Parameters of Hemostasis and Blood Lysosomal Enzyme Activity in Allergic Necrotizing Inflammation Against the Background of Suppression and Stimulation of Immune Processes

A. M. Avanesov, G. A. Drozdova, G. M. Drogova, A. V. Pasechnik, and V. A. Frolov

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 124, No. 8, pp. 157-160, August, 1997
Original article submitted December 20, 1995

Changes in the hemostasis system are experimentally shown in rabbits with modeled allergic inflammation (Arthus phenomenon) of the maxilla. Suppression of immune processes has an adverse effect on this system, while immunostimulation improves hemostatic parameters. Immunosuppression impairs lysosomal mechanisms of inflammation, while stimulation of the immune system normalizes these mechanisms.

Key Words: *inflammation; immunity; hemostasis; lysosomes*

Surgical interventions in patients with impaired immune defense system and severe disturbances in the blood coagulation system (for instance, in leukemia) is a serious problem of operative dentistry. Many carcinogens induce synthesis of procoagulant substances [1] and modulate various functions of mononuclear phagocytes [7]. This can led to infectious and postsurgical hemostatic complications associated with stress and disturbing both the immune and hemostasis systems. In light of this it seems interesting to study the dynamics of some hemostatic and immune parameters in maxillary inflammation, since stomatological operations are usually performed under conditions of inflammation. Simultaneously, blood activity of some lysosomal enzymes was measured, since lysosomes are known to be involved into inflammation reactions [3,4].

MATERIALS AND METHODS

Experiments were performed on 40 male Chinchilla rabbits weighing 2.5-3 kg. Necrotizing inflammation of the maxilla was modeled by inducing the Arthus phenomenon. To this end, native horse serum (0.3 ml/kg) was 6 times injected under the maxillary mucosa at 5-day intervals. The number of platelets, clotting and fibrinolysis times, and the content of platelet factor 4, fibrinogen, plasmin, plasminogen, and activators and inhibitors of fibrinolysis were measured before modeling the pathological process and 1, 2, 3, and 4 weeks after its first manifestation [1]. Activities of the lysosomal enzymes N-acetyl-β-D-glucosaminidase and β-D-glucuronidase in the blood were determined spectrophotometrically [2,6]. In some animals, 3 weeks after induction of Arthus phenomenon soft tissues in the inflammation focus were dissected (surgery model). Immunosuppression in this group was attained by intramuscular injection of cyclophosphane in a dose of 20 mg/kg for 3 days before modeling the Arthus phenomenon, while immunostimulation was effected by single subcutaneous injection of complete Freund's adjuvant containing 0.15 mg/kg BCG on day 3 of cyclophosphane treatment. The state of the immune system was assessed by the content of antibody-producing cells in the spleen, plasma titer of hemagglutinins, and lysozyme activity.

Department of Pathological Physiology, Department of Maxillofacial Surgery and Stomatology, Russian University of Peoples' Friendship, Moscow

0007-4888/97/0008-0760$18.00

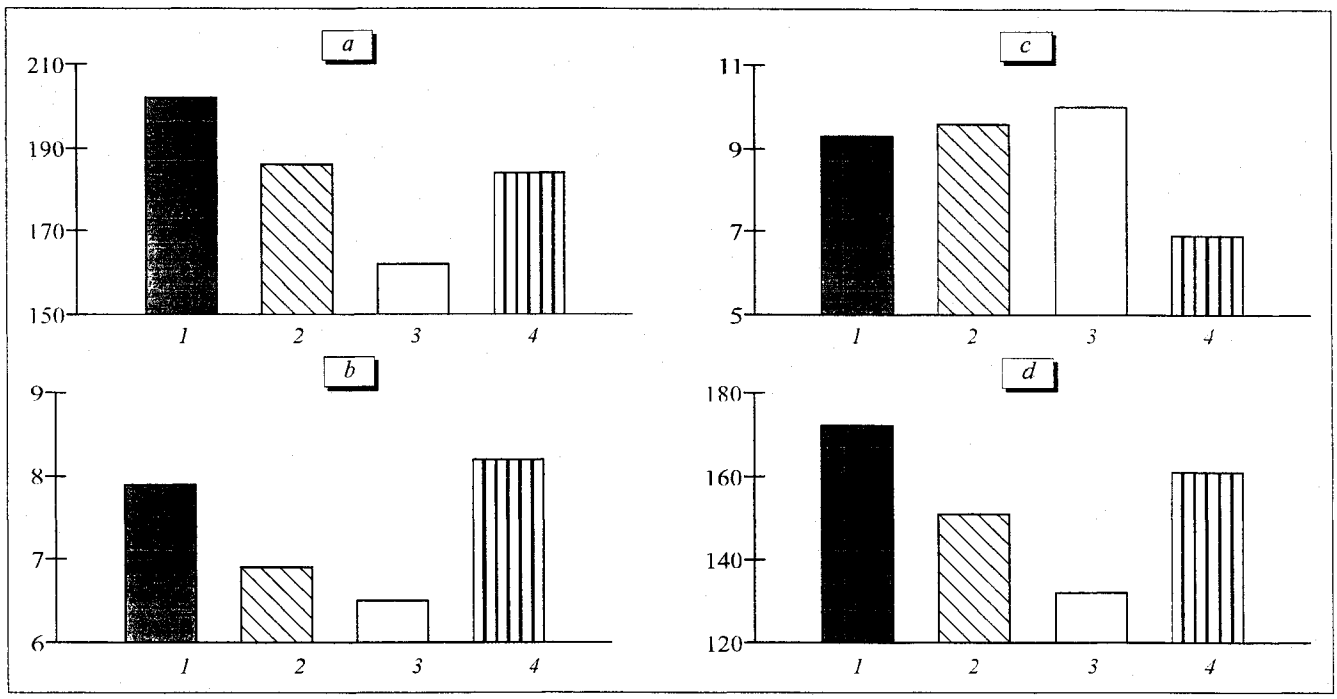

Fig. 1. Parameters of hemostasis 4 weeks after modeling of the Arthus phenomenon in nonoperated (*1*) and operated (*2*) animals under conditions of immunosuppression (*3*) and immunostimulation (*4*). *a*) platelets, $10^3/mm^3$; *b*) fibrinogen, μg; *c*) clotting time, min; *d*) time of fibrinolysis, min.

The data were processed statistically using the Student test, the differences between the mean values were considered to be significant at $p \leq 0.05$ ($T \geq 2$).

RESULTS

Allergic necrotic inflammation was accompanied by phasic changes in some parameters of hemostasis (most of these parameters considerably differed from the control). We compared the most important parameters of the hemostasis system before and after the surgery under conditions of immunosuppression and immunostimulation (Fig. 1).

Surgical intervention markedly decreased platelet count and the content of fibrinogen, had no effect on clotting time, and considerably accelerated fibrinolysis 4 weeks postoperation in comparison with the control (4 weeks without surgery). Cyclophosphane-induced immunosuppression aggravated these shifts. After stimulation of the immune system with BCG vaccine, the content of fibrinogen, platelet count, and fibrinolysis time become close to those in animals with Arthus phenomenon (week 4).

Figure 2, *a*, *b* shows the dynamics of N-acetyl-β-D-glucosaminidase and β-D-glucuronidase activity in the plasma of control animals to whom an injury of the maxillar area was inflicted 3 weeks after the start of experiment. The dynamics of both activities is similar and characterized by a rise 1 week after injury, which can be attributed to the development of local aseptic inflammation.

As seen from Fig. 2, *c*, *d*, four weeks after the start of experiment N-acetyl-β-D-glucosaminidase activity in animals with maxillar injury decreases to a considerably lesser extent than in rabbits with inflammation but without injury, while β-D-glucuronidase activity in these groups is similar. Thus, additional injury has no effect on lysosomal enzyme activity in animals with inflammation, because necrotic allergic inflammation is a very potent factor.

Figure 3 shows N-acetyl-β-D-glucosaminidase and β-D-glucuronidase activity in animals with and without surgery 4 weeks after the start of experiment.

The data on enzyme activity in animals with inflammation are the same as in Fig. 2. Immunosuppression considerably increases N-acetyl-β-D-glucosaminidase activity in nonoperated animals and considerably decreases it in operated rabbits. β-D-Glucuronidase activity in nonoperated animals does not differ from the control level, while in operated animals it markedly decreases.

A pronounced tendency towards normalization of both enzyme activities was noted after immunostimulation.

Thus, immunosuppression has an adverse effect on the dynamics of the hemostasis system in allergic inflammation complicated by traumatic injury and leads to impairment of the lysosome mechanism of

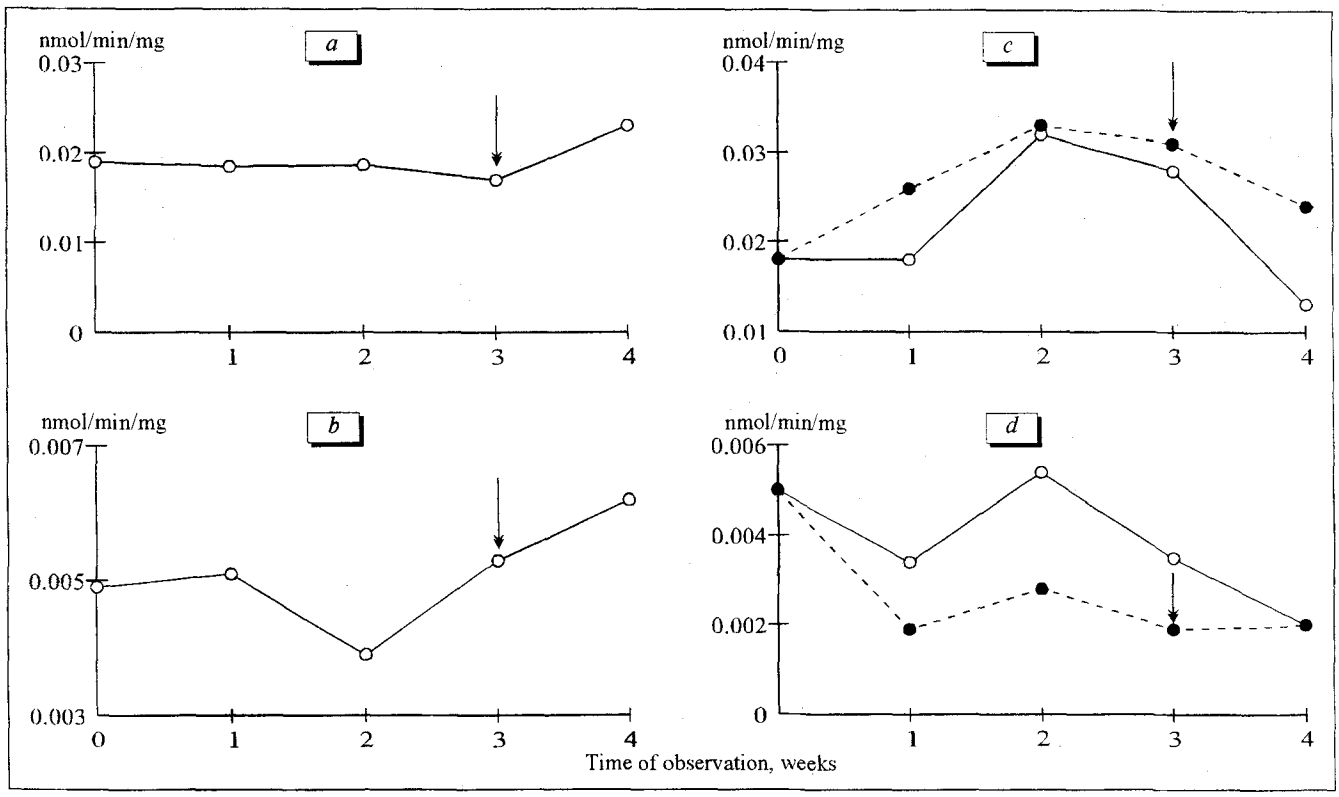

Fig. 2. Dynamics of N-acetyl-β-D-glucosaminidase (*a*, *c*) and β-D-glucuronidase (*b*, *d*) activity in intact animals (*a*, *b*) and rabbits with allergic necrotic inflammation (*c*, *d*) and surgical trauma of the maxilla. Arrow indicates surgical intervention. *c*, *d*: solid and dashed lines indicate animals without and with trauma, respectively.

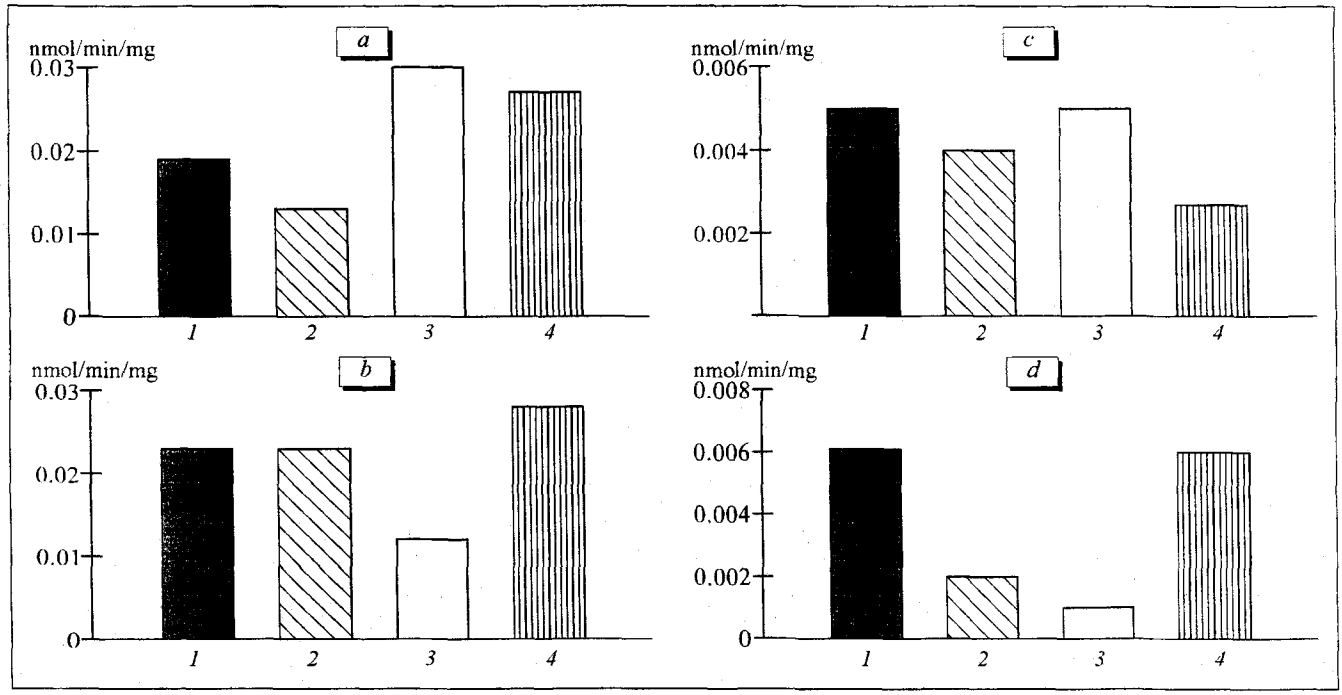

Fig. 3. N-acetyl-β-D-glucosaminidase activity after 4 weeks of allergic necrotic inflammation without (*a*) and with (*b*) surgical trauma and β-D-glucuronidase activity under the same conditions (*c*, *d*). Control (*1*); inflammation (*2*); inflammation against the background of immunosuppression (*3*) and immunostimulation (*4*).

inflammation, while immunostimulation normalizes these processes.

REFERENCES

1. V. P. Baluda, Z. S. Barkagan, E. D. Gol'dberg, *et al.*, *Laboratory Tests for the Hemostasis System* [in Russian], Tomsk (1980).
2. A. J. Barret and M. F. Hit, in: *Lysosomes* [Russian translation], Moscow (1980), pp. 25-156.
3. I. P. Metelitsina and S. S. Rodin, *Oftalmol. Zh.*, No. 4, 205-206 (1992).
4. N. E. Penkin and N. N. Mayanskaya, *Lysosomes: the Role in Adaptation and Reparation* [in Russian], Novosibirsk (1987).
5. S. P. Syatkin, *Vopr. Med. Khimii*, No. 1, 136-138 (1981).
6. J. W. Callahan and J. A. Lowden (Eds.), *Lysosomes and Lysosomal Storage Diseases*, New York (1981).
7. A. Rambalodi, G. Alessino, B. Casali, *et al.*, *J. Immunol.*, **136**, 3848-3855 (1986).