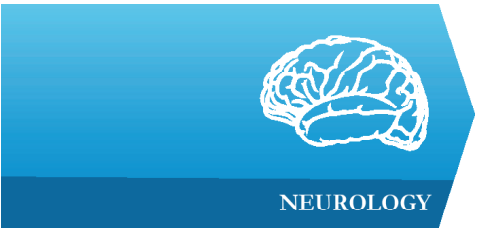
Case Report



Acute onset of Lambert Eaton myasthenic syndrome in prostate adenocarcinoma: a case report

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Abstract

Lambert Eaton myasthenic syndrome (LEMS) is a rare disorder of the neuromuscular junction. The representative clinical triad consists of proximal muscular weakness, areflexia and autonomic dysfunction. The diagnosis is based on the clinical findings confirmed by voltage-gated calcium channels antibody titer and neurophysiology. We present a 69 year old male with prostate adenocarcinoma and 30 years history of smoking, referred for muscle weakness in the lower limbs and difficulty to climb the stairs.

Keywords: Lambert Eaton myasthenic syndrome, voltage-gated calcium channels, neurophysiology

Introduction

Paraneoplastic neurological syndromes are non-metastatic neurological complications of systemic cancers, resulting from a cross-reaction against intracellular antigens [1].

Lambert Eaton Myasthenic Syndrome (LEMS) is a rare neuromuscular junction disorder, first described by E.H. Lambert, L.M. Eaton and E.D. Rooke in 1956 [2,3]. LEMS can be paraneoplastic, affecting men, with a median age onset at 60 years [4]. A small-cell lung carcinoma (SCLC) with neuroendocrine characteristics is found in more than half of the patients, but other associated neoplasms are described [5]. In non-tumor related LEMS most patients are female with a peak of disease at 35 and 60 years [4]. The most important clinical features are proximal muscular weakness associated with areflexia and autonomic dysfunction [6]. The diagnosis is facilitated by serum determination of autoantibodies against voltage-gated calcium channels (VGCC), present in the majority of patients with LEMS [7]. The nerve conduction study shows a significant decrease of the compound muscle action potential (CMAP), without atrophies of the muscles [8]. An important post-exercise increment is observed after contraction, as a result of the facilitation of calcium ions entry into the cell and releasing the acetylcholine vesicles. Moreover, a high-frequency stimulation with 50 Hz shows an increased CMAP amplitude, but the technique is painful and it is recommended to avoid it [8].

We present the case of a patient with acute onset and typical symptoms of LEMS, in the context of a preexisting prostate adenocarcinoma.

Case Report

We present the case of a 69 year old male, with a past medical history of prostate hypertrophy and cardiovascular risk factors, former smoker of 4 packs/day for 30 years, abstinent for about 20 years. The patient was referred to the emergency room for proximal muscular weakness with acute onset

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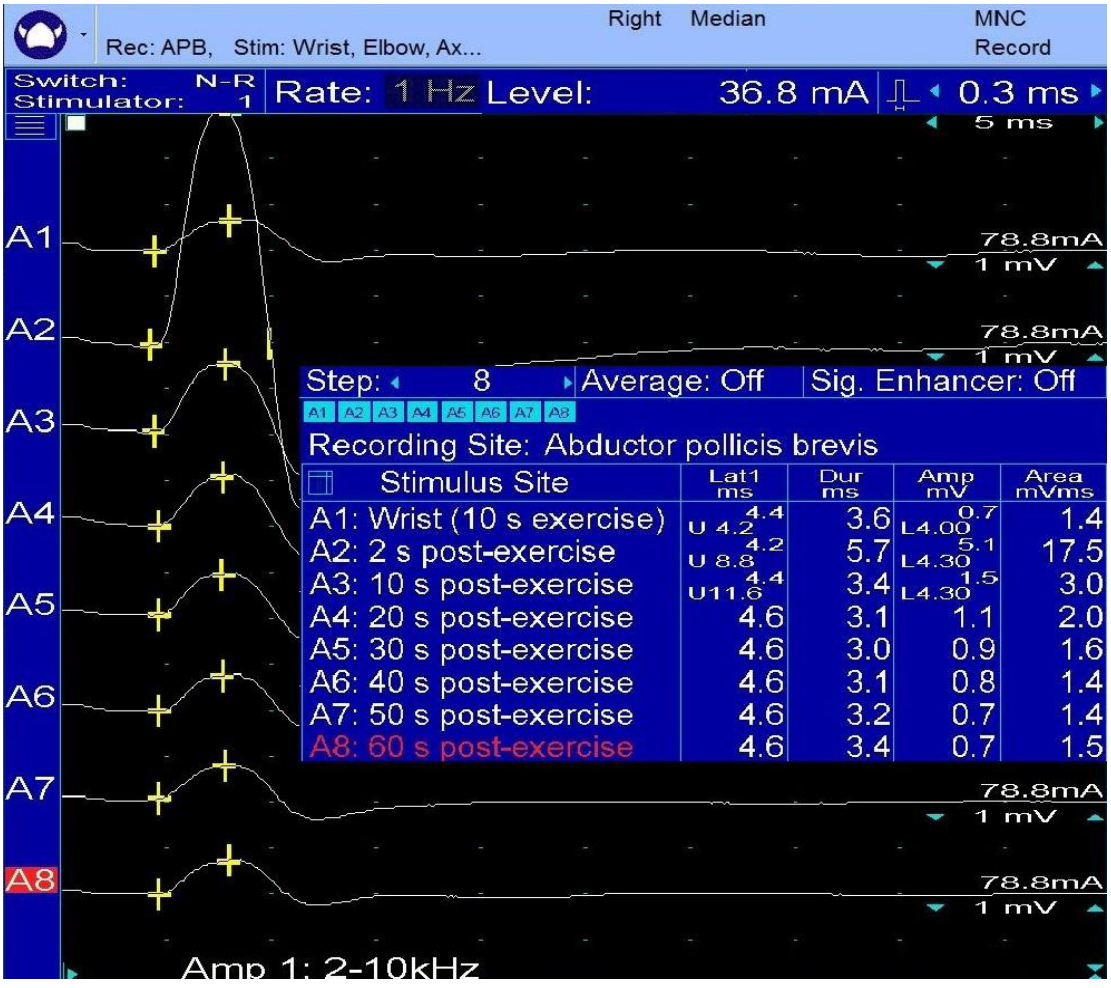
in the lower limbs. The symptoms worsened during the next two days. From day 4 the patient could no longer climb the stairs and from day 5 he had difficulty walking with the cane. Moreover, he described a history of viral respiratory infection 3 weeks before and the symptoms were interpreted as an acute polyradiculoneuritis. The first electroneuromyography (ENMG) examination showed an overall reduced motor CMAP amplitude but the diagnosis was overlooked. The symptoms worsened again, with muscle weakness appearing in the upper limbs. As a result, guidance towards a referral center for neurological diseases was made.

The patient's skin color are pale and he lost 10 kg in 3 months. He had no respiratory complaints, but he suffered from severe xerostomia. Neurological reexamination performed 1 month after the symptoms onset showed a slight bilateral ptosis, without dysphagia. The patient reported generalized muscular weakness associated with a weakness sensation of the neck and abdominal muscles (Figure 1). Deep tendon reflexes were absent in the left upper limb and both lower limbs.

He had a mild anemia. The values of the tumor markers were: CEA (Carcinoembryonic Antigen) = 16 ng/ml (NV (Normal Value) < 4.3 ng/ml, for smokers) and PSA (Prostatic Antigen) = 6.93 ng/ml (NV < 4 ng/ml). The lumbar puncture was normal. Anti-neuronal antibodies were negative, but the VGCC antibodies were present in serum at a value of 510 pmol/l (NV < 40 pmol/l). Detection of SOX 1 antibodies was not performed.

The second ENMG examination showed a global CMAP reduction, with sensory nerve action potential amplitude (SNAP) slightly diminished on the bilateral sural nerve. Needle electrode examination was normal. After 10 seconds of voluntary isometric contraction, the CMAP amplitude and CMAP area of the abductor pollicis brevis muscle increased up to 728% (Figure 2).

Figure 1. Bilateral ptosis and generally diminished muscle strength.



Stimulus Site	Lat1 ms	Dur ms	Amp mV	Area mVms
A1: Wrist (10 s exercise)	U 4.2 4.4	3.6	L4.00 0.7	1.4
A2: 2 s post-exercise	U 8.8 4.2	5.7	L4.30 5.1	17.5
A3: 10 s post-exercise	U11.6 4.4	3.4	L4.30 1.5	3.0
A4: 20 s post-exercise	4.6	3.1	1.1	2.0
A5: 30 s post-exercise	4.6	3.0	0.9	1.6
A6: 40 s post-exercise	4.6	3.1	0.8	1.4
A7: 50 s post-exercise	4.6	3.2	0.7	1.4
A8: 60 s post-exercise	4.6	3.4	0.7	1.5

Figure 2. Increasing of the amplitude and area of abductor pollicis brevis CMAP (Compound Muscle Action Potential) after 10 seconds of contraction.

We performed a first computed tomography of the thorax, abdomen and pelvis (CT – TAP), screening to notice the presence of a neoplasm. Chest and abdominal CT showed mediastinal and abdominal lymphnodes with maximal dimensions of 31/23 mm and no signs of lung tumor. The pelvic CT scan evidenced hypertrophy of the middle lobe of the prostate, heterogeneous iodophilia with microcalcifications and micronodules at the level of periprostatic fat. Also, osteocondensation bone lesions in the pelvis and D11 thoracic vertebra were observed. The MRI raised suspicion of a prostate adenocarcinoma with T3bN1Mx staging and the histopathological examination confirmed an acinar prostatic adenocarcinoma, Gleason score 8 (4+4), grading 4 (WHO 2016). Moreover, the paraclinical examinations were carried out to achieve the differential diagnosis with other malignant diseases: non-small cell and mixed lung carcinoma, thymoma and lymphoproliferative disorders. The medical treatment with Bicalutamide 150 mg/day was initiated, but the patient did not tolerate it, and a cure with Goserelin 3.6 mg/day combined with Flutamide 750 mg/day was started. The immunosuppressive therapy with Azathioprine 100 mg/day and therapy with acetylcholinesterase inhibitors such as Pyridostigmine 240 mg/day was unsatisfactory. The neurological symptoms were improved with 3,4-diaminopyridine, 30 mg/day.

Considering a DELTA–P score at 3/6, a screening for the SCLC was performed every 6 months. The second CT - TAP showed a numerical and dimensional progression of the mediastinal adenopathies with numerical progression of osteocondensation bone lesions (1/3 upper of the bilateral femur, all thoracic - lumbar spine bodies, right clavicle and bilateral scapula) with normal thoracic CT scan (Figure 3).

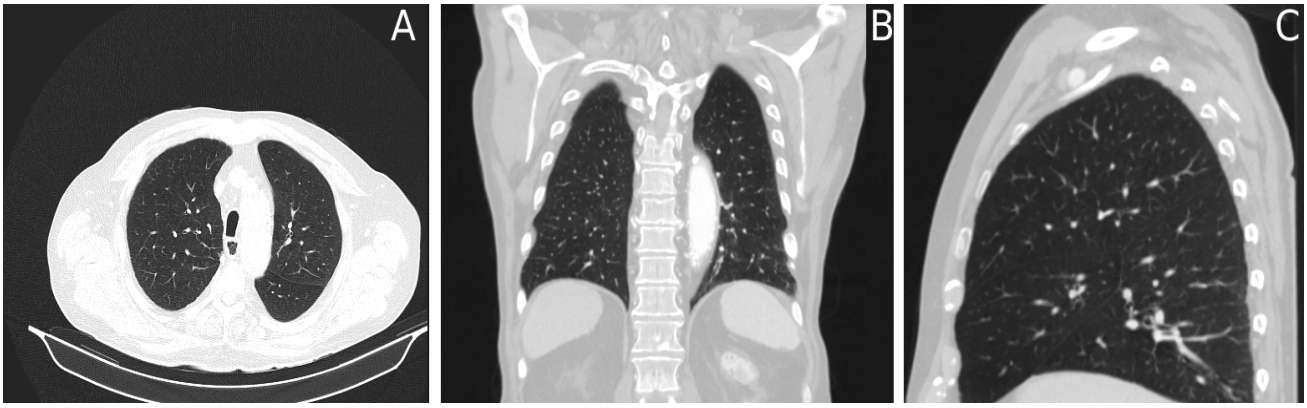


Figure 3. (A) Axial, **(B)** coronal and **(C)** sagittal contrast-enhanced computed tomography (CT) images of the chest.

Discussion

The diagnostic of LEMS is based on history and typical clinical findings, confirmed by electrophysiological studies and serologic testing [9]. However, our patient confirms that LEMS is a rare disease and the diagnosis confirmation can easily escape to the first evaluation. In addition, our patient's case has several particularities. First of all, we want to emphasize that the neurological manifestations were evidenced before the oncological diagnosis. Moreover, the acute onset of the LEMS symptoms is nonspecific and the association between LEMS and prostate adenocarcinoma is very rare. The first description was made by S.K. Agarawal in 1995 and, 20 years later, C. Monteiro reported the second case of LEMS associated with prostatic adenocarcinoma [10,11]. Furthermore, considering the patient's smoking history and the fact that prostatic neoplasms are a very common disease, this might also be a random association with a SCLC. Mainly, in our case, a DELTA-P score of 3 suggests a high risk of SCLC association [7]. On the other hand, the patient did not have any clinical evidence for an overlapped respiratory disease and the two series of chest CT scan were negative. Neurological symptoms were controlled with 3,4-diaminopyridine, but unfortunately, the patient died 16 months after the initial symptoms because of prostatic neoplasm progression and bone metastasis.

In conclusion, our case highlights the importance of performing the increment technique when CAMPs are globally diminished on ENMG examination. Moreover, in current neurological practice, we must extend the clinical reasoning to a LEMS when we have in front of us an oncological patient with clinical signs in favor of a neuromuscular junction disorder.

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