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Overview of Disease

Myasthenia Gravis is an autoimmune disorder that affects the neuromuscular junction by disrupting transmission. This disease is somewhat rare occurring in about 2-7 people in every 10, 000 (Drachman, 2012). Physician Thomas Willis first observed the disease's general signs of muscular weakness and exhaustion in the late 1600s (Conti-Fine et al., 2006). However, this disease did not become widely recognized until the 1930s when Mary Walker found that the drug used to treat curare poisoning also alleviated symptoms of myasthenia gravis (Conti-Fine et al., 2006).

There are several symptoms that characterize this disorder, which typically involve problems with voluntary muscles. People usually experience ptosis, which is the drooping of an upper eyelid, and diplopia, which is double vision from problems with ocular muscles (Aminoff & Douglas, 2017). Myasthenia gravis can also affect how patients talk and swallow. These " bulbar symptoms" may also " include weakness of jaw, facial, and neck muscles" (Amato & Russel, 2016). Common problems include difficulty in whistling, swallowing, and closing the jaw (Amato & Russel, 2016). While muscle weakness is commonly localized to the cranial area, this disorder can also appear elsewhere. For example, it may also affect the muscles of limbs and of those involved in breathing (Aminoff & Douglas, 2017).

There are a few treatment options that are effective for myasthenia gravis. This includes giving cholinesterase inhibitors and/or removing the thymus gland (Drachman, 2012). Using glucorticoids as a means of immunosuppression is another way to treat this disorder (Drachman, 2012).

Disease Mechanisms at the Molecular to Cellular Level

Myasthenia gravis affects the normal function of neuromuscular junctions, which is how voluntary movements are facilitated. Normally, vesicles release neurotransmitter acetylcholine from neuronal presynaptic terminals, which then bind to crowded acetylcholine protein receptors on the muscular postsynaptic membrane so that depolarization can cause normal contraction (Drachman, 2012). However, this disease affects protein macromolecules by IgG autoantibodies binding to these receptors and blocking acetylcholine binding (Aminoff & Douglas, 2017). This abnormal binding can lead to a few consequences that interfere with normal transmission aside from just blockage. These autoantibodies can make receptors crosslink with each other and cause rapid endocytosis of the receptors or they can also directly degrade them through " complement-mediated, membrane-attack complex lysis of AChR" (Amato & Russel, 2016). Folds on the postsynaptic membrane are also leveled, which decreases surface area (Drachman, 2012). Therefore, all of these changes lead to a significant decrease in the protein receptors necessary for acetylcholine to bind. If acetylcholine cannot bind then no action potential is generated and the muscle cannot contract leading to muscle weakness and fatigue (Drachman, 2012). Overall, myasthenia gravis prevents the important cellular function of neurotransmission for voluntary skeletal muscles.

There are no known genetic mutations associated with myasthenia gravis. However, it is considered that certain gene variants might contribute to the probability of developing this disorder (" Myasthenia Gravis", 2018). More

research is needed to investigate which variations might affect the immune system and whether it can be inherited.

Disease Mechanisms at the Tissue to Organism Level

Myasthenia gravis mostly affects two types of tissues in the human body. Since the pathogenesis of this disorder is concentrated at the level of the neuromuscular junction, it mostly affects neural and muscular tissue. The thymus gland might also be affected since about 75% of patients with this disease have an atypical thymus (Drachman, 2012). There is no real problem in nerves creating or releasing their chemical message but rather the problem lies in muscle postsynaptic membranes receiving the message (Drachman, 2012). Therefore, it is the muscular system that is mostly affected.

Overall, this disease impacts simple everyday movements. If the disease is localized to just the cranial and facial area then functions such as blinking, vision, chewing, smiling, speaking, and swallowing may be affected (Drachman, 2012). It can also become generalized and start affecting the muscles of the limbs, which happens in about 20-30% of patients (Amato & Russel, 2016). These effects can greatly reduce everyday quality of life. However, this can be controlled if diagnosed early so symptoms can be reduced with treatment. Myasthenia gravis does not usually affect life expectancy unless it progresses to myasthenia crisis, where respiratory muscles experience weakness and cause difficulty in breathing (Aminoff & Douglas, 2017). This can affect quality of life if constant care is needed for normal breathing.

Epidemiology

There are a few characteristics that influence the likelihood of acquiring myasthenia gravis. There are no known environmental parameters associated with acquiring myasthenia gravis nor are there public health interventions since this is an autoimmune disease that can happen to anyone. While it appears that ethnicity does not influence the development of this disorder, age and gender do. Myasthenia gravis can occur at any age but it is most common in women over 20 and under 40 and in men over 50 but under 70 (Drachman, 2012). This disorder is most common in women when looking at the age group of under 40 but then switches to men in older patients after their 40s (Amato & Russel, 2016). According to some evidence, 10% of babies born from women with myasthenia gravis get temporary myasthenia gravis that usually goes away after a few weeks (Amato & Russel, 2016).

In a study by Lawrence H. Phillips (2003), it was found that there has been an increase in the frequency of myasthenia gravis. However, he suggests that this may be from progress in diagnosing, an increase in quality of treatment leading to higher survival rates, and a general increase in human life expectancy, which affects the populations affected by this disease (Phillips, 2003).

Research Article Summary

A recent study was done to investigate a new treatment for patients suffering from serious myasthenia gravis. Bryant et al (2016) questioned if autologous hematopoietic stem cell transplant (HSCT) would be successful in

treating patients with severe myasthenia gravis symptoms. Since autologous HSCT had been used to treat other serious autoimmune disorders, the researchers investigated its potential use in providing lasting remission in patients with this disease (Bryant et al., 2016). This was a retrospective study that examined the effects months after the surgery treatment.

The researchers analyzed the results from 7 patients with threatening symptoms that had undergone autologous HSCT at a Canadian hospital (Bryant et al., 2016). The patients had been diagnosed with grade III to grade V myasthenia gravis and had little success with the normal treatments for this disease (Bryant et al., 2016). In addition, they experienced either emergency visits and/or ICU prior to the transplant (Bryant et al., 2016). Results were evaluated at 29+ months by measuring occurrence of emergency visits to the hospital and " Myasthenia Gravis Foundation of America (MGFA) clinical classification, therapy status, and postintervention status" (Bryant et al., 2016).

The researchers found that all patients were in " complete stable remission (CSR)" by the final follow-up, which meant that there were no myasthenia gravis symptoms and no disease therapy needed (Bryant et al., 2016). Almost all patients (besides one) stopped other disease therapies and almost all patients no longer had hospitalizations (Bryant et al., 2016). However, the one patient that did require ICU after the transplant was admitted for an unrelated reason. Still, some patients experienced temporary mild complications. Complications included viral reactivation, mucositis, and febrile neutropenia (Bryant et al., 2016). While one patient did die, it was

related to their lymphoma and CSR from myasthenia gravis persisted until death (Bryant et al., 2016).

Bryant et al. (2016) concluded that autologous HSCT may be an efficient treatment in treating patients with extreme cases of myasthenia gravis. However, it should be remembered that this study was limited to a small size of only seven patients and more research should be conducted before concluding such. While complications from the transplant were temporary or alleviated, it is important to consider the types of patients able to undergo this treatment. There are several complications and secondary effects that may occur and all risks should be carefully considered to assess beneficial outcome. Nevertheless, this research was important in finding another possible useful treatment for severe myasthenia gravis for when the other usual medications and therapies are not successful in alleviating symptoms. It is also noteworthy that autologous HSCT did appear to lead to long-term CSR, which can greatly improve quality of life in these patients.

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