CHARACTERISTICS OF A NEW TRANSPLANTABLE RAT OVARIAN TUMOR (OYaK)

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A new transplantable tumor of the ovary of a noninbred rat (OYaK) is described. The tumor was obtained by transplantation of an ovarian tumor developing from an ovary transplanted into the spleen of a castrated rat.

The most widely used method of induction of ovarian tumors in rats is by autografting the ovary into the spleen of castrated animals [7]. In this case tumors develop 8-11 months after autografting in 70-80% of the animals. However, these tumors are unsuitable for use for the development of new therapeutic methods because the latent period of their production is too long, they grow very slowly, and animals with these tumors, if they reach the age of 10-12 months, do not easily tolerate large doses of therapeutic compounds.

In experimental chemotherapy the tumors used are mostly pure strains, so that the investigations can be carried out on large numbers of animals with tumors of identical size growing at identical rates.

However, although primary ovarian tumors can be obtained both in inbred mice and rats [9-12] and also in noninbred rats [3, 4], only one strain of ovarian tumors in rats has been described in the Western literature (the Osborne – Mendel tumor [8]), and in the USSR there is one strain of ascites carcinoma of the ovary (OYa [6]), which, in the opinion of the authors cited, is an adenocarcinoma of the ovary.

The object of the present investigation was to obtain a transplantable ovarian tumor of rats for use as an experimental model for the development of rational methods of treating ovarian tumors.

EXPERIMENTAL METHOD

One of the primary tumors obtained by transplanting the ovary into the spleen of castrated noninbred rats by the Biskinds' method was used in these investigations. This tumor appeared 9 months after autografting. Three months later, when the tumor measured 3×4 cm, it was used for transplantation. The tumor had a granulosa-cell structure (Fig. 1) and consisted of small round cells with a dark nucleus and a small quantity of cytoplasm. In some places the tumor cells formed small clusters, separated from each other by thin layers of connective tissue. Sometimes the tumor cells showed luteinization, when they became much larger and polygonal in shape.

EXPERIMENTAL RESULTS

In the first generation the tumor was transplanted into ten castrated rats (females and males) aged 1 month, into which a cortisone pellet weighing 25 mg was implanted (to suppress immune reactions). Growth of the primary tumor only became apparent after 3 months in 50% of the animals (in 2 of the 3 females and 3 of the 7 males). The tumors grew slowly, and after 5 months their diameter was only 5-6 cm; their granulosa-cell structure was preserved.

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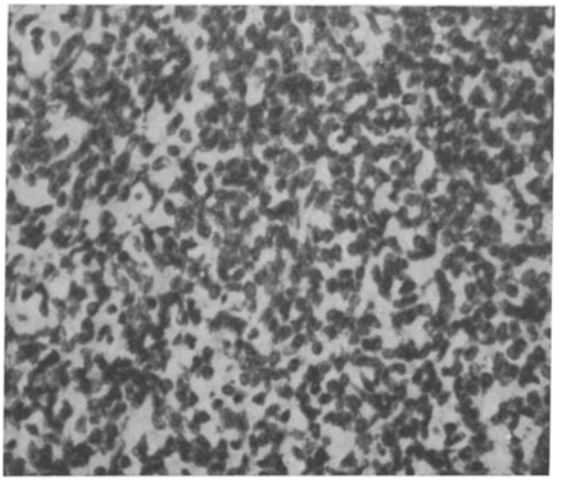

Fig. 1. Granulosa-cell tumor of ovary developing from ovary grafted into spleen of castrated rat (description in text). Hematoxylin-eosin, 200×.

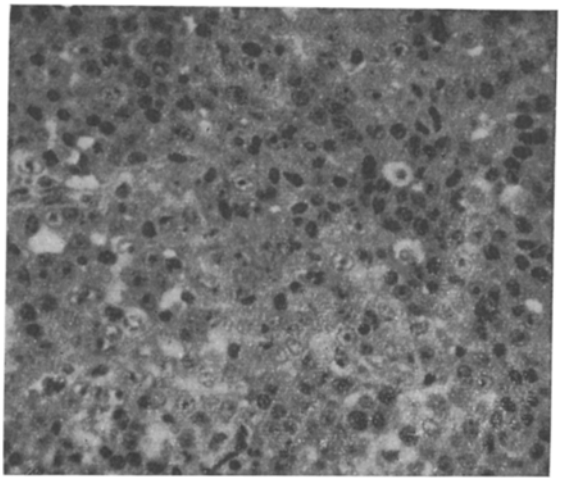

Fig. 2. Structure of granulosa-cell tumor in fourth generation (description in text). Hematoxylin-eosin, 200×.

In the second generation the tumor was transplanted into female and male rats, also at the age of 1 month. Growth of the tumor was found 1.5 months after transplantation in 43% of the animals (in 8 of the 20 females and 5 of the 10 males). The rate of growth was considerably accelerated: after 2.5 months the diameter of the tumor was 5-6 cm.

In the third generation the tumor was transplanted only into females aged 1 month, and 1 month later it had taken 58% of the animals (22 of 38 rats), although its rate of growth was unchanged.

In the fourth generation the tumor took in 87% of animals (both females and males), first becoming palpable after 15 days, and reaching a diameter of 3-4 cm 3 weeks after transplantation. In the fourth generation, morphological changes also appeared in the tumor, although as before it retained its granulosa-cell structure. The tumor cells were arranged in clusters and small bands, separated by layers of lose connective tissue. However, the small and dark tumor cells were fewer in number. The main mass of the tumor cells were larger in size, with a large, pale nucleus, and with little chromatin (Fig. 2).

After the fourth generation, induction of the strain was stopped and the tumor was frozen at -70° by Kiseleva's method [5]. After it had been kept for 3.5 years in a frozen state, the tumor was inoculated into

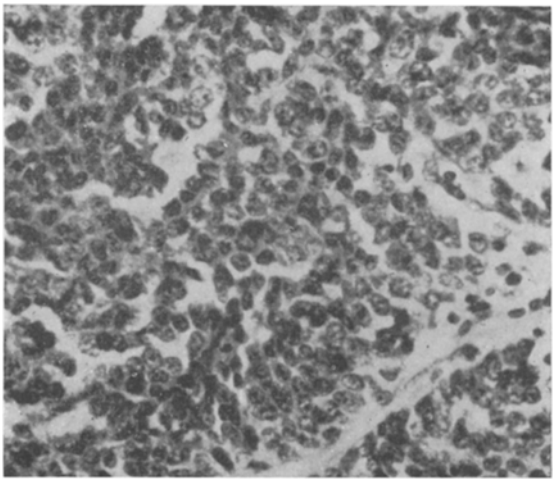

Fig. 3. Structure of granulosa-cell tumor in 45th generation (description in text). Hematoxylin-eosin, 200×.

young rats aged 3 weeks and it developed in 2 of 3 males 14 days after transplantation. During subsequent transplantations (until the tenth generation) the latent period of development of the tumor and its rate of growth were not significantly different from those in the fourth generation, but the percentage of successful takes was somewhat lower (mean 60%). Starting with the tenth generation, the number of successful takes of the tumor again reached 80%.

The 50th generation of the ovarian tumor has now been obtained. The strain has been called OYaK (initials of the Russian words for rat ovarian tumor). The tumor is transplanted into females and males at the age of 3-4 weeks. The percentage of successful takes varies from 80-90. Tumor nodules become palpable 5-7 days after transplantation. The mean diameter of the tumor on the 21st day is 6-7 cm. The life span of rats with tumors is 2-4 months. Spontaneous regression of the tumors is observed in 10% of cases. Morphologically, the tumor has become more malignant: polymorphism of the tumor cells and their nuclei and large number of mitoses are noteworthy. The tumor grows as large groups of cells forming bands separated from each other by very wide layers of lose connective tissue, rich in cells. Extensive foci of necrosis and hemorrhage are observed in the tumor tissues (Fig. 3).

The transplanted ovarian tumor thus obtained possesses marked reactivity both toward hormonal action and toward chemotherapeutic compounds [1, 2].

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