Lambert-Eaton Myasthenic Syndrome

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Risk

- Unknown true incidence. Few studies of very specific regions outside USA report prevalence between 0.48 and 3.42 per million.
- 60–84% of LEMS patients have SCLC.
- LEMS mostly affects middle-aged adults, with rare occurrence in children.

Perioperative Risks

- Increased risk for fall when ambulating, due to proximal lower extremities weakness
- Hypotension due to autonomic dysfunction
- Prolonged emergence secondary to persistent muscle weakness
- Respiratory compromise or collapse after extubation

Worry About

- Failing extubation, necessitating unplanned ICU admission.
- Exacerbation of muscle weakness postoperatively.
- Concomitant presence of SCLC may complicate respiratory function.

Overview

- Autoimmune disorder affecting the presynaptic NMJ.
- Most patients present with slow progressive lower extremities muscle weakness.
- LEMS is different from MG:
  - LEMS affects the proximal lower extremities more than MG.
  - Primarily affects presynaptic mechanisms, whereas MG primarily affects postsynaptic mechanisms.
  - Muscle weakness transiently resolves with activities in LEMS.
  - LEMS is strongly associated with SCLC.
- Pathophysiology: Antibodies attack VGCC, diminishing the release of calcium and subsequent reduction in the release of acetylcholine in the presynapse.

Etiology

- LEMS is an autoimmune disease. IgG antibodies target the P/Q type VGCC at the presynaptic endplate of the NMJ.
- The strong prevalence of SCLC in patients with LEMS suggests the presence of the same antigen in SCLC and at the presynaptic NMJ.
- Cerebellar degeneration may be present in some patients with LEMS. This is likely due to the presence of the P/Q type VGCC in the cerebellum.
- Acetylcholine is necessary for the autonomic function and its reduction in LEMS may result in autonomic nervous system dysfunction.

Usual Treatment

- First line treatment with 3,4-diaminopyridine, which blocks potassium at the neurosynapse, allowing for the release of acetylcholine. It also directly facilitates neurotransmission at VGCC.
- Removing or treating the SCLC tumor may be considered if diaminopyridine is ineffective in alleviating symptoms.
- In cases of severe weakness prednisone and azathioprine may be added to treatment therapy. This treatment must be initiated slowly because it may cause acute weakness prior to having their positive impact.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Ptosis	Drooping of eyelid	Cranial nerve assessment	Symptoms reported by pt
RESP	Respiratory weakness	Dyspnea	Supplemental O_2 dependence Difficulty taking deep breaths	PFTs, including inspiratory force measurements. Phrenic nerve stimulation recordings CXR, CT scan
CNS	Autonomic dysfunction	Dry mouth Erectile dysfunction	Reduced saliva Impotence	Symptoms reported by pts
MS	Proximal lower limbs weakness	Aching, fatigued or stiff muscles affecting gait	Depressed or absent DTRs	Plasma levels of P/Q type VGCC antibodies Electromyography

Key References: Titulaer MJ, Lang B, Verschuuren JJ: Lambert–Eaton myasthenic syndrome: from clinical characteristics to therapeutic strategies, *Lancet Neurol* 10(12):1098–1107, 2011; Weingarten TN, Araka CN, Mogensen ME, et al.: Lambert-Eaton myasthenic syndrome during anesthesia: a report of 37 patients, *J Clin Anesth* 26(8):648–653, 2014.

Perioperative Implications

Preoperative Preparation

- Confirm adequate respiratory function. Verify use of supplemental oxygen at home.
- Prepare for possible ICU admission if unable to extubate due to muscle weakness.
- Consider use of monitored anesthesia care or regional anesthesia whenever possible instead of general anesthesia.
- Assess baseline strength of extremities.

Monitoring

- Standard monitoring
- Arterial line in patients presenting with respiratory compromise or significant autonomic dysfunction
- Nerve stimulation monitoring

Airway

- Avoid intubation whenever possible.
- Consider use of supraglottic airway instead of endotracheal intubation to avoid muscle relaxation.

Preinduction and Induction

- Depolarizing and nondepolarizing muscle relaxants can be used if muscle relaxation is required.
- If unable to avoid endotracheal intubation, consider intubating without muscle relaxants. Avoid neuromuscular relaxants whenever possible. Remember that inhaled anesthetics each have efficacy in neuromuscular blockade.

Maintenance

- Both IV and inhalational anesthetics have been given safely to LEMS pts. Vigilance to administer minimum requirements of anesthetics will likely minimize perioperative complications.
- Hypotension may occur as a result of autonomic dysfunction; vasopressors may be given as boluses or continuous infusion.
- Pts on prednisone should receive a perioperative dose of hydrocortisone.

Extubation

- Ensure return of safe cognitive function, muscle strength, and ventilatory function before extubation.

Postoperative Period

- Judicial use of opioids in the PACU to avoid respiratory compromise.
- Increased susceptibility to respiratory failure and reintubation.
- Consider continued monitoring of pulse oximetry after discharge from PACU.

Anticipated Problems/Concerns

- Muscle weakness
- Respiratory compromise

Landouzy-Dejerine Dystrophy (Facioscapulohumeral Muscular Dystrophy)

Francis Veyckemans

Risk

- Prevalence estimated to be 1:20,000
- Affects equally males and females
- Third most common familial myopathy after myotonic dystrophy and Duchenne muscular dystrophy

Perioperative Risks

- No greater risk of malignant hyperthermia than normal population.
- Possible risk of acute rhabdomyolysis if succinylcholine and/or a halogenated agent is used. However, the dystrophin-glycoprotein complex is not involved in Landouzy-Dejerine dystrophy, and no case of anesthesia-induced rhabdomyolysis has been reported so far.
- Perioperative respiratory complications
- Supraventricular paroxysmal tachycardia

Worry About

- Muscle weakness

Overview

- Muscular dystrophies are a heterogeneous group of genetic muscle disorders leading to progressive weakness and muscle wasting. They were grouped together based on a common histologic picture: variations in fiber size and areas of muscle necrosis

progressively replaced with fat or connective tissue. They are classified based on three phenotypic considerations: predominant distribution of affected muscles, whether facial muscles are affected or not, and mode of inheritance.

- Its clinical presentation varies widely. Approximately 30% of people with a mutation do not present any clinical sign; this could be due to mosaicism. For those presenting with clinical signs, the distribution of muscle weakness varies widely. Two main clinical forms are described below.
- Congenital or infantile form: Facial muscles are affected before 5 years of age, and the muscles of the shoulder and hip girdle around 10 years: muscular involvement is bilateral and symmetric, resulting in apparent facial diplegia and poor expression of emotions. Sensorineural hearing loss is common. Hyperlordosis and scoliosis appear in late childhood and adolescence.
- Usual form: Muscular involvement is asymmetric and starts during adolescence. The first signs affect the face and the shoulder girdle: difficulties drinking with a straw, pursing the lips or whistling, inability to close the eyes (risk of keratitis during sleep), and protruding lips (tapir mouth). All muscles of the shoulder are affected but the deltoid is usually spared, which results in a preserved deltoid bulk despite surrounding muscles atrophy: this produces scapular winging when the arms are abducted. The foot dorsiflexors and the hip are affected later and result in stepping and difficult walking (need for a cane). Weakness of abdominal wall muscles is frequent and can result in some abdominal wall protrusion. The following signs are also frequent: (1) early onset and bilateral sensorineural hearing loss, which varies from mild to moderate; (2) bilateral retinal exudative telangiectasia, called Coats disease, with marked tortuosity of retinal arterioles. Respiratory muscle involvement is usually mild, but severe cases can result in early onset and progression of severe restrictive pulmonary dysfunction, and cor pulmonale. A few cases of hypertrophic cardiomyopathy and cardiac arrhythmias (mainly supraventricular paroxysmal tachycardia) have been observed.
- The evolution is slow and progressive: 20% become wheelchair bound, and less than 5% of pts end up with some form of ventilation support during sleep.
- Paraclinical examinations: CPK: Normal or mildly elevated (<1500 UI/L); RFT: Restrictive pattern in severe forms; EMG: Myopathic changes.

Etiology

There are currently two different known genetic causes of LDD:

- Type 1 [OMIM 158 900] is the most frequent (85% of cases); it is caused by a shortening of the D4Z4 zone in the subtelomeric region of chromosome 4q (4q35.2). This zone is usually hypermethylated and includes tandem repeats of a fragment containing a DUX4 (nuclear protein) open reading frame. The normal number of these repeats varies between 11 and 100: it is lower than 10 in case of myopathy but results in insufficient repression of the usually silent DUX4 gene only if there is a functional pLAM sequence nearby. In this case the degree of chromosomal shortening is correlated with the severity of the disease ,and its earlier age of onset
- Type 2 [OMIM 158 901] is due to a mutation of a gene on chromosome 18p11.32 encoding for protein SMCHD1: this produces a hypomethylation of chromosomes 4 and 10, including both alleles of the D4Z4 zone and has the same consequence on repression of DUX4 gene

Usual Treatment

- Supportive. Some experimental trials are ongoing.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
MS	Muscle weakness: Poor facial, expression, inability to close eyes, weakness in shoulder girdle	Usual activities? Chronic muscle or joint pain?	Eye closure? Ability to perform head lift maneuver? Shoulder girdle amyotrophy Cough?	CPK: Normal or mildly elevated Neuromuscular monitoring: Use unaffected muscle!
RESP	Involvement: Usually mild			PFT
CV	Rarely: Atrial dysrhythmias, hypertrophic cardiomyopathy			ECG Cardiac ECHO if ECG abnormal or murmur
HEENT	Hearing loss			

Key References: Mercuri E, Muntoni F: Muscular dystrophies, *Lancet* 381(9869):845–860, 2013; Nitahara K, Sakuragi T, Matsuyama M, et al.: Response to vecuronium in a patient with facioscapulohumeral muscular dystrophy, *Br J Anaesth* 83(3):499–500, 1999.

Perioperative Implications

Preoperative Preparation

- ECG: If it shows any abnormality (e.g., rhythm, conduction) a transthoracic cardiac echography is useful (cardiomyopathy, pulm Htn secondary to chronic cor pulmonale?). Check SpO_2 on room air and, if you anticipate using muscle relaxants, whether the pt is able to perform the head lift maneuver in order to know if clinical assessment of adequate muscle reversal will be possible. A diagnosis of LDD should not hide the usual preoperative concerns (e.g., allergies, hemostasis, smoking habits, venous access). Pt should be allowed to enter the OR with hearing aids, if any.

Monitoring

- ASA standards
- Neuromuscular monitoring, use a muscle group that is not or only minimally dystrophic and checking its baseline TOF ratio before administering any muscle relaxant.
- Central venous access: Ultrasound-guided jugular or subclavian vein catheterization is recommended because muscular atrophy in the head and neck region makes usual surface landmarks less reliable.
- Locoregional anesthesia: Hyperlordosis could make neuraxial blocks more difficult to achieve; regarding peripheral nerve blocks, regional amyotrophy and dystrophy increase muscular echogenicity and could make nerve identification more difficult.
- Obstetrics: There seems to be an increased risk for breech presentation in mothers with LDD.

Airway

- Although no case of difficult mask ventilation/intubation has been reported in LDD, the upper airway should be carefully assessed because, in addition to factors independent of LDD (e.g., retrognathism), facial muscle atrophy could result in reduced mouth opening and neck mobility.

Induction

- All induction agents can be used; susceptibility to malignant hyperthermia is not greater than in the normal population, but LDD is considered to be phenotypically similar to Duchenne and Becker muscular dystrophies and could thus carry a risk of acute rhabdomyolysis in case of exposure to succinylcholine and or halogenated agents. However, very few cases of uneventful use of enflurane or sevoflurane have been reported. Great care should be given to eye protection.

Muscle Relaxants

- Succinylcholine is best avoided as in any muscle disease; in individual case reports on the use of vecuronium and atracurium, normal sensitivity and faster recovery were observed; rocuronium has been used without problem and reversed with sugammadex.

Maintenance

- TIVA with propofol has been used successfully; see Induction regarding the use of halogenated agents.

Extubation

- Awake, ideally after a period of pressure support ventilation

Postoperative Period

- Chest physiotherapy
- Pain management: Should be titrated to effect, as for any other pt; in severe forms, overnight stay in PACU or ICU is a wise option.
- Chronic pain: Chronic muscle and joint pain is not unusual.

Anticipated Problems/Concerns

- Postop muscle weakness and respiratory failure in severe cases