MORPHOLOGICAL ANALYSIS OF THE THYMUS AND LYMPH NODES DURING GROWTH OF A SYNGENEIC TRANSPLANTABLE HEMANGIOPERICYTOMA IN MICE

N. I. Koval'skaya and V. M. Bukhman

UDC 616-006.311-092.9-07:[616.438+616.428]-091

KEY WORDS: mice; hemangiopericytoma; morphometry; thymus; lymph nodes.

Interaction between tumor and host is a very important problem in modern oncology. The development of tumors of different genesis is accompanied by changes in lymphoid and hematopoietic tissues. For instance, disturbances of hematopoiesis, notably a leukemoid reaction, changes in the lymph nodes (LN), and thymus have been discovered and described [1, 2, 4-6, 8, 13-15]. Investigations on LN have been carried out mainly on clinical material without observation over a period of time, and the results are often highly contradictory [5, 9, 10, 12-15]. Accordingly determination of the more precise behavior of LN during growth of tumors appeared interesting. Previously, using a model of syngeneic transplantable hemangiopericytoma (HAPC), the development of a leukemoid reaction with erythroid hematopoiesis in the red pulp of the spleen and transient erythrocytosis in the blood, followed by anemia, was found in mice. In the present investigation a morphological and morphometric analysis was made of the thymus and of several LN in the course of development of HAPC in mice.

EXPERIMENTAL METHOD

Experiments were carried out on sexually mature male (CBA × C57BL/6j) F_1 mice weighing 24.0 ± 2.0 g, reared at the Stolbovaya Nursery, Academy of Medical Sciences of the USSR. The animals were divided into two groups: a syngeneic HAPC was transplanted subcutaneously into mice of group 1 in the dorsal region, whereas a suspension of spleen cells of syngeneic animals was injected subcutaneously into the mice of group 2 (control), in a dose of 5×10^6 cells per animal. The animals were killed 1, 2, 3, 7, 10, 14, and 17 days after transplantation of the HAPC (five mice at each time, total 70), and the tumor, thymus, axillary regional and contralateral regional LN, mesenteric LN, Peyer's Patches, liver, lungs, and kidney were removed. The tumor, thymus, and LN were weighed and all the material was fixed in Bouin's flud. Paraffin sections, cut to a thickness of 4 μ, were stained with azure II-eosin and with hematoxylin and eosin, and morphological and morphometric analysis was carried out. By means of an Avtandilov's grid the areas of the cortex and medulla of the thymus and the relative percentages of blast cells, mitotically dividing cells, cells in a state of pycnosis, and macrophages in the cortex and medulla and the number of Hassall's corpuscles in a certain area of the medulla were calculated. Activity of the B-dependent zone in LN, the number and degree of maturity of the germinative centers, the area of the medullary cords and the number of lymphocytes, blast cells, plasmablasts, and plasma cells in them, and also the intensity of delymphatization and the abundance of the T-dependent zone (the number and activity of postcapillary venules, the abundance of the specific cell reaction around them, and delymphatization) were assessed by a ranking method. The numerical results were subjected to statistical analysis, the significance of differences being determined by Student's t test at the $P < 0.05$ level.

EXPERIMENTAL RESULTS

Tumor growth was accompanied by a decrease in weight of the thymus and in the body weight (Fig. 1a, b), which was particularly marked on the 10th-14th day after transplantation of the HAPC. A decrease in the area of the cortex and some increase in the area of the thymus (inversion) were observed on the 14th-17th day

N. I. Pirogov Second Moscow Medical Institute. Research Institute for Biological Testing of Chemical Compounds, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR V. V. Kupriyanov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 94, No. 10, pp. 88-91, October, 1982. Original article submitted May 5, 1982.

 0007-4888/82/9410-1416$07.50

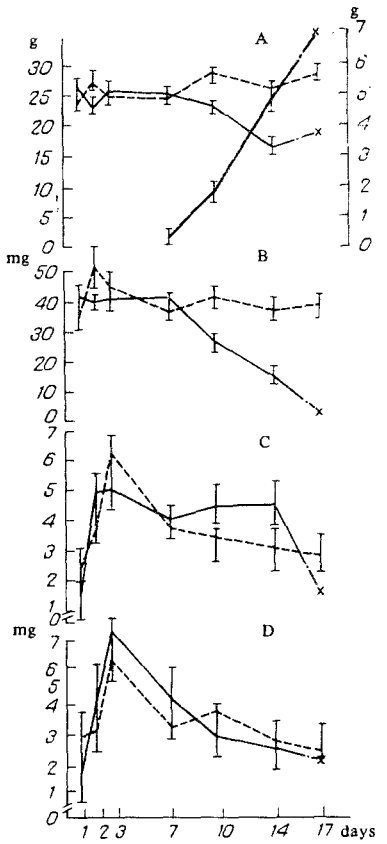

Fig. 1. Changes in body weight and weight of tumor (A), thymus (B), and regional (C) and contralateral regional (D) axillary LN associated with growth of HAPC. Abscissa, time after transplantation of tumor (in days); ordinate: A: on left) body weight, on right) weight of tumor (in g); B) weight of thymus (in mg); C) weight of regional axillary LN (in mg); D) weight of contralateral regional axillary LN (in mg). Continuous line – experiment; broken line – control. A cross indicates a single observation.

after transplantation of the HAPC and in some cases the boundary between cortex and medulla disappeared, so that the parenchyma of the thymus consisted of diffusely arranged lymphocytes with single blast cells and plasma cells. The number of blast cells, pycnotic cells, and mitoses fluctuated in the course of development of the HAPC during the first 3 days after transplantation, with a peak of the blast cells in the cortex and a sharp decrease in the frequency of pycnosis in them on the 2nd day. A sharp decrease in the number of mitoses and an increase in the number of cells with pycnosis were observed in the medulla on the 2nd day, followed by a sharp rise (to a peak) of both these parameters on the 3rd day. The number of macrophages and of Hassall's corpuscles in the thymus did not change significantly at any time during growth of the HAPC, and within each group there was considerable scatter of the values. No changes described above were observed in the control, but the wide scatter of the values also was a feature. During growth of the HAPC progressive atrophy of the thymus was thus observed, mainly on account of a decrease in area of the cortex, as was demonstrated previously in studies of other tumors [1, 2, 6, 11, 13, 15]. Evidently this atrophy of the thymus was nonspecific in character, for it has been observed in starvation [11], after injection of certain antigens [7], and in infectious diseases and stress [3]. The role of the thymus in the onset and development of tumors of different genesis is highly contradictory [2], and the causes of the atrophy observed in the organ are not clear. Atrophy of the thymus may perhaps be a response to lymphocytopenia in the blood and (or) the result of exhaustion of the proliferative activity of the organ in response to the action of substances secreted by the tumor, inhibition of certain components of the immune system, or endocrine imbalance in the course of tumor development [2, 3, 11, 15].

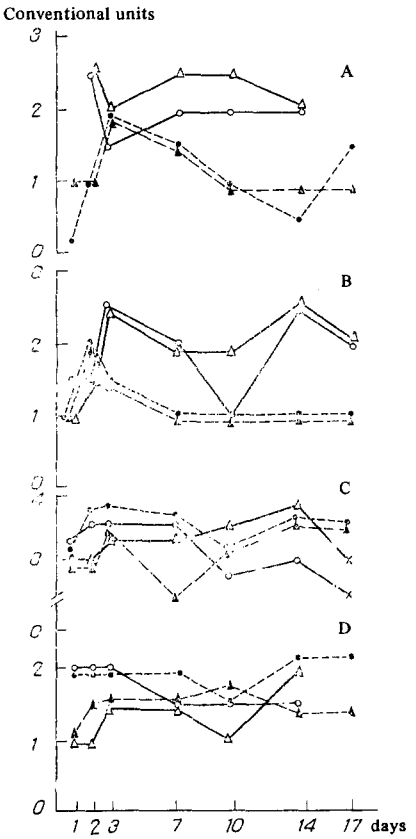

Fig. 2. Changes in activity of T- and B-dependent zones in LN associated with growth of HAPC. Abscissa, time after transplantation of tumor (in days); ordinate, activity (in conventional units) of B-dependent (circles) and T-dependent (triangles) zones in experiment (continuous line) and control (broken line). A) Regional ipsilateral LN, B) contralateral axillary LN, C) mesenteric LN, D) Peyer's patch. ×) One observation.

The weight of the regional axillary LN of the experimental mice was a little higher than in the control (Fig. 1C). On the 2nd day after transplantation of the HAPC the T- and B-dependent zones of LN were more active than in the control. On the 3rd day activity of both zones fell to the level of activity of the corresponding zones in the control, then increased until the 7th day, and remained at that level until the 14th day, much higher than the corresponding parameters in the control. Activity of the T-dependent zones was rather higher than activity of the B-dependent zones throughout growth of the HAPC (Fig. 2A).

In the contralateral regional axillary LN, the weight of which did not differ significantly from the weight of the control LN during development of the HAPC (Fig. 1D), activity of the T- and B-dependent zones exceeded that in the control, except on the 2nd and 10th days after transplantation of the HAPC (Fig. 2B). The ipsilateral and contralateral regional axillary LN thus exhibit activation of T- and B-dependent zones during growth of an HAPC. In remote LN (mesenteric LN and Peyer's patch) no signs either of activation or of exhaustion of T- and B-dependent zones could be observed compared with the control during development of the HAPC (Fig. 2C, D).

Neither tumor cells nor foci of ectopic hematopoiesis could be found in any of the LN studied.

No tumor cells were found in serial sections of the liver, kidneys, and lungs by histological analysis. Foci of granulocytic infiltration of different sizes were found in the lungs and, to a lesser degree, in the liver.

Data in the literature are concerned mainly with morphological and histochemical analysis of LN in cancer patients [5, 8, 10, 12]. Some correlation has been found between activity of different zones of LN and the prognosis of tumors: activation of T-dependent zones is observed in the absence of metastasization and in pa-

tients with a longer period of survival [5, 8, 14]; the state of the B-dependent zones and the discovery of sinus histiocytosis have been interpreted differently [5, 8, 10, 12]; weak activity or exhaustion of LN is regarded as a bad prognostic sign [8, 10]. The results confirm existing views on the connection between metastasization and activity of regional LN. Meanwhile absence of a response of the remote LN will be noted.

The results are evidence that growth of HAPC in mice is accompanied not only by a leukemoid response of myeloid type [4], but also by atrophy of the thymus, activation of T- and B-dependent zones in the regional ipsilateral and contralateral LN, with preservation of the usual structure of distant LN (mesenteric LN and Peyer's patch). Activation of LN may be connected with the immunologic response to the tumor or it may be a compensatory reaction to the developing lymphocytopenia in the blood and gradually increasing atrophy of the thymus.

LITERATURE CITED

1. N. I. Belyanchikova, G. I. Vornovitskaya, S. N. Khramkova, et al., Byull. Éksp. Biol. Med., No. 7, 476 (1981).
2. E. V. Gruntenko, Immunity and the Origin of Malignant Tumors [in Russian], Novosibirsk (1977).
3. Yu. I. Zimin, in: Progress in Science and Technology. Series: Immunology [in Russian], Vol. 8, Moscow (1979), pp. 173-198.
4. N. I. Koval'skaya, N. I. Belyanchikova, V. M. Bukhman, et al., Byull. Éksp. Biol. Med., No. 7, 82 (1981).
5. I. A. Kulaev and V. A. Kovalenko, Vopr. Onkol., No. 2, 9 (1981).
6. C. D. Baroni, L. Ruco, G. S. Franceschi, et al., Immunology, 31, 217 (1975).
7. C. D. Baroni, L. Ruco, G. S. Franceschi, et al., Immunology, 31, 217 (1975).
8. N. T. Berlinger and V. Tsakraklides, Cancer (Philadelphia), 37, 692 (1976).
9. M. H. Claesson and G. R. Johnson, Eur. J. Cancer, 14, 515 (1978).
10. G. Dobrescu and M. Barsu, Arch. Union Med. Balkan., 19, 18 (1981).
11. L. Efskind, T. Godal, T. Gude, et al., Cancer Immunol. Immunother., 3, 207 (1978).
12. P. Jaisa and A. Pasternak, Neoplasma, 28, 205 (1981).
13. M. Klobusicka, F. Kalafut, and L. Novotna, Neoplasma, 24, 583 (1977).
14. E. Pihl, R. C. Nairn, A. P. Nind, et al., Cancer, 36, 3665 (1976).
15. V. Toma and C. Stugren, Rev. Roum. Biol. Ser. Biol. Anim., 25, 55 (1980).

EFFECT OF GANGLIOSIDES SECRETED BY ASCITES HEPATOMA 22a CELLS ON INTENSITY OF PROTEIN SYNTHESIS IN THESE CELLS AND ON THEIR SENSITIVITY TO INDOCARB

G. I. Shaposhnikova, N. D. Zvezdina, L. A. Mal'chenko, N. A. Teplits, N. V. Prokazova, G. A. Buznikov, and L. D. Bergel'son

UDC 616.36-006-008.939.52:616.36-006-008.939.6-02:615.357:577.175.823

KEY WORDS: mouse ascites hepatoma 22a; gangliosides; indocarb; protein biosynthesis.

The important biological role of gangliosides is largely determined by their location on the cell surface. Cell recognition and cell adhesion, and the ability of normal cells to exhibit contact inhibition and the loss of this property during malignant transformation all depend on the ganglioside composition of membranes. The membrane receptor of Vibrio cholerae is a ganglioside; gangliosides of the cell surface participate in reception of other bacterial toxins, viruses, interferon, and peptide hormones [4]. There is evidence of the role of gangliosides in serotonin reception [2, 12].

Laboratory of Lipid Chemistry, M. M. Shemyakin Institute of Bioorganic Chemistry, Academy of Sciences of the USSR. Laboratory of Embryonic Physiology, N. K. Kol'tsov Institute of Developmental Biology, Academy of Sciences of the USSR, Moscow.

(Presented by Academician of the Academy of Medical Sciences of the USSR A. P. Avtsyn.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 94, No. 10, pp. 91-93, October, 1982. Original article submitted March 1, 1982.

0007-4888/82/9410-1419$07.50