A TRANSPLANTABLE METASTASIZING CHONDRO-RHABDO-MYO-SARCOMA OF THE RAT

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With the exception of certain mixed tumors of the testis, ovary, and kidney, neoplasms containing striated muscle are very infrequent in man, and only a few have been described in animals. In a comprehensive review of the literature on animal tumors, in 1896, Caspar (1) mentioned but 3 cases of rhabdo-myomata, i.e., a melanotic rhabdo-myoma of the tail and perianal connective tissue of a stallion, reported by Kolessnikoff; a rhabdo-myoma of the vagi of a horse, described by Gratia; and an adeno-sarco-rhabdo-myoma of the kidney of a hog found by Johne. J. Wolff (2) cited a case of rhabdo-myoma of the shoulder of a horse, discovered by Monod, and Magnusson (3), quoting Boncek, reported an adeno-rhabdo-myoma of the heart of a cow. A giant-cell rhabdo-myo-sarcoma of a trout was described by Adami (4), and Fibiger (5) has reported a rhabdo-myoma of the codfish. However, the rat tumor described in the present paper is apparently the first rhabdo-myoma to be recorded in a rodent, in spite of the number and variety of neoplasms which have been observed in rats and mice. This tumor is interesting not only for its rarity, but also because of its morphology and its biological character.

The growth was found in a black and white female rat, between fifteen and nineteen months old, of a group of animals experimentally infested with Cysticercus fasciolaris. This rat, however, had not developed sarcoma of the liver. When first observed the tumor was a small circumscribed hemispherical mass about the size of a pea, situated beneath the skin of the upper epigastrium, in the median line of the body. It was firm and elastic.
and was apparently adherent to the ensiform process of the sternum. During the first few weeks of observation there was no material increase in size of the tumor, but at the end of two months, when the animal was mated, it was noted that the mass had grown slightly. Three weeks later the rat was isolated pregnant, and it was then recorded that the tumor had about doubled in size since the last observation. The rat gave birth to two young, only one of which she reared. Throughout lactation and subsequently the tumor grew rapidly. One month after gestation, a fragment of tumor was surgically removed, and was used for the subcutaneous inoculation of 93 rats. At this time the growth measured 5.5 x 3.5 x 3 cm. The rat survived the operation thirty days, during which period the tumor grew with great rapidity attaining a size of 6.5 x 5.9 x 4.4 cm. At autopsy the growth surrounded and largely replaced the ensiform process, its capsule being closely adherent to the sternal end of the two caudal pair of ribs. It was irregularly nodular, distinctly lobulated, and covered by a thin fibrous capsule. The consistency was firm and tough, with small soft and cartilaginous areas scattered throughout. In certain parts the tumor was friable and short plugs of tissue could be expressed from the cut surface by pressure. The color was grey white to pinkish, with small scattered areas of hemorrhage and large and small patches of necrosis. Gross metastatic tumor deposits were present in the lungs.

Microscopically, the tumor showed a rather complex structure which varied in different parts. It was composed partly of muscle cells and fibers and partly of small round or polyhedral cells, suggesting embryonal cartilage cells. These two types of cells occurred separately in parts of the tumor, though generally they were freely intermixed, one or the other predominating. Figures 1 and 2 respectively show low and high power views of areas of the tumor in which the muscle elements predominate. The muscle elements showed a wide diversity in shape and size many of them being morphologically fibers while others had the appearance of giant cells. Some of the fibers were thick, short or elongated cylinders with blunt, serrated, or tapering ends;
others were long, slender, and often fusiform, while still others were club-shaped and occasionally branching. They were generally multinuclear and possessed an abundant acidophilic protoplasm. In many of them longitudinal striations were visible and some showed both longitudinal and cross striations.

![Image of chondro-rhabdo-myo-sarcoma of rat](image)

**Fig. 1.** $\frac{R^{92}}{0} \times 250$

An area of the spontaneous chondro-rhabdo-myo-sarcoma of the rat composed largely of muscle elements.

(see fig. 2); others bore a close resemblance to smooth muscle cells. The giant cells consisted of round, oval, or irregular shaped masses of acidophilic protoplasm containing one to many nuclei, multinucleated cells being the rule. The nuclei of the fibers were generally rod-shaped or oval, while the cell nuclei were mostly
vesicular. They occupied either the central or peripheral part of the cell, being sometimes arranged in the form of a ring. The

![Image](image-url)

**Fig. 2.** $\frac{R_{02}}{0} \times 1000$

A striated muscle fiber from the spontaneous tumor

cromatin was not abundant and was distributed in small scattered granules. One to two nucleoli were generally demonstrable. There was considerable cellular degeneration, associated
with irregularity in the shape of the nuclei and changes in their staining properties. In places the degeneration involved the stroma and even resulted in necrosis which often covered large areas. Glycogen was demonstrated in the protoplasm of some of the cells. The fibers were either scattered indiscriminately among the cellular elements or ran in bundles. These bundles were most abundant at the periphery of the tumor and at the borders of the lobules. The muscle elements were loosely embedded in a stroma of rather delicate fibrous tissue of moderate cellularity, which in places was arranged in the form of a network, in the meshes of which lay the muscle cells. It either surrounded individual cells or divided the cells into small groups. The cells did not completely fill the spaces, but lay free in the meshes of the network. This appearance was probably due to shrinkage incident upon fixation and embedding of the tissues.

The other cells which formed a constituent part of the tumor were mostly rather small and round or polyhedral in shape. They possessed relatively large vesicular nuclei and scanty cytoplasm. The chromatin of the cells varied in amount and was distributed in small granules. The nucleolus was represented by one or two large granules. These cells for the most part showed but little difference in size, and generally took a uniform stain; though in areas they were fairly large and hyperchromatic. Most of them possessed a single nucleus, though cells containing two to several nuclei were sometimes observed. They were usually more compactly arranged than the muscle elements and were occasionally split up into islands by strands of stroma. In areas they formed a loose meshwork which enclosed the muscle elements. Mitotic figures were present in both types of cells and were particularly abundant in the small cells. The stroma throughout the tumor was relatively scanty, although in places bands of fibrous tissues penetrated the growth dividing it into distinct lobules.

Scattered through the tumor were large and small islands of cartilage (see fig. 3). The central parts of some of these islands consist of differentiated cartilage cells, while the cells comprising other islands were solely embryonal in type. The cartilaginous
islands showed a marked tendency toward necrosis. Embedded in the tumor were several small trabeculae of osteoid tissue. The tumor was rich in blood-vessels consisting largely of dilated capillaries.

The metastatic nodules in the lung contained both types of cells, the muscle elements preponderating. In these secondary tumors the muscle elements were smaller than those of the primary growth and showed no definite cross striations.

![Image of adult cartilage with surrounding tissue](image)

**Fig. 3.** $\frac{R}{0} \times 250$

An island of adult cartilage with a part of the surrounding tissue composed of small round or polyhedral cells resembling embryonal cartilage cells.

Transplantation of the tumor was successful and it is now in the eighteenth generation. In its initial difficulty of propagation this tumor resembled a carcinoma rather than a sarcoma. Of the grafts introduced subcutaneously into the 93 rats of the first generation only three produced tumors, and only five tumors were obtained from the 48 rats of the second generation. The third generation, however, showed 80 per cent of successful inoculations
A rat bearing a transplanted tumor of the ninth generation photographed 110 days after inoculation. The tumor weighed 2.14 times as much as its host.
and the subsequent generations showed generally a moderate to a high percentage of takes. The rate of growth of the transplanted tumors has also increased since the early generations. The daughter tumors often attain enormous sizes, sometimes greatly outweighing their hosts before death ensues.

Fig. 5. $\frac{R_{92}}{1 A} \times 160$

An area of a tumor of the first series transplanted showing muscle giant cells and fibers and a few of the round or polyhedral cells.
Figure 4 shows a photograph of a young rat bearing a tumor of the ninth generation. This animal was killed and photographed

![Image of tumor fibers](image)

**Fig. 6.** \( \frac{R}{4A} \times 800 \)

Striated muscle fibers in a transplanted tumor of the fourth generation
one hundred and ten days after inoculation. After the re-
moval of the tumor the rat weighed 105 grams while the tu-
mor weighed 225 grams or 2.14 times as much as its host.

Unlike most other rat sarcomata this tumor on transplantation
grows progressively in almost every animal in which a graft
becomes established. The older transplanted tumors show a
tendency toward liquefaction necrosis.

Tumors resulting from each of the first 13 successive inocula-
tions have been examined histologically. They bore a close

\[ \text{Fig. 7. } \frac{R \times 92 \times 1000}{1A} \]

Multinucleated fiber in a transplanted tumor of the first generation showing a
mitotic figure.

resemblance to the spontaneous tumor except that osteoid tissue
was absent in all of them and cartilage was observed in only
2, both of which were derived from the first transplantation.
All the transplanted tumors examined contained the other
constituents in varying proportions, from tumors consisting
largely of muscle to others in which the small round or polyhedral
cells predominated. The muscle elements consisted of both
fibers and cells as in the original tumor.
Figure 5 is an area of a tumor of the first series inoculated showing many muscle giant cells and fibers and a few of the small cells. The continued presence of fibers with cross striation in each successive generation is worthy of note; in fact, cross striations were demonstrated in some of the muscle fibers of every transplanted tumor examined.

![Image](image.jpg)

**Fig. 8.** $\frac{R}{15\ A} \times 400$

Lung metastasis of a transplanted tumor of the fifteenth generation showing both muscle elements and the smaller cells.

Figure 6 shows cross striated fibers in a tumor of the fourth generation. That the muscle elements were growing actively was evidenced by the presence of a large number of mitotic figures. These division figures were frequent in the cells and sometimes there was observed in a fiber a karyokinetic figure. Such a nuclear division in a fiber is shown in figure 7.
One tumor obtained from the first transplantation produced lung metastases, which contained a relatively small amount of muscle in which cross striations were not demonstrable, and one tumor from the fifteenth transplantation produced very extensive lung metastases which contained a large amount of muscular tissue.

Figure 8 shows an area from one of these lung metastases in which both types of cells are represented.

![Image of lung metastases](image_url)

**Fig. 9.** $\frac{R}{3A} \times 500$

An embolus in a blood-vessel of a transplanted tumor of the third generation

Emboli were occasionally observed in the blood-vessels of tumors of later generations (see fig. 9).

**SUMMARY**

The chondro-rhabdo-myxo-sarcoma of the sternum of the rat described above was a transplantable metastasizing tumor in which cross-striated muscle fibers have persisted through fifteen generations, although the cartilaginous elements early lost their power of differentiation.
REFERENCES

(1) Caspar, M: Ergebnisse d. allg. Path., 1896, iii, 705.