Upper Motoneuron (UMN) Diseases

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Familial (s. Hereditary) Spastic Paraplegias

**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).

\*nearly normal in brainstem but show increasing atrophy at more caudal levels in spinal cord (“dying back”)

* **neurons of origin** and **PNS** are unaffected.

| **Type** | **Genetic Nomenclature** | **Inheritance** | **Gene Locus** | **Population** | **Product** |
| --- | --- | --- | --- | --- | --- |
| Complicated | SPG1 | X-linked | Xq28 |   | L1CAM (L1 cell adhesion molecule) |
| "Pure" (uncomplicated)       | SPG2 | X-linked | Xq28 or Xq21\* |   | Proteolipid protein |
| SPG3 | AD | 14q12-q21 | European, North American | ? |
| SPG4 | AD | 2p21-24 | European, North American |   |
| SPG5A | AR | 8p11-q13 | Tunisian | ? |
| SPG5B | AR | ? | Tunisian, European | ? |
| SPG6 | AD | 15q11.1 | North American | ? |
| SPG7 | X-linked | ? | Single family | ? |
| Spastic paraplegia with amyotrophy | ALS4 | AD | 9q34 | Single family | ? |

\*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 (30-50%).
	1. mild (!) decrease in proprioception below knees
	2. 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 (± spinal cord atrophy).

FSP can mimic treatable disorders:

1. vitamin B12 deficiency
2. dopa-responsive dystonia
3. cervical spondylosis
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.

* 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 >>](http://www.neurosurgeryresident.net/Spin.%20Spinal%20Disorders%5CSpin.%20Bibliography.pdf)

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