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Case report

Concurrent Adrenal and Pituitary Adenomas in a Dog: A Case Report of Cushing's Disease

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Abstract: Neoplasms of endocrine organs occur in all animal species and are more commonly observed in dogs, cats, and horses. The simultaneous occurrence of pituitary and adrenal gland neoplasia can appear isolated or as a part of multiple endocrine neoplasias-like syndromes. This report describes a case of isolated simultaneous neoplasia of the pituitary and adrenal glands in a dog, leading to the development of Cushing's disease. The necropsy revealed a large adenoma 2.5 cm of the pituitary gland and medullary neoplasia of the left adrenal gland. This case, due to its rarity and complexity, presents a significant interest for the veterinary community.

Keywords: endocrine neoplasm; pituitary neoplasia; adrenal gland neoplasia; pituitary adenoma.

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1. Introduction

Pituitary tumors are relatively common in dogs and have been increasingly recognized in cats in recent decades [1,2]. Pituitary abnormalities occur in a 2:1 dog-to-cat ratio. Sporadically, we can also find pituitary neoplasms in horses [3] and lama Alpaca [4]. In dogs, the most common pituitary tumor is corticotroph adenoma, characterized by a large number of chromophobe cells and often associated with the clinical syndrome of cortisol excess (Cushing's syndrome). However, invasive adenomas and adenocarcinomas have also been reported [5,6]. In contrast, in cats, the most common pituitary tumor is the somatotroph adenoma but hormonally silent adenomas are underdiagnosed due to the lack of a hormonal syndrome [7]. Adrenal gland neoplasia is the most commonly affected endocrine disorder in domestic ferrets and older dogs (aged 7 years and above). Numerous cases of adrenocortical adenoma and carcinoma have also been reported in cattle [8,9]. In contrast, such neoplasms are rare in cats [10], horses [11], and small ruminants.

Whether occurring simultaneously or separately, neoplasia of the pituitary and adrenal glands accounts for approximately 90% of Cushing's disease cases in dogs. Also known as hyperadrenocorticism, Cushing's disease has several underlying causes, all leading to excessive cortisol production. In cases involving just pituitary adenoma, the condition is classified as Pituitary-Dependent Hyperadrenocorticism (PDH). In contrast, neoplasia (benign or malign) of one or both adrenal glands results in Adrenal-Dependent Hyperadrenocorticism (ADH). Regarding prevalence, studies indicate a rate of 0.20%, suggesting that around 2 out of every 1,000 dogs in general veterinary practice may present with Cushing's syndrome [12]. Notably, there is a marked sex prevalence; among 107 dogs diagnosed with PDH, 74.8% were females, while 25.2% were males [13].

This study describes the macroscopic and histological features observed in simultaneous neoplasia of the adrenal and pituitary glands.

2. Casse description

A 12-year-old mixed-breed female dog was submitted for necropsy following a history of cachexia, enophthalmos, lethargy, polyuria, and polydipsia, along with significant abdominal distention and bilateral alopecia. While the biochemical blood parameters were within normal ranges, alkaline phosphatase (ALP) and alanine aminotransferase (ALT) levels were elevated. These clinical signs suggest a potential endocrine disorder.

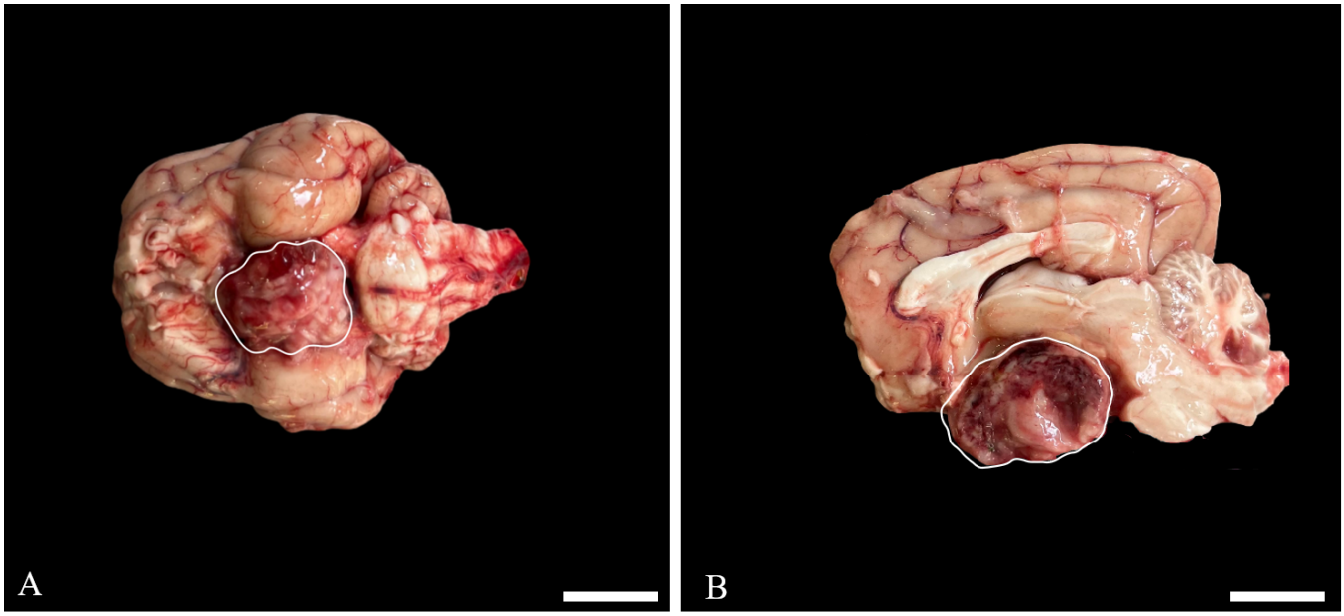

Figure 1. Brain and pituitary gland. Dog. A well-demarcated mass measuring approximately 2.5 cm was observed within the pituitary gland (indicated by the white circle), compressing the surrounding tissue (Image A). The cross-section of the pituitary gland revealed a heterogeneous mass displaying a white-to-red appearance (Image B). (Scale bar 2 cm).

During the necropsy, several findings were noted. The pituitary gland was enlarged due to a mass measuring approximately 2,5 cm, which exhibited significant expansive growth and compression of adjacent tissues. Although the mass was not encapsulated, it was well vascularized and showed no visible infiltration into the surrounding tissue (Figure 1). The left adrenal gland is enlarged, measuring approximately 3x1.5 cm, with a smooth, well-defined surface. On the cross-section, a soft and yellow mass, exhibiting homogeneous features was observed partially replacing the adrenal medulla. The mass is well-circumscribed, with no infiltration into surrounding tissues. Adjacent adrenal tissue appears compressed but intact, with no signs of malignant transformation. The right adrenal gland showed medular hiperplasia with nodular aspect (Figure 2), while normal ratio of cortex and medulla in dogs is 1:2 [14].

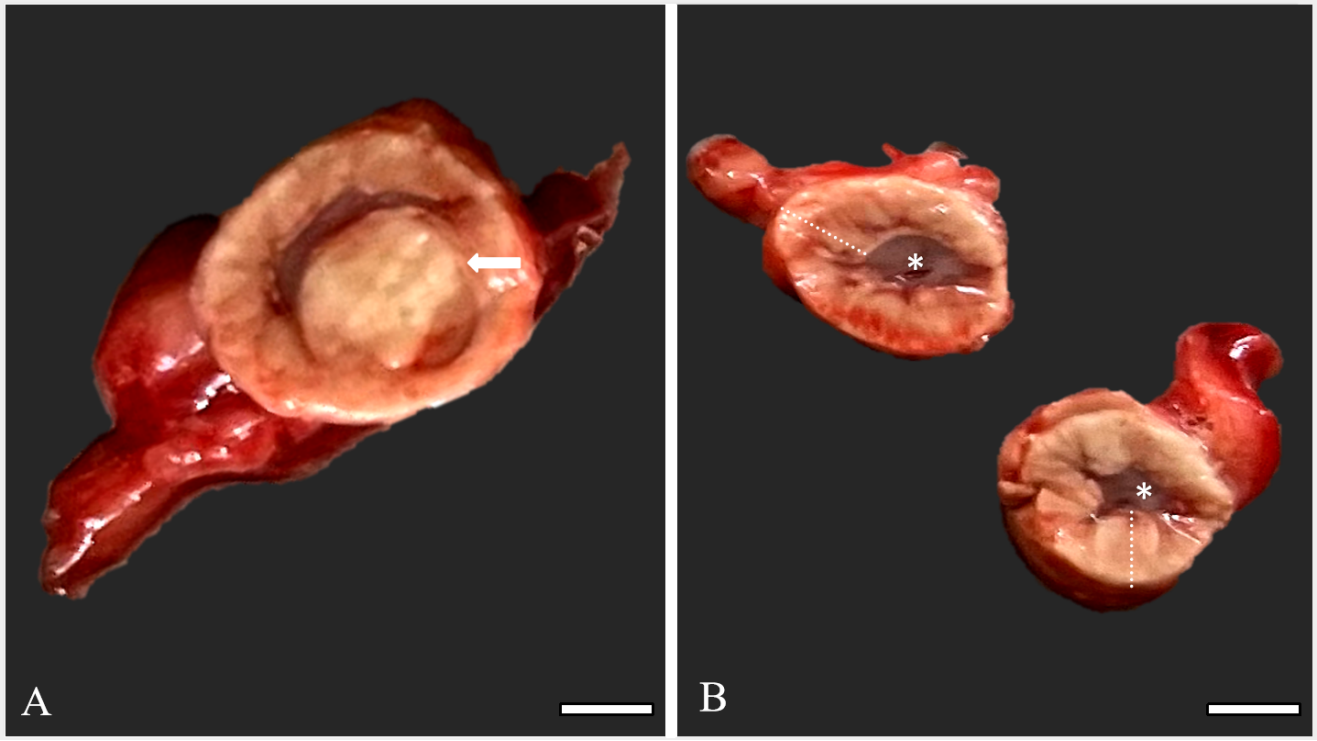

Figure 2. Left adrenal gland (Image A). Replacing the adrenal medulla, a well-demarcated, yellow mass was observed (arrow) within the left adrenal gland. The right adrenal gland showed hiperplasia of cortex with nodular aspect showed with doted line. (Image B) (Scale bar 1 cm).

For histological evaluation, pituitary and adrenal masses were fixed in 10% neutral buffered formalin (NBF) and subsequently embedded in paraffin following standard protocols. According to the manufacturer's protocols, two-micrometer-thick sections were prepared and stained with hematoxylin and eosin (H&E). The histological slides were examined under an Olympus BX51 microscope, and bright field images were captured using an Olympus SP350 digital camera and processed with Olympus cellSens software for further analysis.

Replacing the pituitary gland, a well-demarcated, unencapsulated mass was observed. The mass is supported by a discrete fibrovascular stroma and consists of packets of hypertrophied polygonal to round cells with distinct cell borders arranged in nests with trabecular patterns. The cytoplasm is basophilic and lightly granulated with one central nucleus. Minimal nuclear and cellular pleomorphisms with rare mitotic figures are observed (Figure 3 images A and B).

Within the adrenal medulla, a well-demarcated and encapsulated mass composed of sheets and cords, of polygonal cells was observed. The cells resemble normal adrenocortical cells. The tumoral cells have abundant clear and occasionally vacuolated cytoplasm. The cytoplasm is slightly eosinophilic, resembling zona reticularis cells. The nuclei are round to oval with dispersed chromatin and discrete nucleoli. Mitotic figures are rare. The tumor is surrounded by a thin fibrous capsule, separating it from the adjacent normal adrenal tissue. The capsular invasion was not observed (Figure 3 images C and D).

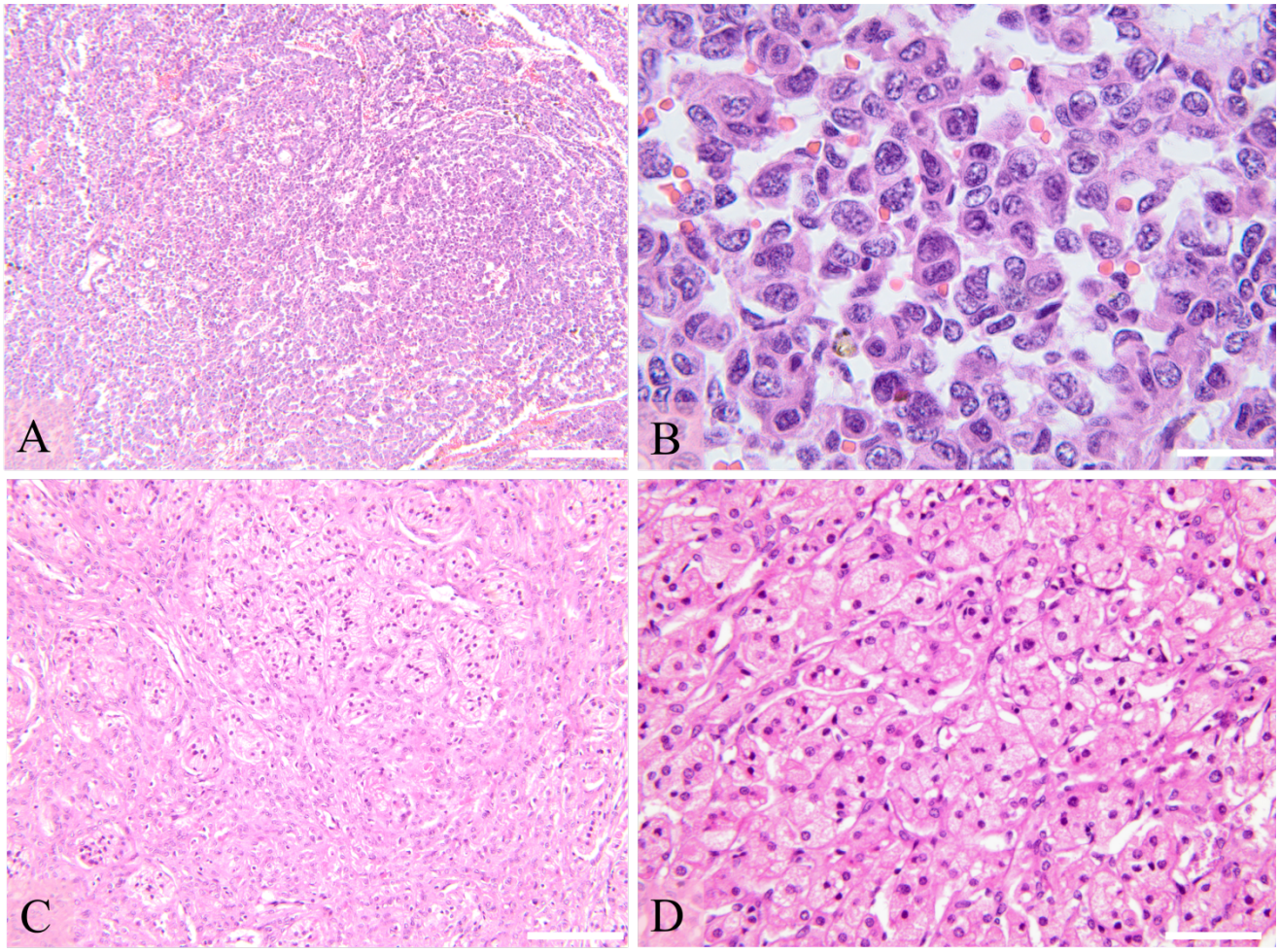

Figure 3. Histological features of pituitary adenoma (Image A and B). The tumor consists of packets of hypertrophied polygonal to round cells with a trabecular pattern. The cytoplasm is basophilic and lightly granulated with minimal polymorphism. No infiltration in adjacent tissue was noted. Histological features of adrenal gland adenoma. (Image C and D). Within the adrenal medulla, a well-demarcated, encapsulated mass composed of sheets of polygonal cells is observed. The tumor cells have abundant clear and occasionally vacuolated cytoplasm, with a slight eosinophilic feature. The nuclei are round to oval with dispersed chromatin and small nucleoli. Mitotic figures are rare. Hematoxylin and eosin stain. Ob. x20 (Image A and C), Ob. x40 (Image B and D). Scale bar 100 μm (Image A and C) and 50 μm (Image B and D).

3. Discussion

Neoplasia of the pituitary and adrenal cortex both contribute to hyperadrenocorticism. However, there are several mechanisms of cause-effect in Cushing disease. In most cases, pituitary-dependent and adrenal-dependent hyperadrenocorticism occur independently of each other. In cases when they appear simultaneously they can have an adrenal or pituitary-driven mechanism [14,15]. The majority of Cushing's cases in dogs are pituitary-dependent, where a pituitary adenoma overproduces ACTH [16]. Adrenal hyperplasia is commonly seen as a secondary effect of pituitary tumors in pituitary-dependent adrenocorticism (PDH) but it does not typically progress to malignancy. This transformation is rare because most hyperplastic adrenal cells do not undergo malignant changes [17].

Cushing's disease constitutes about 2% of total clinical practice and has a diverse range of underlying causes, including incidentalomas (incidental findings of adrenal tumors) and large pituitary adenomas. In the majority of cases, the adenohypophyseal neoplasms associated with Cushing's disease are solitary and are predominantly classified as adenomas rather than carcinomas [13]. According to veterinary literature, the majority of pituitary tumors arise from adenohypophysis [1,18].

Adrenal neoplasia in dogs, particularly with adrenocorticism, is assessed using protocols like those of the ACVIM [19]. Besides hematological testing, the ACTH stimulation test is another diagnostic tool, especially helpful in differentiating iatrogenic from spontaneous cases [20]. Further differentiation between pituitary-dependent hyperadrenocorticism (PDH) and adrenal-dependent hyperadrenocorticism (ADH) can be achieved with the high-dose dexamethasone suppression test (HDDST) or endogenous ACTH levels. Imaging, such as abdominal ultrasound or MRI, is essential for visualizing adrenal or pituitary abnormalities. The integration of clinical signs, hormonal test results, and imaging findings ensures an accurate diagnosis. Misdiagnosis can occur if concurrent conditions mimic Cushing's disease, highlighting the need for careful evaluation. Most adrenal incidentalomas are benign, but excluding ACC or metastases remains critical. Challenges arise from breed differences, variable tumor presentations, and limited diagnostic tools, often necessitating reliance on statistical data, which may not be universally applicable [20]. Species-specific variability further complicates standardization, emphasizing the need for a tailored, multidisciplinary approach [21].

Adrenalectomy is usually the primary treatment for adrenal tumors that cause clinical signs or manifest malignant characteristics, such as local invasion or thrombus formation. Although, the risk or perioperative mortality rate for adrenalectomy in dogs ranges from 20% to 24% [22].Previously there existed hypotheses that dogs could be a suitable model for comparative analysis of Cushing disease. However, recently it was proved that several main differences can not make it possible. Firstly, incidence and susceptibility make it tricky. Cushing's disease is significantly more common in dogs, with an incidence of 1–2 cases per 1,000 dogs annually, compared to 1.2–2.4 cases per million humans annually [23]. Initially, the differences in hormonal receptor expression and absence of human ACTH-producing cell lines complicate efforts to draw parallels between dog and human Cushing’s. As well as differences in tumor behavior [17].

4. Conclusions

This report highlights a relatively rare case of simultaneous adrenal and pituitary tumors in a dog. Both tumors were benign but contributed to Cushing’s syndrome. Despite the large size of the pituitary tumor, neither neoplasm caused notable clinical symptoms during the dog’s life, with tumors only identified during necropsy. Concurrent adrenal and pituitary neoplasia is uncommon and usually occurs separately.

Cushing’s disease remains a challenging disorder to diagnose in animals due to the unclear onset of pathology and limited access to diagnostic technology. As a result, it is often diagnosed too late for effective classical treatment. This case also reinforces the importance of the hypothalamic-pituitary axis as a critical area for further study, offering valuable insight into the complex nature of endocrine disorders in veterinary medicine.

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