
原 著

Growth of Yoshida Sarcoma in the Thymus

by

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INTRODUCTION

One of the most prominent features of the behavior of carcinomas is their great tendency to produce secondary growth in regional lymph nodes¹⁾. They appear to have found a comfortable home in the nodes and enjoy there an abundance of nutrients for growth; lymphoid tissue containing carcinoma cells may function as a feeder for cancer cells²⁾.

There are published many reports on susceptibility of the spleen, liver, kidney and muscle to transplanted tumor³⁾, but none allows a comparison of tumor growth in the thymus with that in other organs.

In the present study, the thymus was chosen as one of the lymphatic apparatuses, since 92% of the cells composing the thymus tissue are considered to be lymphocytes⁴⁾. The present paper will deal with susceptibility of the thymus to YOSHIDA sarcoma cells comparing with other tissues or organs.

MATERIALS AND METHODS

The animals used were male Donryu rats, aged 30 days, weighing 45 to 55 g. They were supplied commercially and fed ad libitum on water and stock diet MF, manufactured by Oriental Kobo Co.

Ascites tumor cells of YOSHIDA sarcoma were obtained through the courtesy of the laboratory of TAKEDA Chemical Co., Osaka, and maintained in our laboratory by successive inoculation into the abdominal cavity of Donryu rats. Prior to each experiment, ascites cells were withdrawn from the rats' peritoneal cavity 4 to 5 days after transplantation and the cell suspension was prepared so as to contain 10,000 cells in an aliquot of 1 μ l of TYRODE solution.

The thymus of Donryu rats was exposed under ether anesthesia through a upper median sternal incision and 1 μ l of the cell suspension was injected into the thymus, using a microsyringe.

For the comparison of susceptibility to tumor, the subcutaneous tissue, liver, spleen and peritoneal cavity were chosen and transplanted with an equal number of cells. In the case of the liver and spleen, Aron Alpha, Sankyo Pharmaceutical Co., was applied to the needle hole after injection to prevent leakage of inoculated cells into the peritoneal cavity.

"Take" of tumor was determined by visible growth of tumor in the organs except for the liver in which tumor mass was not clearly recognized but change of color disclosed proliferation of tumor cells in the region of transplantation.

RESULTS

1. YOSHIDA Sarcoma Tumor in the Thymus:

YOSHIDA sarcoma cells proliferated in the thymus and became visible as a mass on the 4th day after transplantation, involving the whole thymus by the 9th day and resulting in death of the animals. Necropsy showed an enlarged thymus being replaced wholly by YOSHIDA sarcoma cells, which extended as far as the aorta and trachea (Plate 1).

Microscopic observation of specimens on the 7th day after transplantation showed that YOSHIDA sarcoma invaded a wide area of the thymus, replacing normal tissue cells with tumor cells. At the margin of tumor mass sarcoma cells seemed to have phagocytized thymocytes, because some of the tumor cells contained, in their cytoplasm, fragments stained by



Plate 1 On the 7th day after implantation. Tumor involves about 80% of the thymus. The intact area is seen only in the right inferior lobe. Arrows show the border between tumor and intact region.

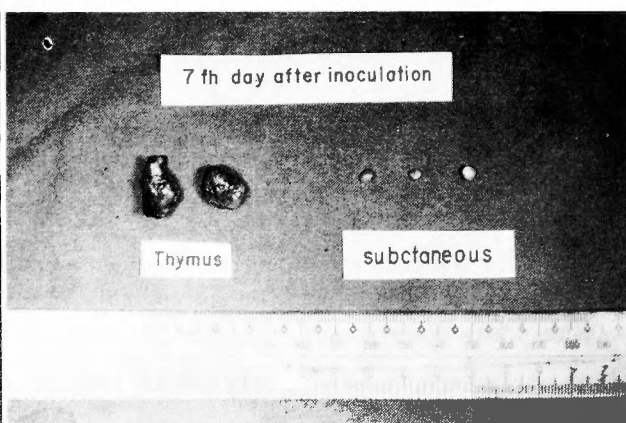


Plate 2 On the 7th day after implantation. Tumors excised from the thymus are considerably larger than those from the subcutaneous tissue.

hematoxylin which were considered to have been derived from nuclei of destroyed thymocytes (Plates 3 and 4).

2. Relative Susceptibility of the Thymus to Tumor Implantation:

YOSHIDA sarcoma cells were implanted into the thymus, subcutaneous tissue, spleen, liver and peritoneal cavity, and incidence of "Take" and growth of

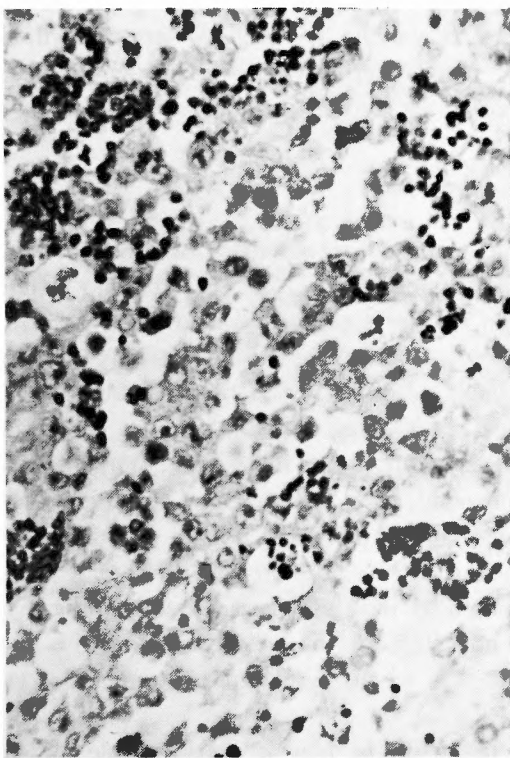


Plate 3 Yoshida sarcoma cells are seen infiltrating into the thymus tissue. Pyknotic thymocytes remain like islands. Hematoxylin and eosin, $\times 600$.

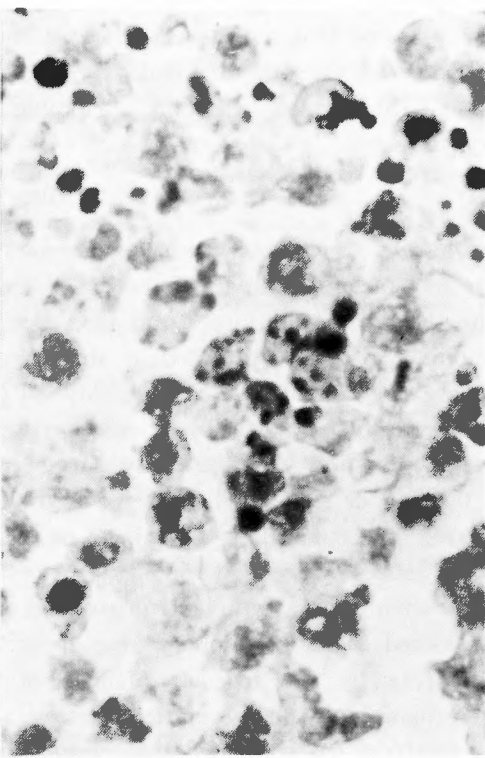


Plate 4 Yoshida sarcoma cells, possibly phagocytizing thymocytes ; some of the sarcoma cells are seen to contain fragments which are thought to be derived from the nuclei of destroyed thymocytes. Hematoxylin and eosin, $\times 1,500$.

tumor in these organs of tissues were compared with those in the thymus on the 7th day after implantation. The data are indicated in Table 1 and 2. It can be seen in the tables that the thymus group showed higher incidence of "Take" and larger size of tumor than the other organs. In the organs mentioned above, except for the thymus, incidence of "Take" and size of tumor were nearly equal on the 7th day after implantation, and the inoculated tumor cells grew at almost the same rate.

Further observation of the subcutaneous

Table 1 Incidence of "Take" of Y.S. tumor on the 7th day after implantation

Organ and tissue	Incidence of "Take"	%
Thymus	14/14	100
Subcutaneous tissue	24/48	50
Spleen	7/16	44
Liver	3/10	30
Peritoneal cavity	6/11	55

Table 2 Average size and weight on the 7th day after implantation

Organ and tissue	Number of animals	Average size of tumor (mm ³)	Average weight of tumor (mg)
Thymus	5	2169	561
Subcutaneous tissue	11	136	32
Spleen	7	161	
Liver	3	110	

Size : (Length $\times$ Width)³/₂.*
* Chambers, H., Scott, G. M. : J. Pathol. Bacterol.,
33 : 553, 1932.

group indicated that the size of these tumors on the 9th day was as large as those in the thymus on the 5th to 6th day when the mass became visible (Plate 2). This suggests that the thymus was more favorable place for growth of the tumor than the subcutaneous tissue.

DISCUSSION

DELONG and COMAN³⁾ have provided evidence of equal susceptibility of the rat to tumor transplantation in the muscle, kidney, liver and spleen. They found no difference among the weights of tumor and incidence of "Take" when fragments of WALKER rat carcinoma 256 were implanted in those organs. The results of the present experiment, however, suggest higher susceptibility of the thymus to tumor transplantation than the subcutaneous tissue, spleen, liver and peritoneal cavity, i.e., the tumor grew more rapidly in the thymus and were generally larger in size than those in the other organs. What does this higher susceptibility of the thymus depend on? Existence of a certain growth-promoting substance like Promine⁹⁾ or absence of immune reaction in the thymus have been suggested by some workers¹⁰⁾. Attention, however, should be directed to the fact that the thymus is a lymphoid organ and composed mostly of lymphocytes. The thymus is considered to be a lymphocyte producer⁷⁾ and 92% of the cells composing the thymus are lymphocytes⁴⁾. Particular affinity of tumors to the lymphatic apparatus has tacitly been recognized by many investigators⁸⁾¹¹⁾.

LEIGHTON has suggested that lymphatic tissue might play a nutritive role for secondary growth of tumor as a feeding trough; biological interaction and passage of nutritive material like DNA have been observed experimentally between thymocytes or lymphocytes and other cells¹⁾²⁾⁶⁾.

FISHER and FISHER⁵⁾, in an electron microscopic study of hepatic metastases of WALKER tumor, have revealed that tumor cells, possibly by a pinocytic mechanism, received various nutrients directly from the host's hepatic cells. Microscopic appearance of YOSHIDA sarcoma cells in the margin of the tumor mass suggested the same mechanism might be operating also in the present case.

SUMMARY

YOSHIDA sarcoma cells were implanted into the rat thymus and other tissues, and the growth of tumor was observed for the purpose of comparing tissue susceptibility.

The thymus was more susceptible to implantation of YOSHIDA sarcoma as well as more favorable for growth of the tumor than the subcutaneous tissue, liver, spleen and peritoneal cavity.

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REFERENCES

- 1) Aoyama, T. : The modification effect of cellular interaction on the radiation sensitivity of rat thymocytes. Proc. Intern. Conf. Radiation Biology and Cancer, Kyoto, Japan, 135, 1966.
- 2) Bryant, B. J. : Reutilization of leukocyte DNA by cells of regenerating liver. Exptl. Cell Res., **27** : 70, 1962.
- 3) DeLong, R. P. and Coman, D. R. Relative susceptibility of various organs to tumor transplantation. Cancer Res., **10** : 513, 1950.
- 4) Dixon, F. J., Weigle, W. C. and Roberts, J. C. : Comparison of antibody responses associated with the transfer of rabbit lymph-node, peritoneal exudate, and thymus cells. J. Immunol., **78** : 56, 1957.
- 5) Fisher, E. R. and Fisher, B. : Host influence on tumor growth and dissemination. In : Biological Basis of Radiation Therapy, edited by Schwartz F. E., Lippincott Co., Philadelphia and Tronto, 1966.
- 6) Humble, J. G., Jayne, W. H. W. and Pulvertaft, R. J. V. : Biological interaction between lymphocytes and other cells. Brit. J. Haematol., **2** : 283, 1956.
- 7) Kindred, J. E. : A quantitative study of the hemopoietic organs of young albino rats. Am. J. Anat., **67** : 99, 1940.
- 8) Leighton, J. : Spread of Cancer. Academic Press Inc., New York and London, 1967.
- 9) Szent-Gyorgyi, A., Hegyeli, A. and McLaughlin, J. A. : Cancer therapy : A possible new approach. Science, **140** : 1391, 1963.
- 10) Thorbecke, G. J. and Keuning, F. J. : Antibody formation in vitro by haemopoietic organs after subcutaneous and intravenous immunization. J. Immunol., **70** : 129, 1953.
- 11) Willis, R. A. : The Spread of Tumors in the Human Body. Butterworths Co. Ltd., London, 1952.
- 12) Yoshida, T. : Yoshida Nikusyu (Yoshida Sarcoma). Nara Shobo, Tokyo, 1965.

和文抄録

胸腺における吉田肉腫の増殖について

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吉田肉腫細胞 1 万個を呑竜ラットの胸腺に移殖し、胸腺における腫瘍の増殖状態を調べた。これは胸腺がリンパ球の造成器官であり胸腺細胞が大部分リンパ球であるといわれているところから、腫瘍細胞のリンパ組織での増殖を観察するためである。

胸腺内に移植された吉田肉腫細胞は、移植後 4 日目より肉眼的腫瘍の形成がみられ、9 日目には全胸腺組織が腫瘍に置換されて動物は死亡する。

次に腫瘍細胞移植に対する胸腺の感受性を他の組織の場合と比較するため、胸腺の他に皮下、肝臓、脾

臓、腹腔内に同じように 1 万個の吉田肉腫細胞を移植し、移植 7 日目における腫瘍の“Take”とその腫瘍の大きさを比較観察した。その結果、胸腺以外の組織での腫瘍“Take”は 50% であるのに対し、胸腺でのそれは 100% であり、また現われた腫瘍の大きさも胸腺の場合の方がはるかに大きかった。このことから、胸腺は他の組織に比し、腫瘍細胞移植に対し、はるかに感受性が高く、したがって腫瘍細胞に好増殖地を提供していることがわかった。