38) Immunological Suppression of Carcinogenesis in T-cell Depressed SHR.
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A strain of SHR has been established by Okamoto and Aoki as an animal model for human hypertension. We have found that the SHR show a progressive decline of T-cell functions by aging, the appearance of natural thymocytotoxic auto-antibody and a deficiency of thymic hormone relating to T-cell differentiation. Recently we have reported that administration of various immunopotentiators (IPs) could bring about the restoration of T-cell functions and the induction of transplantation resistance against syngeneic tumors in SHR. The present study was designed to restore the depressed T-cell functions and to suppress carcinogenesis by means of immunological methods.

(Methods)

3-methylcholanthrene (MCA) was injected into back of the rats. Regular palpation and measurement of tumors were carried out to record the development and size of tumors. Allogeneic thymus grafts or administration of IPs were used to restore T-cell functions in SHR.

(Results)

(1) After injection of 2mg of MCA the tumor incidence was 95.5% in SHR while, by contrast, was only 30.0% in WKA rats with normal T-cell functions.

(2) By means of allogeneic thymus grafts and administration of neurotrophin (NSP), restoration of T-cell depression, induction of Killer T-cells and activation of NK cells were achieved.

(3) The tumor incidence and latency periods were significantly distinct between SHR grafted with thymuses and non-treated SHR. Within 180 days after injection of MCA 66.7% of SHR grafted with WKA thymuses developed tumors, whereas 100% of the non-treated SHR developed tumors within 130 days. The latency periods were also prolonged in SHR treated with NSP, by comparison with non-treated SHR. (see figure)

Figure. Effect of allogeneic thymus grafts and NSP on incidence and growth of MCA-induced tumors in SHR.

(Summary)

The results presented here show that the tumor incidence in T-cell depressed SHR after injection of MCA was higher than that in WKA rats with normal T-cell function. The depression of T-cell functions in SHR was almost completely restored by allogeneic thymus grafts or injection of NSP. At the same time, the generation of Killer T-cells was induced, and the activity of NK cells against K-562 cells was enhanced. The tumor incidence was suppressed and average latency periods were also prolonged in SHR grafted with WKA thymuses. The administration of NSP was effective in prolonging latency periods for the development of tumors. From these results, we suggest that the SHR is a suitable animal model for the investigation of the role of cell-mediated immunity in carcinogenesis.