EFFECT OF ^{60}Co γ-RAYS AND FAST NEUTRONS ON INTRAVASCULAR PLATELET AGGREGATION AND ON PROSTACYCLIN ACTIVITY OF BLOOD VESSEL WALLS

V. P. Baluda, G. N. Sushkevich, E. M. Parshkov, and T. I. Lukoyanova

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In the early period after irradiation the viscosity of the blood is increased, blood coagulation is activated, and blood clots and thrombi are formed in the vessels of the microcirculation. The change in the rheologic properties of the blood is of great importance to the mechanism of postradiation disturbance of the hemodynamics and the development of hypoxia of organs and tissues [1-3, 5, 7].

Adhesion of platelets to the blood vessel wall and their subsequent aggregation are key reactions in the processes of intravascular blood clotting and thrombus formation. The rate and intensity of these reactions largely depend on the regulating influence of prostaglandins, among which an important role is played by prostaglandin I_1 (PG I_2, prostacyclin). This substance is synthesized by endothelial cells and it is the most active physiological inhibitor of platelet aggregation [6, 9].

The action of γ-rays and neutrons on platelet aggregation and on the antiaggregation (prostacyclin) activity of the blood vessel wall was studied in the present investigation.

EXPERIMENTAL METHOD

Experiments were carried out on male CBA mice weighing 18-20 g, Wistar rats, and guinea pigs. The mice were exposed to ^{60}Co γ-rays in doses of 3, 7, 10, and 100 gram-roentgens (Gy) (dose rate 0.16-0.17 Gy/sec) and also with fast neutrons with an energy of 0.85 MeV in doses of 1.5, 3.7, and 10 Gy (dose rate 0.7 Gy/min). The animals were decapitated 1-6 h after irradiation and the femora were removed, cut into fragments 2-3 mm long, and fixed by Reynolds' method. The material was embedded in an Epon mixture. Ultrathin sections were studied in the JEM-5g and 100C electron microscopes. Because of the method used to fix the bone marrow together with the femur, which was removed only at the time of trimming the blocks, it was possible to preserve the cytoarchitectonics of the hematopoietic tissue and the intravascular distribution of platelets in the microcirculation.

Rats and guinea pigs were irradiated with ^{60}Co γ-rays in doses of 8 and 4.5 Gy respectively (LD 80/30 and LD 90/30, dose rate 0.84 Gy/min). Prostacyclin activity was determined in the wall of the abdominal aorta [4, 8]. Healthy animals, anesthetized with pentobarbital sodium were used as blood donors.

EXPERIMENTAL RESULTS

The electron-microscopic investigations showed that during the first few hours after irradiation of mice with γ-rays and neutrons, over the whole range of doses indicated above vasodilatation took place in the capillary network of the bone marrow. Platelets lumped together into aggregates of 4-5 to 20 cells or more accumulated in the sinuses (Fig. 1A, B). With an increase in the dose of irradiation, especially in the case of fast neutrons, the number of aggregates and the number of platelets forming them increased. Fibrin threads also were found in the blood vessels. These threads could be either directly connected with the aggregates of platelets or at a distance from them. Besides these formations composed of platelets and fibrin, stasis

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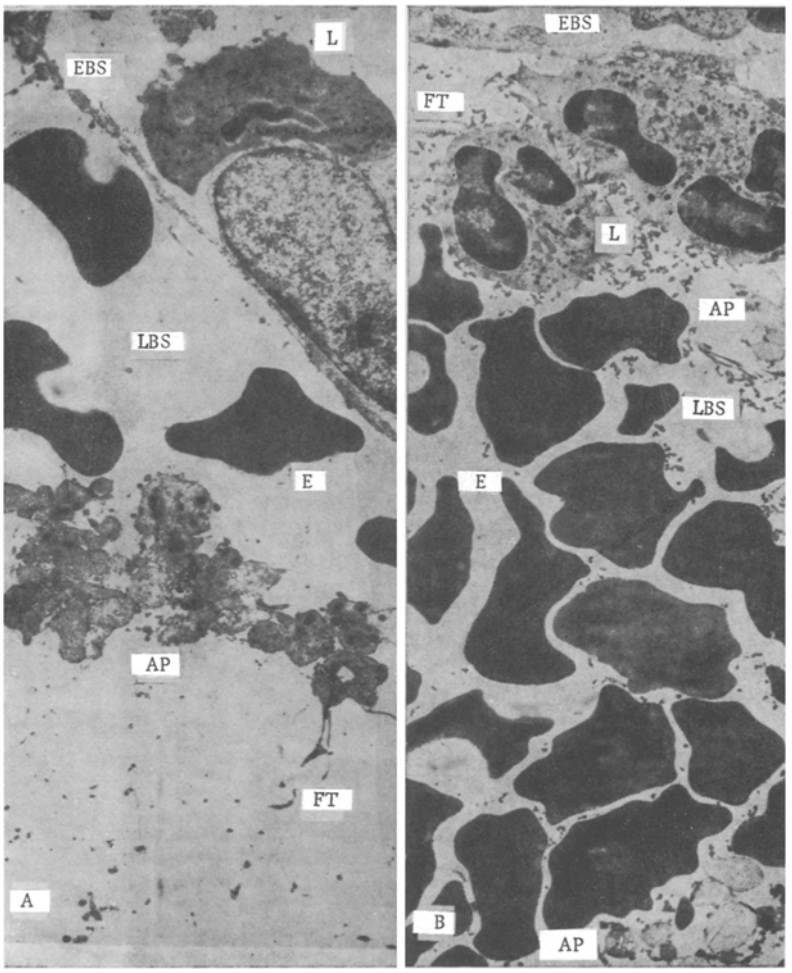

Fig. 1. Aggregation of platelets and fibrin formation in blood vessels of bone marrow of mice 3 h after whole-body γ-ray and neutron irradiation. A) γ-Ray irradiation in a dose of 7 Gy; B) neutron irradiation in a dose of 3 Gy. EBS) Endothelium of blood sinus; LBS) lumen of blood sinus; AP) aggregated platelets; FT) fibrin threads; E) erythrocytes; L) leukocytes. Here and in Fig. 2, magnification 2200 ×.

of erythrocytes and "agglutination" of granulocytes were observed in the microvessels of the bone marrow of the irradiated animals. As a rule these agglutinated granulocytes were in close contact with the aggregated platelets and fibrin threads (Fig. 1B). Platelet aggregates were found not only in capillary sinuses, but also in the arterioles of the bone marrow. In the latter case, spreading of the platelets over the surface of the endothelial cells was observed, with the formation of a basal layer on which the platelet aggregates, sometimes completely filling the lumen of the vessel, was formed (Fig. 2).

Experiments on rats and mice showed that γ-ray irradiation causes marked inhibition of prostacyclin activity of the blood vessel wall. As Fig. 3 shows, 1-6 h after irradiation the wall of the abdominal aorta had almost completely lost its ability to inhibit platelet aggregation. A considerable decline in prostacyclin activity also was observed 1 day after treatment with ionizing radiation. Later (after 3-5 days) a tendency was observed for this index to rise, but at the height of the disease (7th day) the prostacyclin activity fell again. On the 10th day of radiation sickness the vessel wall in the rats and guinea pigs not only did not inhibit platelet aggregation but, on the contrary, stimulated it.

The investigations thus showed that the action of ionizing radiation leads to intravascular aggregation of platelets in the microcirculation and to increased position of platelets onthe endothelium. This may be

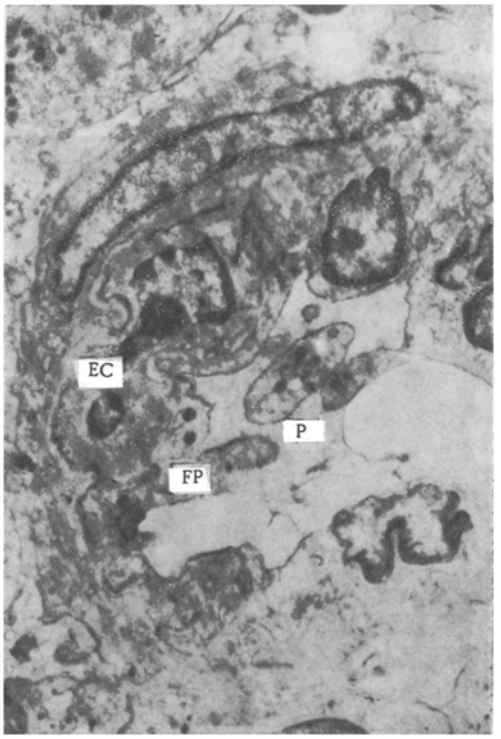

Fig. 2

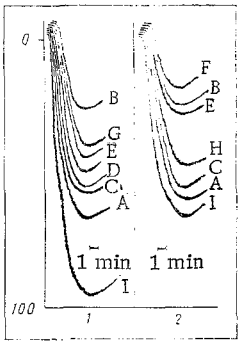

Fig. 3

Fig. 2. Aggregation of platelets in lumen of arterioles of mouse bone marrow 3 h after whole-body γ-ray irradiation in a dose of 100 Gy. EC) Endothelial cells; FP) platelet fixed to surface of endothelial cell; P) platelets in lumen of vessel.

Fig. 3. Antiaggregation activity of blood vessel walls of rats (1) and guinea pigs (2) at different times after γ-ray irradiation in doses of 8 and 4.5 Gy respectively. A) Aggregation of platelets suspended in plasma; B) effect of blood vessel walls of healthy animals on platelet aggregation; C-I) effect of blood vessel wall of animals 1 h (C), 6 h (D), 1 day (E), 3 days (F), 5 days (G) 7 days (H), and 10 days (I) after irradiation on platelet aggregation. Ordinate, platelet aggregation (in %).

due to a fall in prostacyclin activity, which plays an important role in the maintenance of the unaggregated state of the platelets and nonthrombogenicity of the intima of the vessels, in the vascular wall.

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