Association of Testosterone with Metastasis in Brain Tumor Cells

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***Abstract*—**Previous studies have shown that metastasis in cancer cells is influenced by sex steroid hormones. The aim of this study was to investigate the effects of cytotoxic dose of testosterone on glioblastoma (A172) (brain tumor) cells in cell culture. A172 cells were exposed to cytotoxic dose (0.1 mg/ml) of testosterone solution. Real time PCR was used to measure Bax gene expression level. Our results indicated that exposure to 0.1 mg/ml of progesterone led to significant decrease in antimetastasis KAI1 gene relative expression level (P<0.001). Our findings indicated that cytotoxic dose of testosterone decreases KAI1 gene expression level in A172 cells; according to which, cytotoxic dose of testosterone may have a potential to induce metastasis in A172 cells.

***Index Terms*—** Testosterone, Glioblastoma, Metastasis

I. Introduction

Among androgens testosterone plays a pivotal role in the maintenance of accessory organs and is involved specifically in the regulation of normal spermatogenesis [1]. There is a growing body of evidence for the importance of gonadal hormone action in the function of the reproductive and other systems, including bone and cardiovascular system. Sex hormones (androgenic, estrogenic, and progestinic) are produced by both sexes, though the quantity and mode differ by sex and age. [2] It has also been shown that testosterone may involve in cancer development or treatment. [3], [4]

Glioblastoma (GBM) is the most aggressive primary tumor of the central nervous system and accounts for ~ 50% of all adult gliomas. Current management is based on cytoreduction through a combination of surgery, radiation therapy, and chemotherapy. [5] Glioblastoma the deadliest type of brain cancer establishes a synergistic relationship with its local environment to support tumor growth, migration, and therapy resistance. Glioblastoma cells remodel the normal brain microenvironment and in turn this altered microenvironment supports tumor growth. [6] Previous studies also have shown that sex steroid receptors are existing in brain cells including astrocytes indicating that sex steroids may have regulatory role in brain cells function and development. [7]

The studies concerning with the effects of testosterone on cancer cells have mainly focused on the association between testosterone and prostate cancer development. In this study we have examined effects of testosterone on glioblastoma cells metastasis potential in cell culture.

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II. Material And Methods

A172 cells (glioblastoma cell line) were purchased from National Cell Bank of Iran (Pasteur Institute, Tehran, Iran). Cells were grown and incubated in standard situation. Then, cells were sub-cultured into 75cm2 flasks, 96-well plates or 6-well plates. Cytotoxicity of different doses of the testosterone was assayed using MTT method. Real time PCR was used to measure KAI1 gene expression level. Analyses were conducted using the SPSS20 and ANOVA.

III. Results

MTT assay showed that 0.1 mg/ml of testosterone has cytotoxic effects on A172 cells. Exposure to 0.1 mg/ml of testosterone led to significant decrease in antimetastasis KAI1 gene expression level in A172 cells compared to control cells (P<0.01) (Figure I).

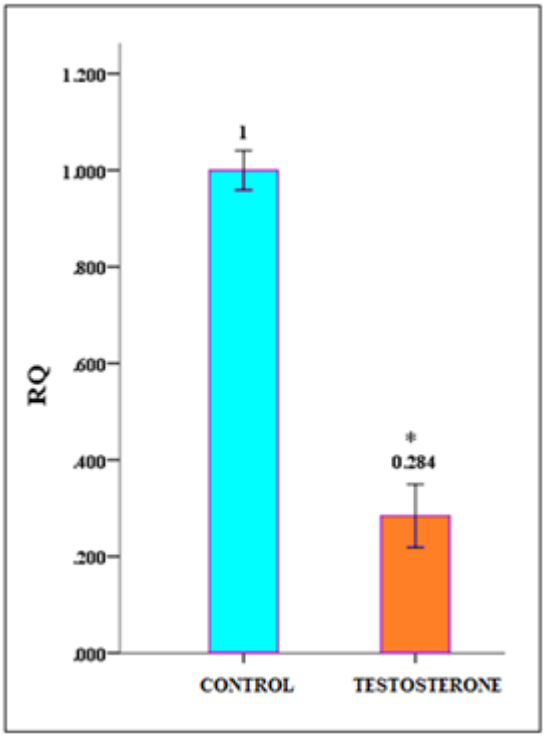

Fig. 1: KAI1 gene expression level in A172 cells exposed to cytotoxic dose of testosterone compared to control group. * indicates significant difference compared to control group at P<0.001.

IV. Discussion

We have shown that testosterone may have a potential to induce metastasis in brain tumor cells. Evidences indicate that sex steroids are implicated in development and progression of primary brain tumors. The findings are suggesting greater prenatal testosterone and lower prenatal estrogen exposure in brain tumor patients. [8] A recent study demonstrates that testosterone transiently impacts cerebrovascular physiology in adult male mice which should help gain new insights into neurological and metabolic diseases linked to hypogonadism in men of all ages. [9] The research has shown that treatment with testosterone propionate can develop local tumors and promote metastasis through lymphatic channels to the lungs. [10] Prospective studies show that high serum levels of testosterone are associated with increased incidence of postmenopausal breast cancer. [11] Androgen therapy in patients with prostate cancer may also adversely cause to cancer metastasis [12], indicating the influence of testosterone in prostate cancer metastasis. However, in contrast to our findings there are reports showing that testosterone may prevent metastasis in cancer patients. [13] Further research are required to clarify the association between testosterone and brain tumors development and metastasis.

V. Conclusion

It can be concluded that cytotoxic dose of testosterone may have a potential to induce metastasis in A172 cells.

Acknowledgment

We appreciate all who helped us to exert this study.

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