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EPIDEMIOLOGY AND CLINICAL MANIFESTATIONS OF SHENLEYN-GENOH DISEASE IN CHILDREN

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Abstract:

This article is dedicated to the analysis of Shenleyn-Genox disease (ShGD) – hemorrhagic vasculitis, a condition that leads to damage in the microcirculatory system, affecting the skin, joints, gastrointestinal tract, and kidneys. The disease is most common in children, with an incidence rate of 3-26.7 cases per 100,000 children. ShGD is characterized by the deposition of immune complexes consisting of immunoglobulin A (IgA), which leads to damage in blood vessels and tissues. The article discusses the disease's pathogenesis mechanisms, clinical manifestations, diagnostic methods, and treatment approaches, emphasizing the importance of assessing the disease's activity and selecting effective treatments. The development of the disease may be influenced by genetic and infectious factors. Currently, further research is required to better understand the full pathogenesis of the disease and improve treatment strategies. Additionally, the article highlights the existence of new diagnostic criteria and ongoing questions regarding the effectiveness of treatment.

Keywords: *Shenleyn-Genox disease, hemorrhagic vasculitis, IgA, diagnosis, pathogenesis, treatment, children.*

INTRODUCTION. Shenleyn-Genox disease (hemorrhagic vasculitis) is a condition that leads to damage of the microcirculatory system, affecting the skin, joints, digestive system, kidneys, and sometimes other organs. It is characterized by the accumulation of immunocomplexes belonging to immunoglobulin A (IgA) class. One of the most common systemic vasculitis in children, with an incidence of 3-26.7 cases per 100,000 children.

Views on the etiology, development mechanisms, and treatment methods of the disease have evolved, but questions regarding laboratory markers and assessment of disease activity remain unresolved. Kidney involvement plays a crucial role in the pathogenesis of Shenleyn-Genox disease and determines treatment approaches. In 26-60% of children, the kidneys are affected.

The need for research focuses on assessing disease activity, predicting its course, and determining effective treatment methods. Currently, the pathogenesis mechanisms of the disease are not fully understood, so it is essential to develop specific criteria for identifying kidney involvement and nephritis risk [1].

The primary goal of this article is to provide a comprehensive analysis of the impact of Shenleyn-Genox disease on children, examining the disease's development mechanisms, diagnostic methods, complications, and treatment approaches.

MATERIALS AND METHODS. During the research and writing of this article, we used various scientific literature and electronic resources, including scientific articles, books, journals, reviews, and official documents. The data was obtained from databases like PubMed, Web of Science, Google Scholar, and periodicals in the field of neuroimmunology. To ensure the accuracy and reliability of the information presented, modern and verified sources were used.

Discussion. Shenleyn-Genox disease (SGD) is a systemic vasculitis characterized by the deposition of immunocomplexes composed of IgA immunoglobulins in small blood vessels. The disease originates from the disorganization of microcirculation vessels and aseptic inflammation. SGD presents with three clinical symptoms: abdominal pain, arthritis, and erythema without thrombocytopenia. The disease may lead to kidney damage in the form of glomerulonephritis and gastrointestinal bleeding [2, 3].

SGD is the most common systemic vasculitis among children, with the initial incidence rate ranging from 3.0 to 26.7 per 100,000 children worldwide. In Russia, this indicator is 23-25 [4]. The disease predominantly affects children aged 4-6 years, with fewer cases in adolescents, though it is more severe in them, and renal failure may develop [5].

SGD occurs in patients aged 6 months to 86 years, but 75% of cases occur in children under the age of 8. The disease is more common in boys and tends to peak in late autumn and early spring.

Etiological and Mechanistic Factors in the Development of Shenleyn-Genox Disease

The exact causes of Shenleyn-Genox disease remain unidentified; however, it is often associated with

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nasopharyngeal or intestinal infections, food allergies, and certain infections such as upper respiratory tract infections, which can trigger the onset of SGD. Research shows that chronic infections (e.g., sinusitis or tonsillitis) are common in children with SGD [6].

The role of various infectious agents in the development of SGD is emphasized, but the specific etiological causes have not yet been proven. Beta-hemolytic group A streptococci, Helicobacter pylori, and other bacteria, viruses, as well as medications (antibiotics, anti-inflammatory drugs, thiazide diuretics), are also considered potential triggers of the disease.

Additionally, some factors, such as food allergies or insect bites, may contribute to the development of SGD. Furthermore, the disease may only develop in individuals with specific genetic predispositions. The effects of external factors and infectious agents have not been fully determined [7].

Genetic Factors of SGD

Currently, significant attention is being given to studying the genetic basis of Shenleyn-Genox disease. Research has focused on identifying changes in polymorphic genes, with the role of the histocompatibility system (HLA), genes synthesizing anti-inflammatory and pro-inflammatory proteins, complement system, and genes regulating cell protection against oxidative stress being studied in the context of SGD development [8, 9].

M.M. Amoli and colleagues (2022) identified the HLA-DRB101 genotype to be more frequent in patients with SGD. A study by H. Peru et al. (2018) found that HLA-A2, HLA-A11, and HLA-B35 alleles were associated with disease development, while HLA-A1, HLA-B49, and HLA-B50 alleles posed a lower risk [10, 11, 13].

The effects of genetic polymorphisms and genes responsible for synthesizing proteins related to the coagulation system are not fully understood. Polymorphisms of MTHFR, prothrombin, and factor V genes did not show significant differences in children with SGD, but the MTHFR gene's 665 C/T polymorphism led to the development of hematuria.

Thus, more than 39 genes influencing the development of SGD have been identified, but there is still no clear information about the combined effects of different genes and their prognostic role.

Pathogenesis and Immunopathology of SGD

Although the pathogenesis mechanisms of Shenleyn-Genox disease are not yet fully understood, it is classified as a systemic vasculitis. It is characterized by the deposition of immunocomplexes composed of IgA immunoglobulins in tissues, especially in kidney glomeruli, the gastrointestinal system, and skin capillaries. Both external factors (infections) and genetic predisposition play a crucial role in the development of the disease.

In the disease's development, infectious agents and vaccines can trigger the immune complex reaction. According to the molecular mimicry theory, certain infections may produce complexes resembling the antigens of small blood vessels, leading to an autoimmune attack. In the active phase of the disease, there is an increase in IgA levels, which may be related to the production or release problems of IgA [12, 13].

Deposits of IgA in skin biopsies and other tissues are detected, showing similarities between SGD and IgA nephropathy. Disruptions in IgA glycosylation may lead to the formation of aggregates. Immunocomplexes accumulate in tissues, activating the complement system, which leads to tissue damage [14].

Thus, the role of IgA in pathogenesis remains significant, especially considering its increased levels in many patients.

Changes in the Hemostasis System in SGD

Recent studies show that changes in the hemostasis system in the pathogenesis of SGD lead to the development of a hypercoagulable state. Studies have shown elevated levels of plasma fibrinogen, D-dimers, thrombin-antithrombin complexes, prothrombin fractions 1 and 2, and Von Willebrand factor antigen in children with SGD. Depending on the disease's activity, these markers may change; for example, D-dimer concentrations can increase up to 10 times in SGD [15].

Von Willebrand factor antigen is considered a marker of endothelial damage, and its levels may be related to the disease's activity. In SGD, the concentrations of thrombomodulin, tissue plasminogen activator, and plasminogen activator inhibitor-1 also increase, which is associated with local activation of the endothelium [16].

Some studies have also shown an increase in homocysteine levels [112].

However, changes in the hemostasis system in SGD have not been fully explored in terms of their pathophysiological and prognostic roles, and future studies will help to better understand the disease's pathogenesis.

Diagnosis and Treatment of Shenleyn-Genox Disease (SGD)

The diagnostic criteria for SGD are based on those proposed by the American Rheumatology Society. Among the four criteria presented in 1990, the presence of at least two allows for the diagnosis of

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SGD, which provides 87% sensitivity and 87.7% specificity. In 2010, new diagnostic criteria were introduced, which include the presence of skin rashes (palpable purpura) and additional signs (abdominal pain, arthritis, kidney damage, histological changes) necessary for confirming SGD. The sensitivity of these new criteria is 100%, and specificity is 87.8% [109].

In the diagnosis of SGD, laboratory tests are often not related to the severity or activity of the disease, although serum IgA levels increase in half of the patients. In many cases, SGD does not require specific treatment, and only symptomatic treatment (anti-inflammatory medications) is used [32]. Questions remain regarding pathogenetic therapy to prevent kidney damage. Studies have shown that the use of prednisolone has reduced abdominal pain and arthralgia in some cases, but it has not prevented kidney damage. New studies have not shown the effectiveness of immunosuppressive treatment.
Therapy including methylprednisolone, urokinase, and cyclophosphamide may be effective in correcting coagulopathy in SGD. In cases of glomerulonephritis, combined therapy is applied, including corticosteroids, azathioprine, cyclophosphamide, and others [162]

CONCLUSION

Shenleyn-Genox disease (SGD) is a systemic vasculitis associated with inflammation of small blood vessels and the deposition of IgA immunoglobulins. The disease primarily occurs in children, with the average age group being 4-6 years old. Its development may be caused by infections, food allergies, and genetic predisposition. Clinically, SGD manifests with abdominal pain, arthritis, and erythema without thrombocytopenia, often affecting the kidneys, gastrointestinal system, and skin.
Diagnosis is based on traditional criteria, where skin rashes and additional signs (abdominal pain, arthritis, kidney damage) are considered confirming factors. The new diagnostic criteria introduced in 2010 have increased sensitivity and specificity, which helps in effective identification of patients.
In the treatment of SGD, many authors emphasize symptomatic treatment, as the disease often resolves on its own in some cases. However, questions remain regarding pathogenetic therapy, as some studies have not shown the effectiveness of prednisolone or immunosuppressive treatment. In cases of glomerulonephritis, combined therapy involving corticosteroids and other drugs is applied.
Further research is needed to fully understand the pathogenesis of SGD and improve diagnostic and treatment strategies. New approaches must be developed in the future for more effective treatment of the disease.

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