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EFFECT OF THE PRE-OPERATIVE IRRADIATION AND SUBCUTANEOUSLY CANCER TISSUE IMPLANTATION ON THE ANTITUMOR ANTIBODY LEVELS Report II.

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癌の術前照射並に摘出癌組織の治療的移植の抗癌抗体価に及ぼす影響

(第 II 報)

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(昭和38年5月11日受付)

術前照射によつて担癌個体の血清中に抗癌抗体が生成され、之れによつて個体が抗癌態勢を取る事を第 I 報に於いて実証して術前照射の臨床的意義を明かにした。この事実に基づいて更に被照射摘出癌組織を皮下に浅く移植して抗原として投与し抗体価を持続せしめようと企てた成績も亦所期

の成果を得た. 第 II 報に於いては更に例数を増してこの事実を確認すると共に, 術前照射を受けない担癌個体には抗体の生成を認めなかつた事実を報告し, 放射線生物学的作用機構に於ける自家抗体の重要な役割を明かにしたいと思う.

Summary:

As already reported in the first report of this series, I proved that the tumor-bearing individuals could be placed in the anticancer state by raising autoantibody if the cancer cells are destroyed by irradiation and whose destructed cells would create the autoantigens.

In this report, I am going to re-confirm the above fact by adding another 13 cases conducted later, and at same time, I would like to prove that the pre-operative irradiation enables to create the antitumor antibody since I failed to prove the antibody in the non-irradiated tumor-bearing individuals.

Introduction:

This study is not merely indispensable in studying the method of pre-operative irradiation to cancer but it is also an essential study to solve the fundamental problems of Radiotherapy. To prove my hypothesis concerning the autoantibody which is to be created by the

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destruction of cancer cells after irradiation, a difference between the cancer tissue and the tissue of cancer possessing organ as antigen must be proved.

In October 1962, Dr. Itakura, the Department of Pathology at the Hokkaido University, has already found the abovementioned difference through his study as appeared under the title of "Investigation of human tissue antigens by Gel-precipitation test" which gave an important support to my study.

Concerning the antigency of irradiated cancer cells, this writer is, at present, preparing to determine the difference by the "tannic acid-treated sheep erythrocytes agglutination test."

In this report, I would like to mention that the same test as stated in the first report had been conducted on the 13 cases so as to further attempted to confirm the fact of the previous report. Subsequently, I made an investigation on the antigency of the collapsed products being irradiated through examining the state of creation of autoantibody in the tumor-bearing individuals without pre-operative irradiation.

Materials and Methods:

There were 13 cases in the first experiment consisting of; 10 cases of stomach cancer, a case of each ileocaecal cancer, rectum cancer and sigmoid cancer. All cases were examined by the same method in the previous report. That is, they had been completed with the preoperative irradiation (2000—3000 r. skindose) either by Co-60 gamma ray, 200 KVP apparatus, or body cavity tube equipment, and they all went the radical surgery at 10—21 days intervals following the irradiation.

Antigens were produced from the above extirpated cancer tissues by the same method as stated in the first report which finally enabled me to confirm the antigen antibody reaction.

In the second experiment, the same test was attempted on the 7 cases consisting of; 2 cases of stomach cancer and 5 cases of cervix cancer by making the antigens from extirpated cancer tissues, without conducting the pre-operative irradiation.

Results:

Table 1 represents the result of the first experiment which shows the change of autoantibody titer in the tumor-bearing individual by the pre-operative irradiation as time proceeds. Table 2 represents the result of the second experiment which shows the change of antibody titer in those 7 cases without pre-operative irradiation. Diagram 1 shows the result of table 1 by graph.

As it is apparent from the above tables and diagram, a remarkable rise of antibody titer was noted in the bloods of tumor-bearing individuals completed with the pre-operative irradiation in a period of 10-21 days following the irradiation. As shown in the diagram 1, when those titers are shown by curved lines with the lapse of time, generally they showed a highest peak around 20-30 days following surgeries and then showed a trend of gradual depression. But their reaction finally disappeared roughly in 60 days. Contrarily, a few cases completed with therapeutical transplantation showed a further accerleration of the antibody titers. No creation of autoantibody could be seen in those 7 cases without pre-operative irradiation.

Table 1 Change of Autoantibody Titer in Bloods in the Tumor-bearing Individuals by Pre-operative Irradiation. (Experimented by Tannic Acid-Treated Sheep Erythrocytes Agglutination Test)

| | on on | TT la itstaa | 0 | | | 0 | | 0 | | | | 10 | 0 | 0 | 10 |
|---|--|-----------------------------|---|----------------|----------------|--|--|----------------|--|--------------------------------|--------------------------------|--|---|---|---|
| | of Progress Therapeutic | | | | | 1 | | | | 15 | | 1 | _ | + | 1 |
| | Revolution | | Fine | * | Recu- | Fine | * | " | | Recur- | Fine | = | * | , | , |
| | ation | 193i T | _ | | | | | | | | | | | 2560 | |
| | tirpa | Days | | | | | | | | | | | | 09 | |
| | utoa | rəti T | - | | | | | 10 | | 10 | | 10 | | 640 | |
| t) | ng th of a | Days | | | | | | 61 | | 53 | | 09 | | 34 | |
| Tes | owir | TətiT | 160 | | | l Î | | 8 | | 10 | 320 | 40 | 1 <u>î</u> | 160 | 1 |
| tion | foll | Days | | | | 61 | | 37 | | 43 | 30 | 30 | 09 | 24 | 51 |
| ıtına | days the | Titer | 160 | 160 | 40 | 160 | 80 | 160 | | 1280 | 88 | 80 | 80 | 80 | 80 |
| Aggu | of and | Days | 28 | 34 | 27 | 16 | 27 | 26 | | 18 | 20 | 20 | 20 | 17 | 36 |
| Erythrocytes Ag | Pre. Number of days following the extirpation ive surgery and the change of autoantibody ation | Titer | 80 | 80 | 20 | 80 | 40 | 320 | 640 | 640 | 80 | 40 | 40 | 8 | 320 |
| | | Дчуу | 13 | 20 | 13 | ∞ | 13 | 13 | Π | 10 | 10 | 10 | 10 | 10 | 15 |
| | | Təti T | 20 | 40 | 20 | 40 | 20 | 80 | 40 | 80 | 20 | 20 | 40 | 20 | 40 |
| daane | After Pre. operative Irradiation | Days | 10 | 21 | 10 | 12 | 15 | 12 | 16 | 10 | 10 | 10 | 12 | 15 | 12 |
| Acid-1 realed | Takizawa's Classificatio- 1 | | | × | X | × | × | X 23 | × 1 | X X | × 1 | × | × | × | X 2 |
| | e Irra- ge X XNo. | | 2000r | 3000r | 3000r | 2000r | 2000r | 3000r | 2000r | 3000r | 3000r | 2000r | 2000r | 2000r | 3000r |
| od by ramme | | No. of daysXNo. of field | $\begin{array}{c} \text{Co60} \gamma \\ 200 \times 10 \times 1 \end{array}$ | BCT 500×6×2 | BCT 500×6×2 | $\begin{array}{c} 200\mathrm{KVP} \\ 200{\times}10{\times}1 \end{array}$ | $\begin{array}{c} 200\mathrm{KVP} \\ 200\!\times\!10\!\times\!1 \end{array}$ | BCT 500×6×2 | C_0 — 60γ . $200 \times 10 \times 1$ | BCT $500 \times 6 \times 2$ | BCT $500 \times 6 \times 2$ | $\begin{array}{c} 200\mathrm{KVP} \\ 200\!\times\!10\!\times\!1 \end{array}$ | $\frac{\text{Co}-60\gamma}{200\times10\times1}$ | $\frac{\text{Co}-60\gamma}{200\times10\times1}$ | $\begin{array}{c} \mathrm{BCT} \\ \mathrm{500} \times 6 \times 2 \end{array}$ |
| TOTAL COLUMN | Sex | | OI- | Ol- | € | €0 | OH- | € | € | € | $\bigcirc\vdash$ | €0 | €0 | OH- | € |
| 1 | A ge | | 28 | 26 | 54 | 22 | 59 | 63 | 62 | 39 | 20 | 53 | 33 | 42 | 20 |
| 4 | Histologi- cal Findi-Age ngs | | Adenocar- zinoma | * | | u | ű | ï | u | * | | * | | | ĸ |
| | Name of | | Heocecal Cancer | Stomach | " | " | | n | Rectum | Stomach | " | | | Sigmoid | Stomach |
| Capelinence by Lannic Acid-Treated Sheep Erythrocytes Agglutination Test, | Name of Patient | | Nagashi- ma | Takata | Yamam- oto | Shiraishi | Wada | Harada | Kataoka | Katsutani | Nitta | Kagawa | Oyasu | Okada | Ueoka |
| | No. | | П | 2 | က | 4 | 5 | 9 | 7 | ∞ | 6 | 10 | 11 | 12 | 13 |

 $\frac{\text{Table}}{\text{(Experimented by Tannic Acid-Treated sheep Erythrocytes Agglutination Test)}} \, ^2 \, \text{Antibody Titer in Bloods in the Tumor-Bearing Individuals Without Pre-Operative Irradiation}$

| No. | Name of Patient | Name of Disease | Histlogical | Age | | No. the | Therapy | | | | | |
|-----|--------------------|--------------------|---------------------|-----|---|------------|---------|------|-------|------|-------|------------------------|
| | | | Findings | | | Days | Titer | Days | Titer | Doys | Titer | |
| 1 | Kubo | Cervix cancer | Adenocar- zinoma | 52 | 우 | 0 | (-) | 10 | (-) | 20 | 40 | Radium 3000 mg/std. |
| 2 | Fukukawa | " | | 62 | 우 | 0 | (-) | 10 | (-) | 30 | 80 | 12 |
| 3 | Kishino | " | Adenocar- zinoma | 47 | 우 | 0 | (-) | 10 | (-) | 34 | (-) | Radical Surgery |
| 4 | Iwai | ,, | ,, | 48 | 우 | 0 | (-) | 10 | (-) | 20 | (-) | " |
| 5 | Kashima | ,, | ,, | 41 | 우 | 0 | (-) | 20 | (-) | 40 | (-) | 79 |
| 6 | Hasegawa | Stomach cancer | ,, | 52 | 6 | 0 | (-) | 10 | (-) | 20 | (-) | " |
| 7 | Oda | ,, | ,, | 62 | 우 | 0 | (-) | 10 | (-) | 20 | (-) | 12 |

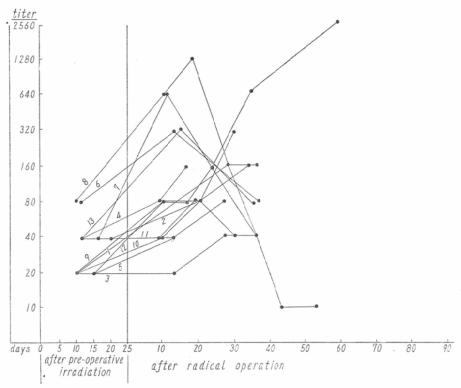


Diagram 1 Number of Days Following surgery and the Change of Autoantibody Titer by Graph.

Conclusion:

As a result of the above experiments, this writer had proved the creation of autoantibody in the bloods of tumor-bearing individuals with the lapse of time following irradiation when the cancer cells are destroyed by irradiation, however, no antibody was proved in the cases without the pre-operative irradiation. Although the change of their titers showed almost same pattern on the graph, some of the cases in therapeutical transplantation group showed a steady accerleration and duration for a long time.

From the above results, it is presumed that the collapsed products of cancer cells caused by irradiation have a definite peculiarities as autoantigens.

Reference

Dr. Itakura. Japanese Journal of Cancer Clinics, Vol. 8, No. 10, Oct. 1962.