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ACCELERATED GENERATION OF METASTASES OF A RENAL CELL CARCINOMA IN CANINES. CASE REPORT

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Abstract: Renal cell carcinoma (RCC) is an uncommon neoplasm in canines, representing between 0.3% and 1.5% of all neoplasms. This predominantly malignant carcinoma originates in the renal tubular epithelium and often metastasizes to organs such as the lungs, liver, lymph nodes and adrenal gland. Clinical signs are usually nonspecific, making early diagnosis difficult. A 15-year-old mixed-breed female canine presented at the UST Veterinary Teaching Hospital with hyporexia and low body weight. Physical examination revealed corneal ulcer and umbilical hernia, while tests detected an abdominal mass in the left kidney, confirmed as grade 3 solid--type RCC through histopathology following nephrectomy. The patient initially showed recovery but developed widespread pulmonary metastases seven weeks post-surgery, leading to euthanasia. This case highlights the rapid progression of RCC with accelerated metastases post-nephrectomy. Although metastasis at diagnosis is usually present in less than 50% of cases and surgical intervention is palliative in advanced cases, metastases can arise rapidly, as occurred in this report. It is concluded that the case underscores the aggressiveness of RCC in canines, with metastases potentially developing rapidly after nephrectomy, despite the initial absence of metastases. Continued evaluation and careful postsurgical management are essential to address associated complications.

INTRODUCTION

In general, renal neoplasms in domestic animals are uncommon. In canines, they are estimated to account for between 0.3% and 1.5% of all neoplasms (S. Carvalho et al., 2016; Edmondson et al., 2015). These neoplasms may develop as primary or metastatic, when the primary tumor is located elsewhere. Primary renal neoplasms in dogs are frequently malignant, with origins that can be epithelial (carcinoma) in 60% to 80% of cases, mesenchymal in 25%, and nephroblastoma in 5% (Henry, 2011; Meuten, 2017).

Renal cell carcinoma (RCC) originates from cells of the proximal or distal contouring tubular epithelium or the collecting duct and usually metastasizes to the lungs, liver, lymph nodes and ipsilateral adrenal gland (Edmondson et al., 2015; Meuten, 2017).

RCC has been reported mainly in male dogs and across a wide age range, from 3 to 15 years (Edmondson et al., 2015; Lucke & Kelly, 1976; Meuten, 2017; Woldemeskel, 2013)nuclear size, nuclear pleomorphism, tumor differentiation, invasiveness, Fuhrman nuclear grade, and clear cell morphology were significantly associated with survival times (overall and tumor specific. Dogs with RCC often present with nonspecific clinical signs such as hematuria, lethargy, cachexia, among others, which are not necessarily caused by a renal tumor. Consequently, approximately 11% of renal tumors are diagnosed incidentally, although there are also cases where they have been detected due to abdominal masses or even pulmonary metastases (Edmondson et al., 2015; Meuten, 2017).

Ultrasonography and radiography have frequently been used as standard diagnostic techniques in veterinary clinics during the general care of patients with various disorders (Holzmann et al., 2023). However, for renal neoplasms various diagnostic techniques may be necessary, such as macroscopic patterns, histology, or immunohistochemical markers to confirm both the tissue origin and urothelial proteins, and even sentinel lymph node analysis (Meuten, 2017; Vail et al., 2020).

CASE DESCRIPTION

A 15-year-old spayed female mixed-breed canine patient was presented at the Veterinary Teaching Hospital of Santo Tomás University in Talca due to low body weight and hyporexia. During the general physical examination, a superficial corneal ulcer with abundant unilateral purulent ocular discharge in the left eye and the presence of an umbilical hernia were evidenced. Blood and biochemical analysis revealed a slight alteration of GGT levels. An abdominal ultrasound was performed, revealing a mass in the left flank, the presence of biliary sludge in the gallbladder, and unstructured urinary sediment. A sample of the ocular discharge was taken for culture and antibiotic sensitivity testing.

A therapeutic plan was established for the patient, consisting of ophthalmic ciprofoxacin for 15 days and ursodeoxycholic acid for 30 days. Concurrently, coagulation tests, two thoracic radiographs, and an abdominal ultrasound were conducted. The results showed no alterations in prothrombin time or activated partial thromboplastin time (APTT), nor were any radiographic findings consistent with metastasis detected (Fig. 1A). The ultrasound detected an undifferentiated mass in the left mesogastric region (Fig. 2). Finally, an exploratory laparotomy was performed after two weeks.

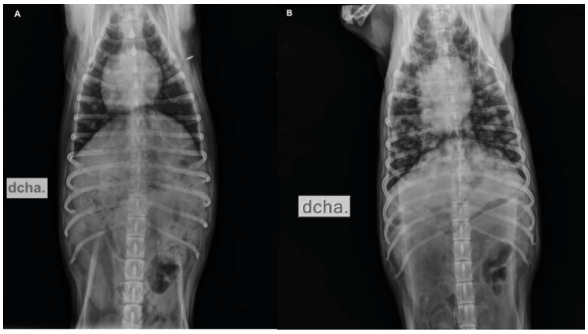

Fig. 1: Thoracic radiograph of a spayed female mixed-breed dog, ventrodorsal view: (A) Initial radiograph showing no signs suggestive of thoracic metastasis. (B) Radiograph taken seven weeks after initial diagnosis, revealing a generalized nodular pattern consistent with metastasis.

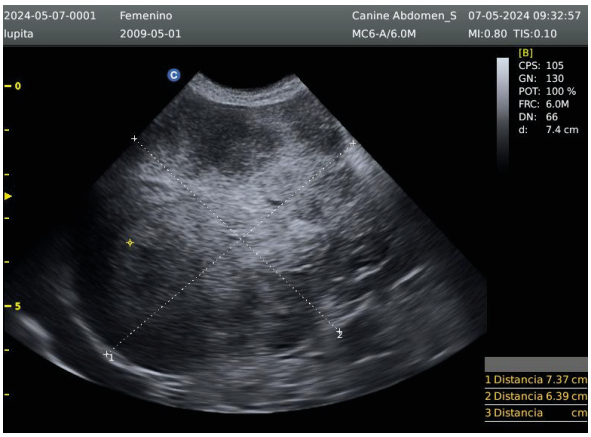

Fig. 2: Abdominal ultrasound detecting a mass in the left mesogastric region.

During surgery, it was evident that the abdominal mass was located in the left kidney, leading to a unilateral nephrectomy and subsequent submission of the mass for histopathological analysis (Fig. 3). During the patient's in-hospital follow-up, slight postoperative hematuria was detected, and a complete blood count was performed, which showed no significant alterations. The patient recovered satisfactorily. The oral postoperative therapeutic regimen included pregabalin at 6mg/kg/BID for 14 days, metamizole at 25mg/kg/BID for 5 days, tramadol at 3mg/kg/BID for 5 days, and amoxicillin/clavulanic acid at 20mg/kg/BID for 14 days. Additionally, subcutaneous administration of sodium chloride with meloxicam at 0.1mg/kg/EOD was provided for 7 days.

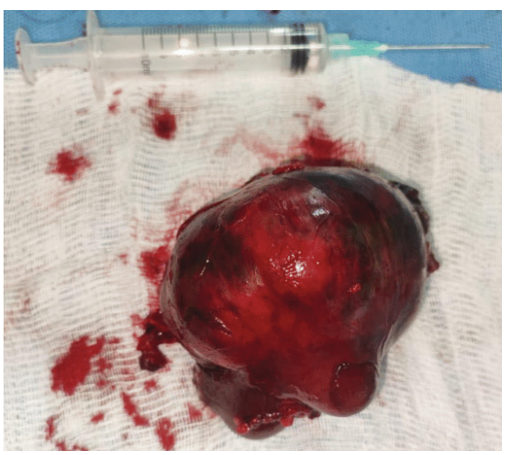

Fig. 3: Neoplasia and kidney extracted during the left unilateral nephrectomy.

Histopathologic analysis of the obtained mass revealed a cellular proliferation with an epithelioid appearance, forming a solid cellular mass without tubular, papillary, or trabecular structures. This epithelial proliferation is composed of tall cubic epithelioid cells with eosinophilic granular cytoplasm and a rounded basal or central nucleus that is highly pleomorphic (Fig. 4), which is suggestive of *grade 3 solid-type* renal cell carcinoma.

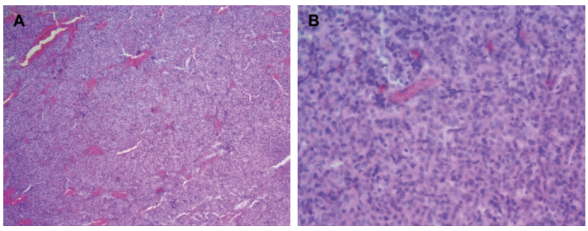

Fig. 4: Microscopic images of a histopathological section of the neoplasm with H&E staining, showing tall cubic epithelioid cells with eosinophilic granular cytoplasm and a rounded basal or central, highly pleomorphic nucleus: (A) General appearance of the lesion at 4x magnification. (B) Cellular detail of the same histopathological section at 40x magnification.

Two weeks after the surgery, consent for referral to oncology was not obtained, and a renal function check was performed, revealing a slight increase in urea and BUN in the biochemical profile. Two weeks later, the thorax was re-evaluated with two radiographic views, showing no evidence of nodular patterns.

Seven weeks post-surgery, the patient began exhibiting hyporexia, decay, apathy and episodes of orthopnea. Blood analysis, urianalysis, and thoracic radiographs were performed. The complete blood count was consistent with an inflammatory process (alterations in hematocrit, erythrocyte count, hemoglobin, segmented neutrophils and lymphocytes). The general biochemical profile and urinalysis suggested compromised renal filtration or even renal failure (alterations in calcium, urea, BUN, creatinine, gama GT, AST, and elevated proteinuria indicated by an increased urine protein/creatinine ratio). The radiographs detected a generalized nodular pattern consistent with metastasis (Fig. 1B). Finally, euthanasia was performed in accordance with established guidelines and protocols.

DISCUSSION

While renal neoplasms in domestic animals are infrequent (S. Carvalho et al., 2016; Edmondson et al., 2015), those that occur in dogs are usually malignant (Henry, 2011; Meuten, 2017) and more common in males aged between 3 and 15 years (Lucke & Kelly, 1976; Woldemeskel, 2013). However, the present case was reported in a female canine within the age range described in the literature. It has been described that breed may influence the development of certain cancers due to genetic selection (Cullen & Breen, 2017); nonetheless, some authors state that there is no breed predisposition for the development of RCC (Woldemeskel, 2013), with the exception of the German Shepherd breed (Lingaas et al., 2003)multifocal tumors in the kidneys, uterine leiomyomas and nodules in the skin consisting of dense collagen fibers. We previously mapped RCND to canine chromosome 5 (CFA5. However, in this report, the patient was a mixed-breed dog and did not come from a group subjected to genetic selection.

The present case was brought to consultation due to weight and feeding deficiencies, signs that have been described in 31% of RCC cases, along with hematuria, lethargy, vomiting, or abdominal pain (S. Carvalho et al., 2016). Due to the nonspecific natural of the clinical signs, the patient was diagnosed incidentally when a mass was detected in the abdominal cavity during a radiograph, which is consistent with how this type of neoplasm has been diagnosed in some previous reports (S. Carvalho et al., 2016; Edmondson et al., 2015; Karikalan et al., 2018; Meuten, 2017).

In cases of unilateral RCC, nephrectomy of the affected kidney is indicated as part of the treatment and is even performed as palliative treatment if the patient presents with metastases (Krabbe et al., 2014; Pontes et al., 2022; Vail et al., 2020). Despite the high association between this type of surgery and intra- and postoperative complications such as acute kidney injury (AKI) and chronic kidney disease (CKD), the latter occurs in one-third of nephrectomized patients and, when complicated, leads to euthanasia in one-third of these patients (Johnson et al., 2024). In the present case, the patient showed no evidence of metastasis at the time of surgery, although nearly two months later, nodulations suggestive of metastasis and compromised renal filtration and renal failure were observed.

Histopathological analysis of the extracted mass revealed tall cubic epithelioid cells arranged in a solid mass with granular cytoplasm and a rounded basal or central nucleus, consistent with descriptions in previous publications on the structure of solid-type RCC. However, it has been published that this carcinoma can also present with tubular and papillary structures in addition to the solid form. Histopathological classification is useful not only to guide treatment but also to provide information about prognosis and factors predicting clinical outcomes. Solid-type RCC has been identified as one of the most predominant forms, alternating predominance with papillary-type RCC. Moreover, 78% of pre-nephrectomy RCC cytologies performed using fine needle aspiration presented "malignant epithelial tissue" (S. Carvalho et al., 2016; Edmondson et al., 2015; Friedrichs & Young, 2020; Usta et al., 2024; Vail et al., 2020).

Several factors influence the survival of a patient with neoplasms. While there are patients with untreated neoplasms who have greater survival than those who undergo surgery, there are also cases where surgical intervention can enhance patient survival (Vail et al., 2020). For example, Carvalho et al. estimated a median survival of 532 days for nephrectomized patients due to RCC. However, 22% of these patients have a median survival of nearly two years, 76% died in just under a year due to progressive deterioration related to RCC, and approximately 2% had a survival of 2.5 years, eventually dying from unknown or unrelated causes (S. Carvalho et al., 2016).

Metastases is another factor influencing the survival of patients with RCC. Patients without metastases at the time of diagnosis have a survival of 533 days, whereas those with metastases have a survival of less than one-third of that (141 days) (S. Carvalho et al., 2016). However, the present case involved a female dog without metastasis at the time of diagnosis, who developed generalized thoracic nodulations consistent with metastasis within a 7-week period. This is similar to metastases in the lungs, regional lymph nodes, serosal surfaces, etc., described by other authors, which are present in less than half of RCC cases at diagnosis but in nearly 70% of cases at the time of death (P. H. Carvalho et al., 2011; S. Carvalho et al., 2016; Usta et al., 2024). Given the published information on the survival of nephrectomized patients with RCC, the rapid development of metastases in this patient, leading to various renal and respiratory complications and resulting in euthanasia, is noteworthy, with a survival of approximately 49 days.

In conclusion, although nephrectomy is considered a palliative treatment even in patients with metastases (S. Carvalho et al., 2016) , the progression of the metastatic process can be sudden, even in patients without metastases prior to surgery who recover satisfactorily from it. Metastases, as observed in the presented patient, can invade the lungs within 2 months post-surgery and induce hyporexia, inspiratory dyspnea, cyanosis, among other complications.

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