

The Influence of WR-2721 on Metastatic Tumor Spread After Irradiation

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The Line 1 alveolar cell carcinoma is a transplantable murine tumor which, unlike most others, kills the host by means of metastatic spread (1). Attempts to cure this tumor with localized radiation therapy often fail, in spite of local tumor control, because the metastases evade the treatment (2). These facts suggest that host-tumor interactions may play a particularly important role in determining the ultimate survival of the tumor bearing animal. In order to initially evaluate the possible importance of normal regional tissues in host-tumor interactions we examined the influence of WR-2721, a radioprotective drug, on local tumor control and on subsequent survival of the tumor bearing animal after localized radiation. Previous experience indicated that the drug did not protect solid tumors, but did protect the normal tissues included in the radiation field (3,4).

Graded single doses of radiation (HVL=1.29 mm cu) of 3000 - 7000 rads localized to the tumor region were given to 160 tumor bearing mice 7 days after I. M. injection of 10^6 viable Line 1 carcinoma cells into the right leg. Sham irradiation was given to 32 mice to serve as controls. Half of the mice in the experiment were given radiation only and the other half were given a single IP injection of WR2721 just prior to radiation exposure. For the purpose of analysis surviving animals were those that were locally tumor free and survived 100 days after treatment. In addition to these animals being included as "locally cured", any animal that died of metastases prior to 100 days but showed no evidence of local tumor were also considered to be locally cured.

The results of the experiment are shown in the top portion of Table I. As stated previously the differences between the percent of animals "locally cured" and the percent that survived are a result of animals that died of metastases despite local control. Also shown in the lower portion of Table I are the total cures and the total percent of animals locally cured that had metastases.

These data indicate that the protection of normal tissue with WR-2721 can decrease the metastatic spread seen after irradiation and suggests that: 1) regional normal tissues are important in controlling metastatic spread; and 2) radiation injury can impair the functional integrity of this regional mechanism. Studies are presently in progress to determine the nature of this regional mechanism and to further examine its response to irradiation in the presence and absence of WR-2721.

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Table I. The influence of WR-2721 on local tumor control, and metastatic spread after irradiation.

Dose (rads)	WR-2721 (mg/kg)	% Local Control ¹	% Survival ¹
3000	0	0	0
	400	6.3	6.3
4000	0	37	27
	400	33	33
5000	0	50	36
	400	30	20
6000	0	75	33
	400	75	53
7000	0	94	50
	400	94	69
TOTAL LOCAL CURES			% WITH METASTASIS
RADIATION ONLY		41	43%
WR-2721 +RADIATION		37	25%

¹See text for explanation