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Abstracts

Articles appearing in the August 2019 issue

Altered CSF levels of monoamines in hereditary spastic paraparesis 10: A case series

Objective To perform a comprehensive clinical characterization and biochemical CSF profile analyses in 2 Swedish families with hereditary spastic paraparesis (HSP) 10 (SPG10) caused by 2 different mutations in the neuronal kinesin heavy chain gene (*KIF5A*).

Methods Structured clinical assessment, genetic studies, and neuroradiologic and electrophysiologic evaluations were performed in 4 patients from 2 families with SPG10. Additional CSF analysis was conducted in 3 patients with regard to levels of neurodegenerative markers and monoamine metabolism.

Results All patients exhibited a complex form of HSP with a mild to moderate concurrent axonal polyneuropathy. The heterozygous missense mutations c.767A > G and c.967C > T in *KIF5A* were found. Wide intrafamilial phenotype variability was evident in both families. CSF analysis demonstrated a mild elevation of neurofilament light (NFL) chain in the patient with longest disease duration. Unexpectedly, all patients exhibited increased levels of the dopamine metabolite, homovanillic acid, whereas decreased levels of the noradrenergic metabolite, 3-methoxy-4-hydroxyphenylglycol, were found in 2 of 3 patients.

Conclusions We report on CSF abnormalities in SPG10, demonstrating that NFL elevation is not a mandatory finding but may appear after long-standing disease. Impaired transportation of synaptic proteins may be a possible explanation for the increased dopaminergic turnover and noradrenergic deficiency identified. The reasons for these selective abnormalities, unrelated to obvious clinical features, remain to be explained. Our findings need further confirmation in larger cohorts of patients harboring *KIF5A* mutations.

NPub.org/NG/9309a

Systematic review and meta-analysis of cardiac involvement in mitochondrial myopathy

Objective Our goal was to perform a systematic review of the literature to demonstrate the prevalence of cardiac abnormalities identified using cardiac investigations in patients with mitochondrial myopathy (MM).

Methods This systematic review surveys the available evidence for cardiac investigations in MM from a total of 21 studies including 825 participants. Data were stratified by genetic mutation and clinical syndrome.

Results We identified echocardiogram and ECG as the principal screening modalities that identify cardiac structural (29%) and conduction abnormalities (39%) in various MM syndromes. ECG abnormalities were more prevalent in patients with m.3243A>G mutations than other gene defects, and patients with mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) had a higher prevalence of ECG abnormalities than patients with other clinical syndromes. Echocardiogram abnormalities were significantly more prevalent in patients with m.3243A>G or m.8344A>G mutations compared with other genetic mutations. Similarly, MELAS and MERRF had a higher prevalence compared with other syndromes. We observed a descriptive finding of an increased prevalence of ECG abnormalities in pediatric patients compared with adults.

Conclusions This analysis supports the presence of a more severe cardiac phenotype in MELAS and myoclonic epilepsy with ragged red fibers syndromes and with their commonly associated genetic mutations (m.3243A>G and m.8344A>G). This provides the first evidence basis on which to provide more intensive cardiac screening for patients with certain clinical syndromes and genetic mutations. However, the data are based on a small number of studies. We recommend further studies of natural history, therapeutic response, pediatric participants, and cardiac MRI as areas for future investigation.

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Redefining the phenotype of ALSP and *AARS2* mutation–related leukodystrophy

R Lakshmanan, ME Adams, DS Lynch, et al. 2017;3:e135. doi.org/10.1212/NXG.0000000000000135