Transplantable Renal Tumor of the Rat*

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SUMMARY

A pleomorphic renal tumor with a histologic structure resembling Wilm's tumor occurred spontaneously in an adult rat and is being maintained by serial transplantation in suckling rats.

This paper reports the observation and successful serial transplantation of a spontaneous rat tumor of renal origin with a structure resembling Wilm's tumor (embryonal nephroma). Several tumors of similar morphology have previously been observed in adult experimental and domestic animals. (See bibliographies in references [1, 4, 5].) Olcott's tumor (4) grew on transplantation to littermates but was not transplantable to unrelated rats. One of Greene's rabbit tumors was serially transplanted for at least seven passages in the anterior ocular chamber or testis (3), but apparently no tumor of this morphology is currently being maintained in any warm-blooded host (2). In humans, tumors of similar morphology (Wilm's tumors) are well known in infants but are much less common in adults (1).

A spontaneous tumor was observed in a female breeder rat of roughly 1 year of age which had had at least one litter. The animal was of Wistar strain, originating from either Carworth Farms or Charles River Laboratories. It was thought to be pregnant, but when it failed to deliver, it was sacrificed and found to have a large intra-abdominal tumor surrounding and distorting the left kidney and displacing but not invading other abdominal organs. No metastases were found. On cutting into the tumor, solid but friable large white areas predominated, but other areas were deep red, and others showed liquid necrosis. Several structures resembling renal collecting tubules ran in a radial pattern through the tumor mass. On histologic examination uniform, deeply staining, nonvacuolated cells of moderate size were arranged in dense nodules separated by thin fibrous septa (Figs. 1, 2), and tubular formations and structures resembling glomeruli were scattered but frequent (Fig. 3). In other areas there was a much looser arrangement of polygonal cells, and in such areas large sinusoidal blood vessels were numerous (Fig. 4) accounting for the red color of these areas on gross examination. Little or no spontaneous hemorrhage was observed. Mitoses were rare. Neither smooth nor striated muscle cells were recognized.

Initial passage of the tumor was accomplished by injection of 0.2 ml. of a thick (approximately 25 per cent) tumor suspension intraperitoneally into newborn rats (less than 24 hours old) by syringe and 21-gauge needle. It was maintained thereafter by inoculation of a similar suspension either intraperitoneally or subcutaneously into rats of various ages. This inoculum contained over 100 million cells per rat. Successful transmission was accomplished both subcutaneously and intraperitoneally from a fifth-generation tumor, with

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Figs. 1-4.—Histologic sections of the spontaneous tumor.

Fig. 1.—Section of dense white area showing characteristic dense nodules and fibrous septa. X 160.

Fig. 2.—Higher magnification of Figure 1. X 320.

Fig. 3.—Areas with tubular and glomerular formation and loosely arranged polygonal cells. X 160.

Fig. 4.—Area showing large blood sinuses. X 160.
FIGS. 5-8.—Histologic sections of transplanted tumors. All
× 160.

Fig. 5.—Subcutaneous transplant, fifth passage, showing
tubule and glomerulus formation.

Fig. 6.—Same tumor as in Figure 5 but showing nodular
and loose arrangement of polygonal cells.

Fig. 7.—Metastasis in lung from subcutaneous transplant,
sixth passage. Rat inoculated at age 13 days and died at age 44
days.

Fig. 8.—Intraperitoneal transplant, seventh passage, show-
ing tubule formation.
doses of 10 million cells, into suckling rats. Tumors were palpable by 2 weeks with the larger dose but not until 4 weeks with the smaller dose. Inocula of less than 10 million cells have not yet been studied.

The tumor is now in its eighth transplant generation. Nodules grew in between 40 and 50 per cent of all rats given inoculations of the tumor, whether newborn (less than 24 hours old), suckling (1–14 days old), weanling (2–6 weeks old), pregnant females (mothers of litters given injections simultaneously), or other adults, and at all passage levels. Recipients less than 2 weeks old were most satisfactory, however, because tumor growth was more rapid and uniform. Such rats usually had palpable tumors by 2–3 weeks after inoculation and were moribund by 2–6 weeks, whereas adults usually had slower tumor growth and few died sooner than 2 months after inoculation. Intraperitoneal implants became palpable and killed at a slightly faster rate than did subcutaneous implants. Histology of the tumors in adult rats was not different from that in young recipients. Transplantation from an adult recipient was successful on the one occasion when it was tested.

The rate of tumor growth in suckling rats in the sixth and seventh transplant generations was slightly faster than in the earliest passages, and direct invasion of liver and diaphragm, metastases to the lungs (Fig. 7), and slight ascites (1–5 ml.) occurred frequently in the higher passages. Gross appearance resembled the original tumor except for lack of macroscopic tubules and growth of the intraperitoneal tumors as multiple implants on visceral and parietal peritoneum. No liver metastases were seen, but one animal had numerous large foci of hepatocellular necrosis, predominantly periportal in distribution, suggesting vascular infarction. Most animals were sacrificed for study and passage when tumors became massive, but those left for observation usually died (if given inoculations intraperitoneally as sucklings) 2–6 weeks after inoculation, with cachexia, intra-abdominal hemorrhage, respiratory insufficiency, and jaundice as apparent mechanisms of death. Microscopic appearance of tumors of all passage levels showed all the same characteristics described above (Figs. 5–8).

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