Upper Motoneuron (UMN) Diseases

Last updated: April 22, 2019

FAMILIAL (s. HEREDITARY) SPASTIC PARAPLEGIAS

<table>
<thead>
<tr>
<th>Type</th>
<th>Genetic Nomenclature</th>
<th>Inheritance</th>
<th>Gene Locus</th>
<th>Population</th>
<th>Product</th>
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<tbody>
<tr>
<td>Complicated</td>
<td>SPG1</td>
<td>X-linked</td>
<td>Xq28</td>
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<td>Xq28 or Xq21*</td>
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<td>Protocoll protein</td>
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<td>8p11-q13</td>
<td>Tunisian</td>
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<td>AR</td>
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<td>Tunisian, European</td>
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<td>ALS4</td>
<td>AD</td>
<td>9q34</td>
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</table>

*other mutations in same gene cause Pelizaeus-Merzbacher disease!  

Prevalence – 10 per 100,000

CLINICAL FEATURES

Clinical heterogeneity - some cases are mild and some are severe.

- variability often occur within same family.
- onset in 2-4th decades (infancy ÷ late adulthood).

Uncomplicated ("pure") FSP (more common):  
1) slowly progressive spasticity of lower extremities (weakness of hip flexion & foot dorsiflexion)
At onset, disorder is one of coordination; there may be no muscle weakness!
Spasticity is usually most disabling component!  
- slow, stiff gait, trip easily, unable to run.
- deep tendon reflexes are pathologically increased (often ≥ grade 4).
- crossed adductor reflexes, ankle clonus, extensor plantar responses.  
- gait disturbance progresses insidiously and continuously: paraparesis → paraplegia; most patients become nonambulatory at 60-70 yrs of age (respiratory function is spared - long survival).
- pes cavus may develop (50-50%)
2) mild (?) decrease in proprioception below knees.
3) urinary sphincter dysfunction (urgency and incontinence) late in disease.

No abnormalities of corticobulbar tracts or upper extremities (except possibly brisk deep tendon reflexes).

Complicated FSP - presence of other neurological problems (optic neuropathy, retinopathy, extrapyramidal disturbance, dementia, ataxia, ichthyosis, mental retardation, deafness).

DIAGNOSIS

- of exclusion.

Molecular diagnosis - available only to families who have been linked to one of identified loci.

Electrophysiological studies are most revealing:  

- somatosensory evoked potentials of lower extremities - conduction delay in dorsal column fibers (even without clinically evident sensory loss).
- cortical evoked potentials - reduced conduction velocity and amplitude in lumbar spinal segment muscles (potentials of arms are either normal or mildly slow).
- nerve conduction studies - normal.

MRI of brain / spinal cord – unrevealing (a spinal cord atrophy).

FSP can mimic treatable disorders:  
1) vitamin B12 deficiency
2) IDA/ARPCAM syndrome
3) cerebral spongiosis
4) multiple sclerosis

TREATMENT

- to combat problems associated with chronic paraplegia (BACLOFEN or DANTROLENE for leg spasticity. OXYBUTYNIN for bladder spasticity).  
- intrathecal BACLOFEN is gaining favor because gait may improve!

PRIMARY LATERAL SCLEROSIS (PLS)

- pure UMN component of ALS (just as spinal muscular atrophy is purely LMN version).

In theory, ALS may start as purely UMN disorder but that seems truly exceptional.

SPG - broad group of disorders characterized by lower extremity spasticity and weakness.  
- degeneration of most distal portions of longest ascending and descending axons (esp. corticospinal tracts to legs), fasciculus gracilis, spinocerebellar tracts.
- neuros of origin and PNS are unaffected.

* backpacking; carbohydrate.
• selective loss of large pyramidal cells in precentral gyrus → degeneration of corticospinal and corticobulbar projections.

• < 5% of all cases of motor neuron disease.

**Clinical Features**
- “spastic paraparesis of middle life”:
  1) onset after age 40.
  2) slowly progressive spastic leg weakness (gait disorder) → becomes stable* (patients rarely lose ability to walk with cane or other assistance).
  3) spastic dysarthria and dysphagia (progressive pseudobulbar palsy).

• no sensory, no sphincter symptoms.

*course may be as aggressive as in ALS!

**Diagnosis**
- MRI - no consistent abnormality (many asymptomatic people > 40 yrs. show white matter lesion in brain!).
- CSF - normal (protein content may be increased).
- EMG - no signs of denervation (but sometimes does).
- Magnetic brain stimulation - delayed conduction of corticospinal tracts.
- Sensory-evoked potentials - normal

**Bibliography** for ch. “Spinal Disorders” → follow this [LINK >>](#)