from ventricular obstruction, surgical removal of the hemorrhage should occur as soon as possible. Consider injection of alteplase (TPA) into hematoma, minimally invasive clotevacuation, decompressive craniectomy , or evacuation Of supratentorial ICH by standard craniotomy for select patients. The patient should be assessed by the neurosurgeon both before and after surgery.

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LAMBERT-EATON MYASTHENIC SYNDROME

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Introduction

Lambert-Eaton myasthenic syndrome (LEMS) is a rare autoimmune disease producing antibodies against pre-synaptic voltage-gated calcium channels. It can occur sporadically or as a paraneoplastic syndrome, most often associated with small cell carcinoma of the lung. The clinical presentation may be mistaken for myasthenia gravis, as there are some similarities in their pathophysiology Lambert and colleagues first described weakness due to neuromuscular transmission deficiency in association with malignancy in the 1950s. In the 1970s, an autoimmune etiology was suggested in LEMS seen in association with other autoimmune disorders. The autoimmune theory was confirmed in the early 1980s by a series of studies resulting in normal rats developing LEMS after injecting them with immunoglobulin G(IgG) antibodies from diseased rats.4 Antibody blockage of the P/Q voltage-gated calcium channels was identified in the 1990s as the major etiology of the disease process of LEMS.

Aim

To study the clinical picture and the manifestations of Lambert-Eaton syndrome according to literary sources.

Materials and methods

A theoretical analysis of literary sources and a synthesis of scientific literature for 2015–2018 was used.

Results

Clinical Presentation. LEMS usually presents in adulthood, usually over 40 years of age, although it can present at any age. Due to similarities in clinical presentation, LEMS can be easily mistaken for myasthenia gravis (MG). Wirtz and colleagues examined the patterns of weakness between MG and LEMS and found that MG involved ocular muscles and bulbar muscles more prominently than LEMS. In addition, all LEMS patients in their study had lower extremity involvement, although the lower extremities were spared in a significant proportion of MG patients.

Proximal muscle weakness, greater in the lower extremities than in the upper extremities, is the typical clinical presentation. The weakness is exacerbated by exercise and heat. Rarely, cranial nerve symptoms such as ptosis, difficulty swallowing, and double vision may also be present. However, if ocular weakness is the only finding, then another diagnosis should be considered. Respiratory failure is rarely the presenting symptom in LEMS patients, although it can develop later in the disease process. Autonomic dysfunction, including dry mouth, blurred vision, constipation, and orthostatic hypotension, occurs in up to 75 % of patients . To direct muscle strength testing, the patient may seem minimally weak. This is due to the nearly continuous influx of calcium and its buildup in the presynaptic nerve terminal with exercise.

Initially, calcium is blocked from entering the presynaptic terminal due to the voltage-gated calcium channel antibodies. Less Ach is released and the muscle contraction is decreased. With continuous contraction from strength testing, calcium accumulates faster than it can be removed by the mitochondria. This buildup of calciumallows more vesicles to attach to the nerve membrane and release Ach, producing a normal or near-normal contraction for the short time that strength is tested in any particular muscle This is referred to as Lambert's sign when the grip becomes more powerful over several seconds of strength testing .On examination, most LEMS patients also have depressed muscle stretch reflexes. The stretch reflex causes amuscle contraction. Briefly exercising the muscle involved in the stretch reflex and then rechecking the reflex results in a normal or near-normal muscle stretch reflex. This finding is again a result of the calcium entryinto the presynaptic terminal with exercise enhancing the muscle contraction. Autonomic dysfunction is evidenced by complaints of dry mouth and findings of sluggish pupils and orthostasis. This is also attributable to the decrease in the number of vesicles of Ach binding to the presynaptic membrane and being released at the muscarinic receptors.

Clinically, 50 to 70 % of LEMS patients will have associated cancer as was originally described by Lambert and colleagues. Small cell lung carcinoma is most commonly associated with LEMS. The cancer cells have proteins that have been demonstrated to match proteins found in the P/Q voltage-gated calcium channels, thus stimulating an autoimmune response. LEMS may precede the diagnosis of cancer by 2 years. In addition to carcinomas, LEMS can be associated with other autoimmune disorders, such as hypothyroidism, pernicious anemia, celiac disease, and juvenile-onset diabetes mellitus

Signs and Symptoms of Lambert-Eaton Myasthenic Syndrome: Proximal limb weakness Legs > arms; Fatigue or fluctuating symptoms; Difficulty rising from a sitting position, climbing stairs; Metallic taste in mouth; Autonomic dysfunction; Dry mouth; Constipation; Blurred vision; Impaired sweating; Weakness on exam is less demonstrable than patient's level of disability; Hypoactive or absent muscle stretch reflexes; Lambert's sign (grip becomes more powerful overseveral seconds); Sluggish pupillary reflexes.

Diagnosis. The most common differential diagnoses for LEMS are MG and myopathy. Distinguishing clinical features such as autonomic symptoms and depressed reflexes help to differentiate these. Electrophysiological testing also has distinctive features. A serological test for voltage-gated calcium channel antibodies is positive in 85 % of patients with LEMS. With electrophysiological testing, CMAP amplitudes are small but latencies and conduction velocities are normal. Repetitive stimulation at 2 Hz may produce a decrement in CMAP amplitudes. This decrement is a normal physiological function amplified by the disease. With slow repetitive stimulation (less than 5 Hz), the amount of readily available Ach is depleted after each stimulation, releasing less Ach each time. This lasts for the first few stimuli, at which point mobilization of stored Ach occurs. In normal patients, the amount of Ach released with each stimulus is still enough to reach action potential threshold, despite the decrease in amount released. In LEMS, the amount released does not reach threshold for all the action potentials to occur, resulting in a decrement in amplitude of the first few CMAPs. This is also seen in MG. After exercise for 10 seconds or with repetitive stimulation exceeding 20 Hz for 10 seconds, the CMAP amplitude will immediately increase by greater than 200 % review of 50 patients, the mean increase in amplitude was 890 % after exercise. The initial small CMAP amplitude is due to the decreased influx of calcium due to the voltage-gated calcium channel antibodies. With brief sustained muscle contraction, as described earlier, calcium concentrations are increased in the pre-synaptic nerve terminal, more Ach is released, and the CMAP amplitude is briefly increased. This can last up to 30 seconds. Single-fiber examination demonstrates increased jitter, consistent with a neuromuscular junction deficit. Blocking may also be seen, demonstrating that either not enough quanta were released to reach threshold or

the time to reach threshold was too long and the response was not recorded. Blood work useful in clarifying the diagnosis includes creatine kinase, thyroid functions and calcium channel antibodies. Because of the high incidence of lung cancer associated with LEMS, a chest computed tomography or magnetic resonance to look for cancer needs to be part of the evaluation.

Treatment of LEMS depends on the etiology of the disease. When associated with cancer, treating the cancer will usually improve symptoms significantly. It has been demonstrated that calcium channels in the cancer cells cross-react with the presynaptic voltage-gated calcium channels. Removal of the cancer may reduce the autoimmune response and antibody production. Regardless of the presence of cancer, using immunosuppressive drugs such as azathioprine and prednisone are useful but not as helpful when compared with their use in treating other autoimmune diseases. Intravenous immunoglobulin has also been used with some success. Pyridostigmine, an anticholinesterase inhibitor, can also reduce symptoms. Inhibition of acetylcholinesterase will decrease the amount of breakdown of Ach, thus increasing the amount found in the synaptic cleft. This increase in Ach concentration allows more end-plate potentials to reach threshold, resulting in a larger number of action potentials and greater muscle contraction. Plasma exchange has been used to filter out the antibodies causing the disease and has been suggested to be the first line of treatment in acute situations. The use of plasma exchange has had limited success because the benefit dissipates more quickly than in other diseases such as MG. It has been suggested that immunosuppressive drugs are needed to maintain the benefits of plasma exchange. Another drug used for the treatment of LEMS is 3,4-diaminopyridine (3,4-DAP). 3,4-DAP is a potassium channel blocker, which helps to maintain depolarization of the nerve terminal by preventing repolarization. This allows more calcium to enter the nerve terminal and release more Ach. If cancer has not been found in patients presenting with LEMS, they should be screened for small cell lung carcinoma every 6 months with chest imaging for at least 2 years. In addition, evaluation for other autoimmune disorders should be done.

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INTRAVENTRICULAR CERLIPONASE ALFA FOR CLN2 DISEASE

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Introduction

Neuronal ceroid lipofuscinosis type 2 (CLN2) disease, a form of Batten's disease, is a rare, autosomal recessive, pediatric neurodegenerative disease resulting from pathogenic variants in the gene encoding lysosomal enzyme tri-peptidyl peptidase 1 (*TPP1*). A deficiency of TPP1 results in accumulation of lysosomal storage material that causes degenerative changes in neurons throughout the central nervous system and retina. Affected children are functionally normal until the age of 2 to 4 years and subsequently have seizures and delayed language acquisition followed by a rapid decline in motor ,language, cognitive, and visual function over a period of 4 to 6 years and death by early adolescence. There has been no approved therapy for this disorder.

Natural-history cohorts of children with CLN2 disease have shown progressive decline in motor and language function. A database of children with the disease has characterized disease severity and progression with a disease specific clinical rating scale, including motor, language, and visual function, and incorporates the frequency of grand mal seizures. Specific disease genotypes do not consistently correlate with phenotype, although pathologic variants