Giant Axonal Neuropathy

By Joshua Khani
What is Giant Axonal Neuropathy (GAN)?

- Dysfunction or disorganization in nerve cells
  - Swellings of axons caused by bundles of neurofilaments
- Autosomal recessive disorder
  - 25% chance of inheriting
- Incidence is unknown
- Progressive neurodegeneration
  - Generally appears in infancy
## Signs and Symptoms

<table>
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<tr>
<th>Initial (1&lt;sup&gt;st&lt;/sup&gt; Decade)</th>
<th>Advanced (2&lt;sup&gt;nd&lt;/sup&gt; Decade)</th>
<th>Late (3&lt;sup&gt;rd&lt;/sup&gt; Decade)</th>
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<tr>
<td>• trouble walking</td>
<td>• inability to walk</td>
<td>• bedridden</td>
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<td>• unusual posture</td>
<td>• loss of sensation and strength in limbs</td>
<td>• seizures</td>
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<td>• curly, lackluster hair</td>
<td>• loss of muscle control and coordination (ataxia and dysarthria)</td>
<td>• dementia</td>
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<td>• impaired reflexes</td>
<td>• hearing and visual problems</td>
<td>• mental retardation</td>
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Example of GAN
Clinical Testing

- Biopsy of peripheral nerve cells and other areas of the nervous system
  - Shows swollen axons
- Microscope examination of hair
  - Abnormal variations in diameters of the follicles and twisting of the hair along the long axis
- Electron Microscope of skin
  - Shows accumulation of spiraling filaments
- Other signs
  - Abnormal responses to stimulation in the visual and auditory cortex
  - MRI show white matter abnormalities
  - Moderate to complete reduction of nerve conduction velocity
Genetics of GAN

- Only one gene associated with Giant Axonal Neuropathy
- No other phenotypes correlated with a mutation of the GAN gene
- GAN encodes for the protein gigaxonin
- Gigaxonin plays a role in the architecture of the neurofilaments
  - Gigaxonin controls degradation of a microtubule-associated-proteins (MAPs)
  - The accumulation of MAP-1 B-LC, MAP8, and TBCB in a cell leads to neuron death
- The test for the GAN is done by sequence analysis
  - Located on chromosome 16 at locus 16q24.1
More Genetics

- Mutations: Missense, nonsense, frameshift
- GAN is ~65,000 base pairs long
Treatments

After assessment of abilities and progression of disorder, treatments are symptomatic and include a team of professionals.

- Neurologists, ophthalmologist, orthopedic surgeons, physiotherapists, psychologists, and speech and occupational therapists

- Even with this team, the disease cannot be stopped and life cannot be prolonged significantly
Questions?
Resources

- [http://www.nature.com/nrn/journal/v4/n9/fig_tab/nrn196_F5.html](http://www.nature.com/nrn/journal/v4/n9/fig_tab/nrn196_F5.html)
- [http://video.aol.com/category/giant-axonal-neuropathy](http://video.aol.com/category/giant-axonal-neuropathy)
- [http://journals.cambridge.org/download.php?file=%2FDMC%2FDMC46_10%2FS0012162204001215a.pdf&amp;code=6b07cc7f754eadb7d298f403f4d38dc7](http://journals.cambridge.org/download.php?file=%2FDMC%2FDMC46_10%2FS0012162204001215a.pdf&amp;code=6b07cc7f754eadb7d298f403f4d38dc7)
- [http://neuromuscular.wustl.edu/time/child.html#gan](http://neuromuscular.wustl.edu/time/child.html#gan)