Stiff-Man Syndrome (SPS/SMS)
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http://www.med.yale.edu/neurol/programs/neuromuscular/stiff_man.html

Introduction
Stiff-Man Syndrome is a rare disease of severe progressive muscle stiffness of the spine and lower extremities with superimposed muscle spasms triggered by external stimuli or emotional stress. Typically symptoms begin between the age of 30 and 50 and respond to benzodiazepines. EMG shows a characteristic abnormality and anti-GAD (glutamic acid decarboxylase (an amino acid, HOOCCH2CH2CH(NH2)COOH, obtained by hydrolysis from wheat gluten and sugar-beet residues, used commercially chiefly in the form of its sodium salt to intensify the flavor of meat or other food; any of the class of enzymes that catalyze the release of carbon dioxide from the carboxyl group of certain organic acids) antibodies, which are very specific, are present in 60% of people with the disease.

Key words: Stiff Person Syndrome, Moersch and Woltman Syndrome, Anti-GAD antibody, Stiff man syndrome

History
Stiff-man syndrome (SMS) was first described by Moersch and Woltman (1956) in a case report of 14 patients seen over 27 years. A literature review by Gordon (1966) including one patient of his own and 33 from the literature more sharply delineated the characteristics of the disease and postulated that the symptoms might be due to a failure of inhibitory function. A follow-up report of the Mayo clinic experience by Lorish (1989) describing 13 patients seen over 30 years established standard criteria for diagnosing the disease. A cumulative literature review by Jankovic (1991) included 2 patients of his own and 82 others is the most recent large scale report of the disease. Effective treatment with a benzodiazepine was described by Howard in 1963.

Clinical Presentation

Epidemiology
SMS is very rare. The prevalence has not been reported however it may be as rare as 1 per 1,000,000 persons. There is no clear racial or ethnic predisposition although the disease may be more common in women than in men. Patients with SMS often have other autoimmune disease. A related disorder has been found in association with lung or breast cancer and is distinguished by the production of anti-amphiphysin antibodies (a hybrid organism having a diploid set of chromosomes from each parental species).

Clinical features
Although most often the disease begins insidiously and progresses over years; in some cases symptoms can develop over weeks. The first symptom is usually a persistent progressive stiffening of the back or a limb which may be worse under pressure (e.g.: crossing a busy street). A sensation of aching or stiffness may be noted. This progresses with time and is described as
stiffness, rigidity, hypertonia (*increased rigidity, tension, and spasticity of the muscles*) or increased tone. Additionally patients experience spasms of the involved muscles which are characterized as severe, tremendous, intense and painful. The examiner may feel there is a volitional component. When stiffness and spasms are present together patients have difficulty ambulating and are prone to unprotected falls i.e. falls like a tin soldier. When in spasm the muscles are hard to palpation and may produce abnormal joint position: extension or contraction. Spasms may be triggered by sudden noise, touch, electrical shock, passive or volitional movement and are typically relieved by sleep. The onset of stiffness may less commonly begin in the face and arms however the spine and legs almost invariably become involved with time. An increase in the normal curvature of the lumbar spine or hyperlordosis is common. In the GAD antibody positive form of Stiff-man syndrome there is a strong association with other autoimmune diseases such as diabetes, hyperthyroidism, hypothyroidism, pernicious anemia and vitiligo. Often before the diagnosis is established people are considered for psychiatric evaluation because symptoms wax and wane over time and are apparently worsened by heightened emotional states. Patients with SMS have been described at fearful, afraid and depressed; it is important to consider the impact of the symptoms of SMS on the patient’s overall well-being.

**Pathophysiology**

The symptom complex of SMS suggests a derangement of physiology mediated by spinal cord reflexes however the specific mechanism of disease has not been defined. Stiffness, spasms, pain, trigger response and falls could all result from failed modulation of spinal cord reflexes. The neurons controlling these functions use gamma-aminobutyric acid (GABA) as a neurotransmitter and are called GABAergic neurons. GAD (glutamic acid decarboxylase) is an enzyme which produces GABA and is localized to the synaptic nerve terminal. GAD is the protein antigen that is specifically bound by the anti-GAD auto-antibodies found in approximately half of SMS patients.

First described by Solimena and coworkers in 1988, at high titer anti-GAD autoantibodies are almost exclusively associated with SMS. Sporadic reports of association with cerebellar ataxia, type I (autoimmune) diabetes and autoimmune polyendocrine syndrome have been made. At low titer anti-GAD antibodies are found in type I diabetes; pancreatic beta cells, like GABAergic neurons, express GAD. Although the presence of high titer anti-GAD antibodies is highly specific for SMS, the role that the humoral immune system plays in pathogenesis of this disease is unclear. It is not known whether the antibodies have a causative role or are the consequence of a process that leads to impairment of neurotransmission.
Diagnosis

Antibody testing

While the absence of antibodies in the serum does not rule out SMS, the presence of anti-GAD autoantibodies strongly supports that diagnosis (99% specific by immunocytochemistry). There are several ways to measure anti-GAD antibodies: immunocytochemistry and Western blotting were the first methods used. Immunocytochemistry allows the detection of antigens in tissue section whereas Western blotting visualizes protein antigens which have been separated by size. ELISA and radioimmunoassay (RIA) use antigen specific binding to attach enzyme linked or radioactively labeled substrates to the antibodies in serum. Developed more recently ELISA and RIA have the advantage of quantitatively assessing the amount of anti-GAD antibody a patient has produced.

Physical exam

Central to evaluation for SMS is a detailed history and neurological exam. The cardinal symptoms are essential to the diagnosis of this disease and isolated laboratory results do not stand alone. The symptoms of stiffness, rigidity or increased tone, spasm or pain are identified by the patient and physician together. The areas of involvement may include the face, neck, abdomen or arms but more typically the legs or lumbar spine are involved. The response to medications is important in discriminating other causes of stiffness e.g. Parkinsonís disease and spasticity. Evaluation may include tests to rule out other causes of stiffness such as multiple sclerosis or transverse myelitis.

Electromyography

Electromyography (EMG) is an important diagnostic tool in evaluating patients for SMS. The typical pattern of continuous low frequency firing of normal motor units or continuous motor unit activity (CMUA) is found simultaneously in agonist and antagonist muscles of the affected region. This abnormal firing pattern is abolished by centrally and peripherally acting agents (general anesthesia, intravenous diazepam, neuromuscular blockade). The EMG findings of SMS may be subtle in patients who are fully treated for the symptoms of SMS.

Genetics

The disease has not been described in members of the same family and there is no known genetic predisposition. An association with human leukocyte antigen (HLA) type has been described.

Treatment

There are several important features specific to the treatment of this disease. Although there seems to be a strong autoimmune link, immunomodulating therapies have yet to produce consistent results. Anecdotal reports of response to prednisone, immunoglobulin or plasmapheresis have appeared. The most consistently effective therapy is benzodiazepines. These drugs produce symptomatic relief and discontinuation often leads to reemergence of symptoms. Other drugs which modulate the function of GABAergic neurons are employed with variable efficacy. Physical therapy may exacerbate spasms in some patients and should be used carefully in those for whom passive motion may be a trigger of spasm. The course of the disease
is variable; there are reports of patients with SMS who respond well to medication and are able to exercise vigorously. Abrupt withdrawal of therapy may be harmful.

How Stiff Person Syndrome Affects the Muscular and Spinal System

The Muscular and Spinal System

Lordosis
Lordosis is the increase of the spinal posterior concavity.

Lateral view
1. Lordosis
2. Normal

Lordosis is an abnormal forward curvature of the spine in the lumbar region, resulting in a swaybacked posture.

How it takes place
In most cases the cause is unknown and the disorder appears from the onset of skeletal growth. It is more frequent in some races.

In some cases shortening of the ischiotibial muscles can facilitate the adoption of hyperlordotic postures. (As seen below under the muscular system)

Symptoms
It was formerly believed that lordosis caused back pain always. This is really not so. It is generally a problem of appearance and does not cause pain.

Risk
Some studies suggest that hyperlordosis can increase the force exerted on facet joints and, eventually, accelerate their degeneration.

Diagnosis
Hyperlordosis is normally directly observable. It can be confirmed by an X-ray.

Treatment
In itself it does not require treatment. Appropriate physical exercise, adapted by the physician to the specific case, is normally sufficient to offset any risk of overloading the facet joints.
The Muscular System

Paravertebral muscles cooperate with abdominal and psoas muscles in keeping the back straight, resembling the opposing ropes holding a ship's mast. The glutei attach the spine to the pelvis and assure stability to the muscular system.

On the other hand, if muscles at the posterior face of the thigh (ischiotibial) are shortened, there is a tendency to inadequate spinal postures.

The abdominal muscles

They extend from the lower margin of the ribs to the upper pelvis, protecting inner organs. Muscles on the front portion are named "anterior rectus". When contracting they bring ribs near the pelvis frontward, bending the spine forward, but these muscles are not efficient in terms of movement: when they are at their utmost contraction the spine only curves about 30 degrees forward.

The abdominal muscles placed on the lateral portion of the trunk are named "oblique" and "transversus". When the left transversus contracts, ribs are brought near the pelvis on the left side, making a wider separation on the right side between the ribs and the pelvis. When the oblique ("major" and "minor") contract, hips rotate without moving the shoulder. If they contract along with the anterior rectus, they bring ribs near the pelvis in a crossed fashion, the right shoulder toward the left hip or viceversa.

The transversus contraction acts as a girdle, keeping viscera tightly against the spine.

The paravertebral muscles

They extend throughout the back of the trunk. Paravertebral muscles unite the posterior lower portion of the ribs with the pelvis, and attach vertebrae one on top of the other, and these with the scapula.
When contracting, the vertebral "tails" (spinous processes) come closer, straightening the trunk and bending it backward.

The psoas muscle

The psoas extends from the last thoracic vertebra along the five lumbar vertebrae to the thigh, crossing the pelvic region. When contracting, the leg is brought forward near the vertebrae until the chest touches the knee.

When flexing the spine forward, the psoas is more efficient than abdominal muscles, in terms of movement. The abdominal and the psoas muscles jointly contribute to the first 30-degree flexion; past this angle, only the psoas permits the spine to continue bending forward.
**The gluteus**

The gluteus extends from the pelvis to the posterior part of the femur, forming the buttocks. When contracting they pull the leg backward and outward. When extending the back backwards, the gluteus and ischiotibial muscles cooperate with the paravertebral muscles.

The gluteus and other pelvic muscles, such as the pyramidal, maintain a dynamic tension within the pelvic waist, providing a stable support to the spine.

**The ischiotibial muscles**

They extend along the posterior part of the thigh, from the back of the pelvis to the knee. During back extension, the glutei and the ischiotibial muscles cooperate with paravertebral muscles.

If ischiotibial muscles are shortened, the lumbar area is consistently arched more than normal - which is known as lordosis - and may result in paravertebral muscle contraction.