Neurol Sci (2015) 36:2145–2146
DOI 10.1007/s10072-015-2315-x

LETTER TO THE EDITOR

Lambert–Eaton myasthenic syndrome and prostatic adenocarcinoma

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Received: 1 February 2015 / Accepted: 29 June 2015 / Published online: 5 July 2015

Introduction

Lambert–Eaton myasthenic syndrome (LEMS) is characterized clinically by proximal muscle weakness, reduced or absent tendon reflexes and autonomic symptoms, combined with typical neurophysiological criteria or with the presence of pathogenic auto-antibodies to voltage-gated calcium channels (anti-VGCC) [1]. Typical neurophysiologic findings are low compound muscle action potentials (CMAPs) with decrement of more than 10 % at low-frequency repetitive nerve stimulation (RNS) and an increment of more than 100 % of CMAPs after maximum voluntary contraction or after high-frequency RNS. LEMS can be paraneoplastic or non-tumor related (NT-LEMS); in the former it is frequently associated with small cell lung cancer; however, combination with other malignancies should be considered. Prostate cancer has been reported as an extremely rare association with LEMS. In the four reported cases, three were small cell prostatic tumors [2–4] (two of these had both neuroendocrine and small cell characteristics) and one was an adenocarcinoma [5]. We report a rare case of a patient with LEMS associated with prostatic adenocarcinoma, with clinical criteria and anti-VGCC positivity, but normal neurophysiological study.

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Case report

A 77-year-old man was referred for neurological observation due to walking difficulties for the past 3 years. He felt weakness after some minutes of walking needing to rest; and had trouble standing up from the sitting position suggesting proximal lower limbs weakness. These symptoms were worse in the morning. He also reported urinary incontinence, dizziness with orthostatism and dry mouth. More recently, he had episodic diplopia. There were no bulbar or sensory complaints. The symptoms began 1 month after the diagnosis of prostate adenocarcinoma. The diagnosis of the tumor was based on prostate biopsy; the patient was initially under hormonal therapy, but due to side effects he stopped it and was submitted to orchidectomy. On the first neurological examination he had lower limb proximal muscle weakness grade 4 in 5 with areflexia. Cranial nerve examination was normal, except for reference to horizontal diplopia without objective ophthalmoparesis. Sensory signs were absent. Symptomatic orthostatic hypotension was present with systolic blood pressure dropping from 130 to 100 mmHg after 3 min of assuming the upright position.

Nerve conduction studies revealed normal median nerve CMAPs (amplitude of 11.5 mV and latency of 3.3 ms) with no increase in amplitude after maximum voluntary effort or after RNS low and high frequencies (from 3 up to 50 Hz); no other nerves were tested. Looking for a tumor-related LEMS, thoracoabdominal computed tomography scan, tests for tumor markers and anti-neuronal antibodies were performed and all were normal or negative. Auto-antibodies against acetylcholine receptors (anti-AchR) and anti-muscle-specific tyrosine kinase antibodies (anti-MuSK) were negative. Anti-VGCC antibodies, tested by radioimmunoassay, were high positive.

The patient was initially treated with pyridostigmine up to 240 mg per day with mild benefits: he felt less weak while walking and was able to climb stairs without assistance. However, significant diarrhea limited its use. After anti-VGCC antibodies confirmation, 3,4-diaminopyridine was initiated, up to 10 mg three times a day; there were only mild benefits and the patient was unable to increase the dose due to significant nausea and dizziness. Prednisolone up to 40 mg per day during 4 months, followed by monthly intravenous immunoglobulin during 7 months was tried without any significant response. The hypothesis of tumor relapse or changing of characteristics was discussed with the urologists but his age and the presence of mild to moderate symptoms of heart failure precluded a more invasive attitude. Prostate-specific antigen was always normal.

Discussion

The presence of the clinical triad: proximal weakness, areflexia and autonomic symptoms suggested the diagnosis of LEMS. Post-exercise facilitation of tendon reflexes or improvement of muscle strength to normal range after muscle contraction was not present in our patient. Dry mouth, one of the most common autonomic features [1], was reported along with less common features as the orthostatic hypotension. Although RNS studies are very sensitive to the diagnosis of LEMS, some patients may have normal CMAPs and RNS [6]; therefore, a normal electromyography is not an exclusion criteria in the presence of anti-VGCC antibodies combined with the clinical triad [1]. Moreover, the RNS was performed only on one nerve and it was not repeated during the clinical evolution possibly preventing the appearance of the typical neurophysiological changes.

Our patient illustrates the difficulties of the diagnosis of LEMS—the first symptom (lower limbs weakness) was very unspecific and the patient was referred to the neurologist only when it was disturbing (3 years later) and associated with other symptoms. This diagnosis delay is a common occurrence in LEMS, especially in NT-LEMS [1]. The association with adenocarcinoma of the prostate is very rare, a reason that also contributed to this delay. Finally, treatment is also a challenge with variable and not always satisfactory results.

Conflict of interest The authors report no conflict of interest.

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