Morphology of Transplantable Chorionic Tumors in Rats

Makoto Miyamoto, Keishi Matsumoto and Toru Sugaya
Department of Pathology, Osaka University Medical School, Osaka

Miyamoto, M., Matsumoto, K. and Sugaya, T. Morphology of Transplantable Chorionic Tumors in Rats. Tohoku J. Exp. Med., 1973, 111 (2), 175-178 — Three lines of transplantable chorionic tumors have been established. They were numbered m-673, m-731 and m-786. At present they are transplanted over 25 generations and in this paper the morphology of both m-673 and m-731 was described. Biological behavior and morphological characteristics of parent tumors resembled those of the human choriocarcinoma. Histological appearance of these two lines were similar to each other and with the advance of generations of transplantation, PAS positive substance in the cytoplasm gradually decreased. The specific enzyme, 3β-ol-dehydrogenase-isomerase system of normal rat placenta on this tumor (m-673) was detected.

More than 20 cases of chorionic tumors were induced in our laboratory and the result was presented at the 31st Annual Meeting of the Japanese Cancer Association. Three lines out of them have been successfully transplanted over 20 generations and they were numbered m-673, m-731 and m-786. At present, m-673 is at the 30th generation, m-731 at the 25th and m-786 at the 25th. In this paper, the morphology of the established lines of m-673 and m-731 will be described mainly.

Materials and Methods

The experimental procedure and the morphology of the original tumor of m-731 have been described elsewhere (Miyamoto 1971; Miyamoto et al. 1972). Rats used for recipients were Wistar-Furth strain kept by brother-sister mating in our laboratory. One-month-old male and female weanlings were used for this serial transplantation. At each generation, a portion of tumor was removed and inoculated into the leg subcutaneously and the peritoneal cavity respectively after mincing it into pieces smaller than 1 mm³ in size.

Morphology

Incidence of tumor growth on the recipient was shown in Table 1. The positive take of tumors in recipients gradually increased in number and the period of survival time in recipients was shortened as well. Rats died with the direct effect of tumor growth either by cachexia or by accumulation of ascites. Mostly,
the type of growth was solid in subcutaneous tissue and nodular in peritoneal cavity attached to the major omentum. For the first several generations, microscopic appearance resembled the original tumor (gen. o). Particularly, plenty of PAS positive homogeneous materials were present in the cytoplasm, though they gradually decreased in quantity on both m-673 and m-731 with the advance of the generations. There appeared syncytial giant cells at the 2nd generation of m-731 which were quite similar to those of syncytium of villi in human being (Figs. 1 and 2). Approximately at the 20th generation, most recipients of m-673 and m-731

<table>
<thead>
<tr>
<th>Generation</th>
<th>Primary tumor</th>
<th>Metastatic tumor in the lung</th>
<th>Primary tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1/20F</td>
<td>1/20F</td>
<td>3/15M</td>
</tr>
<tr>
<td>2</td>
<td>1/2M</td>
<td>Discard</td>
<td>2/5F</td>
</tr>
<tr>
<td>13</td>
<td>2/4M</td>
<td>–</td>
<td>2/3F</td>
</tr>
<tr>
<td>25</td>
<td>3/4F</td>
<td>–</td>
<td>4/4F</td>
</tr>
</tbody>
</table>

M: Male  F: Female  Positive take/Host

Fig. 1
Fig. 1. Huge syncytial trophoblastic tumor cell seen at the 2nd generation of m-731, resembling human syncytiotrophoblastic cells. Hematoxylin and eosin stain. ×20. Slide No. 5229.

Fig. 2
Fig. 2. Higher power of Fig. 1, showing the absence of cell membrane with multiple nuclei. Hematoxylin and eosin stain. ×40. Slide No. 5229.
developed ascites at terminal. It was hemorrhagic on m-673 and was yellowish on m-731 in color. In such cases, $5 \times 10^5$ cells/ml of the ascites were used for the next explant on both m-673 and m-731. In one month, the abdomen of these recipients enlarged and approximately 10 ml of the ascites were able to be removed, with solid tumor formation in the major omentum in plate shape, either hemorrhagic on m-673 or whitish on m-731 in color. Pulmonary metastases were found in some recipients of m-673 and microscopic appearance was the same as that of the site of the inoculation (Fig. 3).

Fig. 3. Pulmonary metastasis through the vascular channels. Hematoxylin and eosin stain. $\times 20$. Slide No. 7981.

Fig. 4. Photomicrograph of hemorrhagic nodule in the lung. Tumor cells grow on the lumar surface with cavity formation containing blood in it. Hematoxylin and eosin stain. $\times 10$. Slide No. 4298.

**COMMENT**

Of the original lesion of m-673 at necropsy, there were multiple hemorrhagic metastases in the lung (Fig. 4) even though the primary lesion in the placenta was small, nodular and hemorrhagic, which was quite like human chorionic tumors on its biological characteristics. Explants from the metastatic nodules in the lung behaved in the same way as the original one showing multiple metastases to the lung of recipients after inoculation into the leg subcutaneously. However, this tumor was not able to be established as a transplantable one. Only one recipient
inoculated from the primary lesion developed new growth in the leg, which has been continuously transplanted up to date. Histologically, giant cell formation was present at each generation and sinus form in the tumor was always found, though PAS positive material in the cytoplasm varied in quantity. Through generations of m-731, histological pattern was unchanged. However, it was quite interesting that huge syncytial giant cell at the 2nd generation of m-731 resembled that of human being at the early pregnancy (Hertig and Gore 1971). Cytological and histological appearances of both lines resembled each other.

As described above, spontaneous chorionic tumors were rarely found among rodents (Park 1971), and it was further difficult to conclude that those experimentally induced tumors were of placental origin, notwithstanding that morphological characteristics and biological behavior of these tumors fully explained themselves to be of placental origin. However, the authors found the conversion of $^3$H-pregnenolone to $^3$H-progesterone using a piece of tumor of m-673 in vitro, while no $^3$H-progesterone was identified from $^3$H-pregnenolone in the liver, spleen or muscle. The result of our work demonstrated for the first time that transplantable tumor of m-673 forms progesterone from pregnenolone, indicating the presence of a $3\beta$-ol dehydrogenase-isomerase enzyme system, which has been selectively found in the steroid hormone secreting organs such as the ovary and the placenta in rats (Matsumoto et al. 1969). Further study on these two lines (m-673 and m-731) is under the process to demonstrate the origin to be placental.

References