relationship was found between the frequency of apoptotic lymphocyte and dose.

These data show a trend towards increase of the numbers of apoptotic lymphocytes with increasing dose. In addition, there were significant peaks on apoptosis induction at 4 and 6h after irradiation, and the morphological findings of the irradiated groups were typical apoptotic cells that were hardly observed in the control group.

Thus, apoptosisinduction assay in human peripheral lymphocytes could be a useful biological technique to evaluate radiosensitive target organ injury. Since the apoptosis induction assay is simple, rapid and reproducible, it will also be a good biological technique for the early dose prediction of many victims simultaneously inaccidental multi-casualties.

Key word: Apoptosis induction low dose; early dose prediction; peripheral lymphocyte; ionizing radiation; multi-casualties; biodosimetry

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P#24

Mini-pig Model Simulating Radiation Accidents for Evaluation of Acute Radiation Syndrome

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Introduction

Absence of a realistic model of accidental irradiation makes difficult the evaluation of new therapeutic strategies. There have been some limitations that the findings of rodents may be different from humans and non-human primates are expensive for intensive studies. Purpose of this study is to evaluate whether mini-pig radiation model would be corresponding to humans and acceptable for evaluating acute radiation syndrome and therapeutic trials for victims of radiation accidents. Here, we clinically and pathologically evaluated new animal model using mini-pigs that has physiologically and functionally close to humans, with special reference to hematopoietic and intestinal changes that are the most important cause of death in radiation accidents

Methods

Minipigs (6month-old, body weight 20kg) were irradiated from X-ray accelerated by microtron (simulated dose 2Gy, 4Gy, 7Gy and 12Gy) in whole body. The simulated dose was compared to radiation dose detected by TLD. Blood cell count and bone marrow biopsy findings were serially examined by

time sequence. Blood counts were daily evaluated for each blood cell and were compared with bone marrow findings from sequential bone marrow trephine biopsy at 30minutes, 18 hours, 3 days, 7 days, and 14 days after whole body irradiation. Gastrointestinal changes were evaluated by sequential endoscopic biopsies from stomach, jejunum, and rectum.

Results

Mini-pigs irradiated by 12Gy died due to sepsis and GI syndrome with bowel perforation at the period of 8 days to 11 days. Deaths by 7Gy irradiation might be attributed to hemorrhage and sepsis. In both 7Gy and 12Gy, E. coli was cultured from postmortem blood. Animals irradiated by 2Gy and 4 Gy survived. Blood cell counts showed quite similar pictures to humans according to time sequence. Mini-pigs irradiated by 7Gy and 12Gy showed abrupt decrease of WBCs from 30 minutes until 14 hrs after irradiation, with following slow decrease to less than 500/μl. RBC counts abruptly decreased until 14hrs and were slowly recovered. Platelet counts abruptly decreased until 36hrs with subsequent transient recovery and finally decrease to bottom. With 2Gy and 4Gy, WBCs showed relatively slow decline. In the serial observation of bone marrow section, CD34+ progenitor cells and Ki67+ proliferating cells were well correlated with radiation dose. In gastrointestinal system, jejunal mucosa was the most vulnerable and exhibited similar histologic changes to humans. Both hematopoietic and intestinal findings of minipigs were quite similar to those of humans.

Conclusion

These observations suggest that mini-pig model would be appropriate as an animal model corresponding to humans. It might be effective in therapeutic trials for better survival on victims of radiation accidents and nuclear terrorism.

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P#25

Suppression of Azoxymethane-Induced Colorectal Tumors in *iNOS* -/- C57BL/6J Mice.

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Nitric oxide (NO) is known to be involved in the pathogenesis of colorectal cancer in both rodents and humans. iNOS is responsible for the over production of NO in a variety of parenchymal cells and macrophage. In the present study we utilized iNOS gene knockout mice to investigate the role of iNOS on chemically-induced colorectal polyposis. Azoxymethane (AOM) at a dose of