

## HIGH PREVALENCE OF OVARIAN TUMORS IN MANED WOLVES (*CHRYSOCYON BRACHYURUS*) AT THE NATIONAL ZOOLOGICAL PARK

Linda Munson, D.V.M., Ph.D., and Richard J. Montali, D.V.M.

**Abstract:** Ovarian neoplasms were identified at necropsy or surgery in four of nine adult female maned wolves (*Chrysocyon brachyurus*) from the Conservation and Research Center of the National Zoological Park. All affected wolves had produced pups 4-9 yr previously. Three of four wolves had dysgerminomas, tumors of primordial germ cell origin that are rare in other mammals. Two of these three wolves were related, and one of the three had extensive metastatic disease. Two of the dysgerminomas were in the ovarian stalk, an atypical location for primordial germ cells. The high prevalence of dysgerminomas in this population may be due to environmental or genetic factors. Another maned wolf had a granulosa cell tumor (Sertoli pattern) and an ovarian papillary adenoma, which are common in domestic dogs. These tumors were accompanied by endometrial carcinoma, endometrial hyperplasia, and pyometra, suggesting an endocrine function of the granulosa cell tumor. The high prevalence of ovarian neoplasia represents another major health problem in this endangered species.

**Key words:** Dysgerminoma, granulosa cell tumor, papillary adenoma, ovarian tumor, maned wolf, *Chrysocyon brachyurus*.

### INTRODUCTION

Maned wolves (*Chrysocyon brachyurus*) are endangered in the wild (CITES, Appendix 2) and have poor reproductive performance in captivity. Although tumors have been reported in the maned wolf<sup>4,5</sup> and are a significant cause of death in nondomestic canids,<sup>1</sup> the prevalence of neoplasia in this species has not been assessed. Ovarian tumors are uncommon in most mammals, accounting for only 1-6% of canine neoplasms<sup>10</sup> and 6% of neoplasms in women.<sup>8</sup> This paper reports four cases of ovarian neoplasia in maned wolves at the National Zoological Park; affecting 44% of the adult females in the collection since 1975.

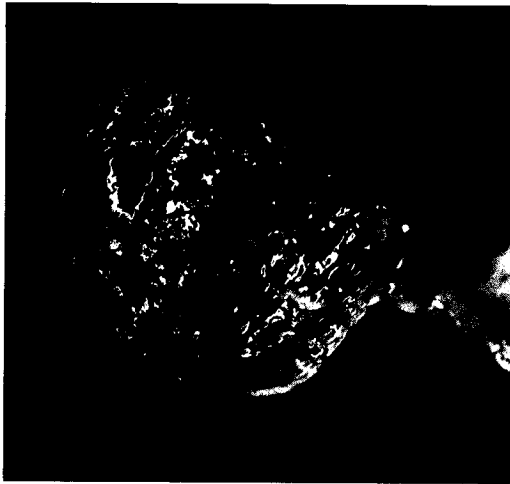
### CASE REPORTS

#### Case 1

A 12-yr-old wild-caught female wolf that produced four pups in three litters (the last litter was 5 yr previously) had a 10-cm ovarian mass, an 8-cm-diameter firm nodular mammary mass, and an enlarged (6-cm-di-

ameter) inguinal lymph node. The masses and node were removed surgically. The right ovary was replaced by a soft, gray friable encapsulated mass with large areas of infarction and hemorrhage (Fig. 1). Histologically, the neoplasm projected from the hilus, compressing normal ovarian tissue to one border. The mass was composed of solid sheets of cells divided into large lobules by a few fibrous septa. Neoplastic cells were large bizarre round cells with vesicular cytoplasm and large central nuclei with large nucleoli (Fig. 2). Large areas of coagulative necrosis and hemorrhage were present, and capsular and vascular invasion were noted. A minimal infiltration of stromal septa by lymphocytes was also present. The diagnosis was ovarian dysgerminoma. The remaining ovary had few oocytes and many small primary follicle-like structures without oocytes (sex-cords). The mammary mass was an adenocarcinoma that had metastasized to the inguinal lymph node. The wolf had no clinical recurrence until 13 mo post-operatively. At that time, she was weak and lethargic. Multiple omental masses and enlarged subiliac lymph nodes were noted on abdominal palpation. Metastatic disease was confirmed by evaluation of impression

From the Department of Pathology, National Zoological Park, Smithsonian Institution, Washington, D.C. 20008, USA.



**Figure 1.** Ovarian dysgerminoma in a maned wolf (Case 1). The ovary is replaced by a solid encapsulated mass.

smears of omental masses, and euthanasia was elected. At necropsy, the omentum and mesentery contained numerous friable masses of various sizes (0.3–4 cm), with areas of hemorrhage and necrosis. The subiliac lymph nodes were enlarged markedly (15 × 10 × 4 cm) and had both firm and friable areas. At the proximal end of the right uterine horn (the site of the previous ovariectomy), a 12-cm friable pink mass was present. The left ovary contained numerous corpora lutea and small numbers of Graafian follicles. Histologically, the uterine mass, omental masses, mesenteric masses, and some of the subiliac masses were metastatic dysgerminoma. The firm areas in subiliac lymph nodes were metastatic mammary adenocarcinoma.

#### Case 2

A 14-yr-old female wolf had an ovarian mass, as determined by abdominal palpation. She had produced seven pups in six litters; the last litter was 6 yr previously. The left ovary was effaced by an 8-cm-diameter multilobulated encapsulated gray mass. No normal ovarian tissue was identified. Unilateral ovariectomy was performed. On cut section, the left ovarian mass

was soft, friable, and tan/gray with multiple areas of infarction and hemorrhage. Histologically, the mass was composed of large bizarre round cells with large central vesicular nuclei, prominent nucleoli, and vesicular cytoplasm. Foci of necrosis and hemorrhage were numerous, and some lymphocytes were present in the few stromal septa. The mass was diagnosed as a dysgerminoma. This female has had no clinical evidence of metastatic disease for 12 mo.

#### Case 3

A 17-yr-old wild-caught female wolf (dam of wolf in Case 2) that had produced two pups 4 yr previously had chronic cystinuria, progressive hyperplastic gingivitis, weakness, and seizures. Euthanasia was elected because no definitive diagnosis was obtained and symptomatic treatment was unsuccessful. Significant necropsy findings were a pheochromocytoma, hepatic nodular hyperplasia, severe unilateral renal atrophy, and marked hyperplastic gingivitis. Ovaries appeared normal grossly. Histologically, a multilobulated mass was present in the ovarian hilus and was composed of a solid sheet of primitive round cells similar to those in Cases 1 and 2. Ovarian dysgerminoma was diagnosed. The remainder of the ovary had two degenerating corpora lutea but a paucity of oocytes or developing follicles.

#### Case 4

A >19-yr-old wild-caught female wolf that produced five pups in three litters (the last litter was 9 yr previously) had weakness, lethargy, and radiographic evidence of pyometra. Euthanasia was elected because of her advanced age and lack of clinical response to prostaglandin  $F_{2\alpha}$ . Significant necropsy findings were chronic cystic endometrial hyperplasia with pyometra, endometrial carcinoma, pheochromocytoma, adrenal cortical adenoma, chronic interstitial nephritis, and hyperplastic gingivitis. The right ovary was enlarged (3 × 4 × 2 cm), firm, and nodular. The left ovary was

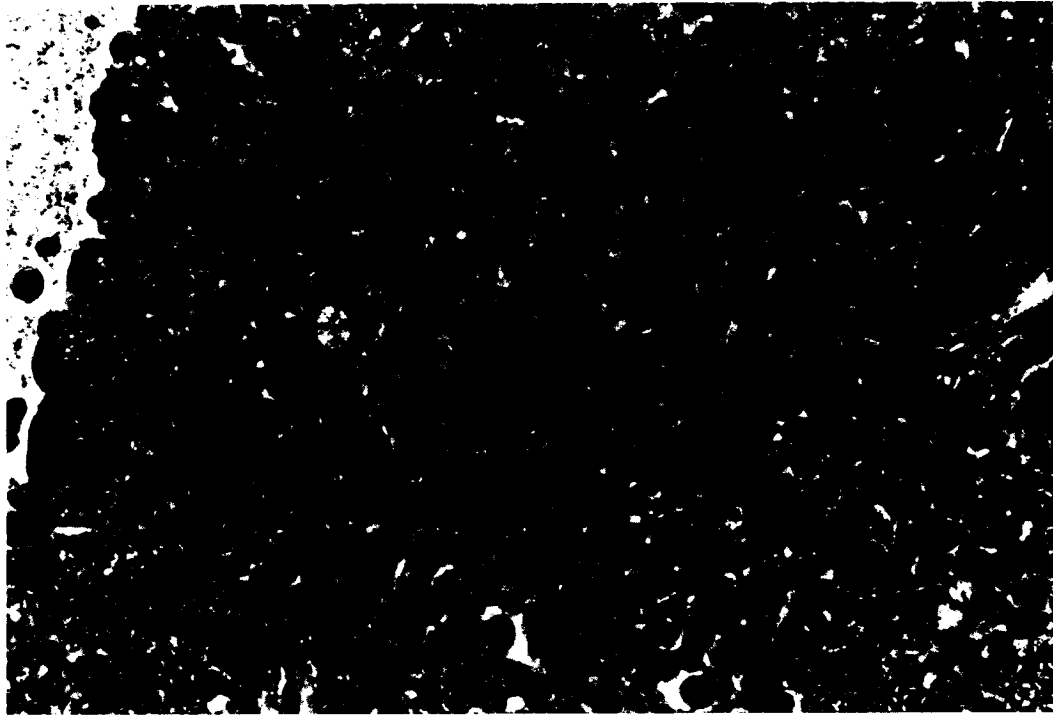


Figure 2. Ovarian dysgerminoma in a maned wolf (Case 1). Note the solid sheets of uniform neoplastic primordial germ cells with abundant mitosis (arrows) and a rare giant cell (arrowhead). H&E,  $\times 250$ .

atrophied ( $0.5 \times 0.25 \times 0.25$  cm). Histologically, the majority of the right ovary had been replaced by a poorly demarcated multilobulated mass, composed of cords and folliclelike structures of cells arranged along thin fibrovascular septa (Fig. 3). The cells were cuboidal to columnar with abundant eosinophilic vacuolated cytoplasm and round open nuclei. The diagnosis was a granulosa cell tumor with Sertoli pattern. On the ovarian surface, there was a small papillary mass composed of cuboidal epithelial cells covering a stomal core. This mass was diagnosed as a papillary adenoma. The remainder of the right ovary and entire left ovary had few oocytes and no folliculogenesis.

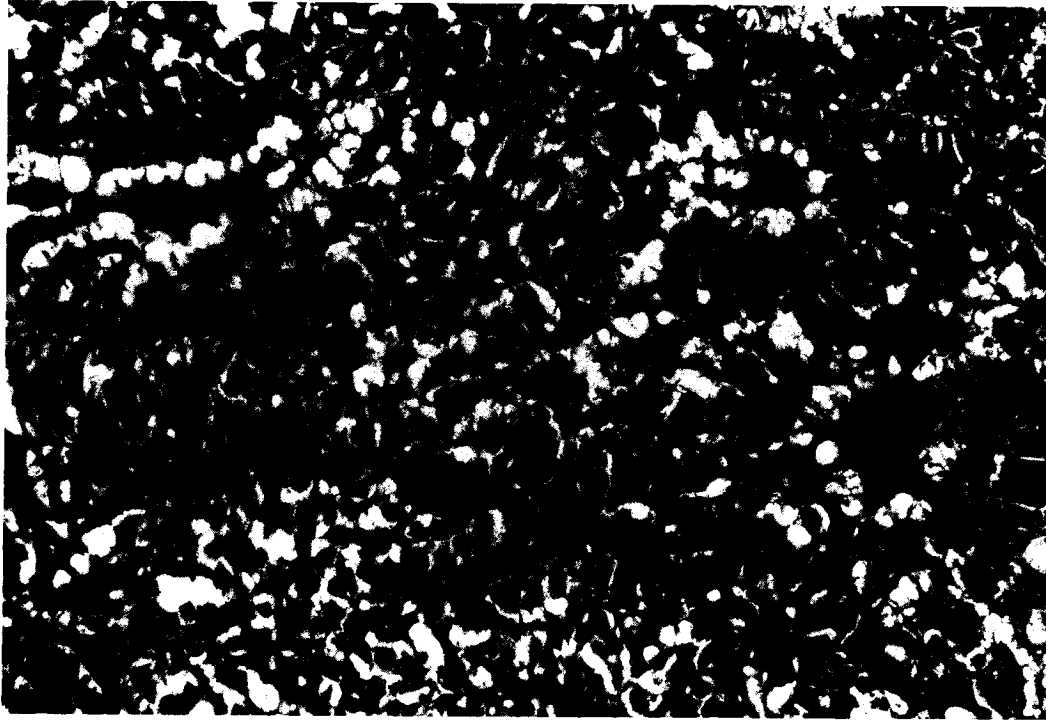
#### DISCUSSION

Ovarian neoplasms were present in four of nine adult female maned wolves, and three of the five ovarian neoplasms were

dysgerminomas. One wolf had a granulosa cell tumor and a papillary adenoma.

Dysgerminomas are neoplasms of primordial germ cells that do not undergo further differentiation.<sup>9</sup> Germ cell tumors in humans develop in the gonad or in extragonadal sites on the midline along the embryonic migration route of primordial germ cells from the yolk sac to the ovarian cortex. Arrested migration of primordial germ cells in the ovarian hilus may have occurred in the two maned wolves with dysgerminomas in the ovarian hilus. The site of origin of the third case could not be determined because all ovarian tissue was effaced.

Dysgerminomas usually are rare in mammals, ranging from 2% of primary ovarian neoplasms in women to 9–10% in domestic bitches.<sup>10</sup> It is interesting to note that the prevalence of dysgerminomas in women varies considerably by geographic region.<sup>9</sup> The high prevalence of dysgerminomas in



**Figure 3.** Granulosa cell tumor in a maned wolf (Case 4). Neoplastic granulosa cells form tubular structures (Sertoli pattern) and a rare follicular structure (arrow). Vacuolization of the cytoplasm suggests endocrinologic function. H&E;  $\times 250$ .

maned wolves at the Conservation and Research Center may indicate a regional focus, although no dysgerminomas have been identified in any other exotic species at this site. The only other reported dysgerminoma in a nondomestic carnivore was in a snow leopard (*Felis uncia*) at another zoological institution.<sup>3</sup>

Dysgerminomas have been reported in closely related women, as was noted in maned wolves (Cases 2 and 3).<sup>9</sup> It is possible that maned wolves have a genetic predisposition to dysgerminomas, as they do for other disease problems such as cystinuria and gingival hyperplasia.<sup>5</sup> This predisposition would be maintained within the population because the tumors were not noted until after all affected wolves had produced pups.

In women, dysgerminomas are associated

with gonadal dysgenesis.<sup>9</sup> Small gonads and infertility have been noted in maned wolves at our institution. Infertile maned wolves, particularly close relatives of wolves with dysgerminomas, should be evaluated for abnormal gonad size or other signs of abnormal gonadal development. The lack of folliculogenesis in the wolves in this study was probably due to advanced age and not to dysgenesis.

Dysgerminomas are usually clinically inapparent.<sup>9</sup> All dysgerminomas are considered potentially malignant<sup>9</sup> but only metastasize in 10–20% of affected domestic bitches.<sup>6,10</sup> Anaplasia and increased cell to stroma ratios, as was noted in Case 1, are associated with metastatic potential in women.<sup>8</sup> Metastatic patterns in women are similar to those in Case 1, with extension of neoplastic cells to the peritoneum and

regional lymph nodes.<sup>7</sup> Early removal of unilateral dysgerminomas that have not invaded the ovarian capsule may be curative.<sup>7-9</sup> Stromal cell neoplasms of the ovary, including granulosa cell tumors of different histomorphological patterns, are more common in domestic bitches.<sup>6,10</sup> Luteinization of granulosa cells usually indicates endocrinological activity, particularly of progesterone.<sup>2,6,10</sup> The presence of endometrial carcinoma, cystic endometrial hyperplasia, and pyometra in Case 4 supports histomorphologic evidence of endocrinologic activity of the granulosa cell tumor. Of women with steroid-producing granulosa cell tumors, 10–15% develop endometrial carcinomas.<sup>8</sup> Fifty percent of bitches with granulosa cell tumors develop cystic endometrial hyperplasia.<sup>2,6</sup>

Papillary adenomas also are common in domestic bitches<sup>2,10</sup> and are thought to arise from the surface epithelium of the ovary. Because granulosa cell tumors and papillary adenomas are common in aged domestic dogs, they also would be expected in an aged maned wolf. This case is notable only by increasing the prevalence of ovarian tumors in this species.

The prevalence of ovarian neoplasia in maned wolves at the National Zoological Park is greater than that noted for other mammals. Additional neoplasms reported in maned wolves at our institution have involved endocrine glands (two pheochromocytomas, an adrenal cortical adenoma)<sup>5</sup> and hormonally sensitive tissue (mammary carcinoma) (L. Munson, pers. obs.). Neoplasia of endocrine or endocrine-sensitive organs represents another major health problem in this endangered species.

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