RENAL TUMORS IN THE RABBIT

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New growths of any kind are evidently rare in rabbits. Although the rabbit is very extensively used for laboratory purposes, we have found reports of only thirty-five tumors. Twenty-four of the recorded tumors were uterine. Of these Stilling and Beitzke (1) have reported thirteen cases, noting a distinctly hereditary tendency to tumor formation. The youngest animal in their series was four years old. Boycott (2) has recorded four cases, and Wagner (3), Selinow (4), Katase (5), Marie and Aubertin (6), Leitch (7), and Shattock (8) have found one each. Shattock and Leitch both agreed that the case described by Lack (9) was really a primary uterine tumor with metastases. Schmorl (10) reported one case of carcinoma of the lung and a second case with carcinoma of the stomach. Von Dungern (11) and Baumgarten (12) each described a case of sarcoma, while Schultz (13) has done some very interesting work with a transplantable round cell sarcoma. Petit (14) has recorded a primary carcinoma of the lung and a carcinoma of an accessory pancreas in the omentum, and Bashford (15) has found a carcinoma of the mamma and a sarcoma of the subcutaneous tissue.

Of the thirty-five tumors recorded, only two were tumors of the kidney. The first, described by Lubarsch (16) in 1905, was similar to the two that we are reporting. In Lubarsch’s case the growth occupied the upper half of the left kidney, and was sharply marked off from the renal tissue. Upon microscopic examination it was found to be composed mainly of gland-like structures of varying form and width, embedded in a very cellular stroma. Lubarsch noted that the histological structure bore
a close resemblance to the human renal tumor commonly described as an adenosarcoma; no cartilage, squamous epithelium, or striated muscle were found, and no Malpighian corpuscles were mentioned. Pieces of the tumor were inserted into the kidneys of four rabbits, with negative results. The kidney had been previously inoculated with embryonic salivary gland tissue but the author did not believe that the tumor grew from this implant; he thought, however, that the injection might have stimulated tissue rests to growth.

The second renal tumor was reported by Nürnberger (17) in 1912. The growth was situated in the upper half of the right kidney and produced a spherical smooth elevation of the surface about the size of a cherry; a sagittal section through the organ showed a tumor measuring 1.5 cm. by 1.3 cm., and displacing about one-third of the renal tissue. Microscopically, the tumor was composed of numerous cysts of varying size lined with cubical or flattened epithelium, and of large numbers of gland-like tubules lined by high columnar epithelium taking a basic stain and showing many mitotic figures. In some of the tubules the epithelium formed more than one layer; in others there was no lumen, the structure appearing as a solid cord. Between the tubules and cysts there was a cellular connective tissue. Smooth muscle fibers were noted under the capsule of the tumor; no striated muscle, cartilage, bone, or elastic tissue was present. Nürnberger recorded his case as a mixed tumor, and compared it to the embryonal glandular tumors found in man.

Our two neoplasms occurred in adult male rabbits, both having been found on the same afternoon; and although we have autopsied over four hundred rabbits during the last three years, no other tumors have been seen. We were not able to ascertain the ages of the rabbits, neither could we determine whether they were both from the same litter, since animals obtained from different persons had been put into a cage together.

Case I. Adult male rabbit. Death was due to surgical shock following an experimental operation. At autopsy, several hours after death, a spherical tumor 1.4 cm. in diameter was found about the center of the outer border of the left kidney (fig. 1).
Apparently it was of cortical origin, since it did not involve the medulla. It was sharply marked off from the renal tissue, fairly firm, and whitish gray in color. A thin prolongation of renal capsule covered the tumor. No metastases were found.

The microscopic structure is shown under moderate magnification in figure 2. The greater part of the tissue consists of cellular masses \((n)\) of irregularly rounded shape, in some of which tubules \((t)\) are to be seen. They occur in all stages of differentiation from a mere radially arranged cluster of nuclei to a completely formed tubule. The structure of these cellular masses and the fact that they are differentiating into tubules makes it certain that they correspond to the nephrogenous tissue of the embryonic kidney. A similar tissue occurs in a type of human renal tumor which has been described as an adenosarcoma. (Birch-Hirschfeld (18), and Trappe (19)).

In figure 3, an island of nephrogenous tissue is shown in which several tubules have been formed. No connective tissue fibers could be demonstrated in the nephrogenous tissue by Mallory's phosphotungstic acid hematoxylin stain. No mitoses were to be seen in any part of the tumor.

Between the masses of nephrogenous tissue there is usually only coarse connective tissue, but in some areas, as is shown in figure 2, there are a number of irregular tubules lined by flattened epithelium. The nuclei of these cells take a deep hematoxylin stain. These tubules sometimes connect with well developed Malpighian corpuscles. The corpuscle shown in figure 4 has parietal flattened epithelium and a capsular space, and resembles the corresponding adult structure except that there is a complete absence of blood capillaries. A number of well formed corpuscles are to be seen in some sections, and there are a great many incompletely formed. They always lie between the masses of cellular nephrogenous tissue, and none of them contain any blood capillaries. No Malpighian corpuscles are mentioned in the rabbit tumors reported by Lubarsch and Nürnberg, but they have been seen occasionally in tumors of this type occurring in children.
Case II. Adult male rabbit. Killed by ether. Autopsy performed immediately afterwards. A large tumor was found at the inner aspect of the caudal pole of the left kidney (fig. 5), not involving the medulla; the inner extremity of the growth was soft and irregular and had ruptured the renal capsule. No metastases were found.

A few small areas of this tumor show islands of cellular nephrogenous tissue such as occurred so abundantly in the first case, but in all other parts the nephrogenous tissue is completely differentiated into masses of solid cords and tubules (fig. 6). Lumina are visible in many of the cords. The greater part of the tissue shows marked retrogressive changes; there is an accumulation of hyaline material in the connective tissue, and the epithelial cords are disintegrating. In some parts, the degeneration of the tissue is so extensive that the epithelial tissues are no longer recognizable as such (fig. 7). No definite Malpighian corpuscles were found in this tumor, and no mitoses.

Rabbits were inoculated with fragments of fresh sterile tumor from Case II, as follows: three subcutaneously, one in the kidney, one in the anterior chamber of the eye, and two intravenously (with emulsified tumor). Negative results were obtained in every case.

The second case may be regarded as similar to the first, though in a much later stage of development. There are a few small areas that closely resemble the structure of the first tumor, but almost everywhere the cellular masses characteristic of the first tumor have differentiated into solid cords and tubules. The growth has ruptured the renal capsule, but it is evidently not very malignant, since there are no mitotic figures and since retrogressive changes have begun in nearly all parts of the growth.

Including our two cases, there are now reports of four tumors of the rabbit kidney. It will be noted that these tumors have

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1 This case affords a strange coincidence. A piece of tumor from Case I had just been transplanted into the cranial pole of the left kidney, when the animal died from the anesthetic. An autopsy performed immediately revealed a large tumor at the caudal pole of the same kidney (this is the tumor described as Case II). No other tumors have been seen by us although the kidneys of over 400 rabbits have been examined during the last three years.
many points of resemblance. Thus, in the gross, they all appeared to be of cortical origin, and were sharply separated from the renal tissue. The only evidence of infiltration was seen in our Case II, in which the renal capsule was penetrated. Microscopically, three of the growths were composed mainly of glandular structures strongly suggesting renal tubules, and the fourth, our Case I, contained a number of these tubular structures. The presence of Malpighian corpuscles is this tumor is convincing evidence that we are dealing with renal tissue.

Our Case I is in some respects the least differentiated of the group, since it contained a large amount of cellular tissue not yet differentiated into tubules; it corresponded closely in structure with the metanephrogenous tissue at the stage when this begins to form tubules. There was a small amount of this metanephrogenous tissue in Case II, but the greater part of this tumor, as well as the tumor reported by Nürnberg, was of tubular structure.

These rabbit tumors thus correspond closely with those neoplasms of the human kidney commonly described as adenosarcomata. The simplest interpretation of their origin is to regard them as having developed from portions of the metanephrogenous tissue which became enclosed in the kidney during its early development but failed to form connections with the collecting tubules. Since no striated muscle is present, they are not comparable to the mixed tumors of the kidney which occur so frequently in children, and which are best explained as derived from portions of the primitive segments.

Since there is a commendable tendency at the present time to limit the word sarcoma to malignant growths in which the type cell is a fibroblast, it seems inadvisable to classify these tumors as adenosarcomata. They are not mixed tumors as this term implies; the type cells are nephroblasts which grow at first in masses or diffusely without special arrangement (so-called sarcomatous tissue) and later differentiate into tubules. Hence we suggest the term *nephroblastoma* for those tumors in which the type cells tend to form renal tissue only.
REFERENCES

(4) Selinow: Uteruscarcinom beim Kaninchen. (Cited from Centralbl. f. allg. Path., etc., 1908, xix, 122.)
PLATES
EXPLANATION OF PLATES

Fig. 1. Case I. Mid-sagittal section of kidney showing tumor. Photomicrograph, × \( \frac{1}{2} \).

Fig. 2. Case I. The rounded cellular masses are islands of nephrogenous tissue, in which tubules may be seen in different stages of formation. Between the rounded masses are numerous tubular structures lined by a low flattened epithelium. Many Malpighian corpuscles are present. (In some areas only the islands of nephrogenous tissue are to be seen.) × 100.

Fig. 3. Case I. Island of nephrogenous tissue under higher magnification. Several tubules are shown. (The nuclei of the tubules are represented much darker than they appeared in the section.) × 300.

Fig. 4. Case I. A Malpighian corpuscle, complete except for the entire absence of blood capillaries. The parietal flattened layer and the capsular space are well shown. Photomicrograph, × 325.

Fig. 5. Case II. Mid-sagittal section of kidney showing tumor. Photomicrograph, × \( \frac{1}{4} \).

Fig. 6. Case II. Island of tubules corresponding to the cellular masses shown in Fig. 2. The connective tissue contains some homogeneous material. × 150.

Fig. 7. Case II. A part of the tumor showing advanced regressive changes. The tubules have disintegrated and the connective tissue shows a large amount of hyaline material. Photomicrograph, × 300.
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PLATE 1

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