Clinical Report of Three Cases of Acute Radiation Sickness from a $^{60}$Co Radiation Accident in Henan Province in China

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Acute radiation sickness/Radiation accident/Clinical report.

On 26 April 1999, three persons were accidentally exposed by high dose $^{60}$Co irradiation. They suffered from severe (one case) or moderate (two cases) hemopoietic form of acute radiation sickness (ARS). As part of the comprehensive treatment, strict reverse isolation and granulocyte-macrophage colony-stimulating factor (GM-CSF) therapy were applied. All the patients recovered after an appropriate treatment for 83 days. In our experience, the correct diagnosis and effective treatment at an early stage proved to be helpful to the patients in pulling out from the critical stage of acute radiation sickness. To avoid menstruation by the female patient just in the critical stage, we modified her menstruation cycle by test-osterone. In our view, GM-CSF should be given as early as possible with enough dosage for promoting early hematological reconstruction. The experience obtained from the medical management of these patients is valuable for the treatment of such patients in the future.

The use of nuclear energy and nuclear technology have brought great benefits to the mankind, but radiation accidents that happened occasionally have aroused great concern throughout the world. To improve the research on the prevention of radiation accidents, the International Atomic Energy Agency (IAEA) has established a world-wide computer database in 1986, and a similar system is also working in China. This article shows a comprehensive and authentic report of the whole process of a radiation accident which took place on April 26, 1999 in Henan province in China.

INTRODUCTION OF THE ACCIDENT

On 26 April 1999, a $^{60}$Co radiotherapy equipment that had been left unused for a long time, was sold to a waste management agency as scrap metal. Then the workers in the agency disassembled the equipment and opened the container where a radiation source of $^{60}$Co was located. As reported, they knew nothing about radiation sources and the radiation damage, thus, they didn’t know what would be the consequence of removing the radiation source from the container. At 5:00 pm on 27 April, a scrap metal dealer, case C in this accident, bought the radiation source – being unaware of its nature and potential harm - and took it away by tricycle to his home and put it near the bed of his wife (case A in this accident) and his son (case B). The relative geographical locality between the victim and source was as shown in Fig. 1 (a and b). Case A and B go to bed at 8:00 pm, then, they felt nausea and vomited frequently. So case C came to Case A and B’s room from his room and sleep with them to look after them, but 1 hour later, he began to vomit too. Case C went to see a rural doctor for help at 4:00 am on 28 April. They were treated as food-intoxication but their symptoms were not mended for 3 days. The radiation source was reclaimed in a lead container at 5:00 pm on 28 April. Fortunately, a doctor knowing about radiation sickness (ARS) suggested them to go to a special hospital to determine if they had been exposed to radiation or not. Then they were admitted to the Hospital of Occupational Disease Prevention in Zhengzhou of Henan province 4 days after the accident. Seven people were exposed to various doses in this accident, four of them were treated in the Hospital of Occupational Disease Prevention in Henan and the other three (case A, B and C) were transferred to The First Clinical Department of Chinese Center for Medical Response to Radiation Emergency, Tianjin, by plane 10 days after the incident.
Fig. 1. Sketch map of the location of the victim (case A) in the radiation field. (quoted and modified from Ref. 1). (a) shows the horizontal position of the victim from the source. (b) shows the vertical distance between the exposed person and the radiation source.

The radiation source

The initial activity of the radiation source of $^{60}$Co was $1.01 \times 10^{12}$ Bq (2730 Ci) in July, 1987, and that was $2.11 \times 10^{13}$ Bq (577 Ci) when the accident happened. The dose rate of it at the distance of one meter away was 48.7 R/min. The source was mounted in a cylinder drawer which was made of stainless steel (Fig. 2). 13

![Active core of $^{60}$Co source](image)

Fig. 2. Location of the active core in the drawer. The large cylinder was the radiation source ‘drawer’ which was made of stainless steel (diam.5.5 cm × 59.5 cm), the small cylinder was the carrier of the radiation source (diam.3.8 cm × 5.6 cm), the dark area represents the active core of the source (diam.22.8 mm × 20.5 mm).

CASE REPORT

Diagnosis and estimate of physical and biological dose (average dose to the whole body) for the three ARS cases are shown in Table 1. The physical dose of all the three victims was estimated by simulating measurement (dose reconstruction). The biological dose was estimated by chromosome aberration (dicentric and ring) and cytokinesis blocked micronucleus assay. The brief procedure of chromosome aberration and micronucleus assay was based on the method of Technical reports series No 405 of IAEA. 25

Case A

Case A, is a 38-year-old married female, of whom the general symptoms and distinct phases are shown in Table 2 and Table 3. To 32nd day, her hair was lost almost completely. Additionally, her arm pit hair and pubic hair were completely depilated by that time, too. She also had an epistaxis about 5ml in her right nostril on the 23rd day, it was stopped by compression. A dark purple deposit strip appeared at the bottom of her nailbed on 35th day, and then disappeared gradually with the growth of the nail.

<table>
<thead>
<tr>
<th>Case</th>
<th>Gender</th>
<th>Age</th>
<th>Exposure time (h)</th>
<th>Physical dose (Gy)</th>
<th>Biological dose (Gy)</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>female</td>
<td>38</td>
<td>20</td>
<td>6.1</td>
<td>5.1 (4.5~5.6)</td>
<td>Severe ARS</td>
</tr>
<tr>
<td>B</td>
<td>male</td>
<td>8</td>
<td>20</td>
<td>3.4</td>
<td>2.5 (2.2~2.7)</td>
<td>Moderate ARS</td>
</tr>
<tr>
<td>C</td>
<td>male</td>
<td>37</td>
<td>9.3</td>
<td>2.4</td>
<td>2.6 (2.4~2.8)</td>
<td>Moderate ARS</td>
</tr>
</tbody>
</table>

*a*: The physical dose showed in this table is absorbed whole body average doses estimated for the victims by experiment simulation.

Table 2. General symptom for the three patients

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Case A</th>
<th>Case B</th>
<th>Case C</th>
</tr>
</thead>
<tbody>
<tr>
<td>nausea</td>
<td>++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>vomiting</td>
<td>21 times</td>
<td>10 times</td>
<td>10 times</td>
</tr>
<tr>
<td>(4thh~11thh)</td>
<td>(4.5thh~10.5thh)</td>
<td>(6thh~10thh)</td>
<td></td>
</tr>
<tr>
<td>reddish face</td>
<td>+(6thh~3thd)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>conjunctiva hyperemia</td>
<td>++,(6thh~3thd)</td>
<td>+(1std~3thd)</td>
<td>+(1std~3thd)</td>
</tr>
<tr>
<td>hyposalivation and anorexia</td>
<td>++,(1std~3thd)</td>
<td>+(1std~3thd)</td>
<td>+(1std~3thd)</td>
</tr>
<tr>
<td>headache</td>
<td>+(1std~3thd)</td>
<td>+(1std~3thd)</td>
<td>+(1std~3thd)</td>
</tr>
<tr>
<td>fatigue and weakness</td>
<td>+,9thd</td>
<td>+,17thd</td>
<td>+,17thd</td>
</tr>
<tr>
<td>trichomadesis</td>
<td>++,(13thd~32thd)</td>
<td>+(17thd~28thd)</td>
<td>+(17thd~28thd)</td>
</tr>
</tbody>
</table>

Notes: "+" shows the degree of the symptom; order numbers in the parentheses show the time for beginning and ceasing of the symptoms; h: hour; d: day.

Table 3. Duration of the distinct phases of ARS for these three patients, days

<table>
<thead>
<tr>
<th>Case</th>
<th>Initial phase</th>
<th>Latent phase</th>
<th>Manifest illness phase</th>
<th>Recovery phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0 ~ 3</td>
<td>4 ~ 8</td>
<td>9 ~ 34</td>
<td>35 ~</td>
</tr>
<tr>
<td>B</td>
<td>0 ~ 3</td>
<td>4 ~ 16</td>
<td>17 ~ 32</td>
<td>33 ~</td>
</tr>
<tr>
<td>C</td>
<td>0 ~ 3</td>
<td>4 ~ 24</td>
<td>25 ~ 32</td>
<td>33 ~</td>
</tr>
</tbody>
</table>

Notes: numbers in the table show the days after the accident.

On 23rd day, she got fever because of the relapsing of chronic tympanitis. Her body temperature remained between 37.5 to 38°C for 4 days. Papules sparingly distributed all over her body on 34th day and mended after treatment with sulfur ointment (sulfur is the acting material) for scabies. Moderate degree of hepatosplenomegaly was detected on the 60th day, along with pain. HBcAb(+) and HBeAb(+), but the function of liver was normal. We had to face the danger of massive haemorrhage because her menstruation appeared just in the manifest phase of ARS Additionally, there was a wound on her right knee that occurred before the accident and had not recovered yet.

There was not obvious infection developed in the whole course of ARS. She was successfully treated from the manifest illness phase and entered the recovery phase on 34th day.

Case B
Case B, is a male 8-year-old schoolboy, of whom the general symptoms and distinct phases were shown in Table 2 and Table 3. His hair was lost on the 2nd/3rd weeks after the accidental exposure. The dark purple deposit band appeared at the bottom of the nail beds on 37th day. It disappeared gradually with the growth of the nail.

He also had intercurrent syndrome as Moderate degree hepatosplenomegaly, HBsAg(+), HBeAb(+), HBeAb(+), and abnormal function of the liver(GPT and GOT increase) on 14th day. The condition was mended after protective treatment with Essentielle Forte. Hepatosplenomegaly and amiotransferase level returned to normal on 32nd day (Fig. 3, green). Papules all over his body were seen on 32nd day and taken a good turn on 49th day after being treated with sulfur ointment as scabies. In the whole course of ARS, there wasn’t obvious infectious sign, pulled out from the manifest illness phase and entered the recovery phase on 32nd day.

Case C
Case C, is a 37 years old male, of whom the general symptoms and distinct phases of ARS were shown in Table 2 and Table 3 too. His hair was lost in about two to three weeks and there was no obvious loss of amripit and pubic hair. The dark purple deposit band appeared at the bottom of the nail beds on 37th day and disappeared gradually with the growth of the nail.

He presented a complication of skin radiation injury which shown slight erythema and pain on the outside of his second right finger on the 15th day, and then, a blister appeared 5 days later. That was absorbed and scabbed on 28th day after the accident. The scab fell off after treatment on 33rd day. He also had HBsAg(+), HBeAg(+), HBcAb(+), and abnormal of liver function(GPT and GOT increase) on 10th day. The amiotransferase returned to normal level after the protective treatment with liver protectant on 33rd day.
(Fig. 3, blue). Papules appeared all over the body on 32\textsuperscript{nd} day and the condition was mended 18 days later after being treated with sulfur ointment as scabies. In the whole course of disease, there wasn’t obvious infectious sign, then he pulled out form the manifest illness phase and entered the recovery phase also on the 32\textsuperscript{nd} day.

**Hematological examination**

Changes of leucocytes and hematoblasts of these three patients are shown in Fig. 3 and Fig. 4. Some specific counts of WBC and PLT are shown in Table 4.

**Poisson’s disribution of “dic + r”**

Uniform or non-uniform radiation could be judged by Poisson’s disribution $u$ test of “dic + r”. The distribution of “dic + r” in the cell was showed in Table 5. “$u$” and “$\sigma^2$” can be calculated according to the equation (1) and (2). $\sigma^2$: mean square; n: cell number; x: number of “dic + r” per cell;

![Change of Leucocyte](image1)

![Change of Hematoblast](image2)

<table>
<thead>
<tr>
<th>Cases</th>
<th>Counts of WBC on 1\textsuperscript{st} day</th>
<th>Lowest counts of WBC</th>
<th>Lowest counts of PLT</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>$15.60 \times 10^9/L$</td>
<td>$0.05 \times 10^9/L$</td>
<td>$2.00 \times 10^9/L$ (22\textsuperscript{nd} d)</td>
</tr>
<tr>
<td>B</td>
<td>$14.00 \times 10^9/L$</td>
<td>$0.15 \times 10^9/L$</td>
<td>$16.00 \times 10^9/L$ (20\textsuperscript{th} d)</td>
</tr>
<tr>
<td>C</td>
<td>—</td>
<td>$0.40 \times 10^9/L$</td>
<td>$18.00 \times 10^9/L$ (23\textsuperscript{rd} d)</td>
</tr>
</tbody>
</table>

**Notes:** numbers in the parentheses show the days after the accident.

<table>
<thead>
<tr>
<th>Case</th>
<th>Cell number</th>
<th>“dic + r” per cell</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>A</td>
<td>150</td>
<td>33</td>
</tr>
<tr>
<td>B</td>
<td>300</td>
<td>192</td>
</tr>
<tr>
<td>C</td>
<td>300</td>
<td>170</td>
</tr>
</tbody>
</table>

**Fig. 3.** Changes of leucocytes and administration of cytokines to Chinese ARS patients. The arrows show the application of GM-CSF and EPO. G/L: $\times 10^9/L$. This Fig. also shows the relationship between the phase of liver dysfunction (GPT and GOT increase) and the leucocyte counts (especially in the manifest illness phase).

**Fig. 4.** Changes of hematoblasts and platelet transfusion to three ARS patients. The arrows show the transfusion. Plt: platelet suspension, G/L: $\times 10^9/L$. 

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Table 6. Results of Poisson’s distribution u test of “dic + r”

<table>
<thead>
<tr>
<th>Case</th>
<th>( \bar{y} )</th>
<th>( \sigma^2/\bar{y} )</th>
<th>u</th>
<th>uniformity coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>2.3800</td>
<td>1.7747</td>
<td>6.6961</td>
<td>non-uniform</td>
</tr>
<tr>
<td>B</td>
<td>0.5133</td>
<td>1.3094</td>
<td>3.7954</td>
<td>non-uniform</td>
</tr>
<tr>
<td>C</td>
<td>0.5933</td>
<td>1.1522</td>
<td>1.8662</td>
<td>uniform</td>
</tr>
</tbody>
</table>

\( \sigma^2 \): cells contain “dic or \( r \)”; \( \bar{y} \): mean \( \sum x_o/n \). The results of u test showed in Table 6. In these three cases, case A and B are non-uniform radiation but case C is uniform radiation.

\[
u = \frac{(n-1)\sigma^2/\bar{y} - (n-1)}{\sqrt{2(n-1)(1-1/\sum x_o)}}
\]

\[
\sigma^2 = \sum \frac{x_o - (\sum x_o)^2/n}{n-1}
\]

CLINICAL TREATMENT

Radioprotective drugs

Patients A and C were individually applied 4 mg oestra- diol benzoate and 300 mg of “408 tablet” (a kind of Chinese radioprotective drug ) on 5th day. The dosage of the same drugs applied to patient B was half of that given to his parents’.

Prophylactic antibiotics

Rational antibacterial management was performed to all the patients according to the results of blood culture and antibiotics-sensitivity test. The relapse of chronic typhus in patient A was mended soon.

Hematopoietic growth factor

Granulocyte Macrophage Colony Stimulating Factor (GM-CSF) was used to all three patients when the WBC < 1.0 × 10^9/L. Patient A was given erythropoietin (EPO) when her Hb < 90 g/L. The applied dosage of GM-CSF for patient A was 400 pg/m^2/d (from the 9th day) and it was decreased to 200 pg/m^2/d from the 33rd day and stopped on the 37th day. The dosage of GM-CSF for patient B was 200 pg/m^2/d (from the 18th day) and it was decreased to 50 pg/m^2/d from the 33rd day and stopped on the 36th day. The administration dosage of GM-CSF for patient C was 400 pg/m^2/d (from the 26th day) and stopped on the 35th day. The dosage of EPO for case A was 120 U/kg/d from the 10th day to the 36th day. (Fig. 3)

Transfusion of blood and γ-globulin

To enhance the immunity function, avoid hemorrhage and infectious complication, γ-globulin and whole blood which was irradiated by γ-ray at 25 Gy and fresh platelet suspension of the same ABO blood type were applied to all three patients. (Fig. 4)

Isolation, nutrition and clinical care

To prevent exogenous infection, case A was transferred into the laminated air-flow room after disinfection, while case B and C were transferred to laminated air-flow isolator 10 days after the accident. We accommodated axenic and nutritious diet to them, cleaned their skin, nostril, mouth and anal hole every day, and performed the culturing of the blood, urine, feces, mouth smear and local lesions, periodically.

DISCUSSION

Radiation accidents could be classified according to the range of estimated physical dose, biological dose, clinical manifestations and primary laboratory test results, especially the clinical manifestations at the early stage. Case A received asymmetrical irradiation for about 20 hours and then began to vomit 4 hours after exposure. She vomited for 21 times lasting for 7 hours. She was considered as a patient suffering of severe bone marrow form of ARS according to the radiation dose, clinical symptoms and hematological signs.

For all three patients, the relationship of the vomiting time and the estimation of radiation dose was different from that mentioned before. The vomiting time was related with not only the dose of radiation, but also the radiation dose rate. When the dose was deduced from the vomiting time (see Table 2) there was some dose-effect relationship, but the radiation dose rate was more important. According to the summary data of Baranov, the relationship between beginning vomiting time (Tp, h) and dose rate (p, GYh) is: Tp = 2.48p^0.50. The time of beginning vomite of these three patients were not coincident with the results acquired according to this equation. The reason of this may be that there were so many uncertain factors, for example, the distance between the victims and the radiation source was not definite when they acted in the room. However, one of the most important factors is the uniformity coefficient of accidental exposure to radiation. “dic + r” showed Poisson’s distribution in cells at low LET uniform radiation, \(|u| < 1.96\), the value of \(\sigma^2 / \bar{y}\) near 1, however, “dic + r” would not show Poisson’s distribution in cells at non-uniform radiation, \(|u| > 1.96\). According to the results of Table 6, case A and B received non-uniform radiation, this may be the main reason why their symptoms and signs were not coincident with the data of Baranov.

Comparing to the accidents happened before in China, patients in this accident presented characteristics as follow: (1) The critical stage came earlier than at other patients in former accidents, i.e. at case A on the 9th day and case B...
on the 17th day. The manifest illness phase of case A lasted for 25 days.

(2) Reviewing their anamnesis, they were all carriers for hepatitis B virus before the accident. Immune dysfunction is considered to be the reason why hepatitis B became active in the course of ARS. Liver dysfunction was appeared along with immune dysfunction when the leukocytes decreased sharply after exposure, and then, liver dysfunction was mended along with the recovery of immune dysfunction when the leukocytes increased at the recovery stage. It was showed clearly in Fig. 3.

(3) All three patients had latent infection of scabies because of their bad rural sanitation. Following the radiation exposure their active scabies manifested due to the decrease of their immune function.

(4) Menses of patient A had just been due in the manifest illness phase. To prevent haemorrhage at the menses, 100 mg propionate testosterone was given i.m. for seven days before the expected time of the menses. Thus, the menses was efficiently postponed for about a week.

(5) The major pathological change of the bone marrow form of ARS was the hematopoietic dysfunction. GM-CSF is helpful for the recovery of the bone marrow function. GM-CSF had been used effectively in the Chinese radiation accident in Henan, like to other radiation accidents in Belarus, Brazil, China, Iran, Israel, Salvador, Thailand and Turkey. EPO was used for the patients in this accident for the first time. It was proved that it was useful to treat anaemia and could improve the recovery of reticulocytes.

(6) The wound on the right knee of patient A that had appeared before the accident presented a difficulty for the treatment in the critical stage. Efficient treatment for prevention of new infection and hemostasis ensured the healing of the wound smoothly.

Cytokines and other multicausal agents can stimulate the proliferation and differentiation of residual hematopoietic stem and progenitor cells. Recently, the combination of hematopoietic growth factors and/or pleiotropic factors are more acceptable in the treatment of victims in radiation accidents.6,7 The combination of GM-CSF and EPO was administrated to patient A in this accident and it has proved efficient. The target cells of GM-CSF include granulocytes, macrophages, eosinophilic granulocytes, megakaryocytes and multipotential hematopoietic progenitor cells, so GM-CSF was chosen firstly. G-CSF is more efficient to the proliferation of granulocytes, so it was used more common in the treatment of radiation accidents recently. Granulocyte colony-stimulating factor (G-CSF) and GM-CSF were recommended by the consensus treatment guidelines have been established in Europe and the United States2,8 to be administrated soon after radiate. And the combination-use of G-CSF, GM-CSF, interleukin(IL-3 or IL-11), thrombopoietin (TPO)/megakaryocyte growth and development factor (MGDF) will be more acceptable in the future.9

In conclusion, the treatment for patients in this accident was successful by the effort of the medical staff, and we have accumulated valuable data for emergency treatment in radiation accident. However, we had learned important lessons from this radiation accident. The cause of this accident was the insecure storage of spent radiotherapy sources like some earlier accidents.9,10 It reminds both the health authorities and the radiation protection services that the management of radiation sources should be improved. Nowadays atomic energy has been widely used in industry, agriculture, medicine, research and we face a potential risk of radiation accidents due to disordered management of radiation sources, especially in developing or disintegrating countries.11 Severe radiation accidents are relatively rare. Thus, when medical doctors in primary care are confronted with such an unexpected radiation exposure, they may be unable to offer professional help because of the lack of sufficient expertise.12 Hence, we should perform more regular and intensive medical training in this subject to general practitioners and also to medical specialists all over the country. Additionally, health education of the public also about the causes and consequences of a possible radiation damage needs urgent improvement.

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