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P221 Boron neutron capture therapy for experimental bladder cancer: Systemic or intravesical approach

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Introduction & Objectives: To investigate the antitumoral and pro-inflammatory effect of Boron Neutron Capture Therapy (BNCT) generated by neutron irradiation following systemic or intravesical Boron administration, and to compare it with conventional radiotherapy (RT) in an orthotopic bladder cancer (BC) model.

Materials & Methods: Sixty-four Wistar rats were used; half of them were exposed to carcinogen for 16 weeks to induce BC. In the 22nd week, 4 animals with and 4 without BC induction were sacrificed following systemic (2 each) or intravesical (2 each) borophenylalanine (BPA) administration, and Boron measurement in bladder tissues was performed with Inductively Coupled Plasma-Mass Spectrometry (ICP/MS). The remaining animals were categorized as follows: control (n=4), control+RT (n=8), control+BNCT-Syst (n=8), control+BNCT-IV (n=8), cancer (n=4), cancer+RT (n=8), cancer+BNCT Syst (n=8), and cancer+BNCT-IV (n=8). All irradiations were done in the 23rd week at Istanbul Technical University MARK TRIGA-II reactor and Kocaeli University Radiation Oncology department Sacrification of survived animals was performed at the 25th-28th weeks, and bladder and perivesical tissues were collected. WHO 2016 classification was used for staging and bladder weight was used for tumor burden evaluation. H&E and immunohistochemistry determined the number of pro-inflammatory cells and TNF-a expressions within them. Additionally, TNF-a expressions in all bladder tissues among all cancer groups were examined by Western blot (WB). Finally, perivesical tissues were evaluated for inflammation.

Results: The levels of boron in carcinogen-received animals were 4.39 ppm for systemic and 10.89 ppm for intravesical administration, whereas the levels in those that did not received carcinogen were 1.51 ppm for systemic and 1.82 intravesical administration. Papillary urothelial carcinomatous lesions were observed in 100%, 100%, 87.5%, and 71.4% of the Cancer, Cancer+RT, Cancer+BNCT-Syst, and Cancer+BNCT-IV groups, respectively. The decrease of tumor burden in Cancer-RT, Cancer+BNCT-Syst, and Cancer+BNCT-IV groups compared with the Cancer group varied from 15 to 25%. The incidence of bladder inflammation in all animals receiving RT, and systemic and intravesical BNCT was 50%, 33.3%, and 20%, respectively. In the intravesical BNCT groups, the rate of inflammation was 7.7% in colon and 6.6% in uterus, while it varied from 25% to 37.5% in the systemic BNCT groups and RT groups. Immunohistochemistry and WB revealed that TNF-a expressions were lower in Cancer+BNCT-IV group compared with Cancer-RT and Cancer+BNCT-Syst groups.

Conclusions: Like RT, systemic or intravesical BNCT has resulted in a partial decrease in the tumor burden. Lower adverse effects had also been observed in BNCT following intravesical BPA administration. Our study suggests that intravesical BNCT may be a potential radiotherapeutic alternative in BC in the future.