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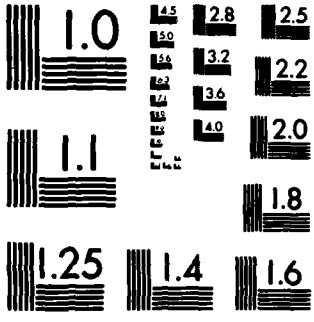

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Spontaneous Transitional Cell Carcinoma in the Urinary Bladder of a Strain 13 Guinea Pig

Creighton J. Trahan and William C. Mitchell

United States Army Medical Research Institute
of Infectious Diseases (USAMRIID)
Fort Detrick, Frederick, MD 21701-5011

Carcinoma of a Guinea Pig Bladder

The animal described in this report was procured, maintained and used in accordance with the Animal Welfare Act and the "Guide for the Care and Use of Laboratory Animals" as promulgated by the Committee on Revision of the Guide for Laboratory Animal Facilities and Care, Institute of Laboratory Animal Resources, National Research Council. USAMRIID is fully accredited by the American Association for Accreditation of Laboratory Animal Care.

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Spontaneous tumors in guinea pigs are very rare. To date, only 318 cases have been reported. This report describes the clinical pathology, gross pathology, and light microscopy histopathology of a spontaneous transitional cell carcinoma in the urinary bladder of a male Strain 13 guinea pig.

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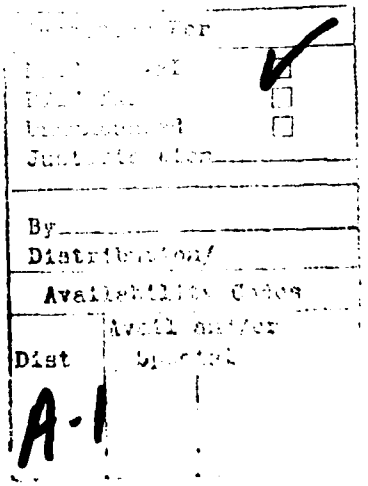
Despite extensive use of the guinea pig (Cavia porcellus) as an experimental animal, there exists a paucity of reports of spontaneous tumors in this species (1-9). The most recent review of the literature (10), conducted in 1960, brought the total number of reported spontaneous neoplasms in guinea pigs to 138. Subsequent publications (3-6, 11-19) now indicate that there are 318 reported cases of spontaneous tumors in the guinea pig. This report describes a case of transitional cell carcinoma of the urinary bladder of a guinea pig.



Case Report

A group of 20 male Strain 13 guinea pigs was received at our facility from Veterinary Resources Branch/National Institutes of Health (VRB/NIH) on March 30, 1983. The animals, selected from NIH's production colony, were part of a shipment of "proven breeders" destined for integration into USAMRIID's Strain 13 breeding colony.

The entire lot was quarantined for two weeks, vaccinated with a Bordetella bronchiseptica bacterin (20), then released and dispersed into the breeding colony. During morning rounds on February 8, 1984, one of these guinea pigs, No. 138, was noted to be emaciated and slightly weakened. The animal was anesthetized[1,2] and blood was drawn for complete blood cell count, differential white cell count, and serum chemistries. Because of the poor physical state of the animal at this time, it was sacrificed[3] and submitted for a complete diagnostic necropsy.

Results

Clinical Pathology: The complete blood cell count[3] revealed a leukopenia ($5.8 \times 10^3/mm^3$), eosinopenia ($0.0 \times 10^3/mm^3$), and a slight neutrophilia ($4.7 \times 10^3/mm^3$). Serum chemistries[4] revealed elevated glucose (156 mg/dl), BUN (128 mg/dl), aspartate amino transferase (AST) (178 IU/l), phosphorus (8.85 mg/dl), cholesterol (69 mg/dl), and triglycerides (238 mg/dl).

Gross Pathology: A single, roughly round, 2-cm diameter, papillary tumor protruded into the lumen of the urinary bladder, completely filling the collapsed bladder. The mass was attached to the ventrolateral mucosa by a fine, narrowly-based fibrous stalk, 0.75-cm long. The bladder contained no urine, and there was no evidence of urinary obstruction.

Light Microscopy: The tumor was covered by a uniform layer of transitional stratified epithelium which had multifocal areas of ulceration and necrosis. The mass was composed of variably-sized lobules of cells, usually further subdivided into smaller, often coalescing sublobules. Separating the lobules was a variable amount of highly vascular stroma which ranged from solidly cellular to extremely loose. Abundant loose stroma frequently abutted the urothelium. Within the sublobules, the cells were arranged in a wide variety of patterns including solid sheets, bundles and streams, and faint whirls and islands. Within the stroma, and also within the stalk, were similar cells arranged in small islands, nests, cords, and ribbons.

The cell shape varied from spindled, to oval, to round (Figure 1). Cell borders were usually indistinct. The cell types seen were a combination of the small cell variant, the clear cell variant, and the spindle cell variant (21). The small cells were densely packed and had scant, pale, basophilic cytoplasm with small hyperchromatic nuclei. The clear cells were round to

oval, and had large amounts of pale, basophilic granular cytoplasm with pale, basophilic vesicular nuclei. The spindled cells had lesser amounts of pale, basophilic cytoplasm than the clear cells, but more than the small cells. The spindled cells had darker, more granular, more variable chromatin patterns within the nuclei than the other two cell types. Up to four cells/high powered field exhibited mitosis, with bizarre forms frequently present. The nucleus to cytoplasm ratio, which varied with the cell type, was from 3:1 to 1:3.

Within the tumor were multiple, randomly scattered, variably sized foci (30μ to 1 cm) of necrosis and hemorrhage. The overall histologic features of this neoplasm were diagnostic of transitional cell carcinoma as described in standard veterinary pathology texts.

Bilateral renal lesions included moderate, multifocal chronic interstitial nephritis with moderate, multifocal, chronic glomerulonephritis affecting approximately 75% of the nephrons. Minimal, multifocal nephrocalcinosis was also noted. Liver tissue sections examined revealed mild, multifocal, acute to subacute necrotizing hepatitis. The pancreas had diffuse, moderate, fatty infiltration of approximately 50% of the acinar tissue.

Discussion

Spontaneous tumors of the lower urinary tract of domestic animals are rare, with the exception of cattle raised where bracken fern (Pteridium aquilinum) is indigenous. The urinary bladder neoplasms in these cases are associated with a syndrome known as chronic enzootic haematuria (21). Studies have shown that bracken fern is a potent inducer of bladder cancer in both domestic and laboratory animal species (22-24). In the canine population, primary urinary bladder tumors account for less than 1% of all canine neoplasms. In the feline, the extremely low incidence of bladder tumors observed may well be due to a difference in metabolic pathways used for the processing of certain amino acids, with a resultant low level of orthoaminophenol metabolites in the urine. The occurrence of bladder tumors is also very infrequent in the equine, ovine, and porcine species (21).

In the commonly used laboratory animal species, spontaneous primary neoplasms of the lower urinary tract are also infrequent. In mice, these tumors are extremely rare, with no inbred strain having been developed which has a high incidence of spontaneous bladder cancer (25). In the rat, primary tumors of the urinary bladder are generally uncommon except for the BN/BiRij strain, which is reported to have a relatively high incidence of ureter and urinary bladder tumors (26). In nonhuman primates, urinary bladder tumors have been induced with 2-nitronaphthalene and related chemicals used in the dye industry, as well as with percutaneous infection with cercaria of Schistosoma haematobium. Overall incidence of spontaneous urinary bladder neoplasia in nonhuman primates remains very low (1). In the laboratory rabbit, and Syrian and Chinese hamster, tumors of the lower urinary tract are extremely rare (1, 27-28).

The guinea pig appears to be refractory to induction of bladder neoplasia with certain known carcinogens (22). This lack of susceptibility may be due to a metabolic difference in aromatic amine acetylation-deacetylation reactions when compared to other species (22, 29). Only five spontaneous tumors of the lower urinary tract of guinea pigs have been reported (14,15). Of these, two were described as transitional cell carcinomas of the urinary bladder.

The leukopenia, due to lymphopenia and eosinopenia, observed in this guinea pig was most likely due to systemic stress induced by the transitional cell carcinoma, and by the renal and hepatic lesions. The slight neutrophilia could be classified as the noninflammatory type, usually associated with the endogenous release of adrenocorticosteroids in diseases such as bone fracture, intoxications, and neoplasia (30). The hyperglycemia observed could be attributed to elevation of adrenocorticosteroids commonly seen in moribund animals. Elevations in serum BUN, phosphorus, cholesterol, and triglycerides are commonly associated with chronic renal disease. The cachexia and ensuing state of protein catabolism, as well as the necrotizing hepatitis, are the most probable causes of the increased level of serum AST.

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Footnotes

[1] Vetalar®, Parke Davis, Morris Plains, NJ.

[2] Rompun®, Haver-Lockhart, Shawnee, KS.

[3] T-61®, National Lab. Corp., Somerville, NJ.

[4] Coulter® MHR, Coulter Electronics, Inc., Hialea, FL.

[5] Cobas-Bio®, Roche Analytical, Nutley, NJ.

Figure 1 Transitional cell carcinoma of urinary bladder. Cellular variation demonstrated by clear cell variant (large white arrow), small cell variant (white arrowhead), and oval or spindle cell variant (large black arrow). All cell types are arranged in a solid sheet. Hematoxylin and eosin. Line = 50μ.

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