Other Neuromuscular Disease

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## I. Muscle & Nerve Disease

<table>
<thead>
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<th>Muscle &amp; Nerve Disease</th>
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<tr>
<td>Muscular dystrophy</td>
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<td>Myasthenia Gravis</td>
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<td>Metabolic disease</td>
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<td>Idiopathic fibrosis of muscle</td>
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<td>Pyomyositis</td>
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<td>Myositis ossificans</td>
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<tr>
<td>Hereditary neuropathy</td>
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<td>Syringomyelia</td>
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<td>Arthrogryposis multiplex congenita</td>
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Management

• Accurate diagnosis
• Effective treatment
• Genetic counsel
Chief complaint

- Delayed developmental milestones
- Abnormal gait
- Cavus, equinus
History

• Birth history: birth weight, Apgar score
• Growth & development
• Family history: positive
• Static or progressive
• Seizure
Physical examination

- Walking, performing simple tasks, run
- Skin: tuberous sclerosis, neurofibromatosis
- Face: SMA, congenital myotonic dystrophy
- Tongue: fasciculation in LMN lesion
- Ophthalmologic examination
- Muscle testing: muscle power, tone and bulk
- Neurological evaluation
Orthopedic Manifestations

- Delayed development
- Abnormal gait
- Foot deformity (cavus, equinovarus, flatfoot)
- Spine deformity (scoliosis, lordosis)
- Hip subluxation or dislocation
- Joint contracture
- Weakness
Other Manifestations

- Lung: insufficiency
- Heart: heart block, bradycardia, cardiac myopathy, CHF
- Brain: mental retardation, encephalopathy
- Phalanx: dysarthria, dysphagia
- Malignant hyperthermia
Diagnostic Test

• Hematologic study
• EMG
• Nerve conduction study
• Muscle biopsy
• Nerve biopsy
• Genetic & molecular biology study
Hematologic study

- CPK, SGOT, aldolase
EMG

neuropathy > myopathy

1. Denervation fibrillation

2. High amplitude increased duration motor unit potential

1. Low amplitude short duration polyphasic wave

Electromyography (motor units during active contraction)

Werndig-Hoffmann disease
Nerve conduction study

- peripheral neuropathy
- Velocity
  - 45 - 65 m/sec
  - infant: <
Muscle biopsy

- Rectus abdominis, vastus lateralis, gastrocnemius, deltoid, biceps
- Liquid nitrogen(-160°): L/M with special stain
- Routine histology & E/M
Nerve biopsy

- Sural nerve
  - Distal location
  - No autonomous zone
Other

- EKG, PFT, MRI, ophthalmologic examination
Genetic & molecular biology study

- dystrophin test: ELISA (enzyme linked immunosorbent assay), western blot
- **DNA marker** : PCR (polymerase chain reaction), Southern blot analysis
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<tr>
<th></th>
<th>Myopathy</th>
<th>Peripheral Neuropathy</th>
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<tr>
<td>Muscle atrophy</td>
<td><strong>Proximal</strong>, symmetric</td>
<td>Distal, asymmetric</td>
</tr>
<tr>
<td>Bulbar sign</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Fasciculation</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Sensory abnormality</td>
<td>-</td>
<td>+, -</td>
</tr>
<tr>
<td>DTR</td>
<td>decreased</td>
<td><strong>Lost</strong></td>
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<tr>
<td>EMG, muscle biopsy</td>
<td>myopathy</td>
<td>neuropathy</td>
</tr>
<tr>
<td>NCV</td>
<td>Normal</td>
<td>decreased</td>
</tr>
<tr>
<td>CPK</td>
<td>increased</td>
<td>normal</td>
</tr>
<tr>
<td><strong>Myalgia, muscle contracture, Hypotonia</strong></td>
<td>+</td>
<td>+</td>
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II. Myopathy
1. MUSCULAR DYSTROPHY

- Non-inflammatory
- Progressive degeneration of skeletal muscle
- Nervous system involvement: (-)
Classification of Muscular Dystrophy

Sex-linked muscular dystrophy
- Duchenne
- Becker
- Emery-Dreifuss

Autosomal recessive muscular dystrophy
- Limb-Girdle
- Congenital muscular dystrophy
Classification of Muscular Dystrophy

Autosomal dominant muscular dystrophy

Fascioscapulohumeral
Distal
Ocular
Oculopharyngeal
A. Duchenne M. Dystrophy

- **Dystrophin**: component of cell membrane cytoskeleton, 0.002% of skeletal muscle protein
Duchenne M. Dystrophy

- Most common
- 3-6 years of age
- X-linked recessive
- New mutation: 1/3
Duchenne M. Dystrophy

- **Skeletal muscle**: proximal muscle group, pseudohypertrophy, contracture of tendo Achillis & iliotibial band
- **Cardiac muscle**: sinus tachycardia, right ventricular hypertrophy, and heart failure (10%)
- **Brain**: mental retardation, encephalopathy
1. Gower sign
2. Meyeron (sliding through) sign
3. Ober test
Readings shown as times normal and in ranges of possible values seen in specific diseases. Differences in technique cause variability in range of normal values.
Duchenne M. Dystrophy

Normal

Duchenne M. Dystrophy
Duchenne M. Dystrophy

• Prenatal diagnosis as early as the 12th week of gestation by chorionic villi biopsy, amniotic fluid
Treatment

• physical therapy
• orthoses
• surgery: contracture, weakness, scoliosis
  • (medication: steroid, azathioprine, aminoglycoside)
  • (myoblast implantation)
  • (Gene, stem cell therapy)
• genetic and psychological counseling
B. Becker M. Dystrophy

- Less severe
- X-linked recessive trait
- Onset: > 7 years of age
- Slow progressive
Becker M. Dystrophy
C. Emery-Dreifuss muscular dystrophy

X-linked recessive trait: emerin deficit

Mild muscle weakness in the first 10 years

Tendo Achillis, elbow, & neck extension contractures
Emery-Dreifuss muscular dystrophy

- Early neck extension contractures
- Cardiomyopathy
- Sudden death due to complete heart block
D. Limb girdle type muscular dystrophy

Autosomal recessive: *sarcoglycanopathy* (plasma membrane)

Pelvic girdle > shoulder girdle, 10-15 years of age

Face involvement: -

Sx: similar to Becker
E. Facioscapulohumeral dystrophy

Autosomal dominant, 10-20 years of age

Gene defect: FRG1 on 4q35

Face, shoulder girdle, upper arm

Popeye appearance

Severe lumbar lordosis in infantile type

Tx: scapulocostal fusion (rare)
F. Congenital muscular dystrophy

- Merosin (α2 chain of Laminin-2) deficit
- Contracture, hypotonic, pseudohypertrophy, floppy baby
- Fukuyama type: severe cardiomyopathy & brain malformations, mental retardation, seizure
- Non- Fukuyama type: no mental retardation, most survive into adulthood
Congenital muscular dystrophy
2. Myotonic Dystrophy

- Inability of skeletal muscle to relax
- Myopathy involving face, eyes, jaw, neck and distal limb muscle
- **Myotonia**: delay in relaxation of hand grip, elicited by striking the thenar eminence or deltoid
- **Autosomal dominant**, affect myototonin protein kinase gene
- Most common muscular dystrophy in adults
Myotonic Dystrophy

- Fish mouth, ptosis, expressionless face, frontal baldness, wasting of temporal & masseter muscles
- Ambulation: Sx+20 Y
- Mental retardation, cardiac arrhythmia, malignant hyperthermia
- Developmental delay & high morbidity in congenital type
Myotonic Dystrophy

Myotonic Dystrophy

Frontal balding

'Hatcher' facies due to atrophy of temporalis muscle

Ptosis and drooping mouth due to weakness of facial muscles

Wasting of sternocleidomastoid muscle

Cataracts

Gynecomastia

Percussion myotonic reaction: thumb moves sharply into opposition and adduction on percussion of thenar muscles and returns to initial position slowly

Electromyogram showing spontaneous myotonic discharge evoked by needle insertion

dive-bomber sound
3. Myasthenia Gravis

- Antibody to acetylcholine receptor at NM junction
- Most common in adult, 10%—child, 1%—infant
- Thymus abnormality: common
- Hormonal regulation: after puberty female predominance (14:1)
• Neonatal transient myasthenia gravis
  10–15% of infants in myasthenia gravis mother
  Neostigmine, exchange plasmapheresis. High-dose immune globulin
• Congenital myasthenic syndrome
  Not an autoimmune disease, acetylcholine receptor anomaly
  Presynaptic: cholinesterase inhibitor
  Postsynaptic: cholinesterase inhibitor, 3,4-diaminopyridine, quinidine or fluoxetine
  Synaptic type: no effective drug treatment
  Poor suck, a weak cry
  Variable severity
  Arthrogryposis multiplex congenita may present
• Juvenile myasthenia gravis
  Onset: 10 years or older in 75%
  Ptosis, ophthalmoparesis
  Extremities weakness in fewer children
  Myasthenia crisis (respiratory difficulty) in 40% of untreated patient
4. Metabolic disease of muscle

- Transient and recurring weakness or paralysis of skeletal muscle: calcium, chloride, and sodium “ion channel” gene mutation
- Periodic paralysis
  - Hypokalemic periodic paralysis
  - Hyperkalemic periodic paralysis
McArdle's Syndrome; Myophosphorylase Deficiency

- Autosomal recessive
- Disorder of muscle glycogen metabolism
- Muscle pain, cramping, weakness, and myoglobinuria following exercise
- Relieved by rest
5. Idiopathic fibrosis of muscle (Progressive Fibrosis of the Quadriceps)

- Extension contracture of the knee develops in early childhood due to fibrosis of the quadriceps muscle
- **Multiple injections** into the thigh muscles during early infancy? Distal vastus intermedius
- Gluteus and deltoid muscle contracture +
6. Pyomyositis

- A deep bacterial infection of skeletal muscle in severe septicemia or immunocompromised patients
- S. aureus resistant to methicillin
- Iliopsoas, obturator, adductor—similar Sx to septic hip
7. Myositis ossificans

- Traumatic Myositis ossificans
- Repeated microtrauma and overuse injuries
- Severe neurologic disorders
8. Polymyositis / Dermatomyositis

- Inflammatory myopathy, 2–15 years old
- Severe proximal muscle weakness
- Dermatomyositis > Polymyositis
- Skin rash
- Calcification (subcutaneous, muscle)
III. Neuropathy
1. Spinal dysraphism

- Spina bifida cystica
  Meningocele
  Myelomeningocele

- Occult spinal dysraphism
  Spinal lipoma
  Diastematomyelia
  Dermal sinus
  Tight filum terminale

- Spina bifida occulta

- Rachischisis
2. Poliomyelitis

- Flaccid paralysis, muscle imbalance, growth—postural anomaly, soft tissue & joint contracture, LLD

- Surgery:
  - Release of soft tissue & joint contracture
  - Tendon transfer
  - Corrective osteotomy
  - Arthrodesis
  - LLD correction
Postpoliomyelitis syndrome

- Overuse syndrome: fatigue, muscle & joint pain, new muscle weakness, functional loss, cold intolerance, new atrophy
- Conservative treatment
3. SPINAL MUSCULAR ATROPHY

- Pathologic continuation of apoptosis (survivor motor neuron gene defect) - degeneration of anterior horn cell (motor neuron disease)
- Autosomal recessive, chromosome 5q11-q13
- Acute event without progression
- Hypotonia – weakness – thin muscle mass – negative DTR (LMN) – congenital contracture (10%)
- Fasciculation & fine tremor of the fingers
Spinal Muscular Atrophy

- **Type I**
  (acute Werdnig - Hoffman disease): - 6M,
  pathologic fracture due to in utero osteoporosis

- **Type II**
  (chronic Werdnig - Hoffman disease): 6-24M
  never able to walk

- **Type III**
  (Kugelberg-Welander disease): 2-10Y
  not to able to run, walk for several years, ventilator
Bell shaped thorax, frog-leg & jug-handle U/E
Physical examination

- Developmental milestone delay
- Gait
- Foot deformity
- Muscle testing
Treatment

• contracture
• hip dislocation±
• scoliosis
4. Hereditary Neuropathy

- Hereditary motor and sensory neuropathy
- Hereditary sensory neuropathy
- Hereditary spinocerebellar ataxia (Friedreich ataxia)
A. HEREDITARY MOTOR & SENSORY NEUROPATHY

- Type I, II, III: pediatric onset
- IV, V, VI, VII: late onset
## Classification of HMSN

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<tr>
<th>Type</th>
<th>Terminology</th>
<th>Inheritance</th>
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<tr>
<td>I</td>
<td>Charcot-Marie-Tooth syndrome (hypertrophic form)</td>
<td>Autosomal dominant</td>
</tr>
<tr>
<td></td>
<td>or Roussy-Levy syndrome (areflexic dystaxia)</td>
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<tr>
<td>II</td>
<td>Charcot-Marie-Tooth (neuronal form)</td>
<td>Autosomal dominant</td>
</tr>
<tr>
<td>III</td>
<td>Dejerine-Sotta disease</td>
<td>Autosomal recessive</td>
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## Classification of HMSN

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<th>Type</th>
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<tr>
<td>IV</td>
<td>Refsum disease</td>
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<tr>
<td>V</td>
<td>Neuropathy with spastic paraplegia</td>
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<tr>
<td>VI</td>
<td>Optic atrophy with peroneal muscle atrophy</td>
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<tr>
<td>VII</td>
<td>Retinitis pigmentosa with distal muscle weakness and atrophy</td>
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1) HMSN type I

- Charcot-Marie-Tooth disease, hypertrophic form
- **Autosomal dominant**, abnormal gene: 17p11.2 locus – peripheral myelin protein 22
- X-linked abnormal gene: Xq13.1 locus – connexin 32
- **Demyelinating disorder**
- sensory involvement: large myelinated nerve fibers (proprioception & vibration)
- autonomic involvement: pallor, cold feet
HMSN type I

- 5 – 15 Y, clumsy, falling, tripping
- peroneal muscular atrophy, **stork-like leg**, ankle dorsiflexor weakness, foot drop
- **pes cavus**: plantar flexed 1st metatarsal --- tripod effect --- hindfoot varus, forefoot supination: Coleman block test
- claw toes & hand
Diagnosis

- P/E, nerve conduction velocity, muscle biopsy
- sural nerve biopsy (onion bulb: proliferated Schwann cell cytoplasm),
Roussy-Levy syndrome (areflexic dystaxia)

- HMSN type I
- + static tremor in the hand
Treatment

- Progesterone receptor antagonist
- Stabilization of the ankle
- Plantar release, tibialis posterior tendon transfer, calcaneal osteotomy, mid tarsal osteotomy, triple arthrodesis
- Claw toes
- Hip dysplasia
- Scoliosis
2) HMSN type II

- Charcot-Marie-Tooth disease, **neuronal type**
- Autosomal dominant, abnormal gene: KIF1B (1p35-p36)
- Slow progression & less disability
- sural nerve biopsy: axonal degeneration
3) HMSN type III

Dejerine–Sottas disease
Similar to type I but more severe
Kyphoscoliosis
Argyll-Robertson pupil
B. Hereditary Sensory Neuropathy

- Familial autonomia (Riley-Day syndrome)
- Congenital insensitivity to pain & anhidrosis
1) Familial autonomia (Riley-Day syndrome)

- decreased number of small unmyelinated nerve fibers
- common in Eastern European Jews
- poor sucking & swallowing, excessive sweating & erythema
2) Congenital insensitivity to pain & anhidrosis (CIPA)

• Boys > girls
• High fever, frequent burns & traumatic injuries
• Total absence of unmyelinated nerve fibers: pain, temperature & autonomic function
C. FRIEDREICH ATAXIA

- Most common hereditary ataxia, 7 – 15 years, autosomal recessive
- Neurodegenerative disorder, decreased frataxin in mitochondria (GAA repeat)
FRIEDREICH ATAXIA

- Dorsal root ganglia cell loss: posterior column, spinocerebellar tract, peripheral nerve degeneration
- Ataxia, cardiomyopathy, scoliosis, cavus, DM
- + Babinski sign, areflexia: degeneration of corticospinal tract with involvement of peripheral sensory neurons (UMN + peripheral sensory neuronopathy)
5. Syringomyelia

- A disorder in which a **cyst** or cavity forms within the **spinal cord**
- This cyst, called a **syrinx**, can expand and elongate over time, destroying the spinal cord
6. Arthrogryposis multiplex congenita

- Decreased fetal movements (akinesia)

Extrinsic

Intrinsic: Neuropathic form—CNS and spinal cord are malformed, Myopathic form

- A rare congenital disorder that is characterized by multiple joint contractures

- Clubfoot, hip dislocation, patellar dislocation

- Can include muscle weakness and fibrosis

- Non–progressive disease
IV. Orthopedic Managements

- Foot deformity (cavus, equinovarus, flatfoot)
- Spine deformity (scoliosis, lordosis)
- Hip subluxation or dislocation
- Joint contracture
- Weakness
Thank You