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DENİZ NAK

AYLİN ALASONYALILAR DEMİRER

BİLGİNER TUNA

YAVUZ NAK

MUSA ÖZGÜR ÖZYİĞİT

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Vaginal prolapse related to ovarian granulosa cell tumor in an Anatolian Shepherd.

Deniz NAK^{1*}, Aylin ALASONYALILAR DEMİRER¹, Bilginer TUNA¹, Yavuz NAK¹, M. Özgür ÖZYİĞİT²

¹Department of Obstetrics and Gynecology; Faculty of Veterinary Medicine, University of Uludağ,
16059 Bursa - TURKEY

²Department of Pathology, Faculty of Veterinary Medicine, University of Uludağ, 16059, Bursa - TURKEY

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Abstract: A 4-year old, primiparous, female Anatolian Shepherd dog was presented for evaluation of type II vaginal prolapse with alopecia of the left perineal skin. Hematological analyses demonstrated leukocytosis and thrombocytopenia. Estradiol (E2) and progesterone (P4) levels were 156 pg/mL and 2.3 ng/mL, respectively. The vaginal smear was predominantly (at least 80%) made up of anuclear superficial cells. An abdominal ultrasonography revealed a heterogeneous multicystic mass with anechoic areas adjacent to the caudal pole of the left kidney. An ovariohysterectomy was performed. Ten days after the surgery, the prolapsed vagina was completely regressed. A histopathological examination of the ovarian mass demonstrated that it was a granulosa cell tumor.

Key words: Dog, ovarian tumor, vaginal prolapsed

Kangal ırkı bir köpekte ovaryumdaki granulosa hücre tümörü ile ilişkili prolapsus vajina olgusu

Özet: Kangal ırkı 4 yaşlı, daha önce bir doğum yapmış dişi bir köpek sol perineal bölgede alopesi ile birlikte prolapsus vajina tip II şikayetleri ile Doğum kliniğine getirildi. Kan muayenesinde lökositosis ve trombositopeni tespit edildi. Östradiol (E2) ve progesteron (P4) seviyeleri sırasıyla 156 pg/mL ve 2.3 ng/mL idi. Vajinal smearda anükleer süperfişiyel hücreler (en az % 80) baskın hücre topluluğunu oluşturduğu dikkati, çekti. Ultrasonografide sol böbreğin kaudaline yakın anekoik alanlar içeren heterojen multikistik bir kitle gözlemlendi. Overiohisterektomi sonrası operasyondan 10 gün sonra prolapsus vajinanın tamamen gerilediği görüldü. Ovaryumun histopatolojik muayenesinde granulosa hücre tümörü teşhis edildi.

Anahtar sözcükler: Köpek, ovaryum tümörü, prolapsus vajina

* E-mail: deniznak@gmail.com

Introduction

The most common causes of vaginal/vestibular masses in the bitch are vaginal prolapse, vaginal neoplasia, and urethral neoplasia protruding into the vaginal vault (1). Vaginal prolapse is the protrusion of edematous vaginal tissue into and through the opening of the vulva, occurring during the pro-estrus and estrus stage of the sexual cycle (1,2). It does not occur during anestrus (2). Although it occurs almost always in intact female bitches (2), it has also been reported in an ovariohysterectomised bitch (3). True vaginal prolapse may occur near parturition, as the serum concentrations of progesterone decline and oestrogen increase (2,4). It occurs less commonly in diestrus and normal pregnancy (2,5). The disease can be caused by vaginal tumors (6) or trauma (7), but this is fairly rare.

Ovarian tumors are relatively uncommon in the bitch. The majority of ovarian tumors are epithelial tumors, sex cord stromal tumors, and germ cell tumors. Sex cord stromal tumors include granulosa cell tumors (GCTs), theca cell tumors or thecomas, and luteomas (2). Granulosa cell tumors may have the ability to produce estrogen and progesterone, resulting in clinical signs related to the reproductive tract. However, to the best of our knowledge, there are no published data available about vaginal prolapse related to ovarian granulosa cell tumors. The present report describes a clinical case of a vaginal prolapse, type II, which developed due to an ovarian granulosa cell tumor in a 4-year-old Anatolian Shepherd bitch.

Case history

A 4-year-old, primiparous Anatolian Shepherd bitch, weighing 34 kg, was presented to the University of Uludağ, Department of Obstetrics and Gynecology clinic with a 7-day history of type II vaginal prolapsed (Figure 1). The bitch had been in estrus, 4 weeks before this presentation, and the estrus cycle was regular. The bitch was treated with aglepristone (Alizine, Virbac) in a dose of 10 mg/kg of body weight subcutaneously, once daily, on 2 consecutive days, for the prevention of pregnancy after 2 weeks of unwanted mating. No vaginal prolapse had been observed during any previous pro-estrus or estrus periods. The bitch was fed a home-prepared diet and housed as a bandog.



Figure 1. Alopecia and type II vaginal prolapse in an Anatolian Shepherd bitch.

Results and discussion

During a physical examination, the animal appeared healthy with no abnormalities other than a protruding tissue of vulva, lichenification, and hyperpigmentation, with alopecia on the left perineal skin. Rectal temperature, heart rate, respiratory rate, mucous membrane color, and capillary refill time were all within normal ranges. A hematological examination (Abbott Cell-Dyn 3500 hematological analyzer, Gml Inc, Ramsey, Minnesota, USA) revealed an increased total white blood cell count (WBC) ($17.3 \times 10^9/L$; normal range $5.4-15.3 \times 10^9/L$) and a decreased platelet count ($118 \times 10^9/L$; normal range $160-525 \times 10^9/L$). The differential cell count indicated an increased neutrophil count (89.9%; normal range 51%-84%). The remaining hematological findings were within normal ranges (8). Neutrophilic leukocytosis and thrombocytopenia were determined in the bitch. Estradiol (E2) and progesterone (P4) concentrations were assayed by the Immulite System (Immulite 1000, Siemens/DPC, New Jersey, USA) using Immulite estradiol and progesterone test kits (Diagnostic Products Corporation, California, USA).

Concentrations of estradiol (E2) and progesterone (P4) were 156 pg/mL and 2.3 ng/mL, respectively. Vaginal cytology revealed more than 80% anuclear superficial vaginal epithelial cells, which was compatible with a smear from late pro-estrus or early estrus. An ultrasound examination (Terason Portable Ultrasonography System, Teratech Corporation, Burlington, USA) of the abdomen identified a large, 12-cm, roundish, heterogeneous ovarian mass in the left mid-abdomen, just caudal to the left kidney. The mass was composed of large, multiple, ill-defined, hypoechoic structures and multiple echogenic septa were visible internally (Figure 2). Scanty fluid was seen in the uterine lumen and the uterus was mildly increased in size. Other abdominal organs were considered within normal limits and no other pathological structures were revealed. Radiographic examination of the thorax and abdomen revealed no specific pathological findings related with metastasis. The ovarian mass was not well viewed. A presumptive diagnosis was made as type II vaginal prolapse related to an ovarian mass. An ovariectomy

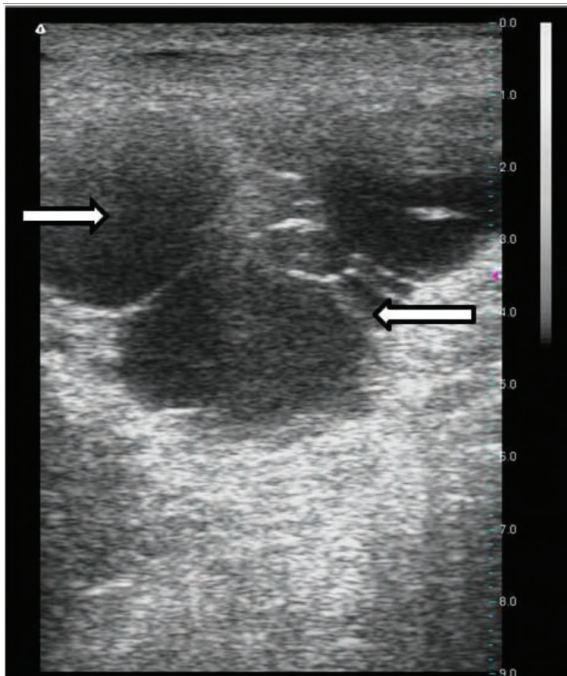


Figure 2. Sagittal ultrasonographic image of the left ovary including the ovarian granulosa cell tumor in the dorsal recumbency. A mass was heterogeneous with multicystic anechoic fluid-filled areas (right arrow) separated by echoic septa (left arrow).

was recommended for treatment of the ovarian mass and vaginal prolapse. The dog was premedicated with 2 mg/kg intramuscular xylazine HCl (Alfazyne 2%, Alfasan) and anesthesia was induced with 4 mg/kg intravenous propofol (Propofol 1%, Fresenius Kabi AB). General anesthesia was maintained with isoflurane (Forane Likid, Abbott) in oxygen. For prophylaxis, at induction, 8.75 mg/kg intramuscular Amoxicillin/clavulanic acid (Synulox, Pfizer) was administered and then the standard protocol was continued. The dog was closely monitored during the surgery with pulse oximetry and electrocardiography. The ovariohysterectomy was performed through a midline incision. The bitch had an uneventful recovery. The protruding vagina was completely regressed 10 days after the ovariohysterectomy.

Grossly, the left ovarian tumor (12 × 12 cm) had irregular, protruding nodules, red to brownish in color. Its cut surface displayed solid and multicystic components. The cysts (2-4 cm in diameter) contained serous reddish fluid. The right ovary (1.5 × 2.0 cm) was normal in size (Figure 3). The uterine horns were mildly enlarged (up to 2 cm in diameter) and showed slightly annular constrictions (Figure 3). A mild amount of red-brown serous exudate was seen in the uterine lumen. The endometrial surface was covered in a disseminate manner by a dark red-brownish exudate. The endometrium was slightly thickened, hemorrhagic, and edematous. Ovarian and uterine samples were fixed in 10% neutral formalin and embedded in paraffin. The sections (5 µm) were stained with hematoxylin and eosin



Figure 3. Reproductive tract of the bitch, showing mild enlargement of uterine horns and a left ovarian tumor.

(HE). A histological examination revealed that the ovarian neoplasm consisted of a central population of proliferating granulosa cells, with interposed irregular fibrovascular septa. An outer capsule of fibrous tissue surrounded the neoplastic tissue. The neoplastic cells were mostly cuboidal and occasionally slim columnar cells with central nuclei and a moderate amount of pale staining foamy cytoplasm. There were extensive areas of hemorrhage within the center of the tumor. A “Call-Exner” body formation was detected in the neoplastic areas, whereas mitoses were not observed (Figure 4). A left ovarian GCT was diagnosed, while the contralateral ovary presented a corpus luteum formation. In the uterus, moderate cystic glandular hyperplasia of the endometrium was observed. A moderate lymphoplasmacytic infiltrate with neutrophils and mononuclear phagocytes and diffuse hemorrhage with edema were also observed within the endometrial connective tissue. A moderate hypertropia has been observed in the myometrium. Compared to other vaginal disorders, vaginal prolapse is an uncommon condition in the bitch (4). Vaginal prolapse is usually seen during the pro-estrus

and estrus stage of the sexual cycle and the first 3 estrous cycles in younger bitches (<2 to 3 years). No breed predisposition has been described, although it appears that the incidence of the condition is higher in large breed bitches (2). In accordance with this literature, the bitch was a large breed bitch, but was 5 years old and in diestrus.

The mean age at diagnosis of GCT is 7.7 years, with a reported range of 14 months to 15 years (2,9). Most of the bitches with GCT were nulliparous. GCTs are usually unilateral, although bilateral masses have been reported. GCTs vary between 0.4 cm to greater than 10 cm in diameter. Smaller tumors are usually solid, and larger tumors often are friable and cystic (2,9-11). The present case was in agreement with the above reports, except for being primiparous. The tumor was unilateral and there were corpora lutea on the other ovary. Clinical signs referable to increased serum estrogen concentrations include persistent or erratic estrus, vulvar swelling and serosanguineous vulvar discharge, purulent vulvar discharge, polyuria/polydipsia, and other signs of concurrent cystic endometrial hyperplasia-

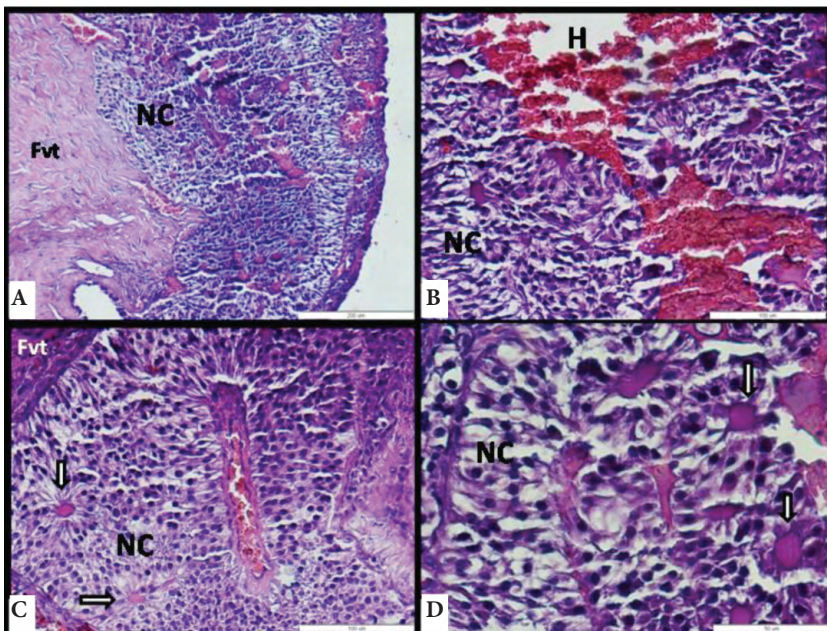


Figure 4. A: Granulosa cell tumor (GCT), composed of clusters of neoplastic cells (NC) surrounded by fibrovascular tissue (Fvt), HE. Bar 200 μ m. B: Cystic pattern in the tumor disrupted by a hemorrhage (H) HE. Bar, 100 μ m C: GCT demonstrating “Call-Exner” body formation (arrow). HE. Bar, 100 μ m D: GCT, demonstrating “Call-Exner” body formation (arrow). HE. Bar, 50 μ m.

pyometra complex, non-regenerative anemia with agranulocytosis and thrombocytopenia resulting from estrogen-induced bone marrow toxicity, and skin changes characteristic of hyperestrogenism, including bilateral symmetrical alopecia of the trunk, lichenification, and hyperkeratosis (2,9-11). In our case, there was type II vaginal prolapse and changes in the skin on the left perineal area. Neutrophilic leukocytosis and thrombocytopenia were detected in the hematological examination. GCTs are often functional, elevations in serum estrogen concentration alone, or together with serum progesterone elevation may occur. Reported serum estrogen concentrations in a functional GCT range from 55 to 166 pg/mL. Reported serum progesterone concentrations range from 0.64 to 11.0 ng/mL, with values greater than 2 ng/mL indicative of active progesterone secretion by the tumor (2). In our case, estradiol (E2) and progesterone (P4) levels were 156 pg/mL and 2.3 ng/mL, respectively. GCTs are usually well encapsulated, with no local invasion. Metastasis is reported to occur in 10%-20% of cases. Reported sites of metastasis include the omentum, mesentery, peritoneum, diaphragm, liver, kidneys, urinary bladder, and intra-abdominal lymph nodes (2,10,11) In this case, no evidence of metastatic disease was observed. The tumor may be visualized by radiography as a soft tissue density mass or by ultrasonography as a mass, with complex echogenicity caudal to the kidney. Ultrasonography is helpful for diagnosing the origin of ovarian masses and for checking for abdominal metastasis. Ovarian

tumors can be recognized ultrasonographically as a mass lesion in one or both ovaries. Tumors may be predominantly solid, solid with a cystic component, or primarily cystic and complex (2,12,13). In the present case, an ovarian mass was imaged ultrasonographically as a cystic component, caudal to the left kidney. Most likely, the tumor could not be well shown radiographically because it had a multicystic structure. Ultrasonography was considered diagnostic because it revealed information on organ architecture and relationships of radiographically, silhouetting soft tissue structures. Surgical removal of the ovary with the tumor is the recommended treatment, with complete ovariohysterectomy most often indicated. Ovariohysterectomy may hasten the resolution of vaginal prolapse by removing the primary endocrine stimulus, the estrogen-secreting ovary. The regression of prolapsed vaginal tissue is reported to occur after 4 to 8 days or within 21 days of the ovariohysterectomy (2). In our case, the prolapsed vagina was completely regressed 10 days after the ovariohysterectomy.

Initially, in this case, only a type II vaginal prolapse was diagnosed during the clinical examination, but after the detailed clinical and histopathological examinations, an ovarian granulosa cell tumor was diagnosed as the cause of the vaginal prolapse. An exact diagnosis led us to a suitable treatment choice. Both the ovarian tumor and prolapsed vagina were completely treated by ovariohysterectomy. Furthermore, a cause was demonstrated for the uncommon prolapsed vagina in the bitch.

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