

Bilateral ovarian dysgerminoma with metastasis in female dog's mesenteric lymph node: a case report

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Abstract

Dysgerminoma is a rare malignant neoplasm, associated with hormonal dysfunctions, which occurs in canine and feline females from middle age to elderly, without racial predisposition. In the present report, we described a case of ovarian dysgerminoma in a dog, only abdominal distension, persistent vulvar bloody discharge and apathy. The animal in question underwent exploratory laparotomy, where general neoformations were detected in the ovaries, and a lymph node with abnormal characteristics was also found. Therefore, surgery for ovariosalpingoisterectomy and puncture of a fragment of the lymph node altered for incisional biopsy was performed. The diagnosis was made through histopathological examination of the ovaries of the fragment derived from the lymph node, the result of which indicated the presence of dysgerminoma in both ovaries and in the lymph node, characterizing a metastasis. In view of this result, the chemotherapy protocol with the association of carboplatin and vinblastine was instituted, which proved to be effective and not very toxic to the animal, with no clinical sign of metastasis being identified after its use.

Keywords: Dysgerminoma; Female dog; Surgery; Chemotherapy.

Introduction

According to Wellons and colleagues [1], dysgerminoma, which can also be called a germinoma, is a tumor that can be located in the testicles, ovaries and extragonal zones, with the same histological basis, consisting of

large, round, oval cells or polygonal with clear cytoplasm and large, round nucleus with one or two prominent nucleoli, grouped in nests separated by fibrous septa with abundant lymphocytes, called Langhans cells, with areas of necrosis and granulomatous reaction. The most

common locations are ovaries, testicles and pineal gland [1].

For Klain [2], dysgerminomas are germ cell tumors, microscopically resembling testicular seminomas, which occur in males, both in dogs and in cats. As a result, dysgerminomas have been called "ovarian seminomas". Dysgerminoma is a rare malignant neoplasm, associated with hormonal dysfunctions, which occurs in canine and feline females from middle age to elderly, without racial predisposition [3-4].

The most common form of presentation of this neoplasm is the unilateral form, however the bilateral presentation has been described. Tumor growth is due to expansion, and metastases can occur in lymph nodes and abdominal organs [4]. There are reports of lung and brain metastases [3]. According to Bustamante et al. [5] in bilateral ovarian dysgerminoma, metastases may occur in the heart, lung, liver, kidneys, pancreas, mesenteric lymph nodes and peritoneum.

Clinically, germ cell tumors do not normally produce signs of hormonal dysfunction, with ascites and abdominal distension being the most common signs [6-7]. According to Cotran [8], females dogs can clinically present irregular hives, fever, pyometra, vaginal discharge, vomiting and diarrhea. However, according to Dune & Bechara [9], normally half of the cases of bitches affected by ovarian dysgerminoma

present endocrine clinical symptoms and in some cases, cause an increase in chorionic gonadotropin (HCG).

North and Banks [10] also mention that prolonged estrus, alopecia, breast hyperplasia, cystic endometrial hyperplasia, attractive vulva, and, very occasionally, myelosuppression, due to hyperestrogenism can be observed. Other clinical signs that may be visible include lethargy, weight loss, the presence of a palpable abdominal mass and low back pain. Grenlee & Patnaik [11] mentions that the clinical signs associated with dysgerminomas are often those characteristic of pyometra.

Dysgerminoma is a very rare tumor in domestic animals, with few cases reported in dogs, cats and cows, respectively in decreasing order of frequency, so it is probably more common in dogs than in other species [12]. In women, on the other hand, it is considered the most common germ cell tumor [13]. Dysgerminomas are more common in young women at the age of 30 [14]. However, according to Smith [15], in the canine species, there is a greater prevalence of case reports developed in female dogs ten years of age or older.

According to Dune & Bechara [9], the occurrence of dysgerminoma is more frequent in patients with gonadal dysgenesis, including pseudo hermaphroditism. According to Britt & Howard [16], there is an apparent predisposition for the involvement of

dysgerminoma by the left ovary in female dogs.

In the present case report, we sought to describe a case of ovarian dysgerminoma in a dog, presenting only abdominal distension, persistent vulvar bloody discharge and apathy.

Case report

An animal of the canine species, female, 12 years old, of the poodle breed, weighing approximately 12 kg, was seen in a public service of veterinary clinic in the state of Ceará, presenting a history of abdominal pain, bloody vulvar secretion for about thirty days, sadness and decreased food intake.

According to the owner, the animal had anti-rabies and anti-viral vaccinations in days, as well as deworming. He used to eat commercial feed, lived in an exclusively home environment, never had a previous disease and there were no contact animals.

On physical examination, normal mucous membranes were found, normal hydration, rectal temperature of 39.4°C, heart rate of 100 beats per minute, pulse with 70 beats per minute and respiratory rate of 30 movements per minute. There were no changes in palpable external lymph nodes.

Upon examination of palpation of the abdominal region, there was a relative distension, with the presence of a mass of an indefinite character and

painful sensitivity associated with moans by the animal. The animal was submitted to complementary exams, such as: complete blood count, serum biochemistry (creatinine and alaninaminotransferase).

Radiographic and ultrasonographic studies were not performed, due to disagreement by the owner. The complete blood count and serum biochemistry exams did not illustrate changes worth noting, obtaining values within the standards of normality to the species. Without a conclusive result, the animal was referred for an exploratory laparotomy surgical procedure, since an intra-abdominal tumor neoformation was suspected.

The animal received as preanesthetic medication acepromazine and tramadol, in doses 0.5mg/kg and 3mg/kg intramuscularly, respectively. Anesthetic induction was performed with the use of propofol, at a dose of 4mg/kg intravenously, and the maintenance of the entire surgical procedure was performed with the use of inhaled anesthetic isoflurane.

After accessing the abdominal cavity, all organs were explored, with the presence of formations (Figure 01) with cystic neoplastic characteristics in both ovaries, measuring approximately 5 cm in diameter. The uterus was normal. The entire reproductive organ and tumor tissues were removed.

An alteration in the mesenteric lymph node was also seen, with involvement of the caudal vena cava, also having characteristics of tumor formation. A small fragment of the

lymph node was collected by means of incisional biopsy. Both the lymph node sample and the ovarian neoformations were sent for histopathological analysis.

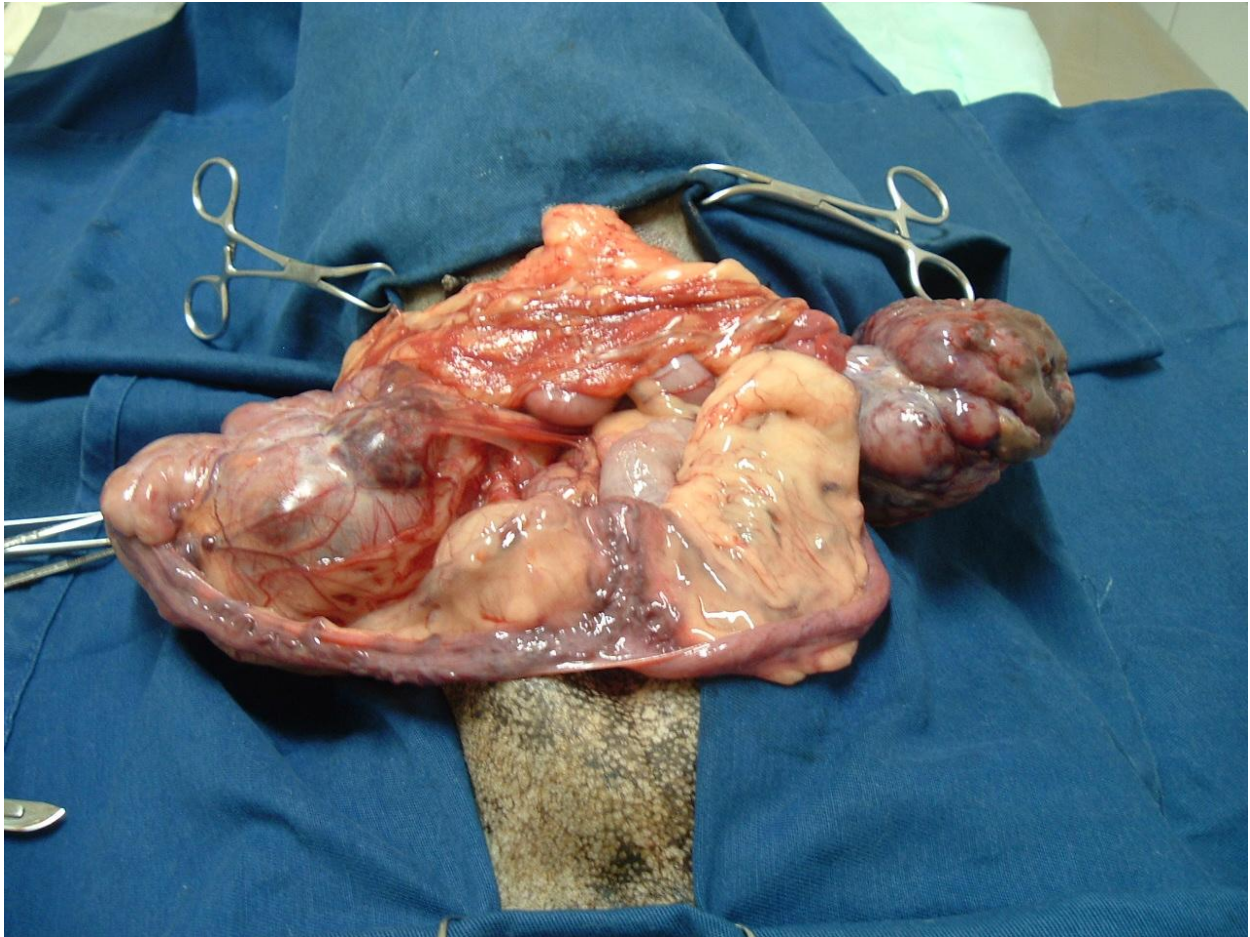


Figure 1. Pathological specimen showing the presence of nodules with neoplastic characteristics in both ovaries.

Histopathological analysis performed on ovarian tumors revealed that the neoplasm reproduced blocks and strands of polygonal cells that exhibited broad cytoplasm and gross chromatin nuclei, multiple and evident nucleoli that invaded the capsule in several areas, and presented about 10 mitoses per microscopic field increase, thus having a conclusive picture for

dysgerminoma. In the histological analysis of the lymph node fragment, cells with a cellular pattern similar to the ovarian dysgerminoma were evidenced, characterizing a metastasis.

After the result of the histopathological analysis, and 15 days after the surgery, the animal was sent for chemotherapy treatment, whose protocol consisted of the administration

of carboplatin in the dose of 300mg / m² intravenously every 30 days, in a total of four administrations; and vinblastine sulfate at a dose of 2mg / m²

intravenously every 30 days for a total of four applications. The 15-day interval between the administration of each chemotherapeutic agent was respected.

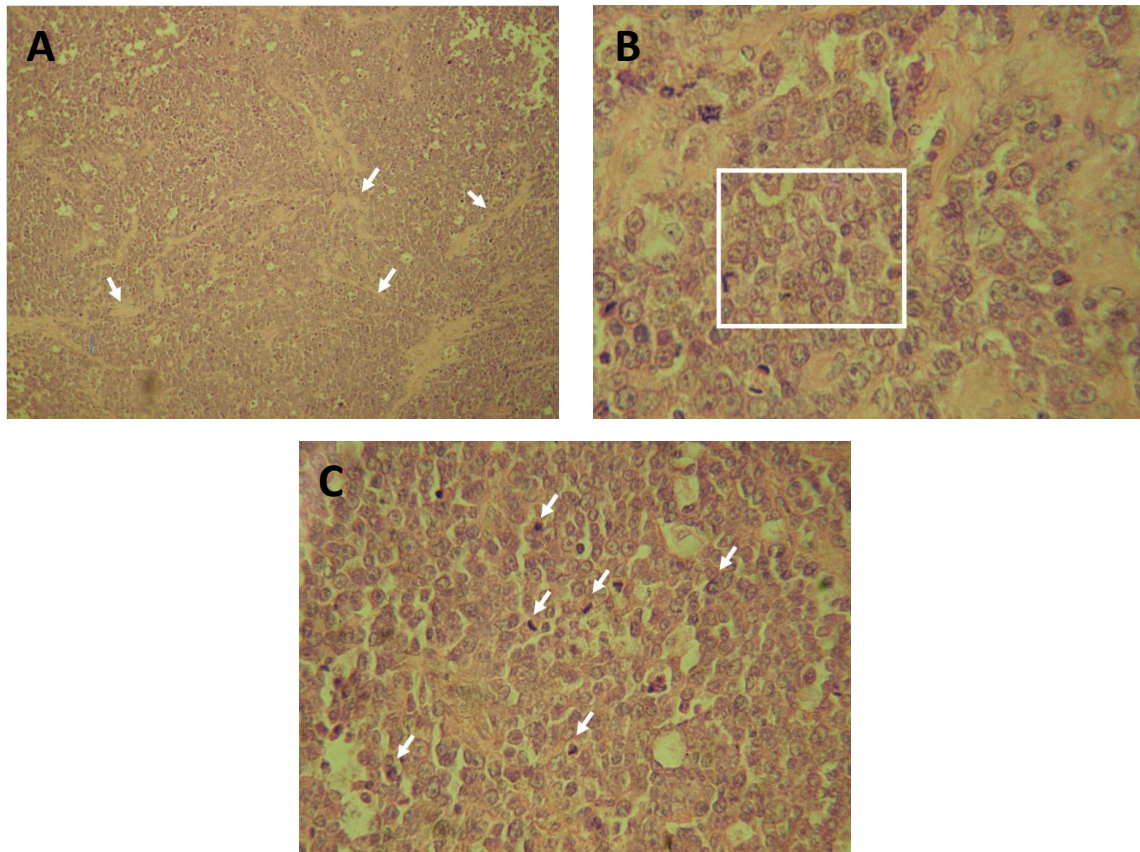


Figure 2. **A.** Histopathological analysis of ovary showing several septa characteristic of dysgerminoma (white arrows) (Hematoxylin-Eosin staining, 10x). **B.** Histopathological analysis of the ovary showing the presence of polygonal cells showing a large cytoplasm and a coarse chromatin nucleus (white board) (Hematoxylin-Eosin staining, 100x). **C.** Histopathological analysis of ovary showing the presence of several cells in mitosis of ovarian dysgerminoma (white arrows) (Hematoxylin-Eosin staining, 40x).

Possible immunosuppression caused by chemotherapeutic agents was also instituted as a preventive measure, the provision of immunostimulating medication (Promundog®), administering three tablets, orally, every 24 hours, throughout the treatment period and 30 days after its termination.

For administration of carboplatin, the animal was contained in an ambulatory care table and, subsequently, its cephalic vein was catheterized, with the use of a number 24 catheter.

After catheterization, 0.9% sodium chloride was infused

intravenously for a period of 30 minutes. After this period, carboplatin was infused for a period of not less than 30 minutes.

After the administration of the carboplatin chemotherapy, 0.9% sodium chloride solution was infused for another 30 minutes, so that the blood vessel was washed in order to avoid accidents during catheter removal.

For administration of vinblastine sulfate, the animal was contained and had its cannulated cephalic vein as previously described. The 0.9% sodium chloride solution was infused for a period of 5 minutes, followed by a slow intravenous administration of the chemotherapeutic agent, and then the physiological solution for washing was infused for another 5 minutes of the blood vessel.

After the first chemotherapy cycle, hematological and serum biochemical alterations were not observed, as well as no physical alterations, with the owner reporting only a slight decrease in food intake, after five days of vinblastine administration, returning to normal after three days.

After the second and third cycles, no changes in hematology and serum biochemistry were observed. The owner reported that three days after the administration of carboplatin, in the second cycle, the dog had emetic episodes, and therapy with 0.5 mg / kg metoclopramide was instituted every 8

hours, orally until resolution of the condition.

The owner of the female dog was contacted, 30 days after the end of the 4th chemotherapy cycle, and reported that the dog was healthy, showing no sign of note.

Discussion and Conclusion

According to the clinical staging / TNM criteria [17] applicable to ovarian tumors, T2 / N1 / M1a was determined for this clinical case. Regarding staging, the fact that it is limited to both ovaries (T2), with invasion, in macroscopic and microscopic evaluation, of a mesenteric lymph node (N1) and showing signs of implantation in the peritoneal cavity (M1a), may indicate a reasonable prognosis for this case.

Dysgerminoma is a very rare tumor in female dogs, derived from germ cells of the ovary. They usually occur in elderly animals and most commonly present in unilateral form and up to 20% of them are capable of producing metastases [18]. In the case described, the dog was advanced in age, in line with the literature [15, 18], but presented bilateral ovarian involvement, which is a fact that highlights the rarity of the case in question [4].

The reported animal had metastasis in the mesenteric lymph node [5], the most common fact in bilateral dysgerminoma, in which our report fits [18]. Corroborating with the literature,

where it is mentioned that the metastatic extension of the tumor occurs initially through the lymphatic system, therefore it is of fundamental importance to surgically analyze the possible involvement of the paraortic and pelvic ganglia. Hematogenic dissemination is later and can reach the liver, lung and bones [19].

A retrospective study was conducted in humans and the authors assessed the prevalence and impact on the prognosis of lymph node metastases in ovarian germ cell malignancies. This study included 372 patients, diagnosed with ovarian dysgerminoma. Of this total, 244 underwent lymph node dissection, in 28.3% of patients the presence of lymph node metastasis was detected [20]. The rate of metastasis in female dogs, as already mentioned, is around 20%, which can occur in lymph nodes and abdominal organs [19], thus showing that the presence of metastases in bitches and women is relatively rare, having values similar percentages.

The symptoms found in the dog, at the time of the anamnesis, were compatible with those described in the literature for dysgerminoma, with bloody vaginal discharge, abdominal distension, lack of appetite, abdominal pain and sadness, conditions that raised the suspicion of a neoplastic condition at the time of the consultation.

As for clinical signs, the literature clarifies that usually female dogs with dysgerminoma have bloody vaginal

discharge as a symptom, with a characteristic of prolonged heat, or purulent, abdominal distention and fever [6, 8, 10]. They may also present with vomiting, diarrhea, irregular hoops, pyometra, lethargy, weight loss and rarely myelosuppression [10-11].

No hematological changes were found in the blood count performed on the dog at the time of the first consultation, consistent with what is cited in the literature, where it is reported that no abnormal laboratory findings can usually be correlated with ovarian tumors [21].

The most correct way to define the diagnosis of dysgerminoma is to remove the affected ovary and perform a histopathological exam on it [22]. The histopathology of the ovary removed from the bitch revealed cell characteristics compatible with dysgerminoma, being in line with the previously mentioned studies, presenting cells with a broad cytoplasm and a coarse chromatin nucleus, multiple and evident nucleoli, and about 10 mitoses or more per field. microscopic image of great magnification [23].

Pelvic and paraortic ganglion biopsies should be performed in order to perform an appropriate surgical intervention [24]. Thus, by incisional biopsy, metastasis was found in the mesenteric lymph node, which was deformed at the time of the exploratory laparotomy.

The traditional treatment for ovarian dysgerminoma is ovariectomy surgery; when the disease is present in the extra-ovarian environment, treatment with adjuvant chemotherapy is recommended [2]. The therapy instituted in this report was the performance of exploratory laparotomy, and after the detection of the ovarian neoformations, even without having an exact knowledge about what the nodulations were about, the complete removal of both ovaries was carried out, being this the appropriate procedure, suggested by the pre-existing literature, for treatment.

With regard to chemotherapy, in humans, a good association of drugs has not been found, yet it seems that combinations containing cisplatin, etoposide and bleomycin are preferred due to the lower recurrence rate and shorter treatment. In patients whose ovaries have been completely removed, the relapse rate is unknown after treatment with platinum derivatives [25].

In contrast, in the case in question, the combination of a platinum derivative, carboplatin with vinblastine, was used. The association of these drugs proved to be effective, because, despite the fact that routine post-treatment tests were not performed, the patient did not show clinical signs of metastasis. In humans, carboplatin may be associated with hypersensitivity reactions. An important retrospective study reported that the hypersensitivity reaction,

associated with the use of carboplatin, was found in 24 of 205 patients (12%) treated for gynecological malignancies [26].

Animals treated with carboplatin may have renal disorders, gastrointestinal effects such as anorexia, emesis and constipation, liver disorders, leukopenia, and anemia and myelosuppression may also occur [27].

According to the literature, in the case in question, the dog showed only cases of emesis after one of the chemotherapy cycles, the situation being reversed with the use of oral anti-emetic. With the use of vinblastine sulfate, only a decrease in food intake was observed after five days of its administration, returning to normal three days after application, thus corroborating with the literature, where gastrointestinal changes are mentioned, such as constipation, anorexia, nausea, vomiting, abdominal pain, diarrhea and rectal bleeding in humans.

It is known that leukopenia is an expected effect of vinblastine sulfate, however, contradicting the literature, no hematological changes were found during the entire treatment. As for treatment, it was found that the association of carboplatin and vinblastine was effective for the absence of symptoms related to metastases. In addition, the carboplatin / vinblastine chemotherapy protocol proved to be safe, as it did not present intense toxicity levels.

Thus, from the present study, it is seen that it is important that ovarian dysgerminoma should be placed on the list of differential diagnosis in bitches that present, at the time of the consultation, symptoms such as abdominal pain and persistent bloody secretion. For this clinical case, it is emphasized that exploratory laparotomy was decisive for its resolution, since no imaging exams were performed.

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