Refractory Anemia Occurring in Survivors of the Atomic Bombing in Nagasaki, Japan

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Refractory anemia was one of the first pathologic effects noted as a result of exposure to radioactive agents. Since the original description, published over forty-five years ago, a number of reports have appeared in the literature describing the occurrence of refractory anemia as a late effect of repeated exposures to x-rays or various radioactive materials.1, 2, 3 The susceptibility of the hematopoietic tissues to irradiation is well known and the severe effects on the bone marrow accompanying acute radiation injury have been described by a number of observers.4-6 However, to date refractory anemia has not been described as a late manifestation of radiation injury among survivors of the atomic bombings. The present paper is a report on six cases of refractory anemia occurring in Nagasaki survivors four to seven years after the atomic bombing. Autopsy findings are presented in five of the six cases.

Methods and Material

During the investigation of late radiation effects by the Atomic Bomb Casualty Commission (ABCC), three patients were encountered with symptoms of refractory anemia. Previously, as part of the investigation, autopsies had revealed a refractory anemia in two individuals. Subsequent to the recognition of these cases a survey was made of all of the death certificates in Nagasaki during the years 1949 to 1951 inclusive. One additional case of refractory anemia was discovered.

Routine hematologic studies, including bone marrow examinations, were made on the three patients studied in the ABCC clinic. Data on the other three were furnished by their physicians. In addition to the usual clinical and laboratory data, a careful radiation history was recorded. This included the exact location of the individual at the time of the bomb burst and the development of any subsequent radiation symptoms. In this report the exposure distances are recorded in meters from the ground center beneath the bomb explosion.

Case Histories

Case 1, T. C.

T. C., a fifty-one year old Japanese male school teacher, was exposed to the atomic bomb at a distance of 500 meters and subsequently developed an acute radiation syndrome. He
remained in a critical condition for months with anemia, hemorrhagic diathesis, and epilation. His hair began to grow back about the third month.

The patient never fully regained his health; he had a severe anemia and often complained of malaise and dizziness. His position as the principal of a mission school taxed his strength, and when a "work camp" arrived from the United States in August, 1949, he joined the party and performed hard manual labor. His symptoms became progressively more severe from that time on.

Early in 1950 he was diagnosed as suffering from anemia, probably due to ankylostomiasis, and he received antihelminthic therapy without benefit. On April 8, 1950 he was admitted to the Ureshino National Hospital, where hematologic studies revealed a red blood count of 960,000 per cu. mm., a leukocyte count of 2,900 and thrombocytopenia. From a bone marrow examination the diagnosis of refractory anemia was made. The patient was given several blood transfusions and liver injections, with very little improvement. On May 5, 1950, following a sudden attack of chills and fever, hematemesis occurred. A generalized hemorrhagic diathesis developed, his condition rapidly became worse, and he died on May 13, 1950.

The autopsy findings were as follows:

**Gross Findings**

There were numerous petechiae scattered over the body and hemorrhages were found in the epicardium, kidneys, base of the brain, and the mucosal surfaces of the stomach and intestinal tract. The spleen measured 11 x 7 x 2.5 cm. and weighed 44 Gm.; the capsule was smooth and free of adhesions; the parenchyma appeared hyperplastic. The liver measured 27 x 19 x 6 cm. and weighed 2650 Gm.; the capsule was smooth and the parenchyma a pale yellow-brown with a prominent lobular pattern. The remainder of the organs were not remarkable.

**Microscopic Findings**

Bone marrow. There was a moderately diffuse increase in fat with a delicate reticulum network (fig. 1). There was a marked diminution in hematopoietic cells including both erythroid and myeloid elements. A large percentage of the remaining cells were of the lymphoid series. Erythropoiesis was particularly diminished, with only rare normoblasts being present. A small number of myelocytes and earlier myeloid cells were seen, but more mature granulocytes were very few in number. Megakaryocytes in diminished number were present.

Liver. An extensive fatty change was present which was most marked in the central zones where it progressed to a hyaline necrosis (fig. 2). A few mononuclear cells were present in the portal triads.

**Summary.** In this case there was a fairly typical fatty marrow almost devoid of hematopoietic activity but leaving a delicate reticulum. All hematopoietic elements were reduced in number, particularly the mature forms and perhaps most conspicuously, the erythroid precursors.

**Case 2, F. H.**

F. H., a forty year old male pathology technician, was exposed to the atomic bomb at a distance of 1040 meters. The patient was working in a room with a large number of people. He was one of four survivors. He suffered flash burns on the arm and left leg, and one week following he had a temperature of 40 C., which continued for one week. A month after exposure, complete epilation occurred. The past history and family history were not contributory.

In September, 1951 the patient developed fatigue and abdominal pain, and at that time a diagnosis of peptic ulcer was considered. In November, 1951 he was treated for ankylostomiasis, but during February the abdominal pain increased and was accompanied by diarrhea. At this time x-ray studies revealed a gastric ulcer, and the patient was treated by diet therapy. On May 19, 1952, due to the persistence of complaints, the patient visited the Medical School of Nagasaki University, where a severe anemia and leukopenia were discovered. He was admitted to the hospital.

On physical examination, the pulse rate was 80 and the blood pressure 90/40. The patient
Fig. 1.—Bone marrow from the femur of case I showing diffuse fatty infiltration (×400).

appeared chronically ill with marked pallor, and he appeared to have lost weight. There were scars of flash burns on the arms and left leg. The superficial cervical lymph nodes were palpable but not enlarged. On auscultation of the chest the breath sounds were distant, and a soft blowing systolic murmur was heard at the cardiac apex. The abdomen was flat and no organs or masses were palpable, but slight epigastric tenderness was present.

Hematological findings were as follows, Red blood count was 1,770,000 per cu. mm., hemoglobin 5.7 Gm. per cent, reticulocyte count was 0.2 per cent, and the platelets numbered 93,330 per cu. mm. The white blood count was 1,800 per cu. mm., with a differential of 2 per cent segmented forms, 16 per cent stab forms, 50 per cent lymphocytes, 28 per cent monocytes, and 4 per cent eosinophils. Bone marrow examination showed 8.5 per cent segmented forms, 7.5 per cent stab forms, 11.5 per cent neutrophils, 10 per cent lymphocytes, 7.5 per cent promyelocytes, 5.0 per cent myeloblasts, 1 per cent polymorphonuclear basophils, 5.5 per cent polymorphonuclear eosinophils, 22.5 per cent lymphocytes and 1 per cent reticulum cells. For 200 leukocytes there were 22 erythroid cells composed of 8 normoblasts, 13 late erythroblasts, and 1 early erythroblast. The megakaryocytes were decreased and the marrow showed definite erythroid hypoplasia.

Hospital Course

The patient continued to complain of tiredness, abdominal pain, anorexia and a persistent fever. The red blood count varied between 2,000,000 per cu. mm. on June 15 and 800,000 on July 16, and he maintained a persistent leukopenia. The differential showed a marked
a granulocytosis with a relative lymphocytosis, although terminally a few myelocytes were seen. A second marrow examination on June 23, 1952 showed a marked reduction in erythroid elements, and the megakaryocytes, although present, were decreased in number. The myelocytic series, except for defective granulation, was essentially normal. Although the marrow was cellular, it did not appear to be leukemic, and was compatible with a diagnosis of refractory anemia.

The patient was treated with penicillin, iron, Vitamin B₁₂, and many small blood transfusions but failed to improve. He expired on July 26, 1952.

Autopsy findings were as follows:

**Gross Findings**

The skin and organs were very pale. Numerous petechiae were found in the epicardium and corpus callosum of the brain. Small mesenteric nodes varying in size up to that of a pea were present, and there were numerous small retroperitoneal nodes. The small intestine showed several ulcers not related to the lymphoid follicles. The spleen measured 11.5 x 7.0 x 2.0 cm. and weighed 92.5 Gm. The liver weighed 1300 Gm. and the cut surface revealed that the lobules were not well demarcated.

**Microscopic Findings**

*Lymph nodes.* There were no significant changes.

*Spleen.* Hemosiderosis was present.
Liver. There was extensive central necrosis.

Bone marrow. The myeloid elements were relatively increased with slight immaturity, while the erythrocytic precursors and megakaryocytes were moderately decreased. A large amount of hemosiderin was present.

Subsidiary microscopic findings included the presence of pulmonary edema, chronic cystitis and focal hyperparomatogenesis.

Summary. The findings were compatible with a diagnosis of refractory anemia, and there was no organ infiltration to suggest a diagnosis of leukemia.

Case 3, M. C.

M. C., a twenty-two year old female office clerk, was exposed to the atomic bomb at a distance of 1250 meters. At the time of the explosion she was standing inside a wooden house with about twenty friends, almost all of whom died within a short while. The patient suffered flash burns on the left side of the face and cut wounds on the right side of the face and right leg. A few days later she noticed a low-grade fever and developed loose stools. A month after the bombing she developed oropharyngeal lesions which lasted five days, and at the same time, swelling and bleeding of the gums occurred. Twenty days after the bombing epilation started and became almost total.

The patient's father, mother and one sister died as a direct result of the bombing; otherwise the family history and past history were noncontributory.

The patient was seen in the Commission's clinic on February 15, 1952 in a routine survey of adult survivors of the atomic bomb. She complained of tiredness and left lateral chest pain. The patient had noted that she developed infections easily since her exposure to the atomic bomb.

Examination at the time of this visit was negative except for the presence of radiation cataracts.

Laboratory Examinations

Hookworm ova were found in the stool specimens, and the guaiac test was positive. The S.T.S. and urine were both negative. The hematology was as follows: red blood count 3,465,000 per cu. mm., hemoglobin 9.4 Gm. per cent, hematocrit 32.5 per cent, MVC 99 cu. microns, MCH 27 micromicrograms, MCHC 29 per cent, reticulocytes 0.5 per cent, Wintrobe sedimentation rate 30.0 mm. (1 hr.), platelets 399,965 per cu. mm. The leukocyte count was 4,650 per cu. mm., with a differential of segmented forms 60.5 per cent, stabs 2.0 per cent, lymphocytes 23.5 per cent, monocytes 1.5 per cent, eosinophils 10.5 per cent, and basophils 2.0 per cent. Slight anisocytosis was seen. The chest x-ray revealed a strand of increased density at the right base but no evidence of active disease.

Subsequent Course

At a local hospital in April, 1952 a provisional diagnosis of pernicious anemia was made and she was treated with Vitamin B12 and liver extract. Bone marrow examination revealed granulocytic segmented forms 10.5 per cent, stabs 9.5 per cent, juveniles 11.0 per cent, myelocytes 10.5 per cent, promyelocytes 8.0 per cent, myeloblasts 1.0 per cent, polymorphonuclear basophils 2 per cent, polymorphonuclear eosinophils 1 per cent, lymphocytes — small 38 per cent, reticulum cells 6 per cent, and plasma cells 2.5 per cent. There were 201 nucleated red blood cells per 200 nucleated white blood cells, normoblasts 109, late erythroblasts 75, and early erythroblasts 17. The marrow was hypocellular with decreased megakaryocytes and increased lymphocytes. No megaloblasts were seen and the hemoglobinization of the erythroid elements was defective.

The patient was seen a second time by Commission physicians on May 23, 1952 and was found to be in extremis. For a month the patient had been bedfast with bleeding gums and persistent bleeding from the vagina. On examination there was extreme pallor, evidence of old hemorrhage about the gums, and active bleeding from the vagina. The pulse rate was 130. There were no enlarged glands and the liver and spleen were not palpable. The tongue, although pale, showed no atrophy of the papillae.
The red blood count was 770,000 per cu. mm. with 2.0 Gms. per cent hemoglobin and a hematocrit of 7.0. The platelet count was 13,000, white blood count 3,900 per cu. mm. with a differential of 5 per cent segmented forms, 5 per cent stabs, 49 per cent lymphocytes, 3 per cent monocytes, 1 per cent eosinophils, 2 per cent metamyelocytes, 9 per cent myelocytes, 21 per cent promyelocytes, and 5 per cent myeloblasts.

The patient was immediately hospitalized and transfused with 300-400 cc. of blood. Three unsuccessful attempts were made to aspirate marrow from the sternum and iliac crest. She expired on May 26, 1952, seventy-two hours after admission. Eighteen hours after death an abdominal incision was made and specimens were obtained from the liver, spleen and right kidney. A section of the sternum for bone marrow examination was taken.

**Pathohistologic Findings**

**Bone marrow.** There was a diffuse and extensive fibrosis involving the entire marrow space of the available section (fig. 3). Enmeshed singly or in small clumps throughout the fibrous tissue were greatly diminished numbers of hematopoietic cells. Among these it was noted that there was a relative diminution of early myeloid forms, with only a few myelocytes and occasional nonsegmented leukocytes present in proportion to the segmented forms. The erythroid elements were more conspicuously those of the erythroblastic level; normoblasts were few in number. Megakaryocytes were present but were for the most part smudged or bizarre. A large proportion of the cells present were lymphocytes and plasma cells.
Spleen. The capsule was very slightly thickened, and the lymphoid germinal centers were small with congested sinusoids. Moderate quantities of hemosiderin were present, and the red pulp was diffusely infiltrated by a great variety of cells, including large and small lymphocytes. Erythroblasts, normoblasts, and a few myelocytes could be distinguished and a number of degenerating megalocytes were present.

Liver. There was moderate congestion of the central portions of the liver lobules, with fatty degeneration and foci of early hyaline necrosis in these areas. The peripoortal connective tissue was moderate in amount and was diffusely infiltrated with small round cells, mostly lymphocytes. The sinusoids contained small islands of round cells with dark nuclei and a slightly basophilic cytoplasm resembling that of erythroblasts and normoblasts. Occasional hypersegmented or degenerating neutrophilic leukocytes were seen, together with a few large cells with degenerating nuclear masses which probably represented megalocytes.

Summary. The single marrow section studied was compatible with refractory anemia in which the marrow cavity showed extensive fibrosis. In this case hematopoietic cells persisted in the fibrous tissue. This picture could not be differentiated from that seen in refractory anemia due to other toxic agents. Extramedullary hematopoiesis, particularly erythropoiesis, was present in the spleen and liver.

Case 4, K. K.

This fifty-one year old farmer was exposed to the atomic bomb at a distance of 1500 meters. He received injuries to the left parietal region and subsequently developed some of the symptoms of the acute radiation syndrome, namely, vomiting, fever, diarrhea and epilation. Apparently the patient recovered fairly completely, but he continued to complain of general weakness.

The past history was not contributory.

In September, 1951 the patient developed furunculosis of the right cheek and he noted pain and bleeding of the gingivae. The left side of his face became edematous and his temperature was elevated to 39 C. Palpitation and dizziness on exertion also developed at this time.

He was seen at the clinic of the ABCC on 24 October 1951. Physical examination revealed an extremely pale and acutely ill Japanese male. The temperature was 38.2 C; pulse, 90; and blood pressure, 110/58. Small bilateral cervical nodes and small axillary nodes were noted. The examination of the fundi revealed old and new hemorrhages, some of them flame-shaped. The heart was slightly enlarged to percussion and a soft systolic murmur was heard over the precordium. The liver was questionable palpable one finger breadth below the costal margin. The spleen was not palpable.

Laboratory Data

Hematology. Red blood count was 600,000 per cu. mm. with a hemoglobin of 2.0 Gm. per cent. White blood count was 5,000 per cu. mm. with a differential of 23.5 per cent segmented forms, 4.5 percent stabes, 55 percent lymphocytes, 11.5 percent monocytes, 1 per cent eosinophils, 2.5 per cent basophils, 1 per cent metamyelocytes, 1 per cent myelocytes. One normoblast was seen and the platelets were markedly reduced in number.

Sternal marrow aspiration was carried out and grossly normal clumps of marrow were obtained. On microscopic examination, some areas of active cellularity were present. Erythroid elements were markedly decreased, and there was a decrease in myeloid activity with a slight shift to immaturity. There was an increase in mononuclear cells, eosinophils, plasma cells, reticulum cells and mast cells.

On the basis of these findings, a diagnosis of refractory anemia was made, and the patient was advised to enter the hospital immediately.

During the hospital course the hematological values of erythroid elements remained unchanged. The white blood count fell to 2,800 per cu. mm. In spite of therapy with iron, penicillin and blood transfusions, the patient expired on November 2, 1951, ten days after admission.
Autopsy Findings

Extreme pallor of mucous membranes and organs, as well as numerous petechiae were noted. Several small mesenteric lymph nodes varying in size up to the size of a pea were found, which, on cross section, were yellowish-white in color. The spleen weighed 45 Gm., it was firm in consistency with normal elasticity, and the capsule was tense. The liver weighed 940 Gm., was firm in consistency, and showed no other abnormality.

Microscopic Findings

Bone marrow. Two sections of marrow were available. In each there were large areas of hemorrhage and replacement of marrow cells by fat. Elsewhere there was active hematopoiesis with the marrow appearing hyperplastic in some zones (fig. 4). The marrow appeared definitely abnormal in that there was a lack of myeloid maturation with relatively few segmented forms being seen. Large numbers of eosinophilic elements were present. The erythroid cells were relatively and absolutely reduced, and megakaryocytes were very few in number. Lymphocytes were increased and pigment was abundant.

Spleen. There was marked hemosiderosis. Liver. There was subcapsular atrophy and extreme central congestion with areas of hyaline necrosis. In the extremely congested central sinusoids there were numerous white
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blood cells, some of them identified as myelocytes, but erythroid elements could not be definitely discerned. In the periportal connective tissue there were small foci of lymphocytic infiltration.

Summary. The marrow had several features unlike those of the other cases in this series. Those areas that were hemorrhagic appeared to have been largely replaced by fat. Elsewhere the marrow had a pseudohyperplastic appearance, but on closer study proved to contain many lymphocytes and plasma cells with a striking diminution in erythropoiesis and an almost complete absence of megakaryocytes.

Case 5, M. S.

M. S., a seventy-one year old Japanese male school supplier, was exposed to the atomic bomb at 3800 meters. He had no radiation symptoms following the bombing.

The patient began to notice mild fatigability in 1948. In September, 1951 he developed a fever and noticed the presence of petechiae on his arms and chest, and later these extended to cover his entire body.

It is of interest that at about this same time he started supplying various inorganic chemical compounds to schools. These compounds included hydrochloric acid, sulphuric acid, nitric acid, potassium hydroxide, sodium hydroxide, ammonia, zinc, magnesium, sulphur and other ores. He obtained bulk materials from the pharmacists and packed and labeled the containers in his shop. This was his only known contact with chemical substances, none of which is known to be implicated in causing refractory anemia.

His blood counts at this time were as follows: red blood cells, 1,000,000 per cu. mm.; white blood cells 1400 per cu. mm., with a differential showing 26 per cent segmented forms, 2 per cent eosinophils, 70 per cent lymphocytes, and 2 per cent monocytes.

The patient was treated with Vitamin B12, reduced iron and blood transfusions. Chloromycetin, penicillin and a sulfonamide preparation were also used in an effort to control the fever. (There was no history of the patient's receiving Chloromycetin before the development of the anemia.) The patient died on October 9, 1951. Permission for autopsy was not granted.

Case 6, I. Y.

This fifty-six year old Japanese male accountant was exposed to the atomic bomb at a distance of 4,400 meters. On the day following the bombing, he walked through the area directly beneath the bomb burst and spent a considerable period of time in the ruins of a steel factory nearby. However, he did not have any symptoms of the acute radiation syndrome.

The family history is of interest in that one of his sons died of leukemia in 1947, but this boy was not exposed to the atomic bomb.

The patient was apparently well until 1948, when he began to complain of general lassitude, palpitation on exertion, and edema of the lower extremities. In April, 1951 a swelling of the left side of the face was noted, as well as a more marked sense of fatigue and a gradual weight loss. On the 9th of September, 1951 the patient first noted tinnitus, slight deafness, and vertigo. He entered the hospital of the Nagasaki Medical School on September 10, 1951.

On physical examination, the blood pressure was 90/45. The patient was slightly emaciated and a noticeable pallor was present. The heart was slightly enlarged to the left and a systolic murmur was heard over the precordium. There was no enlargement of the lymph nodes, spleen or liver. The remainder of the examination was not remarkable.

Laboratory Findings

The red blood count was 870,000 per cu. mm.; hemoglobin equalled 17 per cent; the leukocyte count was 1,300 per cu. mm. with a differential showing 76.5 per cent lymphocytes. The platelet count was 22,750 per cu. mm.; the bleeding time was twenty minutes, and the coagulation time six and one-half minutes. Urine and spinal fluid examinations were negative. Stool examinations revealed the ova of ascaris and Ankylostoma.

The patient went rapidly downhill and expired on September 15, five days after entering
the hospital. A bone marrow examination performed shortly after death showed the following: 7.4 per cent erythroid elements, 69.6 per cent lymphocytes, 0.6 per cent monocytes, 0.4 per cent promyelocytes, 3.2 per cent myelocytes, 5.2 per cent metamyelocytes, 5.0 per cent stab forms, and 9.4 per cent granulocytic segmented forms.

**Autopsy Findings**

**Gross Findings**

There was marked pallor of the mucosal surfaces and organs. Areas of hemorrhage were found throughout the intestinal tract. The lymph nodes were not enlarged. The spleen weighed 100 grams, was brownish in color and showed slight congestion. In cross section, the pattern of the trabeculae was not remarkable, but the follicular pattern was obscure. The liver weighed 1250 grams. The bone marrow of the femur was fatty and the sternal marrow appeared pale.

**Microscopic Findings**

*Bone marrow.* The hematopoietic cells were largely replaced by fat, and the remaining cells were for the most part lymphocytes, plasma cells, and reticulum cells (fig. 5). There were scanty focal areas of cellular activity. There were small islands of complete erythroid
maturation, but only scattered myeloid forms, mostly of late stages, were present. Megakaryocytes were absent.

Summary. The fatty replacement in this marrow was not so diffuse as that in Case 1. However, in large focal areas, there was practically complete fatty infiltration. It was not clear whether the remaining blood-forming cells represented residual islands of hematopoiesis or isolated foci of regeneration. The absence of megakaryocytes was striking.

DISCUSSION

All of the cases in this paper conform to a diagnosis of “refractory” hypoplastic anemia presenting the classical triad of anemia, leukopenia and thrombocytopenia, without significant organ enlargement. Moreover, bone marrow examinations failed to reveal the presence of leukemia and in no case was there evidence of a hypersplenic syndrome. In five cases the diagnosis was confirmed at autopsy. In the sixth case the information was meager, and this patient was not personally studied by the authors. However, this case was included, since all the evidence indicated that the diagnosis of refractory anemia was correct.

It is well known that refractory anemia may present a very variable bone marrow picture. The bone marrows in this series varied from normal cellularity to almost complete aplasia, and in one case to fibrosis. In this case, in addition to myelofibrosis, extramedullary hematopoiesis was present. The different bone marrow pictures represented in this series are shown in the accompanying illustrations.

Four of the patients were exposed to the atomic bomb explosion at distances of less than 1500 meters, and all four developed definite radiation symptoms. It can be assumed that these patients received a significant insult to their hematopoietic system from atomic radiation. Moreover, it is known that the highest incidence of leukemia has occurred in those survivors who were within a radius of 1500 meters. In all there were 5075 known survivors at distances under 1500 meters from the ground center of the atomic bomb explosion in Nagasaki. Unfortunately there are no accurate statistics on the incidence of aplastic anemia among the general population of either Japan or the United States. However, in clinical experience aplastic anemia is a rare disease, seen even less frequently than leukemia. In view of this fact, the occurrence of four cases of refractory anemia in a population of 5075 individuals representing the survivors under 1500 meters in Nagasaki is suggestive of a probable cause and effect relationship between the exposure to the atomic bomb and the subsequent development of refractory anemia. However, such a relationship is by no means conclusively demonstrated. In the other two individuals exposed beyond 3800 meters, the distance and lack of symptoms of the acute radiation syndrome make it improbable but not impossible that radiation per se was a factor in the subsequent occurrence of refractory anemia in their cases.

It is of interest that five similar cases of refractory anemia have been studied in Hiroshima, Japan. These cases will be subsequently reported, together with a survey of the hematopoietic problems arising from late radiation effects. It is well established that one of the outstanding features of the acute radiation injury occurring in heavily irradiated survivors of the atomic bombing was the rapid occurrence of severe hematopoietic damage. This damage ranged from complete hypoplasia to minor degrees of bone marrow depression. Similar
findings have been reported in animals exposed to radiation under experimental conditions. Moreover, there are a number of recorded cases of refractory anemia among early radiologists and other individuals exposed to unshielded radiation over a long period of time. The unusual features of the cases reported in this paper are (1) the radiation insult was due to a single exposure to ionizing radiation, and (2) the fatal hematopoietic damage developed after a latent period of four to seven years without exposure to other known bone marrow toxic agents. The pathogenesis of this disorder remains an enigma, but it is interesting to note that leukemia developing among survivors of the atomic bombing occurs under similar circumstances and after a similar latent period. Since refractory anemia is a much rarer condition, far fewer cases have been found in contrast to the more common leukemia. Further, some studies have shown that erythropoietic tissue is more resistant to radiation than myelopoietic tissue. This has not been universally accepted since other investigators have found the erythropoietic tissues to be quite sensitive to ionizing radiation.

Due to the fact that radioactive isotopes might have been deposited in the bone marrow after exposure to the ionizing effect of atomic energy, the bones of three individuals in this report were analyzed for the presence of any remaining radioactivity. Completely negative results were obtained. This is not conclusive, however, since these studies were made seven years after exposure.

**SUMMARY**

In this paper the case histories of six Nagasaki atomic bomb survivors who developed refractory anemia are presented. Four of these individuals received undoubted radiation injury. The fact that refractory anemia may occur as a late manifestation of exposure to atomic radiation is pointed out.

**SUMMARIO IN INTERLINGUA**

Iste reporto presenta le casos de 6 superviventes del bombardamento atomic de Nagasaki qui disveloppava anemia refractori. Quatro de iste individuos habeva sin ulle dubita lesiones de radiation. Es sublineate le facto que anemia refractori pote occurrer como retardate manifestation del exposition a irradiation atomic.

**REFERENCES**

7 Bomford, R. R. and Rhoads, C. P.: Refractory anemia; Clinical and pathological aspects, Quart. J. Med. 10: 175, 1941.
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Refractory Anemia Occurring in Survivors of the Atomic Bombing in Nagasaki, Japan

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