Congenital myasthenic syndromes

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Congenital myasthenic syndromes (CMS) are a group of diseases caused by genetic defects affecting neuromuscular transmission and are heterogeneous in inheritance and pathophysiology. These are classified as:

1. Presynaptic defects: including Choline Acetyl Transferase deficiency, Paucity of synaptic vesicles, Lambert-Eaton like CMS
2. Synaptic defect: Endplate ACh esterase deficiency
4. No identified defect

CMS should be considered in any patients presenting with weakness/fatigability of limbs and oculobulbar muscles, early onset (since neonatal period) with a positive family history. Electrodiagnostic findings (RNS, SFEMG), response to anti-cholinesterase medications and absence of anti-AChR, MuSK, VGCC antibodies are helpful clues. Diagnostic problems rise when CMS is late onset (in adult), there is no clinical response to anticholinesterases, family history is negative, symptoms are episodic and opthalmoplegia AND cranial involvement are absent. In EMG, decrement may not be present in all muscles, or present only intermittently and the patient is easily misdiagnosed as congenital myopathy, seronegative MG (late onset) or metabolic myopathies. Electrodiagnosis shows decrement after 2-3 HZ Repetitive nerve stimulation (RNS) but this is not present in all patients with different subtypes and is especially absent in Choline-Acetyl transferase deficiency, Na-channel CMS, some cases of Rapsyn deficiency. If negative, try higher frequencies or try conditioning with 5 minutes 10HZ stimulation. Single-Fiber EMG is also a very sensitive technique for detecting neuromuscular junction disorders and is useful in special cases. During EMG if repetitive CMAP is seen after a single stimulus, endplate cholinesterase deficiency or slow-channel syndrome should be considered and in the case of low amplitude CMAP with significant increment after high frequency RNS, Lambert-Eaton like CMS is diagnosed. Clinical, diagnostic and therapeutic aspects of different subtypes will be discussed in details.

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