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Последние взгляды | **Последние данные** | **Последние исследование**

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HEREDITARY DEFICIENCY OF BLOOD COAGULATION FACTOR I-HYPOFIBRINOGENEMIA, CLINICAL OBSERVATION

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Key words: *hypofibrinogenemia, prothrombin, hematoma, hemarthrosis.*

Summary: *Rare coagulation disorders (RCD) include monogenic coagulopathies caused by a deficiency of plasma proteins involved in hemostasis, not related to von Willebrand disease and hemophilia A or B. RBCD include hereditary deficiencies or abnormalities of fibrinogen, prothrombin (factor II), blood coagulation factors V, VII, X, XI, XII, XIII. All these violations in the vast majority of cases lead to violations of the formation of fibrin. Blood clotting is the process by which normal liquid blood turns into a clot that closes the damaged vessel and protects against bleeding. The external and internal pathway of thrombus formation proceeds with the participation of coagulation factors. This process involves the formation of fibrin, the protein that forms the basis of a blood clot. Fibrin as a scaffold gives the thrombus strength. With coagulopathy, due to a lack of coagulation factors, fibrin formation does not occur. Without fibrin, a thrombus is not able to securely attach to the site of damage. Uncontrolled bleeding occurs, which can lead to death. Hypofibrinogenemia is a pathological condition characterized by a decrease in the content of fibrinogen in the blood below 2 g / l. Fibrinogen is the main protein of the hemostasis system; a thrombus is formed from it, which stops bleeding when the vascular wall is damaged.*

INTRODUCTION

Hypofibrinogenemia is a hemorrhagic syndrome that occurs due to a level of plasma fibrinogen below normal, sometimes called fibrinogenopenia or fibrinopenia. It is more of an anomalous condition in the subject than a disease because it never spontaneously manifests clinically; its biological characteristic is a permanently reduced level of plasma fibrinogen, between 30 and 60 mg/100 ml. The first cases were published in the specialty literature in 1935 (Risak); since then and to date, 30 cases of the congenital form and many cases of the acquired form have been reported. Hypofibrinogenemia does not represent a well-defined clinical picture, because the patient never bleeds spontaneously. When these patients develop a hemorrhagic syndrome, it is determined by one of the following

reasons: the occurrence of another disorder of hemostasis, different from the main defect of the patient (thrombopenia, capillary fragility, lack of one of the plasma coagulation factors); an open or closed wound due to a very severe injury; a major surgical intervention to which the patient was subjected (cutting off the umbilical cord does not entail hemorrhage). In these cases, bleeding is obvious and takes on the clinical aspect of the hemorrhagic syndrome of afibrinogenemia, but in a milder form.

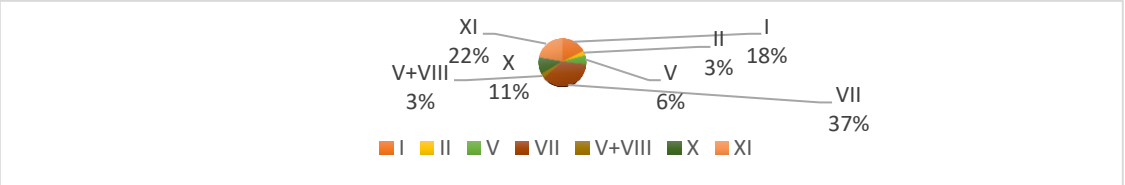
Hypofibrinogenemia can be divided into: congenital (Risack's constitutional fibrinogenemia) and acquired. Congenital hypofibrinogenemia is inherited as a Mendelian autosomal recessive trait; it represents a heterozygous state, while afibrinogenemia, as we have seen, is a homozygous state. Its frequency is more than afibrinogenemia; the possible susceptibility is determined more than reported cases, since there is a high percentage of clinically silent cases. Bleeding in hypofibrinogenemia is the same type as bleeding in afibrinogenemia. It can be caused by the following circumstances: after moderate injuries (never after minor ones), it is moderate and slightly prolonged, but easily subsides by the use of conventional means (often it is an alarm signal leading to the diagnosis of the disease); due to major injuries or surgical interventions, a true hemorrhagic syndrome occurs, as in afibrinogenemia, but of a more limited amplitude - this is the only circumstance when the expression of this disorder takes on the clinical aspect of the disease. A positive diagnosis of hypofibrinogenemia is made in the same way as for afibrinogenemia. However, it should be noted here that in the case of hypofibrinogenemia, the diagnosis is much more difficult due to the lack of clinical manifestations. Since, most often, we are talking about the effect of a severe injury or surgical intervention that causes unusually heavy bleeding, this circumstance attracts the attention of a doctor who prescribes the necessary laboratory tests and, based on these results, explains the situation. Differences are established in relation to any hemorrhagic diathesis, representing light bleeding. Laboratory studies confirming a positive diagnosis also establish a differential distinction justified by the patient's history and previous data. Evolution and complications of hypofibrinogenemia. In all cases, the disease is benign and devoid of complications. Those of the carriers who are aware of their defect should, as a preventive measure, beware of injuries and warn the doctor in case of surgical interventions. Danger threatens those who do not know about their vice and consider themselves normal; when they suffer a severe injury or undergo (without careful examination) surgery, they may develop severe hemorrhage, which is difficult to control. This is the only critical situation in this disease.

Fibrinogen deficiency: There are 2 types of fibrinogen deficiency. Type I, or quantitative deficiency, is afibrinogenemia or hypofibrinogenemia, when fibrinogen is absent or its amount is reduced. Type II - dysfibrinogenemia, a qualitative defect in fibrinogen, when the fibrinogen antigen can be reduced or it is within the normal range, but its activity is disproportionately reduced. The frequency of afibrinogenemia is

approximately 1 in 1,000,000 in the population. The frequency of hypofibrinogenemia is much higher, up to 1 in 500,000. Dysfibrinogenemia is inherited in an autosomal dominant manner, and therefore it is rather problematic to estimate its real frequency.

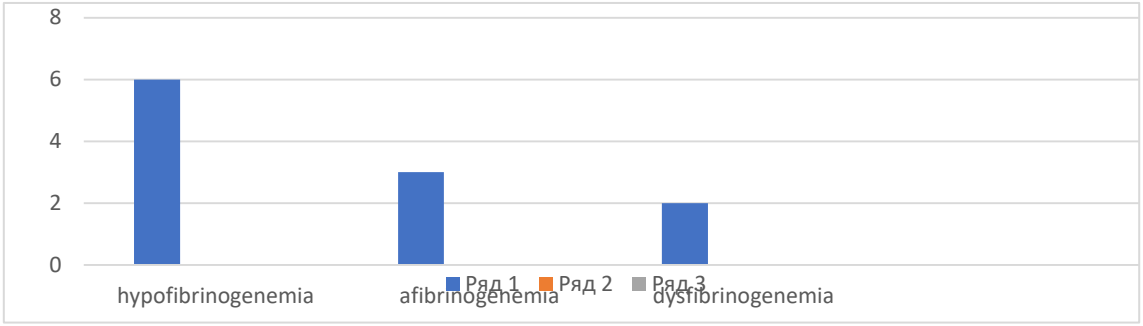
Coagulation factor deficiency % of patients in the group of rare hereditary coagulopathy in the Republic of Uzbekistan. The total number of patients was: 61. Of these, fibrinogen deficiency I-11 (18.0%), deficiency of factor II (prothrombin) II-2 (3.3%), hypoproaccelerinemia V-4 (6.6%), V +VIII2(3.2%), hypoproconvertinemia VII-23(36.5%), factor X deficiency (Stuart-Prauer) X-7(11.1%), factor XI deficiency (Rosenthal factor) XI-14 (22.2%), (Fig. 1)

Fig. 1. The frequency of occurrence of hereditary rare hereditary coagulopathy in the Republic of Uzbekistan (%).



Coagulation factor deficiency; % of patients in the group of rare hereditary coagulopathy in the Republic of Uzbekistan.

Fig. 2. Types of deficient factor I in the Republic of Uzbekistan (%) (hypofibrinogenemia-6 (54.5%), afibrinogenemia-3 (27.3%), dysfibrinogenemia-2 (18.2%)



Coagulation factor I deficiency; % of patients in the group of rare hereditary coagulopathy in the Republic of Uzbekistan.

SCIENTIFIC NOVELTY

Early detection and improvement of diagnosis and treatment of patients with hypofibrinogenemia in the Republic of Uzbekistan, as well as reduction of disability and mortality among them.

MATERIALS AND METHODS OF RESEARCH.

The diagnosis is based on the data of the anamnesis: signs of increased bleeding in other family members (both male and female); clinical signs of the disease and laboratory data. The level of fibrinogen is examined in blood plasma as a component of the coagulogram along with INR, APTT, thrombin time. Correction of this condition is carried out by introducing fresh frozen plasma and eliminating the etiological factor.

Laboratory study in hypofibrinogenemia The coagulation tests with which we examine these patients give results that can be grouped as follows:

a) Selection tests (TC, TH, PTT, PTTK, TQ) show a more or less prolonged time (depending on the degree of fibrinogenemia). As for TCP, it is normal.

b) T thrombin and reptilase are increased, indicating a lack of fibrinogen.

c) T.E.G. shows a low "ma", despite the fact that the platelets and their quality are normal; hence another indicator of fibrinogen deficiency.

d) Dosing of fibrinogen confirms the diagnosis: it shows low numbers, usually around 50 mg/100 ml. These levels are compatible with leading a normal lifestyle. However, when fibrinogen falls below this threshold (due to exaggerated consumption, due to known situations) and if during this period of critical hypofibrinogenemia a severe injury or surgical intervention occurs, then the carriers of this defect get a clinical manifestation of the disease.

e) R.C. wide and fast (due to low fibrin material in the clot). This has the consequence of releasing a significant mass of red blood cells from the poor material of the clot, which may give the false impression of fibrinolysis.

f) All other tests, which, as we have seen, gave normal results in afibrinogenemia, show normal numbers in this case as well.

Clinical case: patient M., 15 years old. The diagnosis of "hereditary coagulopathy: hypofibrinogenemia was established in a patient at the age of 1 year at the RSPMCH, where he was observed until reaching the age of majority, during the observation period, prolonged bleeding from wounds was noted. For hemostatic purposes, he received cryoprecipitate on demand. Patient's coagulogram data: APTT 79 sec., PTI 12%, fibrinogen 0.5 mg/l. The main reasons for treatment are recurrent intense nosebleeds, bruises, abrasions, stab wounds of a traumatic nature. With a hemostatic purpose, replacement therapy with cryoprecipitate is carried out on demand. In 2020, the parents of patient M. are in a consanguineous marriage: the mother's grandmother and the father's mother are half-sisters (they have a common mother). The parents of patient M. are also in a related marriage: the fathers of the mother and father of the patient are cousins. In our opinion, the most likely reason for the homozygosity of the examined patients for the identified rare mutations was closely related marriages, which was confirmed by genealogical data.

RESULTS AND DISCUSSION.

Laboratory data after treatment: APTT 34 sec., fibrinogen 2.1 g/l, Quick prothrombin 92%, FVII 108%, FII 115%, FV 100%; FVIII 114%, FIX 98%, FX 106%, FXI 91.0%, FW 150%, FXII 101%, XIIa-dependent fibrinolysis 6 min, platelet aggregation with ristomycin 85%, platelet aggregation with collagen 73%, platelet aggregation with ADP 79%. In the general analysis of blood in a patient, hemoglobin rose by 102 g/l, erythrocytes 3.8 x 1012/l, platelets 202 x 109/l; leukocytes 7 x 109/l;

Thus, taking into account the anamnestic, clinical and laboratory data, the patient was diagnosed with a hereditary deficiency of F I (hypofibrinogenemia). FFP transfusions were continued at a dose of 600 ml/day (15 ml/kg of body weight), after stabilization of the patient's condition, the daily dose of FFP was reduced, and he was discharged from the RSPC of Hematology 9 days later.

The treatment of hypofibrinogenemia pursues the same goal and uses the same means as in afibrinogenemia, bearing in mind the fact that we are talking about the same basic deficiency, but only of different amplitude. The treatment regimen is more limited, since the patient's fibrinogen level is slightly higher, and the severity of hemorrhagic episodes is less. Usually, 3-4 fibrinogen perfusions are sufficient to stop them, applied once a day every 4 days. The perfusion dose is calculated as in afibrinogenemia, but is administered in its entirety only in the first perfusion, in the following dose is reduced by half.

To stop bleeding, replacement therapy with clotting factor concentrates should be used. When conducting specific replacement therapy, preference should be given to the use of recombinant or highly purified virus-inactivated plasmatic concentrates of blood clotting factors in relation to FFP;

A key aspect of improving health and quality of life in the treatment of hypofibrinogenemia is the prevention of bleeding: life-threatening bleeding and hemorrhage (into the central nervous system (CNS), gastrointestinal tract (GIT), etc.); In addition to specific hemostatic and replacement therapy, the hematologist may use additional drugs in the treatment of patients with hypofibrinogenemia, for example, hormone therapy in women with recurrent severe uterine bleeding.

Tranexamic acid and other antifibrinolytic agents can be used to relieve menorrhagia and mild bleeding from the mucous membranes, with the exception of renal bleeding. Antifibrinolytic drugs may be used alone or in addition to clotting factor concentrates.

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