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GRANULOSA CELL TUMOR IN A GARTER SNAKE (*Thamnophis sirtalis*)

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Abstract: A granulosa cell tumor was identified in a captive six year old Garter Snake (*Thamnophis sirtalis*). Metastasis to both kidneys was manifested as miliary white foci and structure distortion.

INTRODUCTION

A recently compiled list of neoplasms in reptiles shows a wide variation of the types of neoplasms among the various species and families.² In snakes, there is only one case reported involving the reproductive system.⁴ This appears to be the first report of an ovarian tumor in a reptile.

CASE REPORT

The six year old female Garter Snake (*Thamnophis sirtalis*) was raised by and in care of a private owner. At two years of age the snake was noted to pass "large quantities of sticky, yellowish mucus" from the cloaca. One year later she was mated with a sibling. After about one week she passed a large amount of blood. There were no offspring from this mating. Six months later she was allowed to mate again with the same male. This time she passed blood shortly after copulation. She became very weak and had to be carefully nursed before she returned to normal condition. No further mating attempts were done. The animal did have some difficulty swallowing larger pieces of food but aside from this appeared clinically normal throughout the next 2.5 years. Three days prior to death the snake lost her muscle tone and became progressively weaker. She was still eager for food and readily took water

from an eye dropper. She died in a mild convulsion.

On necropsy, there were three abnormal follicles in the ovary varying in diameter from one to two centimeters. They contained clear, slightly yellow fluid and small, irregular proliferations formed by white firm tissue. Both kidneys were poorly lobulated and seeded throughout with white foci, some of which coalesced to form small nodules. The anterior half of the aorta was greatly thickened (2 times the normal diameter) and tortuous.

Histologic examination revealed that the proliferations in the follicles consisted of irregular, predominantly tubule forming cells of epitheliomatous appearance, interspaced by fibrous connective tissue. There was no inflammatory response. In the tubes, the cells were randomly arranged, although a tendency to form trabeculae and rosettes was noticed. A peculiar feature was the peripheral lining of each area of infiltration by a rim of homogeneous eosinophilic, mucin negative, periodic acid-Schiff positive, material. This lining had on many occasions infoldings into the tumor masses (Fig. 1). Tumor cells were oriented in an epithelial-like arrangement along the rim. Rosette-like structures, with a center of identical eosinophilic material, were also observed. The tumor cells were small, with a high nucleoplasm: cytoplasm ratio.

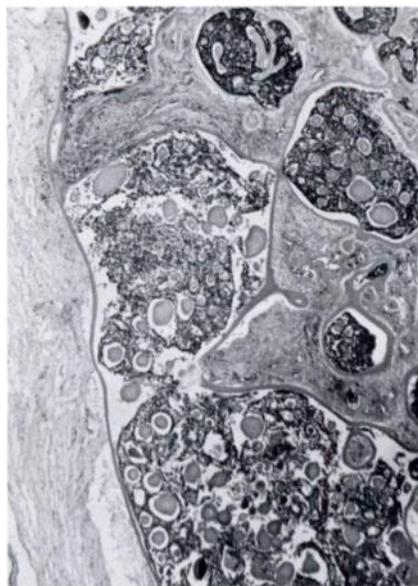


FIGURE 1. Neoplastic infiltrate in the ovary. The tumor masses are surrounded by rims of hyaline material. It often appears as globules among the cells or as infoldings. Fibrous connective tissue separates the tumor masses. H&E stain, $\times 40$.

Few mitotic figures were seen. The scanty cytoplasm was eosinophilic. In the randomly arranged areas the cells were round. In areas of trabeculum formation the cells were spindle-shaped, while the rosettes were lined by cuboidal cells with basally situated nuclei. Based on these characteristics the neoplastic infiltration was identified as a granulosa cell tumor.

In the kidneys, relatively large masses of tumor cells formed a typical insular pattern. There was indication that the tumor metastasized along renal portal veins, entering the kidneys on the surface of the lobules. Further spread occurred along tubules as indicated by plugs of tumor cells and by single tumor cell layers situated between epithelium

and basal membrane. The presence of infiltrating tumor around an otherwise intact artery was suggestive of lymphatic spread. Rosette-shaped accumulations of crystals, probably urates embedded in tumor masses also were observed (Fig. 2). The tumor-containing areas were in contrast to the normal remains of the kidney rich in connective tissue, and had low numbers of isolated tubules and glomeruli. Some characteristic gout tophi, surrounded by giant cells were observed in the interstitium. No evidence of metastasis was seen in any other organ.

There was marked sclerosis of the aortic intima with thrombosis and recanalization of the lumen.

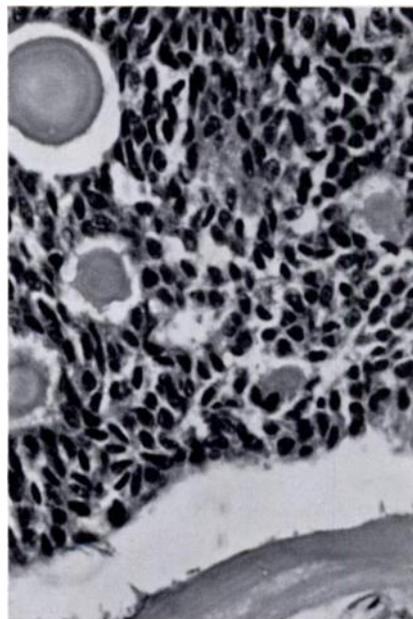


FIGURE 2. Metastatic infiltrate in the kidney. There is a mixed population of very dense spindle-shaped cells and a more cuboidal cell type. Hyaline globules similar to the ones seen in the ovarian tumor masses are also present. H&E stain, $\times 400$.

DISCUSSION

The mucin-producing Brenner tumor occurs in the ovary in man.⁷ In the snake the eosinophilic material in and around the tumor prompted us to perform a mucin stain, which was negative. The granulosa cell tumor in man usually shows a variety of patterns in one tumor. The cell patterns may be trabecular, randomly arranged and follicular.⁶ These descriptions are applicable to the case of the Garter Snake. In man the most distinctive feature of the granulosa cell tumor, although not present in all cases, are microfollicular arrangements of tumor cells; the Call-Exner bodies.⁵ In the Garter Snake these were not identified with certainty. The eosinophilic material associated with the tumor is reminiscent of the polysaccharide-rich *zona pellucida* which is believed to be elaborated by the follicular cells of ovarian follicles.

A recent study of granulosa cell tumors in women indicates that there is usually a long clinical history.³ The presenting signs include abnormal vaginal bleeding. Analysis of the patient's post treatment histories revealed that in all cases granulosa cell tumors should be

considered malignant but to a variable degree as expressed by high or low mitosis. Detection of metastasis occurred as late as 19 years after removal of the primary mass.

In our case, the excellent record of observations of the animal suggests that this tumor was of slow growth and low malignancy, having developed over a period of four years or possibly longer. This is in agreement with the benign appearance of the neoplastic islands. A peculiar feature in the Garter Snake was the presence of urate masses within the areas of tumor. In cases of reptilian gout, urate masses of identical shape and size usually are surrounded by giant cells thus producing gout tophi.^{1,7} In this case the renal tubular epithelial cells probably were lifted from the basement-membrane by tumor cells, thus they became isolated from the host defence mechanisms, while urate crystals were deposited in the degenerated cells.

The arteriosclerosis caused such marked thickening that the esophagus became constricted in the area of the heart so that food morsels were difficult to swallow. Death resulted probably from terminal renal failure.

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