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CASE REPORT

Adrenal Incidentaloma Diagnosed as a Pheochromocytoma in a fifteen-year-old Dog - An Unexpected Finding with Deadly Consequences

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ABSTRACT

Adrenal incidentalomas are masses of the adrenal gland discovered inadvertently during diagnostic procedures, from which a significant percentage are pheochromocytomas and these tumors are rare. Here we report a case of a 15-year-old male dog whose main complaints were a soft cervical mass and mild generalized weakness. Blood cell count, routine biochemistry, arterial blood pressure and electrocardiogram were performed. Diagnostic imaging revealed a 3.5 cm mass next to the right adrenal gland. Surgery was performed and histopathology examination of the mass confirmed a malignant pheochromocytoma. The dog died 96 hours later after surgery. At necropsy, metastasis was found in cervical lymph node. Considering vague and episodic clinical signs, pheochromocytoma *antemortem* diagnosis is uncommon. The main aim of this case is to highlight this endocrinology disorder, increasing the awareness of clinicians to this difficult diagnostic condition.

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INTRODUCTION

Adrenal incidentalomas are masses of the adrenal gland discovered inadvertently during diagnostic techniques for other disorders unrelated to the incidental mass (Willenberg and Bornstein, 2011). A significant percentage of these tumors are pheochromocytomas (Mantero and Arnaldi, 2000) rare endocrine tumors of the chromaffin cells, with a prevalence ranging from 0.13 to 0.01% considering all kinds of canine tumors (Platt *et al*., 1998). Affected dogs are usually older, with a mean age of 11 years (varying from 7 to 16 years) and male dogs appear to be overrepresented. Clinical signs, caused mainly by excessive catecholamine secretion and consequent systemic hypertension, include generalized weakness, episodic collapse, panting, tachypnea, seizures and cardiac or ocular abnormalities (Herrera *et al.,* 2008).

Case history: At the Veterinary Teaching Hospital of Technical University of Lisbon (FMV-UTL), a fifteen-year-old, neutered male and mixed breed dog was brought with a swelling on the left side of the cervical region. Clinical examination showed a soft and fluctuant mass on palpation and a left heart murmur. Fine-needle aspiration of the mass was performed and the results showed the presence of a salivary gland mucocele. Surgery for removing the mucocele was indicated but before that, a complete panel was performed including a blood cell count and routine biochemistry analysis [white blood cell count $11.3x10^3/\mu L$ (6-17); red blood cell count $7.7x10^6/\mu L$ (5.5-8.5); platelet count $350x10^3/\mu L$ (200-500); hemoglobin 14.2 g/dL (12-18); hematocrit 43% (37-55); glucose 120 mg/dL (70-138); total protein 7.0 g/dL (5.0-7.4); albumin 3.2 g/L (2.7-4.4); urea 20 mg/dL (0-54); creatinine 1.2 mg/dL (0.5-1.4); ALT 81 u/L (12-130)], electrocardiogram, abdominal ultrasound and arterial blood pressure measurement (150 mmHg and 90 mmHg of systolic and diastolic pressure, respectively). Almost all parameters showed no abnormalities. However, abdominal ultrasound revealed an unexpected mass with 3.5 cm in diameter, located between the caudate lobe of the liver and the right adrenal gland. No consistent abnormalities were found in the remaining organs. Further investigation of the mass location was performed with a computed tomography scan (Fig. 1). No relevant findings were observed and the exact mass location remained inconclusive. Exploratory laparotomy was then performed, as well as, the removal of the mucocele. During the surgery, the mass was found in the right adrenal gland and was very hemorrhagic, encap-

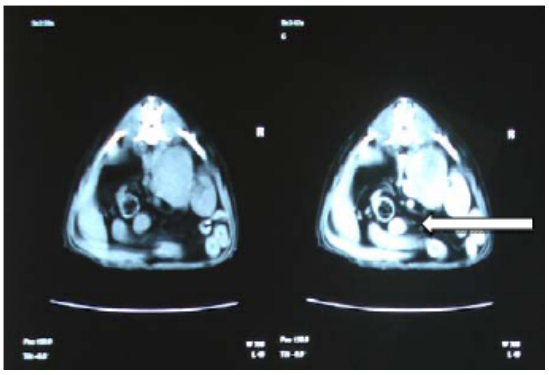

Fig. 1: A circular mass was detected on CT scan, located between the caudate lobe of the liver and the right adrenal gland (white arrow). Distortion of vena cava caused by tumor compression can be observed. Image obtained by CT, without and with iodinated endovenous contrast, respectively.

sulated and firm. Curiously, no vascular invasion or thrombosis was detected in the caudal vena cava and surrounding blood vessels. Right adrenalectomy was done and the mass was sent for histopathology evaluation.

RESULTS

Microscopic analysis revealed the suprarenal invaded by neoplastic tissues composed of polyhedral eosinophilic cells with multiple hyperchromatic nuclei, low mitotic index, and granular cytoplasm separated by a fine fibrovascular stroma (Fig. 2 and 3). The definitive diagnosis of pheochromocytoma was established. Postoperative complications such as hypertension, cardiac arrhythmia, respiratory distress and hemorrhages were presented, causing death after 96 hours. At the necropsy, hemothorax, hemoperitoneum, lung congestion and an extensive subcutaneous hemorrhage were found. Kidneys presented a diffuse tubular necrosis, as well as glomerular and interstitial fibrosis. A massive necrosis with mild signs of calcification was found in the liver and also a pyogranulomatous inflammation in the peripancreatic adipose tissue. Right cervical lymph node was invaded by neoplastic tissue with the same characteristics as the one found in the adrenal gland (Fig. 4).

DISCUSSION

Due to the vague and episodic nature of clinical signs as well as the lack of a sensitive and specific screening test, *antemortem* diagnosis of pheochromocytoma is generally uncommon. In this case, no blood pressure measurements abnormalities were found, which is explained by an episodic and random catecholamine secretion. Clinical signs are usually paroxysmal and not evident during dog examination (Herrera *et al.,* 2008). Adrenalectomy is the treatment of choice for pheochromocytoma. However, this type of procedure has a high mortality rate (20-25%), even when performed by experienced surgeons (Herrera *et al.,* 2008). Whenever a diagnosis of pheochromocytoma is done, treatment with phenoxybenzamine should be prior to adrenalectomy since it blocks the α-adrenergic response to circulating epinephrine and norepinephine, decreasing dog mortality

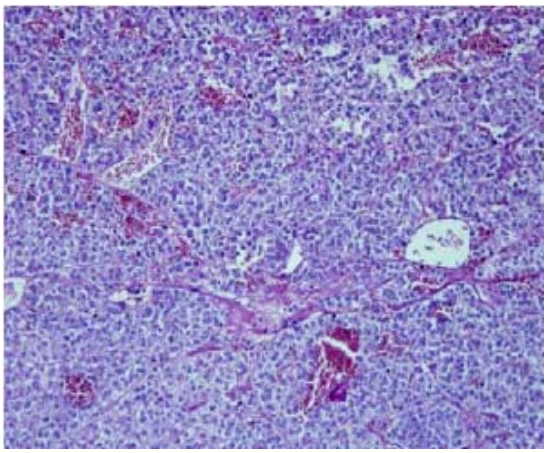

Fig. 2: Histopathogical profile of the right adrenal gland invaded by neoplastic tissue. Microscopically, the mass consisted of polyhedral eosinophilic cells, with multiple hyperchromatic nuclei, granular cytoplasm separated by fibrovascular stroma, typical of pheochromocytoma H&E stain (100x).

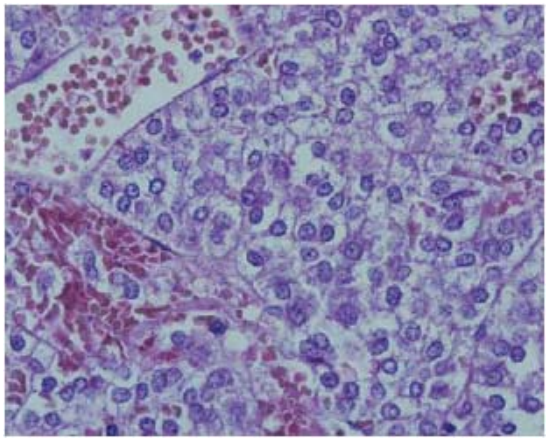

Fig. 3: Histopathogical profile of the right adrenal gland invaded by neoplastic tissue, highlighting cell morphology with ampholytic cytoplasm, hyperchromatic nuclei and prominent nucleoli. Cells are arranged in lobular structures separated by stroma with numerous blood vessels. H&E stain. (400x).

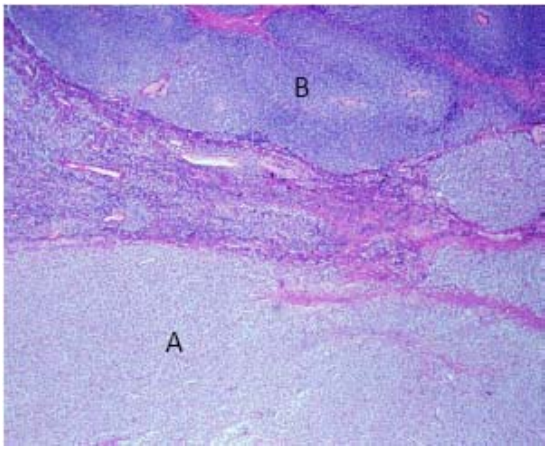

Fig. 4: Histopathogical profile of right cervical lymph node invaded by neoplastic tissue with the same characteristics as the one found in the adrenal gland (A) and conversely healthy lymph node tissue (B). H&E stain (40x).

rates' significantly (Herrera and Nelson, 2010). Nevertheless, life-threatening complications are common, namely metastasis or tumor-induced venous thrombosis. Abdominal ultrasound has been recently documented to be 100% sensitive and 96% specific in identifying the presence of tumor thrombus in the caudal vena cava, being considered a good screening tool for identifying vascular invasion or tumor thrombus in dogs (Davis *et al.,* 2012).

Careful evaluation of these complications is important since 25% of dogs presenting adrenal tumors had vena cava thrombosis (Kyles *et al*., 2003), requiring venotomy to allow thrombus removal (Guillaumot *et al*., 2012). Additionally, it should be taken into account not to invade the adrenal capsule but rather remove the adrenal gland as a single piece in order to avoid neoplastic tissue dissemination.

Since cervical lymph node was already affected and no vascular invasion was detected, lymphatic metastization might have occurred. Considering the fact that approximately 30% to 40% of affected dogs with pheochromocytoma present metastasis at necropsy, these tumors should always be considered malignant in dogs. Usual reported sites of metastasis include liver, lung, regional lymph nodes, bone, spleen and central nervous system (Barthez *et al.*, 1997) and are more frequent in dogs with vein thrombosis and tumors with $\geq$ 5 cm in length (Massari *et al.,* 2011). According to Massari *et al.* (2011) dogs with adrenal gland tumor with major axis length $\geq$ 5 cm, metastasis or vein thrombosis had a poorer prognosis. Despite this fact, a successful *en bloc* excision of neoplastic gland with invasion of caudal vena cava, without nephrectomy, has been recently described in a dog with vein thrombosis, allowing a 49-month survival (Guillaumot *et al*., 2012).

Pheochromocytoma is a rare condition receiving little attention in spite of its malignant character that usually acts as a silent killer. The main aim of this case study is to highlight this uncommon endocrinology disorder, increasing the awareness of the medical community to this difficult diagnostic condition.

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