Oncothermia treatment induced immunogenic cancer cell death – New possibilities for therapeutic cancer vaccine

Gabor Andocs[1], Csaba Kovago, Nora Meggyeshazi, Oliver Szasz
(1) Department of Radiological Sciences, School of Medicine and Pharmaceutical Sciences, Toyama University, Japan

Introduction: Oncothermia method (OTM) is a long time applied tumor treatment modality in the human clinical practice. Experimental results showed that OTM can effectively and selectively destroy the tumor tissue, but recent investigations revealed some unusual immunological aspect of OTM. The immunogenic characteristics of immunogenic cell death (ICD) are mainly mediated by damage-associated molecular patterns (DAMPs). We summarize our results regarding the OTM induced ICD in Study I. Based on these observations we hypothetised a method for in vivo, in situ, personalized tumor vaccination. To prove this theory we designed an other study (Study II.) using immunocompetent animal model.

Materials and Methods: Study I. Animal model: HT29 cell line xenografted to both femoral regions of BalbC/nu/nu mice were treated on one side with a single shot OTM treatment for 30 minutes of -1 cm diameter tumors. Sampling was made after 0, 1, 4, 8, 14, 24, 48, 72, 120, 168, 216 h in 3 mice each group by keeping 5 animals as sham treated controls. Histomorphological analysis (HMA) and immunhistochemistry (IHCH) and TUNEL assay were performed to analyze samples. Study II. C26 mouse colorectal adeno-carcinoma cell line allograft was applied to both femoral region of BalbC mice. One of the lesions (right leg) were treated with a single shot mE HT treatment for 30 minutes, the other Cleft leg) was kept for individual control of every animal. The groups formed for parallel study were: (1) Sham control; (2) injected with 7.5 ml/kg Marsdenia tenacissima, intraperitoneal; (3) mEHT treated; (4), combined mEHT and Marsdenia tenacissima injection 30 min before mEHT. Various histomorphologic and immunhistochemical analysis, TUNEL assay were tested in treated and control tissue samples.

Results: Study I. Oncothermia treatment can induce programmed cell death (apoptosis) in the tumors. Tunel assay proved the apoptotic cell death. OTM treatment induced cell death is higly immunogenic, showing many aspects of the key molecular pattern dynamic changes what is characteristic of ICD. OTM treatment can induce strong and very unusual local immune reaction at the site of the treatment. Study II. OTM treatment, induced an apoptotic tumor death. The Marsdenia tenacissima injection was not effective alone, however the combined therapy was effective far from the OTM localization.

Conclusions: These experimental findings can be the strong scientific theoretical basis to develop a special oncothermia treatment-based immunotherapeutical approach to fight against not just solitaire tumors, but malignant metastatic disease.