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<td>Tezuka, Hiroshi; Harano, Chikao; Shirabe, Raisuke</td>
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http://naosite.lb.nagasaki-u.ac.jp
Scar Cancer in the Atomic Bomb Survivors

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Two cases of skin cancer developed on the scar of A-bomb flash burn in Nagasaki were reported and discussed, comparing with four similar cases reported from Hiroshima. Skin cancer of A-bomb survivors differs little from other skin cancer in regard to age, sex, location and histological findings, but the latent interval is shorter. One of our cases belongs to "acute wound cancer of burns" with 4 month interval between the irradiation and onset of cancer. It must be kept in mind that the A-bomb survivors with scar cancer had effects of the radiation on virtually all organs of the body. For instance our two cases were both exposed at the close distance of 1.3 km and 2.4 km respectively, and no scar cancer was found among those exposed in a longer distance. No definite conclusion on the responsibility of the radiation to the incidence of skin cancer can be drawn at the present. Only continued study and more additional case records will provide conclusive evidence on this problem.

Scar cancer developed on the matrix of scar tissues of the skin has been reported by many authors. SHIGEMATSU21) and MURAKAMI14) have reported statistic study of scar cancer due to burn wound, and SUZUKI23), MIYAZAKI13), TO29) and ONOZUKA16) on cases of scar cancer due to wound. In the West, TREAVES and PACK27), ARNDT2) and others have reported on scar cancer. In our follow-up study of A-bomb survivors with scars due to burns and injuries, we found two cases of scar cancer resulted from radiation burns.

Prior to this paper four case reports appeared in Japan reporting on scar cancer developed after A-bomb radiation burns by MIKI11), ITO6), TAMAGAWA24) (1955) and YANAGIHARA28) (1961). Therefore, the total number of these cases reached to six by this time. In this paper our two cases will be described.

Case 1. H. I., a 50-year-old male, was exposed to the A-bomb in the open 1.300 m away from the hypocenter. His radiation burns involved his face, left forearm, and back of the left hand. Shortly after radiation developed severe symptoms of acute radiation sickness including vomiting, fever, and epilation which disappeared...
Table 1. Scar Cancer in A-Bomb Survivors of Nagasaki and Hiroshima

<table>
<thead>
<tr>
<th>No</th>
<th>Author</th>
<th>Age</th>
<th>Sex</th>
<th>Distance from H·C</th>
<th>Acute radiation sickness</th>
<th>Type of injury</th>
<th>Location of lesion</th>
<th>Intervall before onset of cancer</th>
<th>Histological finding</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Shirabe</td>
<td>1954</td>
<td>50</td>
<td>Male</td>
<td>Vomiting, Fever, Haemorrhage, Epilation</td>
<td>Burn</td>
<td>Back of left hand</td>
<td>1/3Yr.</td>
<td>Squamous cell carcinoma</td>
</tr>
<tr>
<td></td>
<td>(Nagasaki)</td>
<td></td>
<td></td>
<td>1,300 m</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Shirabe</td>
<td>1955</td>
<td>54</td>
<td>Female</td>
<td>Vomiting, Diarrhoea, Epilation</td>
<td>Burn</td>
<td>Left leg</td>
<td>10</td>
<td>Squamous cell carcinoma</td>
</tr>
<tr>
<td></td>
<td>(Nagasaki)</td>
<td></td>
<td></td>
<td>2,400 m</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Miki</td>
<td>1955</td>
<td>62</td>
<td>Female</td>
<td>-</td>
<td>Burn</td>
<td>Head</td>
<td>8.3/4</td>
<td>Squamous cell carcinoma</td>
</tr>
<tr>
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<td>(Hiroshima)</td>
<td></td>
<td></td>
<td>1,000 m</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Ito</td>
<td>1955</td>
<td>62</td>
<td>Male</td>
<td>-</td>
<td>Wound</td>
<td>Head</td>
<td>4</td>
<td>Squamous cell carcinoma</td>
</tr>
<tr>
<td></td>
<td>(Hiroshima)</td>
<td></td>
<td></td>
<td>3,000 m</td>
<td>(-)</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>5</td>
<td>Yanagihara</td>
<td>1961</td>
<td>57</td>
<td>Male</td>
<td>-</td>
<td>Wound</td>
<td>Face</td>
<td>15</td>
<td>Squamous cell carcinoma</td>
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<tr>
<td></td>
<td>(Hiroshima)</td>
<td></td>
<td></td>
<td>2,000 m</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>6</td>
<td>Tamagawa</td>
<td>1955</td>
<td>50</td>
<td>-</td>
<td>-</td>
<td>Burn</td>
<td>-</td>
<td>5</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>(Hiroshima)</td>
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Table 2. Age of Patients

<table>
<thead>
<tr>
<th>Author</th>
<th>Age</th>
<th>Average of Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kitamura (Skin cancer)</td>
<td>8—83 Yr</td>
<td>46.8 Yr</td>
</tr>
<tr>
<td>Kitamura (Scar cancer)</td>
<td>26—61</td>
<td>47.1</td>
</tr>
<tr>
<td>Shigematsu (Burn scar cancer)</td>
<td>44.6</td>
<td></td>
</tr>
<tr>
<td>Murakami (Burn scar cancer)</td>
<td>18—77</td>
<td>44.8</td>
</tr>
<tr>
<td>Amdt (Burn scar cancer)</td>
<td></td>
<td>47.6</td>
</tr>
<tr>
<td>Tezuka et al</td>
<td>50—62</td>
<td>54.6</td>
</tr>
</tbody>
</table>

(A-Bomb burn scar cancer)

spontaneously. Radiation burn was healed in 2 months leaving scars on the involved skin areas. Four months after A-bomb injury, however, a small ulceration started from the scar on the back of the left wrist, gradually increasing its size and severity. All therapeutic means failed to cure it, only making it worse with neuralgic pain around the ulcer. He visited our clinic on November 16, 1946, 1 1/4 year after the injury.

Physical examination revealed normal general and hematological findings except moderately increased red cell sedimentation rate. There was, however, a cancerous ulcer of $8 \times 10$ cm$^2$ extending from the back of the left hand to the distal part of the forearm as illustrated in the picture (Plate 1). The rim of the ulcer formed an elevated uneven
surface presenting hemorrhagic appearance and odorous secretion from foci of cancer. Bordering with this ulcer there were spread burn scars on the back of the forearm and fingers. As the result of described condition both flexion and extension of the left fingers were restricted to a considerable degree with impaired function of all finger joints. The left cubic lymph node was enlarged to a soy bean size and its consistence was solid indicating metastasis. No metastasis, however, was found in the left axillary lymph nodes.

Treatment and Course: Amputation of the left arm was performed on November 16, 1946, and the patient was discharged in one month. Three months after the surgery, metastases to the left axillary lymph nodes were noted and they were removed surgically. Following the removal cancerous infiltration of a wide area extending from the axilla to the anterior wall of the thorax, too extensive for radical operation, appeared. Consequently marked cachexia was noted and finally the patient expired on July 1, 1947 after massive hemorrhage from the axillary fistule. Histological diagnosis was squamous cell carcinoma.

Case 2. T. F., 54-year-old female, was exposed to the radiation in the open, 2,400 m from the hypocenter. Her face, right side of the neck, right upper arm, forearm, hand, lower half of the left leg and back of the left foot had radiation burns and received temporary treatment on her way home. One week later, symptoms of acute radiation sickness, vomiting, diarrhea and epilation, were noticed. Burns were treated with ointment and salve at home and were cured in 3 months, leaving only the scar from which developed a small ulcer one month later. Remission and relapse have alternated but the ulcer steadily progressed. The patient came to our clinic on September 8, 1955, ten years and one month after the A-bomb radiation.

Physical examination revealed good general condition. Hematological study revealed mild anemia (erythrocytes 3,500,000, hemoglobin 66% Sahli). As illustrated in the picture (Plate 2) a large ulcer of $15 \times 20$ cm$^2$ was found on the left lower leg, although walking was not impaired. The rim of the ulcer was elevated and its surface was uneven, covered by odorous hemorrhagic serous secretion. Burn scar around the ulcer was not distinct, but the skin was grossly rough. The left knee and ankle were swollen diffusely with marked dilation of veins. The contour of the patella was not clear. The left inguinal lymph nodes were solidly enlarged to a thumb-size and firmly attached to the surrounding tissues, indicating malignant metastasis.

Course: Immediate amputation of the leg was recommended to the patient who stubbornly refused the surgery and went home, only to aggravate the lesion by home therapy. She died on January 7, 1958. Autopsy revealed (1) skin cancer on the left lower leg (squamous cell carcinoma), (2) cancerous infiltration beneathe the skin cancer and
into the tibia, (3) sclerotic change of the aorta and coronary arteries, (4) mild arteriosclerosis of the kidney, (5) mild increase of intrahepatic interstitial tissues, (6) edema and congestion of the lungs, (7) fibrous adhesion of the right pleura, (8) left ovary cyst, (9) bilateral cyst formation of the kidneys, (10) gall sand in the gall bladder, (11) senile atrophy of solid organs, and (12) diffuse edema of all mucous membranes. These senile atrophic changes without noticeable metastasis indicate that she was a good candidate for surgery which could have prolonged her life if performed immediately after the first examination.

Cases reported from Hiroshima.

As shown in the table 1, 4 cases of scar cancer have been reported from Hiroshima. Their descriptions are far from completion. The sixth case is only casually referred in Ito’s paper.

Discussion

1. Age.

Age is known in 5 cases, ranging from 50 to 62 years of age which belong to the cancer age. Average age is 54.6 years, as shown in the table 2, slightly older than the reported average age of onset of scar cancer of the skin, 44.6 years according to Shigematsu and 47.6 years according to Arndt, although the number of cases is too small to be significant.

2. Sex.

Ratio of male and female is 3 to 2. Reported ratio of skin cancer is 67.8 to 32.2 according to Ohtake et al., and that of scar cancer due to burns is 3.8 to 1 according to Murakami and 3.7 to 1 by Treaves. All agree in higher incidence among males.

3. Type of Scar.

Our two cases were caused by burns, but cases in Hiroshima had wound as well as burns as causes of scar cancer. Incidence of scar cancer among skin cancers in Japan is 13.8% according to Ohtake and 17.9% according to Aiko. These figures are extremely high when compared with Treaves’ figure, 1.1%. Scar of burn is the commonest ground for skin cancer among all reported cases of known precancerous skin conditions in Japan according to Kitamura.

4. Location of Lesion.

According to Ohtake et al., locations of skin cancer are: face 55%, head 8.3%, trunk 6.4%, penis and scrotum 5.5%, upper extremities 7.3%, and lower extremities 17.4%. As far as scar cancer due to burns is concerned, face 34.8%, abdomen 1.52%, upper extremities 12.12%, lower extremities 51.51% according to Shigematsu, and lower extremities 52%, head 32%, upper extremities 15%, and face and trunk 1% according to Murakami. Treaves, on the other hand, states that
burn cancer involves the area which is uncommon for other types of skin cancer. He reported 10 cases of trunk lesions, 5 cases of hand lesions, 2 cases of neck lesions, 3 cases of hip lesions, 2 cases of arm lesions, 2 cases of back lesions and one case for lower leg, another for knee and another for foot.

Thus skin cancer in general and scar cancer are rather different in their common sites of lesions. In the A-bomb survivors, however, only head, face and extremities are involved. They are common location of scar cancer, and not specific to radiation scar.

5. Histological Findings.

All verified scar cancer cases among A-bomb survivors had squamous cell carcinoma. This agrees with SAGA's finding in 38 scar cancer due to burns; all but one basal cell carcinoma were squamous cell carcinoma. Most cases reported by SHIGEMATSU were also squamous cell carcinoma, and only two had adenocarcinoma. There was found, however, no change specific to A-bomb survivors, but only those changes commonly seen in squamous cell carcinoma.

6. Relation to Exposed Distance and Acute Radiation Sickness.

Our two cases were both exposed in close distance of 1.3 and 2.4 km from hypocenter and acute symptoms of radiation sickness developed. Among cases in Hiroshima, one was exposed in 3 km distance without developing acute radiation sickness, another one was exposed in 1 km and probably developed acute radiation sickness, although it was not mentioned in the paper. Geographically, Nagasaki is a hilly city, unlike Hiroshima which situates on a flat plain. This characteristic explains why some people were well protected against heat burns by hills even when they were exposed in close distance, while others of considerable number suffered from extensive burns of second and third degrees in 2.5 km distance, and developed large scars or keloid formations. Our two cases belong to the latter group, developing skin cancer from the scar. It is noteworthy that no skin cancer was found among those who were exposed in long distance. We suspect, therefore, that radiation of A-bomb could be responsible to the incidence of scar cancer among the survivors.

7. Interval before Onset of Cancer.

The interval between the exposure to A-bomb radiation and the onset of skin cancer in the A-bomb survivors varies from 4 months to 10 years, or 7.2 years in the average. On the other hand, latent interval of ordinary scar cancer due to burn varies from 4 months (not in Japan) to 64 years, or 37 years in the average according to KITAMURA, and from 4 years to 64 years, or 36.8 years in the average according to SHIGEMATSU who reviewed 66 cases reported in Japan, of which 54% were between 30 and 60 years. MURAKAMI reported on 116 Japanese cases, stating that the shortest interval was 5 years, the longest 73
years, and 36.1 years in the average.

The scar cancer due to burn of unusually short interval between the burn and onset of cancer is named "acute wound cancer of burns" by Treaves\(^2\), who reported on 6 cases with intervals of around one year. Arndt reported on 19 similar cases which he called "Brandnarbenkarzinom ohne Intervall". Other examples of extremely short intervals are 16 days of Bang, 25 days of Hugenerin, 30 days of Stauffer and 3 weeks of Gaurier\(^2,1\), whereas in Japan 5 years of Murakami\(^4\) is the shortest interval ever reported.

As compared with these long intervals of scar cancer of burn, the average interval of 7.2 years in A-bomb survivors is strikingly short. Particularly, 4 months of the case 1 is the shortest interval in Japan and should be a typical case of Treaves' "acute wound cancer of burns".


Among explanations of pathogenesis of skin cancer, stimulation theory is widely accepted. As internal factor developmental disturbance is mentioned, and as external factors precancerous conditions such as chronic ulcer, scar, and naevus are mentioned. Kaneno\(^7\) includes Paget's disease, Bawen's disease and cornu cutaneum in precancerous conditions, and suspects vulgaris, scar and naevus as external factors, and emphasize the importance of burn scar which exhibits histological findings resembling carcinoma; hyperplasia of basal cell layer of the skin irregular lines of prickle cells, splitting of nuclei, narrow intercellar space, and degeneration of cells. Sasaki\(^2\) puts emphasis on chronic ulcer and burn scar as precancerous state, based upon his own experience. From the fact that common locations of scar cancer are peripheries of the body such as head and lower extremities, Murakami\(^1\) came to the following conclusion: Scar tissues with poor systemic or local blood supply are suitable for development of cancer, because epithelial regeneration under such condition is liable to degenerative change which can be accelerated in the presence of ulcer by promoting regenerative mechanism. Treaves\(^2\) states that thick and hard scar interferes with blood circulation, and its superficial layer can be destroyed easily, thus developing uncontrollable ulcer by any minor stimulus aided by stimulation of blood clot and infection, finally leading to cancer. In regard to acute wound cancer of burns he calls attention to the rapid cancerous change in elderly patients of burns who have atrophic and keratotic skin. Arndt\(^2\) has the same view with Treaves in regard to etiology of scar cancer, reporting that Brandnarbenkarzinom ohne Intervall was found only among elderly patients.

Our cases also suggest that radiation burn, after temporary healing, develop to ulcer by unknown reasons and change to cancer by stimulation of blood, infection, drug and others. Nevertheless, the
relationship between A-bomb radiation and incidence of skin cancer in those exposed in close distance from the hypocenter is to be answered. According to Shono's momentaneous radiation dose in Hiroshima and Nagasaki was 600 to 800 r in 1 km, and 10 r in 2 km radius, undeniably harmful amount for any human being, even though it rapidly decreased. As the result, in close exposure the whole body was exposed to a high amount of radiation, giving damage to all organs. Therefore, it is only logical to suspect the role of radiation as an etiological or facilitatory factor in addition to the above-mentioned causes of skin cancer.

Obo, Mori, Ishida have confirmed statistically the higher incidence of malignant neoplasms among A-bomb survivors. Tomonaga has pointed out the correlation between the incidence of leukemia and the amount of radiation to which the patients were exposed. Our study on carcinoma of the thyroid gland also indicates the higher incidence of malignancy among the exposed. These are a few examples of recent interest in the relationship between A-bomb radiation and incidence of malignant neoplasm.

Some accelerating effect of A-bomb radiation is indicated by the following facts: (1) Interval between burns and cancer formation is relatively short. (2) High incidence was found in the group exposed in closer distance of 1 to 2 km from the hypocenter. (3) Acute wound cancer of burns, which had not been reported in Japan, was found among A-bomb survivors.

Radiation cancer of the skin due to roentgen ray or radium ray usually results from ulcer developed after repeated irradiation with roentgen or radium, and pays no respect to sex or location, unlike other skin cancers. Latent interval of radiation cancer is shorter than other skin cancers, 15.8 years in the average according to Ikeda and 24 years according to Petersen, showing striking resemblance to scar cancer found in A-bomb survivors.

Ito states in his report that it is premature to draw any conclusion on the relationship between the A-bomb radiation and incidence of cancer, because any etiologic theory of pathogenesis of cancer is still in hypothetic stage, although radioactive particles seem to possess a certain carcinogenic action. The number of our cases is not large enough to determin if radioactive particle released by A-bomb explosion has any significant role in incidence of skin cancer. We have the impression, however, that skin cancer following radiation burn has some significant difference from the usual types of skin cancer.

**SUMMARY**

1. Two cases of skin cancer developed on the scar of A-bomb radiation burn in Nagasaki were reported and discussed, comparing with four similar cases reported from Hiroshima.
2. Skin cancer of A-bomb survivors differs little from other skin cancer in regard to age, sex, location and histological findings, but the latent interval is shorter. One of our cases belongs to acute wound cancer of burns with 4 month interval between the radiation and onset of cancer.

3. It must be kept in mind that the A-bomb survivors with scar cancer had effects of the radiation on virtually all organs of the body. For instance our two cases were both exposed at the close distance of 1.3 km and 2.4 km respectively, and no scar cancer was found among those exposed in a longer distance.

4. No definite conclusion on the responsibility of the radiation to the incidence of skin cancer can be drawn at the present. Only continued study and more additional case records will provide conclusive evidence on this problem.

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