



DIFFUSE LARGE B-CELL LYMPHOMA INVOLVING THE UTERUS AND OVARY IN A BITCH

LINFOMA DIFUSO DE GRANDES CÉLULAS B ENVOLVENDO O ÚTERO E O OVÁRIO EM UMA CADELA

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RESUMO

Linfomas do trato reprodutivo feminino são raros em cães. Este relato descreve um caso de linfoma difuso de grandes células B (DLBCL) envolvendo ovário e útero em uma cadela Rottweiler, não castrada, com 1,3 anos de idade, que apresentou paresia de membros pélvicos e leucocitose inflamatória. À ultrassonografia abdominal, observaram-se distensão uterina e aumento ovariano, sendo realizada ovariossalpingo-histerectomia. Macroscopicamente, os tecidos apresentavam aspecto firme, homogêneo e esbranquiçado ao corte. Histologicamente, ovário e útero encontravam-se infiltrados por neoplasia densamente celular composta por grandes células redondas, com núcleos vesiculares, nucléolos evidentes e elevada atividade mitótica (30 mitoses por 2,37 mm²). À imuno-histoquímica, as células neoplásicas apresentaram forte imunomarcacão para PAX-5, confirmando linhagem B, além de



índice proliferativo Ki-67 de aproximadamente 80%. Adicionalmente, a ausência de imunomarcção para marcadores de linhagem germinativa e epitelial permitiu excluir os principais diagnósticos diferenciais, especialmente disgerminoma e neoplasias epiteliais ovarianas. Com base nos achados histopatológicos e imunofenotípicos, estabeleceu-se o diagnóstico de linfoma difuso de grandes células B. Este caso destaca a importância da imunohistoquímica na diferenciação entre linfoma e tumores de células germinativas, particularmente o disgerminoma, no trato reprodutivo feminino canino.

Palavras-chave: Linfoma difuso de grandes células B; Canino; Imuno-histoquímica; Ovário; Útero.

ABSTRACT

Lymphomatous involvement of the female reproductive tract is rare in dogs. This report describes a case of diffuse large B-cell lymphoma (DLBCL) involving the ovary and uterus in a 1.3-year-old intact female Rottweiler presenting with pelvic limb paresis and inflammatory leukocytosis. Abdominal ultrasonography revealed uterine distension and ovarian enlargement, and ovariohysterectomy was performed. The tissues exhibited a firm, homogeneous, and white appearance on cut sections. Histologically, both the ovary and uterus were infiltrated by a densely cellular neoplasm composed of large round cells with vesicular nuclei, prominent nucleoli, and high mitotic activity (30 mitoses per 2.37 mm²). Immunohistochemical analysis demonstrated strong nuclear immunoreactivity for PAX-5, confirming the B-cell lineage, and a Ki-67 proliferative index of approximately 80%. In addition, the absence of immunoreactivity for germ cell and epithelial markers excludes the main differential diagnoses, particularly dysgerminoma and epithelial ovarian neoplasms. Based on the histopathological and immunophenotypic findings, a diagnosis of diffuse large B-cell lymphoma was established. This case highlights the importance of immunohistochemistry in differentiating lymphoma from germ cell tumors, particularly dysgerminoma, in the female canine reproductive tract.

Keywords: Diffuse large B-cell lymphoma, Dog; Immunohistochemistry; Ovary; Uterus.

1 INTRODUCTION

Lymphoma is one of the most common malignant neoplasms in dogs, accounting for 7–24% of all canine tumors and 83% of all hematopoietic malignancies (Novotny et al., 2017). It represents a heterogeneous group of lymphoid tumors with diverse clinical presentations, biological behaviors and prognoses. Among the various subtypes, diffuse large B-cell lymphoma (DLBCL) is the most frequently reported subtype in dogs. It is characterized by the diffuse proliferation of large lymphoid cells with vesicular nuclei, prominent nucleoli, and high mitotic activity (Valli et al, 2011).

While extranodal lymphomas are frequently described in dogs, involving organs such as the skin, gastrointestinal tract, central nervous system, and kidneys, primary lymphomas of the female reproductive tract are exceedingly rare, with uterine involvement being particularly uncommon (Novotny *et al.*, 2017; Ko *et al.*, 2013; Jo *et al.*, 2023).

Most uterine lymphomas reported in veterinary and human medicine are secondary manifestations of systemic lymphoma or rare primary extranodal presentations (Ko *et al.*, 2013; Hadi *et al.*, 2015). Owing to their rarity, uterine lymphomas are often misdiagnosed as other uterine conditions, such as leiomyoma, uterine carcinoma, and inflammatory diseases (Ko *et al.*, 2013). Accurate diagnosis of uterine lymphomas requires a combination of histopathological and immunohistochemical analyses, which are essential for distinguishing lymphomas from other uterine neoplasms and inflammatory conditions (Novotny *et al.*, 2017).

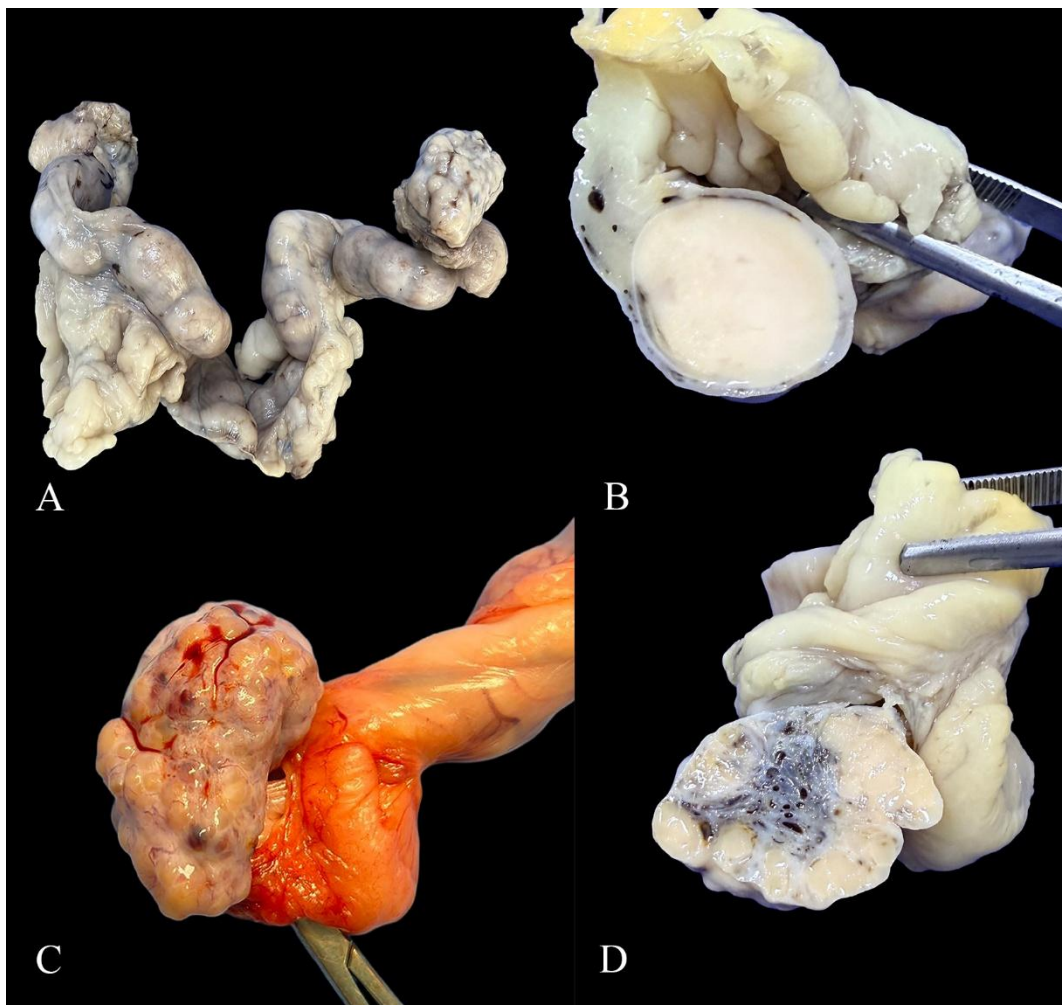
The present report describes a rare case of diffuse large B-cell lymphoma involving the ovary and uterus of a bitch, without sufficient evidence to determine whether the lesion represented primary extranodal disease or secondary involvement. This report emphasizes the histopathological and immunohistochemical findings and discusses the diagnostic challenges associated with reproductive tract lymphoid neoplasms in dogs.

2 CASE PRESENTATION

A 1.3-year-old intact female Rottweiler was presented with pelvic limb paresis, urinary incontinence, and progressive leukocytosis. Hematological evaluation revealed inflammatory leukocytosis ranging from 19,970/mm³ to 28,160/mm³ over five days, accompanied by mild normocytic and normochromic anemia. Thoracic radiography revealed a mixed interstitial and bronchial pulmonary pattern suggestive of early bronchopneumonia, whereas pelvic imaging revealed bilateral hip dysplasia and mild reduction of intervertebral spaces between L3 and L4, L4–L5, and L5–L6. Abdominal ultrasonography revealed uterine distension and enlargement of one ovary, prompting ovariectomy and pathological evaluation of the surgical specimens.

Gross examination revealed the uterus and ovary to measure approximately 40 × 3 × 3 cm. On cut section, the tissues showed a homogeneous white appearance with firm consistency (Figure 1 A, B, C, and D).

Figure 1. Macroscopic examination of the uterus and ovaries. (A) Global view of the surgical specimen showing marked asymmetrical enlargement of the uterus and attached adnexa. (B) Cut surface of the uterus exhibiting a diffuse, homogeneous white appearance with a firm, solid consistency, lacking whorled patterns, necrosis or hemorrhage. (C) Enlarged ovary with a distinctly irregular and nodular external contour. (D) Cut surface of the ovary demonstrating complete replacement of the normal ovarian parenchyma by a solid, white, homogeneous mass.

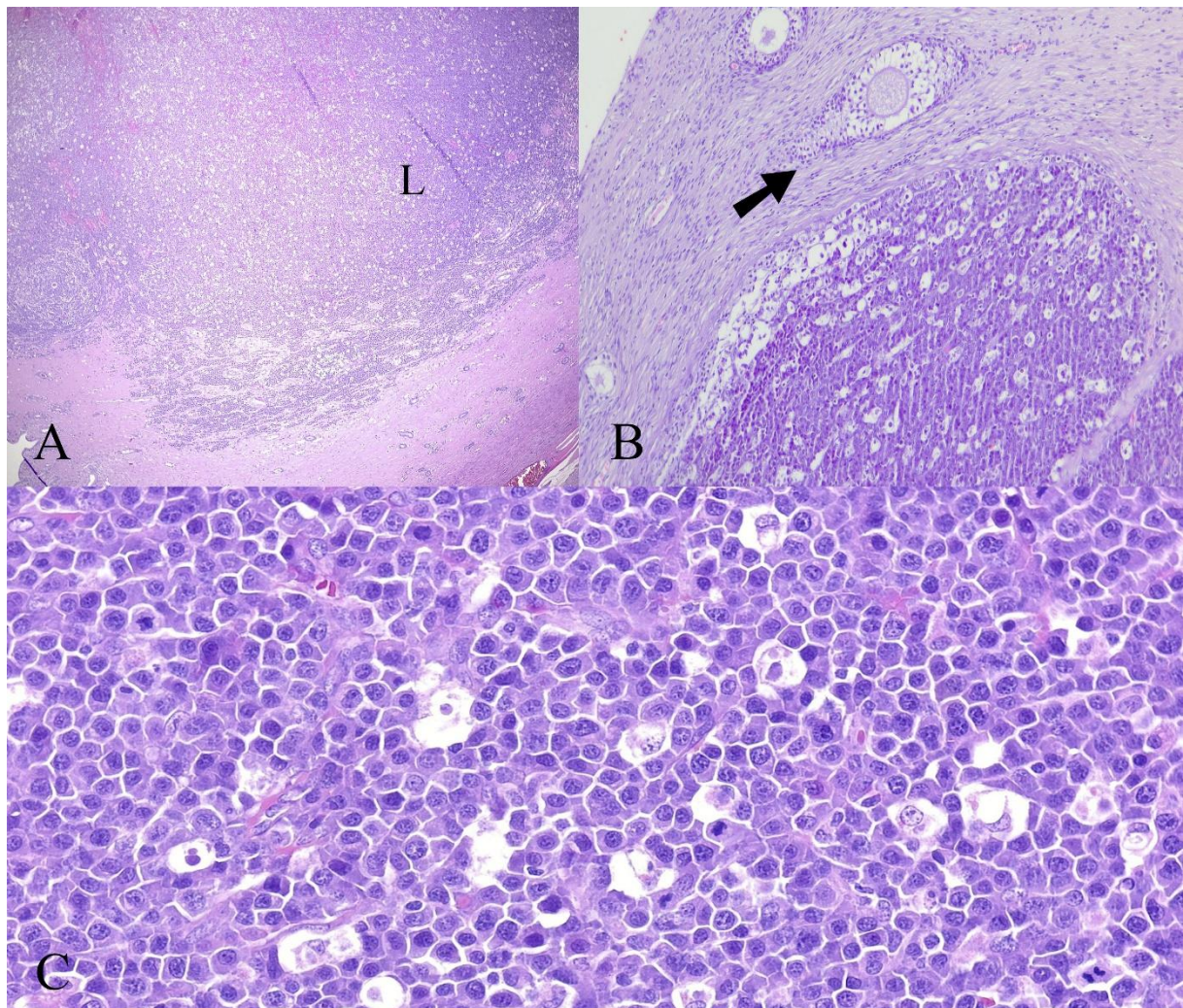


Source: Authors, 2026.

Histopathological examination revealed diffuse infiltration of the ovary and uterus by a densely cellular neoplastic population of large round cells, supported by

scant fibrovascular stroma. Neoplastic cells were predominantly arranged in diffuse sheets, occasionally forming poorly defined nests. The cells exhibited scant to moderate amounts of pale eosinophilic cytoplasm and indistinct to variably distinct cell borders. The nuclei were round to oval, with finely stippled chromatin and one to multiple prominent nucleoli. Marked anisocytosis and anisokaryosis were observed in the patient. Mitotic activity was high, with approximately 30 mitotic figures per 2.37 mm² (Figure 2 A, B, and C).

Figure 2. Microscopic features of uterine and ovarian lesions. (A) Uterine lumen (L) expanded by densely packed neoplastic round cells with secondary compression of the adjacent uterine wall (H&E, 100× magnification). (B) Ovarian parenchyma showing a remaining follicle (arrow) surrounded by a diffuse neoplastic infiltrate, which replaced the normal stroma (H&E, 100×). (C) High-power view of neoplastic cells exhibiting scant to moderate cytoplasm, prominent nucleoli, and marked anisokaryosis. Several mitotic figures are visible, consistent with a high proliferative index (H&E, 400×).

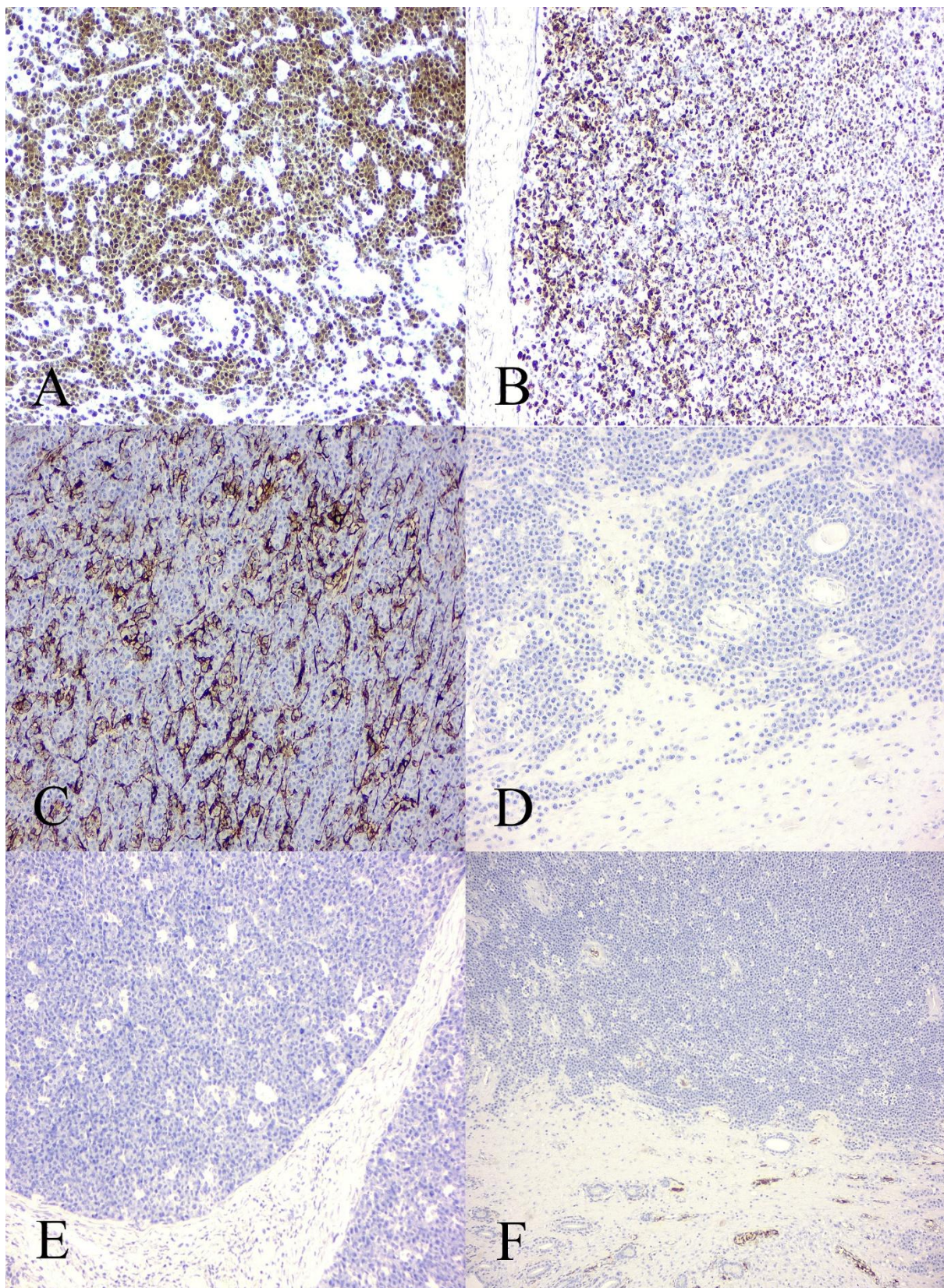


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Within the uterus, neoplastic cells were observed expanding and occupying the uterine lumen, resulting in compression of the uterine wall.

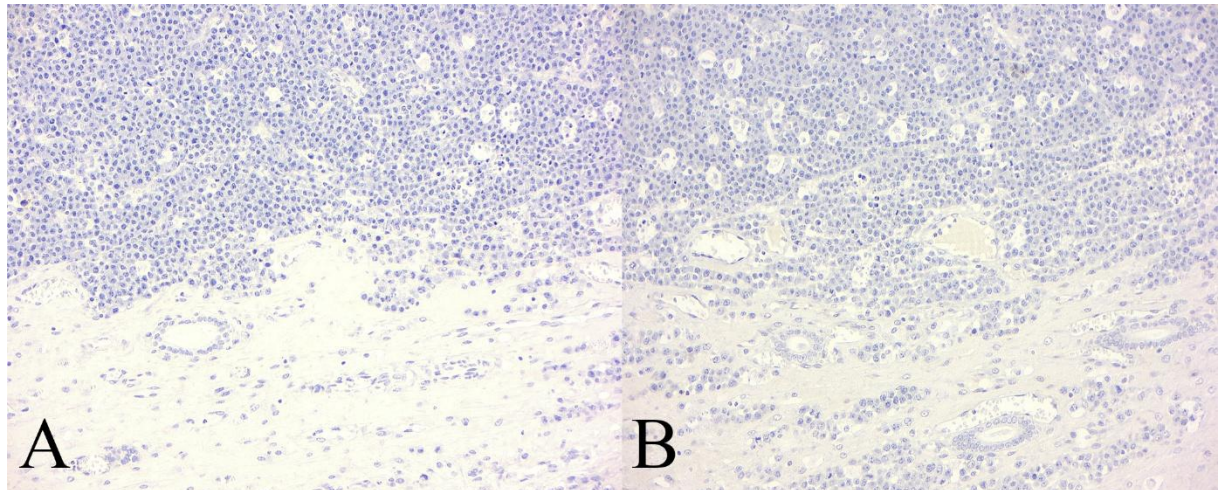
Immunohistochemistry was performed using the streptavidin-biotin-peroxidase method on formalin-fixed paraffin-embedded tissue sections. The immunohistochemical panel included antibodies against PAX-5, Ki-67, CK7, CD117 (c-KIT), D2-40, OCT3/4, PLAP, SALL4, and vimentin. Appropriate positive and negative controls were included in all the reactions. The neoplastic cells showed positive nuclear immunoreactivity for PAX-5, confirming the B-cell lineage. The proliferative index assessed using Ki-67 was approximately 80%, indicating high proliferative activity. Vimentin immunostaining was observed only in the stromal cells. The neoplastic cells were negative for cytokeratin 7 (CK7), CD117 (c-KIT), D2-40, OCT3/4 (Figure 3 A, B, C, D, E and F), placental alkaline phosphatase (PLAP), and SALL4 (Figure 4 A and B).

Figure 3. Immunohistochemical profile of neoplastic cells. (A) PAX-5 immunopositive cells showed strong and diffuse nuclear immunoreactivity, confirming the B cell lineage. (B) Ki-67 nuclear expression was observed in approximately 80% of the neoplastic population, indicating a high proliferation index. (C) Vimentin immunoreactivity was restricted to the cytoplasm of stromal cells (internal control), and neoplastic cells were immunonegative. (D) Neoplastic cells are immunonegative for CD117 (c-KIT). (E) No immunoreactivity for D2-40 was observed in the neoplastic cells. (f) Neoplastic cells are immunonegative for OCT3/4, ruling out germ cell origin.



Source: Authors, 2026.

Figure 4. Additional immunohistochemical markers for differential diagnosis. (A) Neoplastic cells are immunonegative for Placental Alkaline Phosphatase (PLAP). (B) Absence of nuclear immunoreactivity for SALL4, further supporting the exclusion of dysgerminoma.



Source: Authors, 2026.

Based on the histopathological findings and immunohistochemical profile, the diagnosis was diffuse large B-cell lymphoma involving the ovary and uterus. Because complete systemic staging was not performed, the distinction between primary extranodal lymphoma and secondary involvement could not be established.

3 DISCUSSION

Lymphoma is one of the most common hematopoietic neoplasms in dogs and comprises a heterogeneous group of malignancies with variable morphologies, immunophenotypes, and biological behaviors (Valli et al., 2011). According to the World Health Organization (WHO) classification of canine lymphoid neoplasms, diffuse large B-cell lymphoma (DLBCL) is the most frequently diagnosed subtype in dogs and is typically characterized by the diffuse proliferation of large lymphoid cells with prominent nucleoli, high mitotic activity, and aggressive biological behavior (Valli et al., 2011). Therefore, the accurate classification of lymphoma requires the integration of histopathological evaluation and immunophenotyping, allowing the identification of lymphoid lineages and improving diagnostic accuracy (Valli et al., 2011).

In the present case, complete clinical staging, including lymph node assessment, bone marrow evaluation, and postmortem examination, was not performed. Therefore, the lesion is best interpreted as diffuse large B-cell lymphoma involving the ovary and uterus rather than being definitively classified as primary reproductive tract lymphoma. Primary uterine and ovarian tumors are generally uncommon in domestic animals, and when they occur, tumors of epithelial or mesenchymal origin are more frequently reported than hematopoietic malignancies (Agnew; Maclachlan, 2017). Owing to its rarity and nonspecific clinical presentation, uterine lymphoma may initially be mistaken for other uterine conditions, such as leiomyoma, carcinoma, or inflammatory uterine diseases (Novotny et al., 2017). In the present case, the tumor involved both the ovary and uterine lumen, producing uterine distension that was initially detected during ultrasonographic examination.

Ultrasonographic findings in uterine lymphoma are frequently nonspecific and may overlap with those observed in inflammatory or other neoplastic uterine diseases. Reported sonographic features include uterine enlargement, heterogeneous echotexture, lobulated masses, and distortion of normal uterine architecture, often leading to an initial misdiagnosis of leiomyoma, inflammatory disease, or other reproductive tract neoplasms (Hadi et al., 2015). In the present case, ultrasonography revealed uterine distension and ovarian enlargement without specific features suggestive of lymphoma, reinforcing the importance of histopathological and immunohistochemical evaluations for a definitive diagnosis.

Additionally, the neurological abnormalities observed at presentation could not be definitively associated with reproductive tract neoplasms. Although imaging identified mild vertebral and orthopedic abnormalities, central nervous system or spinal involvement by lymphoma could not be excluded because advanced neurological investigation and postmortem examination were not performed. Consequently, whether neurological manifestations represent paraneoplastic, inflammatory, degenerative, or neoplastic-related alterations remains uncertain.

One of the main diagnostic challenges in the present case was differentiating of diffuse large B-cell lymphoma from other neoplasms that may affect the female reproductive tract of dogs. According to standard veterinary pathological classifications, leiomyomas, adenocarcinomas, and various germ cell tumors are the most common neoplastic entities in the canine uterus and ovaries (Agnew; Maclachlan,

2017). Among these, dysgerminoma was considered the principal differential diagnosis owing to the ovarian involvement and the histological features observed in the tumor. Dysgerminomas are malignant germ cell tumors that may occur in the canine ovary and are typically characterized histologically by nests or sheets of large polygonal cells with clear cytoplasm, distinct cell borders, and large nuclei with prominent nucleoli (Park *et al.*, 2009). Because these morphological features may overlap with those observed in other poorly differentiated neoplasms, immunohistochemistry plays a critical role in establishing the correct diagnosis (Park *et al.*, 2009).

Dysgerminomas typically express germ cell markers such as OCT3/4, placental alkaline phosphatase (PLAP), SALL4, and frequently CD117 (c-KIT), which are widely used to confirm germ cell origin in both veterinary and human pathology (Park *et al.*, 2009). In the present case, however, the neoplastic cells were negative for OCT3/4, PLAP, SALL4, and CD117, effectively excluding a germ cell tumor. Conversely, the tumor cells showed nuclear immunoreactivity for PAX-5, confirming the B-cell lineage, while the high proliferative index demonstrated by Ki-67 (approximately 80%) supported the diagnosis of an aggressive lymphoid neoplasm consistent with diffuse large B-cell lymphoma.

Another important differential diagnosis considered was transmissible venereal tumor (TVT), a round cell tumor that commonly affects the genital tract of dogs and may occasionally involve deeper reproductive structures (Ball; Hoddinott, 2018). TVT typically consists of round cells with moderate cytoplasm, frequent cytoplasmic vacuolation, and variable mitotic activity (Ball; Hoddinott, 2018). Although the cytomorphological appearance of TVT may resemble that of other poorly differentiated neoplasms, immunohistochemistry is useful for distinguishing this tumor from lymphoid neoplasms (Ball; Hoddinott, 2018). In contrast to lymphomas, which express lymphoid markers such as PAX-5 or CD79a, TVT generally lacks lymphoid immunophenotypic markers (Ball; Hoddinott, 2018).

An important limitation of the present study is the absence of complete clinical staging, including lymph node evaluation, bone marrow assessment, advanced imaging studies, and postmortem examination. Consequently, it was not possible to determine whether the uterine and ovarian lesions represented primary extranodal lymphoma or secondary involvement as part of a multicentric disease process. Likewise, the lack of clinical follow-up precluded the assessment of treatment

response, disease progression, and overall survival. Nevertheless, the histopathological features and immunophenotypic profile observed in this case allowed for a definitive diagnosis of diffuse large B-cell lymphoma involving the ovary and uterus.

Reports describing lymphoid neoplasms affecting the canine uterus and ovaries remain scarce in the veterinary literature (Novotny *et al.*, 2017; Ko *et al.*, 2013). Therefore, despite the inability to establish the primary or secondary nature of the lesion, the unusual anatomical distribution observed in this case emphasizes the importance of documenting reproductive tract involvement in hematopoietic malignancies. Furthermore, the ovarian localization and morphological appearance of the neoplastic cells closely mimicked dysgerminoma, highlighting the diagnostic value of immunophenotyping, particularly in poorly differentiated round cell neoplasms involving the canine uterus and ovaries.

REFERENCES

- AGNEW, D. W.; MACLACHLAN, N. J. Tumors of the genital system. In: MEUTEN, D. J. **Tumors in domestic animals**. 5. ed. Ames: Wiley-Blackwell, 2017. p. 689-722.
- BALL, E.; HODDINOTT, K. Transmissible venereal tumor of the uterine stump following successful chemotherapy in a 5-year-old mixed-breed dog. **Canadian Veterinary Journal**, Ottawa, v. 59, p. 632-635, 2018.
- HADI, E.; BRUCHIM, I.; HELMAN, I.; HAREL, M.; SARID, D.; KEDAR, Z. Sonographic appearance of uterine lymphoma: case report and review of the literature. **Journal of Clinical Ultrasound**, New York, v. 43, p. 59-63, 2015.
- JO, J.; SON, M.; CHAE, Y.; KIM, H.; PARK, J.; KANG, B.; SUR, J. H. T-cell lymphoma infiltrating the uterus and ovaries of a Golden Retriever: a case report. **Irish Veterinary Journal**, Dublin, v. 76, p. 23, 2023.
- KO, J. S.; KIM, H. J.; HAN, S.; DO, S. H. Primary lymphoma of the uterine horn in a Lhasa Apso dog. **Irish Veterinary Journal**, Dublin, v. 66, p. 24, 2013.
- NOVOTNY, L.; TAYLOR, F.; CLAXTON, K.; DUDOVA, J.; HANSHAW, D.; MISIK, J. Uterine B-cell lymphoma in two dogs: a case report. **Acta Veterinaria Brno**, Brno, v. 86, p. 195-198, 2017.
- PARK, J. K.; GOO, M. J.; HONG, I. H.; KI, M. R.; HAN, J. Y.; JI, A. R.; JEONG, K. S. Immunohistochemistry diagnosis of an ovarian dysgerminoma in one bitch. **Reproduction in Domestic Animals**, Berlin, v. 44, p. 855-858, 2009.

VALLI, V. E.; SAN MYINT, M.; BARTHEL, A.; BIENZLE, D.; CASWELL, J.; COLBOURNE, J.; DURHAM, A.; EHRHART, E. J.; JOHNSON, Y.; JONES, C.; KIUPEL, M.; KRISTENSEN, A. T.; MOORE, P. F.; MOROFF, S.; RUTTEMAN, G.; TASKER, S.; VERNAU, W.; VERNER, T.; ZWINGENBERGER, A. Classification of canine malignant lymphomas according to the World Health Organization criteria. **Veterinary Pathology**, Thousand Oaks, v. 48, p. 198-211, 2011.