The impact of erythrocyte-derived microvesicles on hemostatis disorder during burn injury

Microparticles or microvesicles (MVs) are closed fragments of cell membranes, released into the blood flow by different types of cells, such as: erythrocytes, platelets, white blood cells and endothelial cells. It has been proved that MVs play an essential part in regulation of many vitally important processes: inflammation, cell proliferation, apoptosis, vascular reactions and hemostasis. The role of erythrocyte-derived microvesicles in coagulation system remains practically unstudied.

This problem becomes particularly important during a number of pathological conditions associated with thromboembolitic complications (cardio-vascular diseases, cancer, etc.). Burn injury is one of such diseases, which usually results in thrombophilia (in other words, pronounced hypercoagulation), and even in DIC-syndrom. It is still unclear whether MVs, (mainly erythrocyte-derived) take part in this process.

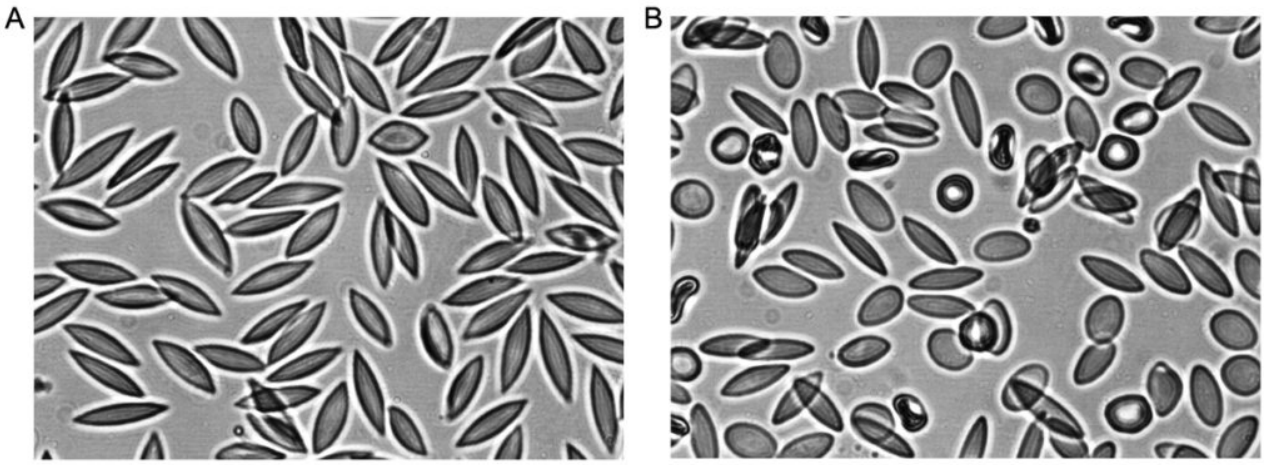

Fig. 1. A.Deformability of erythrocytes in artificial shear flow -in a healthy person.
B. Deformability of erythrocytes in artificial shear flow -in a burn patient

In our previous research we found out that erythrocyte-derived MVs display not only procoagulant activity (activation of blood clot formation), but also anticoagulant (antithrombin and fibrinolytic) activity which prevents blood clot formation. Both the activities are balanced in a healthy person.

Procoagulant activity of MVs is explained by the fact that their membrane surface consists of negatively charged phosphatidylserine clusters which act as catalyst surface for blood coagulation factors. Anticoagulant activity of MVs can be explained by the presence of antithrombins and plasminogen (factor of fibrinolysis system, which is involved in dissolution of fibrin clots) on their

membranes. We also showed that antithrombin activity of MVs accounts for their anti-aggregation properties towards platelets - blood cells, which play an essential role in blood coagulation. Platelet aggregation (or their sticking to each other or to a deformed vessel wall, or to atherosclerotic plaque) usually marks the beginning of blood clot formation.

Burn injury disturbs the balance between procoagulant and anticoagulant activities of MVs. Procoagulant activity increases while anticoagulant one decreases. The ability of erythrocyte-derived MVs to decrease platelet aggregation also goes down. The risk of blood clot formation is the highest after thermal trauma due to the increased vesiculation.

The number of erythrocyte-derived MVs in burn patients demonstrates a 3.5-fold increase compared to the norm. The loss of a part of erythrocytes' membranes when MVs are released from them is accompanied by the change in erythrocyte shape and the increase in hemoglobin concentration in each erythrocyte, which results in reducing their deformability- the ability to change their shape and go through capillaries smaller than erythrocytes themselves.

Our research demonstrated one more reason of reduced erythrocyte deformability after thermal trauma. The prolonged shock after a severe burn leads to hyperglycemia and glycated hemoglobin appears both inside erythrocytes and in their membranes (like in diabetes). It makes erythrocyte membranes more rigid, reducing their deformability.

The decrease in erythrocyte deformability is the main reason of microcirculation disorders, which leads to polyorganic insufficiency during burn injury.

We believe that the results of this research will help outline new ways of prevention and treatment of disorders in hemostasis and microcirculation during burn injury. These ways may be connected with preventing the increase of erythrocyte vesiculation or with intensifying their utilization.

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