



CASE REPORT

Metastatic Kidney Carcinoma Causing Paralysis of Pelvic Limbs in a Dog

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ARTICLE HISTORY (15-238)

Received: May 13, 2015
Revised: July 30, 2015
Accepted: August 09, 2015
Online available: November 29, 2015

Key words:

Canine
Metastasis
Pan-cytokeratin
Renal neoplasm
Spinal cord

ABSTRACT

A 12-year-old male Maltese dog was presented with a history of shivering episodes. Radiographs revealed a mass in the left kidney that was histopathologically classified as a renal cell carcinoma. After nephrectomy, pelvic limbs became paralyzed. Spinal cord and lung metastases were detected via histopathological examination and confirmed by immunohistochemistry. Both pan-cytokeratin and Ki67 assays tested positive in the kidney, lung, and spinal cord. Interestingly, COX-2 had mild immunoreactivity in the kidney, but its labeling was intense in the spinal cord and lung. Though seemingly rare, the spinal cord may possibly be a focus point for metastasis of renal cell carcinomas. Because symptoms can easily be misunderstood, late diagnoses would not be uncommon and may hinder clinical management of the disease.

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To Cite This Article: Calazans SG, Alves CEF, Zanetti NM, Conforti VA, Santilli J, Anjos DS and Magalhães GM, 2016. Metastatic kidney carcinoma causing paralysis of pelvic limbs in a dog. *Pak Vet J*, 36(1): 124-126.

INTRODUCTION

Primary renal neoplasia are rare in dogs, with renal cell carcinomas (RCC) being the most common histological type in the canine species (Woldemeskel, 2013). The majority of patients with RCC are males with an average age of eight years (Bryan *et al.*, 2006; Edmondson *et al.*, 2015).

Dogs with renal tumors commonly present nonspecific clinical signs such as anorexia, lethargy, and weight loss. A palpable abdominal mass may be detected in some cases. Surgical resection is the treatment of choice. Nephrectomy may allow for a cure and has the potential to improve survivability. Additionally, chemotherapy may be offered but the benefits of this treatment remain unknown (Bryan *et al.*, 2006).

The lungs are the most common site of metastasis in primary renal carcinomas in the canine species (Edmondson *et al.*, 2015). In a previous study, pulmonary metastasis of malignant renal tumors was detected by radiographs in 16% of the dogs at diagnosis, whereas metastatic disease was detected in 77% of dogs upon necropsy (Bryan *et al.*, 2006). The aim of this case report was to describe the progression of a metastatic renal cell carcinoma to the spinal cord and lungs in a canine patient.

History and clinical evaluation: A 12-year-old neutered male Maltese dog was presented with a history of shivering episodes after walking up and down stairs. The animal had been previously treated for allergies with corticosteroids and antibiotics. Physical examination revealed distention in the left side of the abdomen, while no abnormalities were detected upon neurological examination. Abdominal radiographic and ultrasonographic images revealed a 4.5 cm X 3.8 cm mass in the left kidney (Fig. 1). Three-view thoracic radiographs showed no signs of lung metastasis. Pre-operative and other laboratory tests were performed. The patient had macrocytic hypochromic anemia, neutrophilic leukocytosis (white blood cells=39.000/μL), high levels of serum alanine aminotransferase (175 U/L), and bacterial cystitis. The animal was treated with dipyrone (25 mg/kg, t.i.d, PO), silymarin (10 mg/kg, t.i.d, PO), and enrofloxacin (5 mg/kg, b.i.d, PO) before surgery.

Celiotomy was performed one week after the beginning of treatment. Upon surgery, the left kidney was easily assessed because the mass involved the entire organ. The mass was firm, brownish/reddish in color, and intensely vascularized. Unilateral nephrectomy was performed and samples were collected for histopathological examination, which classified the tumor

as a renal cell carcinoma. Neoplastic cells had tubular and papillary patterns. There were numerous mitotic figures and areas of necrosis.

The postoperative period was uneventful until fourteen days after surgery when the patient began experiencing ataxia and a proprioceptive deficit in the left hind limb. Within five days of the onset of symptoms, the pelvic limbs were paralyzed. Myelographic examination was attempted, but the contrast did not progress through the spinal canal. Due to the poor health condition of the patient, veterinarians and owners agreed to euthanize the dog.

Necropsy and histopathologic findings: Upon necropsy, no abnormalities were observed in the spinal cord but, unexpectedly, a 9-mm lung tumor was found, contrary to conclusions drawn based on previous thoracic radiographs. The spinal cord appeared normal upon macroscopic examination; however, histopathological evaluation revealed presence of neoplastic cells (Fig. 2). Additionally, immunohistochemical assays were performed to detect the expression of pan-cytokeratin, Ki67, and cyclooxygenase-2 (COX-2). Both pan-cytokeratin and Ki67 assays tested positive in the kidney, lung, and spinal cord. Interestingly, COX-2 had mild immunoreactivity in the kidney, but its labeling was intense in the spinal cord and lung (Fig. 3).

DISCUSSION

To our knowledge, this is the first report of a Maltese breed dog affected by RCC (Khan *et al.*, 2001; Bryan *et al.*, 2006; Gil da Costa *et al.*, 2011). However, it is generally accepted that middle-aged or older male dogs, like the patient described in this report, are at an increased risk for this disease (Edmondson *et al.*, 2015).

Nonspecific clinical signs, such as lethargy, cachexia, vomiting, abdominal or back pain, diarrhea, urinary tract infection, hematuria, polyuria, polydipsia, and hemoabdomen, have been reported (Bryan *et al.*, 2006). In the present case, besides the shivering episodes, the patient had a palpable abdominal mass. Other studies have detected abdominal masses in 14% or 20% of dogs with renal tumors. Three-view radiographs and ultrasonography were performed as recommended for clinical staging (Edmondson *et al.*, 2015). Abdominal radiographs and ultrasonography were able to locate the primary tumor and to estimate its dimensions. No evidence of pulmonary metastasis was observed in thoracic radiographs, even though this exam can detect 7-9-mm nodules (Nemanic *et al.*, 2006). However, computerized tomography is more recommended to detect small, single pulmonary nodules in dogs (Armbrust *et al.*, 2012).

Neutrophilia was the most common hematological finding in dogs with renal tumors in a previous study (Bryan *et al.*, 2006), whose authors suggested that high neutrophil counts could indicate a paraneoplastic syndrome. It is possible that neutrophilic leukocytosis could be induced by colony-stimulating factors produced by the renal tubular carcinoma (Peeters *et al.*, 2001). Indeed, after nephrectomy, neutrophil numbers returned to normal values. In this report, renal carcinoma presented tubular and papillary patterns. These patterns were observed concurrently in three of 13 cases of canine renal cell carcinoma in a previous study (Gil da Costa *et al.*, 2011).



Fig. 1: Lateral decubitus radiograph showing a mass in the left kidney of a 12-year-old male Maltese dog (arrows).

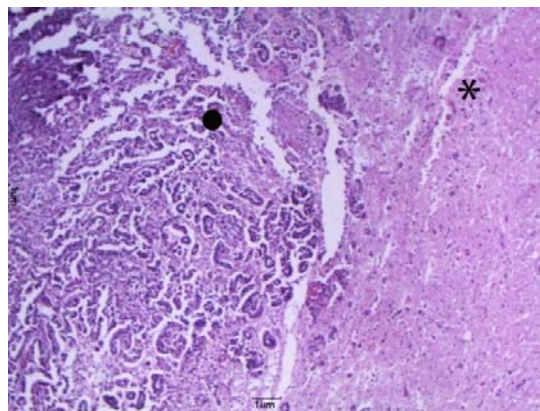


Fig. 2: Photomicrograph of the metastatic carcinoma, characterized by the presence of neoplastic epithelial cells arranged in tubular formation (*) invading the spinal cord, where glial cells in the neuropil are seen (**). (HE, 40x).

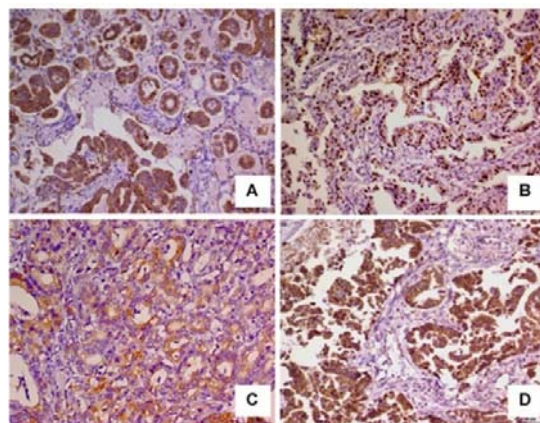


Fig. 3: Photomicrographs of the tumor in different organs of the patient (immunohistochemistry, DAB, counterstaining with Mayer's hematoxylin, 40x). Lung; membranous immunohistochemical reaction to pancytokeratin (AE1/AE3, Santa Cruz) in metastatic tumor (A). Spinal cord; nuclear positivity to Ki67 (MIB-1, Dako) (B). Kidney; mild cytoplasmic COX-2 immunoreactivity (C). Spinal cord; intense cytoplasmic COX-2 immunoreactivity (D).

In the present case, necropsy was essential to confirm metastasis. In a previous study, 69% (21/30) of canine renal carcinomas were metastatic at the time of death (Bryan *et al.*, 2006). Pulmonary metastasis has been commonly reported in canine RCCs (Edmondson *et al.*, 2015). Other authors also have mentioned abdominal organs and bone as possible sites (Bryan *et al.*, 2006).

However, spinal cord metastasis has not been reported in the literature. In the case described herein, spinal cord metastasis rapidly developed post-surgery. The shivering episodes could, potentially, be due to initial metastatic focus in the spinal cord that was being suppressed by corticosteroid treatment. The authors speculate that resection of the primary tumor could have triggered metastasis by mechanisms yet to be understood. Similarly to what has been proposed in cases of breast cancer in women, it is possible that primary tumors could secrete substances that inhibit metastatic progression (Demicheli *et al.*, 2008).

In this report, the diagnosis was confirmed by immunohistochemistry. Cytokeratin staining confirmed the presence of epithelial tumor in the kidney, lung, and spinal cord. According to the literature, papillary and tubulopapillary carcinomas appear to express cytokeratin more often than solid carcinomas (Gil da Costa *et al.*, 2011). Positive staining of ki67 indicated cellular proliferation in the three organs. The presence of metastasis in the spinal cord caused paralysis of the pelvic limbs. To our knowledge, there have been no reports on ki67 being detected in canine renal cell carcinomas. The expression of COX-2 was previously investigated in three other cases of canine RCC that demonstrated moderate to marked immunoreactivity in two dogs (Khan *et al.*, 2001). In the present case, there was intense COX-2 immunoreactivity in the spinal cord, although, in the kidney, this labeling was of mild intensity. Similarly, other authors found stronger COX-2 intensity in metastatic lesions of primary mammary tumors in dogs and suggested that COX-2 metabolites are important promoters of angiogenesis and invasiveness and therefore contribute to metastatic spread (Pereira *et al.*, 2009). In the case described herein, one could speculate that the patient might have benefited from a nonsteroidal anti-inflammatory treatment; however, the diagnosis of metastatic disease was concluded only upon necropsy.

Conclusions: Though seemingly rare, the spinal cord may possibly be a focus point for metastasis of renal cell carcinomas, in addition to the lungs. Because symptoms

can easily be misunderstood, late diagnoses would not be uncommon and may hinder clinical management of the disease. Moreover, three-view thoracic radiographs may not allow for the detection of lung metastatic nodules of up to 9-mm. Immunohistochemistry may be a helpful tool in obtaining a diagnosis.

Author's contribution: SGC, NMZ, JS, DSA, VAC designed and conducted the case report. CEFA and GMM performed the necropsy, and the histopathological and immune histochemical analyses. All authors interpreted the data, critically revised the manuscript for important contents and approved the final version.

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