Short report

A neuromuscular transmission disorder: combined myasthenia gravis and Lambert Eaton syndrome in one patient

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SUMMARY The distinction between myasthenia gravis and Lambert Eaton myasthenic syndrome can usually be made by the clinical and neurophysiological features. A patient was observed with features which suggested a combination of both disorders. This has been described in few patients before. The importance of electromyography in both distal and proximal limb muscles for a correct diagnosis is demonstrated. Only in proximal nerve stimulation tests was proof found of the existence of both syndromes.

Myasthenia gravis and Lambert Eaton myasthenic syndrome (LEMS) are both autoimmune diseases with impaired neuromuscular transmission.¹⁻³ Apart from similarities there are essential differences in pathogenesis and therapy; myasthenia gravis is a postsynaptic disorder at the acetylcholine receptor level, while LEMS is thought to be caused by a presynaptic membrane defect.⁴ Electromyography is probably essential for making the correct diagnosis as clinical features may not be sufficient to differentiate between the two syndromes. We describe a patient with clinical and neurophysiological features which suggest a combination of both diseases. This has been described in few patients before.⁵⁻¹⁵

Case report (fig. upper part)

In 1984 an 80 year old woman visited our clinic with complaints of fluctuating weakness of ocular, bulbar and limb muscles, which had existed for several months. Apart from the weakness which could be provoked by exertion, neurological examination showed no abnormalities. The tendon reflexes were sluggish. There was no post-tetanic poten-

tiation on clinical testing. In her serum antibodies against acetylcholine receptors were found and the patient was treated with one anticholinesterase agent (mestinon up to 360 mg/day). After 6 months she became increasingly dyspnoeic and was admitted to hospital where her vital capacity proved to be only 1000 ml. There was obvious ocular, bulbar and generalised muscle weakness, prominent in pelvic and shoulder girdle. A dry mouth, paraesthesias in the limbs and absent tendon reflexes were noticed. Routine haematological, chemical and serological tests revealed no abnormalities. Antibodies against striated muscle, however, were found in the serum along with thyroid and gastric antibodies. The patient was known to suffer from pernicious anaemia; biopsy specimens from the gastric mucosa showed chronic inflammation without signs of malignancy. Chest radiograph and CT were negative for a possible thymoma. As the tensilon test (10 mg i.v.) clinically still resulted in some improvement of muscle strength, neostigmin (45 mg/day) was added to the mestinon medication. After a few days, signs of a cholinergic overdose developed. Repeated neurophysiological testing revealed abnormal findings which suggested the diagnosis of LEMS (see below). Consequently the patient was treated with corticosteroids (prednisone) up to 60 mg/day, tapering off to a 40 mg alternate day dose. Clinically and neurophysiologically there was marked improvement. The patient was able to eat solid food again, to walk without support, and to take care of herself. At the same time the titre of antibodies against acetylcholine receptors in serum decreased from 42 nmol/l to 2.3 nmol/l. Extensive investigations, including CT scan of the lungs and the abdomen, for possible malignancy were negative.

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Fig Upper part: Clinical history; for myasthenic severity see Oosterhuis.¹⁶ Lower part: Repetitive supramaximal stimulation of the musculocutaneous nerve; recording CMAP from the right biceps muscle (a) 3 Hz stimulation before corticosteroid treatment, (b) 20 Hz stimulation before corticosteroid treatment, (c) 3 Hz stimulation after corticosteroid treatment, (d) 20 Hz stimulation after corticosteroid treatment. Calibrations: horizontal bar 500 ms, vertical bar 5 mV.

Electromyographical data

On neither conventional electromyography nor repetitive supramaximal nerve stimulation were abnormalities in distal limb muscle (right abductor digiti quinti muscle) revealed. In proximal limb muscle, however, conventional electromyography showed some denervation potentials and polyphasic motor unit action potentials. On supramaximal stimulation of the musculocutaneous nerve a small amplitude (2 mV) of the initial compound muscle action potential (CMAP) was seen. Meanwhile the patient received mestinon therapy. Repetitive stimulation at low rate (3 Hz) resulted in a 1000% facilitation; at high rate (20 Hz) facilitation up to

350% of the CMAP was recorded (right biceps muscle; fig a, b).

After corticosteroid treatment the amplitude of the initial CMAP increased to a normal level (12 mV). Pathological increment on both low and high rate nerve stimulation were no longer observed (fig c, d).

Discussion

Neurophysiological testing is an important tool for diagnosis in neuromuscular transmission disorders, even when clinical features may initially appear quite clear. The testing should not be limited to distal limb muscles because proximal limb muscles may be the only site where abnormalities can be found, as has been suggested already by Young and Özdemir.^{17 18}

In our patient clinical features in combination with antibodies against acetylcholine receptors suggested myasthenia gravis. These antibodies are found almost exclusively in myasthenia gravis and occasionally in patients with thymoma without myasthenia gravis.¹⁹ In spite of the combination of antibodies against acetylcholine receptors and striated muscle, known to be associated with thymoma,² no thymoma was found.

In myasthenia gravis neurophysiological testing may show decrease of the CMAP on both low and high rate nerve stimulation. In several patients an incremental response was described on high rate nerve stimulation up to over 100%.^{18 20} A difference in findings between proximal and distal limb muscle is frequently noticed in myasthenia gravis: proximal limb muscle may produce abnormal findings while those in distal limb muscle may be completely normal.¹⁷ In our patient this difference was found as were abnormal findings on conventional electromyography. However, the initial small amplitude and the incremental response of the CMAP on high rate nerve stimulation strongly suggest LEMS. In this disease facilitation has been described on high rate nerve stimulation from 200% to 2000%.^{21 22} The facilitation on low rate nerve stimulation observed in our patient is exceptional, but has been described before.¹⁷ The distinction between findings in proximal and distal limb muscle is remarkable and, to our knowledge, has not yet been reported in patients with LEMS.

Neurophysiological testing of proximal limb muscle in our patient, in combination with some clinical aspects (dry mouth, paraesthesias in the limbs and areflexia) clearly indicated LEMS in addition to myasthenia gravis. LEMS is known to occur predominantly in patients with malignant diseases, especially the oat cell carcinoma of the lung.²² In few patients has LEMS been described in association with autoimmune disorders.^{23 24} Our patient, like Oh's,¹⁰ was known to have pernicious anaemia as well as

Table Patients with features of both myasthenia gravis and Lambert Eaton myasthenic syndrome

Author	Patient		Clinical features	Neurophysiological features: facilitation	Associated disorders	anti-AChR
	sex	age				
Takamori ¹⁵	f	33	MG/LEMS	80%–280% (post-tetanic)	rheumatoid arthritis	
	f	32	MG/LEMS			
	m	33	MG/LEMS			
	f	56	MG/LEMS			
Dahl ⁶	e.a.	m	LEMS	89% (20–50 Hz)	carcinoma of stomach	
Oh ⁹	m	63	MG	580% (20–50 Hz)		
Schwartz ¹¹	e.a.	f	MG	190% (20–50 Hz)	hyperthyroidism	
Mori ⁸	e.a.	m	MG	96% (post-tetanic)		
Cherington ⁵	m	38	MG/LEMS	360% (20–50 Hz)	oat cell carcinoma of lung	+
Fettel ⁷	e.a.	m	MG/LEMS	>100% (20–50 Hz)		
Singer ¹²	e.a.	f	MG	208% (post-tetanic)	thymoma	+
Tabbaa ¹³	e.a.	m	MG/LEMS	83% (post-tetanic)	pernicious anaemia	+
Oh ¹⁰	e.a.	f	MG/LEMS	510% (20–50 Hz)		+

MG = Myasthenia gravis. LEMS = Lambert Eaton syndrome

The second patient described by Takamori had already been described before¹⁴

myasthenia gravis, both of which are known to be autoimmune disorders. The combination of myasthenia gravis and LEMS has been described in few patients before (table). The determination of antibodies against acetylcholine receptors, a highly specific test for myasthenia gravis, has only been possible since 1976.²⁵ Therefore a combination of these diseases would have been less evident in the patients described before 1976.

Corticosteroids are effective in both myasthenia gravis and LEMS.^{26–27} In addition to the systemic effects of corticosteroids there is evidence of a local effect on the neuromuscular junction.^{28–30} Also in our patient this treatment resulted in clinical improvement and normalisation of the neurophysiological findings.

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