Spinal Meningothelial Meningioma in a Dog

İlayda PAZARBAŞILAR[1,3,a], Oya Burçin DEMİRTAŞ[2,3,b], Nur Beyza NAZIR[1,3,c], Sevil VURAL[2,d], Ömer BEŞALTI[1,e,✉]

[1]Ankara University, Faculty of Veterinary Medicine, Department of Surgery, Ankara, Türkiye; [2]Ankara University Faculty of Veterinary Medicine, Department of Pathology, Ankara, Türkiye; [3]Ankara University Graduate School of Health Sciences, Ankara, Türkiye

[a]ORCID: 0000-0002-4131-8440, [b]ORCID: 0000-0003-0850-2374, [c]ORCID: 0000-0002-3000-514X, [d]ORCID: 0000-0003-2111-3381
[e]ORCID: 0000-0002-7819-9094

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✉**Corresponding author**
besalti@hotmail.com

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ABSTRACT

The objective of this study is to report clinical, MRI, surgical, and histological findings of spinal meningothelial meningioma in a dog. The study material was a 9 years old, spayed dog with a history of progressive nonambulatory tetraparesis. The dog had intact cranial and spinal reflexes and deep pain perception. Magnetic resonance images revealed a mass located at the left side C2-C3 level, hyperintense in T1W, isointense on T2W, and well contrast enhancing on postcontrast T1. The mass was microsurgically resected and sub-gross. The dog's neurological status was improved at one week and survived for 15 months without signs of metastasis. Histological and histochemical workup revealed grade I, meningothelial meningioma. Surgical intervention for spinal meningioma can be suggested as the sole treatment in dogs.

Spinal meningiomas are the most common primary spinal tumors that have solitary structures and can be seen in any layer of meninges, especially arachnoid. These tumors are a significant cause of mortality in companion animals depending on their subtypes (4). They could be located in intradural-extramedullary or extradural (3).

Breed and sex predisposition for spinal meningioma was not reported, however, it is observed more commonly between ages five and fourteen years old (10). Computerized Tomography (CT) and Magnetic Resonance Imaging (MRI) along with histopathologic examination are the main diagnostic tool in spinal meningiomas (3). MRI is the method of choice to characterize the tumor deciding about the possibility of surgical resection. However, histological analysis is required to make a definitive diagnosis (3,9).

Tumor classification by World Health Organization (WHO) is modified for defining grades of meningiomas in veterinary medicine. It was stated that grade 1 tumor type has a benign character, but grade 2 and grade 3 are thought to be malign. In addition to histological examination of spinal meningiomas immunohistochemistry is needed to determine for more detail (2,9,12). Meningiomas are stained positive for S100, Vimentin, some of the Cytokeratin (CK) markers, E-cadherin, and CD34 and are negative for GFAP, CD45/CD18, and some of the Claudin antibodies in veterinary pathology (8, 12, 14).

Treatment options for spinal meningiomas are surgical removal, chemotherapy, radiotherapy, or different combinations of them. The prognosis is related to the degree of spinal cord damage, the amount of resected tumor, and the tumor subtype (3).

This study aimed to report the clinical symptoms, diagnostic workup, surgical management, and histopathologic characteristics of cervical meningioma in a dog.

Nine years old spayed mongrel dog admitted to Ankara University Faculty of Veterinary Medicine Department of Surgery was subjected. The dog had a history starting with left hind limb ataxia, combined with

right thoracic limb ataxia in a month. Subsequently, ataxia was generalized with all limbs and more remarkable on the left side by the third month. Within four months, the patient became tetraparesis and was not able to walk for a week. The cell blood count and routine serum biochemistry were in reference limits except for high White blood cell (WBC) and neutrophilia. The dog was mentally alert and had normal cranial and spinal reflexes. The patient was in non-ambulatory tetraparesis in lateral recumbence, with patellar and withdrawal reflexes, and intact deep pain perception in all limbs. Spinal radiographs were normal. Neuroanatomical localization of the lesion was thought in C1-C5 spinal cord segments. Intervertebral disc disease, neoplasia, subarachnoid cyst, and meningomyelitis were considered among differential diagnoses. A cervical MRI was planned to narrow the list.

MRI was carried out with 0.3 Tesla. Anesthesia was induced by butorphanol (0,1 mg/kg) and diazepam (0,5 mg/kg) and it was maintained by Total Intravenous Anesthesia (TIVA) consisting of propofol with a dosage of 0,3mg/kg/min. Images were acquired as sagittal, axial, and transverse views in T1W, T2W, and post-contrast T1W. Gadolinium dimeglumine was used at a dose of 0.1 mmol/kg body weight (BW) intravenously. The lesion was observed as a focal mass. It looked at isointense in T2W and hyperintense in T1W images (Figure 1). In the T2W image, the circumference of the lesion looked hyperintense. The lesion was located on the left side adjacent to the dorsal and left dural margins. Transverse and dorsal images of the T2W sequence showed that left-sided subarachnoid space expanded to compensate for the mass, so the mass was indicated as an intradural-extramedullary origin (Figure 1). Post-contrast T1W image revealed a broad-based attachment to the dura mater and had the appearance of as golf-tee-like mass, located intradural-extramedullary in the C2-C3 region (Figure 1). The mass extended into the intervertebral foramen along the spinal nerve, which mimics a nerve sheath tumor. For a more definitive diagnosis, surgical removal of the mass was planned because of its well-demarcated appearance.

Cephalosporin cefazolin (Eqizolin®500mg/2mL, Turkey) was used at a dose of 20 mg/kg intravenously for prophylaxis. A transdermal fentanyl patch (Duragesic® 50 mcg/h patch, Belgium) was applied before the surgery to provide preemptive analgesia. Intravenously diazepam (Diazem® 10mg/2mL, Turkey) with a dose of 0.5 mg/kg was used for premedication. Propofol (Propofol PF® %1 200mg/20mL, Turkey) with a dosage of 3mg/kg, was used to make induction of anesthesia, and the dog was intubated orolaryngeally. The anesthesia was maintained by isoflurane (Isoflurane USP® %100, USA). Constant Rate Infusion (CRI) of ketamine (Ketasol® %10, Austria) at a dosage of 0,3mg/kg/h with 5ml/kg/h speed was used for perioperative analgesia.

The dog was positioned in sternal recumbency with the head gently flexed in a neutral position. The surgical area was prepared for aseptic surgery. A midline incision was made over the C1-C4 spinous processes. Paraspinal muscles were separated by subperiosteal dissection. The lateral side of C2 –C3 vertebrae, intervertebral foramen, and nerve root were exposed by Gelpi retractors. Hemilaminectomy was performed by preserving nerve roots at C2-C3 intervertebral foramen level by surgical burr. Based on the swelling of the spinal cord and the purplish color change in durameter the hemilaminectomy defect was enlarged. The durotomy was carried out under the operation microscope, and the mass was revealed in greyish color, well-demarcated and it pushed the spinal cord to the right side. The mass was removed by microdissection and aspiration. Blood vessels of the meninges were obscured by electrocoagulation. The dural defect was not repaired for the possibility of recurrence. Fat graft, which was harvested subcutaneously, was placed in hemilaminectomy defect. The operating wound was closed routinely.

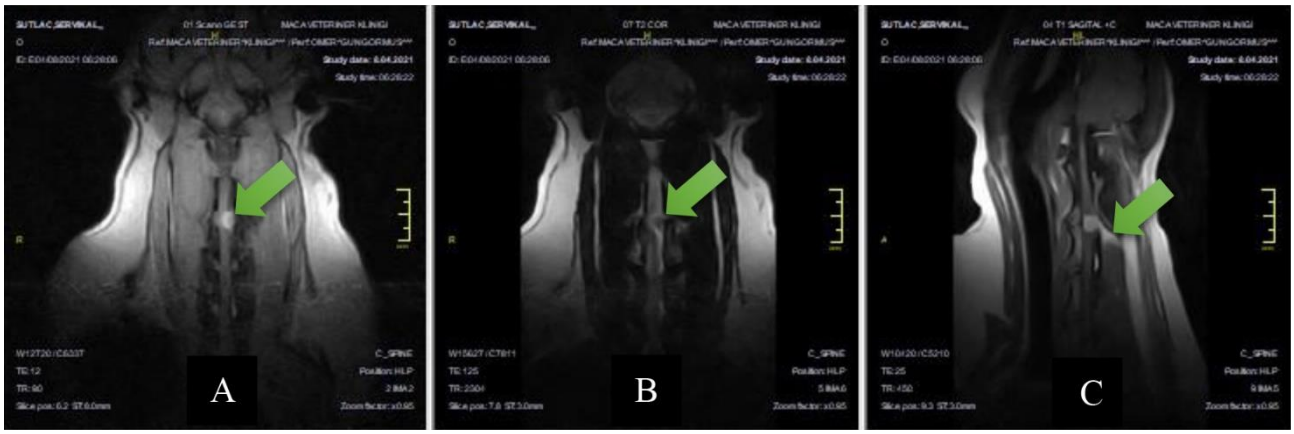

Figure 1. (A) Dorsal postcontrast T1W hyperintense image and (B) Dorsal T2W isointense image show a round-shaped mass on the left side at the C2-C3 vertebrae (green arrow). (C) Sagittal postcontrast T1W MR image shows well contrast enhancement and golf-tee sign located intradural-extramedullary at the C2-C3 vertebrae (green arrow).

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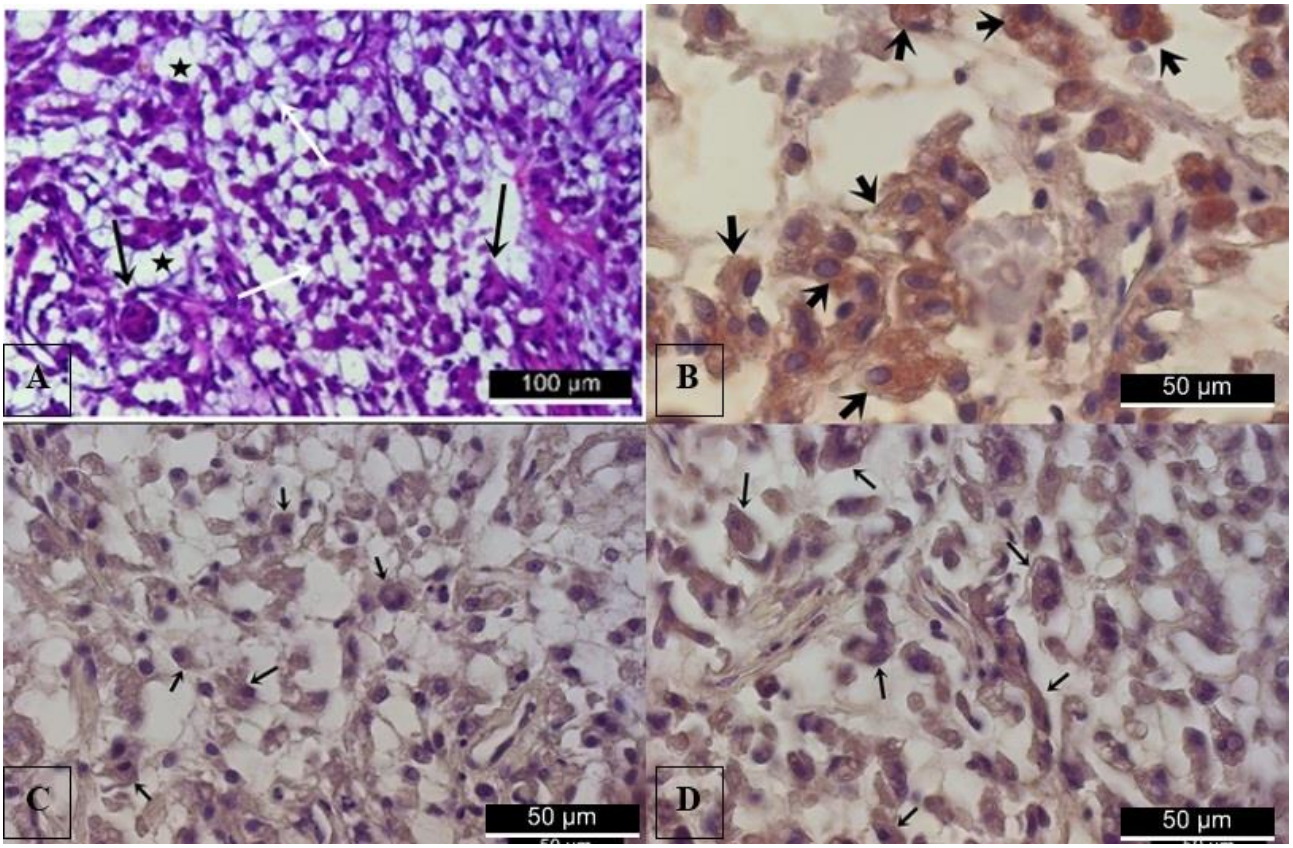

Figure 2. **A:** Histopathological image, meningothelial cells with round/oval basophilic nuclei and abundant eosinophilic cytoplasm with cytoplasmic extensions formed small clusters (black arrows) or a web-like pattern (white arrows). The myxomatous substance is seen in between (black stars) (HE); **B:** CK 8 positive meningoendothelial cells (black arrows), Strept ABC-P; **C:** S-100 positive meningeal cells (black arrows), Strept ABC-P; **D:** Vimentin positive meningeal cells (black arrows), Strept ABC-P.

In the postoperative period, fluid therapy (dose of 2 ml/kg/h) was continued until the patient recovered from anesthesia. Transdermal fentanyl patch had been used as postoperative analgesia for 3 days. Afterward, tramadol with a dose of 2 mg/kg was administered every 8 hours PO to make pain management for two weeks after the surgery. Prednisolone at a dose of 0.5 mg/kg, PO, BID for two weeks and amoxicillin and clavulanic acid at a dose of 25 mg/kg PO, BID for one week were recommended just after the surgery.

The retrieved sample was fixed in 10% formaldehyde, routinely processed, and embedded in paraffin blocks. Then, 5µm thick sections were taken (Leica RM2125, Deer Park, Illinois, USA) and stained with Hematoxylin and Eosin (HE), using an automatic slide stainer (Leica Autostainer XL, Deer Park, Illinois, USA). Immunohistochemically, the sections were stained with StreptAvidin-Biotin Complex Peroxidase (Strept ABC-P) method by using S-100 (1:150, ThermoScientific, Waltham, Massachusetts, USA), Vimentin (1:500 ScyTek, West Logan, Utah, USA) and Cytokeratin 8 (CK8) (1:50 Novocastra, Newcastle, UK) antibodies according to the kit procedure (UltraVisionDetection System Large Volume Anti-Polyvalent, Thermo Scientific, Waltham, Massachusetts, USA). Control sections were treated with normal Mouse IgG serum (Ready to use, Novocastra, Newcastle, UK). Afterward, all of the sections were examined under the light microscope (Leica DM 4000, Deer Park, Illinois, USA) and photographs (Leica MC170, Deer Park, Illinois, USA) were taken from appropriate sites.

Uniform meningothelial cells with large, round/oval, normochromic basophilic nuclei, and wide eosinophilic cytoplasm were seen (Figure 2A). These cells tend to come together as lines or small clusters in which the cytoplasmic borders could not be distinguished, with a blue-colored mucinous material between them. There was no visible mitotic activity. Immunohistochemically, these neoplastic cells were markedly stained positive with S-100, vimentin, and CK 8 antibodies at homogenous brownish color unlike the control sections (Figure 2B-2D). It was diagnosed as a grade 1 endothelial subtype in the light of findings.

The reported case introduces a meningioma that mimics a nerve root tumor in MRI causing nonambulatory tetraparesis. The location of the mass led us to consider a

nerve sheath tumor rather than a meningioma in MRI. However, it was definitively diagnosed as meningothelial meningioma by histopathologic and immunohistochemical examination. Immunohistochemical confirmation with S100, CK8, and Vimentin was carried out. The high-grade positivity of mentioned biomarkers was found to correlate with the literature as spinal meningothelioma (7, 15, 16).

Nerve sheath tumors and meningiomas are the most common intradural spinal neoplasias in dogs, like in humans (5, 6). Meningiomas may account for up to 65% of canine primary spinal cord tumors (8). Differentiation of both tumors can be challenging in some cases by MRI (11, 13, 16).

MRI findings of spinal meningioma in humans and dogs as iso to hypointense on T1W images and slightly hyperintense on T2W images relative to the spinal cord. Dural tails are observed as a result of post-contrast T1W images (8,13). High signal intensity on T1W in human meningioma is considered related to; intra-extra tumor hemorrhage, high lipid content in tumor cells, mild calcification, and high cellular density. Hyperintensity on the T1W image was also reported in a case with cranial meningioma in a dog (6). In our case, T1W hyper-intense and T2W isointense appearance relative to the spinal cord was observed (Figure 1). Additionally, a round-shaped mass was surrounded by hyperintense circumference in the T2W image, and an extension of the tumor along the nerve roots through the intervertebral foramen was seen. This unusual MRI finding was not confirmed by the histological examination regarding to possible causes of human beings. Meanwhile T1 hyperintense and T2 isointense with circumferential hyperintense lesions are thought to be related to hemorrhage and exposed hemosiderin. Extension of the lesion to the intervertebral foramen was reported before and they should be considered in MRI evaluation (8).

Presumptive diagnosis is often possible based on tumor characteristics and location using advanced imaging techniques; however, for definitive diagnosis histological examination is required (1, 3). Additionally, there are no guidelines or criteria for grading the malignancy potential of meningiomas in canine practice, so WHO classification is used basically. Treatments of canine spinal meningiomas consist of medical management and cytoreductive surgery with/without radiation therapy. Survival times after surgery as a sole treatment vary from 4 to 47 months (10, 16). In human grade, I meningioma, surgery is the method of choice for the treatment and results are satisfactory and recurrence postoperatively is low which is found to be approximately 3–15% (5). The case presented in this study is in the same line with grade I.

There was limited information about the surgical technique for removing meningioma, especially at the spine. The location, suitable exposure of the surgical area for manipulation on tumor removal, the method of hemostasis, microsurgical skill, etc. are crucial for a successful surgery. Resection with meticulous hemostasis by electrocoagulation was thought to have a crucial role of one year surviving without neurologic signs, and improvement in neurological status in a relatively short term, which was one week, was thought to be associated with low surgical morbidity on neural tissues. Neurologic improvement in one week after the surgery and remaining silent for 15 months was found successful. The patient was followed up with a detailed neurologic examination over a routine period of 2 months. During that period, there did not exist any proprioceptive deficit or delayed spinal reflexes. Although the surgical technique was not detailed in the veterinary literature, we think that sub-gross total removal of the tumor with minimal trauma is crucial because the outcomes after surgical resection for spinal meningioma remain more unclear compared to cranial meningioma because of the fewer reported cases. The interval between realizing first clinical signs and admission time is reported as about 1 month (13). In the presented case, the first clinical signs were noticed by the owner four months ago, and progressive deterioration resulted in non-ambulatory tetraparesis.

These kinds of studies should be done with more dogs to come up with a result and make a specific tumor classification which helps the management to become easier. Surviving with seamless clinical signs for 15 months can be considered as a clue to suggest surgical intervention for canine meningioma as a sole treatment.

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Ethical Statement

This study does not present any ethical concerns.

Conflict of Interest

The authors declared no conflict of interest

Author Contributors

Case examination, evaluation of clinical findings, interpretation of MRI images, and surgical intervention were done by IP, NBN, and OB. Histopathologic evaluation was done by OBD and SV. The article was written, accordingly. All authors have read and agreed to the submitted version of the manuscript.

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