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Eaton-Lambert Syndrome Associated with Pituitary Apoplexy — A case report —

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ABSTRACT

A case of Eaton-Lambert syndrome associated with pituitary apoplexy is presented. It is thought to be the first reported case. The clinical features, electrophysiological findings and effects and side effects of therapeutic drugs are noted. Endocrinological dysfunctions are discussed in relation to pituitary disorder.

Key words: *Eaton-Lambert syndrome, Pituitary apoplexy, Endocrinological dysfunctions*

Eaton-Lambert syndrome is a rare type of myasthenic disorders. Most of the reported cases have been associated with small cell bronchogenic carcinoma, but some have developed the syndrome without any demonstrable neoplasm[7,23]. Recently, several cases of Eaton-Lambert syndrome have been reported which were associated with autoimmune disorders such as Sjogren's syndrome[2], rheumatoid arthritis[21], hypothyroiditis, and pernicious anemia[20]. Autoimmune etiology for Eaton-Lambert syndrome has also been discussed. To our knowledge, however, no case of Eaton-Lambert syndrome associated with pituitary apoplexy has been reported. This paper reports such a case of Eaton-Lambert syndrome which developed during replacement therapy for panhypotituitarism after surgery for pituitary apoplexy caused by pituitary adenoma. Endocrine dysfunctions are discussed in relation to the combination of this syndrome and pituitary disease.

CASE REPORT

A 54-year old male visited our Department in December 1982 complaining of sudden severe headache, vomiting and double vision. Neurological examination revealed right painful ophthalmoplegia with right oculomotor palsy, right abducent palsy and right trigeninal neuralgia. Skull x-ray films showed ballooning of the sella and erosion of the dorsum sella. Computerized tomography demonstrated parasellar high density and intrasellar enhanced mass several days thereafter (Fig. 1). CSF showed slight xanthochromia. Right carotid angiography revealed irregular wall of the I.C. cavernous portion but not aneurysm. Based on these findings, the condition was diagnosed as pituitary apoplexy with adenoma.

Transsphenoidal surgery was performed on February 17, 1983. Histological examination showed chromophobic adenoma (Fig. 2). Postoperatively, corton at 25 mg every other day and thyradin-S at 0.05 mg daily were administered for panhypopituitarism (Table 1). The patient recovered uneventfully. Ophthalmoplegia improved to a slight double vision when he gazed to the right side and he could resume his work as a painter. However, he was again admitted to our Hospital in March 17, 1984 because of arduousness in standing up. He noted progressive muscular weakness resulting in difficulty in climbing stairs, arising from a chair, and lifting any heavy objects. He also reported that muscular weakness was restored somewhat during exercise.

Neurological examination showed a marked weakness of the four extremities and depressed tendon reflexes. When the patient continued hadgripping for several seconds, there was a striking increase in strength. There were no sensory signs. Cranial nerves examination showed only slight right abducence palsy. His mental faculties were normal. Edrophonium chloride (Tensilon) test was negative. Extensive laboratory tests were conducted, including complete blood count, liver and kidney function tests, serum mineral, serum creatine, creatine phosphokinase, urinalysis and stool test for occult blood, but no abnormality was found. Chest X-ray films,

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Table 1. Panhypopituitarism revealed on endocrinological examination. TSH, PRL and GH showed no response to TRH. LH, FSH and GH showed no response to LHRH. GH and cortisol showed no response to ITT. GH and PRL showed no response to GB154.

TRH test		0'		15'	30'		60'	120'	180'
TSH	(μU/ml)	4.0		4.4	4.9		5.0	4.7	4.6
PRL	(ng/ml)	14.0		15.0	14.0		15.0	16.0	18.6
GH	(ng/ml)	1.0		0.6	1.0		0.6	0.6	0.6
LHRH test		0'		15'	30'		60'	120'	
LH	(mlU/ml)	7.7		10.0	12.0		9.0	9.7	
FSH	(mlU/ml)	5.4		3.4	5.8		5.9	5.7	
GH	(ng/ml)	1.1		0.7	0.6		0.6	0.9	
ITT		0'		30'	60'		90'	120'	
GH	(ng/ml)	0.6		0.6	0.6		1.3	1.1	
Cortisol	(μg/dl)	<1.0		<1.0	<1.0		<1.0	<1.0	
CB 154 test		0	1	2	3	4	6	8	12	24
GH	(ng/ml)	1.1	0.8	1.0	0.7	0.7	0.9	0.8	0.7	0.9
PRL	(ng/ml)	11.0	9.0	7.6	8.0	8.5	9.4	7.3	7.0	8.8

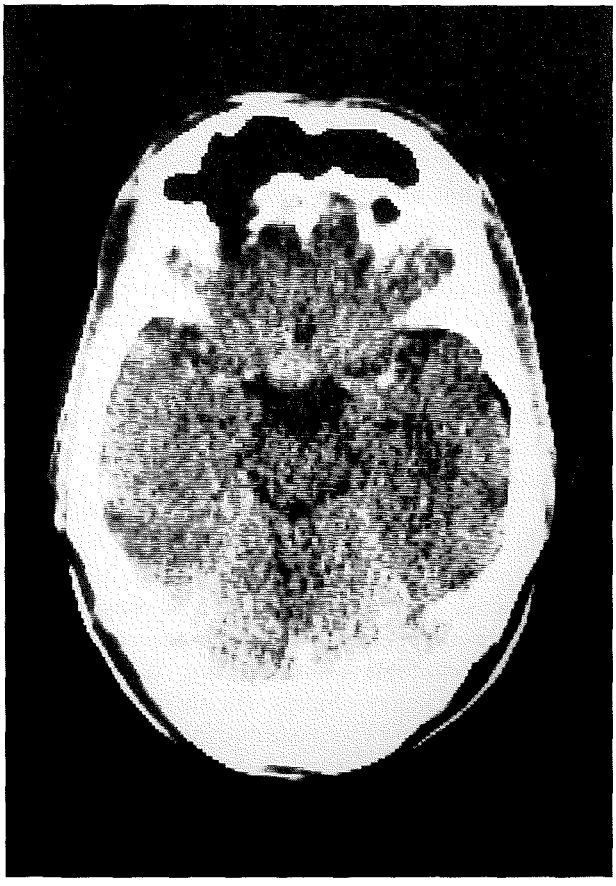

Fig. 1. Cranial CT scan demonstrated an enhanced mass within the sella.

X-ray series of the gastrointestinal tract, liver scintigram and serum carcinoembryonic antigen were all negative for malignancy. Immunological studies, including serum immunoglobulin diffusion test, antinuclear antibodies, complements (C3, C4, CH50), C-reactive protein and erythrocyte sedimentation rate were normal.

Electrophysiological studies showed a small amplitude of the muscle action potential recorded from

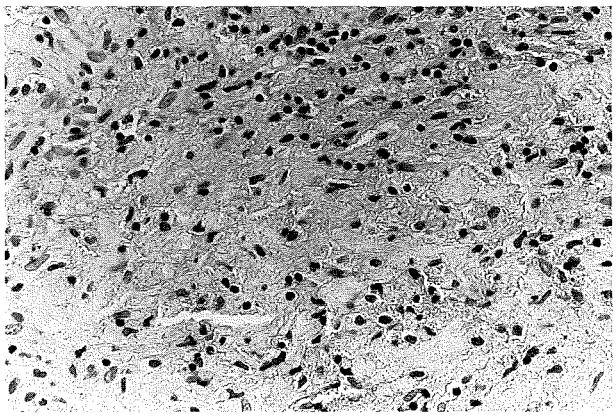

Fig. 2. Histological examination showed chromophobic adenoma in H.E. staining.

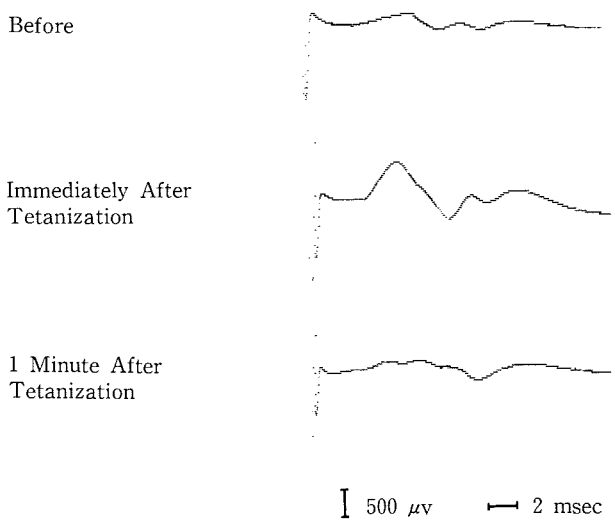

Fig. 3. Response of hypothenar muscle action potentials to a single supramaximal stimulus delivered to the ulnar nerve before, immediately after and one minute after tetanization. Note a marked facilitation immediately after tetanization and depression one minute later.

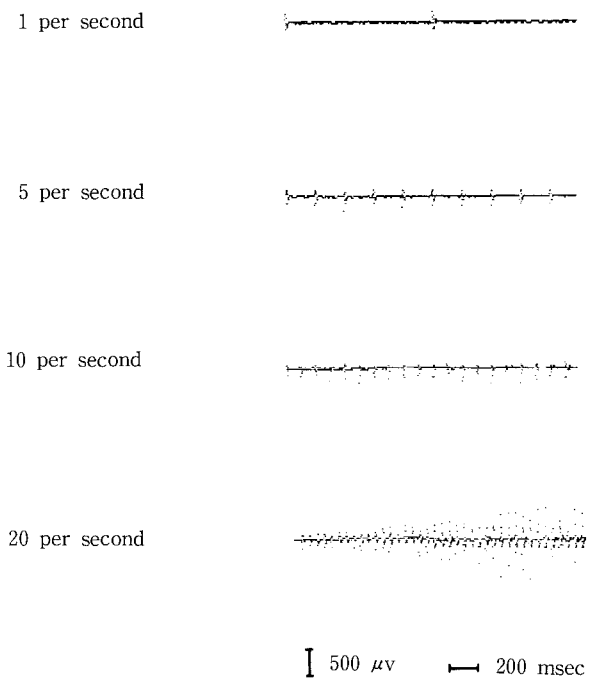

Fig. 4. Response of successive hypothenar muscle action potentials to supramaximal stimuli at various frequencies delivered to the ulnar nerve. Note successive muscle action potentials evoked with repeated nerve stimulation of 20 per second.

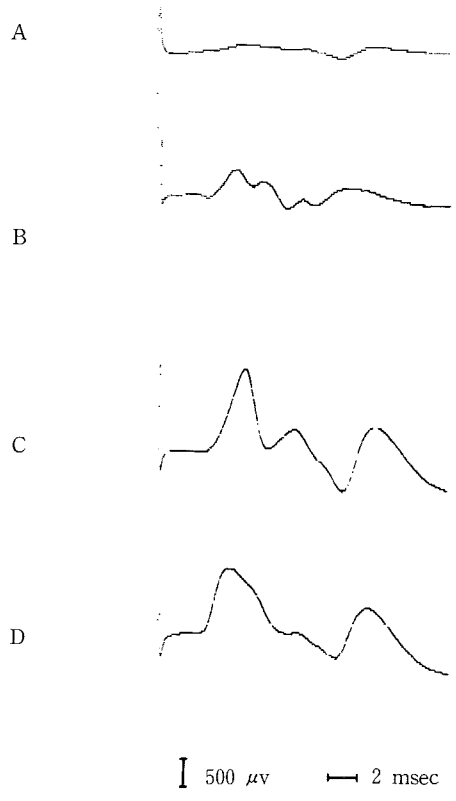

Fig. 5. Response of hypothenar muscle action potentials to a single supramaximal stimulus delivered to the ulnar nerve with no treatment (A), after administration of guanidine HCl at 800 mg/day (B), of 4-aninopyridine at 30 mg/day (C), and of 3,4-diaminopyridine at 100 mg/day (D).

the hypothenar muscle on supramaximal stimulation of the ulnar nerve. The amplitude of a single evoked muscle action potential ranged from 0.2 to 0.3 mV (Fig. 3). Immediately after tetanization for 10 seconds, there was a threefold facilitation of the amplitude of the muscle action potential returning to depression at 60 seconds (Fig. 3). Successive muscle action potentials were evoked with repeated nerve stimulations of 20 per second (Fig. 4). The patient was treated with oral administration of guanidine HCl at 800 mg/day, 4-aminopyridine at 30 mg/day, and 3,4-dianinopyridine at 100 mg/day, separately. These drugs improved his muscle strength. The amplitudes of the muscle action potentials were facilitated 3 to 8 times during administration of these drugs (Fig. 5). However, the patient complained of distal paresthesia when treated with 4-aminopyridine and of epigastralgia with 3,4-diaminopyridine. Thereafter, prednisolone at 15 mg/day was administered and muscle power increased gradually. He now visits our hospital every other week, unaided by train and on foot.

DISCUSSION

The clinical and electrophysiological findings observed in this patient were typical of Eaton-Lambert syndrome: weakness of the proximal limb and girdle muscles and temporary increase in strength in response to voluntary exercise of a few second's duration, and on clectromyography, low amplitudes of muscle action potential, post-tetanic facilitation, and marked facilitation by repetitive nerve stimulations of 20 per second. Administration of guanidine HCl[18], 4-aminopyridine[17], 3,4-diaminopyridine[15] which increased the release of acetylcholine from the nerve terminals at the neuromuscular junction were effective clinically and electrophysiologically. No occult neoplasm could be demonstrated. Immunological studies did not show any abnormality.

The clinical picture is characteristic and the electrophysiological findings are diagnostic, but the etiology of this syndrome has not been clear. Recently, several papers have documented autoimmunity as the etiology of Eaton-Lambert syndrome both because of its association with autoimmune disorders[2,6,20], as well as the effects of prednisone as an immunosuppressor[19], and the effects of plasma exchange[13,16]. Prednisolone was very effective in our patient. This may have been due to immunosuppression[4] or direct action of prednisolone on neuromuscular transmission[1].

Eaton-Lambert syndrome developed in our patient following panhypo-pituitariam caused by pituitary apoplexy. The relationship between this syndrome and pituitary apoplexy is as yet unknown. The frequent association of endocrine dysfunction with myasthenia gravis is well documented in the literature[3,9,11], but few cases of association with Eaton-Lambert syndrome. Eaton-

Lambert syndrome, whether associated with malignancy or not, is due to a presynaptic defect and the number of postsynaptic acetylcholine receptors is normal[14]. The defect in neuromuscular transmission is caused by reduction in the number of acetylcholine quanta released by a single action potential of the motor nerve[5]. Calcium and magnesium ions play an important role in acetylcholine release from the nerve terminals[10]. Lambert[12] has speculated that since calcium is essential in the release mechanism, some as yet unknown substance (polypeptides with considerable biological activity, e.g., ACTH-like activity) interferes with the utilization of calcium in the motor nerve terminals. It may be speculated that an altered metabolism of calcium and magnesium under panhypotituitarism[8] is related to the association of Eaton-Lambert syndrome with pituitary apoplexy. Takenaka[22] reported a case of Eaton-Lambert syndrome with ADH and ACTH producing lung cancer, and emphasized the importance of the association of endocrine dysfunction with the syndrome. No conclusion can be drawn from this single case, but the authors consider it meaningful to document our case of Eaton-Lambert syndrome associated with endocrine dysfunction caused by pituitary apoplexy.

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