



## Case Report

# Spinal Nephroblastoma in a Dog

Sevil Atalay Vural<sup>1\*</sup>, Tuncer Kutlu<sup>1</sup>, Omer Besalti<sup>2</sup> and Pinar Can<sup>2</sup>

<sup>1</sup>Ankara University, Faculty of Veterinary Medicine, Department of Pathology, 06110, Diskapi-Ankara, Turkey

<sup>2</sup>Ankara University, Faculty of Veterinary Medicine, Department of Surgery, 06110, Diskapi-Ankara, Turkey

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The objective of this study is to report Magnetic Resonance Imaging (MRI), histological and immunohistochemical findings of spinal nephroblastoma in a 2-year-old mixed breed dog. There was a mass located at the level of thoracal 12–13 and it was hypo intense in T2 w images and iso/hypo intense in T1 w images, and syringohydromyelia was also accompanying in both cranially and caudally. Macroscopically, the mass was 4 mm in diameter, grey color and well demarcated. Histologically, it was composed of cuboidal to ovoid cells with indistinct borders and a scant to midly amphophilic, generally hyperchromatic nuclei. Tumor cells formed tubules, ribbons and glomeruloid structures within fibrovascular background. Immunohistochemically, neoplastic cells especially in tubules and glomeruloid structures stained pan cytokeratin. On the other hand, fibrovascular stroma and capsule were stained  $\alpha$  –smooth muscle actin ( $\alpha$  – SMA) and vimentin sera.

**Keywords:** Dog, nephroblastoma, spinal cord

## CLINICAL FEATURES

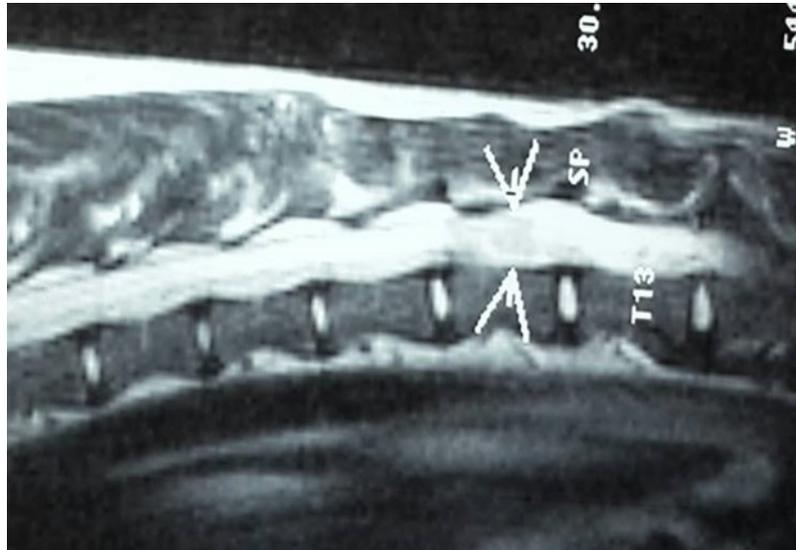
A Mixed breed, two years old male intact dog was subjected. The dog had history of progressive hindlimb ataxia for 6 months and was unable to use hindlimbs since one month. Neurological examination revealed intact flexor, perineal and patellar reflex, and absence of deep pain sensation. Neuroanatomic lesion localization was thoracal (T) 3-lumbal (L) 3 (Figures 1-2). Survey spinal radiography was unremarkable.

The images of the case were obtained with a Magnetic Resonance Imaging (MRI) unit (Siemens superconducting magnet, field: 15 - 20 ms) and T2 weighted images (TR: 2000-4000 ms, TE: 90-110 ms) were adjusted as 2 mm slice thickness. There was an

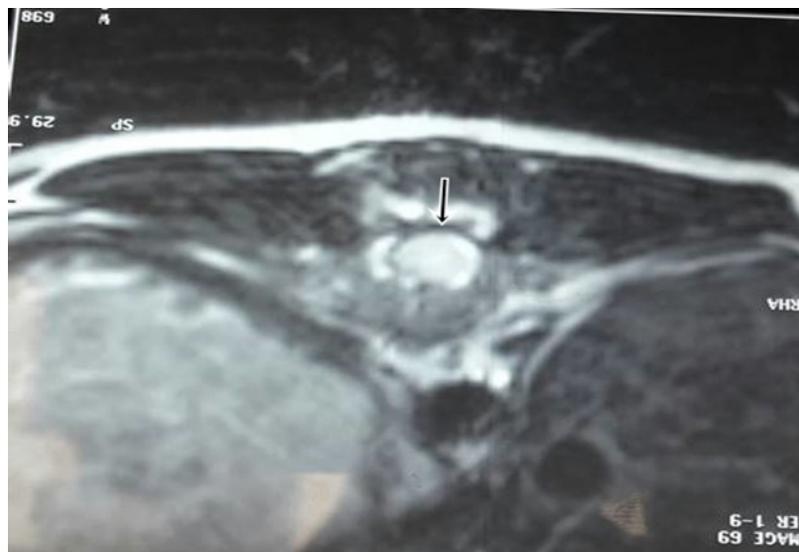
unshaped mass located at the level of T12 –T13, and it was hypo intense in T2 weighted images and iso/hypo intense in T1 weighted images at MRI. Syringohydromyelia was also accompanying the tumor in both cranially and caudally. After tentative diagnosis of spinal tumor the owners asked for euthanasia of the dog and allowed to take samples from related spinal cord. Macroscopically, it was swollen and firm in the transversal section; there was a mass in 4 mm diameter, grey color, well cleavaged.

The mass was fixed in 10% formalin, processed routinely and embedded in paraffin. Paraffin blocks were sectioned at 5  $\mu$ m and stained with Haematoxylin/Eosin (H/E) staining method. Immunohistochemical staining was performed with the Avidin-Biotin Complex Peroxidase (ABC-P; Nova Castro) method using pan cytokeratin (AE1/AE3-L-CE antibody; clone: AE1/AE3, New Castle, UK, 1:100),  $\alpha$  –smooth muscle actin ( $\alpha$  –

\*Corresponding Author E-mail: [sevilvural@yahoo.com](mailto:sevilvural@yahoo.com);  
Phone: +90 312 3170315 - 4276; Fax: +90 312 3164472



**Figure 1.** Hypointense T2 weighted images in sagittal section. (White arrow head: the mass, arrow: syringohydromyelia)

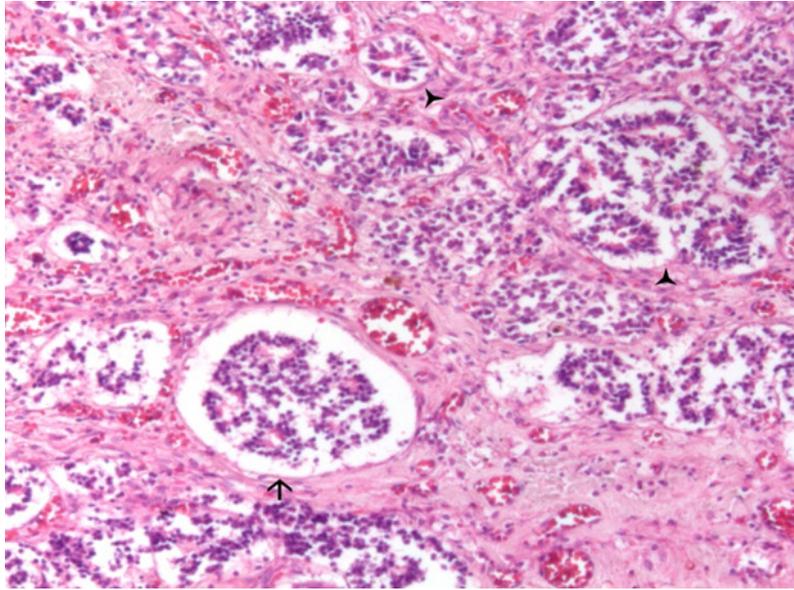


**Figure 2.** Hypointense T2 weighted images in transversal section. (Arrow: syringohydromyelia)

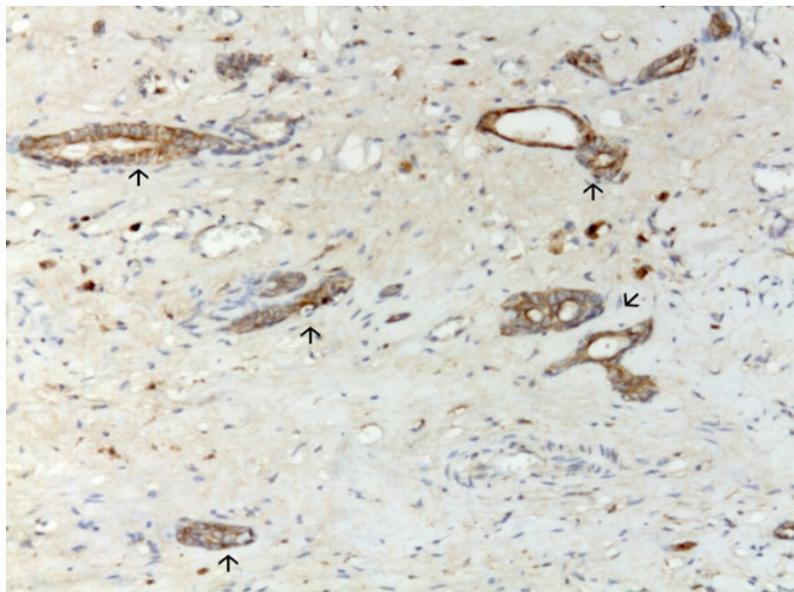
SMA, Sigma, 1:200) and vimentin (Sigma, 1:200) as primary antibodies. As chromogen, 3, 3'-diaminobenzidine (DAB, Nova Castro) was used, and Harris's haematoxylin for counterstaining. Control sections were stained by normal mouse sera.

Microscopically, the tumor had poorly encapsulated intradural and extra-medullary location. It was composed of two distinct cell types, epithelial and blastemal cells. Epithelial cells were composed of uniform cells that were cuboidal to ovoid with indistinct cell borders and a scant to midly amount of amphophilic cytoplasm. Some cells were consisted of vacuoles. The nuclei were generally

hyperchromatic with no nucleoli, mitotic figures were rarely seen. Tumor cells generally formed tubules, ribbons, and glomeruloid structures within fibrovascular background (Figure 3). These epithelial cells were occasionally arranged in tangles of branching and infolded tubules with projecting tufts resembling primordial renal glomeruli with rosettes of cuboidal cells surrounded by a mantle flattened cell. Blastemal cells were fusiform with indistinct cell borders and amphophilic cytoplasm. The aggregates of neoplastic cells were seen on white and grey matter of the spinal cord. Furthermore, the tumor was consisted of widely necrose and



**Figure 3.** Tubules (arrow heads) and glomeruloid structure (arrow), Haematoxylin and Eosin, x100



**Figure 4.** Pan cytokeratin positive on tubules (arrows), ABC-P, x100.

haemorrhage. Mononuclear inflammatory cells were seen in substantia alba and perivascular spaces.

Immunohistochemically, the neoplastic cells especially in tubules (Figure 4) and glomeruloid structures stained pan cytokeratin sera. On the other hand, fibrovascular stroma and capsule were positive stained  $\alpha$  – SMA and vimentin sera. The tumor was diagnosed as spinal cord nephroblastoma originated from ectopic metanephric blastema with typical histological and immunohistochemical staining features.

## DISCUSSION

Primary renal neoplasia is rare in dogs, with a reported incidence of 0.6%. The majority of renal tumors reported in dogs are carcinomas. Nephroblastoma is a rare tumor that tends to be diagnosed in juvenile dogs and it is referred to Wilms' tumor. It is the most uncommon primary malignant renal tumor of children (Montinaro et al., 2013).

Canine spinal nephroblastoma is a rare central nervous

system tumor located intradural extramedullary and showing clinically hindlimb paresis and ataxia. It occurs in young and large breed dogs, between T10 and L2 spinal segments (de Vries-Chalmers et al., 1988; Sale et al. 2004; Terrel et al. 2000; Vaughan-Scott, 1999). Clinical signs associated with spinal cord nephroblastoma are due to the compression caused by the mass (de Vries-Chalmers et al., 1988; Terrel et al., 2000).

Nephroblastomas originate from the metanephric blastema and result from abnormal differentiation of the kidney during embryogenesis. These tumors consist of blastema, epithelial, and mesenchymal components in various stages of differentiation (Terrel et al., 2000). Spinal nephroblastomas are in dogs distinct and independent of renal nephroblastoma. Large breeds such as German Shepherd Dog and Retriever breeds seemed to be predisposed with a high prevalence; the tumor is diagnosed in young dogs, between 3 months and 3 year old (median age, 2 years) with a median survival time of 6 month (Bryan et al., 2006; Montinaro et al., 2013; Nakade et al., 2006; Sale et al., 2004; Terrel et al., 2000; de Vries-Chalmers et al., 1988). In this case of 2 years-old male mixed dog; age and breed predispositions were similar to previous reports. Canine spinal tumor is a rare tumor, with less than almost 50 cases documented in the veterinary literature and previously has not been reported in Turkey. They are classified depending on their origin of tissue, morphologic features, their biological behavior and anatomic location.

Usually nephroblastomas occur as intradural, extramedullary masses, but they can also occur as intramedullary or extradural lesion in dog (Montinaro et al. 2013, Nakade et al. 2006 ) It is especially determined in the region of the spinal cord (T10-L2) adjacent to the kidney (Liebel et al. 2011, Terrel et al. 2000). Terrel et al. (2000) determined the multifocal metastatic type of these tumors at T11-12 and L4-L6. At the same time, metastases involving lungs, liver, intra-abdominal lymph nodes and retroperitoneal space are seen. The mass was located macroscopically between the thoracal (T12-13) spinal cord segments and histopathologically had an intradural extramedullary location. It was composed of embryonic blastemal cells, epithelial cells and mesenchymal cells, and metastasis was not seen. The dogs' signalment, clinical signs, tumor location and histopathology are similar to those previously described but mitosis was not considered to be common in some areas (Sale et al., 2004; Terrel et al., 2000; Vaughan-scott, 1999). Spinal nephroblastoma must be differentiated from some tumors, it has been reported under a variety of names as neuroepitheliomas, poorly differentiated astrocytomas, medullaepitheliomas, hamartomas and ependymomas due to failure to identify the origin of cells (de Vries-Chalmers et al., 1988; Sale et al., 2004; Sfacteria et al., 2010; Terrel et al. 2000; Vaughan-scott, 1999; Vural et al., 2006).

Histopathological pattern and especially immunohistochemical reactivity are quite helpful for differentiation (de Vries-Chalmers et al., 1988; Sfacteria et al., 2010; Terrel et al., 2000; Vural et al., 2006).

The immunohistochemical staining of spinal cord nephroblastoma in dog provides strongest evidence to support the ectopic renal origin of these tumors (Terrel et al., 2000). Nowadays in embryonic renal cells, the Wilm's tumor (WT1) gene protein product and antibody to polysialic acid are positive determined (Sale et al., 2004; Terrel et al., 2000). There are positive immunoreactivity determined by cytokeratin, and vimentin sera (Terrel et al., 2000). The tumor is generally negative for neuroectodermal markers as glial fibrillary acidic protein and neuron-specific enolase. It is thought that the tumors arise from embryonic renal tissue that becomes entrapped in the dura of the spinal canal during fetal development (Sale et al., 2004). In this dog, immunohistochemical staining of the mass revealed strong positive immunoreactivity by cytokeratine in epithelial cells, and vimentin in blastemal and stromal cells. Polysialic acid and WT1 was not performed on the tumor.

## CONCLUSION

This paper describes clinical, MRI, pathomorphological and immunohistochemical findings in a dog with spinal cord nephroblastoma.

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