SOME MECHANISMS OF THE ACTIVATING EFFECT OF CLOSED CHEST TRAUMA

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Experimental studies of the state of the immune system after moderately severe closed chest trauma (CCT) conducted in the writers' laboratory, confirmed by clinical electrophysiological, and morphological data, revealed stimulation of the primary immune response to sheep's red blood cells (SRBC). This response was recorded at the peak of the immune response in the case of immunization of the animals immediately after trauma, and it reached the peak when the antigen was injected on the 15th day of the post-traumatic period [3].

This paper described an investigation into the mechanisms of the immunomodulating effect of CCT described above.

EXPERIMENTAL METHOD

Experiments were carried out on 148 male Wistar rats weighing 180-240 g. Closed chest trauma was inflicted by the falling weight method, devised in the writers' laboratory [2]. All operations were performed under ether anesthesia. Thymectomy was performed through a small aperture in the chest after preliminary division of the upper third of the sternum along the midsternal line. Both lobes of the thymus were removed with pial forceps. In the experiments with trauma to the thymus, the same approach was used and the left lobe was crushed with forceps. In animals undergoing a mock operation the skin was incised and the sternum divided. In all cases the wound was closed in layers.

To prepare cell suspensions the rats' spleens were removed and homogenized in 5 ml of Hanks' solution. The number of nucleated cells was counted in a Goryaev's chamber. To assess the immune response the animals were immunized intraperitoneally with 10^9 SRBC on the 15th day after trauma, and 5 days later (the peak of the immune response) the number of antibody-forming cells (AFC) in the spleen was determined by local hemolysis in agarose gel. T and B lymphocytes in the spleen were counted on the 15th day of the post-traumatic period. B cells were determined by the EAC-rosette-formation method [4], T lymphocytes by the complement-dependent lymphocytolysis test [7] with antithymocytic rabbit serum, exhausted with rat erythrocytes and liver and bone marrow cells [6].

The results were subjected to statistical analysis by Student's test and by the use of the tetrachoric coefficient of association [5].

EXPERIMENTAL RESULTS

The immune response to T-dependent antigen (SRBC) was enhanced by 2.4 times ($P < 0.002$) in the traumatized animals compared with the control rats (Fig. 1). Counting the T and B lymphocytes showed a considerable increase (by 3.3 times) in the number of T cells in the spleen of animals with CCT but not of B cells (Fig. 1). Correlation analysis revealed positive correlation between accumulation of T cells and intensification of the immune response to T-dependent antigen ($r = 0.760$; $P < 0.001$). Meanwhile, investigation of the relationship between the number of B cells in the spleen and the number of AFC did not reveal any significant correlation ($r = 0.189$; $P > 0.05$).

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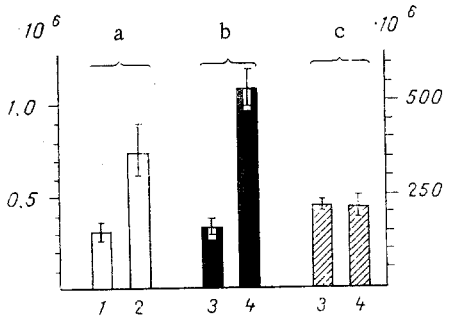

Fig. 1

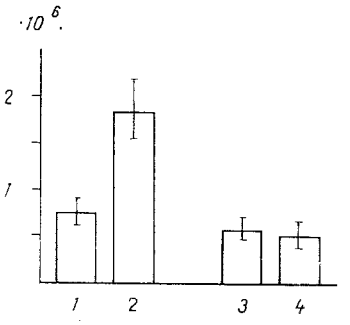

Fig. 2

Fig. 1. Effect of CCT on number of AFC (a) and T (b) and B (c) lymphocytes in the spleen. 1) Intact immunized animals; 2) rats immunized 15 days after CCT; 3) intact unimmunized animals; 4) rats 15 days after CCT. Ordinate: on left — number of AFC in spleen (for groups 1 and 2), on right — number of lymphocytes in spleen (for groups 3 and 4).

Fig. 2. Effect of thymectomy on post-traumatic stimulation of immune response in spleen during CCT. 1) Intact immunized animals; 2) rats immunized 15 days after CCT; 3) thymectomized and immunized animals; 4) thymectomized rats immunized 15 days after CCT. Ordinate, here and in Fig. 3: number of AFC in spleen.

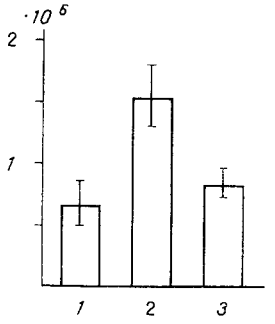

Fig. 3. Effect of thoracotomy and trauma to thymus combined with thoracotomy on immune response in spleen. 1) Intact immunized animals; 2) rats immunized 15 days after thoracotomy; 3) rats immunized 15 days after thoracotomy and trauma to thymus.

The results are evidence, in our opinion, of the leading role of the T system of immunity in stimulation of antibody production after CCT. To test this hypothesis, thymectomy was performed on adult animals, 30 days later (when parameters of the immune response were completely back to normal) CCT was inflicted, and after a further 15 days the rats were immunized with SRBC. Immunized intact and traumatized (CCT) rats, not undergoing the operation, and also thymectomized animals immunized 45 days after the operation, but not subjected to CCT, served as the controls (Fig. 2).

As Fig. 2 shows, thymectomy completely abolished the stimulating effect of CCT on the immune response, whereas in animals with an intact thymus it was preserved.

After thus obtaining proof of thymus-dependent stimulation of the immune response in CCT, the role of direct trauma to the thymus (the possibility of such trauma during CCT was demonstrated histologically) in the immunomodulating effect of CCT was investigated. For this purpose the thymus of rats was injured, and 15 days later SRBC were injected. Rats undergoing a mock operation and intact immunized rats served as the control (Fig. 3).

The experiments showed that thoracotomy, like CCT, significantly ($P < 0.02$) enhanced the immune response (by 2.3 times compared with the response of intact, immunized rats), whereas trauma to the thymus, like thymectomy, abolished this effect.

Activation of the immune response, developing against the background of CCT and thoracotomy, is evidently a universal response to mechanical injury of organs and tissues. Similar results were obtained in rats after laparotomy and laparotomy followed by nephrectomy [10].

The relationship observed between accumulation of T lymphocytes and enhancement of the immune response to T-dependent antigens in the spleen after CCT suggests the selective accumulation of T helper (TH) cells in this organ. However, enhancement of the immune response can be observed also as a result of a decrease in T suppressor (TS) activity. It must be emphasized in this connection that the action of "stimulating" and "suppressing" T lymphocytes on B cell proliferation is determined by the size of the regulatory population: if the number of cells, being a mixture of the two subpopulations, is small, the stimulating effect will predominate, but if it is large, the inhibitory effect will be greater [1]. We therefore consider it right to conclude that the TH/TS ratio in the rate spleen is increased under the influence of CCT on account of the helper subpopulation, for enhancement of the immune response was observed against the background of a more than threefold increase in the number of T lymphocytes but a normal number of B cells. In experiments with trauma inflicted on animals 30 days after thymectomy, the effect of short-living TS is ruled out [9]. At the same time, however, thymectomy leads to abolition of the activating effect of CCT on the immune response. The stimulating effect of chest trauma is evidently determined by the increased inflow of thymic precursors of TH into the spleen. In such a situation trauma to the thymus may inhibit migration of cells from this organ and give an effect similar to that of thymectomy.

The view regarding the mechanisms of activation of the immune response after CCT described above is debatable in many respects. Nevertheless, dependence of the immunomodulating effect of trauma on the thymus, established by this investigation, is important in our view for an understanding of the role of the immune system in traumatic disease.

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