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MECHANISMS OF CHANGES IN WEIGHT OF THE CENTRAL LYMPHOID ORGANS DURING ADENOVIRUS CARCINOGENESIS

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Transplantation of spleen cells of CBA mice at the 25th day of the latent period of carcinogenesis induced by SA7 (C8) virus into newborn syngeneic animals evoked a graft versus host reaction in them. Splenomegaly and a progressive decrease in the weight of the thymus were observed in the recipients. Similar changes in weight of the lymphoid organs were found in animals infected neonatally with oncogenic adenovirus SA7 (C8). The results show that adenovirus carcinogenesis has some manifestations of autoimmune disease.

KEY WORDS: adenovirus; carcinogenesis, autoimmune response; graft versus host reaction; thymus; spleen.

The antigenic profile of tissues undergoing malignant transformation exhibits certain regular features. A common factor in the dynamics of the antigen spectrum of tissues undergoing malignant change is a decrease in the concentration of organ-specific antigens and the accumulation of embryonic antigens associated with tumors [3, 6, 7]. One of the factors which determines the specific character of the antigenic complement of tissues during carcinogenesis is the autoimmune response, frequently observed during carcinogenesis [4, 8]. The writers have shown that in the early stages of carcinogenesis induced by simian adenovirus SA7 (C8) lymphocytes immune to antigens of embryonic fibroblasts appear in the spleens of CAB mice [2].

Considering that immunologic tolerance to certain antigens is due to the functioning of particular populations of co-called T- and B-suppressor cells it is logical to postulate that "injury" to these cells is the cause of the autoimmunity observed in the test system [4, 5, 10]. An expected manifestation of the abolition of the suppressive function may be the increased proliferative activity of a certain population of lymphocytes.

In the present investigation, in order to detect lymphocytes with increased proliferative powers, spleen cells were transplanted from CBA mice in the latent period of carcinogenesis into syngeneic newborn recipients.

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TABLE 1. Weight Index of Thymus and Spleen of CBA Mice after Syngeneic Transplantation of Splenocytes from Mice during Latent Period of Adenovirus Carcinogenesis

Index	25th day of latent period	P	Normal splenocytes	P	Control (intact animals)	P
Splenic	5,64±0,7 (n=4)	—	3,71±0,3 (n=5)	<0,05	3,72±0,4 (n=5)	<0,05
Thymus	4,04±0,7 (n=4)	—	4,88±0,7 (n=4)	<0,05	6,21±0,83 (n=6)	<0,01

TABLE 2. Dynamics of Weight of Thymus and Spleen of CBA Mice in Latent Period of Carcinogenesis

Time of experiment	Splenic index	P	Thymus index	P
10th day of latent period	4,9±0,3 (n=12)	<0,05	—	
25th day of latent period	5,02±0,4 (n=12)	<0,05	5,4±0,6 (n=13)	<0,05
Intact animals	3,72±0,4 (n=5)	—	6,24±0,83 (n=6)	—

EXPERIMENTAL METHOD

Experiments were carried out on CBA mice of different ages. Simian adenovirus SA7 (C8) was used in a titer of 10^{-4} cytopathogenic units/0.1 ml, after serial passage in the writers' laboratory through green guenon kidney cells. Spleen cells from CBA mice aged 25 days, infected on the first day of life with SA7 (C8) virus, were used as donor cells for transplantation into newborn syngeneic recipients in a dose of 9×10^6 cells per animal. The effect of transplantation of spleen cells into the newborn recipients was assessed as the thymus index and splenic index on the 10th day of life. The weight of the lymphoid organs was determined by the formula $\frac{\text{weight of organ}}{\text{body weight}} \times 1000$. The dynamics of the weight of the lymphoid organs was determined as the index of these organs in the early stages of carcinogenesis induced in CBA mice by simian adenovirus SA7 (C8), administered to them on the first day of life. The results were subjected to statistical analysis by Student's t-test.

EXPERIMENTAL RESULTS

The data in Table 1 show that transplantation of spleen cells into newborn syngeneic recipients from animals at the 25th day of the latent period of carcinogenesis induced by simian adenovirus SA7 (C8) led to a marked change in the weight of their lymphoid organs. In animals receiving mouse splenocytes during the latent period the splenic index was considerably increased. After injection of splenocytes from normal 25-day-old animals the splenic index was unchanged.

The difference in the effect of transplantation of splenocytes from animals in the latent period of carcinogenesis induced by SA7 (C8) virus and cells of normal animals of the same age was evidently connected with a change in the proliferative powers of transplanted cells. The experiments showed that by the 25th day of the latent period a population of lymphocytes with increased proliferative activity appeared in the spleens of the CBA mice by the 25th day of the latent period. This is confirmed also by the fact that in animals at the 25th day of the latent period of carcinogenesis (Table 2) the splenic index also was increased. Very probably the increased proliferative powers of these cells, reflected in the increased splenic index, were maintained after transplantation into normal syngeneic recipients, as demonstrated by an increase in their splenic index.

One of the general results of interaction between oncovirus and cell is increased synthesis of cellular DNA and increased mitotic activity [1]. The phenomenon of the increase in the splenic index observed in the present experiments was perhaps due to this mechanism. At the same time, considering that by the 25th day of the latent period cells specifically adsorbed on a monolayer of syngeneic embryonic fibroblasts appear in

the spleens of CBA mice, changes in the weight of the lymphoid organs observed in the present experiments can perhaps be explained by immunological mechanisms. This hypothesis is supported by certain features of the phenomenon observed, resembling the graft versus host reaction. As Tables 1 and 2 show, the increase in the splenic index was accompanied by a progressive decrease in the weight of the thymus; the sum of the indices of the thymus and spleen in these experiments, moreover, was constant [9]. The impression is gained that in this test system there is a "redistribution" of activities of the thymus and spleen.

The characteristic dynamics of the weight of the lymphoid organs observed in CBA mice when infected with oncogenic simian adenovirus during the first day of life (Table 2) was partly due, it seems, to a change in the activity of their spleen cells, for when these cells were transplanted into normal syngeneic newborn recipients similar results were observed: an increase in the splenic index accompanied by a progressive decrease in the index of the thymus. The discovery of cells specifically adsorbed on a monolayer of embryonic fibroblasts and also of cells capable, when transplanted into a syngeneic system, of inducing phenomena resembling the graft versus host reaction in newborn animals in the spleens of CBA mice infected with SA7 (C8) virus, indicates that even in the early stages of carcinogenesis an autoimmune response is formed, evidently by induction by the direct action of the virus on the immunocompetent system.

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MECHANISM OF THE INHIBITORY EFFECT OF BCG VACCINE ON SPECIFIC ANTITUMOR IMMUNITY IN SYRIAN HAMSTERS

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The duration of the inhibitory effect of BCG vaccine on antitumor immunity induced by SV 40 virus in Syrian hamsters and the possibility of restoring immunity after vaccination were investigated. Specific resistance in animals immunized with SV 40 virus and then inoculated with BCG remained inhibited for 1 year after vaccination. A further injection of SV 40 virus into hamsters previously subjected to combined immunization reinduced specific immunity in the animals to tumors. The results show that the phenomenon of abolition of specific antitumor resistance by BCG vaccine is probably cellular in nature.

KEY WORDS: BCG vaccine; SV 40 virus; antitumor resistance.

A role of increasing importance in experimental studies of immunoprophylaxis and immunotherapy of tumors by means of systemic adjuvants (BCG, etc.) is being played by tests of combined specific immunization and nonspecific immunostimulation. Investigations in the writer's laboratory have shown that injection of BCG

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