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Guillain Barre Syndrome

Overview of the Disorder:

A French physician named Dr. Jean Landry first described Guillain Barre Syndrome in 1859. Dr. Landry reported that ten of his patients presented with ascending paralysis (Steinberg & Koski, 2010). Later in 1916, three other French physicians, Georges Guillain, Jean Alexandre Barre and Andre Strohl diagnosed two French soldiers with motor weakness, absent reflexes, diminished deep tendon reflexes, and cerebrospinal fluid with increased protein production (Andary & Klein, 2016). The syndrome identified by these physicians was later named in their honor, Guillain Barre Syndrome.

Guillain-Barre Syndrome (GBS) can best be described as a collection of clinical symptoms that manifests as an acute, progressive, symmetrical, inflammatory polyradiculoneuropathy (Koroshetz & Lyons, 2015). Guillain-Barre syndrome results in decreased motor and/or sensory function, which ascends throughout the extremities. GBS is a disorder in which the body's own immune system attacks the peripheral nervous system and results in acute flaccid paralysis. Guillain-Barre syndrome often occurs subsequently to a gastrointestinal or respiratory bacterial/viral infection (Koroshetz & Lyons, 2015). It has been found that the bacterial or viral infection most often occurs two to four weeks prior to the symptoms of GBS. In GBS, the prior infection causes the patient's immune system to destroy the myelin sheath (which surrounds the axons of peripheral nerves) and/or the axons themselves (Yuki, Nobuhiro, Hartung & Hans-Peter, 2012). As a result of this, the transmission of nerve signals to the muscles and organs decreases in speed or may not transmit at all. Therefore, the muscles and organs these nerves supply can no longer transmit information to and from the brain.

The first symptoms of Guillain Barre Syndrome include varying levels of weakness and paresthesia in the most peripheral parts of the limbs. These symptoms occur symmetrically on both sides of the body and continue to develop proximally. The neural signals to and from the distal parts of the limbs begin to decrease in speed before affecting the proximal portion of the nerve (Koroshetz & Lyons, 2015). This is because the nerves to and from the distal arms and legs must travel the furthest, making them the most susceptible to damage on their path. Symptoms of paresthesia and weakness can increase in intensity over time, resulting in certain muscles that may no longer be functional. If the symptoms of GBS are not treated urgently, a patient can become totally paralyzed (Koroshetz & Lyons, 2015). A life-threatening situation may occur, especially if the cardiac or respiratory muscles become affected. Damage to these muscles can alter the systematic patterns for breathing, heart rate and blood pressure (Yuki et al., 2012).

During the beginning stages of GBS, it is difficult to diagnose because many symptoms are similar to other disorders. Tell-tale symptoms of Guillain-Barre syndrome include nerve degeneration bilaterally (which is more severe distally), quick progression of symptoms, reflexes are absent or decreased, nerve conduction velocity tests reveal decreased transmission speed, and increased protein in the cerebrospinal fluid from a spinal tap (Koroshetz & Lyons, 2015). Guillain-Barre Syndrome can be categorized into four main subgroups based on symptoms and findings. The most common variation of GBS is named acute inflammatory demyelinating polyradiculoneuropathy (AIDP) (Yuki et al., 2012). The other three subgroups of GBS, which are also well recognized, include acute motor axonal neuropathy (AMAN), acute motor-sensory axonal neuropathy (AMSAN), and Miller-Fisher syndrome (Umphred, Lazaro, Roller & Burton, 2013). Currently, there is no known cure for Guillain-Barre syndrome. However, there are treatments that can lessen the severity, accelerate the recovery, and treat the complications of most patients. Treatments can include plasma exchange, immunoglobulin therapy, physical therapy, ventilatory assistance and others to assist body function as necessary (Koroshetz & Lyons, 2015).

Guillain-Barre syndrome is a devastating disorder because of its rapid and unexpected onset, which is not necessarily followed by a quick recovery. After the decline of sensation and muscle strength, which may last for a period of days to months, the symptoms usually stabilize for a period of days to weeks (Andary & Klein, 2016). By three weeks, most patients are experiencing their weakest point within the course of the disorder. Most patients show signs of recovery around four weeks after the symptoms started to appear (Steinberg & Koski, 2010). Once stabilized, most individuals have a good recovery (with minor symptoms of altered sensation and weakness) from even the most severe cases of Guillain-Barre syndrome. Approximately 80% of patients with GBS will make an immense recovery within the first year and a significant number of these patients recover within the first few months (Andary & Klein, 2016). Up to 10% of patients with Guillain Barre Syndrome will be left with residual sensory and/or motor issues multiple years after the diagnosis. Sadly, around 3% of patients may suffer from a relapse of muscle weakness and altered sensation many years after the initial diagnosis (Andary & Klein, 2016).

Throughout the course of Guillain-Barre syndrome, family members, caretakers, and medical staff must reposition the patient and move the patient's limbs to prevent further harm. These precautions should be followed in order to avoid contractures of multiple joints, blood clots, pneumonia, bedsores, improve venous return, and increase flexibility of the muscles. After being discharged from the hospital, patients with GBS should receive outpatient physical therapy to increase their strength and range of motion in order to regain their functional baseline (Umphred et al., 2013). Medical professionals should take into consideration that patients diagnosed with GBS and their families, also face the emotional difficulty of dealing with the sudden readjustment of paralysis and dependence on others for tasks that the patient used to independently perform.

The annual incidence of GBS in the United States according to the Centers for Disease Control and Prevention is 1-2 individuals per 100,000 people (Andary & Klein, 2016). In the

United States, it has been found that the majority of incidences of patients with GBS tend to be between two age ranges. The first peak of GBS incidences occurs around the ages of 15-35, and a second even higher number of patients occurs between the ages of 50-75 years old (Andary & Klein, 2016). United States military personnel are at an increased risk for GBS because gastroenteritis infections have a significantly amplified occurrence among military personnel. Males have also been found to show a slightly higher diagnosis rate for Guillain Barre syndrome with a 1.5:1 ratio to women (Andary & Klein, 2016). Guillain Barre Syndrome has been equally prevalent among all races.

Pathology

Guillain Barre Syndrome is a post-infectious, immune mediated disease. Most patients report an illness, either viral or bacterial, that occurred a few weeks prior to the onset of GBS. The identified infectious agents produce antibodies that negatively react with gangliosides and glycolipids (Yuki et al., 2012). Gangliosides and glycolipids are distributed within the myelin sheath of the peripheral nervous system (Andary & Klein, 2016). *Campylobacter jejuni* infection (*C jejuni*) is the pathophysiologic mechanism of the infection that occurs prior to GBS. *C jejuni* contains a virulence that presents specific antigens in capsules that are shared with nerves. The human immune response to *C jejuni* results in antibodies that also react with ganglioside GM1 in myelin (Yuki et al., 2012). This cross-reaction results in immunologic damage to the peripheral nervous system. Guillain Barre syndrome pathological findings include lymphocytic infiltration of peripheral nerves, followed by macrophage-mediated, multifocal stripping of myelin (Yuki et al., 2012). The combination of pathological infiltration of peripheral nerves and macrophage stripping of myelin, results in defects in the propagation of electrical nerve impulses (Andary & Klein, 2016). These deficiencies in the transmission of electrical signals result in the delay and eventual absence in conduction of nerve impulses causing flaccid paralysis and paraesthesias. The recovery of Guillain Barre Syndrome is determined by the ability of these nerves to re-myelinate.

When Guillain Barre increases in severity, some patients may also experience further inflammation that results in axonal disruption and loss of the nerve (Andary & Klein, 2016). Certain subtypes of GBS have a different pathological presentation as they result in an immune attack directly against nerve axons, but spare the myelin sheath.

Guillain Barre Syndrome pathologically presents as an inflammatory cell attack on the myelin sheath with myelin breakdown and possible axonal degeneration. As noted earlier, GBS includes a wide variety of symptoms and findings. Therefore, the overall syndrome of Guillain Barre was additionally categorized into four main subtypes. The most common subtype of GBS is acute inflammatory demyelinating polyradiculoneuropathy (AIDP) (Umphred et al., 2013). AIDP is characterized by its impairment of both motor and sensory nerves. The myelin sheath of both the sensory and motor nerves is degenerated symmetrically affecting multiple nerve roots. Guillain Barre Syndrome type AIDP is often preceded by a bacterial or viral infection. It has been noted that 40% of the time, AIDP patients test positive for *C jejuni*, which causes the lymphocytic infiltration and macrophage-mediated peripheral nerve demyelination (Andary & Klein, 2016). Patients with GBS type AIDP show impressive recovery compared to other subtypes of GBS. This is attributable to the fact that demyelination of the peripheral nerves is not as detrimental or as long of a recovery as degeneration of the nerve axons. Therefore as time passes, most patients are able to recover from their AIDP motor and sensory losses with re-myelination (Yuki et al., 2012).

The other three subgroups of GBS, which are also well recognized, include acute motor axonal neuropathy (AMAN), acute motor-sensory axonal neuropathy (AMSAN), and Miller-Fisher syndrome (Andary & Klein, 2016). Acute motor axonal neuropathy (AMAN) is a subtype of GBS, which is characterized by axonal destruction of primarily motor axons. Patients diagnosed with AMAN endure a severely rapid and progressive symmetrical weakness, which may proceed into respiratory failure. Of all patients diagnosed with AMAN, 75% of these individuals test positive for prior *C jejuni* (Andary & Klein, 2016). Patients diagnosed with

AMAN typically show increased numbers of antibodies that cause inflammation of the anterior spinal nerve roots. This inflammation leads to a disruption of blood flow to the nervous system. Biopsies of patients with GBS show that affected peripheral nerves demonstrate wallerian degeneration (Andary & Klein, 2016). Patients diagnosed with GBS type AMAN demonstrate severe motor disablement and usually endure a slow recovery over a couple of years due to axonal loss.

A third type of Guillain Barre Syndrome is named acute motor-sensory axonal neuropathy (AMSAN). Guillain Barre Syndrome subtype AMSAN is the most severe because it affects the axons of both sensory and motor nerve roots (Andary & Klein, 2016). Patients with AMSAN have been marked with the worst recovery prognosis because of the rapid severity of axonal degeneration of motor and sensory nerves. AMSAN is associated with an infection of *C jejuni* prior to the presentation of GBS symptoms and exemplifies characteristic signs of muscle wasting (Andary & Klein, 2016).

Miller-Fisher syndrome is the least common of the four main subtypes of Guillain Barre Syndrome. Miller-Fisher syndrome clinically presents as a triad of ophthalmoplegia, ataxia, and areflexia (Andary & Klein, 2016). Ophthalmoplegia is the paralysis of the eye muscles. Acute onset of ophthalmoplegia is a cardinal feature of Miller-Fisher syndrome, along with limb weakness, ptosis and facial palsy (Andary & Klein, 2016). Patients with Miller-Fisher syndrome also present with absent sensory nerves and tibial reflex. In MFS, patients tested positive for accumulation of Anti-GQ1b (Andary & Klein, 2016).

Guillain Barre Syndrome has other variants, which aren't as common as the main four subtypes. These subtypes include acute panautonomic neuropathy, pure sensory GBS, and pharyngeal-cervical-brachial GBS (Andary & Klein, 2016). Acute panautonomic neuropathy affects the sympathetic and parasympathetic nervous systems. Acute panautonomic neuropathy results in severe orthostatic hypotension, bowel and bladder retention, pupillary abnormalities, and decreased production of sweat, tears and saliva (Andary & Klein, 2016). The symptoms of

acute panautonomic neuropathy can be extremely serious, as there may be cardiovascular involvement increasing arrhythmias and the risk of mortality. Recovery from APN is often gradual and incomplete, with significant motor and sensory involvement. The pure sensory subtype of GBS includes a rapid onset of sensory loss, ataxia, and areflexia in an extensive symmetrical pattern (Andary & Klein, 2016). Pharyngeal-cervical-brachial Guillain Barre Syndrome is characterized by isolated facial, oropharyngeal, cervical and upper limb weakness without any lower extremity involvement (Andary & Klein, 2016). In some cases of Guillain Barre Syndrome, there is a combination of nerve injury symptoms of the multiple subtypes of GBS.

Clinical Manifestations and Differential Diagnosis

   The accurate and swift medical diagnosis of Guillain Barre Syndrome is important in order to reduce the mortality and morbidity of patients. If the diagnosis of a patient with GBS is missed or inappropriately diagnosed the treatment will be delayed and less effective. The diagnosis of GBS is difficult because not all patients present with the same symptoms. There are a wide variety of possible symptoms along the spectrum of the disease subtypes. Therefore, when deciding whether or not the diagnosis of GBS is appropriate certain medical syndromes (listed below) should be considered in the decision process. (Randall, 2010).

   According to neurological differential diagnosis protocol, Guillain Barre Syndrome is an acute, progressive, symmetrical, inflammatory, polyradiculoneuropathy. GBS includes the involvement of peripheral nerves, limb and facial muscles, lower cranial nerves, swallowing and respiratory muscles, sensory nerves and the autonomic nervous system (Millichap, 2013). When assessing a patient, the diagnostic characteristics include initial symmetrical weakness of the lower limbs and progression of this weakness from the distal part of the limbs ascending upwards in a matter of hours or weeks (Millichap, 2013). Other characteristics include involvement of the arms and/or facial muscles, areflexia, dysphagia, and respiratory difficulties. Additional

abnormalities of Guillain Barre Syndrome can include sensory loss of light touch, proprioception and other sensory pathways (Millichap, 2013). Patients with Guillain Barre Syndrome may also present with autonomic dysfunction including orthostatic hypotension, cardiac arrhythmias, hyponatremia, and increased protein in the cerebrospinal fluid (Millichap, 2013).

The cause of Guillain Barre Syndrome is an immune response to a foreign viral/bacterial infection. The possible infections include *Campylobacter jejuni* (*C jejuni*), Cytomegalovirus, or influenza virus. When conducting a differential diagnosis for a patient in which GBS is suspected, blood tests and serologic studies should be performed for certain antibodies. Antibodies found to be elevated in patients with GBS include GQ1B for Miller Fisher syndrome, Anti-GM1 for *C jejuni* prior to GBS, or GM1 for AMAN and AIDP (Andary & Klein, 2016). If a patient presents with symptoms that are representative of GBS, other tests should also be carried out to confirm a diagnosis. These tests include a lumbar puncture for CSF scans to check elevated protein levels, and an electromyography (EMG) or nerve conduction study (NCS) to assess conduction slowing and blockage of nerve signals (Randall, 2010). When cerebrospinal fluid tests are run, the results may not be indicative of GBS. This is because elevated protein levels only present after two weeks of symptoms, which is the peak of GBS weakness. The use of EMG and NCS is crucial in the diagnosis of patients with GBS. The findings for these tests may not be present for several days because the appearance of demyelinating features does not appear instantaneously (Randall, 2010). The demyelination of nerves usually features slowing of conduction velocities of motor and sensory nerves resulting in late responses to reflex testing. An MRI may also be used for the diagnosis of GBS to reveal nerve root impairment. Other tests that are run to help diagnose GBS include biochemical screenings to check for ESR and CPK levels, which are elevated in myopathies (Randall, 2010). Pulmonary function tests are important for GBS patients in order to test their neuromuscular respiratory function and predict the diaphragmatic and abdominal muscular strength. If the forced vital capacity, maximum inspiratory pressure and maximum

expiratory pressure are not adequate, the patient will need to be put on mechanical ventilation for respiratory assistance.

Diagnoses, if missed, can result in worse outcomes for the patient due to inappropriate, unnecessary or delayed effective treatments. Therefore, when considering Guillain Barre Syndrome as a possible diagnosis, doctors should first rule out certain diseases. Vasculitic neuropathy should be ruled out, as it is often an asymmetrical progressive weakness caused by previous infections (including Hepatitis, HIV, or Lyme disease). Infections are also the cause of many acute neuropathies whose symptoms appear similar to GBS including Diphtheria, Polio, and Botulism (Randall, 2010). A hereditary disease, Acute Intermittent Porphyria (AIP), can present with initial symptoms similar to GBS as well. AIP displays acute motor multifocal neuropathy with involvement in the arms more than the legs and mild sensory impairment (Randall, 2010). Neurotoxins can also cause symptoms that mimic the classic signs of GBS. Toxins from eating tropical fish, being bitten by a tick/snake/spider, and specific buckthorn berries can all cause symptoms of muscle weakness, loss of deep tendon reflexes, and possible respiratory failure (Randall, 2010). Increased exposure to specific heavy metals including lead, mercury, gold, or arsenic can cause symptoms of progressive weakness, joint pain, widespread sensory loss, axonal loss, autonomic dysfunction, and increased protein levels in the CSF (Randall, 2010). Drug abuse and chemotherapy drugs may also mimic GBS with an onset of paresthesia, weakness and areflexia. Acute cervical myelopathy is important to consider in a differential diagnosis as it presents with decreased deep tendon reflexes, decreased sensation and progressive weakness of the nerves that extend from the cervical spine (Randall, 2010). When diagnosing GBS subtype Miller Fisher syndrome, Wernicke's Encephalopathy is important to differentiate as it also presents with abnormal eye movement, acute ataxia, and gait abnormalities. However, patients with Wernicke's Encephalopathy also present with abnormal changes in their mental status, which does not occur in GBS (Randall, 2010).

When contemplating a patient's symptoms, it is important to have a good understanding of the differential diagnosis for Guillain Barre Syndrome. It is crucial to fully comprehend the patient's onset and progression of symptoms, including the miniscule details of the motor and sensory symptoms. Understanding the progression and preceding events to the symptoms is crucial in GBS diagnosis. As a result of the differential diagnosis previously explained, it is important to make note of exposures to toxins, foods, drugs, and trauma. Notes should also be taken on any prior illness of the respiratory or gastrointestinal tract, as well as, HIV or Lyme disease (Randall, 2010). At times, the diagnosis of a patient with Guillain Barre Syndrome will be clear-cut and the pattern of symptom presentation will be exactly what is expected. However, there will be cases when patient symptoms are atypical. When dealing with obscure patient cases, the Guillain Barre differential diagnosis stated above is very useful in properly evaluating a patient by negating certain diseases through each symptom present.

General Medical Management

The attention and care of medical management for patients diagnosed with Guillain Barre Syndrome is critical to their outcome. In the case of GBS, it is vital to swiftly reach the correct diagnosis to start implementing proper treatments to reduce the progression and seriousness of the symptoms. Patients who are diagnosed with Guillain Barre Syndrome should be monitored in a hospital in close quarters until the symptom progression has plateaued or until the symptoms have begun to dissipate. Although at first, the symptoms of GBS do not seem critical, such as paresthesia in the feet or muscle weakness in the fingers, this condition can progress and result in respiratory distress and cardiovascular complications. Of all patients diagnosed with GBS, 33.3% of patients require admission to the ICU and need to be medically stabilized (Andary & Klein, 2016). When GBS progresses there is a change in the homeostasis of the body including hypoxia, arrhythmias, and blood pressure levels at both ends of the spectrum. Close monitoring and proper

administration of drugs is crucial to the patient's well-being and long term outcome (Andary &

Klein, 2016).

After patients diagnosed with GBS are medically stabilized, they are usually treated on a

neurological floor and medical staff continues to prevent cardiovascular, respiratory and other

medical complications that may occur. Supportive care for patients' diagnosed with GBS during

their length of stay in the hospital is critical for their long-term outcome. For respiratory therapy,

patients may be put on mechanical ventilation after close monitoring of vital capacity and pulse

oximetry. Cardiac monitoring of heart rate, blood pressure, and cardiac arrhythmias allows

detection of any life threatening situations (Hughes, Wijdicks, Benson, Cornblath, Hahn,

Meythaler, Sladky, Barohn, & Stevens, 2005). Vasoactive drugs may be administered in order to

treat blood pressure abnormalities. The prevention of infection, thrombosis, pressure sores and

contractures is administered through physical therapy sessions, appropriate medications,

compression stockings and frequent positioning changes (Hughes et al., 2005). Throughout the

course of Guillain-Barre syndrome, caretakers must reposition the patient and move the patient's

limbs to prevent blood clots, pneumonia, contractures, and bedsores. Medical care is also

necessary in assisting with immobility, neurogenic bowel and bladder issues, and pain. Bowel and

bladder management is necessary to prevent further complications, such as over-distention and

urinary tract infection. Pain interventions used for patients with GBS to improve management of

myalgia include NSAIDs, heat, and Transcutaneous Electrical Nerve Stimulation (TENS)

(Andary & Klein, 2016). Lastly, patients' mental status should be monitored for anxiety and

depression. Psychological issues commonly occur as a result of the rapid onset of the severe

sensory and motor damage to the patient's previously healthy body.

Treatment for Guillain Barre Syndrome includes plasmapheresis (plasma exchange),

intravenous immunoglobulin (IVIG) and physical therapy rehabilitation, as there is no cure for

GBS. Prognosis for patients with GBS includes a complete recovery for 80% of patients within a

year (Burns, 2008). Immunomodulatory therapy has been found to be the most helpful in

accelerating the recovery of GBS. Immunomodulatory therapy includes plasmapheresis or the

administration of intravenous immunoglobulins (Koski & Patterson, 2006; Raphael, Chevret,

Hughes & Annane, 2002).

The use of plasma exchange has been performed over a 10-day period and aids in

removing autoantibodies, immune complexes and cytotoxic components from serum (Burns,

2008). Studies have shown that this plasma exchange has decreased the recovery time of GBS by

50% (Andary & Klein, 2016). Further studies have shown that the efficacy of intravenous

immunoglobulin (IVIG) therapy in patients with GBS is equally as effective as plasma exchange

(Koski & Patterson, 2006; Raphael et al., 2002). IVIG works by several mechanisms to treat GBS

including blocking macrophage receptors, inhibiting antibody production, and neutralizing

pathologic antibodies. IVIG is easier to implement, safer for the patient and more readily

available in contrast to plasma exchange (Koski & Patterson, 2006). The use of

immunomodulatory therapy for patients with GBS is based on the disease's severity and

progression. The more severe and rapid the progression of the disease, the more likely a patient is

to benefit with a faster functional recovery from IVIG treatment (Raphael et al., 2002). The risk

of blood clots is associated with the use of IVIG and should be taken seriously.

Implications for Physical Therapy

Physical therapy is imperative to the rehabilitation process for patients with Guillain

Barre Syndrome. The goal of physical therapy for patients throughout the course of GBS is multi-

fold. As a physical therapist working with a patient with GBS it is crucial to maintain the patient's

musculoskeletal system in an optimal state while steering clear of overworking the patient. It is

also important to enhance the patient's circulation, increase their cardiorespiratory endurance and

pace the recovery process within the limits of active movement while re-innervation occurs

throughout the peripheral nervous system (Burns, 2008).

Studies have shown that patients diagnosed with Guillain Barre Syndrome have continued to improve beyond two years. It is recommended by medical staff that patients recovering from GBS should continue physical therapy and conditioning programs in the outpatient setting (Burns, 2008). Patients recovering from GBS often complain of persistent fatigue and poor exercise tolerance, which limits their function with activities of daily living. The medical prognosis of patients diagnosed with GBS differs depending on the symptoms present in each patient. The most common long-term deficits can include weakness of the anterior tibialis muscle, intrinsic foot and hand muscles, quadriceps, and gluteal musculature (Burns, 2008). Unremitting problems for patients multiple years after the diagnosis of GBS also include sensory deficits of light touch, proprioception and vibration. Muscle aches and cramps are other symptoms of patients with GBS secondary to persistent sensory and motor dysfunction (Burns, 2008).

Physical therapy intervention can take place in the acute stage, the subacute setting or the long-term rehabilitation phase for Guillain Barre Syndrome. The needs of the patient will change as the disease progresses through each of the stages from the acute phase, to the plateau, and later on to the recovery phase. Due to the specific evolution of GBS it is imperative to alter the goals of physical therapy and carefully examine the current status, progression of the symptoms, and needs of the patient (Umphred et al., 2013). Overall, the goals of physical therapy for patient care of GBS include multiple rehabilitation interventions that introduce a graduated program of active exercise while monitoring overuse and fatigue to resume social roles and improve quality of life.

The rehabilitation of patients with Guillain Barre Syndrome during the acute phase is based on supportive management and prevention of long-term medical comorbidities. Patients with GBS often have a significant return of function within the first few months. It is therefore imperative during the acute stage to maintain the integrity of the functioning body systems and appropriately promote increased activity tolerance without over-fatiguing the patient (Khan, Pallant, Ng & Bhasker, 2010). At this stage, it is useful to teach the patient compensatory

strategies to complete any functional activities. During the acute stage, the goal of physical therapy is to prevent contractures, manage pain, improve respiration, manage blood gas levels and protect the skin from potential breakdowns (Burns, 2008). During the acute stage, patients are often unable to move voluntarily or breathe on their own. Therefore, physical therapy should include chest percussion, breathing exercises, control of secretions, and incentive spirometer use for respiratory conditions (Burns, 2008). Improving respiratory function is imperative in decreasing dysphagia and improving oxygen consumption. Respiratory therapy is also important to improve exercise tolerance in order to prevent over-fatiguing and help in weaning patients off mechanical ventilation. Patients in the acute phase of GBS are often flaccid and may be unable to reposition themselves to prevent pressure ulcers and contractures (Hughes et al., 2005). Due to this, physical therapy also focuses on positioning and stretching with passive range of motion to prevent contractures and pressure ulcers. Studies have shown that prolonged, continuous stretching, including the use of splints, is beneficial in preventing contractures and maintaining functional range of motion (Hughes et al., 2005). Splints are often used on the ankle to prevent plantar flexion contractures and on the wrists to maintain proper finger and wrist alignment. Range of motion is important to increase blood circulation and maintain extensibility of the joints. Passive range of motion to stretch all joints should be performed twice a day to decrease any muscle pain or development of possible contractures. PROM exercises are useful, as energy conservation strategies are important for patients diagnosed with GBS to improve overall function and support the recovery process (Hughes et al., 2005; Umphred et al., 2013).

During the subacute stage, physical therapy sessions should include range of motion, activities of daily living exercises, muscle strengthening, and continued respiratory management. It is imperative during the subacute setting to work on bed mobility, transfers and ambulation to prevent skin breakdown. It is crucial during this stage to refrain from over fatiguing patients and being cautious of orthostatic hypotension. Patients in the subacute stage have an orthostatic hypotension precaution because the tone of the blood vessels may not be appropriate. In order to

assess orthostatic hypotension the patient's blood pressure should be taken in accordance to changes in position (supine, sitting, standing, ambulation etc.) (Hughes et al., 2005). Another reason for the orthostatic hypotension precaution is because patients with GBS are usually unable to actively use their leg muscles to pump their blood, causing pooling of the blood in the extremities. Therefore, patients in the acute and subacute phase should contemplate using an ace wrap or compression stockings to help with prevention of blood pooling and blood clots. It is important to slowly progress the patient's tolerance to an upright position and to make sure that these patients are properly hydrated before physical therapy sessions (Umphred et al., 2013).

As strength starts to return for the patient in the subacute phase, physical therapists should incorporate a therapeutic exercise program. A ther-ex program should include low resistance exercises with strict avoidance of antigravity activation of muscles until the patient presents with an MMT grade of at least 3/5 (Umphred et al., 2013). An implemented program should include PROM through the motion desired and then low repetitions of AAROM or AROM for muscle re-education and rebuilding. Facilitatory techniques can be used such as vibration or tapping, if the sensory stimulation permits. Active exercises should be added very slowly and with frequent rests to avoid fatigue. Studies have shown that excessive exercise to fatigue during early reinnervation can lead to further damage rather than increased strength (Hughes et al., 2005). A patient who starts to feel signs of fatigue during exercise may complain of muscle aches and abnormal sensations that continue for longer periods than appropriate. Any exercises that cause over fatigue should be discontinued and re-implemented with decreased resistance until an increase in the patient's strength occurs (Umphred et al., 2013). Every time exercises are implemented, the response from the patient should be monitored closely to assess for weakness, soreness, or muscle spasms.

After a few months of physical therapy, most patients are inclined to stop attending rehabilitation. However, it has been recommended through clinical studies that physical therapy should continue for a few years after the symptoms of Guillain Barre have reversed. During long-

term rehabilitation, the goals for physical therapists should include strengthening, range of motion, and stretching as needed. Patients should continue to increase their endurance and aerobic conditioning, as fatigue is a main complaint from patients diagnosed with GBS (Gupta, Taly, Srivastava, Murali, 2010). Always avoid undue fatigue during therapy sessions until the peripheral nervous system is healed because fatigue stresses the reparations of the motor system. During long-term rehabilitation the patient should aim to become independent in activities of daily living such as bed mobility, transfers, progressive ambulation, and wheelchair management (Gupta et al., 2010). Pain management continues to be important during the long-term rehabilitation stage, as well as, skin care and bed sore prevention. As re-innervation continues to progress, the physical therapist should use PNF to recruit the maximally desired contraction of specific muscle groups. As a patient begins to recover muscle strength, increased repetitions may be implemented in order to redevelop motor-sensory engrams and reintegrate the motor and sensory pathways during movement. The close monitoring of cardiac output is important during rehabilitation to ensure no over fatiguing. It has been shown that keeping a patient at 45% of their predicted maximal heart rate reserve during therapy has allowed improvement of muscle strength, endurance and decreased fatiguing to complete ADL (Garssen, Bussmann, Schmitz, Zandbergen, Welter, Merkies & Van Doorn, 2004).

Previously, a study was performed to report on the effects of physical training on fatigue, fitness and quality of life in patients with Guillain Barre Syndrome. Subjects took part in a 12-week exercise training program which included supervised training sessions 3 times a week for 12 weeks. Each session consisted of 5 minutes to warm-up (65% max HR), a 30 minute cycling session (which consisted of 70% max HR increasing to 90% max HR as the sessions continued) and a cool down of 5-10 minutes, with heart rate monitored continuously (Garssen et al., 2004). The resistance of the bike was also increased from 0 W to 20 W depending on the patient's physical ability as the weeks progressed. This study found that patients who underwent the intensive bicycle training protocol had a 20% reduction of self-reported fatigue, VO_2 max

increases of 20%, and increases in functional outcomes and quality of life (Garssen et al., 2004). The medically supervised training sessions showed decreases in depression and anxiety, as well as, improvement in physical fitness and muscle strength. After the study, most of the subjects stated they were motivated to continue with physical training post-study because of the effects the exercise had on their mental and physical state (Garssen et al,. 2004).

Another study was conducted to clarify the mutual relationship between physical fitness, fatigue, mobility, perceived physical functioning and perceived mental functioning in patients diagnosed with Guillain Barre syndrome. After taking part in a 12-week exercise program, patients with GBS demonstrated an improvement in fitness, mental functioning and mood (Bussmann, Garssen, van Doorn, & Stam, 2007). It was also found that an increase in the patients' perceived mental functioning actually decreased the patients' objectively measured mobility. Complaints of fatigue increased with increased mental functioning, which may be secondary to over thinking symptoms of fatigue during exercise (Bussmann et al., 2007).

Case Scenerio and Recommended PT Program

Natalie is a 27-year-old active female, who is a 3rd grade teacher and runs marathons as a hobby. At the age of 10, Natalie was diagnosed with Type I Diabetes Mellitus, which has been medically stabilized ever since her diagnosis. Natalie recently complained of tingling and dysesthesia in her feet bilaterally, which caused difficulties with her running. Natalie feels that as of last week, she can no longer run as far and feels like her gait pattern has become "uncharacteristic". When Natalie arrived at the hospital she was admitted into acute care. The medical staff disregarded her symptoms as anything other then DM, due to the commonality of such paraesthesia complaints of the lower extremity with Diabetes Mellitus. The doctors altered Natalie's medications for DM and the nursing staff instructed Natalie on the proper techniques for foot care to prevent wounds.

Physical Therapist Kristen Markoe was called upon the next day to assess the patient's functional status before discharging Natalie home. During the sensory evaluation, Kristen noticed the sensory deficits presented in a nerve root pattern. Kristen became alarmed when the patient stated that the paraesthesias had started to affect her lower leg and upper thigh, and no longer just her foot. During reflex testing, Natalie presented with hyporeflexia (1+) of the Achilles and quadriceps tendons bilaterally. Upon evaluation, Natalie presented with decreased MMT strength in her tibialis anterior 3+/5, gastrocnemius and soleus 4/5, fibularis longus and brevis 3+/5, foot intrinsics 3/5, hand intrinsics of 3+/5, quadriceps 4-/5 and glutes 4-/5. While ambulating just 300 feet around the hospital floor, Natalie presented with a minor trendelenberg gait, an inconsistent forceful hyperextension of the knee and an intermittent foot slap. Natalie became visibly upset because she was concerned with her health as she had been able to run a half marathon in New York City just three weeks prior. Kristen told the medical staff to run blood tests, serologic studies (to asses for certain antibodies), a lumbar puncture for CSF scans to check elevated protein levels, and a nerve conduction study because she believed Natalie was undergoing something other than symptoms of Diabetes Mellitus.

The next morning PT Kristen Markoe returned to Natalie's room to check on her test results. Kristen realized Natalie's tests were scheduled for that afternoon, as the doctors did not consider her case to be urgent. Natalie's symptoms had drastically increased since the previous day as she lost complete sensation in her lower extremities with MMT grades of 2+/5 throughout her lower extremities bilaterally. When evaluated, Natalie's upper extremity also became increasingly affected, as her overall bilateral upper extremity MMT was a 3/5 and she was experiencing loss of touch sensation on the dorsal aspect of her forearm and hand. During the evaluation PT Kristen Markoe went to alarm the doctor on-call, when Natalie exclaimed that she was beginning to have difficulty breathing. Immediately, doctors rushed into the room to stabilize Natalie. After tests were run, Natalie was officially diagnosed with Guillain Barre Syndrome, subtype Acute Inflammatory Demyelinating Polyradiculoneuropathy (AIDP). Natalie's symptoms

progressed to the point of flaccid quadraparesis, loss of light touch sensation in all four extremities (glove and stocking pattern), incomplete loss of proprioception in bilateral lower extremities and intermittent use of mechanical ventilation. Natalie had difficulty speaking and breathing on her own for increased periods of time, for which she saw a speech pathologist to aid in her recovery.

Acute Physical Therapy: Natalie's treatment during the acute stage included passive range of motion (PROM) and positioning to prevent contractures/pressure ulcers, respiratory therapy to improve ventilation and breathing efficiency, the use of splints for continuous prolonged stretching, postural drainage to decrease the chance of a respiratory infection and PNF in an attempt to facilitate the neuromuscular system. Natalie was repositioned from supine to side-lying to long-sitting every 2 hours by either the nursing staff or her fiancé, who was educated on the importance of the physical therapy interventions. During positioning, it was noted to keep Natalie's ankles in dorsiflexion, knees and hips in slight extension/neutral rotation, shoulders in slight abduction/external rotation and wrists in neutral to prevent contractures. The nursing staff also donned and doffed compression stockings on Natalie's feet to assist in preventing blood clots.

PROM was conducted for Natalie by her PT Kristen twice a day, twice more by her nurse and again if her fiancé wanted to assist in the rehab process. PROM was performed on each of Natalie's joints including ankles, knees, hips, fingers, wrists, elbows, shoulders, and neck to prevent contractures. Kristen assessed PROM of all of Natalie's joints documenting each joint as full ROM, with slight stiffness at end range for her ankles and fingers. To prevent contractures, Natalie was also given multiple splints. Splints were made to position Natalie's ankles in dorsiflexion and neutral inversion/eversion, wrists in a slightly extended/neutral position, and her fingers in a functional, slightly flexed position.

For respiratory therapy, postural drainage was performed with proper positioning. The physical therapist, Kristen, then completed percussion and vibration for all lobes, followed by

autogenic drainage and active cycle of breathing (to the best of Natalie's capabilities). Lastly, suction with controlled coughing was completed to expectorate any mobilized mucus. Stretching of the patient's thoracic cage was also performed multiple times a day to open up Natalie's chest and improve ROM to allow for deeper breaths and increased oxygenation. External rotation of the shoulders, abduction of the arms, extension of the neck and thoracic spine were motions performed to allow for improved chest excursion to increase lung capacity.

During the two visits a day from her physical therapist, Natalie also participated in electrical stimulation of her muscles, as well as, PNF of her upper extremities and lower extremities. PNF is thought to facilitate proprioceptive neuromuscular systems through diagonal patterns of motion and was used by her physical therapist to reintroduce functional motions and improve proprioception. During the acute phase the PNF exercises were performed as PROM, until the GBS symptoms ceased progression after 3 weeks and a gradual return of function began to occur.

Subacute Physical Therapy: After 3 weeks, Natalie's symptoms of flaccid quadriplegia, loss of light touch sensation in all four extremities, incomplete loss of proprioception in bilateral lower extremities and intermittent use of mechanical ventilation began to diminish and a gradual return of strength and sensation was becoming evident. With the nervous system still repairing itself, it was important not to stress the system with fatigue during rehab sessions. Natalie's blood pressure was taken intermittently throughout the physical therapy sessions to ensure no episodes of orthostatic hypotension. During the subacute stage, Natalie's therapy sessions consisted of maintaining her ROM and decreasing stiffness, increasing her strength with an implemented therapeutic exercise program, improving her functional abilities for ADL, and continuing respiratory management. During Natalie's subacute physical therapy sessions, the main objective was to increase her strength to allow for functional independence with bed mobility, transfers and ambulation. The sessions with Natalie's physical therapist lasted 45 minutes twice a day. Rehabilitation sessions began with a muscle re-education program using

PNF patterns for the lower extremity, upper extremity, pelvis, and trunk. Natalie's physical

therapist started with PROM improving to AAROM in PNF to allow Natalie the chance to

increase her strength and proprioception in functional movement patterns. Natalie was also

educated on an AROM ther-ex program to complete with her fiancé or nursing staff, stressing the

importance of low repetitions dispersed throughout the day to avoid fatigue. The ther-ex program

consisted of ankle pumps, quad sets, glute sets, adductor squeezes, fist opening/closing, wrist

flexion/extension, elbow flexion/extension, shoulder flexion/abduction, and neck

rotation/flexion/extension. Natalie was informed on the importance of these exercises to increase

strength and function but to also realize that fatigue will only extend the recovery process, not

expedite it. Therefore, Natalie should perform only 2 exercises at a time with 10 repetitions of

each exercise and disperse the exercises throughout the day. If Natalie experienced any signs of

fatigue, soreness, muscle aches or abnormal sensations she was to stop the exercise immediately,

include longer breaks, and decrease the repetitions for the next session. The therapeutic exercises

combined with PNF allowed for an improved recovery of muscle re-education and strength.

Natalie was able to achieve an MMT grade of 4- throughout her lower extremities and a 4+

throughout her upper extremities after just 12 weeks of physical therapy.

      Long Term/Outpatient Physical Therapy: After Natalie was able to achieve MMT grades

of 4- and 4+ in her extremities, the goal of rehabilitation became improvement of independence

for functional activities and increasing aerobic conditioning. During long-term physical therapy,

fatigue symptoms were addressed to improve function and active participation in transfers and

ambulation. Strengthening and stretching was still performed to maintain Natalie's improvements

in ROM and muscle power. Natalie was constantly reminded on the importance of avoiding

fatigue during physical therapy to continue her steady progression of recovery. If Natalie

experienced any signs of fatigue she stopped the current exercise immediately, made her physical

therapist aware, and adjustments in her regiment were made for the next session. Natalie's

physical therapist implemented a resisted ROM theraband exercise protocol for her upper

extremity including elbow flexion, extension, as well as, shoulder abduction, flexion, extension, internal and external rotation. Natalie completed all PNF patterns with her physical therapist with appropriate resisted ROM to further improve strength, proprioception and function of entire muscle groups. Natalie also performed bed mobility with minimal assistance from her physical therapist, as they practiced rolling, bridging, and supine-sit 5x for each. As Natalie's strength continued to increase, her strengthening exercises were performed in sitting while adding balance control and proprioception with perturbations. Riding a bike was implemented into Natalie's rehabilitation program as studies showed that bicycling decreases fatigue, increases VO_2 max, and improves strength and function. The protocol for Natalie's bicycle program avoided fatigue and included 2 minutes of a warm up at 50% max HR, a 10 minute increment at 60% max HR, and a cool down of 2 minutes with 0 W resistance throughout the bike session. Overtime, Natalie's rehab sessions included higher repetitions of her therapeutic exercises to increase strength, re-develop motor-sensory engrams and improve cardiovascular functioning, but still refraining from fatigue (Garssen et al,. 2004).

After 26 weeks, Natalie was able to complete a bike riding session for 40 minutes with a 5 minute warm up at 60% max HR, a 30 minute increment at 75% max HR, and a cool down of 5 minutes with a resistance of 10W throughout the ride (Garssen et al,. 2004). On the days when Natalie did not ride the stationary bike, she performed aerobic conditioning by ambulating through the hallways. Natalie was able to ambulate 150 ft using a roller walker (or ambulate within the parallel bars). Towards the end of the walks, Natalie began to demonstrate a slight foot slap, intermittent knee recurvatum and minor trendelenberg gait pattern showing signs of fatigue and was told to sit and rest. Natalie performed weight-shifting exercises from right to left and front to back within the parallel bars to improve strength, normalize the trendelenberg pattern and improve proprioception in her lower extremities. Eccentric quad exercises including stand to sit were also performed to decrease the occurrence of knee recurvatum. While standing within the parallel bars, Natalie practiced single leg stance while concurrently simulating gait by swinging

through with her other leg using concentric/eccentric control of dorsiflexion, to improve all abnormal gait patterns and improve proprioception.

Kristen, Natalie's physical therapist, purchased assistive equipment through Natalie's insurance company prior to her discharge. Natalie planned on using the adaptive equipment until her symptoms of weakness were completely dissipated. Kristen purchased 2 AFOs for the intermittent foot slap, 2 knee braces to assist with the knee recurvatum, a rolling walker for when Natalie would be ambulating short distances, and a lightweight transferring wheelchair for when Natalie would be travelling long distances. After two years, Natalie showed no signs of abnormal fatigue and was able to return to running. Natalie signed up for her first 5K race just two and a half years post-onset of Guillain Barre Syndrome, hoping to be able to complete the race having her, now husband, at the finish line cheering her on.

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