

Disturbance of Coagulative Hemostasis among Patients with Henoch-Schonlein Purpura

Sh.A. Babadjanova¹, Z.S. Islamova², Z.Ch. Kurbanova³,
Khurshida S. Yusufkhojaeva⁴, Feruza Kh.Inoyatova⁵

¹MD, Professor, Department of Hematology, Transfusiology and Laboratory Affairs, Tashkent Medical Academy, 2 Farobiy Street, Tashkent, Uzbekistan, 100109, ²MD, Teaching Assistant, Department of Hematology, Transfusiology and Laboratory Affairs, Tashkent Medical Academy, 2 Farobiy Street, Tashkent, Uzbekistan, 100109, ³MD, Teaching Assistant, Department of Hematology, Transfusiology and Laboratory Affairs, Tashkent Medical Academy, 2 Farobiy Street, Tashkent, Uzbekistan, 100109, ⁴MD, Teaching Assistant, Department of Hematology, Transfusiology and Laboratory Affairs, Tashkent Medical Academy, 2 Farobiy Street, Tashkent, Uzbekistan, 100109, ⁵Senior Lecturer, Professor, Department of Medical and Biological Chemistry, Tashkent Medical Academy, 2 Farobiy Street, Tashkent, Uzbekistan, 100109

Abstract

The Purpose: To examine the state of thrombocytic and coagulation hemostasis among patients with immune microthrombovasculitis.

Materials and Method: The study included 75 patients with immune microthrombovasculitis. Among them, men - 24 (32%), women - 51 (68%), the average age is 42.4±1.3 years. The control group consisted of 15 practically healthy persons.

Results and Discussion: A study of coagulation hemostasis among patients with immune microthrombovasculitis showed the presence of hypercoagulation shift with the increase of fibrinogen concentration, prothrombin index, shortening of the active partial thromboplastin time and blood clotting time, the appearance of hybrid monolith complexes - level increase of D-dimer positive ethanol test.

Conclusions: The most common clinical form of IMTV is the skin-joint form of the disease (62.2%), 89.3% of patients were admitted with an acute form of the disease. Women get sick twice as often (67.3%) than men (32.7%), the highest incidence is in the young age group from 18 to 49 years (87.3%). There is hypercoagulability in case of immune microthrombovasculitis.

Keywords: Immune microthrombovasculitis, coagulation hemostasis.

Introduction

Immune microthrombovasculitis (IMTV) - is an autoimmune disease characterized by generalized vasculitis which involves small skin vessels, the gastrointestinal tract, kidneys, joints, and, rarely, the lungs and central nervous system (CNS). The causes of the disease can include infections of various aetiology, parasitic invasions, various medical products, the introduction of serums, vaccines, etc. IMTV mainly affects microcirculatory vessels, such as arterioles, capillaries, and post-capillary venules³.

IMTV is a widespread disease from the systemic vasculitis group of immunocomplex nature¹¹ and in accordance with epidemiological studies¹⁶, IMTV constitutes 59% of all nosologically forms¹⁹. The annual incidence of IMTV reaches 20-25 per 100,000 of population, and there is an increase in the incidence¹⁴. Children get sick more often than adults⁵ and in accordance with some data, the ratio of IMTV between children and adults is 8:1 – 9:1¹⁷.

The studies of the hemostasis system have led to the conclusion that the leading link in the process of blood

clotting disorders among IMTV patients is the tension of thrombolytic-vascular hemostasis and the acquisition of procoagulant properties by endothelial cells under the influence of immune aggression. In case of hemorrhagic vasculitis, "aseptic inflammation" occurs in small vessels, as well as the formation of immune complexes that circulate within the bloodstream⁹. Under the influence of soluble immune complexes and cytokines activated by them, components of the complement system, aseptic inflammation of micro vessels develops with more or less deep focal endothelial dystrophy and vascular wall disruption¹². As a result, phlebarteriectasia occurs with divergence of endothelial cells, violation of vascular permeability and its integrity⁷. Then, the secondary hemorrhages of skin blood vessels and internal organs develop.

There was a evident activation of coagulation hemostasis, i.e. a state of thrombophilia with a tendency to hypercoagulation and thrombosis, as well as the development of disseminated intravascular coagulation syndrome in acute situations¹³.

In 90 % of cases, the disease debuts with arthritis or arthralgia¹⁵ and joint syndrome is the diagnostic criteria of IMTV²⁰. In general, joint damage (usually knee, ankle, wrist) exists among 60-80 % of patients with IMTV, more often develops among adults and combines with myalgia⁸. As an adult, joint pathology takes the form of chronic or migrating intermittent polyarthritis²².

The high prevalence and increase in the number of patients with IMTV, the severity of the clinical course, determine the important socio-economic significance of this problem.

The Purpose of the Research: To examine the state of thrombocytic and coagulation hemostasis among patients with immune microthrombovasculitis.

Materials and Method of the research. The study included 75 patients with IMTV who were under treatment in the Department of Hematology in the multidisciplinary clinic of the Tashkent Medical Academy. Among them, men - 24 (32%), women – 51 (68%), the age range of patients was from 19 to 70 years, the average age was 42.4±1.3 years. The control group consisted of 15 practically healthy persons in comparable age, as well as 6 men (53.4 %) and 9 women (46.6%), whose average age was 39.4±1.2 years.

We divided all the patients under study into 4

groups in accordance with the clinical implications of the disease. The first group included 14 (18.7%) patients with cutaneous form, the second group consisted of 47 (62.6%) patients with cutaneous-articular form of IMTV, the third group included 8 (10.7%) patients with mixed abdominal form and the fourth group included 6 (8%) patients with mixed renal form of the disease.

Research Method

the research method included patient examination, general blood analysis by the hematological analyzer Mindray BC 5000 (China), blood clot retraction, platelet adhesion and aggregation by the aggregometer Biola Alat-2 (Russia), fibrinogen, prothrombin index (PTI), fibrinolytic activity, activated partial thromboplastin time (APTT) by the coagulometer Humaclo Junior (Germany), antithrombin III, D-dimers by the Roche Cobas C 311 biochemical analyzer (Switzerland).

Results and Discussion

An analysis of the patients distribution by age and gender showed that among patients there was a predominance of women, the number of men was almost half the number of women.

The age composition study of the examined patients showed that the majority of patients were young; 24% (18) were in the age from 18 to 29 years and 60% (45) were patients in the age from 30 to 49 years.

The diagnosis based on clinical symptoms and laboratory data. Patients with a cutaneous form of IMTV were hospitalized with a severe form of the disease. 13 (92.8%) patients of the first group suffered the acute start of the disease. All patients had multiple small-point hemorrhagic rashes on the skin of the lower and upper limbs and within the abdominal area, sometimes of a coalesced character. We observed the maculopapular rash with necrotic skin among 5 (35.7%) patients. 47 patients had the skin-joint form of IMTV, we observed it within the scope of skin lesions in the form of a symmetrical hemorrhagic rash, joint damage. The most characteristic were swelling, soreness, restriction of joint function, often marked symmetrical involvement of the joints: knee, ankle, elbow and wrist. 8 patients constituted the third group with diagnosis of abdominal IMTV on the basis of characteristic spastic pains in various parts of the abdomen, as well as conditions of nausea and vomiting. Abdominal syndrome developed simultaneously with skin rashes. 2 patients had the

enterorrhagia. We found the most severe complications among patients with IMTV referred to 6 patients with kidney damage. The main clinical signs of kidney damage were micro and macrohematuria, proteinuria, cylindruria, edema, and increased blood pressure.

Thus, the analysis of the research results showed that the main part (62.6%) constituted the patients with skin and joint disease, women had the disorder twice as often (68%) as men (32%), the highest incidence is within the young age group in the age range from 18 to 49 years (84%).

Among 75 patients with IMTV who passed treatment in 2019, the state of hemostasis was under study within comparison with the control group (tables 1, 2). In accordance with the table 1, the number of thrombocytes in IMTV group was more high than in the control group, although it remained within normal values. At the same time, there was no significant difference between the thrombocyte values of both groups. The study of thrombocytes functional characteristics showed that the patients of the main group have a distinct increase in the adhesive and aggregation properties of thrombocytes. Thus, in the group of patients with IMTV, the aggregation time increased and constituted 119.3±2.7%, while in the control group it was 66.7±4.1%. this is significantly more high than the initial data. The observed significant activation of thrombocytes aggregation was among 38 patients (88.3%), while 5 (11.7%) patients had the thrombocytes aggregation time within the normal values. The adhesion of platelets in the main group significantly differed from the control group and increased to 62.4±1.2%, and within the control group it was 41.2±0.97%.

Table 1: Thrombocytic indicators among patients with IMTV, M±m.

Indicators of hemostasis	Control group n=20	IMTV, n=43
Thrombocytes (10 ⁹ /l)	232,8±9,75	258,8±6,65*
Retraction (of 0.3-0.5 s)	0,32±0,02	0,25±0,02
Aggregation, %	66,7±4,1	119,3±2,7*
Adhesion, 20-40%	41,2±0,97	62,4±1,2* *

Note: * - accuracy in relation to the control group *- p< 0,05; ** -p< 0,01.

The parameters that characterize the platelet link of hemostasis also include the identification of blood clot retraction. The study of the retraction time among

IMTV patients showed that the initial indicators were more short than in the control group, which indicates an increase in thrombocyte activity, but without any reliable difference.

In order to assess the state of plasma coagulation hemostasis, we studied blood clotting factors, physiological anticoagulants and products of fibrin degradation.

The studies have shown that among the patients with IMTV, the initial values of coagulation hemostasis indicators demonstrated a state of hypercoagulation. (table 2).

In the direction of hypercoagulation, the indicator of blood clotting time (BCT) changed. In the group of patients with IMTV, the BST was shortened to 2.1±0.13 minutes, which is more than half in comparison to the control group (4.8±0.21 minutes). The research results of activated partial thromboplastin time (APTT) showed that a shortening of this indicator occurred among 55 (73.3%) patients. As can be seen, the APTT in the control group was 35.2±0.54 seconds, and in the group of patients, it decreased to 25.2±0.48 seconds. (p<0.001).

Table 2: Indicators of coagulation hemostasis among patients with IMTV, M±m

Indicators of hemostasis	Control group, n= 15	IMTV, n=75
BCT (5 min)	4,8±0,13	2,1±0,12* *
aPPT, sec (45 sec)	35,2±0,54	25,2±0,48* **
PTI, % (90-105%)	86,4±1,24	104,0±1,33* *
INR	1,25±0,04	0,82±0,03* **
Fibrinogen (2.0-3.5 g/l)	2,4±0,19	4,9±0,17* **
Hematocrit, % (40-50%)	41,2±0,9	48,8±0,82*
Von Willebrand factor	96,2±1,2	118,6±1,8* **
Antithrombin III %	100,3±5,2	87,8±3,1 *
FA, sec(140-240 s)	142,2±6,14	256,2±5,18 ***
D-dimers µg/ml	0,58±0,03	2,1±1,6*
Ethanol gelation test	negative	positive

Note: * - accuracy in relation to the control group, * - p< 0.05; ** - p<0.01; ***-p< 0.001

The analysis of coagulation hemostasis state among patients within the IMTV group in accordance with indicators of prothrombin, INR and fibrinogen indicates clearly expressed hypercoagulation. The evidence of

it is a significant increase in the prothrombin index by $104.0 \pm 1.33\%$ in the group of IMTV patients, while in the control group it is $86.4 \pm 1.24\%$ ($p < 0.01$), the average INR values in the main group were significantly shortened in comparison with the control group (1.25 ± 0.04 and 0.82 ± 0.03 , respectively, $p < 0.01$).

An increase in plasma fibrinogen concentration also characterized the state of hemostasis with a tendency to hypercoagulation, so among patients of the main group it was 4.9 ± 0.17 g/l, and within the control group it was 2.4 ± 0.19 g/l. ($p < 0.01$). The hematocrit index in the groups under study did not deviate from the norm and was within the range from 41.2 to 48.8%.

The indicators of coagulation hemostasis also include fibrinolytic activity of blood. In our study, this indicator within the group of patients was significantly more high than in control group. In case of hypercoagulation syndrome, it is important to determine markers of inopexia. Our ethanol gelation test and determination of D-dimer content showed that there is an activation of fibrinolysis processes, which is indicated by an increase in the main group of the fibrinolytic activity indicator almost twice in comparison with the control group. The ethanol gelation test was positive among 61 (81.4%) patients, while within all control group it was negative. The content of D-dimers in blood plasma of patients with IMTV significantly increased, this indicator was almost four times more high than in the control group. It is very important to assess the state of hemostasis in order to study the anticoagulant hemic system, which is to balance shifts in the clotting system. Normally, these important systems of the body are in a state of dynamic equilibrium. For this purpose, the activity of a physiological anticoagulant, antithrombin III (AT III), was under study. In our study, this indicator was more low than the values of the control group and constituted $87.8 \pm 3.1\%$ and $100.3 \pm 5.2\%$, respectively.

Thus, our study of the hemostasis coagulation link among patients with IMTV showed the presence of significant deviations in regard to hypercoagulation shift. We indicated it by an increase in the concentration of fibrinogen, PTI, shortening of APTT and BCT, low INR, and the appearance of degradation markers in relation to fibrin-fibrinmonomer complexes (an increase in the D-dimers level, a positive ethanol gelation test).

Conclusions

1. One found that the most common clinical form

of IMTV is the skin and joint form of the disease (62.2%), with the acute form of the disease referred to 89.3% of patients.

2. Women get sick twice as often (67.3%) than men (32.7%), the most high incidence is in the group of the young age within the range from 18 to 49 years (87.3%).
3. The study of hemostatic parameters among the patients with IMTV indicates a state of hypercoagulation. The evidence of hypercoagulation state was an increase in the aggregation properties of thrombocytes, an increase in the quantity concentration of plasma clotting factors and fibrin degradation products in the blood, and a decrease in the anticoagulant properties of plasma.

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Conflict of Interest: Nil

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