Published on *My46* (https://www.my46.org) 01/20/2022

My46 Trait Profile

Amyotrophic lateral sclerosis

Other Names: Lou Gehrig's disease

Amyotrophic lateral sclerosis is a progressive condition that affects the function of the nerve cells in the brain and spinal cord. It can be caused by mutations in any one of many different genes, by environmental factors, or a combination of these.

Characteristics of Amyotrophic lateral sclerosis

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease involving changes in both the upper motor neurons (UMN) and lower motor neurons (LMN). UMN and LMN are the nerve pathways that send motor information from the brain (UMN) through the spinal cord and out to the muscles (LMN).

Initial symptoms of ALS may include muscle twitching or cramping, weakness of one or more extremities (leading to stumbling or poor grip), and bulbar symptoms (problems speaking or swallowing). Initial symptoms may vary, but typically progress to widespread muscle weakness and wasting (atrophy). Frontotemporal dementia, which affects the parts of the brain that controls personality, behavior, and language, affects about 10% of individuals with ALS.

About 90% of ALS diagnoses are known as sporadic ALS (SALS) the affected individual is the only one in the family with symptoms. For these individuals, the average age of onset is 56 years. The remaining 10% of patients have a family history of ALS (familial ALS or FALS) and an average age of onset of 46 years. For all types of ALS the average disease duration is 3 to 5 years, but can vary significantly. Death usually results from compromised breathing muscles (respiratory failure).

Diagnosis/Testing

The diagnosis of ALS is based on clinical features, electrodiagnostic testing (like EMG test that detects the electrical activity in muscles), and ruling out other health conditions with related symptoms. Family history is the most helpful tool to determine whether an ALS diagnosis is sporadic or familial. Among patients with FALS, about 50% will have a change or mutation in one of the FALS genes. So far, researchers have identified over 40 genes associated with FALS. Mutations in four of these genes (SOD1, C9ORF72, FUS, and TARDBP) account for a great majority of FALS cases; mutations in the remaining genes are found to be causative in a very small percentage of cases.

Genetic testing is available for many of the FALS genes. Knowing which gene is causative will not affect management or predict ones course of disease, but it may be helpful for family members interested in presymptomatic testing (i.e., testing before symptoms appear). Genetic testing strategies usually involve testing the most common FALS genes unless an individuals disease or family history indicates features known to a particular gene or mutation. Individuals with ALS with different causative genes usually have very similar courses with no distinguishing characteristics, although there are a few exceptions. For example, individuals with a certain mutation in the SOD1 gene have a much quicker disease course than average, while individuals with a mutation in the C9ORF72 gene may have a personal or family history of dementia.

Management/Surveillance

Most individuals with ALS benefit from having a team of medical professionals caring for their various needs in a

multidisciplinary clinic setting. This includes a neurologist, pulmonologist, occupational and physical therapist, speech therapist, respiratory therapist, nutritionist, and genetic counselor.

A nutritionist can provide instruction on thickening liquids and pureeing solid foods to allow patients to continue eating for as long as possible despite difficulty swallowing (dysphagia). Some individuals may have gastronomy tubes (i.e., tube put in the abdomen that delivers nutrition directly to the stomach) placed to maintain hydration and an adequate caloric intake.

Medications can be taken to help reduce muscle cramps and spasms. However, the side effects of these medications can cause tiredness.

Devices to help with breathing have also been found to have benefits for individuals with ALS. In 2010, the Food and Drug Administration approved a diaphragm pacing device for certain individuals with ALS. Also known as phrenic nerve pacing, this procedure implants a device that electrically stimulates the diaphragm (the muscle used during breathing) and allows individuals who would otherwise be ventilator-dependent to breathe. The device has provided some benefits to individuals with ALS, but more research is being conducted to further improve this technology.

Speech therapists can provide affected individuals with speech devices that allow them to communicate with others during various stages of the diseases. These range from alphabet boards to iPads and other high-tech computer devices and programs. There are also computers controlled by eye movements which facilitate communication for patients in very advanced stages of disease.

During the final stages of ALS, many individuals are often enrolled in hospice care where palliative care is offered. This includes continued ventilatory support, support for caregivers, and pain medication, if necessary. Bereavement counseling and support groups for family members and friends may also be offered by hospice workers.

Mode of inheritance

Most of the genes associated with FALS are inherited in an autosomal dominant pattern. This means that inheriting one copy of a FALS gene with a mutation is enough for an individual to be affected and show signs of FALS. The mutation can be inherited from an affected parent or it can occur brand-new (de novo) in an affected individual. The percentage of people to have a de novo mutation is not known.

Risk to family members

The risk to family members depends on whether an individual is diagnosed with SALS or FALS. The risk for first degree family members (parents, siblings, and children) of an individual with SALS is about 1%. For a majority of individuals with FALS, the chance for offspring to inherit the genetic mutation and develop symptoms is 50%. However, due to the wide variety of genes associated with FALS, the best way to determine risk is by looking at an individuals family history and genetic testing results from an affected family member.

Special considerations

None

Resources

ALS Association
http://www.alsa.org/
Les Turner ALS Foundation
http://www.lesturnerals.org
Muscular Dystrophy Association - USA (MDA-ALS Division)
http://www.als-mda.org
Genetics Home Reference: Amyotrophic lateral sclerosis
http://ghr.nlm.nih.gov/condition/amyotrophic-lateral-sclerosis

References

Chio, A. et al. (2012)."Extensive genetics of ALS: a population-based study in Italy." Neurology 79(19): 1983-1989.
DeJesus-Hernandez, M. et al. (2011)."Expanded GGGGCC hexanucleotide repeat in noncoding region of C9ORF72 causes chromosome 9p-linked FTD and ALS." Neuron 72: 24556.
Kinsley L, Siddique T. (Updated 31 May 2012). Amyotrophic Lateral Sclerosis Overview. In: GeneReviews at

Created: 04/2013 **Created by:** Lisa Kinsley, MS, LCGC

Updated: mm/yyyy **Edited by:** Seema Jamal, MSc, LCGC