Kobe J. Med. Sci., Vol. 54, No. 2, pp. E108-E113, 2008

Case Report: Iridium 192 - Health Effects during 20 Years after Irradiation

SNEZANA MILACIC[1] JADRANKO SIMIC[2]

Faculty of Medicine, University of Belgrade, Institute of Occupational Medicine and Radiological Protection; Belgrade, Serbia[1];
South East Europe Consultants, Belgrade, Serbia[2]

Received 12 November 2007 /Accepted 19 February 2008

Key words: Iridium 192 (Ir^{192m}), gamma radiation, health effects

This Case Report has presented health effects of high level of irradiation with gamma rays from Ir^{192m} on the patient M. L. during 21 years after the accident. The main purpose of this investigation was to analyze long time consequences of partial high-level irradiation on human health. Locally, short-term irradiation, with high deadly dose, caused acute radiation syndrome with reversible disorder function of the individual, most exposed, organs. Frequency of chromosomal aberrations (dicentric), characteristic for direct irradiation, was increased. However, dicentric analyzes did not give expected result for an acute radioactivity illness. Radio dermatitis had begun already after the incident, while changes on the heart began not earlier than six months and gradually have been increased up to two years after the incident. Irradiated parts of the patient skin have been replaced with auto-transplanted skin and appropriate therapy had been taken. More than two decades after the irradiation, system (leukemia) nor solitary tumor on near organs (liver, heart, lungs, bones) have not been appeared. Radiation illness did not happen in spite of very large dose, because impacts had been local and body was unlikely irradiated. Also, an appropriate therapy was organized and other potential illnesses did not appear.

Iridium-192 (Ir^{192m}) is a meta-stable isotope of Iridium that emitting gamma radiation with a low level of Linear Energy Transfer (LET) and high penetration in human body. This isotope frequently has been used for industrial radiography (7).

Usually, workers daily engaged with Ir^{192m} for a long time period can be injured by radiation and level of tissue damage depends on doses and period of radiation (3).

Consequences of industrial radiography gamma rays accidents (greater than 20Gy) are skin necrosis in various parts of the body (1). Two up to three decades after irradiation exposure malignant disease could be developed (4). Myeloid leukemia, associated with exposition to gamma rays, can be found in clean-up workers 10 years after the accident (2, 6).

Dose equivalents up to 20-30Sv exposed on the fingertips of workers can cause progressive tissue deterioration and successive amputations of the fingers (7). Health risks could arise in a case of environmental pollution with the radioactive isotope Ir^{192m} if it has been lost.

This article has reviewed long-term health consequences of an accidental overexposure from Ir^{192m} radiography source on a human being.

Phone: +381-11-3674-515 Fax: +381-11-643-675 E-mail : m.masha@beotel.net

INCIDENT

Patient M. L. was 53 years old porter in a car factory, when he took a lost source of Ir^{192m} with an initial power of 296 GBq in a factory courtyard on August 14th, 1982. This Ir^{192m} was used for industrial gamma-radiography and when incident had happened starting power was 275 GBq (7.43 Ci). Patient M. L. carried this gamma source three days in the left upper pocket of the worker blouse, and after that he put it in the table where he had worked one up to two hours per day in next 19 days, when the source was detected and removed.

METHODOLOGY

Monitoring of health effects after the irradiation with high level of radiation started three weeks after the accident and has been continued after three, six, and twelve months, as well as later on after two and half and eleven years.

Mentioned monitoring included: clinical symptoms; clinical and laboratory indicators; skin changes; blood changes; chromosomal changes in the karyotype of lymphocytes; changes on the heart, liver, eye lens; in fact all radiosensitive cells and tissues, as well as parts of the body or organs that had been closely to the source of Ir^{192m}. Exposure and absorbed doses on the patient body had been calculated taking into the consideration source power, time of exposure, and distance from the source (9, 10, 11).

RESULTS

Assessment of absorbed dose. Approximately calculated dose was about 22.50 Gy up to 42 Gy for the distance of seven up to five centimeters. Frequency of chromosomal aberrations (dicentrics) confirmed that absorbed dose of gamma rays was high.

Clinical symptoms and signs. Patient M. L. first time was hospitalized on September 3rd, 1982 in the Institute of Occupational Medicine and Radiological Protection in Belgrade with symptoms of acute radio-dermatitis on the parts of body that have been in the contacts with the radioactive source. The most intensive skin changes were on the upper part of right thigh side, front wall of left thoracic girdle (figure 1), on the front side of left thigh, and also on the part of right and left hands joint. Except the insomnia and fast wearing radiation syndrome was not followed with other difficulties or objective findings.

Frequency of chromosomal aberrations was increased. There were dicentric end ring forms; many cells contained both of them (multiple chromosomal aberrations). However, dicentric analyzes, reevaluated few times in short period intervals, did not give expected result for an acute radioactivity illness. Frequencies improperly have varied in the function of time, so that they had increased, contrary to the expectance that it should decrease. Obtained values of absorbed doses on the patient body by this method have been improperly distributed so that it was not possible to implement them for an assessment of biological effect. Probably, it was result of an uneven distribution resulting that lymphocytes from the parts of the body had been closer to the source of radiation were un-proportionally more damaged than those further from the source.

Having in mind that source of radiation was closely to the lymph axillaries nodes additional analyses of lymphocytes karyotype had been carried out. Those analyses have identified significant increase of dicentrics frequency in the long time period after the accident, while in a case of proportional irradiation of the body it could be expected its gradual disappearance.

One year after the accident patient complained on occasional pains in the heart area and increased perspiration during the night. Ulcerous-necrotic changed parts of the skin, breasts

and thigh had been changed with the auto-transplanted skin that had been taken from the inside of the right thigh (figure 2). Skin closely around the auto-transplant, as well as the skin in the area of right hand joint was marble-sided, with telangiectasis, de-pigmented and black pot usual for chronicle radio dermatitis.

Two years after the accident necrosis on the hand joint pro graduated in radiation ulcers, so excision had happened and radio dermatitis chronics ulcers non-specific was confirmed by path-histological (PH) analyses, without the morphological elements for malignity (Table 1). Radiological signs of osteoradionecrosis had not been identified. Twelve years after the accident skin was dark-red on the areas of earlier necrosis, partly edematous and atrophied, without the signs of malignant alterations. Eye lens stay transparent and radiation cataract was not developed.

Figure 1. Radio dermatitis acute on the left side of the thoracis.

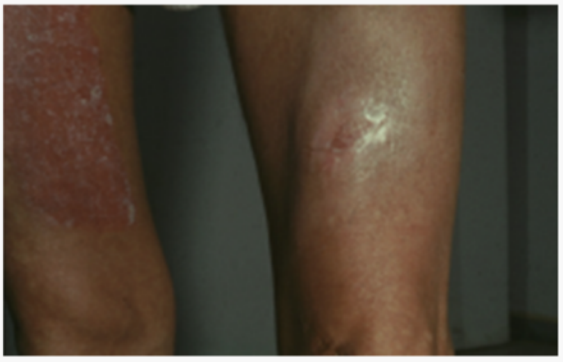

Figure 2. Radio necrosis on the left leg and skin after *auto-transplantation cutis* from the right leg

Table 1. Skin injuries during 20 years after irradiations with Ir^{192m}

Year of examinations	Skin disease	Path-Histological (PH)
1982	Radio dermatitis acute grades II	Dermatitis ulcerous – necrotic
	Auto transplantation cutis	
Therapy		
1984	Radio necrosis (Ulcers radiation)	Dermatitis chronic ulcerous non specifics
Therapy	*Excision*	
	(Tierschu method)	
1993 – 2003	Radio dermatitis chronics	Atrophic, Oedema

Clinical-laboratory findings. Presence of the thrombocytopenia and leucocytopenia in the blood had been identified. The liver was increased 2 cm. Bilirubin in serum had been increased, liver enzymes and factors of coagulation and fibrinolysis were disturbed, in fact factors of pro-thrombus complex. Blood cells count and factors of coagulation completely have been normalized after two years of irradiation. Lymphatic glands had not been increased.

In 1993, eleven years after the accident all elements of haematopoiesis, as well as all liver functions, have been within the physiological framework. By the cytology genetic analyzes of karyotype, chromosome aberrations have been excluded and 14 micronucleus per 1,000 of cells were usual, similarly as in a no exposed population.

Electrocardiography findings (ECG) closely after the incident were without changes. After six months, in February 1983, appearances of ECG were evident, negative T-cog in D1, D2, AVF, and in pre-cordial drain V2-V6.

Such findings had not been followed with subjective difficulties or objective findings on the hearth (Table 2).

Table 2. Cardiac injuries during 10 years after irradiations years

Year of examin a-tions	Duration of time from exposure	Electro-cardiograph changes	Ergo-metri c test	Echo-cardiogram	Blood pressure	Clinical signs and symptoms	Cardiac disease Diagnosis
1982	3 weeks	Normal			Hypo tensions	F100/min Nausea	Acute Radiations Syndrome
1983	6 months	T negative in D1, D2, AVF And V2 - V6		Normal	Hypo tensions	F 75/min	Myocardial ischemia
1983	9 months	T negative in D1, D2, AVF and V2 - V6 Elevation ST		Normal	Normal	F 70/min	Ischemic myocardium sub-epicardial
1983	15 months	T negative in D1, D2, AVF and V2 - V6	Negative	Normal	Normal	F 68/min	Ischemic myocardium post irradiation
1984	21 months	T negative from V3 to V6	Negative	Pericardial adhesion	Normal	Steno cardio	Pericarditis
1984	24 months	T negative from V5 to V6		Pericardial adhesion	Hyper tensions	Brest pain	Chronic Radiations Myopericarditis
1993	10,5 years	Normal			Hyper tensions	Vertigo F 65/min Anorexia	Chronic Radiations Syndrome

Findings did not regress on the coronal-dilatators therapy and maintain balance until 1984, and echocardiogram did not point out pathological changes. On the end of 1984, ergo-metric test did not result of reduced coronary reserves and after patient got tired, even decrease of ST level has happened. Repeated echocardiogram showed a pericardial adhesion.

Two years after the irradiation and twenty months after the appearance on the ST segment of ECG changes started with regression, although they had not been normalized in next few years.

From 1993 ECG findings had been totally normal. The patient M.L. had suffered from vertigo, hypertensions, nausea and anorexia irregularly, from time to time (Table 2).

On the end of 2003, 21 years after the accident, an infarct of the myocardium had happened and patient, 74 years old, died because of acute heart failure caused by coronary thrombus occlusion.

DISCUSSION

Complete, system and acute radiation illness had not happened in spite of very large dose, because impacts were local and body was uneven irradiated. Locally, short-term irradiation with high, deadly dose, caused acute radiation syndrome with reversible disorder of function of individual organs had been the most exposed. The most important changes have happened, besides the most exposed parts of the skin, on the hearth (5, 8, 9).

Closeness of lymph nodes and sternum could cause necroses in lymphatic and haematopoietic tissues, in fact fibrosis and aplasia of bone marrow (5). Changes in karyotype of lymphocytes were structural and unstable, so that they disappeared without clinical consequences (10, 11). Obviously appearance of mutations and stabile aberrations had not happened so that they could not fix themselves during the mitoses and stimulate cancer-genesis. In fact, 20 years after the irradiation, neither system (leukemia) nor solitary tumor on near organs (liver, heart, lungs, bones) had happened (2, 6). Clinical-laboratory disorders have been reversible, probably because of damage function of the parenteral organs and carry over heart system and cells membrane, and possible histological changes are repaired or their functions compensated no damaged part of the tissue (4, 7). Changes on blood cells as well as on the liver have had only reversible character because blood and liver cells have had high reparative capacity (4, 10).

Dermatitis ulcerous – necrotic has been developed as a result of high doses irradiation of 20 – 40 Gy, localized on the skin (1, 3, 7). It has been observed as a skin reaction within few weeks after the incident.

Acute radio dermatitis rarely malignly alternate (1). On the skin around the radiation ulcer (later on auto-transplants) radio dermatitis chronic had been appeared because of little smaller dose on that part of the skin, proportionally to the distance of the direct sheaf on the ulcer level. Sometimes, chronic radio-dermatitis can malignly alternate 20 – 30 years after irradiation (1, 3).

A chronic reaction to radiation can be seen starting 6 to 12 months after irradiation (3, 9, 10). Skin in nearest vicinity of excision was changed to the end with the symptoms of chronicle radio dermatitis and after 21 years it was not malignancy alternate. It means that age after the incident (from 53 to 74) had impact on lower radio sensitivity (5, 8).

Chronic cardiac changes may have their onset from 6 months to several years after irradiation. The clinical symptoms may indicate chronic constrictive disease due to pericardial, myocardial, and endocardium fibrosis. Changes on the heart began gradually, not earlier than six months up to two years after the incident.

The risk of cardiac death in patients with acute myocardial infarction depends on the irradiated part of the heart and age of the patient (8, 12, 13, 14).

Symptoms of hearth function, as well as blood cells and enzymes in serum have been normalized after ten years, probably because smaller part of the heart of the old patient had been directly irradiated. Death happened because of an infarct of the myocardium and that may be connected with the changes of the heart and blood vessels, or late thrombosis occlusions (12, 14). However, classic diagnostic method (ECG) was not sufficient for monitoring late effects overdose on myocardium.

Case of the patient M. L. had pointed out that partial irradiation with high level of gamma rays from Ir^{192m} may not be fatal for human beings if appropriate medical treatment has been applied.

REFERENCES

1. **Becker, J., Rosen, T.** 1989. Acute radio dermatitis from occupational exposure to iridium 192 South Med J. **82(12)**: 1561-1563.
2. **Butenko, Z.A., Smirnova, I.A., Zak, K.P., Kishinskaja EG, Janok EA.** 2000. Leukemia-associated gene rearrangements in blood mononuclears of subjects in long term after radiation exposure. J Exp Clin Cancer Res; **19**: 57-59.
3. **Conde-Salazar, L., Guimaraens. D., Romero, L.V.** 1986. Occupational radio dermatitis from ^{192}Ir exposure. Contact Dermatitis **15(4)**: 202-204.
4. **Gourmelon, P.** 2004. The Medical Diagnosis and Treatment of Radiation Overexposed people; 11th International Congress of the International Radiation Protection Association 23-28 May 2004, Madrid, Spain. Proceeding of the IRPA 11, published on CD *(full papers) 2004; produced by SENDA.* Available online at: www.irpa11.com
5. **Hahn, S.M., Glatstein. E.** 2001. Radiation injury in the book Harison Principles of Interne Medicine, Eugene Brawnvald, ed. (15th edition), Mc. G. Hill, N.Y. Chapter 394. Available online at: http://www.harrisonsonline.com
6. **Inskip, P.D., Kleinerman, R.A., Stovall, M., Cookfair, D.L., Hadjimichael, O., Moloney, W.C., Monson. R.R., Thompson, W.D., Wactawski-Wende, J., Wagoner, J.K.** 1993. Leukemia, lymphoma, and multiple myeloma after pelvic radiotherapy for benign disease. Radiat Res **135**: 108-124.
7. **Jalil, A., Molla, M.A.** 1992. Accidental overexposure to 192Ir source in industrial radiography: a follow-up study. Health Phys **62(1)**: 74-76.
8. **Joensuu, H.** 1989. Acute myocardial infarction after heart irradiation in young patients with Hodgkin's disease. Chest **95 (2)**: 388-390.
9. **Kramer, R, Santos, A.M., Brayner, C.A.O., Khoury, H.J., Vieira, J.W., Lima, F.R.A.** 2005. Application of the MAX/EGS4 exposure model to the dosimetry of the Yanango radiation accident. Phys Med Biol **50**: 3681-3695.
10. **Littlefield, L.G., Lushbaugh, C.C.** 1990. Cytogenetic dosimetry for radiation accidents: «The good, the bad, and the ugly» in The Medical Basis for Radiation Accident Preparedness: Clinical Experience and Follow-up Since 1979. RC Ricks, SA Fry (Eds). New York, Elsevier; 461-478.
11. **Sevankaev, A.V., Lloyd, D.C., Edwards, A.A., Moquet, J.E., Nugis Vyu, Mikhailova, G.M., Potetnya, O.I., Khvostunov, I.K., Guskova, A.K., Baranov, A.E., Nadejina, N.M.** 2002. Cytogenic Investigations of Serious Overexposures to an Industrial Gamma Radiography Source. Radiation Protection Dosimetry **102**: 201-206.
12. **Wolfram, R.M., Budinsky, A.C., Pokrajac, B., Poter, R., Minar, E.** 2005. Vascular brachytherapy with 192Ir after femoropopliteal stent implantation in high-risk patients: twelve-month follow-up results from the Vienna-5 trial. Radiology **236**: 343-51.
13. **Wondergem, J., Strootman, E.G., Frölich, M., Leer, J.W., Noordijk, E.M.** 2001. Circulating atrial natriuretic peptide plasma levels as a marker for cardiac damage after radiotherapy. Radiotherapy and Oncology **58(3)**: 295-301.
14. **Wondergem, J., Persons, K., Zurcher, C., Frolich, M., Leer, J.W., Broerse, J.** 1999. Changes in circulating a trial natriuretic peptide in relation to the cardiac status of Rhesus monkeys after total-body irradiation. Radiotherapy and Oncology **53**: 67-75.