B-blockers as a Novel Management of Osteosarcoma: Pros and Cons emerged from an in vivo Experimental Model

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INTRODUCTION:

β-Adrenergic are Gs-protein-coupled receptors expressed in various types of cancers. Several studies demonstrated that beta-blockers are regulating cancer cellular proliferation, migration, apoptosis, ECM invasion, MMPs/ cytokines activation, and angiogenesis. Recent studies reported that patients treated with neoadjuvant chemotherapy and b-blockers had low risk of recurrence and metastases. Aim of our study was to examine if the administration of β-blockers converts the osteosarcoma growth and the metastatic potential *in vivo* after the administration of highly metastatic 143B human osteosarcoma (OS) cells in SCID mice.

METHODS:

30, 6-9 weeks old, mice, separated into 6 groups were used. On day 1, 143B cells were injected in the tail vein (subgroup 1) or tibia intramedullary (subgroup 2). The control (A1, A2) groups were composed of mice that didn't receive β-blockers, while B1,2 mice were treated with propranolol for 30 days. Finally, in C1 (tibial application of OS) and C2 (tibial application of OS plus propranolol) groups, amputation of the affected joint was performed on the 5th day. On day 30, the mice were euthanized and radiographic, pQCT and whole-body scintigraphy scanning were performed.

RESULTS:

The survival rate was 95%. The amputation was successful without any complications. The size of the tumors was less than 2.00 cm X 2.00 cm. Imaging examinations displayed altered number of local osseous and skeletal or lung metastatic potential in all groups receiving b-blockers. However, X-ray, PET-scan, morphogenetic and histological analysis demonstrated that b-blockers induced lung metastases after the administration of OS cells in via tail vein.

DISCUSSION AND CONCLUSION:

Clinical significance of b-blockers in the management of primary cancers of bones has not been elucidated yet. Our research displayed that propranolol modifies the expression of OS and metastatic potential. Regarding that 30% of OS patients are suffering from hypertension our results showed that in aggressive forms of OS with increased hematogenous metastatic potential, the use of b-blockers should be carefully considered.