Pediatric Neurology Part III: Chapter 146. Hereditary motor-sensory, motor, and sensory neuropathies in childhood (Handbook of Clinical Neurology)

Pierre Landrieu, Jonathan Baets, Peter De Jonghe

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Hereditary neuropathies (HN) are categorized according to clinical presentation, pathogenic mechanism based on electrophysiology, genetic transmission, age of occurrence, and, in selected cases, pathological findings. The combination of these parameters frequently orients towards specific genetic disorders. Ruling out a neuropathy secondary to a generalized metabolic disorder remains the first pediatric concern. Primary, motor-sensory are the most frequent HN and are dominated by demyelinating AD forms (CMT1). Others are demyelinating AR forms, axonal AD/AR forms, and forms with “intermediate” electrophysiological phenotype. Pure motor HN represent<10% of HN but exhibit large clinical and genetic heterogeneity. Sensory/dysautonomic HN cover five classical subtypes, each one related to specific genes. However, genetic heterogeneity is largly greater than initially suspected. Syndromic HN distinguish: “purely neurological syndromes”, which are multisystemic, usually AD disorders, such as spinocerebellar atrophies +, spastic paraplegias +, etc. Peripheral Neuropathy may be the presenting feature, including in childhood. Clearly degenerative, AR forms prompt to investigate a large set of pleiotropic genes. Other syndromes, expressed in the perinatal period and comprising malformative features, are mainly developmental disorders, sometimes related to specific transcription factors. Altogether, >40 genes with various biological functions have been found responsible for HN. Many are responsible for various phenotypes, including some without the polyneuropathic trait: for the pediatric neurologist, phenotype/genotype correlations constitute a permanent bidirectional exercise.

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