Host Resistance against Cancer after Removal of Primary Tumor

by

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Unexpectedly early recurrence or metastasis in the cases of seemingly early operation and fairly long survival or sometimes spontaneous cure in the cases of mere palliative operation have been observed, which has given strange impression to clinicians.

The fact that there can be observed marked fluctuation in the course of tumor arising in a organism can be better explained by possible fluctuation of host resistance than to conceive some alteration in malignancy of the tumor itself. Recently, cancer has come to be investigated under the concept of host-tumor relationship. We also have studied this problem based upon several experiments and clinical experiences.

MATERIALS AND METHODS

1. Experimental animal and experimental tumor: Albino rats of random bred Gifu-strain weighing 100 to 150 gr. were used. Ascites hepatoma AH 130 or Sarcoma Yoshida (from Sasaki Institute, Tokyo) of approximately $5 \times 10^6$ cells was implanted subcutaneously in the back or foot-back.

All the animals died of progressive tumor development when the ascites hepatoma AH 130 reached $6 \times 7 \times 8$ mm. in the foot and 10 mm. of diameter in the back within 10 days. In Sarcoma Yoshida, more rapid development was observed.

2. New congo-red index: Concentration of congo-red in serum of 4 minutes after the injection/Concentration of congo-red in serum of 60 minutes after the injection (Adler-Reimann-Sugiyama), and splenic uptake of colloidal radiogold (Stern and Duwellus).

3. Cytotoxic activity of the serum: O'Gorman's method was followed. Well rinsed tumor cells were suspended in a cell density of 30000/mm³ in serum of normal rats diluted to 5 times with Ringer's solution. A series of successive double dilution of the serum to be investigated was prepared with the same solution, which was then mixed with dilution of complement of guinea pig and incubated for an hour at 37°C. Trypan blue-Tyrode solution of 0.05% was then added to the mixture. After several minutes' staining, cell count of stained cells was performed, which was represented in the term of percentage.

4. Phoretic study of serum protein: Paper electrophoresis was performed.

5. Tanned cell hemagglutination: The antigen for coating tanned cells was prepared following the method of Zilber and his associates. Namely, homogenate of human cancer tissue was subjected to extraction for an hour with water of pH 7.6 in a freezer. Supernatant was adjusted to pH 6.0 and its precipitant was discarded.
was again adjusted to pH 4.0 and its precipitant was dried in a desiccator. Saline solution of 0.015 to 0.02% of the substance was used.

6. Microscopic preparation: Materials were embedded in paraffin and stained doubly with hematoxylin and eosin.

RESULTS

Experiment 1. Reticuloendothelial function of tumor-bearing animals. Reticuloendothelial function was examined with new congo-red index in subcutaneous inoculation of ascites hepatoma AH 130 in the back of the animals (Tab. 1). Utmost hyperactivity of reticuloendothelial function was observed 8 to 10 days after the inoculation, which gradually fell thereafter until final death of the animals. In other words, reticuloendothelial function is activated in relatively early period of tumor growth, and it is lowered in paralell with development of the tumor thereafter.

Table 1  Reticuloendothelial Function of Tumor-bearing Rats  
(Subcutaneous Inoculation of Ascites Hepatoma AH 130)

<table>
<thead>
<tr>
<th>Time of slaughter</th>
<th>No. of case</th>
<th>No. of metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 days after inoculation</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>7 days after inoculation</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>9 days after inoculation</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>10 days after inoculation</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>12 days after inoculation</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

Experiment 2. Period of metastasis establishment in the regional lymphnodes. In subcutaneous inoculation of ascites hepatoma AH 130 in the back of the foot, it was 10 days after the inoculation that metastasis in the regional lymphnodes was observed constantly (Tab. 2), while in the inoculation of Sarcoma Yoshida, it was 4 days after the inoculation (Tab. 3).

Table 2  Time of Regional Node Metastasis  
(Inoculation of Ascites Hepatoma AH 130 in the Back of the Foot)

<table>
<thead>
<tr>
<th>Time of slaughter</th>
<th>No. of case</th>
<th>No. of metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 days after inoculation</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>1 days after inoculation</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>5 days after inoculation</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

Experiment 3. Behavior of metastasized regional lymphnodes after the excision of primary growth. As metastasis in the above, initial metastasis in the regional lymphnodes was constantly observed 10 days after the inoculation of ascites hepatoma AH 130, which, at the same time, corresponds to the period of utmost hyperactivity of reticuloendothelial function. The primary tumor was removed at this stage and the behavior of metastasized
lymphnodes was pursued thereafter (Chart 1). Regression of metastatic tumor was observed in amazingly high percentage as 25%, histological study of which revealed a characteristic appearance, that is, tumor cells were surrounded by newly appearing reticulum cells (Fig. 1) and finally the former was displaced with the latter (Fig. 2), whereas in control animals no reactive finding was observed, allowing progressive growth of tumor cells (Fig. 3). The regression occurred in 9.5% (2/21) when the primary tumor was removed 13 days after the inoculation, what was more, these 2 cases of regression were those of retarded development of the primary tumor.

In the similar experiment using Sarcoma Yoshida, if the primary tumor was removed 4 days after the inoculation, when the initial metastasis was observed constantly in the regional lymphnodes, regression of the metastasized lymphnodes occurred in 20.7%. If the excision was performed 6 days after the inoculation, all the animals died of tumor growth, showing no regression of the metastatic tumor (Chart 2).

Experiment 4: Cytotoxic activity of the serum after the excision of the primary tumor and its fraction. When the primary tumor was removed 10 days after subcutaneous inoculation of ascites hepatoma AH 130 in the back, cytotoxic activity showed higher value and maintained for long in the group of regression in metastatic tumor which then restored to normal as it regressed further, whereas, in control animals and in the animals died of overwhelming growth of metastatic tumor despite the excision of the primary tumor, the activity remained within normal range until the death (Chart 3).

Phoretic study of the serum revealed an increase in gammaglobulin in the former serum, and this increase had a close correlation between cytotoxic activity (Chart 4).

Experiment 5: Change in antibody titer in tanned cell hemagglutination of human serum after excision of the primary tumor. In most of cancer patients, antibody could
Chart 3
Cytotoxic Activity of Serum after Removal of Primary Tumor (Subcutaneous inoculation of ascites hepatoma AH 130 in the back. Mean value.) Solid line represent animals showed regression, broken line animals died of tumor. Normal range (0 to 3.2%).

not be detected or, if any, showed only low titer in the serum by the use of tanned cell hemagglutination with coating of extract from autochthonous tumor. However, in some cases of relatively favorable prognosis, elevation of antibody titer was sometimes observed after the operation, among which the antibody could be detected to be more than 1000 times dilution (Tab. 4).

Table 4 Tanned Cell Hemagglutination

<table>
<thead>
<tr>
<th>Degree of cancer development*</th>
<th>Postoperative course**</th>
<th>Before operation</th>
<th>After operation***</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1st wk.</td>
<td>2nd wk.</td>
</tr>
<tr>
<td>IV</td>
<td>death</td>
<td>5</td>
<td>45</td>
</tr>
<tr>
<td>IV</td>
<td>death</td>
<td>45</td>
<td>0</td>
</tr>
<tr>
<td>IV</td>
<td>death</td>
<td>0</td>
<td>45</td>
</tr>
<tr>
<td>III</td>
<td>death</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>III</td>
<td>favorable</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>II</td>
<td>favorable</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>II</td>
<td>favorable</td>
<td>45</td>
<td>405</td>
</tr>
<tr>
<td>I</td>
<td>favorable</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>III</td>
<td>unknown</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>II</td>
<td>unknown</td>
<td>0</td>
<td>15</td>
</tr>
<tr>
<td>II</td>
<td>unknown</td>
<td>15</td>
<td>5</td>
</tr>
</tbody>
</table>

* Bill of J. S. S. to indicate degree of tumor development.
** Prognosis within 2 years after operation.
*** Numbers indicate dilution of serum. All cases treated here are stomach cancer

Experiment 6.: Reticuloendothelial function of cancer patient. R. E. S. activity in cancer patient, examined by congo-red test, showed hypofunction as is easily presumed.
There was, however, some cases which showed almost normal level (Tab. 5).

### Table 5 New Congo-Red Index in Stomach Cancer

<table>
<thead>
<tr>
<th>Degree of cancer development*</th>
<th>New congo-red index</th>
<th>Control</th>
<th>New congo-red index</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>1.44</td>
<td>Appendicitis</td>
<td>1.41</td>
</tr>
<tr>
<td>IV</td>
<td>1.48</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>1.34</td>
<td></td>
<td>1.32</td>
</tr>
<tr>
<td>IV</td>
<td>1.32</td>
<td></td>
<td>1.47</td>
</tr>
<tr>
<td>IV</td>
<td>1.18</td>
<td></td>
<td>1.42</td>
</tr>
<tr>
<td>III</td>
<td>1.28</td>
<td>Cholelithiasis</td>
<td>1.31</td>
</tr>
<tr>
<td>III</td>
<td>1.14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>1.45</td>
<td></td>
<td>1.31</td>
</tr>
<tr>
<td>II</td>
<td>1.39</td>
<td>Gastritis</td>
<td>1.58</td>
</tr>
<tr>
<td>II</td>
<td>1.39</td>
<td></td>
<td>1.13</td>
</tr>
<tr>
<td>II</td>
<td>1.25</td>
<td></td>
<td>1.39</td>
</tr>
<tr>
<td>II</td>
<td>1.21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>1.19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>1.31</td>
<td>Mean</td>
<td>1.37</td>
</tr>
</tbody>
</table>

* Degree of cancer development is shown similarly to Table 4.

Experiment 7: Lymphnode reaction in cancer patient. The regional lymphnode and the mesenteric lymphnode, which is considered to react well at intraabdominal change, although this cannot be assumed to be regional ones in patients of stomach cancer, were studied histologically. Early death could be observed even in cases in which active lymphatic reaction was demonstrated in the non-metastasized regional lymphnodes (Fig. 4), leading us to the disapproval of the assertion of Black. On the other hand, prognosis seemed to be worse in the cases in which the reaction had spread as far as the mesenteric nodes any way (Tab. 6), while prognosis seemed to be favorable in the cases in which lymphatic structure was preserved relatively intact in the mesenteric nodes.

Case report: Reduction of general resistance and tumor growth. A 54 year old man had a cancer of the size of child's head in lesser curvature of the stomach, at the same time having 2 small metastatic foci in the left lobe of the liver and metastasis in the mesocolon of the transverse colon. He received total gastrectomy, left lobectomy of the liver and resection of the transverse colon. Mitomycin C of 48 mg. in all was administered pre- and postoperatively. One week after the final injection of Mitomycin C (32th post-operative day), epistaxis was observed. Platelet count was 13700. Petechia appeared gradually all over the body (Fig. 5). Prednisolone was at once administered 20 mg. for 3 days, 10 mg. for 3 days and 5 mg. thereafter everyday. At the same time amino acid preparation and fresh blood was administered intravenously. Platelet count increased to 30000 after 1 week, 70000 after 2 weeks and petechia formation ceased. Then a tumor became palpable in the right hypochondric region, which was not observed at laparotomy, and enlarged progressively. Although more 1 week later platelet count became 100000, the tumor enlarged as large as child's head and the patient was driven to cachexy. He died 56 days after the operation.
Table 6 Lymphnode Reaction in Postoperative Early Death (Stomach Cancer)

<table>
<thead>
<tr>
<th>Degree of cancer development*</th>
<th>Interval between opt. and death</th>
<th>Lymphnode reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>3 month</td>
<td>Reticulosi**</td>
</tr>
<tr>
<td>III</td>
<td>5 month</td>
<td>Metastasi**</td>
</tr>
<tr>
<td>II</td>
<td>3 month</td>
<td>Reticulosi</td>
</tr>
<tr>
<td>I</td>
<td>1 month</td>
<td>Metastasi**</td>
</tr>
<tr>
<td>IV</td>
<td>2 month</td>
<td>Reticulosi</td>
</tr>
<tr>
<td>IV</td>
<td>5 month</td>
<td>Metastasi**</td>
</tr>
<tr>
<td>IV</td>
<td>2 month</td>
<td>Reticulosi</td>
</tr>
<tr>
<td>IV</td>
<td>7 month</td>
<td>Metastasi**</td>
</tr>
<tr>
<td>IV</td>
<td>14 month</td>
<td>Reticulosi</td>
</tr>
</tbody>
</table>

* Degree of cancer development is shown similarly to Tab. 4, 5.
** Metastasi means that metastasi was found in all the lymphnodes that could be studied.

Experiment 8: An attempt to activate R. E. S. of tumor-bearing animals. The spleen was extirpated from tumor-bearing rats subcutaneously inoculated in the back with ascites hepatoma AH 130 at the period of reticuloendothelial hyperfunction. The spleen was homogenized and injected in the other tumor-bearing rats. Hereupon, regression of the tumor was observed in considerable frequency (Tab. 7). By the way, it was ascertained by cytotoxic activity test that the homogenate itself had no immediate effect upon tumor cells.

Table 7 Inhibitory Effect of Spleen Homogenate
(Subcutaneous Inoculation of Ascites Hepatoma AH 130)

<table>
<thead>
<tr>
<th>Experimental group</th>
<th>No. of inoculation</th>
<th>No. of take</th>
<th>No. of no take</th>
<th>No. of death</th>
<th>No. of regression</th>
<th>Rate of regression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>54</td>
<td>44</td>
<td>10</td>
<td>34</td>
<td>10</td>
<td>22.7%</td>
</tr>
<tr>
<td>Injection of spleen homogenate from normal animals</td>
<td>54</td>
<td>44</td>
<td>10</td>
<td>35</td>
<td>9</td>
<td>20.4%</td>
</tr>
<tr>
<td>Injection of spleen homogenate from tumor-bearing animals</td>
<td>54</td>
<td>38</td>
<td>16</td>
<td>9</td>
<td>29</td>
<td>76.3%</td>
</tr>
</tbody>
</table>

DISCUSSION

Recently Old reported based on his studies on reticuloendothelial function of tumor-bearing animals that reticuloendothelial function is most activated at the time when the inoculum becomes slightly palpable and the same tendency was observed in artificially induced tumor as well as in spontaneous primary one. In our Experiment 1 and 2 also, reticuloendothelial function was most heightened 8 to 10 days after the inoculation when the early metastasis was observed in the regional lymphnodes, and the function declined gradually thereafter. When the primary tumor was, however, removed in the stadium of
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utmost hyperfunction of the R. E. S., regression was observed in metastasized lymphnodes in considerable frequency, as was seen in Experiment 3.

It has long been assumed that operative aggression enhances the development of residual tumor cells and this is frequently ascertained by clinical experiences that abrupt development of the tumor was seemingly caused by exploratory laparotomy. On the other hand, it is difficult to assume that microscopically viable tumor cells or small metastasis did not remain in all of more than 30% of 5 year survivors of gastrectomized cancer patients. In fact KALLENBACH pointed out according to the findings of autopsy performed within 6 postoperative weeks that tumor cells were left in 1/2 to 1/3 of cases, which were radically operated on and died of some other causes. And there are also many investigators reporting spontaneous regression of human cancer. The findings of our Experiment 3 can be interpreted to be demonstrating a possibility of regression of metastatic tumors, which might be caused by excision of the primary tumor in the stadium of utmost hyperactivity of R. E. S., with resulting predominance of host resistances to residual tumor cells. This was also ascertained, as seen in Experiment 4, by higher and longer lasting serum cytotoxic activity in the group of regression compared with that of normal range in control group, suggesting a favorable influence of removal of the primary tumor on the host.

As has been discussed by SOUTHam, among serological factors in cancer immunity, there exist some factors in the serum of cancer patients deemed to be non-specific, such as inhibitory effect upon tumor cells or lowering of properdin level, as emphasized recently, which can be also seen in the serum of normal man. It is difficult to presume an establishment of immunity against malignant tumor from the concept of “antigen loss” of GREEN. However, it would be of utmost importance to take a concept of postnatal appearance of antigenicity into account, when one intends to interpret a series of autoimmune diseases, recently studied deliberately by WITEBSKY, by the aid of clonal selection theory of BURNET. Hence, presence or absence of specific antibody against tumor is an important problem in association to that of antigenicity of tumor. In fact, there are not a few investigators who ascertained the existence of specific antigenicity and antibody in tumor.

HSU reported that no particular effect could be observed in serum, even in cases in which the resistance could be improved by vaccination. GRACE studied intradermal allergic reaction, using an extract of autochthonous tumor. GRAHAM found antibody in serum by means of complement fixation test against extract of autochthonous tumor.

FINNEY successfully detected antibody against an extract of autochthonous tumor, using tanned cell hemagglutination. He put emphasis upon nuclear fraction in cancer and microsome fraction in sarcoma as the antigen.

It is considered difficult to demonstrate antibodies against tumor, because of its extraordinarily small amount, if any. It is not, however, impossible to assume that demonstration of the antibodies becomes feasible, when the equilibrium is altered and the amount of antibodies comes to surpass that of the antigen by excision of the tumor.

Hereupon, antibodies were detected in serum of cancer patients before and after the removal of the tumor, using tanned cell hemagglutination, which has been employed fre-
quently to demonstrate antibodies in autoimmune diseases because of its subtle sensitivity. There were observed some cases which showed elevation of antibody titer after operation, among those cases of relatively favorable prognosis. In some cases, particularly, antibodies could be demonstrated in the dilution of more than 1000 times postoperatively. These findings roughly come to accordance with those in experiments in animals. Furthermore, the existence of incomplete antibodies against extract of autochthonous tumor in serum have been detected by the authors, using Coombs serum after the SINDO's method as in tuberculosis. This has been impossible up to present.

Even though the time of operation can be decided according to the utmost hyperactivity of R. E. S. in experimental tumor, it is very difficult to expect much from operation in human cancer, when the development of cancer has come to impair reticuloendothelial function of the host. According to the findings of our reticuloendothelial function test in cancer patients (Experiment 6), in considerable number of cases reticuloendothelial function remained in normal range, although there were naturally some cases of hypofunction. It is a matter of fact that favorable prognosis cannot be expected merely from almost normal reticuloendothelial function. However, there is a considerable difference in host resistance regardless of the degree of tumor development revealed at surgery.

Concerning the cases of breast cancer, BLACK reported that prognosis was favorable in those without metastasis in regional lymphnodes and at the same time revealing an appearance principally consisted of sinus histiocytosis, whereas prognosis was unfavorable in those showing degenerative picture. MOORE, BERG and others disapproved of this observation and BERG, IMAI and others attributed significance to stromal reaction of the tumor. Our study of regional lymphnodes in stomach cancer revealed that such reaction was markedly observed in non-metastasized lymphnodes adjoining to the nodes filled with tumor cells. Furthermore, among such cases early death was observed. These findings disagree with the opinion of BLACK. On the other hand, prognosis was favorable in cases in which normal structure was maintained in further distant mesenteric nodes, while prognosis was unfavorable in cases in which metastasis or degenerative picture was observed in these nodes. From these findings, it might be said that prognosis is unfavorable when some changes are to be found in slightly distant nodes, suggesting some sort of invasion of the tumor to the nodes since cancer has become a disease of generalized nature. When the lymphnodes maintain their almost normal structure, there are many cases of favorable postoperative prognosis, which is presumably due to the fact that at this stage cancer remains to be a localized disease.

However, prognosis of cancer brought about by surgery is not favorable and chemotherapy or radiotherapy cannot be deemed to be effective. On the other hand, it has been said that removal of precancerous lesion does not always prevent the occurrence of cancer.

KONDO pointed out a possibility of chemotherapy to decrease host resistance and gave a warning as "adverse effect". There are also many researchers who insist that cortisone or irradiation enhances the development of tumor, weakening the host resistance. As has already been shown in the case report, we have experienced some unpleasant cases which showed rapid growth of tumor presumably caused by disturbance of host resistance. From these considerations, it is strongly suggested that it must be ex-
tremely hazardous to treat cancer without the concept of host resistance.

Buinauskas⁶, Murray³³ and others observed effectiveness of immune serum in cancer treatment obtained from animals immunized with human cancer. Graham²¹ attempted vaccination. Stone⁴⁴ reported that reimplantation of tumor cells treated in low temperature was effective, Ishibashi²⁷ made studies to establish immunity by implantation of autochthonous tumor at a site distant from original site.

Mizukami²⁹ attributed significance to activation of R. E. S. by ligation of the splenic artery. In short, there have been many attempts to promote host resistance regardless of direct or indirect.

Borrel⁶, Biach⁴ and others were, since early days, interested in anti-tumoral character of the spleen, and Braunstein⁸ made further studies systematically on this problem. From such a concept, we have also made Exp. 8, and ascertained that spleen homogenate prepared from tumor-bearing animal of the utmost hyperactivity of R. E. S. has an effect to hinder the growth of tumor, markedly activating reticuloendothelial function of other tumor-bearing animals. Participation of the spleen is not so large in the adults as in experimental animals³³. However, such a marked antitumoral effect of homogenate of the spleen which represents the R. E. S. of animals suggests a new approach to improve the results of cancer surgery at later stadium.

SUMMARY

In recent years, there is a tendency to investigate cancer under the concept of Host-tumor relationship. We have also made a series of experiments from a standpoint of reticuloendothelial function of hosts, and have demonstrated that eventual regression can be observed in metastatic lesion in the residual lymphnodes when the primary tumor experimentally produced is removed at a certain stage of the tumor growth.

Moreover, in human cancer, even if the primary tumor is adequately removed, immediate recurrence can be seen, especially when the host resistance is weakened. The importance of host resistance and its activation in the treatment of cancer is emphasized in this paper.

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23) Grosse, H. Schütz. die Operative Entfernung der Prakanzerose Tats
Fig. 1
Metastasis in Regional Lymphnode (Subcutaneous inoculation of ascites hepatoma AH 130 in the back of the foot). In animals showed regression after removal of primary tumor (1).

Fig. 2
Metastasis in Regional Lymphnode (Subcutaneous inoculation of ascites hepatoma AH 130 in the back of the foot). In animals showed regression after removal of primary tumor (2).
Fig. 3
Metastasis in Regional Lymphnode: Subcutaneous inoculation of ascites hepatoma AH 130 in the back of the front. Non-treated group.

Fig. 4
Case of Active Regional Lymphnode Reaction: 63 year old man, having a symptom in the upper abdomen since 1 month. Operated on as stomach cancer. Although active lymphnode reaction was seen in non-metastasized lymphnodes in excised material, prognosis was unfavorable and died within 5 month after surgery.

Fig. 5
Case Report: 51 year old man, revealing hemorrhagic tendency 1 week after pre-and postoperative administration of Mitoxantrone of 48 mg. for stomach cancer in greater curvature.
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和文抄録

主病巣切除後の担癌宿主の抵抗性

金沢大学医学部第2外科教室

水本 龍二・木庄 一夫

臨床的に早期手術が施行出来たと思われる症例に，
予想外の早期の再発転移を認めたり，末期症例で姑息
的手術に止まった症例にかなりの長期生存，時には
自然治癒を思わせる症例が経験されて，臨床家に奇異
の感を抱かしめることがある。

或る個体に発生した癌の発育や経過に動揺があるこ
とはその癌自体の悪性度が変化したと考えるよりも宿
主たる生体側の抵抗性に変動があったためと考えざる
を得ない。最近かかる見地からHost-tumor relationship
なる立場で癌を検討しない傾向があり，われわれも
2〜3の実験や臨床成績から検討を加えて見た。

1）先づ腹水肝癌 AH 130 及び吉田肉膿を用いて，
初期転移の起こったと思われる時期に主癌巣のみを切除
して，以後の転移巣の動向につき検査した。即ち腹水
肝癌 AH130 をラットの足背に皮下に移植すると，
癌巣は局所に発育するのみならず，移植後10日目に
は，全例，領域リンパ節にも転移を形成して結局腫瘍死
する。この担癌動物の網内系機能を新コンゴロート係数
及び 188 Au 脤摂取率にて逐次検査してみると，移植
後8〜10日目で最も先進し，以後次第に減弱する。か
かる初期転移を形成し，しかも網内系機能の最強先進
している時期に領域リンパ節の転移巣を残し，主癌巣
のみを切除すると，30/40 では転移巣が発育して結局
腫瘍死するが，残りの25%（10/40）では転移巣の自然
退縮がみられた。吉田肉膿で若干の時期は移植後4
日目で，この時に主癌巣を切除すると18.8％（10/53）
に転移巣の自然退縮がみられた。腹水肝癌 AH130 及
び吉田肉膿共に主癌巣切除の時期が遅れると効果が少
ないか，又は全く効果がみられなかった。これらの変
化を組織学的に逐次追求してみると，転移リンパ節の
退縮は，細胞間细胞が主作となっているのが観察され
た。

2）上記の実験例に付き，血液の腫瘍細胞に対する
Cytotoxic effect をしらべてみると，腫瘍死するもので
は正常範囲内の変動であったが正常退縮を示した群で
はCytotoxic effect の上昇が認められ，且つその上昇は
血清中のγ-グロブリンの変動に従って変動している如
く思われた。

3）臨床的な癌が実験癌にみられたような早期のも
のであれば，例え最近述べられている如く血液中癌細
胞の存在や手術側における癌細胞の遺残が存在しても
手術に対する予後に期待が持てるよう，しかし例えば胃
癌患者の網内系機能を新コンゴロート係数でしらべて
みても必ずしも一定の傾向がみられないことが多い。
臨床の癌の時期を予測することは困難である。そこで
胃癌につき腸間膜リンパ節の反応態度につき検査し
た。術後2年間の予後との関係をみると，腸間膜リン
パ節の反応が rich であったものに予後不良のものが多
く，このことは，領域外と考えられる腸間膜リンパ節
に逆変化の及んでいる場合には癌が既に全身的であつ
て，手術後の予後も不良であったものと考えられた。

4）臨床例の胃癌切除後に血清中タノニ酸処理血
球凝集反応の抗体価の変動を追求してみると症例によ
っては1000倍以上の抗体価のみとめられたものがあ
り，かかる例では予後も良好であった様に思わわれ
た。

反対に術後抗癌剤の投与によって，かえって全身抵
抗性の減少を来たし，癌の発育を促進させた症例が
しばしば経験され，生体の抵抗性を考慮せずに癌の治
療に当ることは甚だ危険であると考えられる。

5）末期癌患者の抵抗性を判別して癌治療に利用せ
らとする試みが行われて来たが，われわれも網内系
機能の亢進している時期の担癌動物の脾臓剝が，他の
同様な担癌動物の網内系を著明に刺激して，癌の発育
に抑制的に作用することを明らかにした。