Other Hereditary Sensory Neuropathies

- Sensory PN + Hearing loss: Connexin-31; 1p35
- Sensory PN + Deafness: Xq23
- HSMN + Ataxia: 7q22
- HSN + Cough & GE reflux

HEREDITARY NEUROPATHIES

A) Non Syndromic Hereditary Neuropathies:

1- Hereditary Motor & Sensory Neuropathies (CMT).

2- Hereditary Neuropathy with liability to Pressure Palsy (HNPP)

3-Hereditary Sensory & Autonomic Neuropathies (HSAN).

4- Distal Hereditary Motor Neuropathies (HMN).

B) Syndromic Hereditary Neuropathies:

4- Distal Hereditary Motor Neuropathies (HMN)= Distal Spinal Muscular Atropthy (SMA).

Subtypes &Clinical picture:

Disorder	Gene/Locus	Clinical picture
HMN-5	**7p; GARS**	**Arm> leg weakness;** onset in 2nd- 3rd decade; no sensory involvement
HMN 7	**2q14**	**Vocal cord involvement**
HMARD	**11q13;**	Distal infantile SMA with **diaphragm paralysis**
HMNJ	**9p21; 1-p12**	Childhood-onset distal weakness (Jerash type)
HMN	**2p13; DCTN1**	Progressive hand >leg weakness and atrophy, **vocal fold paralysis & facial weakness**

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B) Syndromic Hereditary Neuropathies:

B) Syndromic Hereditary Neuropathies

1) Demyelinating Dominant

Disorder	Gene / Locus	Associated features
Wardeenburg type IV	22q13; SOX10	CNS & PNS dysmyelination Hirschsprung disease

B) Syndromic Hereditary Neuropathies

2) Demyelinating Recessive

Disorder	Gene / Locus	Associated features
Metachromatic leukodystrophy	22q13; (ArylsulfataseA)	Optic atrophy Mental retardation Hypotonia
Globoid cell leukodystrophy (Krabbe's)	14q31; (Galactosylceramide - galactosidease)	Spasiticity, Optic atrophy Mental retardation

B) Syndromic Hereditary Neuropathies

2) Demyelinating Recessive

Disorder	Gene / Locus	Associated features
Refsum's disease	10 pter-p11.2 PAHX (Phytanoyl-CoA hydroxylase) & 7q21-22; PEX7 (Peroxin-1)	Deafness Retinting pigmentosa, Ichthyosis heart failure
Merosin deficiency	6q 22; LAMA2 (laminin-2)	Neuropathy and muscular dystrophy

B) Syndromic Hereditary Neuropathies

3) Axonal dominant

Disorder	Gene / Locus	Associated features
Familial Amyloidotic Neuropathy (FAP-I & FAP-II	18q21; TTR (Transthyretin)	Painful axonal neuropathy; other organs involved; FAP-II also causes carpal tunnel syndrome
FAP-III"lowa"	11q23; ApoAl (Apoliporotein A1)	Nephropathy, liver disease
FAP- IV "Finnish"	9q32-q34; AGel (Gelsolin)	Corneal dystrophy, cranial neuropathies

B) Syndromic Hereditary Neuropathies

3) Axonal dominant

Disorder	Gene / Locus	Associated features
Acute Intermittent Porphyria	11q23.3; PBGD (Porphobillinogen deaminase	Acute neuropathy follows abdominal crises; psychosis; depression; dementia; seizures
Coproporphyria	3q12;CPO (Copropophrinogen 3 oxidease)	Skin photosensitivity, psychosis, crises of acute neuropathy and abdominal pain
Variegate Porphyria	3q12;CPO (Coproporphurinogen 3 oxidease)	South Africa; similar to acute intermittent prophyria

B) Syndromic Hereditary Neuropathies

3) Axonal dominant

Disorder	Gene / Locus	Associated features
Fabry's disease	Xq22;GLA (galactosidase)	Angiokeratoma Pain Stroke Renal failure Cardiomyopathy
Hereditary Neuralgic Amyotrophy	17q25	Painful episodes of brachial palsy, dysmorphic features

B) Syndromic Hereditary Neuropathies

4) Axonal Recessive

Disorder	Gene / Locus	Associated features
Hereditary tyrosinemia type 1	15q23-q25; FAH (Fumaryl-Acetoacetase)	Hepatic and Renal disease, Cardiomyopathy
Giant axonal neuropathy	16q24; GANI (Gigaxonin)	Kinky/curly hair CNS features UMNL, Optic atrophy, Nystagmus,Ataxia Mental retardation,

B) Syndromic Hereditary Neuropathies

4) Axonal Recessive

Disorder	Gene / Locus	Associated features
Abetalipoproteinemia	4q24; MTP (microsomal triglyceride transfer protein)	Ataxia, Acanthocytosis
Analphalipoproteinemia (Tangier's disease)	9q31; ABC1 (AtP- binding cassette transporter)	Orange tonsils, Organomegaly Atherosclerosis, Painless ulcerations

B) Syndromic Hereditary Neuropathies

4) Axonal Recessive

Disorder	Gene / Locus	Associated features
Cowchock's syndrome	Xq24-26	Mental retardation (60%) Deafness
Congenital Catarcts, Facial Dysmophism Neuropathy (CCFDN;	18 q23-qter; CTDP1 (intron 6)	Cataracts, microcornea, Facial dysmorphism Skeletal deformities

Other Syndromic Hereditary Axonal Neuropathies

- Ataxia telangectasia
- Cerebrotendinous xanthomatosis
- Chediak-Higashi
- Friedreich Ataxia
- Glycogenosis, Type 3
- Mitochondrial: MNGIE; NARP; Leigh; Other
- Neuroacanthcytosis
- Brachial Plexopathy

Diagnosis Of Hereditary Neuropathies

Based on Clinical Presentation and Electrophysiological Findings

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Diagnosis Of Hereditary Neuropathies

- History taking (hereditary cause is suggested)
- Examination
- Lab work to exclude causes of acquired neuropathies
- Neurophysiological study
- Biopsy
- Genetic study

Recurrent Hereditary Neuropathies

- Hereditary Neuropathies

  Liability to Pressure Palsy
- Brachial Plexopathy
- Refsum
- Porphyria

Hereditary Neuropathies affecting UL>LL

- HMN 5A
- CMT 2D
- HMN 5B
- Amyloidosis (
  Carpal tunnel syndrome)

Hereditary Neuropathies Affecting Motor Neurones

- HMN-5A
- HMN 7
- HMARD
- HMNJ
- HMN

Hereditary Neuropathies associated with skin manifestations

- Amyloidosis :Petechiae or purpura
- Refsum: Ichthyosis
- Sensory neuronopathies: Ulcers
- Coproporphyria: Skin photosensitivity,
- Fabry: Angiokeratoma

Hereditary Neuropathies Affecting eye

- CMT-4B2 : Glaucoma
- CMT 6 : optic atrophy
- CMT 7 : RP
- Mitochondrial disorders
- Leukodystrophies: optic atrophy
- Refsum: RP
- FAP- IV: Corneal dystrophy
- Congenital Catarcts, Facial Dysmophism Neuropathy (CCFDN) : Cataract
- Ataxia Telangectasia

Hereditary Neuropathies associated with Hearing Loss

- X-linked
  - Cowchock
  - HMSN X (Connexin 32)
- Recessive
  - CMT 4D (Lom)
  - Refsum
  - Xeroderma Pigmentosum
  - CEDNIK
- Dominant
  - CMT 1A
  - CMT 1B
  - CMT 2E
  - CMT-4D
  - Dejerine-Sottas (Dominant)

Hereditary Neuropathies associated with thickened nerves

- Demyelinating
  - HMSN I & III
  - Refsum
- Neurofibromatosis

Hereditary Neuropathies associated with GIT troubles

- HSN + Cough & GE reflux
- Mitochondrial: MNGIE & Variants
- Riley-Day (HSAN3)

Hereditary Neuropathies associated with Facial Nerve palsy

- Amyloid: Gelsolin

- Tangier disease

Hereditary Neuropathies associated with Dysmorphic Features

- CMT-4D
- Hereditary Neuralgic Amyotrophy
- Congenital Catarcts, Facial Dysmophism Neuropathy (CCFDN;

Hereditary Neuropathies associated with Vocal cord affection

- HMSN II C
- HMN 7

Hereditary Axonal Neuropathies

- HMSN: II ,V ,VI
- HSAN
- Spinal muscular atrophy: Proximal; Distal
- Amyloidosis
- Porphyria
- Fabry's
- Hereditary tyrosinemia type 1
- Giant Axonal Neuropathy
- A-beta-lipoproteinemia
- An- α -lipoproteinemia (Tangier's)
- Cowchock's syndrome
- Congenital Catarcts, Facial Dysmophism Neuropathy (CCFDN;
- Ataxia telangectasia
- Cerebrotendinous xanthomatosis
- Chediak-Higashi Friedreich Ataxia
- Mitochondrial: MNGIE; NARP; Leigh; Other

Hereditary Demyelinating Neuropathies

- HMSN type I, III, IV, XL
- HNNP
- Leukodystrophies
- Refsum
- Wardeenburg type IV

Clinical Case

- 40ys old female patient presenting with gradual progressive weakness both UL & LL, D>P, UL>LL associated with distal wasting
- NC study showed axonal motor affection with no sensory affection

keywords

- UL involvement
- Pure motor
- Axonal

Hereditary Neuropathies Affecting Motor Neurones

- HMN-5A
- HMN 7
- HMARD
- HMNJ
- HMN

Hereditary Neuropathies affecting UL>LL

- HMN-5A
- CMT 2D
- HMN 5B
- Amyloidosis (Carpal tunnel syndrome)

Hereditary Axonal Neuropathies

- HMSN: II
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- Mitochondrial: MNGIE; NARP; Leigh; Other

Online Mendelain Inheritance in Man (OMIM):

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Neuromuscular:

www.neuro.wustl.edu/neuromuscular/

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