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Chromosome aberrations in accidentally irradiated human subjects*

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放射線事故被曝者の末梢白血球染色体異常

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事故によつてX線および γ 線に被曝した2例および濃縮ウランを吸入した3例の放射線取扱者について末梢白血球を培養してその染色体異常を調べた。前2者は被曝後1年程度経っていたが血液

試験管照射の結果から推定される程度の染色体異常を示した。後3者では推定線量は1レム以下であるのに40—50ラドの被曝に相当する頻度の異常が認められた。

1. Introduction

We recently studied the chromosomes in peripheral leukocytes of a number of otherwise normal men who accidentally received whole-body irradiations. The first group of cases consisted of persons exposed to external irradiation of X or γ -rays but the second group to internal irradiation with enriched uranium (3.2%). Incidences of chromosome aberrations observed in the first group were in the range expected from the dose-effect relationship reported by Bender and Gooch (1), Norman et al. (2), and Kelly and Brown (3) but those in the second group were quite unexpected. Importance of chromosome study in case of accidental exposure as a means of medical examination will be emphasized though medical implications of chromosome aberrations observed has not yet been explored.

2. Materials and Methods

Age, radiation history and past radiation dose of cases to be reported and quality and dose of radiation in accidental exposures are shown in Table 1. Two cases in the first group were exposed to external irradiations of X- and γ -rays and studied 12 and 10 months after the irradiation respectively. Doses were estimated from the reading of a fluoroglass dosimeter carried on the breast in case A and calculated

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Table 1. Radiation history and exposure conditions of accidentally irradiated radiation personnel.

Case*	Age in year	Past radiation history		Accidental exposure	
		Duration of radiation work	Accumulated dose recorded	Quality of radiation	Estimated dose
A	20	about 1 y	0	250 Kvp X-ray	66R
B	36	// 2/ 1 y	0	⁶⁰ Co γ -ray	40R
C	32	// 5 y	128 mrem	U (3.2% enriched)	3.9mg($4.6 \times 10^{-3} \mu\text{Ci}$)inhaled
D	50	// 6 y	936 //	U (//)	2.2mg($2.6 \times 10^{-3} \mu\text{Ci}$) //
E	32	// 5 y	425 //	U (//)	3.4mg($4.0 \times 10^{-3} \mu\text{Ci}$) //

* All of them are males. ** From external irradiation.

from the distance and duration assumed for the man to be staying near the radiation source in case B. Case A was exposed to leakage radiation from a X-ray tube housing thus receiving non-uniform exposure and case B to nearly naked γ -ray source of ⁶⁰Co. Both cases were studied again five months later.

Three cases in the second group (Case C, D and E) inhaled uranyl fluoride, UO₂F₂, derived from uranyl hexafluoride in air at an accident and supposed to be exposed to internal irradiation. The amount of uranium inhaled was estimated from urinary excretion for one month after the exposure measured by a fluorophotometric method. The radiation dose seemed to be highest in case C, intermediate in case E and lowest in case D. The blood samples were taken fourty days after the exposure. In all these five persons chromosomes were studied in cells from blood cultures the latter being prepared following the technique of Moorhead et al. (4), the final spreading of the cells being achieved by air-dry method. Number of chromosomes and gross anomalies were counted under a microscope. Karyotypes were prepared in some of the cells according to the Denver classification.

All cases were under the supervision of radiation control officers respectively. Personal radiation monitoring with film badge and health examination including hematological test have been carried out routinely.

3. Results

Erythrocyte count, hemoglobin content, and leukocyte count of the peripheral blood shortly after the accidents are shown in Table 2. All values were in the normal range except erythrocyte count and hemoglobin content in case D. Case D seemed to be suffered from anemia since he started his radiation work in 1960.

Distribution of chromosome counts and incidence of gross anomalies are shown in Table 3. For

Table 2. Hematological findings shortly after the exposure

Case	A	B	C	D	E
Days after the exposure	17	3	8	8	8
Erythrocyte count $10^4/\text{mm}^3$	480	574	450	410*	490
Hemoglobin content/dl	16.0	19.0	14.7	12.6	14.4
Leukocyte count/ mm^3	5250	6700	7300	5600	8500

* Remains around $400 \times 10^4/\text{mm}^3$ since 1960 when he started his radiation work

Table 3a. Distribution of chromosome counts

Case	Chromosome count									Percent aneuploidy
	43	44	45	46	47	48	49	4n	Total	
A (1)			2	67	6	1		3	79	11.8
(2)	1	1	3	94	1				100	5.1
B (1)	2		2	38	7				49	19.1
(2)		2	8	88	1				99	11.1
C			3	92	4			1	100	7.1
D	1	1	3	147	3				155	4.6
E		2		97	1				100	3.0
Control M (28)	1		1	114	3				119	3.4
// M (44)	1		2	134	1	1			139	2.9

Table 3b. Incidence of gross anomalies of chromosomes

	Isochroma- tid break	Chromatid gap or break	Fragment or acentric	Dicentric chromosome	Ring chr- omosome	Large ac- rocentric	Total number of anomalies	Percent abnormal
A	2	1	4	2	0	0	9	11.4
	0	4	4	1	0	0	9	9.0
B	2	1	1	2	0	0	6	12.2
	3	3	0	0	0	0	6	6.1
C	0	6	3	1	0	0	10	10.0
D	1	2	1	0	0	1	5	3.2
E	1	6	4	0	1	1	13	13.0
Control M* (28**)	0	1	0	0	0	0	1	0.8
// M* (44**)	0	3	0	0	0	0	3	2.2

* sex; male ** age in year

the calculation of percent aneuploidy, cells with chromosome counts smaller than 43 and tetraploid cells have been excluded from the number of aneuploid cells. Percent aneuploidy was increased in the case of external irradiation. Dicentric chromosome observed in case A and B seemed to be reduced with the time after irradiation. Dicentric, ring and abnormally large acrocentric chromosomes were also observed in case C, D and E though the estimated radiation doses were much less than in case A and B. In case D a minute chromosome presumably belonging to group G chromosomes was found. Incidences of chromatid gap or break were in the normal range in case A, B and D but slightly high in case C and E. Dicentric and ring chromosomes have never been found in 258 cells of healthy persons as controls.

Karyotypes with a dicentric chromosome in case A and C and that with a ring chromosome in case E are shown in Fig. 1. The cells with a dicentric chromosome appear to be X₁ cells according to the definition by Buckton and Pike (5), that is the cell which from the nature of their contained abnormality is judged to be in their first post-irradiation division, in case A, though the blood sample was taken 17 months after the exposure.

Fig. 1. Examples of karyotype analysis: In case A a dicentric chromosome accompanied with acentric chromosome might probably be derived from chromosome No. 1 and No. 18. The all belongs to X_1 cells according to the definition by Buckton and Pike (5). Similarly, in case C a decentric chromosome might be derived from chromosome No. 2 and No. 12. The cell belongs to X_1 cells as well since it has a fragment. A ring chromosome was observed in case E.

Case	A			B			C						D			E			F		G		XY	abnormal
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22		
A	↓																	↓						dicentric acentric
C	↓											↓												dicentric fragment
E															↓									ring

4. Discussion

It has been well known that chromosome aberrations in man can be induced by radiation and may persist for many years. However data on single whole body irradiations seems to be meager. Bender (6) summarized his cases of accidental irradiation. Other data have never been noticed by the authors. In the present cases A and B, dicentric frequencies are comparable to those reported by Bender. Increased percent aneuploidy has been reported in irradiated persons (7, 8, 9) but the dose effect relationship has not been established. High percent aneuploidy and its decrease with time in the first group may support the correlation between irradiation and aneuploid cells.

Incidence of chromosome aberrations in the second group appeared to be extraordinarily high. But recently Boyd et al. (10) reported significant increase in cells with structural abnormality in women with the body burden of Ra more than $0.1 \mu\text{Ci}$. According to their calculation, the body burden of $0.1 \mu\text{Ci}$ Ra^{226} corresponds to the exposure to the blood with a dose rate of 0.015 rem/week . Estimated radiation doses in the present cases are far less than 1 rem. Thus the present data on uranium cases and those on Ra dial painters seem to be consistent to each other. But the results can not be interpreted on the dose-effect relationship for external irradiation. Existence of hot spot of high dose rate or the chemical toxicity related with the induction of chromosome aberrations would be considered for the interpretation.

Comparison of the incidences of various chromosomal abnormalities in the second group with those in the first group may suggest the clue to analyse the characteristics of internal irradiation by uranium. In

this comparison, the difference in time interval between exposure and examination should be noted. The fact that no increase in percent aneuploidy was observed in uranium cases but that the dicentrics frequency was in the comparable range in these two groups may suggest that in uranium cases lymphocytes were irradiated in peripheral blood, i.e., after their last division in the body. Increased incidence of chromatid aberrations may support this interpretation if chromatid aberrations can be induced in circulating cells, i.e., in cells at G₂ stage, though contradictory opinion seems to be prevailing on this point. External irradiation may include the irradiation of stem cells as well as peripheral cells. Low incidence of chromatid aberrations in the first group may be due to the elimination of the aberrations induced in periphery. But appearance of X₁ cells in case A seems to be contradictory to this interpretation.

In any way, the present investigation indicates that chromosome study is more sensitive than routine hematological test for the indication of exposure. Studies many months after irradiation can reveal the irradiation. Further studies on the dose-effect relationship under various irradiation conditions on the one hand and those on the medical implications of the aberrations would make the chromosome study more valuable for the supervision of accidental exposure.

5. Summary

Chromosomes in peripheral leukocytes from five radiation workers exposed accidentally to whole-body irradiation; two persons to external irradiation of X or γ -rays and three to internal irradiation with enriched uranium. Incidences of chromosome aberrations observed in the first group were in the range expected from the reported data, but those in the second group were extraordinarily high.

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