Stiff-Person Syndrome Fact Sheet

Syndrome Description

The initial definition of stiff-person syndrome included axial stiffness and rigidity with superimposed spasms believed to be associated with anti-GAD antibodies. However, up to 40% of patients lacked the glutamic acid decarboxylase antibodies constituting what was believed to be an anti-GAD-negative variant. GAD-negative status is no longer considered a separate entity from classic stiff-person syndrome. As more cases presented, multiple variations developed: stiff-baby, stiff-trunk, stiff-limb, jerking-limb, SPS with progressive encephalomyelitis with rigidity and myoclonus (PERM), and SPS with paraneoplastic syndrome.

Stiff-person syndrome is often found in a setting of other autoimmune diseases such as Type 1 diabetes, Hashimoto's disease, Graves' disease, vitiligo, pernicious anemia, myasthenia gravis, and epilepsy.

The disease is progressive, debilitating, and incurable. It requires ever-increasing quantities of GABAergic drugs to control the symptoms. Patients are at high risk for suicide.

Patients are shuffled from doctor to specialist and back again, often left in medical limbo without a diagnosis or true understanding of what the disease is, and isn't, and how it should be treated. Due to this lack of education, patients are at high risk in emergency medical situations.

In-depth information on professional websites and in medical textbooks is severely lacking.

Demographics

Research studies indicate that one in a million (7,000 out of 7 billion) people are afflicted with stiff-person syndrome. It affects both men and women. Onset is usually in the third to fifth decades of life but has affected a small number of children. Up to sixty-five percent of patients will become wheel-chair dependent and most will become disabled and unable to work. On average, the patients must take as many as three drugs per day, such as baclofen, benzodiazepines, antiseizure medications, or immunotherapy drugs, at increasingly high doses to control symptoms. No single therapeutic agent is sufficient to control the symptoms. They undergo expensive IVIG and plasmapheresis treatments with mixed results, but no true remission. There are only a few programs willing to consider stiff-person syndrome for stem-cell research studies, even though the outcome is optimistic.

Disability

Stiff-person syndrome is as debilitating as other progressive neuromuscular diseases such as multiple sclerosis, muscular dystrophy, and other dystonias. It is included under the Social Security Compassionate Allowances program. Due to difficulties in gaining awareness of stiff-person syndrome, patients must fight for SSD. The majority of stiff-person syndrome patients will not be able to hold down a steady job due to their condition, the risk of seizures, falls, startle-induced spasms, and the level of controlled medications they are required to take. Combined with the cost of medications, IVIG, immunotherapy drugs, and plasmapheresis, the majority of stiff-person patients carry a heavy financial burden, which can result in bankruptcy.

Research Findings

The cause of stiff-person syndrome is unknown. GAD65 and GABARAP antibodies exist in up to 70% of stiff-person patients. No single predominant allele has been identified. The paraneoplastic variant is associated with anti-amphiphysin and anti-gephyrin antibodies. These antibodies have no clear pathogenic role. Despite extensive research, causation due to a specific autoantigen has not been proven. Mutations of the GLRA1 glycine-receptor are the basis for startle disease and could correlate to the stiff limbs and startle aspect of stiff-person syndrome. There is also correlation with between stiff-person syndrome and several MHC class-II alleles: Dqβ1 and DRβ1.

In some - but not all - cases, stiff-person patients responded to treatment with IVIG, plasmapheresis, and immunotherapy drugs, but none resulted in remission or cure. Though SPS is a rare disease, it is hoped that further studies will lead to finding the cause and developing new forms of treatment.

Current Status of FMS-related Research Spending by NIH

Currently, the limited research into stiff-person syndrome has been conducted by doctors at Mayo Clinic and the NIH. Their research to date focuses on the relation to autoantibodies, not therapeutic interventions.

Recent Therapeutic Success

As of December 2014, there have been advances in hematopoietic stem-cell replacement therapies with "cautiously optimistic outcomes" by Dr. Henry Atkins in Ottowa, Canada; Dr. Richard Nash in Denver, Colorado; Dr. George E. Georges in Seattle, Washington; and Dr. Denis Fedorenko in Moscow, Russia.