PRELIMINARY EARLY EVALUATION OF RADIATION ACUTE SYNDROME SEVERITY IN AN ANIMAL MODEL.

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SUMMARY

To improve the knowledge of Radiation Acute Syndrome radiopathological picture , whole body X-rays irradiation at 2Gy of a primate (Cebus apella paraguayanus) used as model has been performed.
Early evaluations of clinical symptoms and dose and damage biological indicators have shown that this primate has given out similar responses to those of man.

INTRODUCTION

All accidental overexposures, particulary Chernobyl and Goiânia, have made evident the need to evaluate even more precisely the severity of the Radiation Acute Syndrome during the first days in order to decide the specific treatment (1,2) A delay in applying a compensatory treatment may be as fatal as an early supplying of a substitutive one(3). The difficulty in evaluating the RAS severity in the shortest time is due to complex accidental circumstances, variability in clinical response and imprecise knowledge of the underlying radiopathological mechanisms.

In order to increase and to improve the information about these infrequent events it is necessary to obtain data from animal models which may reproduce accidental situations.
Cebus apella paraguayanus is a primate wich has shown cytogenetical radiosensitivity similar to that of man and this fact makes this species an interesting potential model (4).
The variables chosen to define therapeutical behaviour were:
a) Dose biological indicators (5) which may predict how deep and severe overexposure has been.
b) Damage indicators which may predict clinical evolution through the insufficiency degree of affected organs.
The information obtained from both indicators is complementary.
Intensive care of the overexposured animal model necessarily implies some analysis of the mechanisms and stages of radiation induced damage.
According to overexposure dose and dose rate, there are different degrees of insufficiency in different tissues, some of which have high vital hierarchy such as the hemopoietic, gastrointestinal and neurovascular ones. Evolution to lethal condition is not frequent when multiparenchymatous insufficiencies are not evident (6).
It is not simple to distinguish deviations of the physiological state from insufficiencies or transitory stages

strictly physiologically generated by the lost of functional balance. It is necessary to develop a repeatable quantificator to diagnose insufficiency and its severity degree, particularly when RAS clinical and humoral expressions appear relatively late.
All above mentioned leads to a wide physiopathological approach such as that applied to Multiple Organ System Failure (7,8).
Radiation Acute Syndrome objective evaluation needs to take into account severity and chronometry of dose and damage biological indicators.
The aim of this work is to establish multiple correlations between dose and damage indicators observed during the first 2 or 3 days to in order to:
- Found therapeutic decisions.
- Interpret radiopathological mechanisms.
- Train medical staff to assist accidentaly overexposured people.

MATERIAL AND METHODS

An adult female primate has been X-Rays whole- body irradiated with the following exposure conditions: 200 Kvp. 10 mA, 0,25 Gy/min.
Previous dosimetry with a phantom and TLD dosimeters have been performed.The entrance dose has been 2 Gy and oulet dose has been 1.8 Gy.
A LD50 of approximately 4 Gy is supposed.

RESULTS

1) Dose indicators

a) Cytogenetical Dosimetry: dicentrics + rings/cell has been 0.38 dic.+rings/cell (human frequency: 0.34 dic + rings/cell).

b) Taurine quantification: in 24 hours taurine in plasma had not increased as expected, whereas a non identified compound, next in its position in the chromatography column, had.

c) α-amylase has doubled in 6 hours, while TGO, CPK and LDH have increased 24 hours post irradiation 4,20 and 10 times respectively.

2) Damage indicators

a) Blood parameters

-Peripheral blood: the kinetics of blood cells concentration related to time for equal dose, has been similar to that of man, though it has shown a more marked tendency to cell depletion, except for platelets.Neutrophiles increased 260%, 24 hours later.During this time lymphocytes have decreased 50%. From this moment neutrophiles have reached the lowest value (20%) in 20-22 days. Lymphocytes have reduced to minimal value (14%) 8 days post-irradiation.

Platelets have increased 175% in 24 hours for later fluctuations between 75% to 125% of control values.
Reticulocytes have increased 4% in 48 hours; they have reduced to minimum (0.12%) the 6th. day post-irradiation and have fluctuated during follow-up between 0.5% and 1% .

-Bone marrow: Previous to irradiation,slides for mononuclear cells recognition, reccount and recovering have been performed (24 E6 cells/ml.).
A few hours after irradiation cell changes had not been observed yet. On the 14th. day post-irradiation an 370% lymphocyte increase and megakaryocytes disappearance has been observed.
Cultures from a withdrawal made some hours after irradiation have not developed colonies; only a fibroblastic type monolayer has been formed.
The cultures set-up on the 14th. day post-irradiation has developed CFU-GEMM colonies, whose size was similar or slightly inferior to that of man, particularly erytrocytes "burst" type, having few hemoglobinized cells.
More than 50% of granulocytes colonies have inmature cells.
The number of colonies has decreased in all lineages except for some very compact macrophagic colonies, whose number has increased.
The cell stroma was abundant till 14th. day; then its decreased till all cells disappeared one month later.

b) Metabolic parameters

The acid-base balance has moved towards metabolic acidosis. Chloride has significantly increased. Glucemia has doubled in 24 hours and at the same time uremia has decreased.

c) Endocrinological parameters

Premature luteinization of the growing folicule has been observed, with a later insufficient luteal phase.
Thyroid parameters have ranged within control values. T3 has had greatest fluctuations.

CONCLUSIONS

A preliminary assay of primate acute overexposure evaluation has given out similar responses to those of man, even though hemopoietic radiosensitivity (except for platelets) has been more marked than human.
Cell kinetics has been similar.
Deep changes in bone marrow cell stroma has been observed. However, in 50 days recovery has been complete.
The stable platelet concentration is associated with high megacaryocytes proliferation.
Metabolic parameters and acid-base state have been modified with the same trend as that of man but more highly marked.
There has been an outstanding premature luteinization of growing folicule.

Primate has not shown clinical manifestations during the period of observations.
The handling of the animal model has been an adequate stage of operative trainning for medical personnel who treat overexposured people.

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