The Effect of Bevacizumab (Avastin) on Tumor Growth of Malignant Fibrous Histiocytoma in the Animal Model.

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Introduction

Vascular endothelial growth favtor (VEGF) is considered to be a key mediator among the angiogenic growth factors causing tumor growth and metastasis, hence the development of anticancer drugs targeting angiogenesis and clinical trials have been widely conducted. Bevacizumab, one of the specific inhibitor for angiogenesis and a neutralizing antibody against VEGF, has recently been used as a drug against malignant tumors such as colorectal cancer, lung cancer, breast cancer, and renal cell carcinoma(1,2). In this study, we evaluated the effect of bevacizumab against malignant histiocytoma (MFH) in the animal model.

Materials&method

Animals. Male athymic BALB/c nude mice (6 week-old) were used. Animal maintenance was in accordance with institutional principals and procedures outlines in the Guide for the Care and Use of Laboratory Animals at our institution.

Implantation of tumor cells. Human MFH cell line, Nara H, was used in this study. We injected Nara H cells (1.2×10^7) subcutaneously to the dorsal area of nude-mice. Then, we measured weight and tumor dimensions twice a week after implantation of tumor cells. Tumor volume was calculated according to the formula $V=\pi/6\times a^2\times b$, where a and b represent the shorter and the longer dimension of the tumor.

Treatment of established tumor in nude mice. Twenty mice were randomly divided into experimental group(n=10) and control group(N=10). We started treatment 2 days after implantation of tumor cells. We injected 2mg/kg (weight) of bevacizumab (Avastin®,Genentech/Roche), twice a week for 4 weeks, intraperitoneally to the treatment group, while we injected the same amount of PBS intraperitoneally to the control group.

Statistical analysis. We used Student's T test for the statistical analysis. $P<0.05$ was considered as statistically significant.

Results

No significant difference in change of body weight was found between the two groups (Figure1). On the other hand, tumor growth was significantly inhibited in the treatment group compared with the control group after day 12 of the treatment (Figure 2). Finally, the mean tumor volumes of the treatment group and the control group were $1.4\times10^{-5}m^3$ and $6.9\times10^{-6}m^3$, respectively. In the control group, 2 mice died on day 26 and 3 mice died on day 28, while no mouse died in the treatment group. Survival rate was significantly higher in treatment group than that in control group on day 28.

Discussion

Previous studies have demonstrated a critical role of VEGF in regulation of physiological and pathological angiogenesis. We have reported that VEGF was often expressed in bone and soft tissue tumors (3) as well as in various solid tumors. Bevacizumab is an anti-angiogenic drug by binding specifically with VEGF, and its effectiveness has been reported for the adjuvant therapy of colorectal cancer, as well as lung cancer and breast cancer. The current study suggests that bevacizumab may be effective on inhibition of tumor growth in MFH.

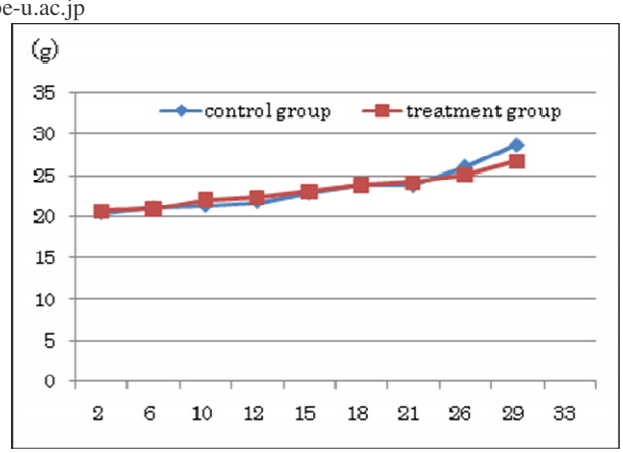

Figure 1. The weight of mice
No significant difference was found between the two groups.

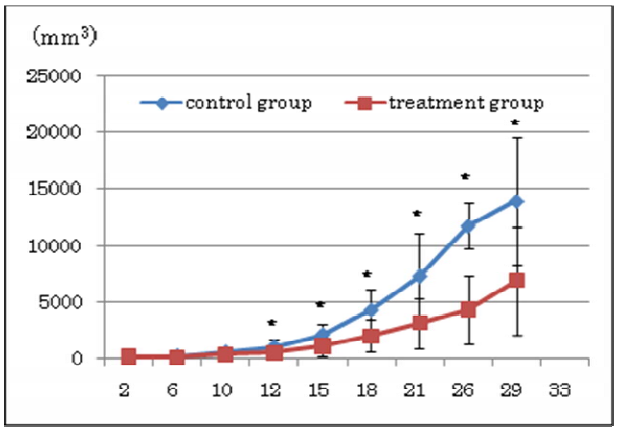

Figure 2. Inhabition of tumor growth by bevacizumab.
After day 12 of treatment, tumor growth was significantly inhibited in treatment group compared with in control group. * $P<0.05$

References

1) Ferrara N, Hillan KJ, Gerber HP, et al. Nat Rev Drug Discov. 3(5):391-400, 2004
2) Steven M, Expert Opin. Biol. Ther. 7(4):509-519, 2007
3) Hara H, Akisue T, Fujimoto T, et al. Anticancer Res. 26:4307-4312, 2006