Primary renal hemangiosarcoma with brain and lung metastasis in a dog

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Abstract
Hemangiosarcoma (HSA) is a malignant tumor derived from the endothelium of vessels, and primary renal HSA is a rare variant of the disease. This study aimed to report a case of unilateral primary renal HSA with pulmonary and brain metastasis in a dog. A 10-year-old mixed-breed male dog was treated at the Hospital Professor Ricardo Alexandre Hippler from Universidade Vila Velha (HV-UVV) with signs of hematuria. A mass in the left kidney was detected by ultrasound, and no metastasis was detected on chest radiography. Unilateral nephrectomy was performed, and the material underwent histopathological examination, which was concluded as HSA. The animal died 48 days after surgery, and a necropsy was performed, showing marked hemothorax and multifocal metastasis of HSA in the lung and brain. The absence of nodules at other sites before surgery indicates a primary renal origin. The late diagnosis of the disease may have contributed to the spread of metastasis and, consequently, the development of hemothorax. Histopathological and necroscopic examinations were essential to confirm the diagnosis.

Keywords: neoplasm, hemothorax, sarcoma, vascular tumor, coagulation.

Introduction
Hemangiosarcoma (HSA) is a malignant tumor derived from the endothelium of the vessels, and it may originate from any vascular site in the body (14). The most frequent primary sites are the spleen, skin and subcutaneous tissue, right atrium, and liver (25), and the mean age of occurrence ranges from 8 to 13 years old (4, 10). Visceral forms are highly metastatic and spread rapidly (9, 25). When metastasis is widespread, the primary site is challenging to determine, and multicentric origin is possible (8, 25).

Primary renal HSA is a rare variant of the disease (13, 17). Animals with renal HSA show nonspecific clinical signs such as anorexia, weight loss, sublumbar pain, and hematuria, and signs of renal failure occur if there is bilateral renal involvement (18, 26). The diagnosis of renal neoplasms can be directed by radiological and ultrasound examinations and is confirmed through histopathological examination (2). Nephrectomy is indicated for unilateral malignant renal tumors without the presence of metastasis (15). Some studies speculate that primary renal HSA may be associated with a better prognosis than other visceral forms of the disease (14, 15).

The lungs are commonly affected by metastasis of HSA (19, 25). Brain metastasis is infrequent in dogs (21, 25). However, HSA is considered the tumor that most commonly causes brain metastasis in this species (21, 25). The present study aimed to report a case of primary renal HSA with pulmonary and brain metastasis in a dog since it is an uncommon form of presentation of HSA in dogs.

Case description
A 10-year-old male mixed breed dog was attended at the Hospital Professor Ricardo Alexandre Hippler from
Universidade Vila Velha (HV-UVV), presenting hematuria, confirmed by urinalysis. Abdominal ultrasound revealed a mass measuring approximately 10 x 7.5 centimeters involving the left kidney. Two and a half months after the first consultation, the patient presented pale mucous membranes and dyspnea. A new abdominal ultrasound examination showed growth of the renal mass to approximately 15.65 x 8.95 centimeters (Fig. 1A). Chest radiography showed no findings of lung metastasis (Figs. 1B and 1C). A left kidney nephrectomy was performed, and the material was sent to the Laboratório de Patologia Animal of the HV-UVV. A chemotherapy protocol was not performed because the animal presented substantial cardiac alterations on echocardiographic examination, and the medication of choice (doxorubicin) is known for its cardiotoxic effects.

Grossly, the mass measured 13.0 x 10.0 x 8.0 centimeters, involved the left kidney and showed a reddish color and a multilobulated external surface (Fig. 2A). The cut surface had a friable consistency, and bloody fluid flowed. Histology revealed a neoformation originating from the renal capsule, with lobules divided by septa of abundant connective tissue (Fig. 2B). It was organized in vascular spaces and a solid pattern, with extensive areas of hemorrhage (Fig. 2C). The cells were fusiform, with a high nucleus:cytoplasm ratio, oval nuclei, finely stippled chromatin, and single to double evident nucleoli, and moderate to severe anisokaryosis and moderate nuclear pleomorphism were observed. One mitosis figure was found in 2.37mm² (FN18). The adjacent renal parenchyma was compressed by the neoformation, which presented hemorrhage between the renal tubules and multifocal degeneration of tubular cells.

The animal returned for consultation a month and a half after the surgery, showing weight loss, prostration, pallor of the mucous membranes, and dehydration. The animal died the following day, resulting in a survival time of 48 days after surgery, and the body was submitted for necropsy.

Necropsy revealed hemothorax (2.5 liters) and disseminated lung nodulation, protruding to the pleural surface, measuring 2 to 5 centimeters, dark red, with an irregular and frequently ruptured surface (Fig. 2D). Histology revealed multifocal nodules of HSA. The brain’s frontal lobe showed at section two black millimetric areas, and histologic examination revealed two focal nodules of HSA (Figs. 2E and 2F).

Discussion

The primary renal origin of HSA is suggested when there is no other site of the same neoplasm in the body (12, 21). In the present case, in the clinical staging before the surgery, no other nodules were found beside the kidneys, and the animal had no history of previous neoplasms (25). These findings are indicative of an HSA of primary renal origin. The pulmonary metastasis probably appeared after the surgical procedure was performed. However, thoracic radiography may not be sensitive enough to detect micrometastasis (5).

There are reports of primary renal HSA metastasis in dogs in sites such as lungs, heart, liver, spleen, skin, and intestinal serosa. However, it is difficult to confirm that the primary lesion is renal in some cases (12, 27). Some studies have shown that renal HSA does not metastasize as often as other visceral HSA (splanic, cardiac, and retroperitoneal forms), it is related to longer survival times, and it is less associated with hemoperitoneum, but this may be associated with an early diagnosis of the disease in these studies (14, 23, 24). The present case was not diagnosed early, and the surgical intervention was performed late, which may have led to a worse prognosis than that reported in the literature.

Dogs with lung metastasis are eight times more likely to have brain metastasis (27). According to one study, approximately 90% of dogs with HSA and brain metastasis also have lung metastasis, as observed in this case (28). Brain metastasis from HSA is usually of millimetric proportions (10), as reported in this case. Nevertheless, they also can be bigger and more disseminated (7).

A similar case of HSA with metastasis in the central nervous system in a dog was reported, with concomitant
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Braz J Vet Pathol, 2023, 16(3), 172-175
DOI: https://10.24070/bjvp.1983-0246.v16i3p172-175

lung, spleen, and ribs metastasis, which also did not appear in image exams before surgery (7). However, in this earlier case, the primary site was the skin, and the animal presented many neurological signs since the lesions were more extensive and more disseminated than those of the present report, with lesions in the brain and the spinal cord (7). Even though the lesions were more disseminated in the previous case, the animal had a 9-month survival time after surgery compared to the animal in the present report, which had only 48 days of survival time. A feasible explanation is the development of hemothorax in the present case, compared to the lack of this finding in the previous case.

The severe hemothorax resulted from the rupture of the pulmonary nodules. It may have been potentiated by coagulation disorders caused by canine HSA, such as disseminated intravascular coagulation (DIC) and microangiopathic hemolysis (9). One study revealed that canine HSA cells expressed significant amounts of procoagulant tissue factor in vitro, which may contribute to DIC (29). The hemothorax led to compressive atelectasis of the lung parenchyma, leading to respiratory failure and death of the animal. Another possible mechanism that may have contributed to the death was hypovolemic shock due to massive blood loss into the chest cavity.

A study of 14 dogs with renal HSA found a mean survival time of 278 days. However, in dogs with associated hemoperitoneum, a survival time of only 62 days was observed (14). Therefore, although studies indicate a longer survival time in cases of renal HSA compared to other visceral types of HSA, it is likely that the late diagnosis and the late surgical intervention, the presence of lung metastasis, and severe hemothorax may have led to a lower survival time in this case.

In conclusion, the primary renal origin of HSA, in this case, was suggested by the lack of detection of other sites affected before the surgical procedure by radiographic and ultrasonographic procedures. Histopathological and necroscopic examinations were essential for confirming the diagnosis of renal HSA and detecting foci of pulmonary and brain metastasis. The delayed diagnosis, the late surgical intervention, and the spread of lung metastasis probably led to a worse prognosis than those reported in the literature for primary renal HSA in dogs.

Conflict of Interest

The authors declare no competing interests.
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