Steroid-induced Increase in Survival of Tumor-bearing Rats

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Summary

2α-Methyl-17β-hydroxy-5α-androstan-3-one significantly increased the survival time of rats bearing mammary fibroadenomas. The extent of survival was related to the hormone responsiveness of the tumor.

Introduction

Numerous clinical studies have indicated that treatment of human breast cancer with 2α-methyl-17β-hydroxy-5α-androstan-3-one (2α-MHA) or its propionate ester produces objective and subjective relief (2, 3, 5, 7). That treatment actually produces significant prolongation of life has been indicated but not proved. The present study involves the treatment of rats bearing mammary fibroadenomas with 2α-MHA to determine the effect of this therapy on survival.

Materials and Methods

Female Sprague-Dawley rats bearing actively growing mammary fibroadenomas, which had been transplanted as previously described (1, 6), were utilized. The tumors were permitted to grow 7–10 weeks prior to the use of the animals. Two separate experiments were run. In Test A, relatively slow-growing tumors were utilized. These animals were selected from groups bearing tumors known to be inhibited by 2α-MHA treatment, as determined by glycine-2-14C uptake into tumor protein (1, 6). Those animals selected for Test B, however, were taken from groups bearing tumors of which most were much less responsive or were irresponsive to 2α-MHA treatment, similarly determined. Test A utilized 18 rats/group; 27 rats were used in each group of Test B. The rats for each test were divided into groups randomly.

The steroid was administered s.c. twice weekly, each dose being 2 mg of 2α-MHA suspended in 1 ml of a vehicle consisting of sodium chloride (0.9%), polysorbate 80 (0.4%), carboxymethyl cellulose (0.5%), and benzyl alcohol (0.9%). The control animals received vehicle only. All animals received treatment until death, except for 2 2α-MHA-treated rats in Test A, which were sacrificed after 380 days with no viable tumors being present.

Results and Conclusions

The survival curves of the control and treated groups for Tests A and B are presented in Chart 1. Two observations can be made: (a) In both tests 2α-MHA significantly increased the survival time of the tumor-bearing rats. The control and treated groups of each test were compared with the use of the rank sum test (4). For Test A, τ = 3.92 (P < 0.0001); for Test B, τ = 3.76 (P < 0.0001). (b) The 2nd observation is that 2α-MHA is significantly less effective in prolonging the survival time of rats bearing relatively fast-growing tumors (Test B) than of rats bearing slow...
growing tumors (Test A), even though the time of onset of death in these 2 treated groups is similar. A comparison of the 2α-MHA-treated groups of Tests A and B with the use of the rank sum test yielded a value for $r$ of 2.76 ($P < 0.01$). Tumors having greater hormone responsiveness as determined by glycine-2-14C uptake into tumor protein are, therefore, more responsive with respect to survival than those having relatively little hormone responsiveness.

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References

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