Demyelinating polyneuropathy (MCV ≤38 m/s)

PMP22 duplication

- present → CMT1A
- absent

Are technical resources and expertise for Next Generation Sequencing available?

- yes → Perform testing of demyelinating panel
- no → Perform targeted gene analysis

Demyelinating panel consisting of at least the following genes:

**AD genes**
- MPZ (CMT1B)
- PMP22 (CMT1E)
- LITAF (CMT1C)
- EGR2 (CMT1D/4E)
- NEFL (CMT1F)
- **Rare AD genes**
  - FBLN5
  - ARHGEF10

**AR genes**
- GDAP1 (CMT4A)
- SH3TC2 (CMT4C)
- NDRG1 (CMT4D)
- MTMR2 (CMT4B1)
- PRX (CMT4F)
- FIG4 (CMT4J)
- SBF2 (CMT4B2)
- SBF1 (CMT4B3)
- FGD4 (CMT4H)
- SURF1 (CMT4)
- HK1 (HMSN-Russe)
- **X-linked gene**
  - GJB1 (CMT1X)

Strong indications for autosomal recessive inheritance:
- At least two affected sibs
- Consanguineous parents
- Onset early childhood and severe progression

- present → male-to-male inheritance
- absent

GJB1 (CMT1X)

Test for AR genes (see under demyelinating panel AR genes)

- present → GJB1 (CMT1X)
- absent

Test for AD genes (see under demyelinating panel AD genes)

- present → Consider:
  - FBLN5 → CMT1 + cutis laxa + age-related macular degeneration
  - ARHGEF10 → asymptomatic slow nerve conduction velocity
- absent

Is there an affected parent/child

- yes → when no causative mutations are identified in known CMT-related genes
- no

Consider only in familial cases:
Whole Exome Sequencing