VETERINÁRIA NOTÍCIAS

Case report

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Meningeal osteosarcoma in a dog's brain

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Abstract: Osteosarcoma is the most common bone cancer in dogs.It has a high invasion capacity and commonly metastasizes. This neoplasia ensues mainly in the medullary canal of long bones of the appendicular and axial skeleton, rarely affecting primarily extra-skeletal sites. Primary meningeal osteosarcomas are extremely rare both in human and veterinary medicine. A male, mixed breed dog was admitted at the Veterinary Hospital with a history of over excitement, decreased neurological reflexes, and seizures. The worsening of its clinical condition led to its euthanasia and anatomopathological examination at the Veterinary Pathology Service. This report describes a primary extra-skeletal osteosarcoma of a dog's meninges. Its clinical signs were indicative of a central nervous system disease later diagnosed by histopathological and immunohistochemical analysis.
Keywords: osteogenic sarcoma, meninges, dog.

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Introduction

Osteosarcoma is the most frequently diagnosed bone neoplasia in dogs. It is characterized by extreme aggressiveness at the primary site, and frequently metastasizes. This neoplasm mainly affects dogs of large or giant breeds at the average age of seven to ten years (GOMES; BRANDÃO; RANZANI, 2008). The vast majority of this neoplasia originates from the medullary canal of long bones of the appendicular and axial skeleton (MOORE, 2001) and rarely affects primarily extra-skeletal sites. The formation of extra-skeletal osteosarcoma has already been observed in humans and dogs, in cutaneous form (including the mammary gland), muscle, gastrointestinal, visceral (liver and spleen), endocrine (thyroid and adrenal glands), urinary tract (bladder and kidney), reproductive tract (testicles and vagina), respiratory tract (lungs), in addition to the central nervous system (HEYMAN et al. 1992; MOORE, 2001; GOMES; BRANDÃO; RANZANI, 2008). In the latter, it is called meningeal osteosarcoma (MO) (RINGENBERG; NEITZEL; ZACHARY, 2000).

MOs have been reported in humans, as well as in an albino rat and a dog. This neoplasm is considered extremely rare in human and veterinary medicine (RINGENBERG; NEITZEL; ZACHARY, 2000; MEDINA et al., 2004). The diagnosis is based on clinical history, radiological and scintigraphic findings, and confirmation is made by histopathological and immunohistochemical analysis (OSIPOV et al., 2002; GOMES; BRANDÃO; RANZANI, 2008). Its main differential diagnosis is osteomatous meningioma (BARNHART; WOJCIESZYN; STORTS, 2002).

This report describes a case of MO in a dog with clinical signs of central nervous system disease, which was later confirmed by histopathological and immunohistochemical analysis.

Case report

An eight-year-old, male, mixed breed dog was admitted at the Veterinary Hospital "Luiz Quintiliano de Oliveira" in Araçatuba (Sao Paulo, Brazil) with a history of excitement, decreased neurological reflexes, and seizures. Its clinical condition deteriorated, and the dog was eventually euthanized. The animal was sent to the Veterinary Pathology Service for a anatomopathological examination. Organ samples were placed in a 10% buffered formalin solution, processed by routine methods, cut 3µm thick, and stained with hematoxylin and eosin (HE).

Gross examination revealed marked congestion on the brain. An area of adhesion was observed in the dura mater from the base of the brain to the skull floor, in the region of the sella turcica, involving the pituitary gland. After removing the brain, it was noted that the meninges of this site had a hardened plaque and were slightly elevated and very irregular. The same lesion pattern was seen in the pituitary gland and the neuropil in the regions of the hypothalamus and optic chiasm. These lesions displayed resistance when cut, suggesting local mineralization. A rigorous skeletal assessment revealed no primary bone tumors or metastasis at distant sites, and lesions were restricted to the base of the brain.

Microscopic analysis of the brain showed the predominance of mesenchymal cells, pleomorphic to anaplastic, with oval to round nuclei, fusiform to starry cytoplasm, distributed in a solid myxoid stroma at the base of the brain, starting from the dura mater. In most areas there was formation of an osteoid matrix and areas of differentiated bone tissue, mimicking bone trabeculae demarcated by osteoblasts and osteoclasts (Figure 1B). Additionally, there were areas of necrosis and tumor infiltration in the adjacent neuropil and in the pituitary gland (Figure 1A). In these places, edematous areas and foci of liquefactive necrosis of the neuropil were also observed.

Immunohistochemical analysis was performed at the School of Veterinary and Agrarian Sciences – Universidade Estadual Paulista (FCAV-UNESP) following the protocol described in Table 1, in order to identify cells of mesenchymal or glial origin.

Table 1 – Primary antibodies used to identify the histological origin of neoplastic cells.

Primary Antibodies	Antigenic Retrieval	Dilution[2]	Secondary Antibodies
Vimentin	Pascal Pressure Chamber (Dako)[1]	1:200	LSAB[3]
GFAP	Pascal Pressure Chamber (Dako)[1]	1:100	LSAB[3]
S-100	Pascal Pressure Chamber (Dako)[1]	1:700	LSAB[3]

1 – Sodium citrate buffer, 10 mM, pH 6,0; 2 – 4°C for 18 hours; 3 – Kit LSAB – DakoCytomation, code K0690-1

Immunohistochemical analysis resulted in the positive cytoplasmic labeling of neoplastic cells for vimentin (Figure 1C) and S-100 (Figure 1D), and negative for GFAP antibodies.

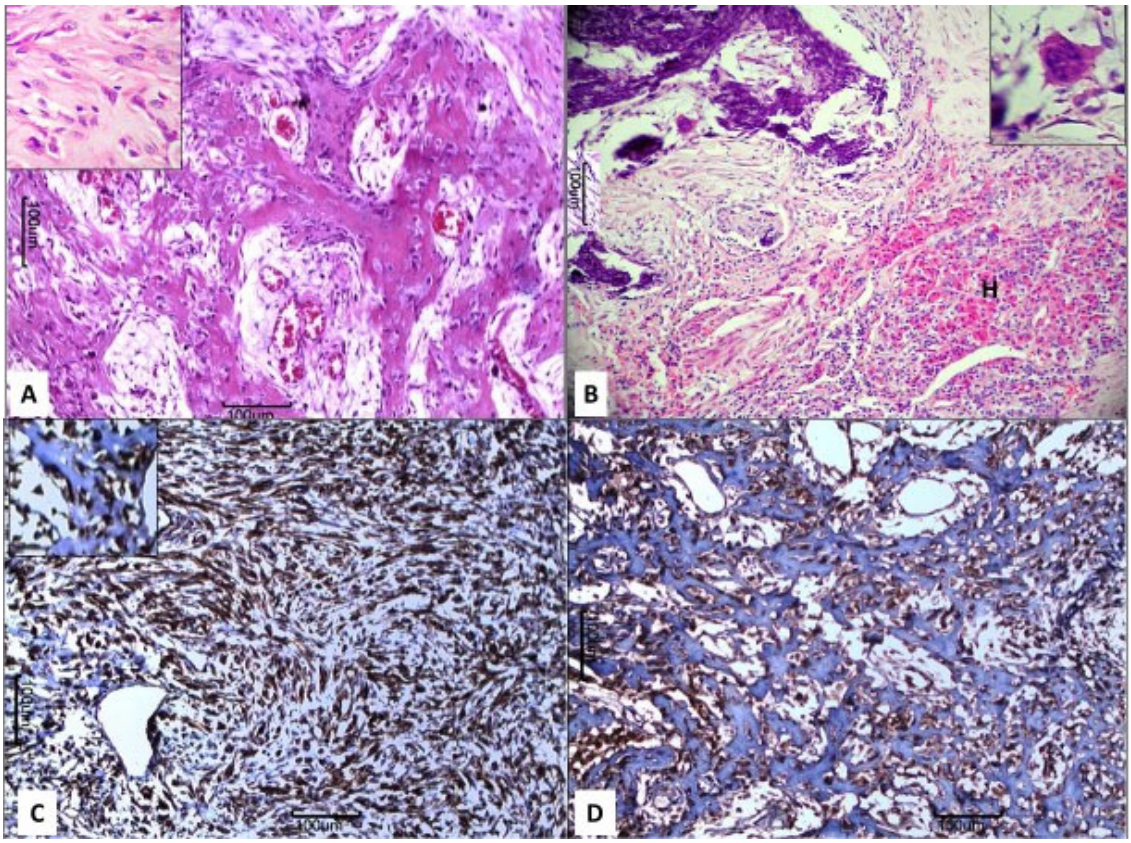

Figure 1. Photomicrographs of meningeal osteosarcoma in a dog. A) Neoplastic mesenchymal cells differentiated of bone trabeculae. Detail: pleomorphic neoplastic cells. Hematoxylin and eosin. B) Tumor infiltration into the pituitary tissue (H). Note the presence of adjacent mineralization (*) and osteoclast adjacent to mineralized tissue (detail). Hematoxylin and eosin. C) Positive labeling for vimentin in tumor (detail). Peroxidase-bound polymers complex. D) Positive tumor cells for protein S-100. Peroxidase-bound polymers complex. Bar = 100 µm.

Discussion

Extra-skeletal osteosarcomas are tumors of mesenchymal origin that produce bone tissue and lack an association with bone or periosteal tissue (RINGENBERG; NEITZEL; ZACHARY, 2000). Meningeal osteosarcoma has been first reported in a dog (RINGENBERG; NEITZEL; ZACHARY, 2000), originating from a focus of dural mineralization. These lesions, known as ossifying pachymeningitis, are common in the dura mater of the brain and

spinal cord of elderly dogs, especially in large breeds. In this case, the lesion involved the brain.

Grossly, MOs can be detected in the form of a mass that is usually pinkish-white, firm and mineralized when cut (PACE; PERSOHN; HEIDER,1995; RINGENBERG; NEITZEL; ZACHARY, 2000). In the case of the present report, the neoplasm was observed in the form of a hardened plaque, slightly elevated and quite irregular, white and firm when cut.

The most common microscopic findings are the presence of the osteoid matrix with atypical, polygonal or fusiform, uni or multinucleated cells with significant nuclear pleomorphism, in addition to prominent nucleoli and frequent atypical mitoses (PACE; PERSOHN; HEIDER, 1995; MEDINA et al.; 2004). Binucleation may also be present, but necrosis is not common. Some authors consider that mitosis is rare, while others less so (PACE; PERSOHN; HEIDER,1995; MEDINA et al., 2004). In the present case, an osteoid matrix, areas of differentiated bone tissue, intratumoral necrosis and necrosis of the neuropil surrounding the tumor (compressive effect) were observed, in the latter associated with edema as reported before (PACE; PERSOHN; HEIDER,1995; MEDINA et al., 2004).

Meningeal osteosarcoma in humans and rats are morphologically similar. Macroscopically, tumors have been observed involving the dura mater, both in humans and in rats, and associated with the tissue of the adjacent brain (PACE; PERSOHN; HEIDER,1995). In the present case, the bone tissue of the skull floor did not reveal any signs of tumor involvement, a fact that reinforces the meningeal origin of this neoplasm.

The observed changes in the dura mater in the present study may represent a causal association, with dura mater mineralization followed by heterotopic ossification and culminating in the malignant transformation of mineralized meningeal tissue. A similar mechanism may apply to other extra-skeletal osteosarcomas, such as feline-induced sarcomas. These neoplasms are often caused by a chronic inflammatory process. The persistence of

cytokines and growth factors at the injury site leads to the formation of metaplastic tissue, which provides an environment conducive to malignant transformation (RINGENBERG; NEITZEL; ZACHARY, 2000).

Studies highlight that in humans, radiotherapy has been identified as a predisposing factor for the development of meningeal osteosarcoma. They occur mainly in patients treated with radiotherapy for other neoplasms (pituitary adenomas, glioblastomas, and meningiomas) (MEDINA et al., 2004), which did not occur in the present case.

The main differential diagnosis of meningeal osteosarcoma is meningioma, which is the most common central nervous system (CNS) tumor diagnosed in humans, dogs, and cats (BARNHART; WOJCIESZYN; STORTS, 2002). Meningioma has a broad classification regarding its histological aspect in dogs (VAN WINKLE et al., 1994, BARNHART; WOJCIESZYN; STORTS, 2002). One of the most common brain sites for the onset of this tumor is the turcic cell. The difference between meningeal osteosarcoma and osteomatous meningioma is in the invasive behavior and rapid growth of the former, given that meningiomas are generally benign and slow-growing, and can occasionally cause proliferation of periosteal bone tissue by tissue irritation (BARNHART; WOJCIESZYN; STORTS, 2002).

The immunohistochemical analysis performed sought to confirm the histological origin of the neoplastic cells. Therefore, an immunohistochemical panel composed of markers for vimentin, GFAP and S-100 protein was used. Intense labeling for vimentin is common in neoplasms of mesenchymal origin in neural tissue (RINGENBERG; NEITZEL; ZACHARY, 2000; BARNHART; WOJCIESZYN; STORTS, 2002; VIOLIN, 2009), like those found in the present case. GFAP is recommended to differentiate tumors of glial origin, whereas S-100 can indicate the origin of neoplastic cells of meningiomas (BARNHART; WOJCIESZYN; STORTS, 2002). However, even though S-100 is a marker of nervous tissue, its marking is not specific enough to confirm

the diagnosis of meningioma (BARNHART; WOJCIESZYN; STORTS, 2002; VIOLIN, 2009) because the protein can be expressed in other cell types.

Conclusion

Drawing on the literature, this neoplasm was classified as a primary meningeal osteosarcoma of the pachymeninge, as there were no changes in the dog's skeleton or skull during the anatomopathological examination. Albeit rare, its occurrence in the CNS must be considered in the differential diagnosis with other tumors of the central nervous system.

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Osteossarcoma meningeal no encéfalo de um cão

Resumo: O osteossarcoma é considerado a neoplasia óssea mais frequente em cães. Tem elevada capacidade invasiva e comumente gera metástase. Essa neoplasia é mais frequentemente observada no canal medular de ossos longos do esqueleto apendicular e axial. É raro que acometa primariamente sítios extraesqueléticos. O osteossarcoma primário meningeal é considerado extremamente raro em medicinas humana e veterinária. Um cão macho e sem raça definida foi atendido no Hospital Veterinário com histórico de excitação, diminuição dos reflexos neurológicos e desenvolvimento de quadro convulsivo. O agravamento do quadro clínico levou à eutanásia do animal e a um exame anatomopatológico pelo Serviço de Patologia Veterinária. O objetivo deste relato é descrever um caso de osteossarcoma extra-esquelético primário de meninge em um cão que apresentou quadro clínico compatível com doença originária do sistema nervoso central e que foi diagnosticado por meio das análises histopatológica e imunohistoquímica.
Palavras-chave: sarcoma osteogênico, meninge, cão.

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