

## Journal of the Hellenic Veterinary Medical Society

Vol 70, No 3 (2019)



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doi: [10.12681/jhvms.21804](https://doi.org/10.12681/jhvms.21804)

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### To cite this article:

KAMPOURI, P., KARIKI, A., BAKA, R., PATSIKAS, M., & POLIZOPOULOU, Z. (2019). Spinal neuroblastoma in a dog: a case report. *Journal of the Hellenic Veterinary Medical Society*, 70(3), 1737–1742.  
<https://doi.org/10.12681/jhvms.21804>

## **Spinal neuroblastoma in a dog: a case report**

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## **Νεφροβλάστωμα νωτιαίου μυελού σε σκύλο: αναφορά σε ένα κλινικό περιστατικό**

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*Date of initial submission: 06-12-2018*  
*Date of revised submission: 10-02-2019*  
*Date of acceptance: 19-02-2019*

**ABSTRACT.** The case report presents the clinical, clinicopathological, diagnostic imaging and histopathological findings of spinal cord neuroblastoma in a dog. It was admitted with a 2-week history of a “weight-bearing” lameness of the left posterior limb that evolved to paraplegia within hours. Neurological examination showed spastic paraplegia compatible with a T3-L3 spinal cord lesion. Differential diagnosis included ischemic myelopathy, myelitis and acute spinal cord compression. The spinal radiographs and cerebrospinal fluid analysis were unremarkable. Cisternal myelography indicated a focal intradural-extramedullary lesion at the level of T12 vertebra. Further diagnostic investigation was not performed because the owner decided to proceed to euthanasia. Histopathological examination of the spinal cord confirmed the diagnosis of intraspinal neuroblastoma.

**Keywords:** dog, lameness, myelopathy, neoplasm, neuroblastoma.

**ΠΕΡΙΛΗΨΗ.** Στην εργασία αυτή παρουσιάζεται περιστατικό νεφροβλαστώματος του νωτιαίου μυελού σε νεαρό σκύλο, που προσκομίστηκε με αιφνίδια παραπληγία. Συγκεκριμένα, στο ιστορικό αναφέρθηκε αρχικά χωλότητα στο πίσθιο αριστερό άκρο που εμφανίστηκε δεκαπέντε ημέρες πριν την προσκόμιση του ζώου και εξελίχθηκε ραγδαία σε παραπληγία. Στη νευρολογική εξέταση διαπιστώθηκε σπαστική παραπληγία (θωρακοσφυϊκό σύνδρομο, Θ3-Ο3) και η αρχική διαφορική διάγνωση περιλάμβανε την ισχαιμική μυελοπάθεια, τη μυελίτιδα και την οξεία συμπίεση του νωτιαίου μυελού. Στα ακτινογραφήματα της σπονδυλικής στήλης και στην ανάλυση του εγκεφαλονωτιαίου υγρού δεν υπήρξαν παθολογικά ευρήματα. Στη μυελογραφία διαπιστώθηκε εντοπισμένη υποσκληρίδια εξωμυελική χωροκατακτητική βλάβη στο ύψος του Θ12 σπονδύλου. Η διερεύνηση του περιστατικού δεν συνεχίστηκε ύστερα από απόφαση του ιδιοκτήτη να γίνει ευθανασία. Η οριστική διάγνωση τέθηκε με την ιστοπαθολογική εξέταση που έδειξε ότι πρόκειται για υποσκληρίδιο νεφροβλάστωμα.

**Λέξεις ευρετηρίασης:** μυελοπάθεια, νεόπλασμα, νεφροβλάστωμα, νωτιαίος μυελός, σκύλος.

## CASE HISTORY

A 2-year-old, client-owned, male, intact, mixed-breed dog, was presented with a history of acute paraplegia evolving within hours. According to case anamnesis the animal developed an acute, weight-bearing lameness of the left posterior limb 15 days prior to presentation that subsequently evolved to paraparesis and paraplegia within hours. The dog had been treated symptomatically with non-steroidal anti-inflammatory drugs (NSAID) without any noted improvement. Physical examination was unremarkable. The dog was paraplegic with preservation of spinal reflexes and deep pain sensation. Neurological signs were compatible with a grade IV T3-L3 spinal cord lesion. Differential diagnosis included ischemic myelopathy, myelitis and acute spinal cord compression due to traumatic intervertebral disk rupture, spinal arachnoid pseudocyst or congenital vertebral anomalies. Myelography showed a marked stop of contrast medium above the caudal end of T12 vertebra, with an evident “golf-tee” sign, suggesting a focal intradural-extramedullary lesion (Figure 1, 2). The owner declined further investigation and elected euthanasia, as the prognosis for recovery was poor.



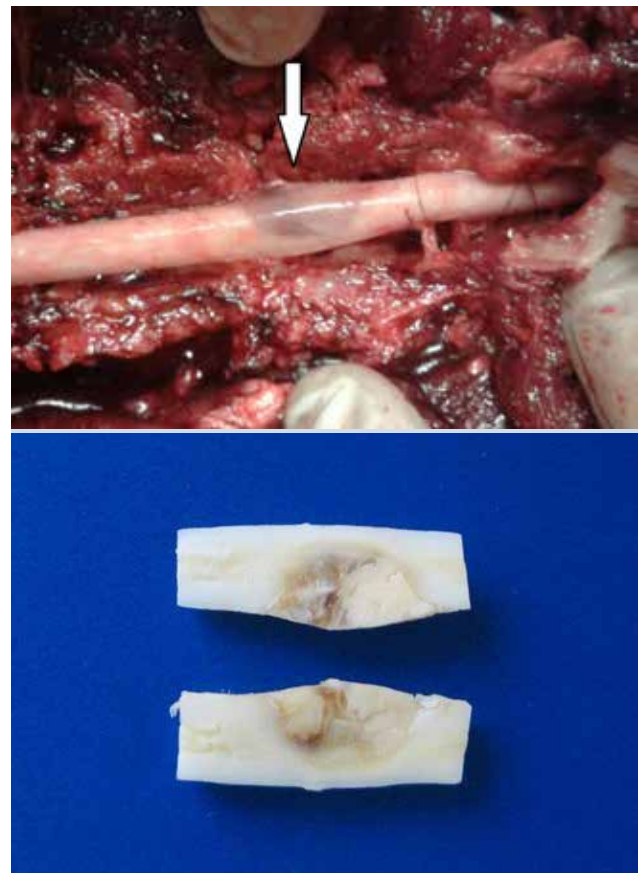
**Figure 1.** Cisternal myelogram of the thoracolumbar region of the spine indicating a complete obstruction (arrow) of the contrast medium at the caudal end of T12 vertebra in lateral view.

Gross macroscopic findings during necropsy included a lentiform, intradural-extramedullary multilobular, partially cystic proliferation with extensive lateral spinal cord compression, leading to a reduction for about 75% of the original diameter (Figure 3, 4). Samples from the mass were embedded in paraffin and were stained with Hematoxylin /Eosin and Giemsa staining. Histology revealed a predominantly extra-axial, lobulated and partially cystic mass which had grown in direct contact to the pia mater, was attached to the nerve root as well as a focal, well circumscribed protrusion into the spinal cord. The mass was lined by a pseudo-capsule of flattened cells. The

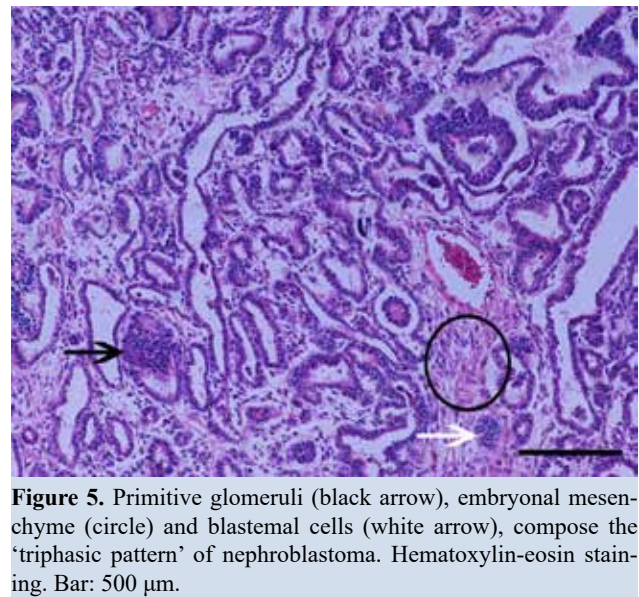
lesion was mostly characterized by an epithelioid tubular pattern with delineated cystic and very cellular solid parts and very occasional glomeruloid features (Figure 5). Notably, there was a multifocal goblet cell differentiation and membrane specifications were seen throughout. The cysts varied in size, contained flocculent mucoid material and exfoliated cells. Between the surface structures, there were polymorphic spindle cells with some cellular exfoliation, high degree of basophilia, anisocytosis and anisokaryosis, round to elongated nuclei, highly hyperchromatic coarse chromatin and some areas with parachromatic vacuolation. Most of the cells contained 1-3 prominent paracentral and moderately anisometric nucleoli. Furthermore, there were small epithelioid nests scattered in between the tubular structures consisting of oval cells with an eosinophilic indistinct cytoplasm and hypochromatic round to oval nuclei and small central or paracentral nucleoli. The adjacent neuroparenchyma (spinal cord and nerve root) was deformed and presented with multiple enlarged myelin tubes, axonal spheroids and multiple gitter cells.



**Figure 2.** Cisternal myelogram of the thoracolumbar region of the spine indicating a “golf-tee” sign (arrow) in ventrolateral view (RH=right side).



**Figure 3, 4.** Intradural- extramedullary mass with extensive lateral spinal cord compression.



**Figure 5.** Primitive glomeruli (black arrow), embryonal mesenchyme (circle) and blastemal cells (white arrow), compose the “triphasic pattern” of nephroblastoma. Hematoxylin-eosin staining. Bar: 500  $\mu$ m.

Cranial to the lesion the histological examination revealed a mild diffuse lympho-plasma-cellular infiltration of the subarachnoid space and a severe bilaterally symmetric extracellular grey matter edema of the intermediate zone. This area and the ventral fascic-

ulus proprius contained numerous axonal spheroids. Caudal to the lesion the spinal cord presented with equal histopathological changes. In addition, the central canal in this segment was mildly enlarged. The histological picture was consistent with the pre-neuro-invasive stage of a spinal nephroblastoma of the young dog, due to embryonic misplacement of cells from the nephrogenic primordium (Figure 5).

## DISCUSSION

Nephroblastoma is a rare neoplasm of the spinal cord occurring in young dogs aged from 6 months to 3 years, but it has also been reported in older animals (McConelli et al., 2003, Liebel et al., 2011). Nephroblastoma is also called Wilm's tumor and is the most common renal tumor in children, although extrarenal spinal localization is rare (Liebel et al., 2011). Large breed dogs seem to be predisposed, especially German shepherds and Retriever breeds (Liebel et al., 2011). The tumor is frequently located between the 10<sup>th</sup> thoracic and the 2<sup>nd</sup> lumbar spinal cord segments and may be intradural – extramedullary (ID – EM) or, less often intramedullary (IM) or extradural (ED) (McConelli et al., 2003, Liebel et al., 2011). Classification of these tumors in animals and humans is controversial, and they are invariably described as ependymomas, neuroepitheliomas, spinal cord blastomas, medulloepitheliomas, hamartomas, nephroblastomas, embryonal nephromas, embryonal adenocarcinomas, renal adenocarcinomas, or Wilm's tumor (McConelli et al., 2003, Liebel et al., 2011). The recommended definition by the World Health Organization Histological Classification of Tumors of Domestic Animals is “thoraco-lumbar spinal cord tumor of young dogs” (Liebel et al., 2011). The histomorphologic and immunocytochemical evidence shows that nephroblastomas represent ectopic growths of undifferentiated metanephric blastema, entrapped within the dura or spinal cord parenchyma during fetal development (Liebel et al., 2011). This theory is supported by immunohistochemical staining using human Wilm's tumor (nephroblastoma) gene antibody, which was used to confirm the presence of primitive renal tissue (McConelli et al., 2003). Nephroblastomas are usually solitary but there are reports of potential spinal metastases (McConelli et al., 2003).

The clinical presentation of the current case is comparable to those of previously reported cases. The presenting signs of the tumor was sub-acute to chronic progressive, pelvic limb ataxia or paresis (T3 – L3 myelopathies) (Liebel et al., 2011).

A tentative diagnosis is based on advanced diagnostic imaging investigation such as myelography, magnetic resonance imaging (MRI) and ultrastructural or immunohistochemical examination of the mass (Ohta et al., 2009). In the majority of soft tissue spinal neoplasms, plain radiographs of the spine are normal, except of vertebral neoplasia cases where vertebral bone lysis with loss of cortical outlines is noted. Myelography, computed tomography (CT) or magnetic resonance imaging (MRI) are helpful for establishing the diagnosis of spinal tumors and for therapeutic planning. Evaluation of cerebrospinal fluid (CSF) rarely reveals neoplastic cells but may reveal increased protein levels with or without elevated cell counts. In the current case, CSF analysis did not reveal either increased protein concentration or elevated cell count. The myelographic appearance of central nervous system (CSN) tumors has been described in several reports as either an intramedullary or intradural-extramedullary space-occupying lesion (Dewey 2008). Nephroblastomas are intradural-extramedullary in origin, but may infiltrate the spinal cord giving rise to the appearance of an intramedullary mass. It can be difficult to differentiate intradural from intramedullary masses with myelography. Myelographic classification of a mass as intradural-extramedullary is based on the presence of a widened subarachnoid space and a filling defect within the contrast medium. If the lesion lies laterally, the spinal cord appears expanded on the lateral view and displaced on the ventrodorsal view. Focal widening of the subarachnoid space caused by a discrete mass in the region forms the “golf-tee” sign as was in the dog presented here (Kealy, McAllister, Gragam, 2005). In one study, it was found that conventional myelography was superior to CT myelography in differentiating intradural-extramedullary tumors from intramedullary tumors (Li et al., 1992).

In our case, based on cisternal myelography findings, the focal “golf-tee” lesion above the caudal end of T12 vertebra was considered compatible with intradural-extramedullary mass (Figure 1). However, the “golf-tee” sign was described in a case of extradural lesion, hence its identification should be interpreted with caution (Nderbisv2000).

A “triphasic pattern” may be observed in histopathologic examination of spinal neoplasms (De Lorenzi et al., 2007). The terminology refers to the presence of three different tumor cell populations, stromal/mesenchymal cells, epithelial cells and un-

differentiated small hyperchromatic blastemal cells (Liebel et al., 2011).

Therapy for dogs with this type of spinal tumor can be supportive (palliative) or definitive (Dewey, 2008). Supportive therapies are directed against secondary sequel of nephroblastoma (e.g., spinal cord edema, pain), whereas definitive therapies are aimed at elimination of neoplastic tissue (Dewey, 2008). Supportive therapies consist of administration of anti-inflammatory dose of glucocorticoids (e.g., prednisone), with or without additional pain-relieving drugs (e.g., narcotics) (Dewey, 2008, Liebel et al., 2011). Definitive therapy consist of cytoreductive surgery and radiotherapy (Dewey, 2008, Liebel et al., 2011). The cytoreductive surgical procedures include hemilaminectomy, dorsal laminectomy with unilateral facetectomy, durotomy, regional durectomy, myelotomy with or without radiotherapy (Liebel et al., 2011). In dogs, the goals of surgery for spinal cord tumors are decompression of the spinal cord, maximal neoplastic tissue resection and collection of samples for morphologic examination (Liebel et al., 2011). The outcome after cytoreductive surgery varies with survival times ranging from 2 months to more than 3 years (Liebel et al., 2011). The efficacy of radiotherapy after cytoreductive surgery or as a sole treatment modality for

nephroblastoma in dogs is not well documented, but a few reports suggest that it may be beneficial (Liebel et al., 2011). Therapies can provide some temporary relief of clinical signs, but many patients will likely be euthanized because of poor general condition. The prognosis is considered poor, however, it may depend on the neuroinvasive and metastatic potential of the neoplasm, while distant extraneural and intraspinal-metastases appear to be rare (Liebel et al., 2011).

### **CONCLUDING REMARKS**

Although rare, spinal cord tumors like nephroblastomas should be included in the differential diagnosis of canine cases with acute or sub-acute spinal cord disease.

### **ACKNOWLEDGEMENTS**

The authors thank Dr. K. Matiasek and Dr. M. Rosati, Neuropathology Laboratory Institute of Veterinary Pathology, Ludwig-Maximilian University of Munich and Dr. D. Psalla, Laboratory of Pathology, School of Veterinary Medicine A.U.Th. for their support in the histopathological diagnosis of the case.

### **CONFLICT OF INTEREST**

None declared by the authors.

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