# INTRAOPERATIVE APPLICATION EXPERIENCE OF VIIA RECOMBINANT HUMAN FACTOR IN PATIENTS WITH ITP AND COMPLICATED SUBDURAL HEMATOMA

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Idiopathic thrombocytopenic purpura is known as the primary immune or autoimmune thrombocytopenic purpura represents the isolated immunomediated thrombocytopenia [11, 18] on the background of marrow normal function [20].

The disease is often revealed in women (72%) and in children until 10 years (40%) [20].

Numerous clinical researches have been shown that the reason of the ITP development is the disintegration of thrombocytes as a result of their phagocytosis antithrombocyte antibodies [11]. In the given process T-limphocytes take immediate part ($CD4^+$) [8, 27], having the right cytotoxic influence on thrombocytes [24]. Besides, the patients with ITP $CD3^+$ limphocytes can change the genes expression connected with apoptosis. In the result of $CD3^+$ limphocytes can get fastness to corticosteroid therapy [23].

This classical theory, explaining ITP pathophisiology (antibodies synthesis against glycoproteids of a cytoplasmatic membrane of thrombocytes-GPIIb-IIIa, GPIb-IX и GPIa-Iia – with their subsequent recognition Fcγ-thrombocytic receptors of macrophages and phagocytes) is considered old one nowadays [16, 18].

It is proved that disease can develop in 10–20% of cases in spite of antibodies formation process. According to other concept, the synthesis of the deformed thrombocytes by megacaryocytes and-or blockade of thrombocytes production provoke antithrombocytic antibodies [19].

In the ITP pathogenesis a special significance has the cytokines liberation disturbance, shown by activation Th0/Th1 of cells. As a result concentration IL-2 and IFN-g increases, but level IL-10 goes down, up to a total disappearance [6, 21].

The great interest represents the research of clinical role $CD8^+$ reactive cytotoxic cells concerning the thrombocytes which existence has been proved lately [19].

At ITP exacerbation, the clinical picture of the disease is expressed by dermal petechiasis eruption, cyanosis of mucosas in a kind of purpura, hypodermic hematomas, nasal bleedings, and plentiful menstruations [18]. From all possible complications intracranial and subarachnoidal hemorrhages are most life-threatening [20].

Due to the ITP diagnostics, a particular interest represents the thrombocytopenia picture (thrombocytes $<100 \times 10^9$/l) [11] in the absence of a massive bleeding or an immune hemolysis on the background of normal indicators of a hemogram [14].

Nowadays 3 basic approaches of the ITP treatment are known [14, 22, 29]. However, in complications and massive hemorrhage, besides the basic treatment, the acceptance of emergency measures according to the references of the American society of hematologists [5], which consist in the appointment of high glucocorticoids, intravenous usage of immunoglobulin and platelet concentrate transfusion are necessary. The mechanism of glucocorticoids action in ITP isn't definitively found out; however there are the data confirming their influence on the reduction of synthesis of antithrombocytic antibodies, the depression of thrombocytes integration and wall capillaries strengthening [10].

The positive result by immunoglobulin treatment is caused by temporary suppression of reticuloendothelial system function, so-called "blockade of macrophages" [2, 17]. In the modern literature there is a disputable question on the transfusion necessity of a platelet concentrate. Undoubtedly, in the case of massive hemorrhage, the given tactics provides short-term haemostatic effect. According to a series of authors [12, 15, 28], in patients with ITP, a massive bleeding at concentration of thrombocytes $<20\times10^9$/l doesn't form the basis for carrying out a specific therapy without fail since it can lead to deterioration of the basic pathology [25]. In such cases it is offered to prescribe NovoSeven – recombinant human factor VIIa (NovoSeven, Novonordisk, Denmark) [7, 9, 13, 26, 31] which is a preparation of a choice for urgent patients with a bleeding [30]. The mechanism of preparation efficacy consists in the connection of recombinant

human factor VIIa with the liberated tissue factor. The given complex activates factors IX, IXa, X and Xa. As a result there is a primary transformation of insignificant quantity of a prothrombin into thrombin which activates thrombocytes in the damage zone, factors V and VIII and, transforming a fibrinogen in fibrin, providing the formation of a haemostatic stopper.

To assume efficiency of this factor at disorder of a coagulative hemostasis, the patients with hemophilia have been allowed to apply the given preparation. The therapy of the Novo Seven preparation doesn't demand laboratory control. Lately, this preparation has been successfully used for treatment of bleeding which has no connections with hemophilia, namely in patients with liver function disturbances, at liver transplantation, and also for treatment of bleeding caused by an operative intervention and trauma [1]. There are data on high hemostatic efficiency of the Novo Seven preparation in the complex infusionally-transfusion therapy of a massive postnatal bleeding that testifies the expediency of its application of massive bleeding at obstetrics in childbirth-women with hemostasis pathology [3]. The preparation application in childbirth- women with ITP has allowed to refuse from the uteri extirpation and to keep reproductive function of women [4]. In the literature there is data about sufficient efficiency of the Novo Sevena appointment at subarachnoidal and parenchymatous hemorrhages [30].

We offer the results of the private experience on intraoperative applications of recombinant human factor VIIa in patients with ITP and complicated subdural hematoma.

The woman of 65 years was admitted with the complaints of headache, diplopia, the general delicacy and fatigability. According to her opinion the patient is ill within 15 days. Due to the anamnesis, the patient was administered prednizalon (120 mg/per day), strumectomy (eutiroxin, 5 mg/per day). The treatment was interrupted the last month. On the basis of objective examination at the moment of admition: the consciousness – clear, arterial pressure – 110/70 mm Hg, pulse – 100/minute, breath – independent, the frequency of respiratory movements – 14/minute With the help of auscultation the lungs were defined vesicular breath, the lien wasn't palpated, the liver was located under a costal arch. In the neurologic status positive meningeal symptoms, disturbance of functions oculomotor and abducing nerves at the left, moderated tetra paresis with positive Babinsky symptom and increasing tendinous reflexes were revealed.

While carrying out MRI (fig. 1) and CT (fig. 2) of the brain it was revealed a number of bilateral, convexital, chronic, subdural hematomas with signs of

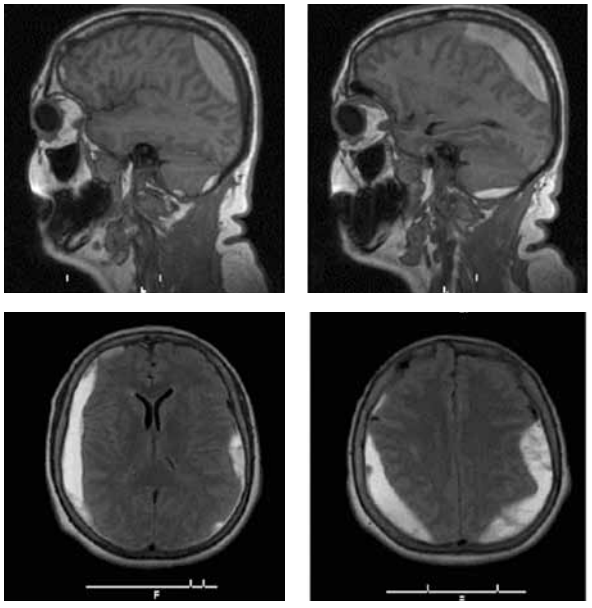

***Fig. 1.*** *MRI of the brain before the operation*

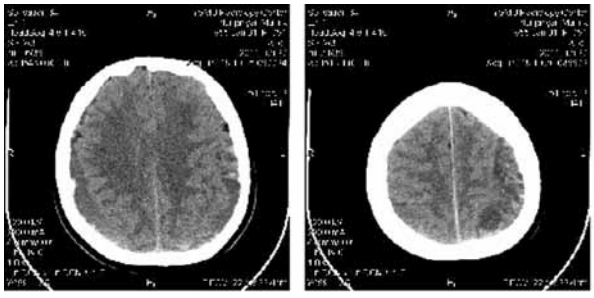

***Fig. 2.*** *CT of the brain before the operation*

fresh repeated hemorrhage, as well as bilateral chronic subdural hematomas in the field of hemispheres of a cerebellum and mosto-cerebullum angle at the left.

The results of laboratory blood analyses were in norm limits, except for the concentration of thrombocytes which made up of $5\times10^9$/l.

Neurosurgeons came to the conclusion about the necessity of carrying out an operative intervention for the purpose of bilateral subdural hematomas ectomia through dilated cutter apertures.

The preparation for surgery included the prednizalon therapy (120 mg/per day) in the result on the third day there was the increasing thrombocytes level of blood up to $26\times10^9$/l that had the basis for an urgent operation.

Before the anesthesic induction of the patient, the analog of the Novo Sevena preparation – the Eptakog-alpha (4.8 mg) was applied. Anesthesia proceeded without complications. The hemorrhage made up less than 500 ml that was the basis for the refusal of blood

transfusion preparations. In the intraoperive period it was not observed complications in the form of the lowered blood coagulability and bleeding. After the operation the patient was exuberated and transmitted into the intensive care ward. The postoperative period proceeded without complications. Within ten days the level of thrombocytes increased up to $255\times10^9$/l. Wounds became healthy by the first intention, progressive disappearance of complaints and disturbances of neurologic character (fig. 3) were perceptible. The patient was discharged from the hospital in a satisfactory condition.

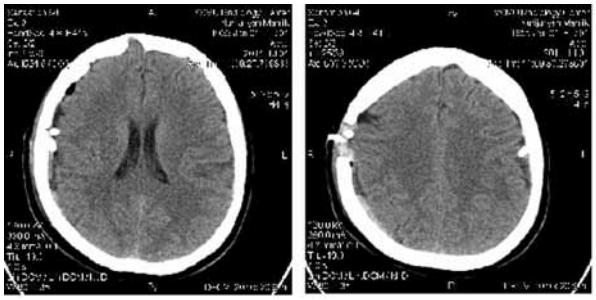

***Рис. 3.*** *CT of the brain after the operation*

Thus, our experience of Eptakog alpha application in the patient with ITP has shown that the preparation is capable to warn bleeding development in the intraoperative period.

The Introduction of modern haemostatic preparations in complex therapy of the ITP complications will allow minimizing the volumes of donor blood components, to reduce the frequency of serious postoperative hemotransfusionic complications.

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