

Upper Motoneuron (UMN) Diseases

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FAMILIAL (S. HEREDITARY) SPASTIC PARAPLEGIAS 1
 PRIMARY LATERAL SCLEROSIS (PLS)..... 1

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):

- 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%).
- mild (!) **decrease in proprioception** below knees
- 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:

- vitamin B₁₂ deficiency
- DOPA-responsive dystonia
- cervical spondylosis
- 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”:

- 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 >>](#)