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## **GUILLAIN-BARRÉ SYNDROME: CURRENT UNDERSTANDING OF THE PATHOLOGY (REVIEW)**

Guillain-Barré syndrome (GBS), also called acute inflammatory demyelinating polyneuropathy, is an acquired immune-mediated neuropathy, the development of which occurs due to an immune reaction to a previous immune-activating event (viral or bacterial infection, surgical intervention, etc.). It is the most common cause of acute neuromuscular weakness and paralysis worldwide. Immune-mediated attack on peripheral nervous system myelin, axons or both is presumed to be triggered by molecular mimicry, with both cell- and humoral-dependent mechanisms implicated in disease pathogenesis [1, 9, 11]. The prevalence of this pathology is 1-2 persons per 100,000 of population each year [5], and about 100,000 people are developing the disorder every year worldwide [12]. Thus, it cannot be classified as a frequently occurring pathology, but its potential fatality and high risk of disability make its study relevant throughout the world [7]. It can affect any person regardless of gender or age [5], including children and adolescences [1, 3].

More than 60% of patients have a respiratory or gastrointestinal infection 1 to 6 weeks before the first symptoms appear. According to serological studies, this infection may be viral or bacterial. Among viruses, a number of authors emphasize the important role of Zika virus [2, 8], and among intestinal bacterial *Campylobacter jejuni* is considered to be one of the reasons of this pathology [5, 13]. Also *Mycoplasma pneumoniae*, *Haemophilus influenza*, Cytomegalovirus, Epstein-Barr virus, influenza A, varicella-zoster, hepatitis, and Chikungunya viruses are considered to be responsive triggers of this disease [15].

Last years, many scientists have paid much attention to the relationship between GBS and coronavirus disease [4, 12, 15]. Several recent case reports may suggest an association between the development of Guillain-Barré syndrome and a previous (up to 4 weeks) SARS-CoV-2 infection. Published studies on SARS-CoV-2-related GBS typically report a classic type of GBS often with a demyelinating electrophysiological subtype [12]. The most likely cause is postinfectious dysregulation of the immune system caused by the virus. It is likely that the main mechanism of nervous system damage in such patients may be an autoimmune reaction to peripheral nerve antigens, since no viral genome was detected in the CSF. In addition, A. Zito et al. emphasize the importance of the fact that the severity of COVID-19 at the onset of the disease probably does not correlate with the clinical outcome of Guillain-Barré syndrome [18]. Thus, in children and adolescents, there are some minimal manifestations of covid-19 or its asymptomatic

course [17], however, complications, including damage to the nervous system, cannot be excluded. In COVID-19 patients, an increase has been observed in cytokines such as interleukin-1 $\beta$ , IL-6, IL-17, TNF- $\alpha$  and interferon- $\gamma$ , as well as with other inflammatory chemokines. Because many of the same cytokines have been implicated in the pathogenesis of typical GBS, the cytokine storm in COVID-19 may play role in the development of GBS [15].

GBS is the leading cause of acute paralysis that can potentially affect all of the human population. GBS is an immune-mediated disease, driven by an immune attack targeting the peripheral nervous system [10]. According to modern concepts, Guillain-Barré syndrome is an acquired immune-mediated neuropathy, the development of which occurs due to an immune response to a preceding immune-activating event, so the leading role in the pathogenesis is attributed to autoimmune mechanisms [18].

GBS can be divided into several subtypes depending on the phenotype, pathophysiology, and neurophysiological features. Additional research is still needed to shed more light into the pathogenesis for a better understanding and treatment of this condition [10, 14].

As for clinical picture, flaccid weakness predominates in most patients with Guillain-Barré syndrome; it is accompanied with sensory abnormalities, but usually is more prominent. Relatively symmetric weakness with paresthesias usually begins in the legs and progresses to the arms, but it occasionally begins in the arms or head. Sphincters are usually spared. Weakness remains the same for a variable period of time, typically for a few weeks, then resolves. Deep tendon reflexes are reduced or absent. Dehydration and loss of weight may take place. According to different authors, respiratory paralysis, that require endotracheal intubation and mechanical ventilation, occurs from 5 to 30% [11, 16]. A few patients have significant, life-threatening autonomic dysfunction causing abnormalities of blood pressure, inappropriate antidiuretic hormone secretion, cardiac arrhythmias, gastrointestinal stasis, urinary retention, and pupillary changes. An unusual variant may cause only ophthalmoparesis, ataxia, and areflexia [3, 11]. Cranial innervation involvement is typical, in particular, swallowing disorders. The severity of the condition in severe cases increases rapidly with the development of peripheral tetraparesis to tetraplegia and ineffective external respiration. At the same time, the state of consciousness of patients is almost unaffected, and even with massive damage to the cranial nerves, patients are available for contact through preserved movements of the eyes or toes or hands [16].

Guillain-Barré syndrome should be suspected in the presence of rapidly progressive bilateral limb weakness with sensory deficit or without it, hyporeflexia or areflexia, facial or bulbar palsy, ophthalmoplegia and ataxia [7].

Inpatient treatment in severe cases lasts up to 3 months and more. Intravenous immunoglobulin and plasma exchange (plasmapheresis) are the most commonly prescribed immunotherapies for GBS with variable efficacy dependent on GBS subtype, severity at initial presentation and other clinical and electrophysiologic prognostic factors, though the mechanisms of action of these measures are not known definitely [7, 9, 11, 14, 16]. The use of corticosteroids in this disease is quite questionable, and in modern guidelines, as a rule, is not recommended, as it may worsen the prognosis [11]. Up to a third of patients potentially need mechanical ventilation, the duration of which depends on the rate of regression of respiratory disorders [8, 16].

Clinical trials are currently underway to investigate some of the potential therapeutic candidates, including complement inhibitors [13].

Physical therapy helps to improve the prognosis and includes massage, changing body position every 1 to 2 hours, exercise therapy, lessons with a speech therapist, and myostimulation. Psychotherapy is extremely important as it combats depression, provides psychological support and builds positive motivation in the patient [5, 16].

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