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Original Article

# Lambert-Eaton Syndrome, an Unrecognized Treatable Pediatric Neuromuscular Disorder: Three Patients and Literature Review

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ABSTRACT

**BACKGROUND:** Lambert-Eaton myasthenic syndrome, a presynaptic neuromuscular junction autoimmune disorder, rarely occurs in children. Patients typically present with proximal lower extremity weakness with areflexia. **METHODS:** We report three children presenting between ages 9 and 10 years diagnosed with Lambert-Eaton myasthenic syndrome 2 years, 1 year, and 5 months later, respectively. Their clinical attributes are correlated with nine other pediatric Lambert-Eaton myasthenic syndrome patients found in our literature review. **RESULTS:** These patients were identified as having Lambert-Eaton myasthenic syndrome during their evaluation for proximal weakness. Low-amplitude compound muscle action potentials classically facilitating >100% with voluntary exercise and/or 50 Hz stimulation were essential to diagnosis. Three of the 12 children had associated malignancies, two of them had lymphoproliferative disorders with onset of symptoms more rapid than the rest, and the third had neuroblastoma. The nine nonparaneoplastic Lambert-Eaton myasthenic syndrome patients responded to immunomodulatory therapy with close return to their baseline function. Complete remission no longer necessitating medication was reported in two patients. Follow-up up to 17 years was available on two patients previously reported. **CONCLUSION:** Lambert-Eaton myasthenic syndrome is a diagnosis that must be considered in children presenting with unidentified proximal muscle weakness. In most children, Lambert-Eaton myasthenic syndrome is a primary autoimmune disorder that is treatable. Nevertheless, a search for malignancy is recommended.

***Keywords:*** Lambert-Eaton myasthenic syndrome (LEMS), neuromuscular transmission disorders, myasthenia, myopathy, pediatric

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## Introduction

Lambert-Eaton myasthenic syndrome (LEMS) is a paraneoplastic or primary autoimmune disorder of the presynaptic neuromuscular junction, characterized by proximal lower extremity weakness, areflexia, and dysautonomia.[1] Initially described in a paraneoplastic setting affecting middle-aged adults with small-cell lung cancer, LEMS occurs as a primary autoimmune disorder in younger adults and rarely children. We present three pediatric LEMS patients with literature review emphasizing this unusual, potentially treatable disorder.

## Methods

The clinical presentation and long-term course of our three patients are reported. PubMed search using "pediatric," "childhood," or "children" with "Lambert-Eaton myasthenic syndrome" or "LEMS" was performed. Patients' selection criteria included clinical presentation, nerve conduction studies demonstrating post-exercise or repetitive motor nerve stimulation facilitation response greater than 100%, and/or positive voltage-gated calcium channel antibodies. Including our three patients, 12 children ages 3 to 19 years are reviewed (Table A and B). Our

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**TABLE A.**
Clinical summary of LEMS in children and adolescents

| Author (Year) | Age at Onset/ Gender | Presenting Symptoms | Clinical Findings | NCS/EMG | CK, AChR Ab, and VGCC Ab |
|---|---|---|---|---|---|
| Shapira (1974) | 10/M | Progressive weakness, visual disturbance, bone pain, cachexia for 1 month | Bilateral ptosis, ophthalmoparesis, right tongue deviation, Gower's sign, proximal > distal extremity weakness and absent MSRs | - CMAP amplitude reduced<br>- 3 Hz: decrement<br>- 25 Hz: 170% increment<br>- MUAPs: small, polyphasic | NA |
| Brown (1974) | 19/F | Progressive proximal weakness for 1 year, calf/thigh muscle tenderness, and dry eyes | Waddling gait, Gower's sign, proximal lower > upper extremity weakness, absent MSRs and later reduced PFTs | - CMAP amplitude reduced<br>- 1 Hz: decrement of 68% from the first CMAP amplitude<br>- 30 Hz: 500% increment<br>- 10 seconds' exercise: 150% increment<br>- MUAP: mildly myopathic | CK normal |
| Chelmicka (1979) | 9/F | Progressive lower extremities weakness for 3 months and difficulty chewing | Mild muscle tenderness, weakness of the neck flexion, proximal lower > upper extremity weakness, hip thrust, and circumduction when walking, initially hypoactive then absent MSRs, perioral skin tightness, and respiratory insufficiency | - CMAP amplitude reduced to 0.5 mV<br>- 10 seconds' exercise: 300% increment<br>- 20 Hz: increment<br>- 2 Hz: 50% decrement<br>- MUAP: variable | - CK normal<br>- AChR Ab: negative |
| Streib (1981) | 16/F | Progressive lower extremities weakness for 6 months | Proximal lower > upper extremity weakness, waddling gait, and normal MSRs | - CMAP amplitude reduced<br>- 2 Hz: small decrement<br>- 10 seconds' exercise: 100% increment<br>- 50 Hz: increment | AChR Ab: negative |
| Squier (1991) | 15/M | Progressive lower extremities weakness and fatigue<br>Backache | Ptosis, mild facial weakness, moderate proximal weakness, followed 15 months later by fatigable weakness and initially hypoactive MSRs that 1 month later became absent | - CMAP amplitude reduced<br>- 3 Hz: 21% decrement<br>- 15 seconds' exercise: 1030% increment<br>- 10 Hz: decrement then increment<br>- MUAP: small polyphasic units | CK normal |
| Argov (1995) | 7/M | Bilateral ptosis, ophthalmoparesis, and unsteady gait | Ptosis, ophthalmoparesis, proximal extremity weakness, absent MSRs in the legs and trace in the arms | - CMAP amplitude reduced to 1 mV<br>- 3 Hz: 75% decrement<br>- 20 Hz: 250% increment<br>- MUAP: normal | AChR Ab: negative |
| Tsao (2002) Patient 1 | 10/F | Progressive lower extremities weakness for 5 months, followed by dysphagia | Neck flexion/extension and proximal > distal extremity weakness, Gower's sign and hypoactive MSRs | - CMAP amplitude reduced<br>- 3 Hz: moderate decrement<br>- 50 Hz: >200% increment<br>- MUAP: normal | - CK normal<br>- VGCC Ab: elevated at 602 pmol/L (normal <20) |
| Tsao (2002) Patient 2 | 9/M | Progressive lower extremities weakness for 12 months | Mild facial weakness, proximal > distal and lower > upper extremity worsening weakness, and hypoactive MSRs | - CMAP amplitude reduced<br>- 3 Hz: decrement<br>- 10 seconds' exercise: 62% increment<br>- 50 Hz: 124% increment<br>- MUAP: small | - AChR Ab negative<br>- VGCC P/Q-Ab: elevated at 161 pmol/L (normal <28) |
| Hoffman (2003) | 9/M | Progressive lower extremities weakness and intermittent dysarthria | NA | - CMAP amplitude reduced<br>- 15 seconds' exercise: 1075% increment | VGCC Ab: elevated |
| Kostera (2009) | 11/M | Progressive lower extremities weakness, muscle fatigue, and frequent falls for 6 months | Mild proximal weakness, waddling gait, Gower's sign, and absent MSRs | - CMAP amplitude reduced<br>- 3 Hz: 45% decrement<br>- 30 seconds' exercise: 82% increment<br>- MUAP: myopathic | - CK normal<br>- AChR Ab: negative<br>- VGCC Ab: elevated |