METASTASIZATION OF TRANSPLANTABLE MAMMARY GLAND CARCINOMA OF Phodopus sungorus Pall. ON INTRAMUSCULAR AND INTRAPERITONEAL INOCULATION

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A study of the frequency and character of metastasization of transplantable mammary gland carcinoma of Phodopus sungorus Pall. (strain OMD) conducted on 47 animals with intramuscular or intraperitoneal inoculation of the tumor (2nd-16th generation of the strain) showed that this transplantable tumor has a high incidence and a distinctive (hematogenous and lymphogenous) type of metastasization. With both methods of inoculation the most characteristic localization of metastases is the lungs (more than 80% of cases). As a rule, metases in the lungs were combined with metastases in lymph glands in different parts of the body (60-80% of cases). After intraperitoneal inoculation, metastases were found particularly often in the paratracheal lymph glands (up to 60% of cases). Frequently metastases were found in the kidneys, spleen and liver. Metastasization in the internal organs (including the lungs) occurred in 24 of 27 hamsters after intramuscular inoculation and in 16 of 20 hamsters after intraperitoneal inoculation.

The striped hairy-footed Jungarian hamster Phodopus sungorus Pall. is a new experimental animal used in cancer research [1-3]. The first transplantable tumors of this animal have been obtained comparatively recently. One of them, strain OMD (transplantable carcinoma of the mammary glands) behaved from the outset as a metastasizing tumor, and it has retained this property during subsequent transplantations [4].

The object of the investigation described below was to obtain more detailed characteristics of the frequency and nature of metastasization of this tumor.

EXPERIMENTAL METHOD AND RESULTS

Museum material, consisting of early (from the 2nd to the 15th) generations of strain OMD, generously provided by O. I. Sokova (to whom the writers express their gratitude) was subjected to microscopic investigation, and a special experiment was carried out to study strain OMD in the 16th generation. This experiment was performed on the first hamsters reared by the writer himself, and derived from 5 pairs of animals belonging to a stock held at the Laboratory of Cytogenetics (Head, Professor E. E. Pogosyants) of the Institute of Experimental and Clinical Oncology.

The museum material investigated was obtained from 28 Jungarian hamsters of both sexes which had died after intramuscular or intraperitoneal inoculation of strain OMD in the 2nd-15th generations.

The experimental material consisted of 20 Jungarian hamsters inoculated intramuscularly (13 animals) or intraperitoneally (seven animals with strain OMD in the 16th generation. Altogether tumors,

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TABLE 1. Growth and Metastasization of Strain OMD after Intramuscular and Intraperitoneal Inoculation

Generation of strain	Mode of inoculation	Number of successful takes		Mean life span after inoculation (in days)	Frequency of metastasization (No. of cases)														Total number of animals with metastases	
					lymph glands							internal organs					total number of animals with metastases in lymph glands	total number of animals with metastases in internal organs		
					peripheral			visceral				lungs	liver	kidney	spleen				
		absolute	in percent		cervical	axillary	inguinal	paratracheal	pararenal	lumbar								absolute	in percent
2-12*	Intramuscular	14/14	100	45.2 ± 3.4	2	3	2	4	3	2		14	0	5	2		6	14	14/14	100.0
7-15*	Intraperitoneal	14/14	100	27.6 ± 2.1	0	0	0	9	2	0		12	2	3	4		11	12	14/14	100.0
16	Intramuscular	13/13	100	34.8 ± 3.3	0	5	3	5†	4	10		10	0	0	2		10	10	11/13	84.6
16	Intraperitoneal	6/7	85.7	21.3 ± 2.1	1	0	1	4	0	1		4	1	2	0		5	4	5/6	83.3

*O. I. Sokova's material.

† In all these cases the tumor invaded the peritoneal cavity.

internal organs, and all lymph glands demonstrable at autopsy from 47 animals dying at different times after inoculation were subjected to histological investigation (paraffin sections, hematoxylin-eosin).

In the experimental investigation successful takes of strain OMD were obtained in almost as many cases (100% by intramuscular and 85.7% by intraperitoneal inoculation) as in O. I. Sokova's experiments (naturally, allowance must be made for the very small size of the group of hamsters in the present series inoculated intraperitoneally), in which it was 100% when both methods of inoculation were used. The mean life span of the animals after inoculation in the present experiments was somewhat less than in O. I. Sokova's experiments, at least after intramuscular inoculation (45.2 ± 3.4 and 34.8 ± 3.3 days, respectively, $P < 0.05$). This difference can be attributed fully to the fact that Sokova used earlier generations of the strain.

Analysis of the result given in Table 1 indicates that tumors of strain OMD are characterized by a very high frequency of metastasization, whether inoculated intramuscularly (from 84.6 to 100%) or intraperitoneally (from 83.3 to 100%). The most constant and characteristic localization of metastases in both cases was the lungs: multiple metastases in the lungs were found in 24 of 27 (88.9%) animals investigated after intramuscular inoculation and in 16 ot 20 (80%) animals investigated after intraperitoneal inoculation (Figs. 1 and 2). As a rule metastases in the lungs were accompanied by metastases in lymph glands in different parts of the body: metastases in the lymph glands were found in 16 of 27 (59.3%) hamsters after intramuscular inoculation and in 16 of 20 (80%) hamsters after intraperitoneal inoculation (Fig. 1). The most commonly affected group of lymph glands after intraperitoneal inoculation of OMD was the paratracheal glands: metastases in this situation were found in 13 of 20 (65%) hamsters inoculated intraperitoneally. It is interesting to note that paratracheal metastases were found in five of those six cases in these experiments in which a tumor inoculated intramuscularly invaded the peritoneal cavity. Besides metastases in the paratracheal lymph glands, metastases of strain OMD also were found in the hamsters in the cervical (three cases), axillary (eight cases), inguinal (six cases), pararenal (nine cases), and lumbar lymph glands (13 cases). The latter are evidently affected somewhat more frequently after intramuscular (12 of 27 cases) than intraperitoneal (two of 20 cases) inoculation. The frequency of metastasization in lymph glands in other parts of the body (except the paratracheal and lumbar glands) is evidently independent of the mode of inoculation.

It must be emphasized that strain OMD metastasizes fairly frequently also in those internal organs which are relatively rarely affected by metastases from other transplantable tumors. For instance, in the material analyzed three cases of metastasization in the liver (Fig. 3), ten cases of metastasization in the kidney, one case of metastasization in the adrenal, and eight cases of metastasization in the spleen were observed. The total incidence of metastasization of the strain

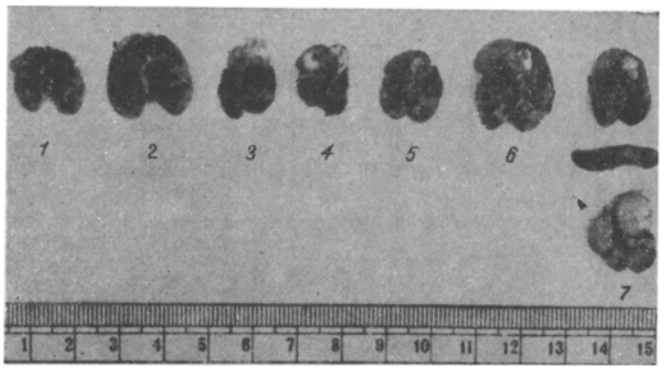

Fig. 1. Strain OMD (2nd-15th generation). Organs affected by metastases from hamsters dying at various times after intramuscular or intraperitoneal inoculation (O. I. Sokova's museum material). 1, 2) Multiple miliary metastases in the lungs; 3, 4) paratracheal metastases in the paratracheal and pararenal lymph glands; solutary metastatic nodule in the spleen.

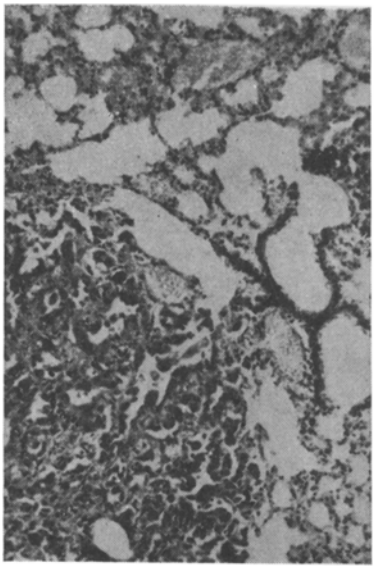

Fig. 2. Strain OMD, 16th generation, 47th day after intramuscular inoculation. Metastasis in the lung (120×).

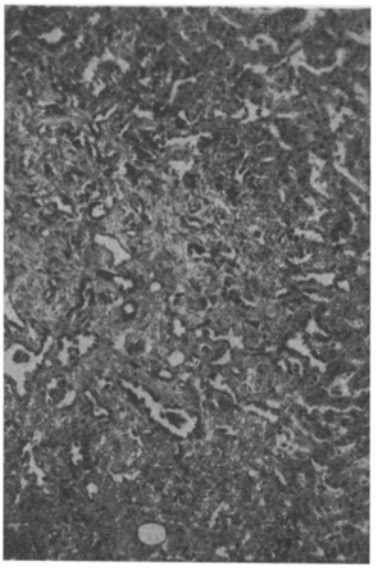

Fig. 3. Strain OMD, 11th generation, 37th day after intraperitoneal inoculation. Metastasis in liver (120×).

OMD in the internal organs was 88.9% (24 of 27 cases) after intramuscular inoculation and 80% (16 of 20 cases) after intraperitoneal inoculation.

As a rule, the morphological structure of the metastases corresponded to the structure of the original tumor which, in the early generations, was marked by predominance of the glandular component, whereas in the 16th generation it had a mainly solid structure.

The writer concludes from his many years of experience in the study of the frequency and distribution of metastases from various transplantable tumors that each tumor characteristically metastasizes either mainly by the lymphogenous or mainly by the hematogenous route.

From this standpoint, strain OMD is particularly interesting as a highly metastasizing transplantable tumor with a well marked mixed (hematogenous and lymphogenous) type of metastasization, giving rise to metastases in many different organs whether inoculated intramuscularly or intraperitoneally.

The high frequency of metastasization of strain OMD in the paratracheal lymph glands after intraperitoneal inoculation and invasion of the peritoneal cavity by an intramuscularly inoculated tumor can be interpreted, it is considered, as evidence to support the early hypothesis that the selective metastasization of certain ascites tumors in this group of lymph glands is determined by the anatomical and physiological features of the lymph drainage from the peritoneal cavity in rodents [2].

LITERATURE CITED

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