ISSN NO: 2770-2936
Date of Publication:24-08-2023

Changes in the Hemostasis System in Children with Hemorrhagic Vasculitis (Henoch-Schönlein purpura)

Avezova Guloim Sattarovna –PhD, dosent,
Babomuratov Turdikul Akramovich- DcS, professor
Department of propaedeutic of children's diseases
Tashkent Medical Academy, Uzbekistan

Abstract. The article discusses changes in the hemostasis system in children with hemorrhagic vasculitis, in particular, damage to the walls of small vessels by immune complexes circulating in the circulatory system and activated components of the complement system, and then activation of all parts of the hemostasis system, as well as changes in the hemostasis system of blood vessels, platelets, plasma. Hemorrhagic vasculitis (IgAV) is classically a childhood disease with an incidence of about 10 cases per 100,000 a year. The pediatric form of this pathology is generally considered benign and self-limited. In contrast, IgAV in adults is less common but often associated with worse clinical course and outcome The results of studies conducted by different authors in different countries on the study of the processes of violation of the mechanisms of blood coagulation in hemorrhagic vasculitis in children are presented.

Keywords. Hemorrhagic vasculitis, hemostasis system, immune complex, thrombin, prothrombin, fibrinogen

The formation of children's health is significantly influenced by such factors as climatic, geographical, environmental, economic, lifestyle and conditions, the level of population migration, ethnic and socio-cultural characteristics, as well as the material and technical base of medical institutions. The state of children's health is a barometer of the socio-economic development of the country.To date, one of the urgent problems is the assessment of a combination of various risk factors (exogenous and endogenous) leading to the development of hemorrhagic vasculitis in children. Hemorrhagic vasculitis ((immunoglobulin-A) vasculitis (IgAV)), formerly called Henoch-Schönlein purpura, is an inflammatory vascular disease that affects small blood vessels, predominantly capillaries, venules, or arterioles, with IgA1-dominant immune deposits.

Currently, hemorrhagic vasculitis (HV) is a common and frequent pathology in the pediatric population. Its frequency is very variable and depends on the region, its level of economic development, diagnostic and statistical features. Hemorrhagic vasculitis (Henoch-Schönlein purpura) is a disease belonging to the group of systemic vasculitis with microcirculatory disturbances as a result of the accumulation of immunoglobulin A (IgA)-containing immune complexes in the blood vessels of the skin, joints, gastrointestinal system, kidneys [4,11]. This disease is one of the most common systemic vasculitis in childhood. Worldwide, the incidence among children ranges from 3 to 26.7 per 100,000 children [5,6]. In the pathogenesis of the disease lies the damage of the intima of small blood vessels in the skin, joints, gastrointestinal system, kidneys with IgA-immunocomplexes. As a result, endothelial dysfunction - decrease in synthesis of fibrinolysis activators, activation of lipid peroxide oxidation system (POL), coagulation-platelet hemostasis processes.

Hemorrhagic vasculitis is a systemic vasculitis (inflammation of blood vessels) and is characterized by deposition of immune complexes containing the antibody immunoglobulin A (IgA); the exact cause for this phenomenon is unknown. In children, it usually resolves within several weeks and requires no treatment apart from symptom control but may relapse in a third of cases and cause irreversible kidney damage in about one in a hundred cases [8].

The course and clinical features of hepatitis B in children depend on which system or organ is damaged. The course and outcome of the disease largely depend on kidney damage. In children, clinical signs of kidney damage in hepatitis B occur in 26-60% of cases [11].The relevance of the study is related to the need to determine clinical and laboratory signs for an objective dynamic assessment of the level of

ISSN NO: 2770-2936
Date of Publication:24-08-2023

disease activity, as well as to develop criteria for predicting the outcome of the disease and determining the most appropriate treatment tactics.

Observations carried out to date have shown that changes in the hemostasis system leading to the development of a hypercoagulable state play a major role in the pathogenesis of GVs. According to D. Yilmaz and co-authors (2005), plasma concentrations of fibrinogen, D-dimers, thrombin-antithrombin complex, prothrombin fragments 1 and 2, and von Willebrand factor antigen are higher than normal in children with GV.Currently, GV is considered an immune complex disease, which is based on damage to the walls of small blood vessels by circulating immune complexes and activated components of the complement system, and then all parts of the hemostasis system are activated [1,3,4,5,6,7,10].The process of formation of circulating immune complexes is genetically determined. The phenomenon of increased circulating immune complexes in GVs is considered as an important evidence of the immune complex nature of vascular damage. Disruption of all components of hemostasis: blood vessels, platelets, plasma coagulation, immunocomplex was found to be secondary to primary processes [1,10].

Various manifestations of clinical symptoms, severity of the disease, consequences largely depend on the state of the coagulation and anticoagulation systems of hemostasis [2,3,7,12].

Autoimmune process in GVs, i.e., circulating immune complexes damage the endothelium of the wall of small blood vessels, causing disorganization of collagen. This hemostasis system enzyme activation mechanism is the first step in a chain reaction [2].The von Willebrand factor, synthesized in the vascular endothelium, is a marker of vascular damage by immune complexes [10]. The level of this factor remains consistently high for several months after resolution of the main symptoms of the disease [7].Antithrombin-III (AT-III), the plasma cofactor of heparin, an important physiological anticoagulant, is often significantly reduced in the acute phase of GV. AT-III deficiency causes microcirculatory blockade, which leads to significantly severe GVs. The more severe hemorrhagic vasculitis, the more pronounced hemocoagulation disorders [1,3,5].A statistically high correlation was established between disease activity and the concentration of D-dimers, von Willebrand factor antigen 1, and prothrombin 2 fragments. In studies conducted by K. Brendel-Müller et al (2001), laboratory signs of activation of the hemostasis system were identified in children with HB. It was found that in the acute period of the disease, the concentration of D-dimers in the blood plasma increased in 15 out of 17 patients. In addition, a statistically significant increase in the concentration of thrombin-antithrombin complex, fibrinogen, and prothrombin fragments 1 and 2 was found, and it was noted that there is a correlation between the change in the concentration of these indicators and the activity of the disease. In GV, the concentration of D-dimers in blood plasma can increase 10 times or more, which in some cases requires differential diagnosis with disseminated intravascular coagulation syndrome.N. Besbas et al (1999) found an increase in the plasma concentration of thrombomodulin, tissue plasminogen activator and plasminogen activator inhibitor-1 compared with HB and the control group, the concentration of thrombomodulin statistically depends on the activity of the disease.

According to the results obtained, the changes in coagulation tests described above in HB are the result of local damage and inflammation of the endothelium, as well as the release of a plasminogen activator-1 inhibitor and reflect the general activation of the hemostasis system.

The von Willebrand factor antigen is currently considered as a marker of endothelial damage in systemic inflammatory diseases, and therefore an increase in its concentration in blood plasma is considered as a sign of the active course of the disease [5].

The concentration of the von Willebrand factor antigen in hepatitis B is associated with the level of IgA in blood plasma (D. De Mattia et al., 1995), which indirectly confirms the possibility of using this indicator as a marker of immune-mediated endothelial damage. (S.J. Park et al., 2013). The level of von Willebrand factor antigen in the mixed form and severe HB reflects the degree of damage and spread of the vascular endothelium [2,6].

However, a correlation between the severity of clinical manifestations and the concentration of von Willebrand factor antigen in hepatitis B has not been shown in all studies. G.K. A large-scale study conducted by Del Vecchio et al (2008) found an increase in plasma concentrations of anti-inflammatory cytokines, fibrinogen, von Willebrand factor antigen, but these indicators were not statistically associated with kidney damage and disease activity.

ISSN NO: 2770-2936
Date of Publication:24-08-2023

A stable, but independent of disease activity, increase in the concentration of the von Willebrand factor antigen in HV (mainly due to its abnormal multimeric forms) was also based on the studies of A. Casonato (1996) [6]. N.N. Petrishchev and T.D. According to Vlasova (1996), the von Willebrand factor antigen and tissue plasminogen activator are highly sensitive as markers of endothelial dysfunction, since a significant part of other signs of endothelial dysfunction is formed not only in endothelial cells, but also in others [5].The synthesis of plasminogen activator inhibitor type 1 also increases dramatically with activation and damage to the endothelium. Some of the endothelial secretory products are released continuously to maintain normal functional activity, while others are produced upon injury or stimulation. Factors that accumulate in the endothelium and are released during its stimulation: von Willebrand factor antigen, tissue plasminogen activator; factors, the synthesis of which does not normally occur, but increases sharply when the endothelium is activated: inhibitors of type 1 plasminogen activator, membrane proteins (receptors): thrombomodulin. In some observations, an increase in the concentration of homocysteine in HS was also observed [2].

Thus, changes in various parts of the hemostasis system are observed in HB, but the significance of pathophysiological and prognostic factors has not been sufficiently studied. Further research in this direction will help determine the pathogenesis of the disease, develop diagnostic and prognostic markers.

References:

1. Берман Ю. О. Взаимосвязь генетических нарушений в системе гемостаза, метаболизма гомоцистеина и течения геморрагического васкулита // Аспирантский вестник Поволжья. – 2013. – № 5-6. – С. 18-22.
2. Дзилихова К.М., Долгина Е.Н., Кисляк Н.С. "Особенности клеточного и гуморального иммуннитета, комплементарной активности сыворотки крови, фагоцитарной функции нейтрофилов и моноцитов и уровень ЦИК у детей, больных геморрагическим васкулитом // Педиатрия. — 1995. - №2. —С. 55-60.
3. Жданова Л. В. и др. Вклад полиморфизма генов тромбофилий в клиническое многообразие геморрагического васкулита //Вестник Российской академии медицинских наук. – 2014. – Т. 69. – №. 3-4. – С. 61-64.
4. Исмамбетова Г. К. и др. Клинические проявления геморрагического васкулита у детей //Здравоохранение Кыргызстана. – 2018. – №. 2. – С. 85-88.
5. Кудряшова М.А. и другие. Нарушения гемостаза при IgA-васкулите (Геноха-Шенлейна) у детей и их коррекция // Педиатрия. Журнал им. Г.Н. Сперанского. – 2019. – Т. 98, № 4. – С. 71-77.
6. Храмцова А. С., Яковлева А. В. Клинико-эпидемиологические особенности геморрагического васкулита у детей //Молодежь-практическому здравоохранению. – 2018. – С. 1018-1020.
7. Ширинбекова Н. В., Ларионова В. И., Новик Г. А. Полиморфизмы генов системы гемостаза у детей с геморрагическим васкулитом // Актуальные вопросы педиатрии: матер. межрегион. науч.-практ. конф., посвященной 90-летию ГБУЗ ПК «Детская городская клиническая больница № 3». – Пермь, 2013. – С. 258-263.
8. Sais G, Vidaller A, Jucglà A, Servitje O, Condom E, Peyri J (1998). "Prognostic factors in leukocytoclastic vasculitis: a clinicopathologic study of 160 patients". Arch Dermatol. 134 (3): 309–15.
9. Casonato A., Pontara E., Bertomoro A. et al. Abnormally large von Willebrand factor multimers in Henoch-Schönlein purpura // Am J Hematol. – 1996. – Vol. 51(1). – P.7-11.
10. De Mattia D., Penza R., Giordano P. et al. von Willebrand factor and factor XIII in children with Henoch-Schönlein purpura // Pediatr. Nephrol. – 1995. – Vol. 9(5). – P.603–605.
11. Mir S., Yavascan O., Mutlubas F. et al. Clinical outcome in children with Henoch-Schönlein nephritis // Pediatr Nephrol. – 2007. – Vol. 22(1). – P.64-70.