Lambert-Eaton syndrome and prostate adenocarcinoma, a case report

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Introduction

Lambert-Eaton Myasthenic Syndrome (LEMS) is a rare neuromuscular disease characterized by progressive muscle weakness due to a disruption of acetylcholine neurotransmission within the neuromuscular junction (NMJ). It has similar clinical features to myasthenia gravis (MG), but exhibits electrographic facilitation upon exercise.[6] Unlike MG, LEMS is due to dysfunction of the presynaptic calcium channels rather than the postsynaptic acetylcholine receptors in MG. LEMS occurs about 46 times less than MG, and is more likely to affect males, whereas MG is known to have higher prevalence in the female population.[1] Literature has shown that LEMS is predominantly associated with small cell lung cancer (SCLC). It is thought that paraneoplastic autoantibodies target the P/Q voltage-gated calcium channels within the presynaptic terminal at the NMJ.[1,5] Although some cases have been reported, the association of LEMS with other malignancies is much more rare and cases in the literature are lacking.[7,8] Here, we present a case of LEMS diagnosed in a male patient with metastatic prostate adenocarcinoma.

Case Description

A 75-year-old male with a known history of metastatic prostate cancer status-post radiation and chemotherapy treatment was admitted to the hospital for planned lumbar radiation treatment and chemotherapy. The neurology team was consulted due to progressive weakness most notably in the proximal lower extremities as well as increased difficulty breathing for 8 months. The patient denied diplopia, dysarthria, dysphagia, dizziness, or voice changes. The weakness was not associated with sensory changes or pain beyond mild muscle aches. Weakness started in the lower limbs then gradually progressed to involve the proximal upper extremities bilaterally, as well as diaphragmatic muscles, resulting in dyspnea on exertion, and eventually made the patient bedridden. However negative inspiratory force was persistently normal throughout the hospitalization. Spine MRI showed potential sites of bony metastases of prostate cancer but did not show evidence of significant spondylosis. The patient denied saddle anesthesia and bowel or bladder incontinence.

Physical examination revealed normal cranial nerve exam, 4+/5 strength throughout the bilateral upper extremities, and predominantly proximal weakness in the lower limbs with 4-/5 strength in the iliopsoas, quadriceps, and hamstrings, normalizing at the ankle. There were diminished reflexes in the biceps, triceps, brachioradialis, and the ankles. Labs were significant for mild hyponatremia, normocalcemia, and normal blood counts. Voltage gated calcium channel antibodies were elevated at 142.5 pmol/L (Normal 0-30 pmol/L). CT scan of the chest revealed clear lung parenchyma without nodules, infiltrates, or effusions, which ruled out a primary lung malignancy. Small subsegmental pulmonary emboli were visualized incidentally.

EMG/NCS was performed which demonstrated normal sensory conduction of the left superficial peroneal nerve. However, motor nerve conduction of the right ulnar at the abductor digiti minimi muscle demonstrated low compound muscle action potential (CMAP) amplitude which more than doubled upon exercising for 10 seconds (Fig. 1). 3Hz repetitive nerve conduction of the bilateral ulnar nerves demonstrated decremental response of ~30% in amplitude with subsequent post-exercise facilitation (Fig 2).

The patient was then treated with a 5-day course of intravenous immunoglobulin and amifampridine for LEMS, resulting in improvements in strength testing as well as subjective dyspnea and was subsequently discharged home on a prolonged prednisone taper.[2] He eventually transitioned to hospice care and passed away due to the underlying metastatic prostate cancer.

Discussion

Compared with MG, LEMS is a much rarer. In the literature, paraneoplastic cases are mostly associated with lung malignancy. However, our case of a patient with prostate cancer highlights the importance of considering LEMS as a cause of weakness in patients with other forms of cancer. Electrodiagnostically, one must be alert to a pattern of widespread low CMAP amplitudes on nerve conduction studies, which may alert the diagnostician to perform exercise testing to look for electrographic facilitation and subsequently pursue repetitive nerve stimulation. The treatment of paraneoplastic LEMS is primarily directed at the underlying neoplasm but also consists of immunosuppression and a trial of pyridostigmine. Additionally, amifampridine, an FDA approved agent for LEMS that may help reduce symptoms.[3,4] Amifampridine works by facilitating the release of acetylcholine within the neuromuscular junction via potassium channel blockade. Unlike SCLC, there are no clear studies of how prostate adenocarcinoma cells trigger the immune system leading to LEMS, but we theorize the mechanism may be similar to that of SCLC. Future studies should focus on understanding this pathophysiology and highlighting the mechanism at the molecular level.

Fig 1. Motor nerve conduction of the right ulnar nerve at the wrist of the ADM muscle demonstrating A) baseline reduced CMAP amplitude of 1.8mV at the wrist B) post exercise (for 10 seconds) facilitation of the same muscle to 4.4mV C) 5 minutes post exercise showed a return to baseline/post exercise exhaustion to 1.4mV.

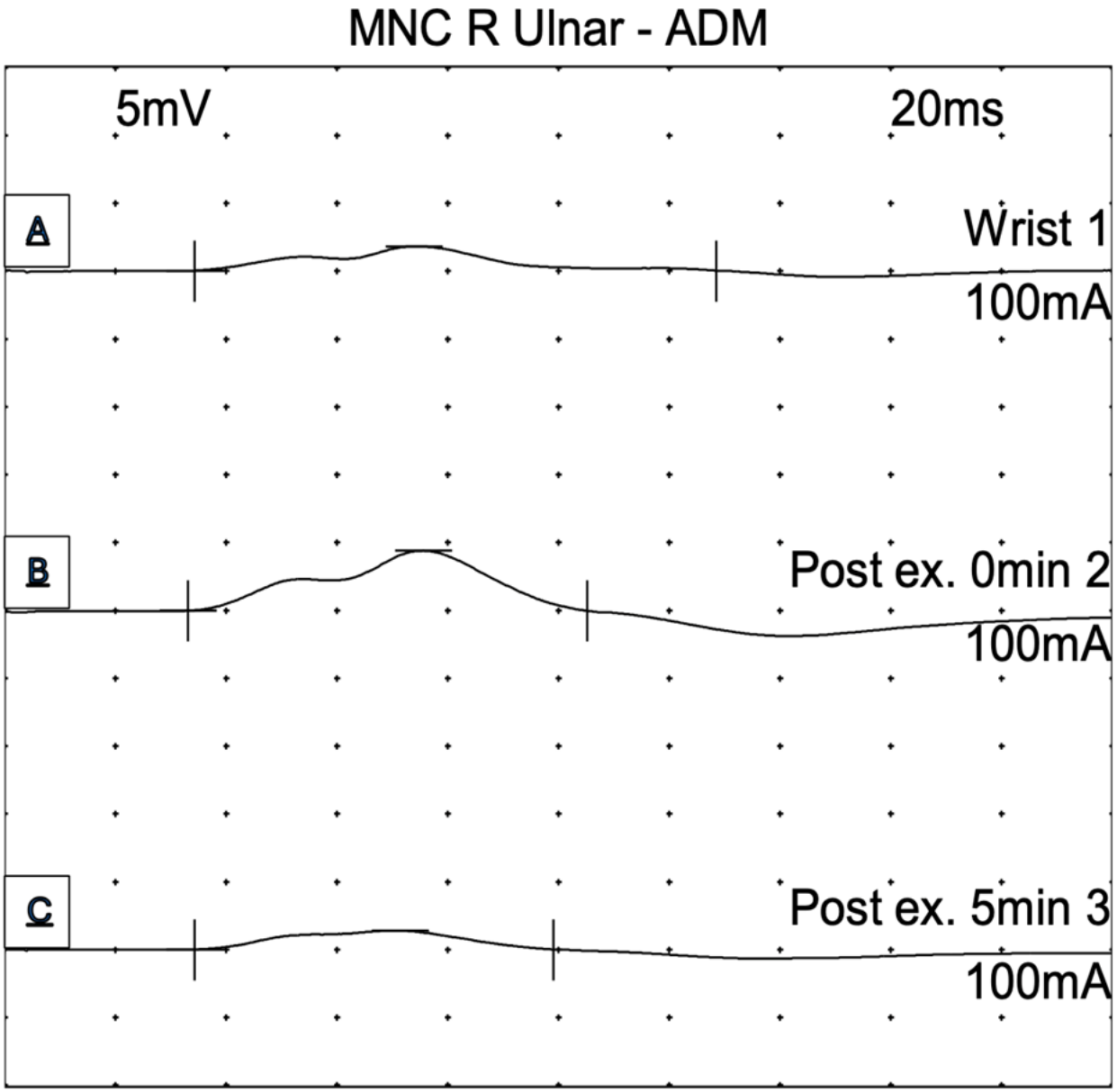
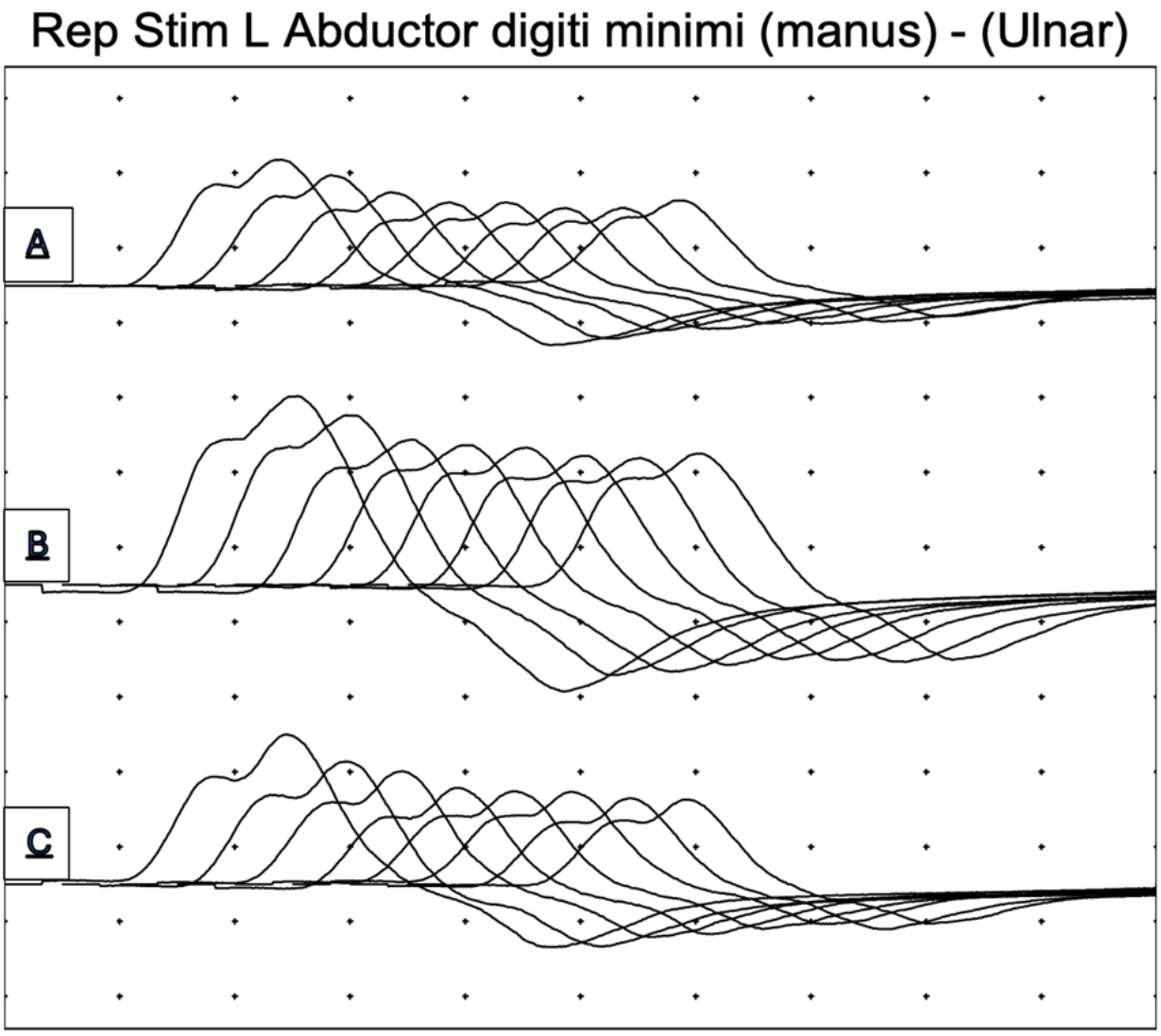


Fig 2. Repetitive nerve stimulation (3Hz) of the left ADM muscle demonstrating: A) 1.6mV at baseline. B) Facilitation immediately post exercise to 2.6mV (60% increase). C) Return to near baseline at 1.9mV 30 seconds post exercise.



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