PERSISTING RING CHROMOSOMES DETECTED BY MFISH IN LYMPHOCYTES OF A CANCER PATIENT- A CASE STUDY

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Background: We report the case of an 84 years old prostate cancer patient with severe side effects after radiotherapy in 2006. He was cytogenetically analysed in 2009 and in 2012 in a comparative study for individual radiosensitivity of prostate cancer patients. Among 40 investigated individuals only this patient showed clonal aberrations. Ring chromosomes were detected in the range of 21-30 % of his peripheral lymphocytes. Three years before radiotherapy of prostate cancer this patient received 5 cycles of 5-fluorouracil/folic acid for chemotherapy of sigmoid colon carcinoma in 2003.

Material und Methods: Blood samples were irradiated *ex vivo* with Cs-137 γ-rays (0.7 Gy/min) in the G_0-phase of the cell cycle. 100 FISH painted metaphases were analysed for control and irradiated samples each. Multicolour in situ hybridisation techniques like mFISH and mBand as well as MYC locus, telomere and centromere painting probes were used to characterize ring metaphases. Metaphase search and autocapture was performed with a Zeiss Axioplan 2 imaging microscope followed by scoring and image analysis using Metafer 4/ISIS software (MetaSystems).

Results: In 2009 chromosome 8 rings were found in about 25 % of lymphocytes. Rings were stable over time and increased to about 30 % until 2012. The ring chromosome 8 always lacked telomere signals and a small amount of rings displayed up to four centromere signals. In aberrant metaphases 8pter and 8qter were either translocated or deleted. Further analyses revealed that the breakpoint at the p arm is localized at 8p21.2-22. The breakpoint at the q arm turned out to be distal from the MYC locus at 8q23-24.

Conclusions: We hypothesize that the ring chromosome 8 has been developed during the 5 FU/folic acid treatments in 2003. The long term persistence might be due to clonal expansion of a damaged but viable hematopoietic stem cell giving rise to cycling progenitor cells that permit cell survival and proliferation.

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