THE EFFECT OF NEONATAL THYMECTOMY ON AUTOALLERGIC MYOCARDITIS

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Over the past few years, as the result of numerous researches, it has been established that neonatal thymectomy leads to a reduction of lymphocytes in the peripheral blood and lymphatic circulation (Miller, 1962; Arnason et al, 1962), marked lymphoid hypoplasia (Wokman et al, 1962), antibody production impairment (Friedman, 1955; Bash, 1966; Miller, 1966) and inhibition of hypersensitivity reactions of a delayed (cellular) type.

The pathogenesis of rheumatism, despite intense experimental studies, is still far from being fully clarified. Parallel to ascertaining the part of streptococci in its etiology, researches are also conducted into the mechanism of allergic reaction in rheumatism. According to Bibikova (1965), Borisova (1967) and others, the allergy of delayed (cellular) type is more characteristic of rheumatism than the immediate sensitivity, as claimed by a number of authors (Rich and Gregory, 1944; Evseev and Razsohina, 1967).

In earlier studies we were successful in demonstrating that the thymus, assumed as an immune response organ, is related to the pathogenesis of rheumatism in general, and to its allergic link in particular. It was established that neonatal thymectomy inhibits the development of experimental myocarditis and arthritis in rats, induced by intravenous injection of beta-hemolytic streptococcus, group A (Kemileva and Uzunova, 1970).

It is the purpose of the present study to trace the influence of neonatal thymectomy on the occurrence and development of autoallergic (autoimmune) myocarditis as a typical form of allergic hypersensitivity of a delayed (cellular) type.

Material and Method

The research was performed on 49 male white rats of the Wistar line, divided up into two groups: experimental, consisting of 30 neonatally thymectomized animals, and a control one, comprising 19 rats subjected to pseudothymectomy.

Neonatal thymectomy was made within 24 hours of birth. Two thirds of every generation were subjected to thymectomy, whilst the remainder were subjected to false thymectomy, including all the stages of the real one except for leaving the thymus intact in situ. The completeness or degree of thymectomy, and the presence or not of regenerated thymus tissue were judged from the macroscopic data of the postmortem examination, and in some instance, also from the histological investigation of mediasti-

num sections. Animals with a residual thymus and septic processes at the site of operative intervention or in other parts of the body, as well as the animals sustaining exhaustion syndrome were omitted from the present study.

Autoallergic myocarditis was provoked in either group of animals upon reaching the age of three months by means of repeated (five times) subcutaneous injections of 0.5 ml rabbit heart homogenate, prepared after the method of Kaplan and associates (1962).

Material for histological study was taken from the myccardium of all the animals two weeks after the last homogenate injection. The whole heart underwent fixation in 10 per cent neutral formalin, and thereby it was cut in two halves in a fashion permitting the dissection line to pass along the longitudinal axis, enclosing both halves and the septum. The histological preparations were treated according to the paraffin method and were stained with hematoxylin-eosin, after Van Gieson and with AZAN for the connective tissue, and with toluidine blue at pH of the solution 2.2, 3.8 and 5.3 for demonstrating acid mucopolysaccharides.

Results and Discussion

The data obtained show that autoallergic myocardial lesions develop in 68.4 per cent of the control, falsely thymectomized rats, and only in 40.0 per cent of the thymectomized (Fig. 1), which gives us sufficient reason to accept that neonatal thymectomy inhibits the development of autoallergic myocarditis.

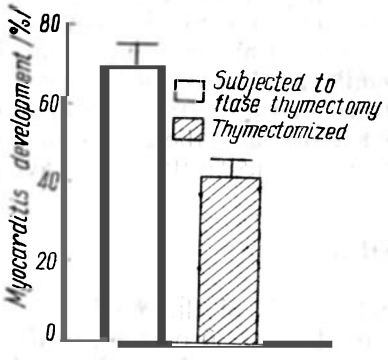

Fig. 1

The histological changes in the myocardium of the animals subjected to pseudo-operation are localized in the blood vessels, in the fibrous ring of valve orifices and in the paravascular connective tissue. The walls of the blood vessels are thickened and stain pale pink with hematoxylin eosin. Within the vascular wall, the different layers are hardly distinguishable. In the perivascular spaces the observations show edema, connective tissue loosening and cellular proliferation from lymphocytes, plasmatic cells and histiocytes. Toluidine-blue staining at pH of the solution 5.3 shows slightly pronounced metachromasia. The methods for connective-tissue demonstration employed (after Van Gieson and with AZAN) point to a disturbed affinity of connective tissue for the dyes used. Instead of the elective red after Van Gieson, the connective tissue in the perivascular spaces is tinged yellow-brown, while with AZAN it displays bluish-violet staining. The changes just described suggest the presence of destructive processes within

the connective-tissue fibers of the type of mucoid dystrophy. The cellular proliferation in the perivascular zones displays a granulomatous character and is manifested by the outgrowth of lymphocytes, histiocytes, mastocytes and single plasmatic cells. These cellular elements are aggregated in a mono- or bipolar fashion around the blood vessels in the form of nodules, similar

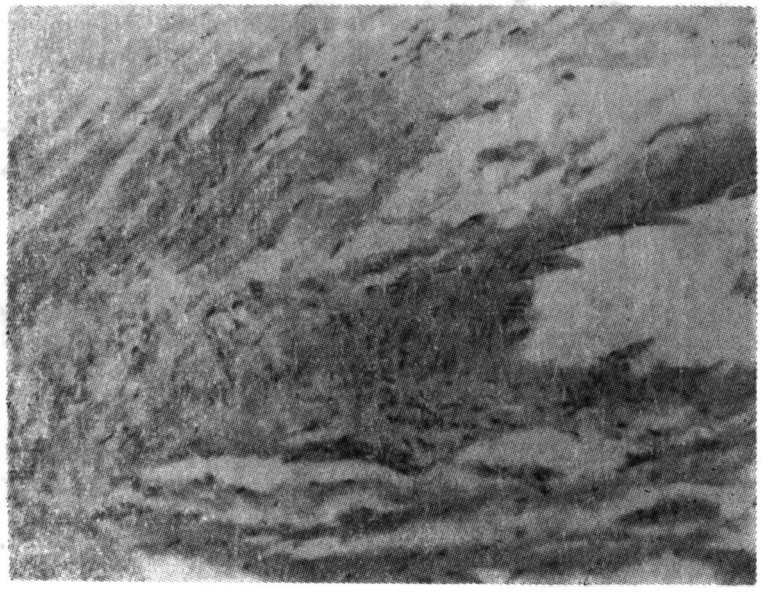

Fig. 2

to the nodes of Ashov-Talalaev in rheumatism (Fig. 2). Loosening, edema and mesenchymal proliferation are also noted in the fibrous annulus of valvular orifices.

In the group of neonatally thymectomized animals, myocardial lesions are likewise detected, but they differ essentially from those in the controls, equally by the number of animals affected, and by the severity of the pathological process. The inflammatory response has the character of focal interstitial or septic myocarditis. Focal proliferation from lymphocytes and histiocytes is present although there is no tendency to form granulomas with their characteristic perivascular localization, as in the control animals, subjected to false thymectomy (Fig. 3). Structural changes in the perivascular spaces, presenting the picture of mucoid edema, are discovered in isolated animals but they are not accompanied by cellular proliferation. The staining methods for connective tissue and the histochemical study with toluidine blue by no means give sufficient reason to accept the presence of pronounced mucoid edema in the connective tissue.

In conclusion, it may be stated that neonatal thymectomy inhibits the development of autcallergic myccarditis in rat which, in turn, warrants the assumption that delayed allergy plays an essential role in the pathogenesis of this particular pathological process.

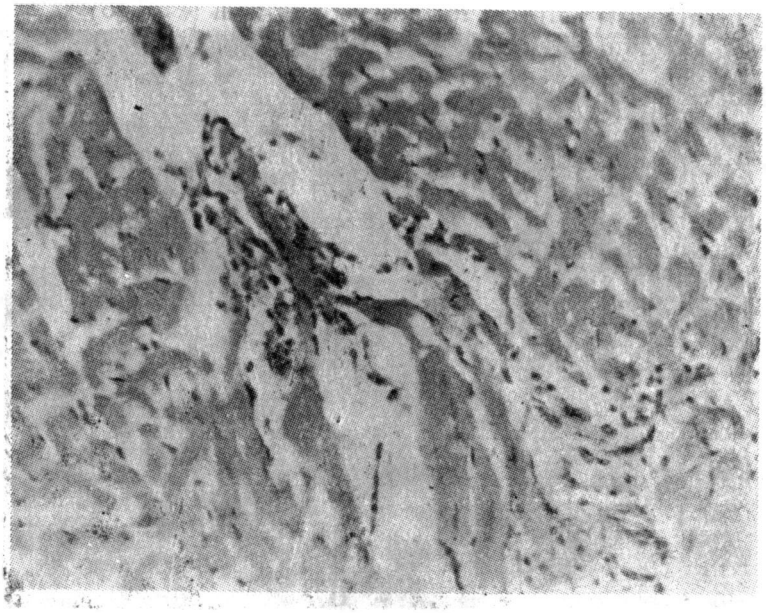

Fig. 3

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ВЛИЯНИЕ НЕОНАТАЛЬНОЙ ТИМЭКТОМИИ НА АВТОАЛЛЕРГИЧЕСКИЙ МИОКАРДИТ

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РЕЗЮМЕ

Автоаллергический миокардит был вызван у неонатально тимэктомированных и ложно тимэктомированных крыс породы Вистар путем подкожного введения гомогената из сердца кролика, приготовленного по методу Kaplan (1962).

Гистологически и гистохимически миокард был исследован у 30 тимэктомированных (опытных) и 19 ложно тимэктомированных (контрольных) животных. Автоаллергические поражения миокарда были установлены у 63,4% контрольных животных и у 40 % тимэктомированных. Это показывает, что неонатальная тимэктомия подавляет развитие автоаллергического миокардита, который считается, что является реакцией сверхчувствительности замедленного (клеточного) типа.

Клеточная пролиферация в миокарде неонатально тимэктомированных животных имеет характер интерстициального миокардита, без тенденции к образованию гранулом, которая наблюдается у контрольных животных. Гистохимическое исследование показало, что деструктивные изменения в околососудистой соединительной ткани неонатально тимэктомированных животных выражены слабее.