Short report

Congenital Lambert-Eaton myasthenic syndrome

B BADY, G CHAUPLANNAZ, H CARRIER

From the EMG Laboratory, Hôpital Neurologique and Department of Neuropathology, Faculté de Médecine, Alexis Carrel, Lyon, France

SUMMARY A 4 year old girl had been hypotonic and areflexic since birth with delayed milestones in motor development. Repetitive stimulation at high rates performed at 3 years elicited an incremental response typical of the Lambert-Eaton Syndrome.

The Lambert-Eaton myasthenic syndrome was first described in adult patients with cancer, especially with small cell carcinoma. However, 30% of patients with Lambert-Eaton myasthenic syndrome do not develop cancer. Some cases have been reported in children but they were always acquired. There is strong evidence of an autoimmune pathophysiology as the electrophysiological features have been passively transferred from man to mice with IgG.

We present the case of a floppy infant whose clinical symptoms had been present since birth and in whom electrophysiological studies gave results similar to those described in Lambert-Eaton myasthenic syndrome.

Case report

A 4 year old girl was born at term; hypotonia and areflexia were noted immediately after a normal delivery. She was the second child of Portuguese parents without known consanguinity. The first child of the family was normal. The mother had seven siblings in good health. The father had 10 siblings but six of them died in Portugal before the age of seven years of unknown cause. The four siblings still living were in good health; three of them were married with normal children.

At 30 days the infant was floppy, with markedly reduced spontaneous motor activity. There was no difficulty in sucking or swallowing. Deep tendon reflexes were absent. There was no facial weakness, ptosis or oculomotor palsy. EEG and CSF were normal. Muscle enzymes levels were in the normal range. A muscle biopsy specimen was obtained at the age of one year. At three years of age she was unable to sit unaided but slight arm and leg movements were observed. She was always hypotonic and areflexic. She had a hip dysplasia and a dorsal kyphosis. At 4 years she could sit and play unaided but she was unable to stand unsupported. Psychometric tests disclosed a moderate mental retardation with a developmental age of 33 months. Guanidine hydrochloride given by mouth (10 mg/kg) induced a significant increase in muscle tone with a better head control for 2 hours. A trial of calcium gluconate by mouth (50 mg/kg) gave no response. Parents did not give consent for a new muscle biopsy for microelectrophysiological studies and electronmicroscopy of neuromuscular junctions.

Electrodiagnostic studies

EMG was performed with concentric needle electrode at 30 days, 1 year and 3 years. A prolonged insertional activity and an increased proportion of short duration (less than 3 ms), or small polyphasic potentials with early recruitment were noted in tibialis anterior, deltoid and quadriceps muscles. Motor conduction velocity was normal in peroneal nerve (47 m/s at 3 years). The amplitude of the motor response was 0.15 mV; no repetitive responses were seen. Sensory conduction velocity was normal in the median nerve (37 m/s at 1 year). Repetitive stimulation studies performed at 3 years demonstrated a decrement of approximately 33% at 1 Hz and 50% at 3 Hz and an incremental response greater than 2000% at rapid rates (20–50 Hz) (fig 1). Rapid rates induced a facilitation for 30 seconds. Guanidine hydrochloride per os (10 mg/kg) given at 4 years increased the amplitude of the motor response in extensor digitorum brevis muscle from 0.4 to 2 mV and reduced potentiation at 50 Hz from 2200% to 400%. Electromyography, nerve conduction velocities and repetitive stimulation studies were normal in both parents.

Muscle biopsy studies

A muscle biopsy specimen was obtained from quadriceps muscle under local anaesthesia at 1 year. There was no morphological abnormality on sections stained with hae-
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Fig  Repetitive stimulation of the peroneal nerve recording extensor digitorum brevis muscle action potential: decrement of approximately 33% at 1 Hz (A) and 50% at 3 Hz (B); increment of 3000% at 20 Hz (C) and 2500% at 50 Hz (D).

matoxylin and eosin or ATPase. Quantitative analysis of 376 muscle fibres disclosed only a fibre type disproportion with small type II fibres. The mean fibre diameter was 24.46 μm for type I, and 15.77 μm for type II. There was 51.5% of type I fibre and 48.5% of type II fibre.

Discussion

The electrophysiological findings in this child are consistent with the diagnosis of Lambert-Eaton myasthenic syndrome. It is noteworthy that she was initially considered as a congenital myopathy on the basis of clinical and EMG findings but the EMG at 30 days and 1 year did not include repetitive stimulation studies. However, motor responses were said to be difficult to elicit. The incremental response at rapid rates of stimulation noted at 3 years was strongly suggestive of Lambert-Eaton myasthenic syndrome, as was the positive result of a guanidine trial. Muscle biopsy findings appeared non-specific and could be secondary to the neuromuscular defect.

Several congenital myasthenic syndromes have already been reported. In most cases ocular and facial symptoms were noted and electrophysiological studies did not reveal an incremental response. The case of the child reported by Albers and co-workers resembles ours as there was no ocular or facial symptoms and a post-tetanic facilitation was noted. However, the clinical course was progressive and led to death in infancy. In addition a decremental response was noted at all rates of stimulation and guanidine produced clinical deterioration.

Our case may represent a new type of congenital myasthenic syndrome with a recessive inheritance sharing the electrophysiological features of Lambert-Eaton myasthenic syndrome. Microelectrophysiological studies are needed to further characterise this disease.

In autoimmune Lambert-Eaton myasthenic syndrome the target for the autoantibody seems to be located at the level of the Ca2+ channel of the presynaptic active zone, as transfer of IgG from Lambert-Eaton myasthenic syndrome patients to mice reproduced the characteristic morphological abnormalities of the disease and reduced the quantal content of end-plate potentials. A recent study has demonstrated that Lambert-Eaton myasthenic syndrome IgG reduced K+ induced 45Ca2+ flux in a cultured small cell carcinoma line suggesting that in Lambert-Eaton myasthenic syndrome associated with this tumour an autoantibody is produced in response to tumour Ca2+ channel antigens and that its cross reaction with similar antigens at the motor nerve terminal is responsible for clinical symptoms.

Thus our patient could have an inherited disease of the Ca2+ channel.

This case underlines the need to perform repetitive stimulation at low and high rates in floppy infants without overt aetiology.
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