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Progressive myoclonic epilepsy: A clinical, electro-physiological and pathological study from south India

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Objective: Progressive myoclonic epilepsy (PME) is a syndrome complex encompassing different diagnostic entities and often cause problems in diagnosis. We describe the clinical, electrophysiological and pathological features of 94 patients with the diagnosis of PME

Methods: Case records of confirmed patients of Lafora body disease (LBD=37), Neuronal ceroid lipofuscinosis (NCL=30), Myoclonic epilepsy with ragged red fibers (MERRF=10), Tay-Sach's disease (TSD=9) and probable Unverricht Lundberg disease (ULD=8) were reviewed.

Results: Patients of LBD (mean age of onset at 14.4 +/- 3.9 years, M: F= 24:13) with triad of PME were evaluated. EEG (n=37) showed varying degree of slowing of background activity in 94.6% and epileptiform discharges in 97.3%. Photosensitivity with fast frequency was observed in 5 patients. CT (n=32) and MRI (n=3) revealed diffuse cortical atrophy. Giant SSEP was demonstrated in 24 patients of LBD while VEP study revealed a prolonged P100 (4) and absent waveform (8). Electrophysiological features of neuropathy were present in one patient of LBD. Diagnosis was established by presence of PAS positive diastase resistant inclusions in sweat glands of axillary skin (n=27), brain (n=2) and liver (n=1) tissues.

The mean age at onset in patients with NCL (n=30) was 4.8+/-6.8 years with M: F=5:1. Subtypes of NCL were: late infantile (n=16), infantile (n=7), juvenile (n=6) and adult (n=1) NCL. EEG (n=37) showed varying degree of slowing of background activity in 93.3% and epileptiform discharges in 80% of patients. Slow frequency photic stimulation evoked response in 5 patients. Giant SSEP was demonstrated in 7 and VEP study revealed a prolonged P100 (2) and absent waveform (7). Electrophysiological features of neuropathy were present in NCL (3/19). Presence of PAS and Luxol Fast Blue (LFB) positive, autofluorescent (AF) ceroid material in brain tissue (n=12) and electron microscopy of brain (n=5) and skin (n=18) samples showing curvilinear bodies established the diagnosis.

Patients with MERRF (mean age at onset: 14.6 $\pm$ 5.8 years; M: F=3:2) had triad of PME and muscle biopsy revealed oxidative reaction product and classical ragged red fibers. Neuropathy was present electrophysiologically in one patient of MERRF.

Children with TSD (mean age at onset: 1.85 $\pm$ 1.00 years; M: F= 7:3) had startle myoclonus, cherry red spot and low Hexose-aminidase levels.

In eight patients of PME without cognitive decline, probable ULD (mean age at onset: 13.8 +/- 9.5 years) was considered after biopsy of skin and/ or muscle ruled out other PMEs.

Conclusions: Classically described phenotypes of PME were noted.

Lafora body disease and Neuronal ceroid lipofuscinosis were the common causes of PME in our series as mentioned in literature. However

Sialidosis was conspicuously absent, probably due to lack of facility to measure a-neuraminidase levels in serum.

Photosensitivity is less common in LBD/NCL in this series than reported in the literature.

Morphological changes were helpful in diagnosis and Could be confirmed by biopsy of peripheral tissues like skin and muscle in majority (60%). Electron microscopy was helpful in NCL and MERRF.

Genetic analysis will help in accurate diagnosis and better understanding in future.

References

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Flow chart – Progressive myoclonic epilepsy: An approach

Clinical

LBD	*NCL*	*ULD*	*MERRF*	*TSD*
Early dementia	Severe dementia	Ataxia	Myoclonus	Startle Myoclonus
Visual failure	Retinal degeneration	Myoclonus	Deafness	Cherry red spot
Occipital seizures	Optic atrophy	Preserved cognition	Neuropathy	1st two years
Early 2nd decade	First decade	1st/2nd decade	Retinitis pigmentosa	

Electrophysiology

LBD	*NCL*	*ULD*	*MERRF*	*TSD*
Giant SSEP	Giant SSEP	Giant SSEP	Neuropathy	–
Photosensitive seizures at high feq	Photosensitive seizures at low freq			

Final diagnosis

Pathological				Biochemical	Genetics
Skin	Liver	Muscle	Brain		
LBD	*LBD*	*MERRF*	*LBD*	*TSD*	*NCL*
NCL (EM)	*TSD*	*NCL*	*NCL*		*LBD*
LBD					*ULD*
					MERRF