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Myasthenia Gravis: an Autoimmune Neuromuscular Disorder

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Abstract

Myasthenia gravis (MG) is an autoimmune disease which is caused by impaired transmission of signals at neuromuscular junction and results in problem with muscle contraction. At neuromuscular junction neurotransmitter acetylcholine is released by nerve ends which binds to the receptor at surface of muscle cells. The patients with MG the acetylcholine receptors are blocked or destroyed or altered by its own antibodies and interrupts the communication between nerve cells and muscle cells. MG includes symptoms like weaken muscles, tiredness by any regular work e.g. chopping vegetables, movement of eye, drooping of eyelids and double vision. MG is classified in five types out of which the two main forms are ocular and generalized myasthenia gravis. Diagnosis and treatment of MG can be done by various process. MG preferably affects young women on their20s and 30s and old men after their 60s.

Keywords: Acetylcholine; Autoimmune disease; Myasthenia gravis; Neuromuscular junction.

Introduction

Immune system of human body protect it from foreign invaders or antigens e.g. bacteria, virus. Immune system fights with these antigens and provides immunity to body.[1]

The body has immune tolerance and is normally able to distinguish its own self-antigens from foreign non-self antigens and does not mount an immunologic attack against itself. At times the body loses tolerance and mounts an abnormal immune attack, either with antibodies or T cells, against a person's own self antigens.[1]

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Autoimmune disease results from the activation of self-reactive T and B cells that, following stimulation by genetic or environmental triggers, cause actual tissue damage. Examples include rheumatoid arthritis, Myasthenia gravis and Type I diabetes mellitus.[1]

An autoimmune disease Myasthenia gravis is a neuromuscular disorder which happens when tissues of human body are attacked by its own immune system and breaks the connection or linkage between nerve and muscle cells- the neuromuscular junction, resulting in muscle weakness. Myasthenia gravis is a Latin word which means "grave muscle weakness".[2]

Myasthenia gravis preferentially affects young women under fourth's and old men above sixty's.[6]

The first reported case of MG is likely to be that of the Native American Chief Opechancanough, who died in 1664.[7]

People living with myasthenia gravis might get weak and tired, sometimes getting weaker from repetitive movements like chopping vegetables.[6]

Symptoms

In myasthenia gravis degree of muscle weakness varies greatly among individuals. MG mostly affects muscles which are responsible for movement of eye and eyelids, facial muscles and swallowing, major symptoms include drooping of one or both eyelids (ptosis), blurred or double vision (diplopia) due to weakness of the muscles that control eye movements, a change in facial expression, difficulty swallowing, shortness of breath, impaired speech (dysarthria), weakness in the arms, hands, fingers, legs, and neck. Sometimes MG gets severe and affect muscles which are responsible for breathing-myasthenia crisis.[2]

Causes

Nerve cells communicate and control muscle cells at neuromuscular junction. When this processes in interrupted and transmission of nerve impulses to muscles are blocked, contraction of the muscles actively is compromised and causes myasthenia gravis.

At NMJ, nerve cell's endreleasesa chemical named acetylcholine which binds to acetylcholine receptors on the surface of muscle cells and activates muscle contraction.[5]

In individuals with MG antibodies are released and blocks or destroy the acetylcholine receptors on the surface of muscle cells at NMJ. This process blocks the transmission and results in problem with muscle contraction.

Main cause of myasthenia gravis is self-antibodies impairing signal transmission at NMJ but in some cases muscle-specific kinase antibodies are also responsible for this.

Thymus gland plays an important role in development of immune system and controls the immune function. Research shows that about ten to fifteen percent individuals with MG have thymomas-most often harmless but can become cancerous and others have more than usual number of cells in thymus. However thymus gland considered related to the myasthenia gravis but its exact function is unknown.

MG is an autoimmune disease but in about three to five percent of patients congenital myasthenia gravis is seen but inheritance pattern is unknown.[2]

Classification

Typically divided into five types: congenital myasthenia gravis, generalized myasthenia gravis, ocular myasthenia gravis, transient neonatal myasthenia gravis, and juvenile myasthenia gravis, depending on time of disease onset, the cause of the neuromuscular dysfunction, and the muscle groups affected.[3]

Congenital Myasthenia Gravis

Congenital disease is the defect caused by having a particular trait from birth or inherited by parents or family. Congenital myasthenia gravis is a genetic defect rather than autoimmune disease which is the cause of other types of this disease.

In this disease communication between nerve and muscle cells at neuromuscular junction interrupted by transformation in normal genetic order- gene order. For e.g. acetylcholine receptor encoding genes affected. The various types of congenital myasthenia gravis are defined by the location and type of genetic defect that causes poor neuromuscular signaling.

Ocular Myasthenia Gravis

Ocular means connected with eye or vision. Ocular myasthenia gravis is related with weakness and fatigue of the muscles linked with eye and eyelids, drooping eyelids and double vision are mostly occurred symptoms. Ocular myasthenia gravis is limited to muscles of these area and do not spread to other region.

Generalized Myasthenia Gravis

Generalized myasthenia gravis is a types in which muscle weakness and fatigue also spreads to the facial muscles and limbs not only to the muscles of eye and eyelid regions.

In some patients it leads to the myasthenia crisis which is a life-threatening disorder characterized by worsening of muscle weakness, resulting in respiratory failure that requires intubation and mechanical ventilation.

Transient Neonatal Myasthenia Gravis

Infants from Mothers who are suffering from myasthenia gravis are likely to develop myasthenia gravis after birth and shows symptoms like impaired sucking and swallowing, a weak cry, and respiratory insufficiency.

Juvenile Myasthenia Gravis

Juvenile myasthenia gravis is not very common and shows the symptoms before the onset of puberty. In patients with juvenile MG symptoms include limited eye muscles movement, trouble in swallowing and tiredness.

Diagnosis

Physical and Neurological Examination

Reviewing an individual's medical history, physical and neurological examination is first step to diagnose MG which further includes testing muscle weakness and fatigue by checking reflexes, muscle strength and tone, coordination, sense of touch, and look for impairment in eye movements.[4]

Endrophoniumtest

In this test to check ocular muscles weakness, injection of edrophonium chloride is provided to the patients of MG which reduces muscle weakness and temporarily cause active muscle contraction by blocking the enzyme responsible for breakdown of acetylcholine which leads to increase in acetylcholine at NMJ.[4]

Blood Test

Occurrence of abnormal antibodies that disrupts acetylcholine receptor at muscle sell surface is detected by blood test along with detection of another type of antibody called muscle specific kinase antibody associated with non-specific process of alteration and damage of nerve-muscle transmission. In some individual neither of these antibodies are detected-seronegativemyasthenia.[4]

Electromyography

In this test fine wire electrodes are inserted into muscles. These electrodes electrically stimulate single muscle fibers and measure the electrical activity traveling between the brain and the muscle.[4]

Imaging

Patients with thymoma have some abnormality in thymus gland which is detected by A computerized tomography (CT) scan or a magnetic resonance imaging (MRI) scan.[4]

Treatment

MG can be controlled by several therapies that improve muscle weakness.

Thymectomy.

In Patients with thymoma in some cases removal of thymus gland is a good way for rebalancing of immune system.

Anticholinesterase Medications

Anticholinesterase agents reduce the muscle weakness and improve the neuromuscular transmission process of breakdown of acetylcholine at the neuromuscular junction.[2]

Immunosuppressive Drugs

These drugs reduce the production of abnormal antibodies. E.g. prednisone, azathioprine.[2]

Plasmapheresis and Intravenous Immunoglobulin

These therapies eradicate the destructive antibodies, but their effect usually only lasts for a few weeks to months.

Plasmapheresis - In this process substitution of harmful antibodies in plasma is done.

Intravenous immunoglobulin - This process leads to temporarily change in the immune system by injecting concentrated antibodies which binds with MG causing antibodies and remove them.[2]

Yingzhe Cui et al in year 2019 published a research paper conforming that the metformin drug widely used for type 2 diabetes has anti-inflammatory functions. The drug functions via activating AMP-activated protein kinase (AMPK). As the circulating autoantibodies and disequilibrium of helper T cells and regulatory T cells are pathological indications of myasthenia gravis (MG). The drug has effect on the imbalance of different T cell populations.

Epidemiology

The study performed by B. S. Singhal et.al in 2008 on the 841 patients, they observed that 836 (611 males and 225 females) had acquired myasthenia (myasthenia gravis). The median age of onset was 48 years (males 53 years and females 34 years). Two hundred and twenty-two (26.31%) patients had ocular and 616 (73.68%) had generalized myasthenia. Serological studies were done in 281 patients with myasthenia gravis for Acetylcholine receptor (AchR) antibodies of which 238 (84.70%) were seropositive.

Conclusion

In case of Myasthenia Gravis epidemiological study at nation level in India is less covered. The disease

needs more attention and in depth research for its prevention, therapeutics is needed. The work done by Yingzhe Cui et al is remarkable in the treatment of Myasthenia Gravis. The anticholinesterase agents reduce the muscle weakness and improve the neuromuscular transmission can be used as therapeutics with other suggested treatment. The naturopathy ayurved also can be studied in detail for the possible diagnosis and treatment of Myasthenia Gravis.

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