

Experimental Evaluation of Tumor Growth Rate Related to Age

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ABSTRACT

The differences of the growth rate of MH 134 tumor inoculated in younger or older mice were experimentally investigated in this study. The age-related tumor growth rate were evaluated as the changes of a tumor size to food pad ratio respectively.

In this study, a 6 weeks-old, a 9 weeks-old and a 20 weeks-old C₃H/He mice were correctly selected and prepared according to age. From the aspect of age factor in tumorbearing host, MH 134 tumor growth rate as well as survival rate after inoculation of 2.5×10^4 , 2.5×10^5 and 2.5×10^6 tumor cells were simultaneously investigated in each age groups.

Interestingly enough, a depressed tumor growth rate was noted in older mice in comparison with those in younger mice, whereas survival rates showed almost the same between in younger and older mice groups.

While as many as 2.5×10^6 of MH 134 tumor cells were inoculated, the differences in tumor growth rate between younger and older mice were apparently pronounced. The rapid tumor growth in young mice, furthermore, were definitely denoted. Meanwhile, the improvement of survival rate in older mice had not become manifest regardless of slow growth, as compared in the two age group. Age affected some aspect of inhibitory tumor growth, whereas this assumption was not consistent with prolongation of survival time.

This results reported here ensured the differences of tumor growth rate in tumor-bearing host concerning age. Needless to say, the reliability of tumor resection as a treatment against cancer has been substantiated even for the elderly patients in order to enable survival rate significantly improve.

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INTRODUCTION

According to actual prolongation of life span, the high incidence of various kinds of carcinoma has been notably approved in the elderly¹⁾. The favorable effects of treatments for cancer are facilitated by a combination of therapeutic procedures with surgery, radiation, chemotherapy and immunotherapy. However, it is well conceived that the most favorable results of cancer treatments are mainly obtained by surgical excision against cancerous tumor. In an attempt to the achievement of further extension of surgical indication, it is on these premises that the operative risk should be eliminated and subsequently a satisfactory outcome following surgery should be ensured even in elderly patients.

It is generally accepted that a high frequency of cancer is observed with advancing age and a growth rate of cancer tumor in the elderly is considerably inhibited as compared to that in the younger.

However, a relatively little information is found in terms of the difference of tumor growth rate between younger and older patients. This study was undertaken to elucidate the specificity of tumor growth patterns in the advancing age experimentally.

MATERIAL AND METHODS

The animals used were 6 week-old, 9 week-old and 20 week-old c_3H/HE mice respectively that have been supplied by Chugai Laboratory, Tokyo. The suspension of tumor cell of MH 134 was prepared by ascites from tumor-bearing mouse and viable tumor cells were counted in a hemacytometer by the trypan blue staining method. The cell suspension with Hank's medium containing 5% fetal calf serum was adjusted to the concentration of 10^6 tumor cell in $10\mu l$ of this suspension.

This suspension containing 2.5×10^6 , 2.5×10^5 and 2.5×10^4 of MH 134 tumor cells were inoculated in food pad in divided three groups which were selected according to mice age of 6 week-old, 9 week-old and 20 week-old respectively.

We have assumed as an experimental protocol that 6 and 9 week-old mice would be the representative state of young person immunologically as well as 20 week-old mice would be those of advancing age. We have studied on changes of inoculated tumor growth rate in individual each groups, which were expressed with the ratio of a diameter of tumor mass to a width of food pad.

Eighteen mice in each groups, which were divided into three groups of 6 week-old, 9 week-old and 20 week-old according to mouse age, were prepared and a total of fifty-four mice were subjected to this study. Furthermore, eighteen mice in three groups were separated by inoculation of 2.5×10^6 , 2.5×10^5 and 2.5×10^4 tumor cells respectively. (Fig 1)

The observation of tumor growth rate as well as survival period were continued to record up to death of tumor-bearing mice in comparison with those of each three



Fig 1. Tumor mass of MH 134 on 7th day after inoculation of 2.5×10^6 tumor cells according to mice age (right : 6 week-old, middle : 9 week-old, left: 20 week-old)

groups to certify the influencing age effect of tumor-bearing mouse and the number factor of inoculated tumor cells. The tumor growth rate after inoculation was calculated by a ratio of tumor area to food pad..

RESULTS

The survival rate was investigated according to number of inoculated tumor cells in each groups divided by mouse age. The mice with inoculation of MH 134 tumor cells of 2.5×10^6 expired in relatively early period as compared with those of 2.5×10^5



Fig 2. Survival after inoculation of MH 134 tumor cells of 2.5×10^6 , 2.5×10^5 and 2.5×10^4 according to mice age.

and 2.5×10^4 as shown in Fig 2.

In comparison with survival rate, it was elucidated that the survival period was approximately proportion to number of inoculated tumor cells in each three groups. However, survival in younger mice were directly influenced on number of inoculated tumor cells while survival rate in older mice were not necessarily similar to those in younger mice.

As far as we can observe, it is of interest to note that prolonged survival with inoculated tumor growth are more likely to obtain old mice rather than in young mice. It is shown that a large number of inoculation of MH 134 tumor cells makes survival reduce in younger mice, while its tendency is discordant in aged mice so that a less number of inoculation of MH 134 tumor cells may allow to bring about the longer survival in younger mice.

When 2.5×10^6 of MH 134 tumor cells were inoculated, the ensuing tumor size was considerably enhanced with the elapse of time, especially after 14 days of inoculation as compared with inoculation of more or less a small number of 2.5×10^5 and 2.5×10^4 MH 134 tumor cells. In the series of MH 134 inoculation, the rapid tumor growth was noted in younger mice rather than in older mice regardless of inoculated number of MH 134 tumor cells.

However, the difference of tumor growth rate between younger and older mice

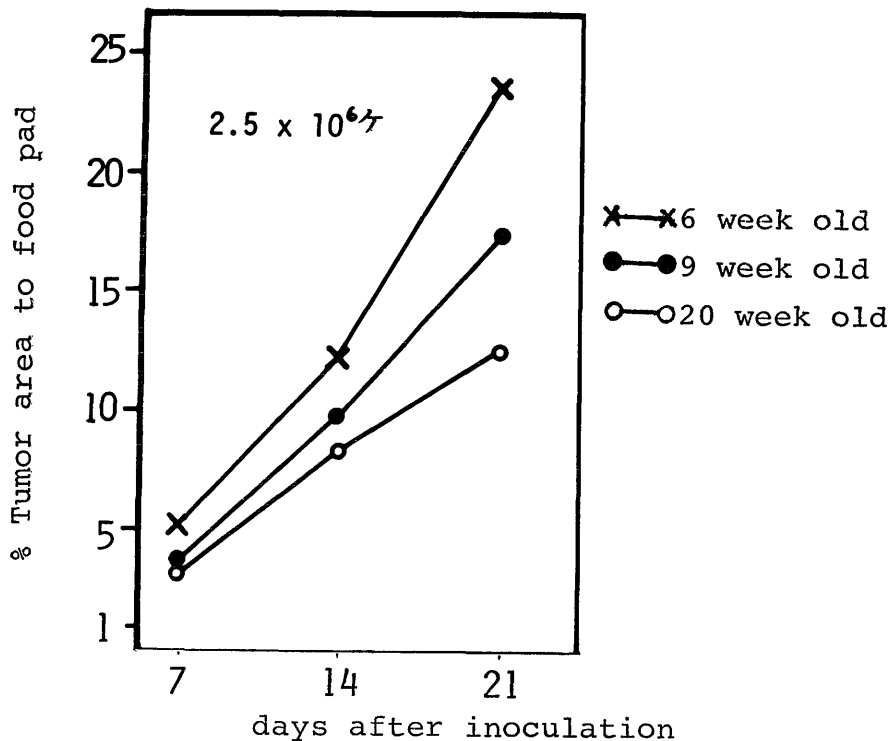


Fig 3. Tumor growth rate inoculated MH 134 tumor cells of 2.5×10^6 according to age.

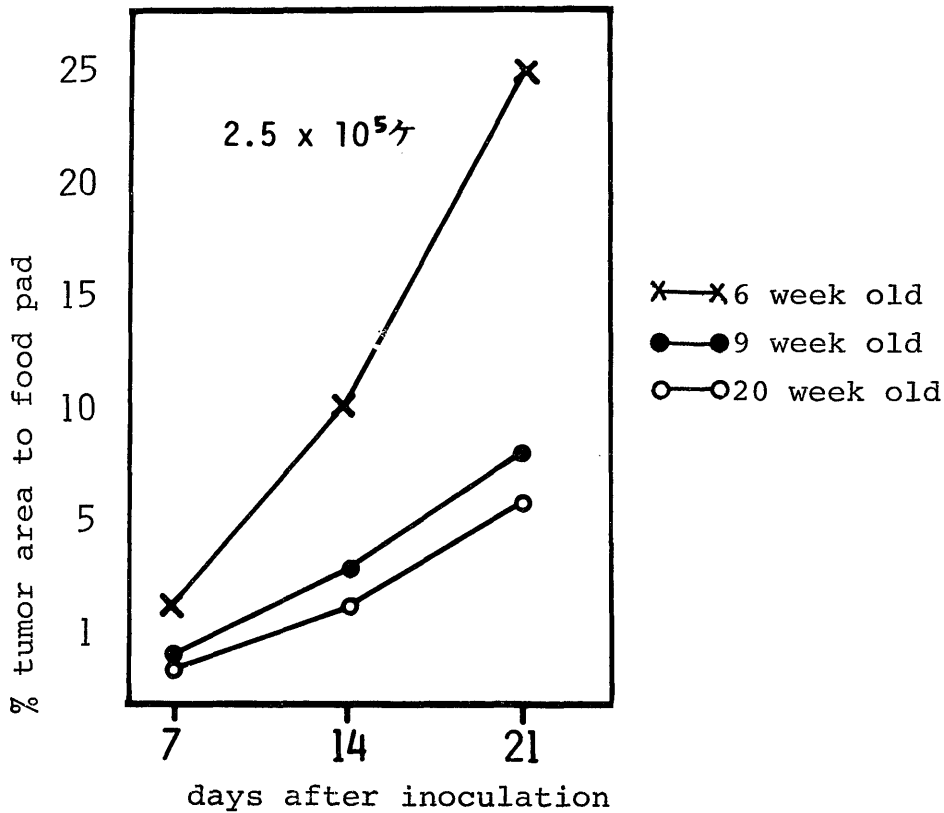


Fig 4. Tumor growth rate inoculated MH 134 tumor cells of 2.5×10^5 according to age.

were extremely defined at inoculation of 2.5×10^6 , 2.5×10^5 and 2.5×10^4 tumor cells as outlined in Fig 3. 4. 5. As compared to inoculation of 2.5×10^5 and 2.5×10^4 tumor cells, the increased tumor sizes were significantly enhanced in young mice of 6 week-old although those in old mice of 20 week-old as well as 9 week-old mice were apparently suppressed.

As shown in Fig 5, a less depressed tumor size were observed at inoculation of 2.5×10^4 tumor cells, demonstrating a minimal difference in regard to age.

As indicated in Fig 5, the inoculation of a small number of 2.5×10^4 tumor cells brought about the depression of tumor growth rate. From the observation of changes in tumor size, the changes of inoculated tumor sizes were markedly increased in younger mice whenever 2.5×10^6 , 2.5×10^5 and 2.5×10^4 tumor cells were inoculated.

In group of 6 week-old mice, the tumor growth rates were rapidly enhanced as compared to those of other groups, especially its modality of tumor growth was characterized after 2 weeks of MH 134 tumor cells inoculation. In groups of either 9 week-old or 20 week-old mice, the patterns of tumor growth were moderately depressed during the course of this study in comparison with that of 6 week-old mice group.

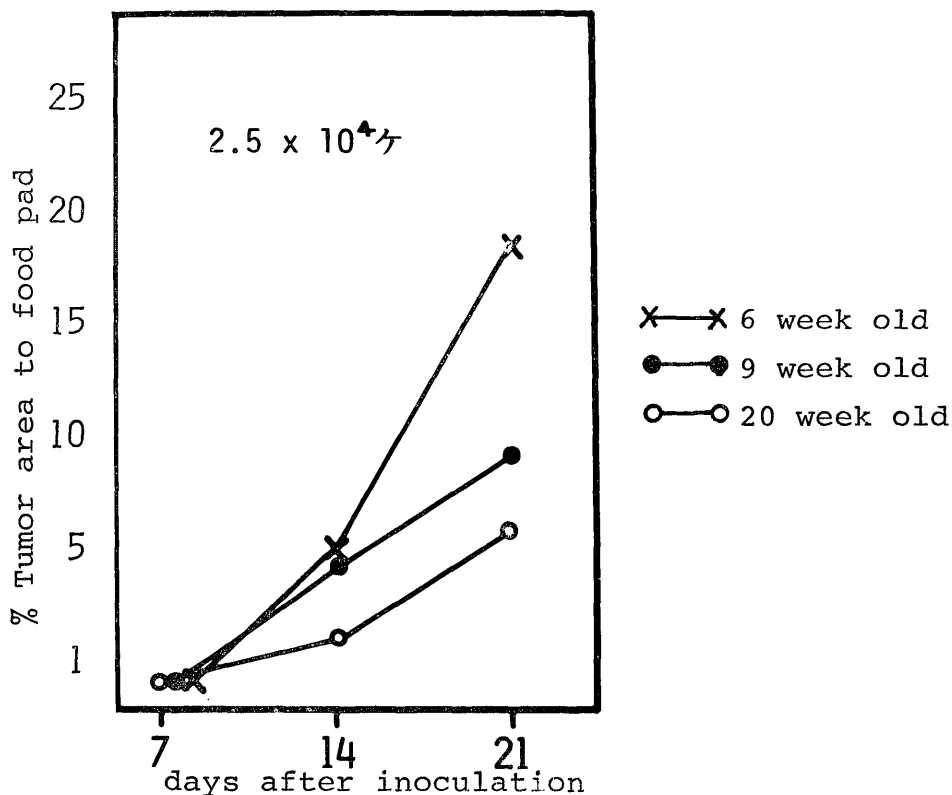


Fig 5. Tumor growth rate inoculated MH 134 tumor cells of 2.5×10^4 according to age.

The growth rate of tumor cells inoculated in older mice were obviously slow despite the demonstration of rapid growth in young mice. Interestingly enough, it is of note that the patterns of tumor growth rate were inversely proportional to immunological responsiveness which might apparently be suppressed in older mice.

DISCUSSION

With advancing age, a high incidence of occurrence of various kinds of carcinoma has undoubtedly noted in all parts of body.²⁾ On recent advances in cancer therapy, it is speculated that the first aim to achieve the ensuing excellent outcome for cancer treatment is large enough to remove tumor mass surgically. In addition, it is generally conceded that surgical excision for cancer is refractory to a gain of satisfactory results as compared to that of any other intensively therapeutic procedures. There is not doubt that surgical resection against carcinoma is considered best suited for management of cancer³⁾⁴⁾.

This study is to certify the reliability of operative treatment even in the aged patients without some of an apprecial risk for surgery in comparison with survival and

tumor growth in relation to age of tumor-bearing host.

As far as we consider in relation to aspect of life span in tumor-bearing mice, it is assumed that likelihood of survival in older tumor-bearing mice is inferior to that in younger mice.

However, it is of interest to note from this study, contrary to what others believe, that old tumor-bearing mice enable their survival rate far prolonged. From these results, it seems worthwhile to document that host resistance in older mice against MH 134 tumor growth is strong enough as compared with that in younger mice.

Furthermore, it was experimentally defined that tumor growth rate was relatively depressed in older mice. However, it was concluded that these results did not lead to a better prognosis in older mice rather than in younger mice in comparative study with special reference to survival period. These experimental results, furthermore, show clinical reliability of enlarging the operative indication for the aged patients under less appreciable operative risk to obtain a further excellent cure rate even in older patients. This study also provides an experimental evidence of the specific behavior in MH 134 tumor growth inoculated in old mice as compared to those in young mice, namely, tumor growth rate is enhanced in young tumor-bearing host rather than in old tumor-bearing host and its tendency has become manifest at the time of inoculation of a large number of 2.5×10^6 tumor cells, on the contrary, it enables survival shortened notably in younger mice.

By comparative study in terms of growth rate of MH 134 tumor cells inoculated in either older or younger mice, it has been argued that MH 134 tumor growth was apparently depressed in older mice but it was not responsible for improvement of survival rate.

Insofar as increasing size of inoculated tumor mass, prolonged survival is unable to be expected regardless of age in tumor-bearing host. However, it is well conceived, otherwise, that the prognosis in older patients with cancer is relatively fair, as a consequence of slow tumor growth as compared to those in younger tumor-bearing host in which tumor growth are prevalent with fashion of far malignant potential. It is emphasized as a result of this experimental study that surgical excision is enough to permit a favorable outcome for cancer treatment even in older patients unless it is otherwise contraindicated.

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