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Case Study

Guillain-Barre Syndrome: Case Study and Literature Review

William Peretti Wobeto[1], Beatriz Beretta Zani[1], Ana Beatriz da Silva Esteves[1], Maria Vitoria da Silva Marangoni[1], Naiélli da Silva Pinatti[1], Kaique Nazaré Sousa Pedro[1], Nayadne Michaela da Silva[1], Days Oliveira de Andrade[1], Idiberto José Zotarelli Filho[2,3*], Uderlei Doniseti Silveira Covizzi[1]

[1]Brazil University, Fernandópolis, Sao Paulo, Brazil; [2]São José do Rio Preto, Sao Paulo, Brazil; [3]Bentham Science Ambassador Program, Brazil

ABSTRACT

Guillain-Barre syndrome (GBS) is an acute demyelinating inflammatory mediated polyneuropathy mediated by the immune system that leads to generalized flaccid paralysis. Most GBS cases are preceded by viral or bacterial infections of the respiratory or gastrointestinal tract, developing an aberrant response that causes autoantibody formation and complement and cytokine activation. Because it is a rare disease, diagnosis is often slow and may worsen the clinical picture. The patient should be evaluated by a multidisciplinary team and the treatment of choice is intravenous human immunoglobulin. We report a case in which the patient had several symptoms resulting from GBS, probably developed by the previous infection, but only had the disease diagnosed late, leading to a worsening of her clinical condition and compromising her quality of life. Since 1976, several studies have established a causal relationship between GBS and vaccines, especially Influenza A, but the pathophysiological mechanism remains unknown. However, it is known that there is a greater chance of GBS development due to Influenza a virus infection than vaccination. Studies reveal that there are environmental and genetic components that may influence susceptibility to disease. However, there is little research on the polymorphism of immune response genes and their influence on the development of the syndrome. Some cases of involvement of people belonging to the same family have been reported in the literature, thus demonstrating that the presence of genetic components influencing the predisposition to GBS cannot be ruled out.

Keywords: Guillain-Barre Syndrome; Polyneuropathy; Immune system; Diagnosis

INTRODUCTION

Guillain-Barre Syndrome (GBS) is considered an acute onset peripheral polyneuropathy and represents the most common cause of generalized flaccid paralysis [1]. Both sensory and motor systems may be affected, and motor disorder is characterized by a gradual decrease in muscle strength, and paralysis moves from the lower to the upper, and at maximum intensity may increase the danger of asphyxiation [2]. The incidence of typical GBS is between 0.81 and 1.89 cases per 100,000 people, being more frequent in men than women, increasing with age. An incidence survey conducted in 2011 showed that it was highest in Bangladesh (2.5 cases per 100,000 people) and lowest in Brazil (0.40 cases per 100,000 people). The severity of GBS cases also manifests differently, being higher in China than in Europe and the United States. Several researchers have collaborated on the spectrum of SBG, gathering clinical and biological data for definitions of biomarkers related to the clinical and scientific landscape of this autoimmune neuropathy [2]. The etiology remains unknown; however, most GBS patients have symptoms of the gastrointestinal tract or respiratory system infections within the six weeks preceding the disease [1-3]. Campylobacter jejuni bacteria appear as an infecting agent in 30 to 40% of cases, but there are reports of other agents such as Mycoplasma pneumonia, Haemophilus influenza, Helicobacter pylori, Epstein-Barr virus, Zika virus, among others [1]. In addition to infections, some vaccines such as rabies, oral polio, diphtheria,

Correspondence to : Idiberto José Zotarelli Filho, MSc, Ph.D, São José do Rio Preto, Sao Paulo, Brazil, Tel: +55(17) 98166-6537; E-mail: m.zotarelli@gmail.com

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tetanus toxoid, hepatitis B, conjugated meningococcal, and influenza A also appears to play a role in the development of GBS [4].

The association between influenza vaccine and GBS emerged in the United States in 1976 when 32% of Ohio's population was vaccinated against influenza A, and neurologists noted that GBS was more prevalent in people who received the vaccine. In a rigorous study, which assessed the relationship between influenza A vaccination and the development of GBS in adults, it concluded that there is one case of the disease for every 100,000 doses administered [5]. In Norway, a population analysis revealed that there was an increased risk of GBS development during and after a pandemic of influenza A infection, but no increased risk of vaccination was observed [6]. Although the Influenza A virus vaccine has been shown to be effective in reducing morbidity and mortality, there is still some resistance to its administration due to the reported risk. Recent studies have shown that infection with influenza A virus is associated with a higher risk for GBS than vaccination against it. Research has shown that acquiring the infection increased the risk of GBS by approximately 16 to 18 times, while influenza A vaccination increased by only 2 times [7]. Therefore, it is important to emphasize that the development of GBS due to influenza a vaccination is a rare event and the benefits of the vaccine are irrefutable. Rare cases have reported the development of GBS following the use of a rabies vaccine made from sheep brain neural tissue. This type of vaccine production, which is even the oldest mode of preparation, has low cost, but confers lower immune power compared to vaccines from cell culture and also provides a higher incidence of neurological complications. However, it is still commonly used in countries in Asia, America, and Pakistan. In these cases, patients did not have the most well-known symptoms preceding GBS, but abdominal pain and difficulty in urinating, and as there are almost no reported cases of GBS development caused by vaccination, little is known about the symptoms and therefore more difficult to diagnose [8,9].

The most common symptoms of GBS are progressive muscle weakness, flexlexia, and increased CSF protein without increased cell count [10,11]. The classic form is acute demyelinating inflammatory polyradiculoneuropathy, accounting for 90% of cases in Europe and North America, and is characterized by progressive muscle weakness, sensory symptoms, and dysautonomia. Axonal forms are most common in Asia and Central and South America and are preceded by Campylobacter jejuni infection. Another type of neuropathy, called Miller-Fischer syndrome, is characterized by ophthalmoplegia, ataxia, and dyslexia [10]. Treatment of GBS patients involves a multidisciplinary team that must prevent and monitor potentially fatal complications. Approximately one-third of patients develop respiratory failure, and intubation, if necessary, should be performed before fatigue or respiratory arrest occurs. Plasmapheresis, which removes autoantibodies, cytokines, and complement, is an effective treatment but should be performed within the first two weeks. However, the treatment of choice is intravenous human immunoglobulin infusion by neutralizing pathogenic antibodies. The use of oral or intravenous corticosteroids was not beneficial for patients [1].

The exact cause of GBS remains unclear and the pathophysiological mechanism may differ depending on the presentation [1-12]. Damage to the myelin sheath is known to be predominantly caused by activated macrophages that penetrate the membrane around nerve fibers causing demyelination. In addition, patients with acute GBS have low CD4+ and CD25+ T cell counts, demonstrating that there is an important role of T lymphocytes in the pathogenesis of the disease. An increase in matrix metalloproteinase 9 (MMP9) has been identified as the cause of Schwann cell membrane invasions [1]. Despite advances in identifying possible triggers for GBS, there is still much to be researched on genetic and environmental factors that may influence individual susceptibility to GBS. Some scientific studies have revealed specific gene polymorphisms associated with a higher risk of disease development, as well as cases of GBS occurring in members of the same family, thus demonstrating that genetic causes should be considered [13-17].

LITERATURE REVIEW

The first description of the disease was made approximately one hundred years ago by three French neurologists who identified high protein concentration and normal CSF cell count of two soldiers. In 1949, clinicopathological features of fifty fatal cases were described which presented axonal degeneration, myelin sheath damage and edema in nerves. A variant of GBS with predominant axonal damage was described in 1986, but some time later was linked to acute axonal motor neuropathy [1]. Several studies have shown that GBS is not an inherited disease, but some individuals may develop it due to some genetic predisposition linked to gene polymorphisms. There are some scientific studies that have attempted to associate certain polymorphisms with increased susceptibility to the development of the syndrome. Studies indicate that GBS pathogenesis is associated with a T cell-mediated immune response. Liu and colleagues in 2016 investigated polymorphism in exon 2 of the CD1A and CD1E gene, whose function is related to the presentation of lipid antigens. The study showed that only individuals with CD1A gene polymorphism were at higher risk for the disease. Due to the presence of an aberrant immune response induced by GBS infection, a Brazilian study by Dourado et al. In 2016, evaluated polymorphisms in the gamma receptor gene (FCGR) in healthy people and people with the disease. The result of the study revealed that in the Brazilian population there is no association between the analyzed polymorphisms and a greater predisposition for the development of the pathology [14].

The polymorphisms of interleukin-17 genes and intercellular adhesion molecule 1, both highly expressed in autoimmune and inflammatory diseases, were analyzed by Kharwar et al., and it has been shown that these genes are increased in individuals with GBS and can be used as a genetic marker of susceptibility [16]. Sharshar et al., demonstrated that the extracellular matrix metalloproteinase gene, MMP-9, responsible for the degradation of the basement membrane and extracellular matrix constituents, was increased in patients with GBS and correlated if with gravity [18]. Rare studies have shown the development of GBS in members of the same family. Aquil et al. described 2 cases of GBS and 2 other probable cases of GBS in members of

the same family, indicating the possible presence of genetic elements in the pathogenesis of the disease [17]. The complete set of messenger RNAs, ribosomal RNAs, carrier RNAs, and microRNAs is called a transcriptome and there are variations depending on the patient's physiological or pathological condition. Advances in sequencing techniques that enable transcriptome analysis have enabled the identification of how cells respond to numerous signals. Huang et al. analyzed the gene expression of seven GBS patients and seven healthy people and concluded that the most differentially expressed genes were FOS, PTGS2, HMGB2, and MMP9, which are involved with inflammatory response, infectious disease, and respiratory disease [19]. Future studies analyzing polymorphisms in differentially expressed genes are needed to understand their relationship with GBS. Therefore, based on the case report of a patient diagnosed with Guillain-Barre Syndrome, the aim of the present study was to review the literature regarding GBS and also to relate its pathology to some known genetic polymorphisms.

CASE STUDY

This is a case report with a literature review where we sought to analyze scientific articles that relate GBS with predisposition linked to genetic factors resulting from gene polymorphisms.

After searching the literature on scientific articles dealing with GBS relating it to gene polymorphism, a small number of publications have been observed and they still do not show a strong link between genetic factors and susceptibility to pathology development. Research describing cases of members of the same family affected by GBS is still very rare. However, there are genetic indicators that seem to interfere with the risk of developing this complex pathology. It was also observed that the symptoms described in the researched articles coincide with the description of the patient's clinical condition evaluated in the case study.

GBS is considered the leading cause of generalized flaccid paralysis in the world [1]. There are a few specific epidemiological data for Brazil. The pathology occurs sporadically, presenting an autoimmune character, preferentially affecting the proximal myelin of the peripheral nerves in an acute/sub-acute form. It is evidenced that, in most cases, there are reports of infections prior to the onset of the syndrome and rare cases arise after vaccination [17]. The diagnosis is made through the clinical picture of the patient, who most often has paraesthesia, tingling, weakness, pain, in addition to CSF analysis and electroneuromyography examination. Despite a favorable evolution occurring in approximately 80% of cases, 20% die or become sequelae [19]. Thus, it is important to continuously seek an understanding of the causes that lead to the development of this pathology.

Most autoimmune diseases are considered polygenic, and affected individuals may inherit multiple genetic polymorphisms that contribute to increased susceptibility. There are still few studies that have analyzed the involvement of gene polymorphisms that predispose individuals to greater susceptibility to GBS development. Even rarer are researches that identified people from the same family group who developed the syndrome [13-17]. However, it is unlikely that a simple Mendelian inheritance can be responsible for GBS alone, requiring the presence of a joint interaction of environmental factors contributing to increased susceptibility to disease [17].

DISCUSSION

The patient R.P.N., dentist, female, age 47 years, affected by GBS was interviewed. She revealed that her symptoms were a weakness of muscle tone, beginning with the fingertips, and pain at the wrist, which made her think she could be affected by carpal tunnel syndrome. As his field is in the dental field, he imagined that the symptoms were linked to repetitive movements. The symptoms of weakness were exacerbating and after 48 hours the pain began to radiate from her arm, incapacitating her to perform movements with her hands. When seeking medical help in an emergency room, she was treated with serum only and was referred for an ultrasound to check for carpal tunnel syndrome. However, other symptoms, such as weakness of the lower limbs and respiratory symptoms have already begun to be observed. The disease has reached the vertebrae and the patient begins to have difficulty walking. As yet undiagnosed, the patient was sent for upper and lower limb electroneuromyography and, at the time of the examination, was asked by the physiologist if there were any infectious conditions, and the patient reveals that she had diarrhea fifteen days before onset of the symptoms. Thus, Guillain-Barre Syndrome was confirmed after puncture and analysis of CSF that showed clear coloration, caused by a probable bacterial or viral infection of the gastrointestinal tract, and as the condition was already stabilized, the doctors chose not to perform the intravenous human immunoglobulin infusion.

At this stage of the disease, the patient was already dependent on care, such as bathing, hygiene, clothing, and food. Added to the difficulties caused by the syndrome, the depression became worse and the patient opted for total isolation. Even after 8 months of disease onset, the patient still has hand tremors after stimulation requiring physical therapy and does not have the same firmness in the lower limbs requiring a gym. To treat the remaining symptoms of GBS and provide the patient with the quality of life, the attending physician prescribed vitamin D, a cytidine disodium phosphate, uridine trisodium triphosphate and hydroxocobalamin acetate drug to alleviate peripheral neural disorders, and another drug. For peripheral neuropathy composed of diclofenac sodium-rich and B complex. Thus, we observed that the clinical picture of the interviewee corroborates that described in the literature, which shows an acute onset, usually preceded by respiratory or gastrointestinal tract infection, and presenting weakness of muscle tone and tingling sensation as one of the first symptoms.

CONCLUSION

GBS is an autoimmune disease characterized by the acute/subacute onset of polyneuropathy, but the underlying causes of the pathology are not yet fully understood. In most cases, previous respiratory or gastrointestinal tract infection and, more rarely, recent vaccination is evident. Because it is an uncommon disease, it often ends up being difficult to diagnose and may lead to worsening of the clinical picture and even the impossibility or difficulty of reversal. This condition occurred with the patient interviewed, since she was not diagnosed at the first medical care, and the cause was identified only after the electroneuromyography examination. Scientific studies support the hypothesis that there are environmental and genetic factors that influence susceptibility to disease development. However, there are still few studies that have evaluated the influence of gene polymorphisms involved with immunity in the pathophysiological process of GBS. Thus, further studies analyzing genetic, epidemiological and molecular aspects are needed to unravel the complex mechanism of this mysterious autoimmune disease and the reasons that lead to greater susceptibility to the syndrome.

DECLARATION OF CONFLICTS OF INTEREST

The authors declare nothing.

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