



Case Report

A Case of Subacute Cerebellar Degeneration Coexisting With Lambert-Eaton Myasthenic Syndrome

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Abstract

Paraneoplastic cerebellar degeneration (PCD) is a neurological disorder characterized by the subacute onset of cerebellar dysfunction, sometimes with dysarthria, dysphagia, nystagmus, mental changes, muscular and sensory deficits. Cancers of the lung, ovary, breast and lymphoma are the most frequent causal neoplasms. Furthermore, PCD may occur in association with the Lambert- Eaton myasthenic syndrome (LEMS). LEMS is a rare syndrome with fluctuating muscle weakness, hyporeflexia and autonomic dysfunction, predominantly affecting men. We present here a case with symptoms of subacute cerebellar degeneration coexisting with LEMS.

Keywords: Paraneoplastic cerebellar degeneration, Lambert- Eaton myasthenic syndrome, small-cell lung carcinoma

Lambert-Eaton Myastenik Sendromunun Eşlik Ettiği Subakut Serebellar Dejenerasyon Vakası

Özet

Paraneoplastik serebellar dejenerasyon (PSD), subakut serebellar bozukluğa eşlik eden dizartri, disfaji, nistagmus, mental değişiklikler, parezi ve duysal defisitlerle karakterize bir nörolojik bozukluktur. En sık akciğer, over, meme kanserleri ve lenfomalarla birliktelik gösterir. Ayrıca Lambert-Eaton myastenik sendromu (LEMS) ile de birlikteliği bilinmektedir. LEMS dalgalanan kas güçsüzlüğü, hiporefleksi ve otonomik bozukluklarla giden ve en fazla erkekleri etkileyen nadir görülen bir sendromdur. Bu makalede, subakut serebellar dejenerasyon bulguları ile birliktelik gösteren bir LEMS vakası sunulmuştur.

Anahtar Kelimeler: Paraneoplastik serebellar dejenerasyon, Lambert- Eaton miyastenik sendromu, küçük hücreli akciğer kanseri

INTRODUCTION

Paraneoplastic cerebellar degeneration (PCD) is a neurological disorder characterized by the subacute onset of cerebellar dysfunction, sometimes associated with dysarthria, dysphagia, nystagmus, mental changes, muscular and sensory deficits^(4,14). Cancers of the lung, ovary, breast and lymphoma are the most frequent causal neoplasms. Different immunological mechanisms may play a

role in the development of PCD. Furthermore, PCD sometimes may occur in association with the Lambert- Eaton myasthenic syndrome (LEMS)^(4,6,14). LEMS is characterized by fluctuating muscle weakness, hyporeflexia and autonomic dysfunction predominantly affecting men⁽¹⁷⁾. Antibodies to voltage-gated calcium channels (VGCCs) have been found by radioimmunassay in about 90% of LEMS patients^(15,16). We report

here a case presenting with symptoms of subacute cerebellar degeneration coexisting with LEMS.

CASE PRESENTATION

A 61 year-old man, with diplopia, slurred speech, nausea, vomiting, ataxia and difficulty of walking was admitted to the hospital in January 2006. He denied any problems other than heavy alcohol use and smoking. He had easy fatigability since 1 month after having a viral upper respiratory tract infection. He had worsening difficulty of walking and slurred speech with vertigo, nausea and vomiting since then. On neurological examination, he had diplopia and severe dysarthria; his vision and gaze were normal other than a horizontorotatory nystagmus while looking to both sides. He had no paresis. Generalized hypotonia was noted. Deep tendon reflexes were normoactive on the upper limbs but hypoactive bilaterally on the lower limbs. He had no Babinski sign bilaterally. He had no dysmetria or dysidiadochokinesia. The sensory examination was totally normal. He had no orthostatic hypotension. He could neither sit nor stand or walk without assistance. He fell to his knees.

Routine blood analysis was normal. His cranial magnetic resonance imaging did

not reveal any abnormality. Lumbar puncture examination excluded any leptomeningeal metastases. Serum level of CA 19,9 was found high (65,9 n= 0-39). HuAb and JoAb were negative. He got worse when we decided to examine him by electromyography (EMG) because of his marked hypotonia, unsteadiness, and unusual pattern of gait with diminished deep tendon reflexes.

An electrophysiological examination revealed normal sensory conduction studies but diminished compound muscle action potentials (CMAP) on the muscles of all extremities. Motor unit potentials were normal in needle electromyography. Immediately after maximum contraction of ADM for 10 seconds, single stimulation of the ulnar nerve at the wrist demonstrated 400% facilitation of the CMAP amplitude recorded on ADM muscle (Figure 1). During repetitive stimulation (ulnar nerve stimulation at the wrist; recording: ADM) mild decrement was detected at lower rates (3 Hz). 20Hz repetitive stimulation could not be sufficiently performed but first 9 potentials demonstrated a tendency to facilitation. The electrophysiological findings suggested a disorder of the neuromuscular junction, being probably presynaptic. LEMS was diagnosed electrophysiologically.

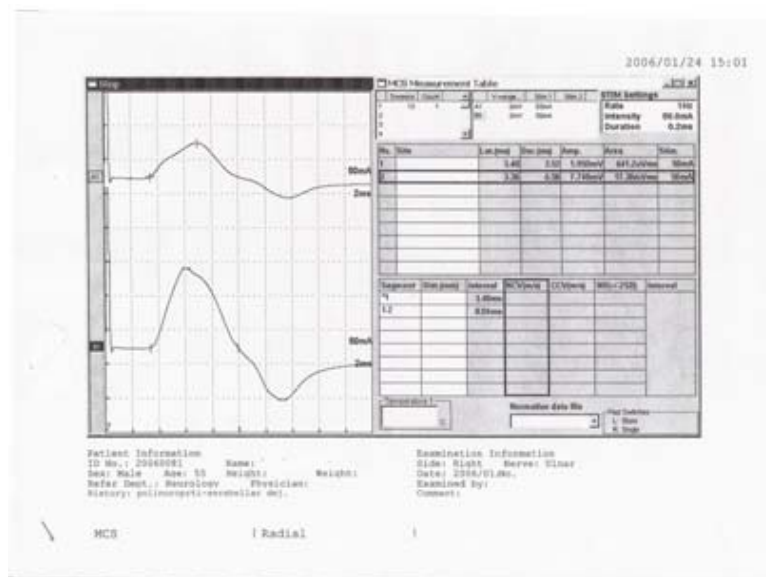


Figure 1: 400 % facilitation after 10 s maximum contraction

Anti-acetylcholine receptor antibody was negative. Anti-VGCC antibody titer was very high (760,n= 0-45). Thorax computerized tomography (CT) detected no abnormality. An abdominal CT disclosed thickening of the gastric mucosa and gastroscopy revealed Grade 1 esophageal varices, cardioesophageal sphincter dysfunction, and gastritis. Pathological examination of this area showed chronic gastritis, foveolar hyperplasia and areas of mild incomplete intestinal metaplasia. He had an F-18 FDG PET scan in which a pathological FDG uptake was observed not only on the right inferior paratracheal and hilar regions, but also on the right anterior segment of superior lobe. On bronchoscopic examination chronic nonspecific bronchitis was detected.

A very mild response to anti-acetylcholinesterase therapy was observed. But his progression continued. And when a proximal muscle weakness of both lower and upper limbs accompanied his previous

symptoms, he was treated with intravenous immunoglobulin (IVIg) with a dose of 0.4 mg /kg/ day and a mild improvement in muscle strength was observed. In his second EMG after IVIg therapy, we detected 800 % facilitation after a single stimulation of the ulnar nerve at the wrist and typical increment during repetitive stimulation (Figure 2).

After 3 weeks of IVIg treatment, metilprednisolone (80mg/day) was introduced and he showed a good response to steroid. He was able to stand and sit with a less effort.

When it was available we added 3,4 Diaminopyridine (3,4 DAP) simultaneously with steroid after which he managed to sit himself and was able to stand and walk with assistance. Despite the improvement in muscle strength, generalized marked hypotonia, diplopia, nystagmus and dysarthria persisted. We didn't detect the possible underlying cancer yet.

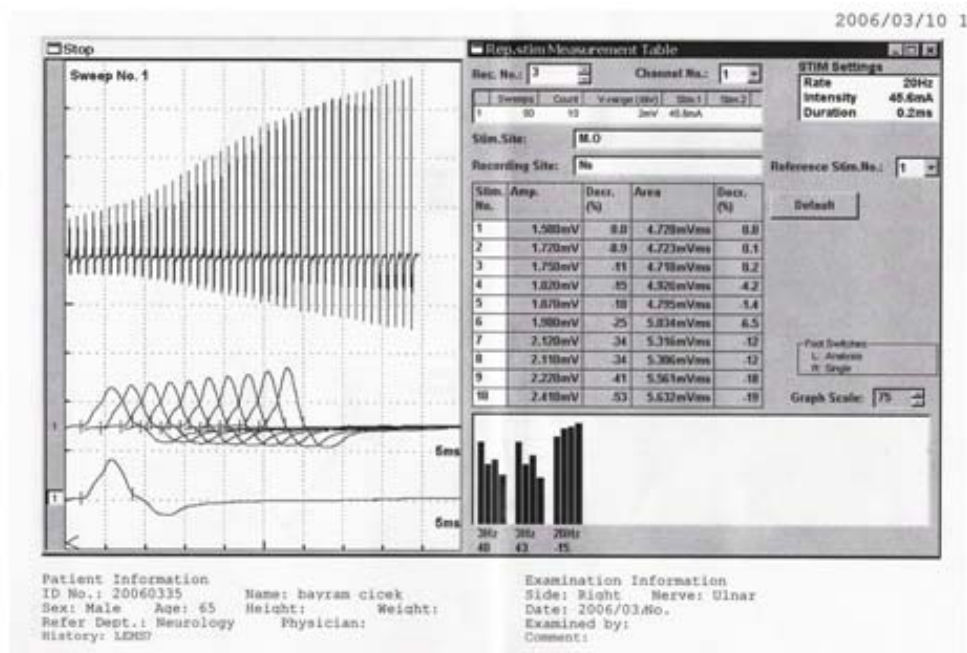


Figure 2: 800 % facilitation after a single stimulation of the ulnar nerve at the wrist and typical increment.

DISCUSSION

Here we reported a HuAb negative patient presenting with symptoms of subacute cerebellar degeneration who was simultaneously diagnosed as LEMS with the typical clinical and electrophysiological findings and also high titer of Ab to VGCC.

PCD may occur with or without Hu antineuronal antibodies in patients with small cell lung carcinoma (SCLC). Approximately 45% of 57 patients were reported to be HuAb+ in series of Mason et al.⁽¹⁴⁾. Patients had presenting symptoms of subacute cerebellar degeneration such as ataxia, nystagmus, dysarthria and diplopia similar to our patient. Eighty percent of HuAb positive and 37,5% of HuAb negative PCD patients developed extracerebellar signs and also LEMS (16%). The prevalence of VGCC Ab was reported so high in HuAb negative PCD patients suggesting that these antibodies may have a role in the pathogenesis of the cerebellar dysfunction⁽¹⁴⁾.

Clouston et al. identified 23 cases with LEMS and PCD, most of them with lung cancer and concluded that the frequency of association of PCD and LEMS was higher than expected by chance⁽⁶⁾.

LEMS is a rare disorder of neuromuscular transmission first recognized clinically by lung cancer, mostly SCLC^(1,7,8,11,17) and subsequently, cases without cancer was also detected^(12,13). Later, associated electromyographic abnormalities, pathophysiology and clinic were reported by Lambert and his colleagues^(10,11,17,18). The incidence of neurological syndrome is probably less than 5 % in LEMS^(8,11). Although SCLC accounts for the vast majority of lung cancers, LEMS with atypical pulmonary carcinoids was also reported^(5,12).

Our patient was a HuAb negative PCD case with high titer of VGCC Ab and diagnosed clinically and electrophysiologically as LEMS. We think that identification of LEMS in these

patients is important, because LEMS may respond to treatment in some aspect.

In the patient group reported by O'Neill et al, symptoms of LEMS preceded diagnosis of the tumor by 5 months to 3.8 years in most (17 of 24) patients. And proximal leg weakness was the most frequent presenting symptom. Depressed limb reflexes, symptoms of autonomic dysfunction such as dry mouth, impotence, constipation, blurred vision and sweating, mild and transient cranial nerve symptoms (diplopia and ptosis), slurred speech were also seen. We did not diagnose the underlying cancer yet (one and a half year) and our patient still have persistent cranial nerve symptoms, slurred speech and cerebellar signs.

IVIg was first tried for the treatment of LEMS in 1992 by Bird⁽³⁾. The results of a single placebo controlled study and a number of single cases published demonstrated that IVIg is useful in the treatment of LEMS patients^(2,3,9). Our patient gave a partial response to IVIg treatment but his symptoms got worse again after 10 months of the first IVIg therapy.

In LEMS without SCLC prognosis was reported to be variable, patients needed continuing doses of immunosuppressive medication and proximal muscle strength was the predictor of outcome after about 11 years of follow up⁽¹³⁾. Also spontaneous remission is not a feature of PCD and efforts directing to underlying carcinoma had no significant impact to the course or severity of it⁽¹⁴⁾. Our patient is still on follow-up for the prognosis.

In conclusion, we think that clinicians should be aware of the coexistence of SCD with LEMS and because of the possible treatment chance of this syndrome; patients with SCD should also be examined electrophysiologically for LEMS.

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