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CLINICAL REPORT

A Case of Cervical Intramedullary *Dirofilaria immitis* Associated with Nerve Sheath Tumor in a Dog

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ABSTRACT

Dirofilaria immitis, a globally widespread nematode known for its high mortality rate, primarily infests the cardiovascular system, notably the pulmonary artery and right ventricle. However, since 1856, instances of adult heartworm infestation in atypical sites have been documented, including the eye, peritoneal cavity, subcutaneous region, skeletal muscle, systemic arteries, and the central nervous system (CNS). Dirofilariasis often manifests asymptomatically, but severe cases can lead to respiratory and circulatory complications, even sudden death. Migration of *D. immitis* to the CNS results in symptoms corresponding to the parasite's location rather than typical heartworm signs. Magnetic resonance imaging (MRI) plays a crucial role in diagnosing CNS parasitic infestations, aiding in lesion evaluation and parasite localization. Additionally, malignant peripheral nerve sheath tumors (MPNSTs), originating from Schwann cells, fibroblasts, and perineural cells, are rare neoplasms with high recurrence rates and poor prognoses. While MPNST metastases are infrequent, they have been reported in various animal species and anatomical sites, including the CNS. Here, we present the first documented case of intramedullary *D. immitis* associated with a nerve sheath tumor in a dog, highlighting the unique intersection of parasitic infestation and neoplastic disease in veterinary medicine.

Introduction

Dirofilaria immitis is a nematode that is frequently encountered worldwide, has a high mortality rate, and usually causes cardiovascular infestation. Heartworms are frequently encountered in the pulmonary artery and right ventricle.[1] However, since 1856, adult heartworm infestations have been reported in abnormal sites such as the eye, peritoneal cavity, subcutaneous region, skeletal muscle, systemic arteries and the central nervous system.[2]

Patients with dirofilariasis are usually asymptomatic. The severity of clinical symptoms is related to the number of adult parasites present in the dog. In severe infections, serious clinical symptoms of the respiratory and circulatory systems can be observed and even sudden death can occur. The most common symptoms are right ventricular dilatation or hypertrophy associated with inflammation of the lung, cough, dyspnoea, exercise intolerance and fatigue. Ascites and hepatomegaly may also be observed in patients due to right heart failure.[3-8]

In cases of *D. immitis* migrating to the central nervous system, the symptoms are usually shaped according to the location of the parasite rather than the clinical signs of heartworm infestation. In the reported cases, parasite migration was observed in the intracranial arteries, ventricular system, subarachnoid, and epidural region of the vertebral canal. The clinical symptoms seen in these cases are usually associated with the degree of myelopathy, mechanical

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compression of the neuropil, local inflammation and vascular damage.[9-11]

In humans, MRI is the most important diagnostic method used in the diagnosis of parasitic infestation of the central nervous system. Magnetic resonance imaging allows the evaluation of lesions along the parasite's migration path and the preoperative localisation of the parasite.[12]

Peripheral nerve sheath tumors are neoplasms originating from Schwann cells, fibroblasts, and perineural cells. These tumors are classified as benign peripheral nerve sheath tumors (schwannoma, neurofibroma) or malignant peripheral nerve sheath tumors depending on histological character and tumor aggressiveness. Malignant peripheral nerve sheath tumors (MPNST) have been reported in different animal species and anatomical locations. Caudal cervical, cranial thoracic region, and cranial nerves are the most commonly affected areas in dogs. The MPNSTs are tumors with high local recurrence rate and poor long-term prognosis. Metastasis of MPNSTs is very rarely encountered and cases have been previously reported in dogs, cattle, and cats.[13] Previously reported case reports of two dogs showed lung, spleen, liver, and kidney metastases. A recent study of soft tissue sarcomas in dogs reported an 11.1% rate of PNST metastasis. One site of metastasis involved the central nervous system, but whether this was due to an MPNST or another type of soft tissue sarcoma has not been clarified. In humans, MPNSTs have an incidence of 0.001% in the general population and more commonly develop in patients with neurofibromatosis type-1 (NF-1).[14] Distant metastases have been described in non-NF-1 patients. The sites of metastases include the lungs, bones, pleura, retroperitoneum, diaphragm, lymph nodes, liver, chest wall, pericardium, thyroid gland, adrenal gland, leptomeninges, and brain. Spinal cord and brain metastases have been reported to be very rare.[15]

The case we present is the first case of intramedullary *Dirofilariasis immitis* associated with a nerve sheath tumor in a dog in the literature.

Case Description

In this case report, a 10-year-old male English bulldog dog was brought to Istanbul University, Cerrahpaşa Veterinary Faculty, Surgery Outpatient Clinic with the complaints of lameness of the right forelimb, weakness in all four limbs and loss of appetite 3 weeks ago. Neurological examination revealed hyperreflexia in the anterior and posterior legs, loss of proprioception in all four legs, and tetraparesis. No morphological abnormality was found on thorax and abdomen radiography. Laboratory examination of the patient revealed HCT 29.9 (reference value: 36.00-56.00 %), ALP 280 U/l (reference value: 13.00-83.00), and ALT 664 U/l (reference value: 17.00-78.00). Abdominal CT scan was ordered due to markedly elevated liver enzyme levels and brain and cervical MRI examinations were ordered based on neurological examination findings.

Treatment and Outcome

The MRI of the cervical region was performed by a 1.5 T MRI unit. In the MRI examination, a mass lesion of 6x8x13 mm in size, located in the medulla spinalis at the C4 level, with an intramedullary location, with prominent peripheral annular contrast enhancement after intravenous injection of gadopentetate dimeglumine (0.1 mmol/kg), and with hyperintense surroundings on T1A sections and hypointense features on T2A sections was detected. Significant edema accompanying the medulla spinalis was noted cranial and caudal to the described lesion (Figure 1).

No abnormality was found in the abdominal CT scan and only increased craniocaudal size of the spleen was observed.

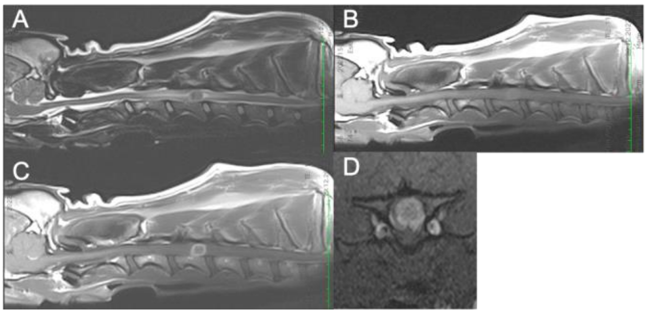

Figure 1. The mass is well defined with T2-weighted (T2W) hypointensity with moderate cord edema cranial and caudal to oval-shaped mass (A), T1-weighted (T1W) peripherally hyperinsity (B). In contrast enhanced T1 images (C, D) ring enhancing lesion at C4 level.

Figure 2. The macroscopic appearance of the mass is a well-defined lesion, intramedullary in location, easily separable from the nerve tissue, without extension into the nerve sheath, and measuring 12×8×6 mm at its widest point.

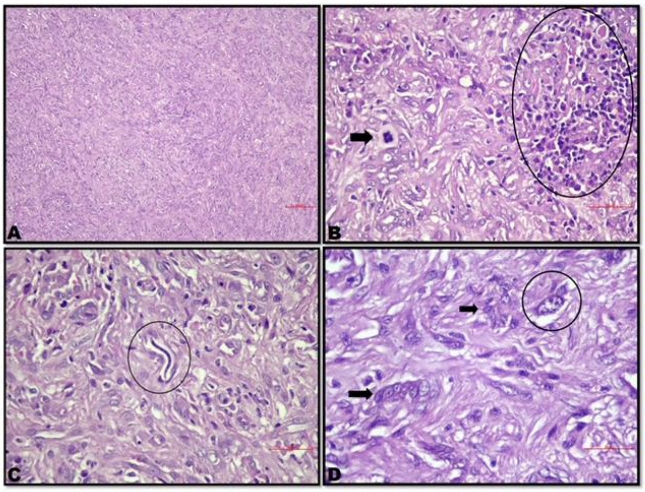

Figure 3. (A) Hypercellular tumoral mass composed of pleomorphic neoplastic cells arranged in a radially whorled pattern (storiform) on a loose collagenous matrix. (H&E). Bar = 10µm. (B) Atypical mitotic figure (arrow). Mononuclear inflammatory cell infiltration, mainly composed of plasma cells (circle). (H&E). Bar = 40µm. (C) Microfilaria in the lumen of a blood vessel (circle). H&E. Bar = 40µm. (D) Multinucleated giant cells (arrows). Bizarre neoplastic cell with a vesicular nucleus and large prominent nucleolus (circle). H&E. Bar = 60µm.

The C4-C5 cervical dorsal laminectomy was performed to remove the lesion detected by MRI and to eliminate the spinal cord compression and then the lesion was removed by durotomy. The lesion was observed to be 6×7×12 mm in diameter, with clear borders, firm consistency, and pale pink colour (Figure 2). The sample was sent to the laboratory for histopathological examination. Mannitol (1g/kg BID IV, Polifleks % 20 Mannitol®) (3 days), prednisolone (1mg/kg BID IV, Prednol®) (5 days), sucralfate (1g/day PO, Antepsin®) (5 days) and ceftriaxone (50 mg/kg BID IM, Novosef®) (7 days) were prescribed post operatively.

In histopathological examination, the mass was diagnosed as malignant peripheral nerve sheath tumor, and parasite sections with nematode morphology were observed in the parenchymal tissue. Histopathologically, the entity was diagnosed as a malignant peripheral nerve sheath tumor by light microscopy. The tumor was a non-encapsulated hypercellular neoplasia composed of pleomorphic, fusiform to round cells with vesicular nuclei arranged partly in storiform, partly in whorls on a loose collagenous matrix. Multi-nucleated giant cells were also noted, and atypical mitotic figures were observed. Perivascular mononuclear inflammatory cell infiltration, mainly consisting of plasma cells, was evident in most of the microscopic fields, and intriguingly, microfilaria-like parasitic foreign bodies were also detected in some small venous vessels (Figure 3).

After the histopathological diagnosis, the patient was tested with the IDEXX SNAP 4Dx® Plus because of the parasite sections in the region and *Anaplasma canis* Ab Positive -*Ehrlichia canis* Ab Positive -Canine Heartworm Ag Positive -Lyme Ab Positive were observed.

Doxycycline (10 mg/kg BID PO, Monodoks®) (3 weeks) was added to the patient's postoperative treatments. Clinical symptoms started to regress after treatment of the blood parasite was started and the lesion was removed. After the operation, it was observed that the patient started to use all four legs, was able to regain a sternal position unassisted, started to move, and his general condition improved.

Clinical Relevance

In humans, MRI is the most important diagnostic method used in the diagnosis of parasitic infestation of the central nervous system. Magnetic resonance imaging allows the evaluation of lesions along the parasite migration pathway and preoperative parasite localisation and may respond to pharmacotherapeutic interventions in medically treated cases. In our case, the entry route of *D. immitis* into the dura could not be determined during MRI or surgery. How adult worms migrate to abnormal sites has not yet been elucidated. Although third- and fourth-stage larvae are thought to be large enough to flow through a capillary bed, adult heartworms lack the mechanical structures necessary to pierce vessel walls and migrate. It has been hypothesised that where adult heartworms are found in abnormal positions, immature heartworms or their larvae may occlude small vessels or capillaries, causing rupture of the vessel and release of the larvae into the abnormal position.[16]

In cases of *D. immitis* migrating to the central nervous system, the symptoms usually occur depending on the location of the parasite rather than the clinical signs of heartworm infestation. The clinical symptoms seen in these cases are usually associated with the degree of myelopathy, mechanical compression of the neuropil, local inflammation and vascular damage. In three previous case reports of dogs, it was reported that adult heartworms found in the epidural space caused paresis or paralysis. [9-11] The diagnosis is made by radiography and myelography. In a case of dirofilariasis in the epidural space in a cat, paraparesis and ataxia in the hind limbs were observed and the diagnosis was made by MRI.[16] Based on the contrast-enhanced MRI, the patient was found to have tetraparesis due to the presence of a lesion at the C4-C5 level and a general condition disorder accompanying the central nervous system findings due to the presence of dirofilaria larvae accompanying the peripheral nerve sheath tumor in the lesion removed from the region. Lesion enhancement was evident after contrast medium injection. The MRI suggested two differential diagnoses: infectious/inflammatory granulomatous with unknown pathogenesis or extradural focal neoplasia (eg, lymphoma, haemangioma).[17]

In the MRI evaluation of this patient, it was thought that the solid structure compressing the medulla spinalis in the region might be a space occupying mass, therefore decompression of the region was performed, and the solid structure was resected at the same time. Blood parasite test was not performed preoperatively because the symptoms of the patient were not suggestive of *D. immitis*. The test was performed post-operatively because the histopathology report showed nematodes and the result was positive. Although cases of *D. immitis* migrating to the central nervous system have been previously reported in the literature, this is the first case of intramedullary localization accompanied by MPNST. It is suggested that due to the coexisting abnormalities that might not be detected in the patient evaluation and the insufficiency of advanced imaging results to make a clear diagnosis, the intraoperative findings, histopathological studies and clinical examination of the patient should be assessed thoroughly. We would like to share this first case of intramedullary *D. immitis* associated with MPNST with our colleagues and share our experiences in diagnosis and treatment.

Conflict of Interest

None to declare.

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