CORTISOL-SECRETING ADRENOCORTICAL CARCINOMA IN A BLUE HEELER

CARCINOMA ADRENOCORTICAL SECRETOR EM UM CÃO BOIADEIRO AUSTRALIANO

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ABSTRACT

Adrenocortical tumors in dogs are uncommon, but clinically important neoplasms, especially when they are functionally active and associated with cortisol overproduction. These tumors can lead to classic signs of hypercortisolism including polyuria, polydipsia, polyphagia, muscle wasting, and abdominal distension. This report describes the clinical, imaging, and histopathological findings of cortisol-secreting adrenocortical carcinoma in a 14-year-old female Blue Heeler dog that presented with progressive abdominal distension, exophthalmos, and systemic hypertension. The initial diagnostic workup revealed hyperlipidemia and increased alkaline phosphatase levels. The low-dose dexamethasone suppression test failed to suppress the hypothalamic-pituitary-adrenal axis, indicating endogenous hypercortisolism. Contrast-enhanced computed tomography revealed a nodular mass in the left adrenal gland with internal calcification, renal vein displacement, and no vascular invasion. The dog underwent adrenalectomy, and histopathological analysis confirmed a diagnosis of adrenocortical carcinoma. The neoplasm displayed a solid and infiltrative pattern, capsular invasion, hemorrhage, and dystrophic calcification. The partial Utrecht histological scoring system yielded a score of 7, suggesting an intermediate malignancy and risk of recurrence. Liver biopsy revealed marked macro- and microvesicular hepatocellular vacuolar degeneration, predominantly in the centrilobular and midzonal areas, which was consistent with chronic glucocorticoid exposure. This case illustrates the importance of integrating clinical signs, hormonal testing, advanced imaging, and histopathological evaluation for the accurate diagnosis and management of functional adrenocortical tumors in dogs. It also emphasizes the relevance of histological scoring systems, such as the Utrecht Score, in predicting biological behavior and guiding therapeutic decisions in veterinary oncology.

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Keywords: Adrenal neoplasm. Cortisol-secreting tumor. Hypercortisolism. Adrenalectomy. Utrecht score.

RESUMO

Os tumores adrenocorticais em cães são neoplasias incomuns, porém clinicamente relevantes, especialmente quando funcionais e associados à produção excessiva de cortisol. Esses tumores podem causar sinais clássicos de hipercortisolismo, como poliúria, polidipsia, polifagia, atrofia muscular e distensão abdominal. Este relato descreve os achados clínicos, de imagem e histopatológicos de um carcinoma adrenocortical secretor de cortisol em uma cadela da raça Boiadeiro Australiano, com 14 anos de idade, que apresentava distensão abdominal progressiva, exoftalmia e hipertensão arterial sistêmica. A investigação inicial revelou hiperlipidemia e aumento da fosfatase alcalina. O teste de supressão com dexametasona em baixa dose não suprimiu o eixo hipotálamo-hipófise-adrenal, indicando hipercortisolismo endógeno. A tomografia computadorizada contrastada identificou uma massa nodular na região da adrenal esquerda, com calcificações internas, deslocamento da veia renal e ausência de invasão vascular evidente. A paciente foi submetida à adrenalectomia, e a análise histopatológica confirmou o diagnóstico de carcinoma adrenocortical. A neoplasia apresentou padrão sólido e infiltrativo, com invasão capsular, hemorragia e calcificação distrófica. A pontuação histológica parcial de Utrecht foi 7, indicando malignidade intermediária e risco de recidiva. A biópsia hepática revelou acentuada degeneração vacuolar hepatocelular, macro e microvesicular, predominando nas zonas centrolobulares e intermediárias, compatível com exposição crônica a glicocorticoides endógenos. Este caso ilustra a importância da integração entre sinais clínicos, exames hormonais, métodos de imagem avançados e avaliação histopatológica detalhada para o diagnóstico e manejo dos tumores adrenocorticais funcionais em cães, destacando também o papel dos sistemas prognósticos histológicos na conduta oncológica veterinária.

Palavras-chave: *Neoplasia Adrenal, Hipercortisolismo, Adrenalectomia, Escore De Utrecht*

1 INTRODUCTION

Adrenal gland tumors in dogs are relatively rare but clinically significant because of their ability to secrete hormones and cause major endocrine disturbances. These tumors are referred to as cortisol-secreting tumors (Rosol; Meuten, 2017). Among adrenocortical tumors, adenomas and carcinomas are the most common, with the latter being characterized by greater aggressiveness, local invasion, and metastatic potential (Rosol; Meuten, 2017). Functional adrenocortical carcinoma, which leads to

excessive cortisol secretion, presents clinical signs such as polyuria, polydipsia, alopecia, and abdominal changes (Machida *et al*., 2008; Mendes *et al*., 2022).

The diagnosis of adrenal tumors involves the integration of clinical findings, laboratory tests, and imaging studies. Computed tomography (CT) and ultrasonography are essential tools for assessing tumor morphology and the extent of the disease (Pagani *et al*. 2016; Lee *et al*. 2022). Although uncommon, the presence of intratumoral calcifications may indicate necrosis and hemorrhage, suggesting malignancy (Labelle *et al*., 2004). A definitive diagnosis relies on histopathological analysis, which evaluates features such as capsular invasion, cellular pattern, mitotic index, and tissue infiltration, which are the key criteria for distinguishing adenomas from carcinomas (Rosol; Meuten, 2017).

The preferred treatment for localized and functional adrenocortical carcinomas is adrenalectomy, which can lead to clinical improvement and favorable prognosis, particularly in the absence of vascular invasion or metastasis (Schwartz *et al*., 2008; Park *et al*., 2023). However, high perioperative mortality and associated complications require careful preoperative assessment and multidisciplinary management (Massari *et al*., 2011).

Despite advances in diagnosis and treatment, detailed reports of functional adrenocortical carcinomas in Blue Heelers are scarce. This highlights the need to document and analyze clinical cases to expand the knowledge of this neoplasm across different clinical and breed profiles. Therefore, the present study aimed to describe a clinical case of cortisol-secreting adrenocortical carcinoma in a female Blue Heeler dog, emphasizing the clinical, imaging, and histopathological aspects and discussing the importance of an integrated approach for the diagnosis and management of this condition.

2 CASE REPORT

A 14-year-old female Blue Heeler presented with clinical signs of polyphagia, polyuria, polydipsia, exophthalmos, and progressive abdominal distension (Figure 1), suggestive of an endocrine disorder. Complete blood count, biochemical profile, and blood pressure (BP) measurements were performed, revealing severe systemic

hypertension (BP, 280 mmHg with cuff no. 4), hyperlipidemia, and elevated alkaline phosphatase levels.

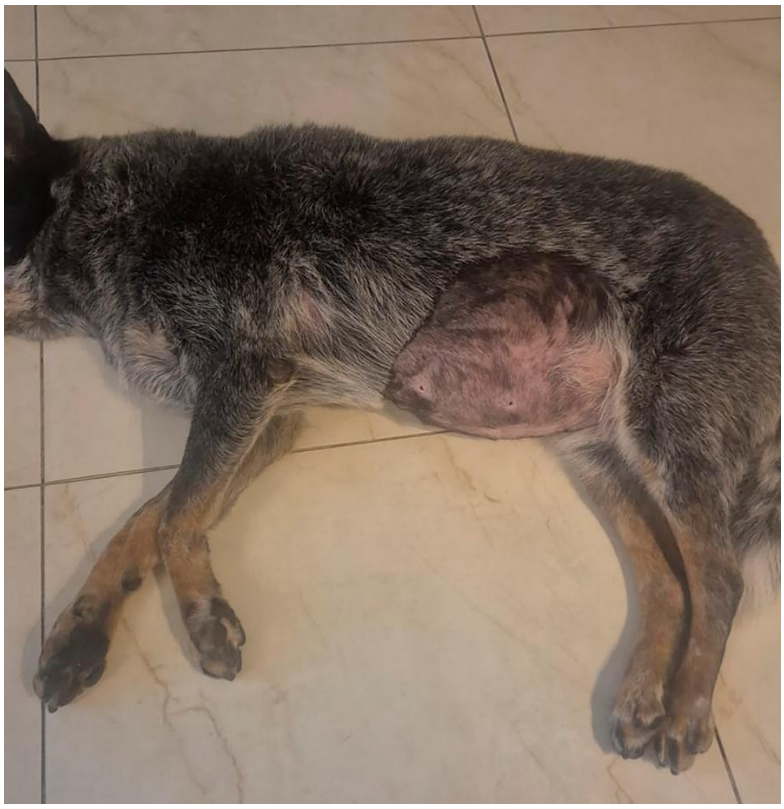

Figure 1: Cortisol-secreting adrenocortical carcinoma in a dog.
Note: The marked progressive abdominal distension, a common clinical sign associated with hypercortisolism.
Source: Author, 2025.

Given the clinical suspicion of hypercortisolism, contrast-enhanced computed tomography scan was performed. The scan revealed a nodular mass in the region of the left adrenal gland containing internal calcifications that caused displacement of the ipsilateral renal vein, but without evidence of vascular invasion (Figure 2). Additionally, hepatomegaly with multiple hepatic nodules was noted, with characteristics consistent with nodular hyperplasia, adenoma, or metastasis as well as left iliomedial lymphadenomegaly.

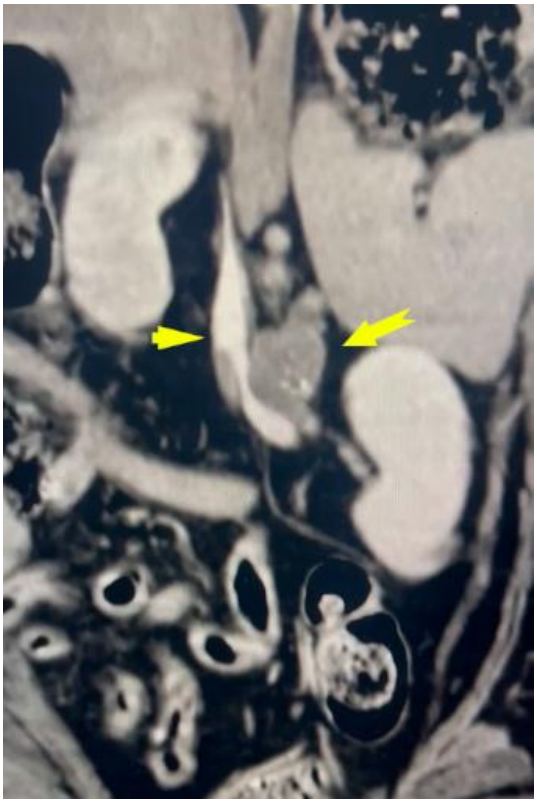

Figure 2 — Cortisol-secreting adrenocortical carcinoma in a dog.
Note: Contrast-enhanced computed tomography scan showing a nodular mass in the left adrenal gland (yellow arrow) with displacement of the ipsilateral renal vein (arrowhead).
Source: Author, 2025.

Based on these findings, a low-dose dexamethasone suppression test was performed using a three-sample protocol (T0h, T4h, and T8h). The test showed no suppression of the hypothalamic-pituitary-adrenal axis, supporting the hypothesis of a glucocorticoid-secreting functional tumor.

Adrenalectomy was elected given the expansive behavior of the lesion and positivity in the low-dose dexamethasone suppression test. Surgical specimens were collected, fixed in 10% buffered formalin, and subjected to histopathological analysis.

Macroscopically, multiple fragments of tissue from the left adrenal gland were received, friable in consistency, brown in color, and measuring collectively 5.2 × 3.5 × 0.5 cm (Figure 3). A liver fragment measuring 0.5 × 0.5 × 0.5 cm was also submitted, soft in consistency and homogeneously brown on cut surface.

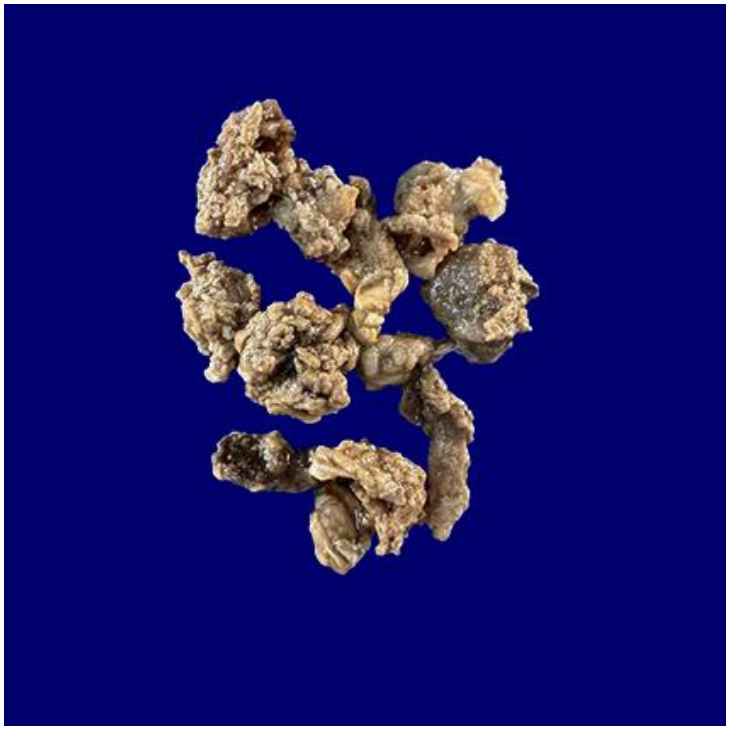

Figure 3 — **Cortisol-secreting adrenocortical carcinoma in a dog.**
Note: Multiple fragments of the left adrenal gland exhibited friable consistency and brown coloration, with a total combined size of 5.2 × 3.5 × 0.5 cm.
Source: Author, 2025.

Histological sections of the adrenal gland revealed poorly demarcated and infiltrative epithelial neoplastic proliferation with capsular invasion and extension into the periadrenal adipose tissue (Figure 4).

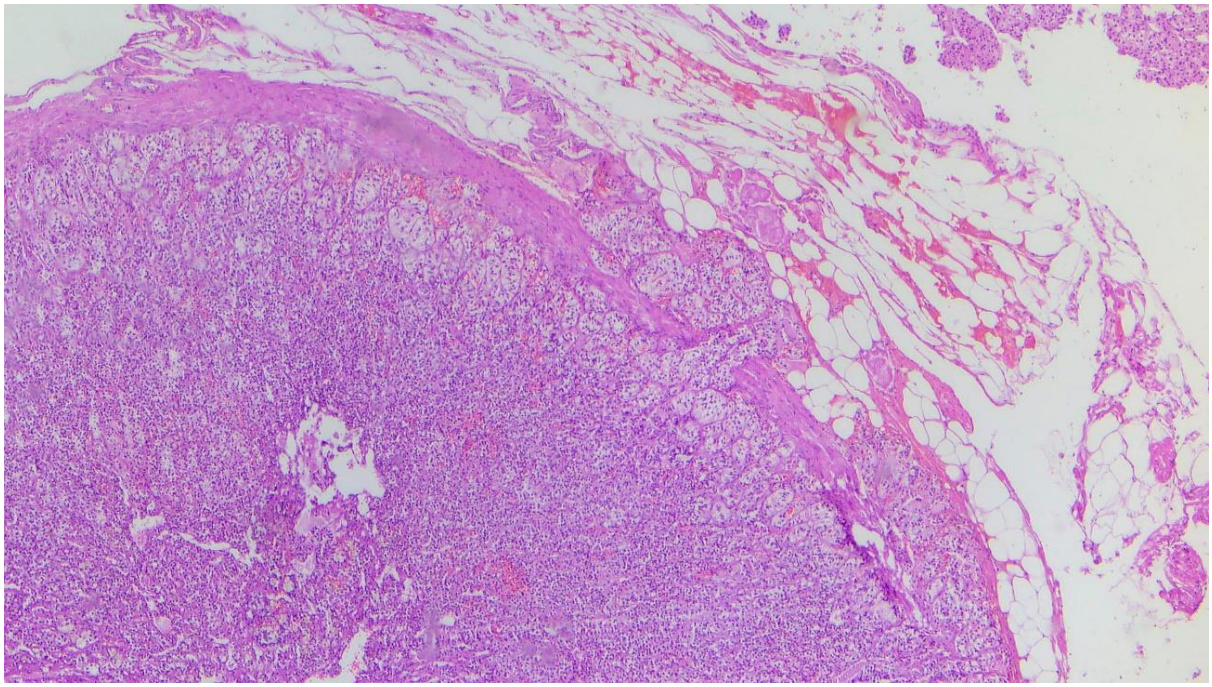

Figure 4 — Cortisol-secreting adrenocortical carcinoma in a dog.
Note: Histological section of the adrenal gland showing a poorly demarcated and infiltrative epithelial neoplasm with evidence of capsular invasion and extension into the surrounding periadrenal adipose tissue (HE, 10x, BAR 100µm).
Source: Authors, 2025.

The neoplasm exhibited a solid and cord-like cellular pattern supported by a fibrovascular collagenous stroma. The cells were polyhedral to slightly cuboidal and moderately sized, with eosinophilic, finely granular, and moderately abundant cytoplasm. The nuclei were oval to round with open chromatin and one to two prominent nucleoli. Three mitotic figures per high-power field (2.37 mm²) were observed with no atypical mitoses. Mild cellular and nuclear pleomorphism (moderate anisocytosis and anisokaryosis), along with multifocal areas of hemorrhage and dystrophic calcification (Figure 5).

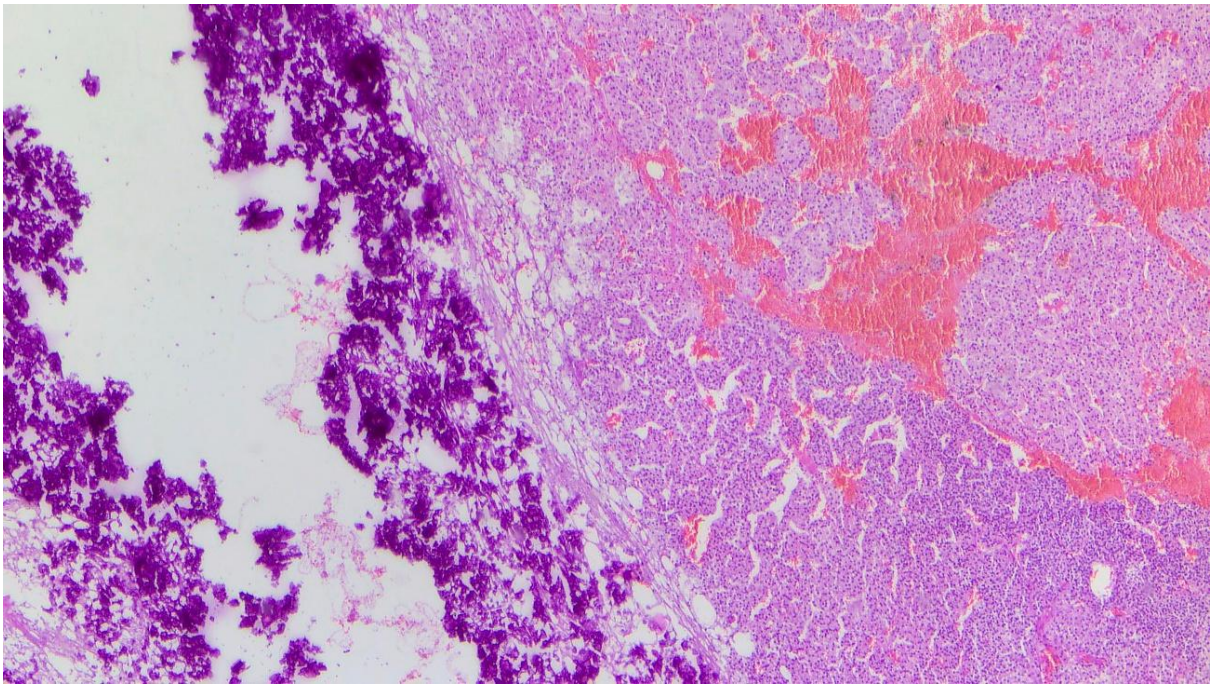

Figure 5 — Cortisol-secreting adrenocortical carcinoma in a dog.
Note: Histological sections of the adrenal gland revealed a poorly demarcated area with hemorrhage and dystrophic calcification (HE, 10x, BAR 100µm).
Source: Authors, 2025.

Additionally, histological assessment was performed using the Utrecht Score, as proposed by Sanders *et al*. (2019), to predict the biological behavior of adrenocortical carcinoma. Two positive criteria were observed: tumor necrosis (3 points) and neoplastic cells with clear or vacuolated cytoplasm in > 33% of the tumor (4 points). The Ki67 proliferative index was not assessed. The partial Utrecht Score was 7.

Liver histology revealed preserved lobular architecture. There was marked vacuolar degeneration of hepatocytes, both macrovesicular and microvesicular, predominantly in the centrilobular and midzonal areas. Hepatocytes exhibited extensive vacuolated cytoplasm with peripheral nuclear displacement in areas of macrovesicular degeneration, and multiple small cytoplasmic vacuoles in the microvesicular form (Figure 6).

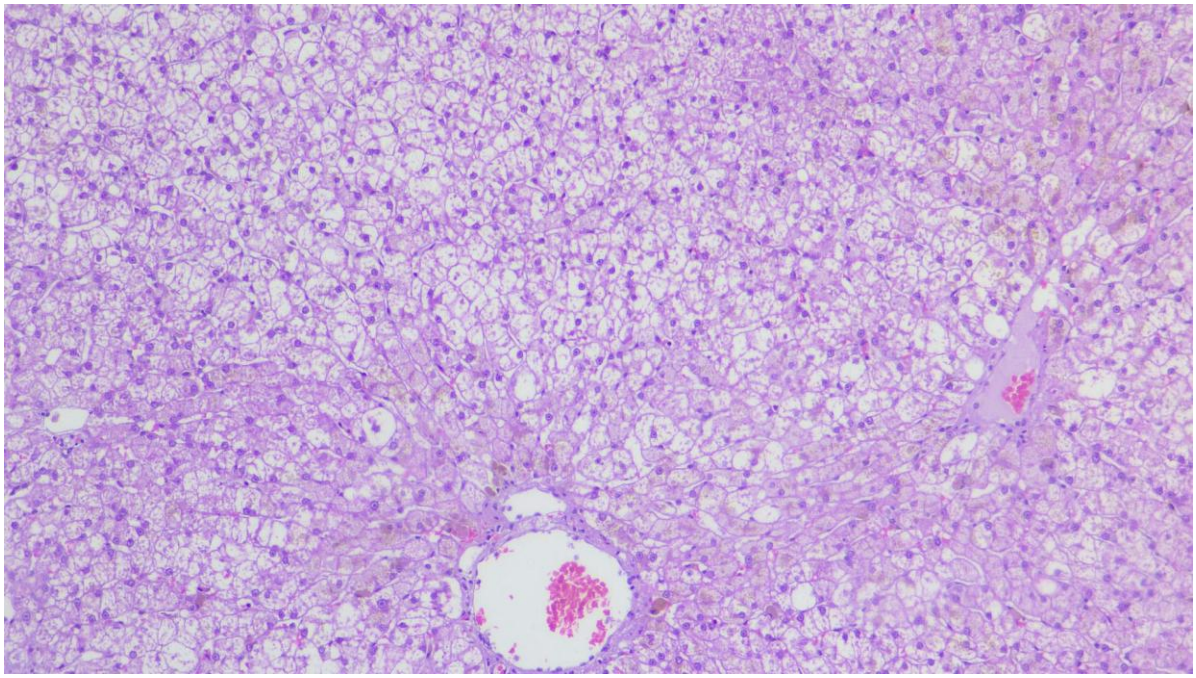

Figure 6 — Cortisol-secreting adrenocortical carcinoma in a dog.
Note: Liver histology showed marked vacuolar degeneration of hepatocytes, both macrovesicular and microvesicular, predominantly affecting the centrilobular and midzonal regions (HE, 40x, BAR 100µm).
Source: Author, 2025.

3 DISCUSSION

Functional adrenocortical carcinoma in dogs is an uncommon endocrine neoplasm, with clinical presentation varying according to the level of hormone production and degree of tumor invasiveness. In the present case, the patient exhibited classic signs of hypercortisolism, such as polyuria, polydipsia, and abdominal distension, consistent with excessive glucocorticoid secretion from the left adrenal gland. These clinical manifestations are often the first indicators of a tumor's functional activity. As highlighted by Park *et al*. (2023), it is crucial to consider functional adrenocortical tumors in geriatric dogs presenting with chronic systemic alterations.

Computed tomography was decisive in identifying a left adrenal nodular mass with calcifications and mass effects, as well as nodular hepatomegaly and lymphadenomegaly. As discussed by Lee *et al*. (2022), CT provides greater sensitivity than ultrasonography in detecting structural changes and in surgical planning, particularly due to its ability to evaluate the tumor's relationship with adjacent structures such as renal vessels and the caudal vena cava.

Functional confirmation was established through the low-dose dexamethasone suppression test, which revealed a failure to suppress the hypothalamic-pituitary-

adrenal axis, consistent with a cortisol-secreting adrenal mass. This test is widely used to screen for and differentiate the causes of hypercortisolism (Mendes *et al*., 2022).

Adrenalectomy was the treatment of choice, in line with the recommendations of Schwartz *et al*. (2008), who advocated surgery as the preferred approach for unilateral adrenocortical tumors without clear evidence of vascular invasion or extensive metastasis. The absence of vascular invasion in histological samples was also associated with a better postoperative prognosis, as reported by Massari *et al*. (2011).

In cases where surgery is not feasible owing to tumor extension, metastasis, or unfavorable clinical conditions, medical treatment with trilostane is an effective alternative for managing hypercortisolism. Trilostane acts as an inhibitor of 3β-hydroxysteroid dehydrogenase, reducing adrenal glucocorticoid synthesis and alleviating clinical signs of the disease. As reviewed by Lemetayer and Blois (2018), this drug has been shown to be safe and effective in most dogs with Cushing's syndrome, including those with functional adrenocortical tumors. Although it does not directly affect tumor growth, hormonal control provided by trilostane significantly improves patient quality of life and is considered the treatment of choice in non-surgical cases. Regular monitoring of cortisol levels and clinical progression are essential for dosage adjustment and the prevention of adverse effects.

Histopathological analysis of the adrenal glands confirmed a diagnosis of adrenocortical carcinoma. According to Labelle *et al*. (2004), the presence of necrosis, cytologic atypia, capsular invasion, and infiltrative growth are the criteria most strongly associated with aggressive behavior. Nonetheless, the absence of aberrant mitosis and vascular invasion in this case suggests an intermediate biological behavior within the prognostic spectrum of the neoplasm. Based on these findings, the Utrecht Score prognostic model proposed by Sanders *et al*. (2019) was applied, combining histological parameters and the Ki67 proliferative index. Although Ki67 was not assessed, the presence of tumor necrosis and clear cytoplasm in ≥33% of the neoplastic cells resulted in a partial score that exceeded the established cut-off for identifying tumors with higher recurrence risk and reduced survival. According to this model, patients scoring between 6 and 11 have a median survival of approximately 51.5 months, classifying this case into an intermediate-risk category.

Liver changes consistent with vacuolar degeneration observed in the histological evaluation of the patient's liver are expected findings in the context of chronic exposure to endogenous glucocorticoids, as occurs in functional adrenocortical tumors. Macro- and microvesicular degeneration of hepatocytes, predominantly in the centrilobular and midzonal regions, reflects lipid accumulation and metabolic disturbances induced by the catabolic effects of cortisol on hepatic metabolism. According to the National Institute Of Diabetes And Digestive And Kidney Diseases (2022), hypercortisolism leads to enzymatic induction, steatosis, and hepatic lipid redistribution, often resulting in hepatomegaly and microscopic structural changes such as those observed in this case. This histological pattern is considered characteristic, although not exclusive, of corticosteroid-induced hepatopathies in dogs.

4 CONCLUSION

This case highlights the importance of integrating clinical evaluation, hormonal testing, advanced imaging, and histopathological analysis for the accurate diagnosis and management of functional adrenocortical tumors in dogs. Adrenalectomy remains the treatment of choice for localized lesions, offering a favorable prognosis in the absence of vascular invasion or metastasis.

The prognosis depends on tumor invasiveness and histological scoring, emphasizing the need for regular postoperative monitoring using imaging and cortisol assessment to detect early recurrence. The correlation between imaging and histopathological findings is essential to understand tumor behavior and guide precise therapeutic decisions in endocrine neoplasms.

ACKNOWLEDGMENTS

This study was partially funded by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior, Brasil (CAPES), Finance Code 001. Additional support was provided by the Fundação de Amparo à Pesquisa e Inovação do Espírito Santo (FAPES).

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