

P55 - Treatment of rabbit VX2 liver cancer by irreversible electroporation

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Irreversible electroporation (IRE) is a method of non-thermal focal tissue ablation that uses electrical currents to irreversibly permeabilize cell membranes. This technique is already being used to treat different tumors such as liver tumors. The aim of the current study is to assess the efficacy of IRE treatment in the rabbit VX2 liver cancer model. A total of 15 New Zealand white rabbits were used in the present study. In 9 animals, 1 mm³ of VX2 tumor was implanted into the middle lobe of the liver. After 9 days of tumor growth, animals were randomly assigned to a tumor control group (n = 6) and an IRE treatment group (n = 6). IRE ablation was performed on IRE treatment group at 1500 V/cm electric field strength using a versatile high-voltage generator and 2 cm diameter parallel-plate electrodes. One and 8 days after treatment was performed, 3 treated and 3 tumor control animals were sacrificed. In addition, the same IRE treatment was performed on 3 non-implanted rabbits (IRE control group) which were sacrificed 19 days after treatment. The treated / implanted lobes were collected and fixed in 10% formalin. Procedures were approved by the Animal Experimentation Ethical Commission, University of Zaragoza (permit number: PI35/22). Formalin-fixed tissues were trimmed, the volume of the tumor was determined and samples were processed according to standard histopathological procedures. In addition, tissue sections were processed for immunohistochemistry using the primary mouse monoclonal antibodies anti-ki67 and anti-p53 (Dako/Agilent, CA, United States). One day after IRE treatment, the cut surface of the IRE-ablated zone was characterized by an irregular mixture of white, discolored, and dark areas. Microscopic evaluation of the IRE-ablated tissue showed areas of coagulative necrosis surrounded by large areas of inflammatory cells and congestion. Immersed in the ablated tissue, sheets of viable tumor cells (Ki-67 and p53 positive) were observed. Eight days after IRE treatment, 2 animals showed a well delineated tumor (volume of 0.25 and 0.55 cm³) composed of large sheets of viable tumor cells with necrotic areas of various sizes. The tumors were surrounded by IRE-ablated liver tissue characterized by the coexistence of areas of necrosis with areas of repair. In one animal, no tumor was observed either macroscopically and microscopically in the IRE-ablated liver tissue. In the IRE control samples, treated tissue was loose completely the characteristic liver architecture and was composed of reparative tissue. Under the conditions of the present study, IRE treatment did not completely ablate the VX2 liver tumor. A previous report using multiple IRE applications resulted in complete ablation of the VX2 tumor [1]. Differences in electrodes and applied electric field parameters may account for differences in treatment efficacy. In the present study, parallel plate electrodes were used, which generate a more homogeneous electric field distribution and allow large volumes to be treated more homogeneously. Differences between the electrical conductivity of tumor and normal liver tissue may also explain treatment failure.

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