THE PHENOMENON OF GENOMIC INSTABILITY IN THE CHILD'S BODY EXPOSED TO PROLONGED RADIATION AT SMALL DOSES AND HEALTH STATE

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In addition to an increased frequency of chromosome aberrations, some researchers have resently reported an increase in general somatic morbidity and in neuropshychical dysadaptation, and a tendency to chronization of diseases in children living on territories contaminated with radionuclides after the accident at the Chernobyl NPP [1]. There is a considerable body of published data about a remote effect of radiation –induction of genomic instability in the offsprings of repeatedly divided cells exposed to radiation at medium and high doses [2,3]. In connection with the fact that destabilization of genome may lead to the above – mentioned states, the aim of the present work has been to assess the reality of this new genetic phenomenon in children exposed to low-intensity radiation at small doses.

Materials and Methods

Cytogenetic examination was carried out in 90 children, constant residents of territories with radioactive contaminations (Novozybkov district, Bryansk region, 16 – 18 Ci/km^2 , ^{137}Cs) exposed to radiation at different stages of ontogenesis: postnatal-irradiated in 1986 (32 subjects), uterine-irradiated in 1986 (15 subjects), born after the accident in 1987-1992 (19 subjects) and in 1994-2000 (24 subjects) from irradiated parents. In 15 children (1986-1998) genomic instability was tested in 3 cell generations using ^{137}Cs γ –irradiation of blood lymphocytes in vitro. The control group was composed of children living in contamination – free regions (16 subjects). The children were examined in the Federal Children's Scientific-Practical Center of Antiradiation Protection (prof. L.S. Baleva) to which they were delivered with various pathologies in the state of health. Cytogenetic preparations, analysis of chromosome aberrations (CA) and sister chromatid exchanges (SCE) were made according to the commonly accepted procedure. Differential staining of sister chromatids with 5 -BDU was used.

Results and Discussion

In all examined groups of children exposed to radiation at different stages of ontogenesis the frequencies of one or other type of radiation-induced CA were significantly increased as compared to the control. No significant intergroup differences in the frequencies of aberrant genomes were revealed although the calculated average doses of technogenic

irradiation from long-lived radionuclides accumulated by the children were different (Fig. 1). Analogous results were also obtained in comparative analysis of the frequencies of other cytogenetic parameters. The absence of dependence of the expression of dysgenomic effects

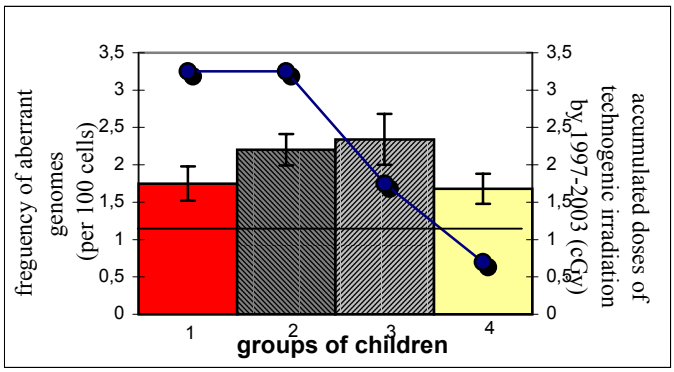

Fig.1. Doses (●) and frequencies of aberrant genomes (■) in children living on territories contaminated with radionuclides: 1 - children born in 1982-early 1986; 2- children born in 1986 (intrauterine irradiation); 3- children born in 1987-1992; 4- children born in 1994-2002
———— - control group

on the level of accumulated doses may be an indicator of both individual radiosensitivity and radiobiological peculiarities of the action of low-intensity radiation at small doses on the organism of children. One of such peculiarities seems to be the transgeneration phenomenon of genomic instability in children of irradiated parents.

In the irradiated children the average frequencies of exchange aberrations of the chromosomal type after testing irradiation in vitro (10 cGy and 100 cGy) were significantly higher than in the control group ($p<0,02$) suggesting increased radiosensitivity of somatic cell genomes in those children (table). An accelerated growth (estimated by the coefficients of

Table. Frequencies of exchange aberrations of the chromosomal type in metaphases of the 1st mitosis of lymphocytes of examined children

Examined children	Dose (cGy)	Echange aberrations of the chromosomal t ype (frequency per 100 cells)
Control (5 subjects)	0 10 100	0 0,33 ± 0,09 8,35 ± 0,39
Born in 1986 (intrauterine irradiation) (5 subjects)	0 10 100	0,32 ± 0,09 0,83 ± 0,14 15,36 ± 1,39
Born in 1987-1991 (5 subjects)	0 10 100	0,50 ± 0,17 1,16 ± 0,25 17,19 ± 2,07
Born in 1994-1998 (5 subjects)	0 10 100	0,16 ± 0,16 0,82 ± 0,33 14,18 ± 2,46

linear regression) of the frequencies of paired fragments+centromeric breaks in 3 successive mitoses of intact and in vitro irradiated (10 cGy) lymphocytes of the children exposed low-intensity radiation as compared with the children of the control group points to induced postradiation chromosomal instability occurring along with reduplication of chromosome aberrations and their preservation in succeeding cell generations. The level of reciprocal SCE in lymphocytes of the 3rd mitosis (in contrast to lymphocytes of the 2nd mitosis) turned out to be significantly higher in the children from the contaminated territories as compared to the children of the control group ($p<0,001$), which is

due to the appearance of genomes with a large number of SCE (fig. 2) and also points to induced genomic instability.

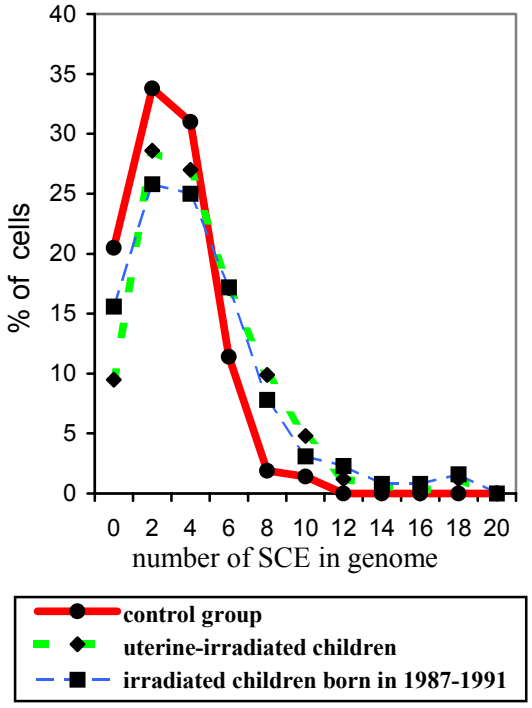

Fig.2. Distributions of lymphocytes of the 3rd mitosis depending on number reciprocal SCE

No essential differences were revealed in the average frequencies and in the distributions of SCE in intact and in in vitro irradiated lymphocytes of the 2nd and 3rd mitoses both in irradiated children and in the control group ($p>0,05$). A wide range of interindividual variability of the frequencies of dysgenomic effects (DE) was observed in intact and irradiated in vitro lymphocytes of the children from radionuclide-contaminated territories. In most of irradiated children with pronounced DE combined abnormalities in the immune system were noted. No significant differences were revealed for CA frequencies depending on the structure of morbidity. In children having disturbances of the central nervous system only the frequency of chromatid fragments was higher than in the group of children having infective-allergic diseases. The highest sensitivity to testing irradiation and most pronounced expression of DE in lymphocytes of the 3rd mitosis were observed in 5 children having the following pathologies: disturbances of the central nervous system, chronic gastritis, chronic pneumonia, extremity malformation.

Conclusion

The data obtained suggest the reality of induction of genomic instability in a growing organism exposed to prolonged low-intensity radiation and the necessity of further studies of the relationships between individual peculiarities of the expression of genomic instability and the health of children**.**

References

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