Diagnosis of the Sarcoma by a Skin-Test.

By
Rai Satake.

(From the Medical Clinic of Prof. T. Kurokawa, Faculty of Medicine, Tohoku University, Sendai.)

(Received for publication on December 26, 1950)

In taking advantage of an opportunity reported elsewhere, a watery extract was prepared from sarcomatous mass, almost pure, and injected intracutaneously to the patients suffering from the sarcoma, carcinoma or various diseases other than any neoplasma. As the results, in the case of sarcoma the skin reaction took place almost invariably while no reaction occurred in the patients suffering from the carcinoma.

Experimental.

Material: Spindle cell sarcoma originated from the great omentum. It was of consistence of the brain mass, and occupied the abdominal cavity in full, so that we thought the latter was filled with the ascites, but get the white, soft mass instead of the watery by puncture while the patient was alive. A portion, about 150 grm., of the mass floating in the abdominal cavity at autopsy, was used for the present investigation.

Extraction: The mass was placed in 95% alcohol for a few days, being shaken from time to time. Alcohol then was discarded, the remaining mass was dried and powdered in a mortar. 2% watery emulsion was made therefrom, shaken thoroughly. To the supernatant liquid, separated by centrifugalization, about 5 volume alcohol was added, and shaken thoroughly. The precipitation, separated by centrifugalization, was washed and dehydrated with alcohol and ether, and then dried in the vacuum exsiccator, followed by powdering. The powder was dissolved in the saline solution, the carbolic acid being added to 0.5% for preservation.

Dosis, estimation: 0.1 cc. emulsion was intracutaneously injected on the palmar face of the upper arm, and the same quantity of 0.5% carbolic acid solution on the other side as the control. At first 0.05 cc. and 0.2 cc. emulsion were tried too, with similar outcome.

In loco the redness, induration and bubbles develop as a consequence. At 1, 2, 3, 4, 5, 24, 48 & 72 hours after the injection they were noted.
The largeness of induration was chiefly marked, the redness and bubbles formation being taken into account also.

On the base, given below, the induration, the diameter of which exceeds 1 cm. at the end of 48 hours after the injection, is taken unconditionally as a positive reaction for the sarcoma. And if the induration, with the diameter a little less than 1 cm. be combined with bubbles, clearly visible, it is taken as a positive case.

(1) In this skin-test, the induration has a boundary clearly determinable than that of the redness, and swells nodularly, in comparison with that was brought about by the control test with carbolic acid or the Mantoux-Mendel's.

(2) It is commonly difficult to say of the width of the redness because of the irregularity of expansion and of indistinctness of its boundary.

(3) The largeness of the induration, determined 24 hours after the injection and 48 hours, i.e. another 24 hours later, practically the same each other in the sarcoma patients only.

In all other cases, that is, even in the patients suffering from the carcinoma and other neoplasma, the induration is to be found as being reduced undoubtedly, when measured 48 hours after the injection.

(4) The observation for a short time such as 1–5 hours cannot be taken as sufficiently adequate. The carbolic acid only, for example, is able to produce the reaction of similar degree if the observation is limited within such a length of time as 5 hours. At 24 hours after the injection no trace of induration exists.

In the cases of sarcoma the induration was invariably found 72 hours after the injection as still existing, while no or almost no induration was found at all 24 hours after the extract injection in the carcinoma cases.

In the skin reaction due to the carcinoma extract, which gives a promising data in the hands of Sec and Matsubara, the latter author relied on observation extending for some hours to one hour only. The extract of mouse sarcoma, it may be here added in passing, can evoke also the skin reaction in patients suffering from carcinoma and in pregnant women.

Results.

It must be noticed first that the extract was applied here to the patients, usually before identifying the nature of tumor.

**Healthy persons:** No positive case in 10 persons. (24 hour test gave 5 positive reaction (induration with over 1 cm. diameter))

**Sarcoma patients:** In toto 12 cases were examined; 11 cases positive, with 1 negative case. All the cases, which gave positive skin reaction in our hands, 11 in number, were proved histologically as the sarcoma. With a single case, which was diagnosed as the sarcoma clinically, especially by the beneficial effect of X-ray, the induration did not exceed 1 cm. at last. The observation was not extended to 72 hours; in fact this case was investigated at the very beginning of the present observa-
Diagnosis of Sarcoma by Skin-Test

**Table I.**

Sarcoma Patients.

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<tbody>
<tr>
<td>1</td>
<td>21</td>
<td>Mediastinal sarcoma</td>
<td>R(+) I(+) 9x9 B(+) 4x4</td>
<td>+</td>
<td>R(+) I(+) 7x7 B(+) 3x3</td>
<td>+</td>
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<tr>
<td>2</td>
<td>56</td>
<td>R., cervical lympho-sarcoma</td>
<td>R(+) I(+) 8x10 R(++) I(+) 3x3</td>
<td>-</td>
<td>R(+) I(+) 6x6 B(+) 3x3</td>
<td>-</td>
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<tr>
<td>3</td>
<td>27</td>
<td>Lymphosarcomatosis</td>
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<td>+</td>
<td>R(+) I(+) 18x22 R(++) I(+) 6x7 B(+) 2x3</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>13</td>
<td>Ovarial sarcoma</td>
<td>R(+) I(±) 22x33 R(++) I(+) 5x6 B(+) 2x2</td>
<td>+</td>
<td>R(+) I(+) 7x8 B(+) 2x3</td>
<td>+</td>
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<tr>
<td>5</td>
<td>52</td>
<td>Osteosarcoma of r. humerus</td>
<td>R(+) I(±) 25x25 R(++) I(+) 7x10 B(+) 2x3</td>
<td>+</td>
<td>R(+) I(+) 14x20 R(++) I(+) 9x10 B(+) 3x4</td>
<td>+</td>
</tr>
<tr>
<td>6</td>
<td>18</td>
<td>Osteosarcoma of l. humerus</td>
<td>R(+) I(+) 14x15 R(++) I(++) 7x7 B(+) 3x3</td>
<td>+</td>
<td>R(+) I(+) 10x11 B(+) 2x3</td>
<td>+</td>
</tr>
<tr>
<td>7</td>
<td>20</td>
<td>Mandibular sarcoma</td>
<td>R(±) I(+) 22x25 R(+) I(+) 7x7 B(+) 2x3</td>
<td>+</td>
<td>R(+) I(+) 12x14 R(+) I(++) 6x7 B(+) 3x4</td>
<td>+</td>
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<tr>
<td>8</td>
<td>50</td>
<td>Cervical lymphosarcoma</td>
<td>R(+) I(−) 25x25 R(+−) I(+) 10x12 R(++) I(+) 5x6</td>
<td>+</td>
<td>R(±) I(±) 11x13 R(++) I(+) 5x5 B(+) 2x3</td>
<td>+</td>
</tr>
<tr>
<td>9</td>
<td>31</td>
<td>Lymphosarcoma in fovea jugul. &amp; axillary fossa</td>
<td>R(−) I(+) 20x20 R(+) I(+) 9x8 B(+) 3x3</td>
<td>+</td>
<td>R(−) I(+) 15x15 R(++) I(++) 8x10 B(+) 4x4</td>
<td>+</td>
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<tr>
<td>10</td>
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<td>Fibrosarcoma in larynx</td>
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<td>Lymphosarcoma in r. tonsil</td>
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<td>R(++) I(+) 7x7 B(+) 2x3</td>
<td>+</td>
</tr>
<tr>
<td>12</td>
<td>50</td>
<td>Pelvis sarcoma</td>
<td>R(±) I(+) 10x10 B(+) 2x2</td>
<td>+</td>
<td>R(±) I(+) 10x10 B(+) 2x2</td>
<td>+</td>
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</tbody>
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R: Redness  I: Induration  B: Bubbles  Numerals: mm.

**Carcinoma cases:** Among 33 cases (thyroid 1, lung 3, esophagus 4, stomach 18, liver 2, pancreas 2, rectum 2, uterus-metastasis only 1) only 2 cases gave us positive reaction against the sarcoma extract. The following two cases are of interesting to note: Each case of the lung and
the pancreas was diagnosed clinically as the sarcoma, and in fact the latter as so even at autopsy; but the skin reaction was always negative, against our expectation. And in reality microscopical examination finally uncovered its character; they were the cancer. Our skin test thus stands on a firm ground.

All the patients with sarcoma and the majority of the carcinoma patients originated from the cliniques of Surgery, Otology and X-ray therapy. Our cordial thanks are due to Professors S.-T. Katsura, Y. Koga and T. Tsuiki for their kindness.

Miscellaneous diseases: 70 patients were taken at random. 6 cases gave a positive reaction, they are 2 cases of phthisis out of 14, 1 case of cholecystopathia out of 5, 1 stomach ptosis, 1 malnutrition and 1 erythema multiforme exsudativum.

The diseases qualified with negative reaction only are, 12 ulcer (stomach and duodenum) 4 ascariasis and etc.

From the data above given, we are doubtless qualified to say, the skin injection of the watery extract of the sarcoma tissue evokes generally a certain reaction in the patients suffering from the sarcoma, while no reaction is produced in the cases with the carcinoma. The difference is decisive.

Although there were detectable exceptional cases, they were very small in number and there were apparently some grounds to account for the discordance.

The present outcome well corresponds to the finding of Kaminer on the diagnosis of the carcinoma. He injected the crystallic carcinoma fatty acid intracutaneously. The reaction sets in in the carcinoma cases almost always (97%), while none in the cases with the sarcoma (4 in number).

He measured the induration, and in fact 2 days after the injection.

If both the outcomes (Kaminer and Satake) be combined, the malignant neoplasma can be diagnosed and differentiated with sure by the skin reaction against the substance which is obtainable from the neoplasma and characteristic of its properties, whether carcinoma or sarcoma. It is highly desirable to deepen this kind of researches along the process of reasoning.

DISCUSSION.

In connection with the present communication Nakagawa's investigations carried out in dealing with the same question might be referred to on this occasion. He seemed successful while the author was trying to improve the serodiagnosis of cancer, devised by Lehmann-Facius and re-
ported the availability of the sarcoma extract besides the cancer extract for discriminating them from each other.

The sera from the carcinoma patients react positively against the carcinoma extract, but does not against the sarcoma extract, but those from the sarcoma patients react equally against both kinds of extracts.

He then however suddenly withdrew his opinion in a later publications. Namely he came to witness negative cases of the sarcoma reaction in a half of the sarcoma patients (4 cases).

Aoki failed to duplicate the views of Nakagawa et al. not only the value of the method to differentiate between both the kinds of malign neoplasma, but also of the procedure of Lehmann-Facius in general. Apparently this criticism did not remain without effect upon the above-referred withdrawal.

In his several experiments Nakagawa made extraction mostly from the sarcoma of rabbits; that of hen, rat and patient was also used. Further it should not be neglected here in referring to the outcome of Nakagawa that the cancer extract reacts invariably positive against the sarcoma sera; it is quite unintelligible from the findings here given.

Similar results to those quoted in the above paragraph were obtainable in the experiments of Matsubara, who applied the same principle as Kaminers to patients of various kinds of neoplasma. This is worth while to be discussed now.

He used the skin-test, similar to Kaminers and according to the present worker's, but he chiefly estimated the area of redness and limited the observation within 4–1 hours after the injection. And human cancer, chorion tissue and mouse sarcoma were extracted. All the extracts caused the skin reaction in the patients suffering from all the kinds of malign neoplasma and from the pregnant women.

According to his publication in 1950, the placental extract produces the positive reaction in carcinoma patients, while none in pregnant women, if the extract is applied intracutaneously and the findings in 1–2 hours only be taken into account. Therefore the extract, prepared in the hand of Matsubara thus involves the matter characteristic to the rapidly developing cells but common to all the kinds of neoplasma, malign as well as benign. In contrast to that author both the extract of Kaminers from the cancer and that of the present writer from the sarcoma contain the matter characteristic solely to either the cancer or the sarcoma.

**Summary.**

From the spindle cell sarcoma originated from the great omentum in a patient, which was obtainable in a form of pure cultivation and was not contaminated with necrotic mass if any, watery extract was prepared,
and injected intracutaneously into the patients suffering from the malign neoplasma.

The cutaneous reaction was followed, and chiefly the induration estimated; its largeness at the end of 24 and 48 hours after the injection was particularly noted.

The results were clear cut, that is, commonly the sarcoma patients gives the positive reaction while the carcinoma patient does not.

The outcome thus harmonizes perfectly with that of Kaminer with the carcinoma extract. The present investigations deal with the sarcoma extract only, and Kaminer dealt with carcinoma only.

The present outcome shows, otherwise expressed, that it is possible to obtain from the sarcoma tissue the substance which brings about the skin test, described in the text, in sarcoma patients only, but not in carcinoma cases. It is highly probable that our success was due to the purity of the sarcoma tissue utilized here.

References.

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