Overview & Orthotic Management of Charcot Marie Tooth

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Purpose of this Presentation ..... 

- Description of CMT
- Some History
- Understand the disease process
  - Pathophysiology
  - Pathomechanics
  - Critical insight into best orthotic designs
- Patient Evaluation
- Orthotic Management Options
Charcot Marie Tooth Disease
Aka:

- Peroneal Muscular Atrophy
- HMSN; Hereditary Motor Sensory Neuropathy
- Charcot-Marie-Tooth-Hoffman
- Tooth’s Motor sensory neuropathy

Description:
A progressive inherited neuropathy that is characterized by motor and sensory loss, predominantly in the feet and legs but also in the hands and arms.

This condition is one of the most common inherited neurological disorders, with 1 in 2,500 affected.
History
1886
2 papers were submitted in similar timeframe

Jean-Martin Charcot
61 y/o

Pierre Marie
33 y/o

Howard Henry Tooth
Cambridge Thesis: “The Peroneal type of Progressive Muscular Atrophy”
29 y/o
CMT1A is an autosomal dominant disease resulting from a duplication of the gene on chromosome 17 that carries the instructions for producing the peripheral myelin protein-22 (PMP-22). The PMP-22 protein is a critical component of the myelin sheath.

HMSN I, characterized by severely reduced motor nerve conduction velocities (NCV) (less than 38m/s) and segmental demyelination and remyelination with onion bulb formations on nerve biopsy. Demyelinating disease process.

CMT2 is a demyelinating disease that begins in infancy. Infants have severe muscle atrophy, weakness, and sensory problems. This rare disorder can be caused by a specific point mutation in the P0 gene or a point mutation in the PMP-22 gene.

CMTX is an X-linked dominant disease and is caused by a point mutation in the connexin-32 gene on the X chromosome. (CMTX1) is X-linked dominant or X-linked intermediate; heterozygous females are more mildly affected than are hemizygous males. Ionescu et al. (1991) presented data suggesting the existence of 2 separate loci for X-linked recessive disorders mapping to other sites:

CMTX2 at chromosome Xp22.2 (302801) and CMTX3 at chromosome Xq26 (302802). CMTX4, which maps to chromosome Xq24-q26, Cowchock syndrome (310490). CMTX5 at chromosome Xq21-q24 (311070).

- Males who inherit one mutated gene from their mothers show moderate to severe symptoms of the disease beginning in late childhood or adolescence (the Y chromosome that males inherit from their fathers does not have the connexin-32 gene).
- Females who inherit one mutated gene from one parent and one normal gene from the other parent may develop mild symptoms in adolescence or later or may not develop symptoms of the disease at all.

CMTX >50 types.
CMT & HMSN: Demyelinating

Dominant

CMT 1A: PMP-22; 17p11
CMT 1B: P0 protein; 1q22
CMT 1C: LITAF; 16p13
CMT 1D: EGR2; 10q21
CMT 1E: P0 protein; 1q22
CMT 1F: NEFL; 8p21
HNPP: PMP-22 deletion; 17p11
HMSN 3 (Dejerine-Sottas)

CMT 2A1: KIF1B; 1p36

CMT 2A2: MFN2; 1p36
CMT 2B: RAB7; 3q13-q22
CMT 2C: 12q23-q24
CMT 2D: GARS; 7p15
CMT 2E: Neurofilament light chain; 8p21
CMT 2F: Distal HMSN; HSPB1; 7q11-q21
CMT 2G: 12q12
CMT 2H: P0; 1q22
CMT 2I: P0; 1q22
CMT 2J: GDAP1; 8q21
CMT 2K: GDAP1; 8q21
CMT 2L: HSPB8; 12q24

HMSN-Proximal: 3q13
CMT 2 + Cataracts: DNM2; 19p12
HMSN + Optic atrophy: MFN2; 1p36
HMSN + Ulcero-mutilation: MFN2; 1p36
HMSN + Ataxia: IFRD1; 7q22
HMN 5B: BSCL2; 11q13

X-linked

Connexin-32 (Females): Xq13
1: Xq22.2
2: Xq26
4: (Cowchock): Xq24
5: PRPS1; Xq22
Sensory PN + Deafness: Xq23

CMT + Intermediate NCV

Dominant

CMT DIA: 10q24
CMT DIB: DNM2; 19p12
CMT DIC: Tyrosyl-tRNA synthetase; 1p34
CMT DIA: P0; 1q22
CMT DIB: P0; 1q22
CMT X (Semi-dominant)

CMT 2E: Neurofilament light chain; 8p21

Recessive

CMT RIA: GDAP1; 8q21.1

CMT + Axonal NCV

Axonal: CMT type II; AR-CMT2; HMSN 5; HMSN 6

CMT & HMSN: Axonal

Recessive

CMT 4A: GDAP1; 8q21
CMT 4B: MTMR2; 11q23
CMT 4C: SH3TC2 (KIAA1985); 5q32
CMT 4D (Lon): NDRG1; 8q24
CMT 4E: EGR2; 10q21
CMT 4F: Periaxin; 19q13
HMSN-Russe (4G): HK1; 10q22
CMT 4H: FGD4; 12q12
CMT 4J: FIG4; 6q21
HMSN 3 (Dejerine-Sottas)
P0; PMP-22; EGR2; Periaxin
HMSN + Juvenile glaucoma
Cataracts (CCFDN): CTDP1; 18qter
Cockayne’s: 5
Congenital hypomyelinating
P0; PMP-22 & EGR-2
Farber lipogranulomatosis: ASAH; 8p22
CDG1a: PMM2; 16p13
Krabbe: GALT; 14q31
MLD: ARSA; 2q13
PMP-22 point mutations
Refsum’s disease
Childhood: PHYH; 10pter-p11.2
Adolescent-Age: PEX7; 6q22
Infant: PEPT1; 7q21
Refsum-like: 20p11
HMSN + CNS: Heterogeneous

CMT 4K: GDAP1; 8q21
CMT 4L: HSPB1; 7q11-q21
HMSN + Ataxia: IFRD1; 7q22
HMN 5B: BSCL2; 11q13

HMSN+Optic neuropathy

Recessive

AR-CMT2A: Lamin A/C; 1q21
AR-CMT2B: MED25; 19q13.3
AR-CMT + Pyramidal signs: (CMT 2H): 8q21.3
AR-CMT + Hoarseness: (CMT 2K): GDAP1; 8q21
AR-CMT, Severe & Early onset: NEFL; 8p21
AR-CMT/Distal HMSN: HSPB1; 7q11-q21

Acrodrystrophy

Andermann (Corpus callosum Δ): KCC3; 15q13
Ataxia with neuropathy: TDP1; 1q31
Giant axonal: Gagoxlin; 16q24
HMSN + Optic neuropathy + Deafness
Infantile axonal + Respiratory failure
Lethal Neonatal
Neuropathy dystrophy
Ouvrier: Early childhood onset

Syndromes
Childhood onset HMSN
CNS + HMSN
Deafness + HMSN

Demyleination Disorders: CMT 1, III (Dejerine-Sottas), 4, HNPP, Neuropathy with focally folded myelin sheaths, Congenital hypomyelinating neuropathy

Genes producing either demyelinating or axonal neuropathies Connexin-32 (CMT-X)
How many of you know specifically what type of CMT you or your family have?
Centre of Excellence
Rochester - Closest
Iowa – Dr. Micheal Shy

EMG Studies
Bloodwork
Patient complaints/presentation

- General foot weakness (foot drop, foot slap, weak push off)
- Unsteady gait (poor balance)
- Decreased proprioception: (where you are in space)
- Chronic lateral ankle sprains
- Glove and stocking hypoesthesia
  - “numbness”
- Atrophy of hand muscles
  - “Hand weakness, dropping things”
  - Thumb opposition
- Atrophy of distal leg muscles
- Claw toes
- Painful calluses
  - Base and head of 5th metatarsal
  - 1st and 5th met heads
Does not affect longevity

Primarily affects pts below elbows and knees

Can predict severity (maybe)

Managed well
A specific sequence of muscle loss results in muscle imbalances which over time develops into the classic CMT deformities of:

- Intrinsic minus toes
- Plantar flexed 1st ray
- Anterior cavus foot
- Forefoot adduction at the mid tarsal joint
- Inverted rear foot with lateral ankle instability
- External rotation of the ankle and knee axes relative to the line of progression
Intrinsics are first to go leaving extrinsic long toe flexors unopposed to create claw toes.

Peroneus longus out lasts its antagonist anterior tibialis with resultant plantar flexion of the first ray.

A rigidly plantar flexed 1st ray is almost impossible to stretch out and weight bearing imparts an inversion twist to the rear foot creating the “tripod effect”.

Posterior tibialis out lasts its antagonist the peroneus brevis with unopposed forefoot adduction.

Long extrinsic toe flexors outlast extensors creating anterior cavus.
Pes Cavus!

Classic characteristics associated with CMT
Classic CMT from behind
Classic CMT hand
Tripod Effect

In static weight bearing, a rigid plantar flexed 1st ray imparts an inversion twist to the hind foot with resultant calcaneal varus.
Lateral Block Test
Path of Pressure

- Normal Human Locomotion
- COG travels through a 2 inch corridor for maximum energy efficiency
- Normal Biomechanical Gait
Quality of the base

- An abducted or adducted forefoot will have an abnormal path of pressure.
- Here as the COG passes over the base it will track lateral and off the base of the 5th metatarsal.
Path of pressure.....evidence
Evaluation

• History
  ○ Occupation, present activities, desired activities.
  ○ Complaints (what is hard to do?, what limits you?)
    • Weakness, instability, balance, reduced activity levels

• Pathomechanical Assessment
  ○ Sensory Testing
  ○ Range of Motion
  ○ Manual Muscle Test
  ○ Gait Deviations
  ○ Balance
  ○ Cadence (gait)

• Ask, Explain, Discuss, Agree
  • Get some specifics on you want
    • may not have even thought about options
  • Describe orthotic options
  • Agree on a treatment plan
Goals: what can we achieve?

Traditional orthotic goals:

- Prevent deformity
- Support and align skeletal structures
- Limit or enhance motion about a specific joint
- .................Balance
Treatment Options
Which Design is Right?

- Determine Patient Goals
- Consider level of gadget tolerance.
- device is like a tool
BALANCE

- Simple physics of balance
- the COG must lie over the base of support
Prevention!!!!

- Simple FO’s/SMO’s
- Post to prevent lateral ankle instability
- Fore-foot varus post
- ST pad and 1st MP trap, and with weight bearing, prevent shortening of LA
- Stretching exercises to prevent tight achilles tendon, hamstrings
Accommodative/corrective FO’s for fixed deformities

Forefoot valgus post for rigid plantar flexed 1st ray
• Inhibit lateral ankle instability with rear foot or fore foot posting
• Prevent forefoot adduction at mid-tarsal joint
• Prevent shortening of longitudinal arch:
  • trap 1\textsuperscript{st} MP with intrinsic post
  • trap calcaneus with ST pad
Off the Shelf Carbon AFO’s
Ground Reaction and dorsiflexion assist
Custom Energy Storing
Align Skeletal Segments

Derotation

- ERD  External Rotary Deformity
- Forefoot adduction at midtarsal joint
- Anterior cavus foot
- ER of ankle and knee axes relative to LOP
- COG not over base of support

- Extended medial foot plate
- Lateral mid tarsal slot strap
- Lateral sub talar slot strap
- Lateral calcaneal base modification
- ST pad and intrinsic FF valgus post
- Dorsi assist ankle joints
- Extended medial proximal trim
Silicone AFO’s
Questions???

Thank you very much!!

.......... and thanks to Ken Cornell, CO & Sean McKale, CO for some of the presentation content.