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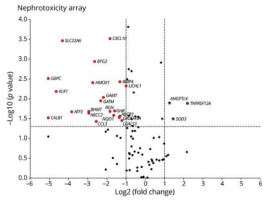
Abstracts

Articles appearing in the October 2019 issue

Impaired kidney structure and function in spinal muscular atrophy



Objective To determine changes in serum profiles and kidney tissues from patients with spinal muscular atrophy (SMA) type 1 compared with age- and sex-matched controls.

Methods In this cohort study, we investigated renal structure and function in infants and children with SMA type 1 in comparison with age- and sex-matched controls.

Results Patients with SMA had alterations in serum creatinine, cystatin C, sodium, glucose, and calcium concentrations, granular casts and crystals in urine, and nephrocalcinosis and fibrosis. Nephrotoxicity and polycystic kidney disease PCR arrays revealed multiple differentially expressed genes, and immunoblot analysis showed decreased calcium-sensing receptors and calbindin and increased insulin-like growth factor–binding proteins in kidneys from patients with SMA.

Conclusions These findings demonstrate that patients with SMA type 1, in the absence of disease-modifying therapies, frequently manifest impaired renal function as a primary or secondary consequence of their disease. This study provides new insights into systemic contributions to SMA disease pathogenesis and the need to identify coadjuvant therapies.

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Next-generation sequencing approach to hyperCKemia: A 2-year cohort study

Objective Next-generation sequencing (NGS) was applied in molecularly undiagnosed asymptomatic or paucisymptomatic hyperCKemia to investigate whether this technique might allow detection of the genetic basis of the condition.

Methods Sixty-six patients with undiagnosed asymptomatic or paucisymptomatic hyperCKemia, referred to tertiary neuromuscular centers over an approximately 2-year period, were analyzed using a customized, targeted sequencing panel able to investigate the coding exons and flanking intronic regions of 78 genes associated with limb-girdle muscular dystrophies, rhabdomyolysis, and metabolic and distal myopathies.

Results A molecular diagnosis was reached in 33 cases, corresponding to a positive diagnostic yield of 50%. Variants of unknown significance were found in 17 patients (26%), whereas 16 cases (24%) remained molecularly undefined. The major features of the diagnosed cases were mild proximal muscle weakness (found in 27%) and myalgia (in 24%). Fourteen patients with a molecular diagnosis and mild myopathic features on muscle biopsy remained asymptomatic at a 24-month follow-up.

Conclusions This study of patients with undiagnosed hyperCKemia, highlighting the advantages of NGS used as a first-tier diagnostic approach in genetically heterogeneous conditions, illustrates the ongoing evolution of molecular diagnosis in the field of clinical neurology. Isolated hyperCKemia can be the sole feature alerting to a progressive muscular disorder requiring careful surveillance.

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B. Rhead, M. Bäärnhielm, M. Gianfrancesco, et al. 2016;2:e97. doi.org/10.1212/NXG.0000000000000097

***CHCHD10* variant p.(Gly66Val) causes axonal Charcot-Marie-Tooth disease**

M. Auranen, E. Ylikallio, M. Shcherbii, et al. 2015;1:e1. doi.org/10.1212/NXG.0000000000000003

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E. Harris, C.L. Bladen, A. Mayhew, et al. 2016;2:e89. doi.org/10.1212/NXG.0000000000000089

A novel *DYNC1H1* mutation causing spinal muscular atrophy with lower extremity predominance

Q. Niu, X. Wang, M .Shi, Q. Jin. 2015;1:e20. doi.org/10.1212/NXG.0000000000000017

