A strain of SHR, which spontaneously develops hypertension and cardiovascular diseases, had a decreasing number of rosette forming T-cells in their thymuses and a progressive decline in cellular immune functions such as blastogenic responses to PHA, delayed type hypersensitivity and allograft rejections by aging (Takeichi et al., Clin. exp. Immunol., 40: 120, 1980). A cell cooperation experiment indicated that the T-lymphocytes of the SHR were selectively impaired in antibody response to SRBC in cooperation with B-lymphocytes (Takeichi et al., Cell. Immunol., in press).

We describe here a naturally occurring thymocytotoxic autoantibody (NTA) that is detectable in the serum of SHR at various ages by means of a complement dependent cytotoxicity test. The NTA occurred from 1 month of age through life and the incidence was more than 60% of SHR at any age. Cytotoxic titers of the NTA in older SHR were higher than those in younger rats up to 2 month old. Thymocytes from all 7 rat strains tested showed similarly high sensitivity to NTA but none of the strains tested produced NTA except the SHR strain. The cytotoxicity of the NTA was strong only for thymus cells, and was very weak or negative for the spleen cells, lymph node cells, bone marrow cells and blood lymphocytes of rats. However, the cytotoxic activity of the NTA was completely absorbed with the thymus, spleen, lymph node cells and brain homogenates and was partially absorbed with bone marrow cells, but not with liver and kidney homogenates. The cytotoxic activity of the NTA was completely lost by treatment with 0.1M 2-mercaptoethanol. Gel-filtration on Sephadex G-200 showed that the cytotoxicity of the NTA was observed only in the first peak containing IgM-globulins.

The SHR had progressive decline of T-cell mediated immunity due to age. Whether there is a correlation between T-cell depression and the appearance of NTA in SHR is not yet known. However, this possibility is suggested by the fact that the cytotoxicity of NTA is specific for thymocytes and also by the fact that the age-related increase in the incidence of NTA is inversely related to the linear decrease of T-cell functions in SHR. T-lymphocytes in the peripheral lymphoid tissues and blood of SHR have the NTA-reactive antigens on their cell surface as shown by absorption test, though they did not show direct cytotoxic sensitivity to the NTA. From these results, it is possible that immature and mature T-lymphocytes are affected by NTA, which is always in excess in the circulation of SHR.


(Summary)

Spontaneous hypertensive rats produced a natural thymocytotoxic autoantibody (NTA) which was cytotoxic for the thymocytes of the various strains of rats tested. More than a 60% incidence of NTA in the SHR occurred from 1 month of age and was observed throughout their life span. The titers of the autoantibody varied among individual rats and progressively increased with age. The NTA was cytotoxic for thymocytes but weak or negative for spleen, lymph node and bone marrow cells. However, absorption test indicated that NTA-reactive antigens were distributed in the thymus, spleen, lymph nodes, and brain of adult rats. The NTA in SHR was an IgM-globulin as determined by sensitivity to 2-ME treatment and by Sephadex G-200 column chromatography. These results suggest that the NTA is responsible for the selective suppression of T-cell functions in SHR.