Hereditary Peripheral Neuropathy Diagnostic Algorithm

Inherited neuropathy suspected
The following tests should be performed in all adult patients:
- HbA1c or glucose tolerance, vitamin B12, monoclonal proteins.
- Order PMP22 Gene, Large Deletion and Duplication Analysis

Charcot-Marie-Tooth disease type 1A (CMT1A) – PMP22 duplication
HNPP – PMP22 deletion

Neglected
But HNPP still suspected
Using Custom Gene Ordering Tool: PMP22 Sequencing

Disorder-specific management

HNPP missense mutations
Disorder-specific management

Consider: NPPAN / Peripheral Neuropathy Genetic Panels by Next-Generation Sequencing, Blood
- Specify subpanel Peripheral Neuropathy Expanded Panel (193 genes)

Nerve conduction studies show:
- Ulnar motor forearm nerve conduction velocity <38 m/s (compound muscle action potential test >0.5 mV)
- AND/OR
- blink reflex R1 >13 ms

Either <50 years of age at onset with no obvious acquired cause
Or Definitive family history

Predominant motor neuropathy
Predominant sensory neuropathy

Expand acquired etiology search:
- Immune-mediated inflammatory, eg, Sjögren, lupus, polyarteritis nodosum
- Metabolic: eg, thyroid disease, vitamin B6 deficiency or toxicity
- Toxic: eg, ethanol, heavy metals, organophosphates
- Infectious disease: eg, CMV, EBV, HIV, HCV, Lyme disease
- PA/VL / Paraneoplastic Autoantibody Evaluation, Serum
- PAC1 / Paraneoplastic Autoantibody Evaluation, Spinal Fluid

Peripheral Neuropathy Gene Panels:
- Hereditary Motor Neuropathy Panel (23 genes)
- Hereditary Sensory Neuropathy Panel (18 genes)
- Metabolic or Syndromic Neuropathies (74 genes)
- Motor and Sensory Neuropathy Panel (82 genes)
- Peripheral Neuropathy Expanded Panel (193 genes)
- SEPT9 Gene, Full Gene Analysis (1 gene)
- Spastic Paraplegia Neuropathy Panel (41 genes)
- Custom Gene Panel (select genes from list) via Custom Gene Ordering (CGO) Tool

Diagnostic of chronic idiopathic axonal polyneuropathy (CIAP)
Consider ordering: NPPAN / Peripheral Neuropathy Genetic Panels by Next-Generation Sequencing (NGS), Blood
Specify one of the following subpanels (see Peripheral Neuropathy Gene Panels box):
- Hereditary Sensory Neuropathy Panel
- Peripheral Neuropathy Expanded Panel