe.

The clinical features of distal weakness, hammer toes and pes cavus in our patient were unusual for LEMS, and led us to consider a diagnosis of long-standing motor neuropathy initially. However, the autonomic features, diagnostic RNS study, and marked response to therapy, confirmed the diagnosis of LEMS.

Although positivity of P/Q VGCC antibodies was initially thought to be mandatory for LEMS diagnosis, seronegative forms of LEMS are well recognized, the pathology being antibodies against other presynaptic molecules such as Synaptotagmin in these cases. The neurological features of LEMS have been shown to be similar in VGCC seronegative patients.

3,4-diaminopyridine and intravenous immunoglobulins have been reported to be beneficial for long-term improvement in muscle weakness by Keogh et al, in a Cochrane review of treatment response in ELS.

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Fig. 2: Low CMAPs, preserved SNAPs* and post-exercise facilitation in lower limbs

Fig. 3: Pseudomyopathic pattern

References


