SPINO CEREBELLAR DEGENERATION
(By Dr. S. Uma Devi M.D)

Spinocerebellar degeneration is a rare genetic disorder with multiple types resulting from degeneration of cerebellum and spine.
Slowly progressive ataxia with other signs
This can be predominantly
1. Spinal form
2. Cerebellar form or
3. Spinocerebellar form.
Atrophy of cerebellum causes incoordination and ataxia
Spinal atrophy causes spasticity.
(Brain stem neurons may be also affected)
The basic differences between some of the common forms in this group are tabulated below. (There are many specific types, more than 29.)
The degree of degeneration varies in each type
There is overlap of symptoms among different types.
Not easy to diagnose types based on clinical criteria alone.

Friedrichs Ataxia and differential diagnosis

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Age of onset</th>
<th>Rate of progress</th>
<th>Reflexes</th>
<th>Sensory signs</th>
<th>Cerebellar deficit</th>
<th>Other important clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Friedrich’s syndrome</td>
<td>First decade</td>
<td>Slowly progressive</td>
<td>Absent DTR</td>
<td>Moderate loss</td>
<td>severe</td>
<td>Disarthenia, nystagnus mental retardation, Skeletal deformity cardiomegaly, Autosomal dominant, recessive or sporadic</td>
</tr>
<tr>
<td>Roussy-levy syndrome</td>
<td>1st or 2nd decade</td>
<td>Slowly progressive</td>
<td>Absent DTR</td>
<td>Moderate loss</td>
<td>Sensory ataxia+</td>
<td>No dysartria no nystagmus, It is intermediate between Friedrichs &amp; Charcoat Mary. (in summary Ataxia, areflexia and atrophy of muscles occur)</td>
</tr>
<tr>
<td>Charcoat-Tooth Syndrome</td>
<td>1st or 2nd decade</td>
<td>Slowly progressive</td>
<td>Absent DTR</td>
<td>Moderate loss</td>
<td>None</td>
<td>Predominant peroneal muscular atrophy, Nerves thickened Optic &amp; VIIIth nerve atrophy, Autosomal dominant</td>
</tr>
<tr>
<td>Bassen-Kornwigs syndrome</td>
<td>1st decade</td>
<td>Slowly progressive</td>
<td>Absent</td>
<td>Moderate loss</td>
<td>severe</td>
<td>May have mental retardation, Acanthocytosis, (Star shaped RBCs), Steatorrhea</td>
</tr>
</tbody>
</table>
Refsum’s Disease
Neuro cutaneous disorder
Accumulation of phytanic acid in plasma and tissues

1st decade
Slowly progressive
Absent
Moderate loss
severe
Nictalopia
Retinal degeneration
Icthyosis
Deafness
Arrhythmias
↑ serum phytic acid
Autosomal recessive

Hereditary spastic paraplegia

1st or 2nd decade
Slowly progressive
Hyperreflexia clonus Plantar extensor
Minimal loss
None
Paraplegia
Impaired bladder and bowel function
May occur in family with Friedrich or OPCD
Autosomal dominant or recessive or sporadic

Nomenclature; has varied over the years. Presently SCA type 1 to SCA22 (excluding No 9) thus far 29 different gene mutations found.

**Genetics:**
Defect: - Expansion of CAG triplet repeat
Normal

![CAGCAG CAGCAGCAG]

Expanded:

![CAG CAGCAG CAGCAGCAG CAGCAG CAGCAGCAGCAGCAG CAGCAG]

This type of abnormal expansion of CAG trinucleotide repeat is the basic genetic defect
CAG is the codon for aminoacid glutamine
Gene for SCA 1 is found on chromosome 6.
Manner of inheritance can be autosomal dominant, recessive, rarey X linked.

**Investigations:**
Elicitation of family history is important in diagnosis.
DNA based testing for the genetic defect - 100% diagnostic
Brain scan confirms the atrophy

**Treatment:**
There is no cure.
Underlying causes like metabolic derangement or vitamin disease is correctable
Physical therapy strengthen the muscles.
Special appliances help walking and other daily activities.
Lot of research is going on in understanding the disordered genetics.

<table>
<thead>
<tr>
<th>SCA Type</th>
<th>findings and comments</th>
<th>Mutation</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCA-1 (3-15%)</td>
<td>Hypermetric saccades, slow saccades, UMN</td>
<td>CAG repeat, 6p</td>
</tr>
<tr>
<td>SCA2 (6-15%)</td>
<td>Diminished velocity saccades, areflexia</td>
<td>CAG repeat, 12q</td>
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<td></td>
<td>Common in Cuba.</td>
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<tr>
<td>SCA3 (MJD, 30-40%)</td>
<td>Gaze-evoked nystagmus, UMN, slow saccades.</td>
<td>CAG repeat, 14q</td>
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<tr>
<td></td>
<td>Common in the Azores.</td>
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</tr>
<tr>
<td>SCA-4 (17 families)</td>
<td>areflexia</td>
<td>Chromosome 16q</td>
</tr>
<tr>
<td>SCA-5</td>
<td>Pure cerebellar</td>
<td>Chromosome 11</td>
</tr>
<tr>
<td>SCA-6</td>
<td>Downbeating nystagmus, positional vertigo</td>
<td>CAG repeat, 19p (Calcium channel gene)</td>
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<td>Symptoms can appear for the first time as late as 65 years old.</td>
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<tr>
<td>SCA-7</td>
<td>Macular degeneration, UMN, slow saccades</td>
<td>CAG repeat, 3p</td>
</tr>
<tr>
<td>SCA-8</td>
<td>Horizontal nystagmus</td>
<td>CTG repeat, 13q</td>
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<tr>
<td>SCA-9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SCA-10 (Zu et al, 5 families)</td>
<td>ataxia, seizures, primarily in Mexicans</td>
<td>Chromosome 22q linked, pentanucleotide repeat</td>
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<tr>
<td>SCA-11</td>
<td></td>
<td>15q</td>
</tr>
<tr>
<td>SCA-12 (rare, O'Hearn et al)</td>
<td>Head and hand tremor, akinseia</td>
<td>5q CAG</td>
</tr>
<tr>
<td>SCA-13 (rare)</td>
<td>Mental retardation</td>
<td>19q</td>
</tr>
<tr>
<td>SCA-14 (rare)</td>
<td>Myoclonus</td>
<td>19q</td>
</tr>
<tr>
<td>SCA-16</td>
<td>Head and hand tremor</td>
<td>8q</td>
</tr>
<tr>
<td>SCA-16</td>
<td></td>
<td></td>
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<tr>
<td>DRPLA</td>
<td>Chorea, seizures, primarily found in Japan</td>
<td>12p CAG expansion</td>
</tr>
</tbody>
</table>
SCA 19, 22?
Mild cerebellar syndrome, dysarthria

SCA 25
ataxia with sensory neuropathy, vomiting and gastrointestinal pain.

2p

Mexican-american pedigree of Grewal et al.
Pure cerebellar
Unknown

Mexican family of Matsuura et al
Gaze-evoked nystagmus, seizures
Autosomal dominant, chromosome 22q13-qter

**Short note on trinucleotide repeat**
Trinucleotide repeats are abnormal nonsense areas in human DNA. They tend to get bigger in time in successive generations causing decrease in age of onset this phenomenon is called **Anticipation**

Other trinuclotide repeat diseases are

1. Huntington's disease
2. Dentato rubro pallidoluysian atrophy
3. Bulbar muscular atrophy
4. muscular dystrophy
5. Juvenile myoclonic epilepsy

What are polyglutamine disease?

Refer next page
CAG repeat

Transcription

CAG repeat

Translation

Polyglutamine

CGG Repeat

CAG Repeat

GAA Repeat

CTG Repeat

Fragile X syndrome

Huntington's Disease
Machado-Joseph Disease
Spinocerebellar Ataxia etc.

Myotonic Dystrophy

Friedreich's Ataxia

www.brain.riken.jp/labs/cagrds