POLYNEUROPATHY + NEURONOPATHY: Points in Differential Diagnosis

Selective Functional Involvement

Motor
Motor Neuropathy: Multifocal (MMN); Distal
Motor Neuron Disorders
Lower Motor Neuron (LMN): BVvL; Fazio-Londe; Madras
Spinal Muscular Atrophies (SMA): 5q; BSMA; Infantile; HMN
ALS: Sporadic; Hereditary
Toxic: Pb; Dapsone; Botulism; Tick
Acute: Porphyria; Axonal GBS (AMAN); Polio; West Nile
Diabetic amyotrophy

Autonomic
Diabetes Mellitus; Amyloid; Paraneoplastic
Immune: Acute; GBS; Vasculitis
Multisystem: Shy-Drager; IOH; Mitochondrial
Hereditary: Riley-Day; Sensory PN; HSAN II
Infections: Chagas; Leprosy; HIV
Toxic: Vacor; Perhexiline; Vincristine
Hyperhidrosis: Arsenic; Hg; Acrylamide
Localized: RSD; Horner's

Treatable neuropathies
Diabetes; Vasculitis; CIDP;
Lymphoma; Infection;
Toxic; Compression
Deficiency: B_{12}; E; Cu
Antibody: GM1; TS-HDS; MAG;
Neurofascin; Contactin-1; GALOP
? FGFR3; Cryoglobulin; M-protein

Sensory: Large fiber & Ataxic
Tabes dorsalis; Vitamin deficiency: B12; E
Toxic: Vitamin B6; cis-platinum; Taxol; MeHg
Hereditary: an-α-lipoproteinemia; Friedreich's;
Ataxia telangectasia; Biemond; OPCA; HSAN
Immune: MAG; GALOP; GD1b; Miller-Fisher
Neuronopathies: Hu; Sjögren's
Rule out: Myelopathy; HTLV1; HIV

Sensory: Small fiber
Leprosy; Amyloid; Idiopathic
Toxic: Kepone; Ciguatera
Metabolic: Diabetes; Increased Triglycerides
Hereditary
HSN I & IV; Tangier's, Fabry's;
Indifference; Thermoanalgesia; Navajo
HSN + Paraparesis (Cavanagh)

Neuropathy + Pain
Diabetic amyotrophy; Vasculitis;
Idiopathic; Polio; HIV; Ca meningitis;
Toxic: EtOH; Arsenic; Ifosfamide
cis-Platinum; Thallium; Thalidomide
Hereditary: Fabry's; HSN I; Erythermalgia
Focal: Median & Post tibial n.
Other: Roots; Plexus

Selective Anatomical Distribution: Most are symmetric and maximal distally in the lower extremities

Extraocular muscle
Botulism
Diabetes
Miller-Fisher
Diphtheria
Rule out:
MG; Myopathy

Proximal Motor
Immune Demyelinating:
GBS; CIDP
SMA; Porphyria
Plexopathy: Brachial; Lumbar
Rule out: Joint pain; Myopathy

Proximal Sensory
Hereditary: Porphyria; Tangier
Neuronopathy: Hu; Sjögren's
Thoracic neuropathy
Rule out: Myelopathy

Skin temperature-related
Leprosy

Upper extremity
Immune: MMN; Vasculitis
CIDP variant
Amyloid: Carpal tunnel
Entrapment: HNPP; Other
Toxic: Lead; Vincristine
ALS; LMN
Rule out: Spinal; CNS

Asymmetric
Mononeuritis multiplex
Neuronopathy: ALS; Sensory
Entrapments
Plexopathies
Toxic

Mononeuritis Multiplex
Vasculopathy; Amyloid;
Leprosy; Diabetes; CMV
Waldenström; Perineuritis
Demyelinating: HNPP;
Multifocal CIDP; MMN
Compression: Multiple
Lymphoma: Intraneural
Wartenberg

CNS
Spinal: Organophosphate; Hexacarbon; AMN; MLD; Lymphoma; Cuban; Vernant's
Optic: Disulfiram; CS_2; Hg; Drugs; NARP; CMT6; Post col & RP; Cuban; Vernant's
Hearing loss: HMSN X, 1A, 1B, 4D, 6; Mitichondrial; Sarcoid
Cerebellum: FA; AT; MLD; Refsum; A-β-lipoproteinemia; SCA 2, 3, 4; IOSCA; Hu & CV-2
Supratentorial: Mitochondrial; Thyroid; Hu; B12; Vasculitis; Neoplastic; Sarcoid
Infection: Lyme; HIV; Rabies; Syphilis; West Nile
Hereditary: Polyglucosan; Fabry; HexA; Porphyria; Prion; ALS; Cowchock; NAD; Krabbe; MLD

Face
Bell's Palsy
Melkersson; Tangier
Polyradiculopathies:
Sarcoid; Lyme; GBS
Motor neuron disorders:
ALS; Kennedy's; Möbius
Rule out: MG; Myopathy

Time Course

Acute
Immune: GBS; Vasculitis
Toxic: Botulism; Thallium; Vacor;
Drugs; Org-phos
Infections: Tick; Lyme; HIV;
Leptospirosis; Rabies; CMV; West Nile
Porphyria; Paraneoplastic (Anti-Hu)
Rule out: Myopathy; MG; Spinal

Relapsing
CIDP ± GBS
Hereditary: Porphyria; HNPP; HNA;
Thermosensitive; Refsum

Childhood Onset
Immune: CIDP; GBS
Hereditary: NAD; HMSN I & III; MLD
Giant Axonal; Lethal neonatal; Tangier
CCFDN; Congen Hypomyelin; Krabbe

Hereditary
CMT Demyel Dominant: IA PMP-22; IB & IE P0; IC LITAF; ID EGR2; IF NFL
HNPP PMP-22, KARS; YARS; Thermosensitive; SOX10; DNM2; 10q24
III (PMP-22; P0; EGR2); CMT + Intermed NCV: 10q24; DNM2; YARS; INF2; GNB4; P0; GJB1
CMT Demyel Rec: III; 4A GDA P1; 4B MTMR2; 4B2 SBF2; 4B3 SBF1; 4C SH3TC2; 4D NDRG1;
4E EGR2; 4F Prx; 4G HK1; 4H FGD4; 4J FIG4; CCFDN CTDP1
CMT X-linked: Connexin-32; Xp22.2; Xq26; Cowchock AIFM1; PRPS1; PDK3; AUNX1; Xq23
CMT Axon, AD: 2A MFN2; 2B RAB7; 2C TRPV4; 2D GARS; 2E NFL; 2F HSPB1; 2G 12q12; 2I P0; 2K GDAP1; 2L: HSPB8;
2M DNM2; 2N AARS; 2O DYNC1H1; 2P LRSAM1; 2Q DHTKD1; HMSN-P TFG; HNA1 SEPT9; VCP; 2T DNAJB2; 2U MARS
2V NAGLU; 2W HARS; 2Y MORC2; 2Z ; MORC2; 2CC NEFH; DGAT2; TFG; MME
CMT Axon AR: 2A LAM A/C; 2B MED25; F HSPB1; 2K GDAP1; P LRSAM1; R TRIM2; S IGHMBP2; T MME; X SPG11;
P0; HINT1; HSJ1; MFN2; PNKP; MCM3AP
CMT + CNS: Andermann KCC3; Deafness; Optic Δ; NAD; GAN Gigaxonin;
AR-CMT2 + Pyramidal 8q21; Lethal Neonatal; TDP1
Myelin, Recessive: Cockayne; Refsum (PAO & Peroxin-1); Krabbe; MLD; CMT 4E; P0; EGR-2
ALS: **AD** SOD; SETX; VAPB; ANG; NFH; TDP-43; FIG4; VCP; Ataxin-2; GRN; HNRNPA1; BSCL2; Matr3; TUBA4A; DAO;
GLE1; SS18L1; ANXA11; ATXN2; BSCL2; FUS; c9orf72; PFN1; UBQLN2; SQSTM1; ErbB4; CHMP2B; CHCHD10; 20p13
AR NF-H; Alsin; PRPH; FUS; Spatacsin; OPTN; SIGMAR1; PNPLA6; c19orf12; PNPLA6; OPTN
SMA: AR Xq12; SMN; SCO2 & TK2 (Mito Δ); ATP7A; P 3q13; VAPB; DYNC1H1; TRPV4
HMN: HSPB 1,3 & 8; GARS; BSCL2; ATP7A; DCTN1; SETX; PLEKHG5; FBLN5; IGHMBP2
Sensory, Dominant: HSAN1 SPTLC1 & 2; ATL1 & 3; DNMT1; GJB3; ARHGEF10; RNF170; PRNP; SCN9A & 11A
Sensory, Recessive: HSAN2 HSN2; HSAN3 (Riley-Day) IKBKAP; Tangier; SCN9A; Dystonin; FLVCR1; MPV17; PRDM12
HSAN4 NTRK1; HSAN5; NGF-β; ATM; FA FRDA; Fabry; DHH; NARP; HSN2; FAM134B; ATSV; CCT5; CLTCL1

Other Features

Paraneoplastic
Myopathy: RIIM; DM-VP; Type II atrophy;
Decorin Antibody; Rippling muscle; Metabolic; Scleromyxedema
NMJ: MG (Thymoma); LEMS (Small cell Ca)
Nerve: Hu; Motor neuronopathy; Isaac's; M-protein
Neuromyopathy (wt loss > 15%); Autonomic (Hu)
Spinal: Necrotizing; Stiffman (Breast +)
Cerebellar: Yo (Gyn); Tr (Lymphoma); Hu; LEMS; Ma
Opsoclonus/Myoclonus - Child (Neuroblastoma), Adult, Ri
Encephalopathy: Hu; Thymoma; Ma2 (Ta)

GI disorders
Neuropathy
Hereditary: Hirschsprung; MEN; Pseudoobstruction
Infection: Polio; Chagas
MNGIE; Diabetes; Amyloid; Hu; POEMS; Porphyria
Vitamin ↓: B_{12}; E
Myopathy: Inflammatory; ↑ Thyroid; Visceral
Dystrophy: Myotonic; Duchenne; Oculopharyngeal;
Oculopharyngodistal
Spinal: Syringomyelia

Large nerves
Leprosy; CIDP; Amyloid;
Acromegaly; Entrapment
Hereditary: Refsum;
HMSN I & III; Noonan
Neoplasm: Focal;
Diffuse: Lymphoma
Local: Entrapment; Tumors;
Mononeuropathy

Demyelination
Immune: GBS; CIDP; MMN; MAG;
Sulfatide; GALOP; POEMS
Toxic: Amiodarone; Perhexiline;
Diphtheria; Na cyanate; Buckthorn
Hereditary:
HMSN I, III, IV; HNPP;
Krabbé; MLD; Refsum
Mitochondrial: MNGIE; NARP

Spontaneous Activity
Complex repetitive
Dystonia
Fasciculations
ALS; MMN; Normal
Hyperekplexia (Startle)
Myokymia
Isaac's; Radiation
Neuromyotonia
Myotonia
Stiffman Syndrome
Tetanus

Antibodies: For M-protein use immunofixation
IgM vs GM1, NS6S or GalNAc-GD1a: Motor neuropathy
IgG vs GM1, GM1b, GalNAc-GD1a: AMAN
IgM vs GM2: Sensory > Motor; Demyelinating
IgM vs GD1b: Sensory; Axonal; CANOMAD
IgM vs TS-HDS or IgG vs FGFR3: Sensory; Pain; Axonal
IgG vs GQ1b: Miller-Fisher; Ophthalmoplegia
IgM vs MAG: Sensory > Motor; Ataxia; Tremor
IgM vs Sulfatide or GALOP: Sensory; Gait Δ
IgG vs Hu: Sensory neuron; IgG vs Yo, Tr, Hu: Cerebellar
IgM vs Tubulin or IgG vs NFASC, CNTN1: Demyelin PN
IgG vs CRMP5: Polyneuropathy + Cerebellar

Nerve biopsy: ↑ Utility
Asymmetric PN
Age > 65 + Disabled
Sensory loss
Abnormal NCV
Diagnoses
Vasculitis; ± CIDP
Systemic: Leprosy;
Amyloid; Sarcoid
Hereditary: MLD
Giant axonal;
Fabry; Krabbé

Alan Pestronk 7/12/2017 More information at Neuromuscular Website: http://neuromuscular.wustl.edu