



NOTE

Wildlife Science

Granulosa cell tumor in 8 African pygmy hedgehogs (*Atelerix albiventris*)

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ABSTRACT. A retrospective study involving eight African pygmy hedgehogs histopathologically diagnosed with granulosa cell tumors was conducted. The age at onset was 2.2–4.5 years, with a median age of 3.6 years. The most common clinical signs were hematuria and abdominal distension, which were observed in >50% cases. Exploratory laparotomy was performed in all cases, and ovariectomy or excision of the abdominal mass was performed. Patients with only hematuria survived for >250 days after surgery, whereas those with initial ascites showed recurrence of ascites or tumor growth and survived for approximately 130 days after surgery. Intraperitoneal injection of carboplatin was performed in three recurrent cases. In one of these three cases, the tumor mass disappeared. Hence, carboplatin can be considered a potential antineoplastic drug for the treatment of granulosa cell tumors.

KEY WORDS: carboplatin, granulosa cell tumor, hedgehog

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Granulosa cell tumors are a type of ovarian interstitial tumors that have been reported in various animal species [1, 6]. However, to the best of our knowledge, only two studies have reported a single case of a hedgehog with ovarian granulosa cell tumors [7, 10]. This study aimed to summarize the clinical characteristics of granulosa cell tumors in eight African pygmy hedgehogs.

The medical records of eight hedgehogs admitted to Miwa Exotic Animal Hospital between October 2009 and December 2018 were reviewed. Eight female hedgehogs (one spayed female) were included in this study. These patients underwent ovariectomy or abdominal tumor excision and were histopathologically diagnosed with granulosa cell tumors. Clinical signs at diagnosis, treatment, complications, and prognosis of these eight cases were evaluated retrospectively and are summarized in Table 1.

The age at presentation was 2.3–4.5 years, with a median age of 3.6 years. The body weight was 401–786 g (median, 527 g). One case was already diagnosed with granulosa cell tumor at another hospital (Case 6). Hematuria was observed in four of eight cases, while abdominal distension caused by ascites was observed in the remaining four cases. Other clinical signs included anorexia in three cases, tachypnea in two cases, stranguria in one case, and pale mucous membrane in one case.

On radiography, a swollen abdominal cavity was observed in four cases (Cases 5–8), mild cardiomegaly was observed in two cases (Cases 1 and 4), and hepatomegaly was observed in one case (Case 3). Ultrasonography was performed in seven cases, revealing ascites in four cases, uterus-like tubular structures in four cases, abdominal masses in three cases, cystic structures in one case, and rounded liver margins in one case.

Surgery was performed under general anesthesia with premedication of meloxicam (0.5 mg/kg) and buprenorphine (0.02 mg/kg) subcutaneously. Anesthesia was induced and maintained by mask inhalation of isoflurane. On laparotomy, cystic or tumor-like ovaries and enlarged uteri were observed in 6/8 cases (Fig. 1), while cystic abdominal masses were observed in the other two cases (Fig. 2). In addition, hemosanguinous ascites was observed in 4/8 cases. The abnormal ovary, uterus, and other intraabdominal masses were excised as much as possible. However, in two cases with intraabdominal tumors complete excision was not possible. Separation of the tumor mass from the surrounding tissues was difficult due to intensive adhesion (Case 6) and dissemination of tumor cells within the abnormal cavity (Case 5). All surgeries were performed safely, and the patients recovered without any adverse events.

Physical examination and abdominal ultrasonography were performed periodically after surgery. Follow-up data on various examinations were collected at the hospital or by telephone consultation with the owners.

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Table 1. Case description in 8 African pygmy hedgehogs diagnosed with granulosa cell tumor

Patient no.	Age at the diagnosis (years)	Clinical signs	Surgery	Post-operative finding	Carboplatin	Survival time (days, after surgery)
1	4.5	Hematuria; tachypnea; anorexia	Ovariohysterectomy	CI	-	258
2	3.2	Hematuria	Ovariohysterectomy	CI	-	380
3	3.7	Hematuria	Ovariohysterectomy	CI	-	>393
4	3.3	Hematuria	Ovariohysterectomy	CI	-	>613
5	2.7	Ascites	Partial tumor excision	Tumor regrowth	Tumor response (decreasing)	>131
6	2.2	Ascites	Partial tumor excision	Ascites recurred	No decreasing of ascites	112
7	3.4	Ascites; anorexia; stranguria	Ovariohysterectomy with partial tumor excision	Ascites recurred	No decreasing of ascites	155
8	4.2	Ascites; anorexia	Ovariohysterectomy	Ascites recurred	-	117

CI: clinically improved.



Fig. 1. Appearance of the excised ovary and uterus (Case 2). A cystic ovary and an enlarged uterus are observed.

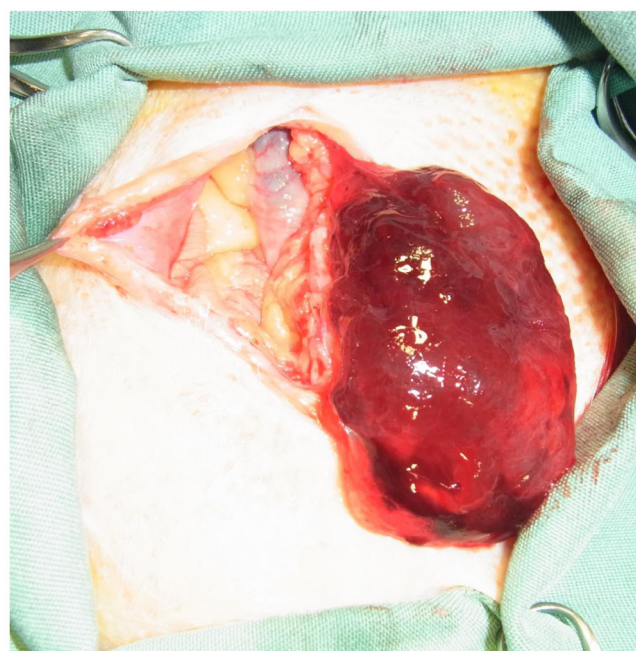


Fig. 2. Appearance of the excised abdominal cystic mass (Case 6). A cystic abdominal mass is observed; separation of the tumor mass from the surrounding tissues was difficult due to intensive adhesion.

Cytological evaluation of the ascites obtained during surgery was performed in four cases (Cases 5–8); no neoplastic cells were identified. The excised ovaries and abdominal masses in all cases were sent for histopathological evaluation; granulosa cell tumors were diagnosed in all cases. Histopathologically, the neoplastic tissue in the ovary of each case showed papillary growth with an indistinct margin (Fig. 3A). Vascular invasion of the tumor was observed in Case 8. Neoplasms were composed of round cells that were diffusely arranged and separated by thin fibrovascular stroma (Fig. 3B). Neoplastic cells had scant cytoplasm and round nuclei, showing mild anisokaryosis. Occasionally, neoplastic cells were arranged in rosette-like structures with acidophilic material in the center (Fig. 3C).

Evaluation of the excised uteri showed endometrial hyperplasia (Cases 4 and 8), mixed endometrial tumors (Case 3), uterine adenomyosis (Case 7), endometrial adenocarcinoma with endometrial stromal tumor (Case 1), and endometrial adenoma with endometrial stromal tumor (Case 2).

In four cases without initial ascites (Cases 1–4), clinical improvement was observed after surgery; all patients survived for

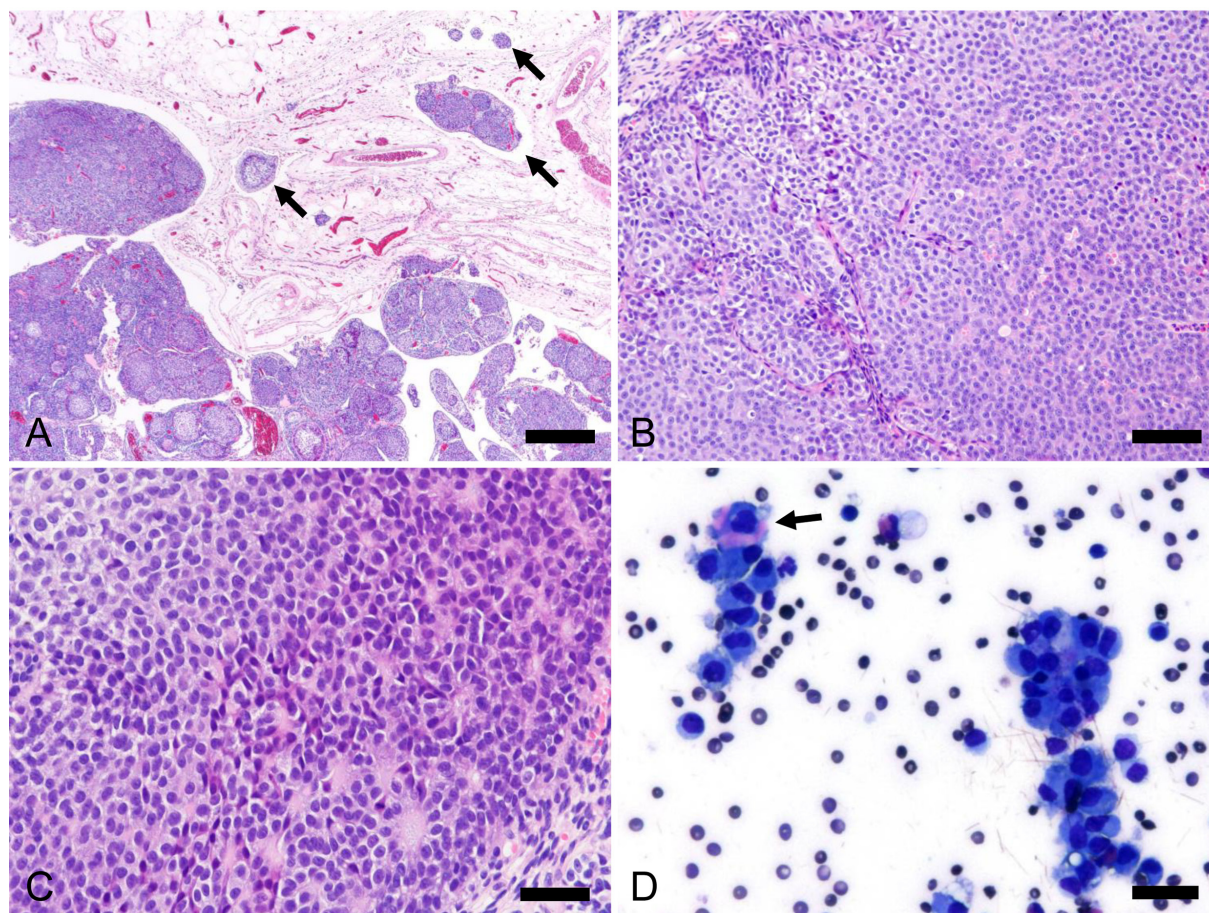


Fig. 3. Histological and cytological findings of granulosa cell tumor in hedgehogs. (A) Papillary growth of neoplastic tissue in the ovary. Vascular invasion of neoplastic cells (arrows). Case 8; Hematoxylin-Eosin stain; bar, 1 mm. (B) Neoplastic tissue is composed of diffuse growth of round cells separated by thin fibrovascular stroma. Case 5; Hematoxylin-Eosin stain; bar, 100 μ m. (C) Occasionally, tumor cells are arranged in rosette-like structures with acidophilic material in the center (lower right). Case 5; Hematoxylin-Eosin stain; bar, 50 μ m. (D) Cytology of ascites. Aggregates of round cells with occasional acidophilic material (arrow). Case 5; Wright-Giemsa stain; bar, 30 μ m.

>250 days after surgery. Two patients died of other diseases unrelated to the tumor at 258 and 380 days after surgery (Case 1 and 2, respectively). In the remaining four cases with ascites at initial presentation (Cases 5–8), recurrence of ascites (3/4, Cases 6–8) or a cystic intraabdominal tumor (1/4, Case 5) were noted on ultrasonography. Cytological evaluation of the recurrent ascites was performed in one case (Case 5) 2 weeks after surgery, and granulosa cell tumor cells were identified. Carboplatin (5–18 mg/kg) was administered intraperitoneally in two cases (Cases 6 and 7) with ascites recurrence and in one case with intraabdominal tumor regrowth (Case 5) (Fig. 3D). Remission of the regrown intraabdominal tumor was identified in Case 5; however, a decrease in ascites was not observed in Cases 6 and 7. In these four cases with initial ascites (Cases 5–8), 3 patients died at 112, 117, and 155 days after surgery (Cases 6, 7, and 8, respectively). In Case 5, the patient was alive 131 days after surgery.

Granulosa cell tumors are the most common spontaneous ovarian tumors found in many domestic and laboratory animal species [2]. The present study describes the clinical characteristics, treatment outcomes, and prognosis of African pygmy hedgehogs diagnosed with granulosa cell tumors. The age at diagnosis ranged widely from middle to advanced age. However, dogs and mice are diagnosed with granulosa cell tumors at a relatively older age, ranging from 8 to 16 years (median: 12 years) and 12 to 24 months (median: 18 months), respectively [2, 8]. The histopathological structure of tumors in hedgehogs is similar to that in other mammals, including dogs and rodents [4, 8].

The presence of ascites has been reported in hedgehogs with proliferative uterine lesions [3] and granulosa cell tumors [7]. In this study, ascites was identified in 50% patients. Furthermore, patients presenting with ascites tended to have a relatively shorter survival than those without ascites, suggesting that presence of ascites may be a worse prognostic factor in this disease.

Cytologically, the ascites collected before or during surgery did not have neoplastic cells in all patients; however, neoplastic cells were identified in postoperative ascites in one case. This may suggest that surgical manipulation can cause dissemination of neoplastic cells into the abdominal cavity. From the authors' histopathological experience, the boundary between the ovary and its surrounding tissue is slightly indistinct in hedgehogs. To prevent intraoperative tumor cell dissemination, efforts should be made to handle the ovary carefully, especially when ascites is present.

Excessive production of sex steroids has been reported in humans, dogs, and rats with granulosa cell tumors [4, 5, 8]. There have been many reports of this tumor with concurrent endometrial hyperplasia in dogs [8]. A similar finding was also observed in our study; endometrial hyperplasia and mixed endometrial tumors were identified in 87.5% (7/8) of the excised uteri. It is, therefore, suggested that in hedgehogs with granulosa cell tumors, overproduction of sex steroids might induce uterine diseases, similar to that observed in humans and dogs.

In dogs with granulosa cell tumors, the distant metastasis rate was reported to be 20% [9]. Local invasion of peri-ovarian tissues has been occasionally observed in malignant granulosa cell tumors in rats [4]. Although tumor metastasis to distant organs such as the lungs was not observed in the present study, additional cases are needed to investigate the metastatic behavior of the tumor in hedgehogs.

Treatment protocols for granulosa cell tumors in dogs and cats have not been established, and complete excision is considered to lead to a good prognosis [9]. In this study, long-term survival after ovariectomy was observed in hedgehogs without ascites. In patients with ascites at diagnosis, recurrence or regrowth of the intraabdominal tumor was observed, and chemotherapy with carboplatin was attempted in three of four cases. Tumor regression in one case indicates that intraperitoneal administration of carboplatin may have a suppressing effect on tumor regrowth; however, its efficacy against ascites could not be identified. Further studies with more cases are needed to develop better treatment protocols and verify the effectiveness of chemotherapy in granulosa cell tumors in hedgehogs.

POTENTIAL CONFLICTS OF INTEREST. The authors have nothing to disclose.

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