HYPERSENSITIVITY OF DELAYED TYPE MANIFESTED DURING THE DEVELOPMENT OF ALLERGIC LESIONS OF THE MYOCARDIUM

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Changes in humoral and cellular responses were studied during the development of allergic lesions of the myocardium in rabbits. These responses, manifestations of hypersensitivity of delayed type, are connected with transformation of cells of the active mesenchyme, responsible for the process of immunogenesis, into lymphocytes and plasma cells. In allergic lesions of the myocardium hypersensitivity of delayed type is manifested as a lympho-marcrophagal reaction in the intermuscular stroma of the heart, the thymus, and the lymph glands and also as blast transformation of the lymphocytes. A complex series of disturbances of immunologic homeostasis arises, in which the primary components are microangiopathies, blast-transformation of lymphocytes and activation of lysosomal enzymes.

KEY WORDS: hypersensitivity of delayed type; allergic myocarditis; cell reactions in hypersensitivity of delayed type.

A leading place among the reactions of cellular immunity is occupied by hypersensitivity of delayed type (HDT), which lies at the basis of many allergic and infectious diseases, autoimmune diseases, etc.

The object of this investigation was to study the immunomorphological manifestations of HDT, using allergic lesions of the myocardium as the experimental model [1].

EXPERIMENTAL METHOD

Chinchilla rabbits weighing 2.0-2.5 kg were immunized repeatedly with a 5% rat heart homogenate. The homogenate was injected together with an adjuvant (10-15% alumina gel) in a dose of 4 ml subcutaneously in the inguinal region once a week, on both sides alternately, for 8 injections [2]. The animals were killed at various periods of immunization (after the 2nd-8th injections of the antigen).

The hearts of 57 rabbits were studied. Pieces of the rabbit's heart were fixed in Lillie's fluid and embedded in paraffin wax. Sections were stained with hematoxylin-eosin, picrofuchsin-fuchselin, iron-hematoxylin, and toluidine blue. The reactions of Brachet, Einarson, Feulgen, and Shabadash were carried out. In several cases small pieces of heart were fixed in a 2.5% solution of glutaraldehyde and in osmium tetroxide by Palade's method [14] and embedded in a mixture of Epon and Araldite. Ultrathin sections were stained with lead citrate as described by Reynolds [15] and studied in the JEM6C electron microscope.

EXPERIMENTAL RESULTS

The distinctive features of the antigenic stimulation used to produce allergy of delayed type were revealed when the antigen was injected together with adjuvant.

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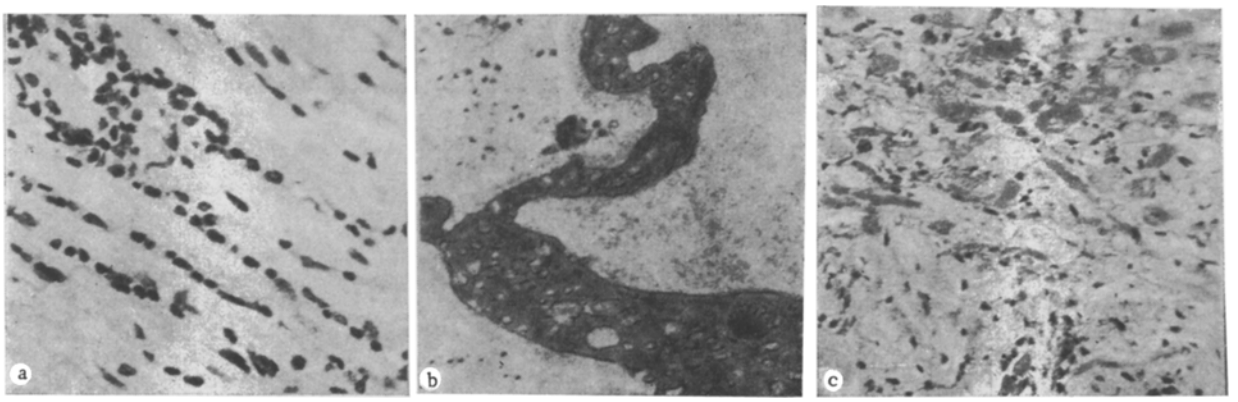

Fig. 1. Rabbit myocardium 1 month after the beginning of immunization: a) extensive infiltration of the intermuscular stroma by lymphocytes (hematoxylin-eosin, 280 ×); b) swelling of the endothelium of an intermuscular capillary (25,000 ×); c) uneven distribution of glycogen in muscle fibers (stained with Schiff's reagent by Shabadash's method, 180 ×).

There is evidence in the literature [3, 4, 8] that lymphocytes and macrophages (Fig. 1a), which were the principal infiltrating cells in these experiments and were discovered in the intermuscular stroma of the rabbit myocardium 30-35 days after the beginning of immunization, react specifically with the antigen in HDT. Considerable changes in the microcirculation – capillaries, arterioles, and, in particular, the venules – took place in the zones of infiltration. Swelling of the endothelium (Fig. 1b) and accummulation of neutral mucopolysaccharides in the basement membrane of the capillaries and the tunica media of the arterioles and venules were observed in them. These changes predetermined the migration of lymphocytes from the blood into the focus of the allergic reaction. This statement was confirmed by ultrastructural changes in the blood vessels of the stroma. The capillary endothelium formed cytoplasmic appendages which fixed the lymphocytes. The latter left the vessel through the endothelial cell.

During the development of HDT (on the 55th-60th day of immunization) blast transformation of lymphocytes was observed in the myocardial stroma. The blast cells were bigger than the lymphocytes and had a well-marked pyroninophilic cytoplasm, rich in acid phosphatase.

An increase in acid phosphatase activity and a decrease in succinate dehydrogenase activity, the basis of the chemical aggression of the lymphocytes [10-12, 16], have been demonstrated by biochemical methods [13] in transformed peripheral blood lymphocytes. Investigations have shown [19] that an increase in the activity of lysosomal enzymes leads to an increase in tissue proteolysis as a result of their liberation through the lysosomal membranes into the tissues.

The cytopathic effect of lymphocytes is one of the chief features of HDT, for it is connected with injury to the myocardium. The lesion consists of balloon degeneration and cloudy swelling of the muscle fibers, followed by their necrobiosis, with homogenization of the cytoplasm and a sharp decrease in its content of mucopolysaccharides and, in particular, of glycogen (Fig. 1c). Single muscle fibers underwent discoid fragmentation and lysis. In many groups changes in the muscle fiber were detected only by electron-microscopic examination. They took the form of condensation of the nucleolus, swelling of the mitochondria, and dilatation of the tubules of the endoplasmic reticulum. A very small decrease in the glycogen content was observed: the glycogen was localized as rosettes chiefly around the mitochondria, which were clustered into large or small groups. The outlines of the nuclei were indented. The amount of chromatin was increased.

The lympho-macrophagal reaction in the stroma of the rabbit myocardium took place against a background of progressive lymphoid hyperplasia and blast transformation of lymphocytes in the lymph glands and thymus and of high serum titers of complement-fixing immunoglobulins. The lymphocyte count in the peripheral blood was increased (60-90 per 100 leukocytes).

The specific features of HDT were determined not only by lymphocytes but also by macrophages. They were localized in the foci of infiltration in the stroma, more especially around dying or degenerating muscle fibers. The functional state of the monocytic system was depressed: after the first injection of antigen the numbers of promonocytes and monocytes were increased, the latter considerably. After repeated injections of antigen the cells showed reduced proliferation but increased differentiation, indicating depression of the "active mesenchyme" and a disturbance of general reactivity.

Coagulation studies revealed the phasic character of the changes.

Analysis of the material showed that these changes in the humoral and cellular reactions during the development of allergic lesions of the myocardium are associated with lymphocyte and plasma-cell transformation of cells of the "active mesenchyme," the structure responsible for the process of immunogenesis. HDT is the earliest phase of the immune response, before antibody formation and the production of plasma cells.

The appearance of HDT is based on factors of cellular immunity. Various cells participate in the development of HDT: thymus-dependent lymphocytes and macrophages. In allergic myocardial injury HDT is manifested as a lympho-macrophagal reaction in the intermuscular stroma of the heart, the thymus, and the lymph glands as well as blast transformation of the lymphocytes.

A complex disturbance of immunologic homeostasis arises, in which the primary changes are microangiopathies, blast transformation of the lymphocytes, and activation of the lysosomal enzymes of the lymphocytes.

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