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Giant Cancer Cell Formation: A Link between Cell Survival and Morphological Changes in Cancer Cells

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Abstract : Introduction: Giant cancer cells (GCC) are common in all types of cancer, especially after poor therapy. Some specific features of such cells include ~10-fold enlargement, drug resistance, and the ability to propagate similar daughter cells. We used murine NK/Ly lymphoma, an aggressive and fast growing lymphoma model that has already shown drastic changes in GCC comparing to parental cells (chromatin condensation, nuclear fragmentation, tighter OXPHOS/cellular respiration coupling, multidrug resistance). Materials and methods: In this study, we compared morpho-functional changes of GCC that predominantly show either a cytostatic or a cytotoxic effect after treatment with drugs. We studied the effect of a combined cytostatic/cytotoxic drug treatment to determine the correlation of drug efficiency and GCC formation. Doses of G1/S-specific drug paclitaxel/PTX (G2/M-specific, 50 mg/mouse), vinblastine/VBL (50 mg/mouse), and DNA-targeting agents doxorubicin/DOX (125 ng/mouse) and cisplatin/CP (225 ng/mouse) on C57 black mice. Several tests were chosen to estimate morphological and physiological state (propidium iodide, Rhodamine-123, DAPI, JC-1, Janus Green, Giemsa staining and other), which included cell integrity, nuclear fragmentation and chromatin condensation, mitochondrial activity, and others. A single and double factor ANOVA analysis were performed to determine correlation between the criteria of applied drugs and cytomorphological changes. Results: In all cases of treatment, several morphological changes were observed (intracellular vacuolization, membrane blebbing, and interconnected mitochondrial network). A lower gain in ascites (49.97% comparing to control group) and longest lifespan (22+9 days) after tumor injection was obtained with single VBL and single DOX injections. Such ascites contained the highest number of GCC (83.7%+9.2%), lowest cell count number (72.7+31.0 mln/ml), and a strong correlation coefficient between increased mitochondrial activity and percentage of giant NK/Ly cells. A high number of viable GCC (82.1+9.2%) was observed compared to the parental forms (15.4+11.9%) indicating that GCC are more drug resistant than the parental cells. All this indicates that the giant cell formation and its ability to obtain drug resistance is an expanding field in cancer research.

Keywords : ANOVA, cisplatin, doxorubicin, drug resistance, giant cancer cells, NK/Ly lymphoma, paclitaxel, vinblastine
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