KERATINIZING EMBRYONAL NEPHROMA OF THE KIDNEYS OF THE CHICKEN

WILLIAM H. FELDMAN, D.V.M., M.Sc., AND CARL OLSON, JR., D.V.M.

Division of Experimental Medicine, The Mayo Clinic, Rochester, Minnesota

Neoplasia occurs commonly among adult chickens. In fact, chickens appear to be more susceptible to neoplastic diseases than any of the other domesticated species. The annual incidence of tumor among fowls one year of age or less is approximately 2 to 3 per cent. With the advent of the second year the incidence of occurrence definitely rises, and the rise continues as the age of the fowl advances so that an annual morbidity rate as high as 10 per cent may occur in certain flocks.¹

The majority of tumors that occur in chickens are malignant, and practically all of the ordinary varieties of neoplasia have been encountered, including embryonal tumors of the kidney. The latter usually present a more or less complex histologic structure and are comparable to the so-called Wilms' tumor of human beings. Carcinomas not uncommonly affect chickens, the majority occurring inside the body; the ovary and the intestines are the organs for which there is predilection. A few cases have been reported in which the tumor arose from the liver, the skin, or the mucosa of the mouth and pharynx.

The material constituting the basis for this report is of interest, because of the unusual circumstance of bilateral embryonal neoplasms of the kidneys containing keratin in an amount characteristic of typical epidermoid carcinoma of the integument.

REPORT OF CASE

A male cross-bred fowl was the progeny of a barred Plymouth Rock cockerel mated to a white Leghorn hen. When the bird was eighty-three days old, it became a part of a transmission experiment on fowl leukemia, receiving an intravenous inoculation of whole blood from a donor with erythroleukosis. At the beginning of the experiment the bird was apparently normal so far as its general appearance was concerned; the weight was the same as for other birds of the same age. The total number of erythrocytes, thrombocytes, and leukocytes, and the differential leukocyte count and value for hemoglobin were normal. There was, therefore, no evidence to indicate functional disturbance.

The first observation of the blood which gave evidence of the presence of leukemia was two hundred twenty-seven days after inoculation, and the first physical symptoms of the illness were noted a few days previous to this; however, the involvement

¹ We include with the tumors affecting the domestic chicken the rather common lymphoid neoplastic entity described by Feldman as lymphocytes.
of the blood may have preceded the physical symptoms by a week or more. Three
days after this observation of the blood, or two hundred thirty days after inocula-
tion, the fowl died.

Necropsy

The carcass was in a state of poor nutrition, and appeared anemic. When the
abdomen was opened, a large, yellowish white, irregularly oval mass measuring 4.5
by 5 by 6.5 cm. was observed in the region of the anterior pole of the right kidney,
protruding into the abdominal cavity. The rough, irregular, nodular surface was
covered with peritoneum. The mass was very firm and tough, and could be cut only
with difficulty. When dissecting the tissue of the right lumbar region, it was found
that the anterior third of the right kidney was attached to the mass. The renal
tissue was flattened and spread in a thin sheet over the dorso-medial aspect of the
tumor. The color and consistence of this tissue and the remainder of the right kid-
ney seemed normal, with the exception of a small, well circumscribed, white area 0.2
to 0.3 cm. in diameter near the dorsal edge of the posterior pole. The right testis
and adrenal gland were pushed to the left of the median plane by the mass. The
total weight of the large tumor and the adherent remnant of renal tissue was ap-
approximately 100 gm.

The left kidney was enlarged slightly if at all, and was of normal color and con-
sistence. Situated directly under the left ureter, and in the middle portion of the
kidney, was a rather smooth, grayish-white mass, measuring 0.5 to 0.8 cm. in di-
diameter. On cross-section through this region the neoplastic mass was found to ex-
tend about 0.5 cm. into the renal tissue; the border line between the tumor and
renal tissue was definite. In the central portion of the tumor were a few small,
discrete, dense, yellowish-gray areas which resembled in appearance certain aspects
of the large tumor in the right kidney.

The liver was enlarged and brownish-red, with indefinite areas of small white
foci which tended to coalesce into diffuse circular masses. On cross-section, these
foci were observed to extend into the depths of the hepatic substance.

The other pathologic changes noted were directly associated with the process of
erythroleukosie. The spleen was enlarged to a size estimated to be about ten times
normal; it was 3 cm. long and 3 cm. wide. On serial cross-sections, no foci of
neoplastic cells were seen; the lungs appeared anemic, but otherwise were normal.
The bone marrow was hyperplastic, as would be anticipated in leukemia.

Gross Appearance and Physical Properties of the Large Tumor: The tumor was
ovoid, and was composed of innumerable closely packed, grayish-yellow, kernel-like
units, separated from each other by a minimal amount of grayish stroma. The kernel-like elements were of variable size, from minute bodies hardly perceptible to the unaided eye, to units measuring from 0.1 to 0.2 cm. in their greatest dimension. The surface of the growth, although covered with a thin, delicate, serous membrane, had a strikingly pebbled appearance (Fig. 1). The uneven surface which resulted from the multiple bosselations gave the tumor a unique appearance.

When the tumor was cut, after fixation, it was not difficult to enucleate the kernel-like units; these were found to be of a tough, compact consistence but apparently did not contain mineral salts. The extreme toughness of the structure of the tumor was evident when an attempt was made to incise it with a heavy knife. It was with difficulty that the blade could be made to penetrate into the depths of the tissue. Little soft tissue was discernible, and this seemed more abundant in the dorsal portion of the tumor, beneath the flattened layer of renal tissue, than in the more pendulous parts. A few large blood channels were at the surface of the growth beneath the serous capsule, but blood vessels of sufficient size to be seen in depths of the gross specimen were not observed.

![Fig. 2. Extensive Cornification of the Neoplastic Tissue from the Tumor of the Right Kidney (× 90)](image)

**Pathologic Histology:** *Tumor of the Right Kidney.* Only a minimal amount of normal renal tissue was present. This was limited to areas near the dorsal surface of the tumor, where renal tissue was seen in the gross specimen.

The neoplastic elements consisted largely of multiple, irregularly contoured islands of strongly acidophilic material which was devoid of demonstrable cellular units (Fig. 2). The acidophilic substance consisted of concentric layers of whorls of coarse, compactly arranged fibrillar material. The periphery of the respective island-like structures was invested by a layer of flattened to cuboid cells which rested on a small amount of connective-tissue stroma.

In the zones between the various whorl-like masses there was highly cellular tissue composed of cuboidal cells, many of which were undifferentiated, whereas others had a tendency to form tubular or adenomatous structures. Mitosis was rarely observed, and not a few well formed blood vessels could be seen. Calcification was not present. The diagnosis was keratinizing embryonal nephroma.

Since many keratins contain large amounts of sulphur, it was considered desirable to determine the sulphur content of the dried keratinized material. Dr. M. H.
Power found that the substance contained 0.65 per cent sulphur. Normal dried chicken kidney contained 0.57 per cent sulphur, whereas dried tissue from a non-keratinizing embryonal tumor of the kidney of a chicken contained 0.61 per cent of sulphur.

**Fig. 3. Numerous Keratinizing Units of the Tumor of the Left Kidney (× 35)**

**Fig. 4. Large Epithelial Pearls in Neoplastic Tissue from the Left Kidney (× 90)**

It is obvious that in the tumor reported the sulphur content of the keratinized material is not sufficient to allow the substance to be classified as keratin. Identification must rest on histologic methods.

*Left Kidney:* The neoplastic features of the left kidney were essentially the same as those of the tumor of the right kidney (Figs. 3 and 4). The involvement, however, was less extensive and was confined to that portion of the organ immediately below and adjacent to the ureter. The tumor was not sharply demarcated
from the nephric tissue, although the diverse characteristics of the two structures were clearly apparent.

The central portions of the tumor contained numerous keratinizing masses, although in a rather broad outer zone the embryonic character was evident. Here

![Image](image_url)

**Fig. 5. Non-Keratinizing Portion of Tumor from the Left Kidney (× 100)**

The characteristic structure of an embryonal neoplasm of nephrogenic character may be observed.

there was the same tendency of the cells to produce irregular adenomatous units, comparable to those seen in the tumor of the right kidney, but the diverse histologic propensities of the cellular elements was a notable feature. Although the more cuboidal cells occurred in nests or irregular masses, polymorphic or spindle-shaped cells were present in large numbers between the more differentiated tubular structures (Fig. 5). Squamous cells were relatively few, and were usually found surrounding some of the smaller deposits of keratin. The adenomatous tubular units were lined with a single to several indistinct layers of cells, and in many instances only a small lumen was patent.

Blood vessels were rather few and small. Calcification was not seen. The diagnosis was embryonal nephroma with keratinization.

*Other Organs*: Examination of sections prepared from the spleen, liver, testes, and lungs failed to disclose metastasis. In the liver were lesions of an acute, multiple, focal necrosis, and in this organ, together with the spleen, were the usual pathologic changes observed in erythroleukosis produced experimentally.

**Comment**

Wells, in 1922, contributed a paper pertaining to keratinizing carcinomas of the kidney of human beings, and in addition to reviewing the pertinent literature up to that time, he also described a case. Wells considered the tumor he described to have resulted from metaplastic transformation of the transitional epithelium of the renal pelvis to epithelium of a squamous nature as a result of chronic irritation from renal concretions. Recently Potts contributed a report of one case of squamous-cell carcinoma of the
pelvis of the kidney of man associated with stone and leukoplakia. Other reports of keratinizing tumors of the kidney of man, including that of Scholl and Foulds, have appeared from time to time, but the total number of such reports is relatively few, which attests to the paucity of this variety of neoplasm among human beings.

Cornification of embryonic mixed-cell tumors of the kidney of man was mentioned by Garceau, but information on the frequency of occurrence of this keratinization in such tumors was not given.

Renal tumors of chickens have been reported by several observers. The most comprehensive data have recently been published by Eber and Malke. These authors recorded 371 tumors which had been found at necropsy among 11,903 chickens. The kidney was affected in sixteen instances. The tumors included one carcinoma, two adenomas, one lipoma, one fibroma, and eleven specimens classified as sarcomas. Eight of the sarcomatous growths were of the mixed-cell type.

Tumors of mixed-cell type of the kidney of chickens have also been described and reported by Mathews, McKenney, and Malke. Metastasis occurred in one of Mathews' cases and in a case reported by Malke. None of these authors mentioned the occurrence of keratin in the material studied. In two reports, however, neoplasms similar to the one described by us were observed. The first of these was described by Borrel and Masson. The tumor occurred in a young cockerel which had been killed for food. The growth involved the entire right side of the lumbar region and obliterated part of the right kidney. The neoplasm, which was considered to have arisen in the kidney, was of an embryonic type, and remnants of what appeared to resemble the primitive kidney were to be seen. The structure was lobulated in appearance and possessed nests of stratified epithelium containing "epithelial pearls." Attempts to transplant portions of the tumor to six chickens of the same breed were unsuccessful.

The second instance of a keratinizing tumor of the kidney of a chicken was reported by Baird. The tumor was adherent to the posterior surface of the right kidney of a Plymouth Rock chicken. The author, however, was unable to determine if the mass was an outgrowth from the renal tissue. The tumor, which was considered to represent "a displaced embryonic epithelial remnant of an early stage renal anlage," was composed of a considerable number of epithelial elements, many of them of a squamous nature, and a very vascular and cellular stroma. Extensive areas of cornification were prominent features of the abnormal histologic changes, and the resemblance of the growth to a keratinizing squamous-cell carcinoma was striking. Attempts
to transplant portions of the tumor to 100 Plymouth Rock chickens gave negative results.

The tumors we observed cannot be considered to have originated from the adult epithelial elements of the renal pelvis through the functional and morphologic transformation known as metaplasia. The presence of embryonic nephrogenic elements in both tumors provides significant evidence that these tumors arose independent of the elements constituting the structure of the permanent kidney. The tumors must be considered as having originated from certain cells which persisted from an early developmental period of fetal existence. Occasionally, due to some congenital mishap, these undifferentiated, multipotent, embryonal cells are not utilized in the formation and subsequent evolution of the permanent kidney, but remain as a more or less isolated autonomous focus of potential mischief. They persist with the capacity for growth which characterizes the elements of fetal existence, but apparently are immune to the inhibitory mechanism which guides and restrains normal tissues. Under the circumstances, neoplasia obviously will occur.

Why these particular embryonal nephromas should reveal such a marked tendency to undergo keratinization is difficult to explain satisfactorily. Embryonal tumors of the chicken's kidney do not ordinarily contain this substance, and in the examination of a large number of specimens of embryonal renal tumors of swine we have failed to observe this condition. Two explanations suggest themselves, both of which are without proof. It may be suggested, first, that the cells of the adenomatous structures, by the process of metaplasia, have assumed a morphologic and functional state markedly at variance with the biologic characteristics of these cells as they ordinarily exist. Second, the functional capacity to produce keratin may have been an inherent property of certain of the cellular elements which, in these embryonal tumors, are characterized by their multipotency. Cells which are capable of giving rise to complex tumors containing such varied tissues as striated muscle, cartilage, bone, unstriated muscle, epithelial tubular structures, and connective tissue might possibly provide epithelial elements from which keratin could be derived.

We are of the opinion that the tumors in our case arose as separate entities from a developmental fault which was common to both kidneys. The structure of the larger tumor (that of the right kidney) did not suggest malignant aggressiveness sufficient to cause metastasis. Furthermore, the absence of secondary foci in the liver, and particularly in the lungs, constitutes presumptive evidence that this tumor did not metastasize. That the tumor of the left kidney could have arisen independently is supported by
the occasional occurrence of bilateral embryonal renal tumors in other species. In a series of forty-six embryonal nephromas of swine observed by one of us (Feldman), the tumors in eight instances were bilateral. Furthermore, observations would indicate that tumors of this character do not often metastasize. In the forty-six tumors, previously mentioned, metastasis occurred in only three.

The possibility that the tumor of the left kidney was derived from that of the right kidney must, however, be considered. If the tumor of the right kidney does represent the parent mass from which the tumor of the left kidney developed, the path of dissemination of the neoplastic cells is obscure. There was no evidence that the tumor had spread by continuity from the growth on the right side. In fact, the firm, encapsulated, and retrogressive character of the tumor would probably preclude such behavior on the part of the neoplastic tissue. Conveyance by the blood stream is, of course, possible, but this is hardly tenable in view of the fact that the other viscera did not reveal secondary tumorous foci.

**Summary and Conclusions**

Bilateral embryonal renal tumors were observed in a cross-bred cockerel, ten months of age. The right kidney was practically obliterated by a tumor which weighed approximately 100 gm. The tumor of the left kidney was much smaller and was confined to the region just under the ureter. Metastasis to the remainder of the viscera had not occurred. Study of pathologic histology as related to these tumors disclosed a variety of cellular elements characteristic of a nephrogenic form of neoplasm of the fetal type. Adenomatous structures were common, and the cells of many of these were undergoing keratinization, with the resultant formation of numerous cornified nodules or epithelial pearls. In the larger tumor cornification was the most prominent feature.

**Bibliography**


