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Primary non-metastatic omental myofibrosarcoma in a horse

[*Miofibrossarcoma omental primário não metastático em um cavalo*]

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ABSTRACT

Myofibrosarcoma in horses is a rare malignant tumor composed predominantly by myofibroblasts. A 15-year-old horse was referred to the Veterinary Hospital of the Federal University of Parana for evaluation of colic signs. Initial physical examination showed icteric mucous membrane and laboratory analysis found anemia, increased serum activity of ALT, GGT, ALP, and bilirubin. In the exploratory laparotomy a highly vascularized abdominal mass in the left hypochondrium region of approximately 50cm x 45cm x 30cm, adhered to the surrounding structures was observed. Due to the size and adhesions to the omentum, the mass was considered surgically unresectable, and euthanasia was performed followed by necropsy. The immunohistochemical and morphological results indicate the diagnosis of myofibrosarcoma since the neoplastic cells immunoexpressed Vimentin, HHF35 and S100. To the authors' knowledge, this is the first equine case of omental myofibrosarcoma described in the literature.

Keywords: immunohistochemistry, myofibroblast, myofibroblastic sarcoma, neoplasia

RESUMO

O miofibrossarcoma em cavalos é um raro tumor maligno, composto predominantemente por miofibroblastos. Um equino, de 15 anos de idade, foi encaminhado ao Hospital Veterinário da Universidade Federal do Paraná, para avaliação de sinais de cólica. O exame clínico inicial apresentou mucosas ictéricas e, nos exames laboratoriais, revelou anemia e aumento sérico de ALT, GGT, ALP e bilirrubina. Na laparotomia exploratória, observou-se massa abdominal vascularizada de aproximadamente 50cm x 45cm x 30cm na região do hipocôndrio esquerdo e aderida às estruturas circunvizinhas. Devido ao tamanho e às aderências ao omento, a massa foi considerada irressecável cirurgicamente, portanto foi realizada a eutanásia e a necropsia. Os resultados imuno-histoquímicos e morfológicos indicam o diagnóstico de miofibrossarcoma, visto que as células neoplásicas imunoexpressaram Vimentin, HHF35 e S100. Portanto, esse é o primeiro caso em equinos de miofibrossarcoma omental descrito na literatura.

Palavras-chave: imuno-histoquímica, miofibroblastos, sarcoma miofibroblástico, neoplasia

INTRODUCTION

Myofibrosarcoma, or myofibroblastic sarcoma, is a rare malignant tumor composed predominantly of differentiated myofibroblasts (Silva *et al*., 2012). In horses, there are three cases of this tumor, an associated with the site of equine influenza vaccination (Kannegieter *et al.*, 2010), in a limb (Silva *et al*., 2012) and an abdominal spindle cell sarcoma of probable myofibroblastic origin (Newman *et al*., 1999). In domestic animals this neoplasm is also rare, being reported in a maxillary region in a dog (Tsuchiya *et al*., 2012), in inguinal region in a dog (Hojo *et al*., 2012) and a restrictive orbital in cats (Bell *et al.*, 2011).

In addition, primary tumors of the omentum are also extremely rare in all species, including horses, in which there are only three case reports in the literature (Shaudien *et al.*, 2007; Harvey *et al.*, 1987; Johnson *et al.*, 1994).

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Neoplasms such as benign myofibroblastic lesions, fibrosarcoma, and leiomyosarcoma are tumors included as differential diagnoses to myofibrosarcoma. The histological distinction can be difficult, but immunohistochemical expression can differentiate myofibrosarcomas from other types of sarcomas more clearly (Silva *et al*., 2012).

The purpose of this study is to describe the clinical aspects, diagnosis, *post-mortem* finding, histologic, and immunohistochemical features of the first primary non-metastatic omental myofibrosarcoma in a horse, contributing to a better understanding of neoplasms in the specie.

CASUISTRY

A 15-year-old, male, mixed-breed horse was referred to the Veterinary Hospital of the Federal University of Parana for evaluation of seven days intermittent abdominal discomfort, anorexia, pyrexia, and distended abdomen.

Physical examination findings included alert attitude, regular body condition, jaundiced mucous membranes, and decreased intestinal motility in the right upper and lower quadrants. Through the nasogastric tube, a liquid compatible with intestinal reflux, with a pH 8 alkaline, was obtained. Transrectal palpation identified a firm mass in the ventral region of the left posterior quadrant. Abdominocentesis yielded a voluminous yellow peritoneal fluid, however, sample cytology was not performed since the case was aggressively deteriorating.

The complete blood count detected a mild anemia with a hematocrit of 28%, hemoglobin of 9.3g/dL, reactive lymphocytes with mild anisocytosis, and hypersegmented neutrophils. Serum biochemical analysis revealed an increase in the concentration of total bilirubin (8.47mg/dL, direct 2.23mg/dL and indirect 6.24mg/dL) and increased activity of aspartate aminotransferase enzymes (AST 862.0 U/L), gamma-glutamyl transferase (GGT 197.1U/L) and alkaline phosphatase (ALP 587.9 68 U/L). All other blood parameters were considered normal.

Due to the rapid and severe deterioration of the patient, the horse was submitted to exploratory laparotomy. A 50cm longitudinal incision was made on midline starting near the umbilical scar. During the abdomen inspection a highly vascularized abdominal mass of approximately 50cm adhered to the surrounding structures and tissues, mainly stomach and omentum, in the left hypochondrium and midline region was identified. As the mass occupied a large part of the abdominal cavity, it was impossible to see deeper structures (Fig. 1A). Surgical removal was unsuccessful due to the size of the mass, high blood irrigation and adhesions mainly to the omentum. For this reason, the horse was euthanized, and a postmortem examination was performed.

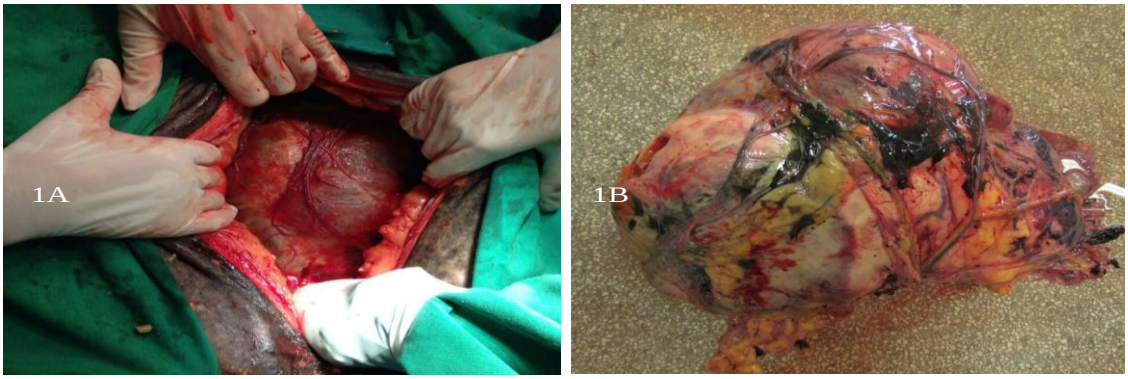

Figure 1. (A) Myofibrosarcoma, abdominal cavity, horse. Highly vascularized mass in the left hypochondrial region and midline. (B) Myofibrosarcoma, abdominal mass, horse. Aspect after necropsy removal revealing a mass of approximately 50cm x 45cm x 30cm.

Necropsy examination confirmed the mass (Fig. 1B) in the left hypochondrium, measuring 50cm x 45cm x 30cm. Macroscopically it had an irregular surface, adhered to the omentum, soft to the cut, yellowish, and with cavitation areas of 2 to 15cm filled with blood. There were no

macroscopic signs of metastasis or any involvement in other organs of pelvic and thoracic cavity. Some organs and tumor samples were removed and fixed in 10% neutral buffered formalin, embedded in paraffin, cut at a 5µm, and stained with hematoxylin and eosin for routine light microscopic examination.

The histopathological examination revealed a neoplastic proliferation of spindle shaped cells with moderate anisocytosis and anisocariosis. The cytoplasm was eosinophilic with slightly distinct edges and the nucleus was rounded to oval, vesicular, with 1 to 4 evident nucleoli (Fig. 2A). The surrounding stroma was composed of a large amount of myxoid tissue and fibroblasts, with areas of multifocal and moderate hemorrhage (Fig. 2B). Few mitotic figures were observed (a mean of 3.2 per 10 fields examined with the x40 microscope objective). Other organs of the abdominal and thoracic cavity were also evaluated histologically, and no tumor cells or other abnormalities were detected.

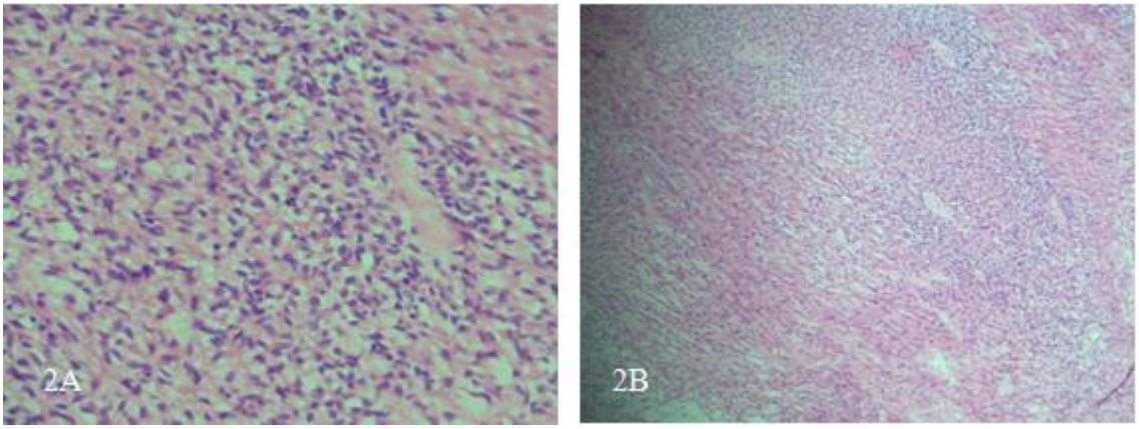

Figure 2. (A) Myofibrosarcoma, Horse. Histological section showing areas of necrosis and focal broad bleeding. Hematoxylin and eosin, 10x. (B) Myofibrosarcoma, Horse. Histological section showing ovoid to fusiform neoplastic cells. Hematoxylin and eosin, 40x.

Since there were no signs of infiltration in the macroscopic and histopathological evaluation of the organs of pelvic and thoracic cavity, it was confirmed that the neoplasm originated in the omentum.

To establish the definitive diagnosis, the tissue samples were sent for immunohistochemical evaluation for the following antibodies anti-vimentin (V9 clone), anti-alpha muscle actin (clone HHF35), anti-S100 protein, anti-CD31, anti-smooth muscle actin (1A4), anti-desmin, anti-cytokeratin AE1AE3, and anti-myoD1 (Dako, Agilente, Santa Clara, United States). The antigenic recovery by the wet heat method was carried out in a steam pan for 20-30 min. The incubation with the primary antibodies was carried out overnight at 4ºC. For development, the Advance system was used. Staining was done with 3,3-diaminobenzidine and counter-staining with hematoxylin. External and/or internal controls were used to validate the reaction. All antibodies used in this reaction have cross-reactivity proven in equine tissue, using dilutions specific to that specie.

In immunohistochemistry, there was a positive expression in the neoplastic cells for Vimentin (Fig. 3A), HHF35 (Fig. 3B), and S100 (Fig. 3C). However, the tumor cells were negative for CD31, 1A4, Desmin, AE1AE3, and MyoD1. Based on the histopathological analysis and immunohistochemical profile, the diagnosis of myofibrosarcoma was confirmed.

DISCUSSION

Myofibroblasts are modified fibroblasts that exhibit a hybrid phenotype, occurring in the stroma of normal tissues, inflammatory tissues, repair tissue and in some reactive and neoplastic soft-tissue lesions (Fisher, 2004). In addition, due to their contractile ability and capacity to synthesize components of the extracellular matrix, cytokines, proteases, and pro-angiogenic factors a variety of benign soft tissue tumors,

malignant tumors and fibrocontractile diseases show myofibroblastic differentiation. In cases of mesenchymal neoplasms with malignant myofibroblastic differentiation, it is defined as myofibroblastic sarcoma or myofibrosarcoma (Eyden *et al.*, 1991).

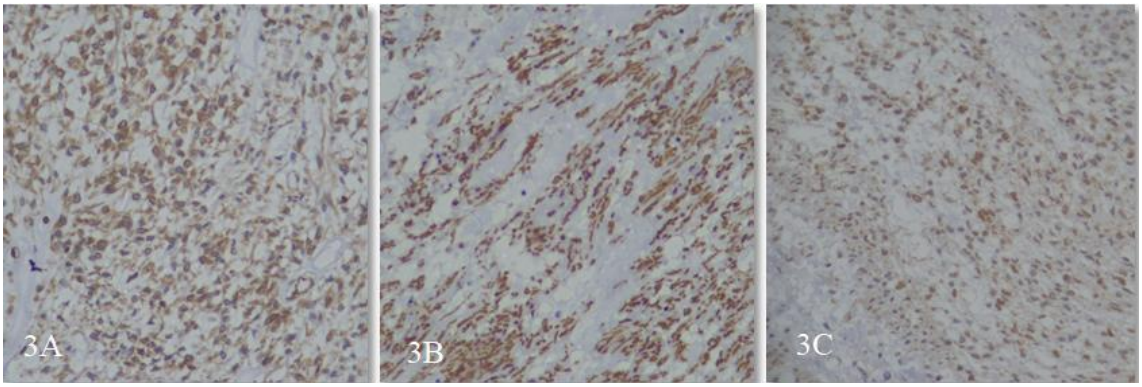

Figure 3. (A) Myofibrosarcoma, Horse. Immunohistochemical expression of vimentin in the cytoplasm of neoplastic cells. (B) Myofibrosarcoma, Horse. Immunohistochemical expression of HHF35 in the cytoplasm of neoplastic cells. (C) Myofibrosarcoma, Horse. Immunohistochemical expression of S100 in the cytoplasm of neoplastic cells.

The etiology of myofibrosarcoma is unknown; however, Silva *et al*. (2012) report a relationship with post-inflammatory or post-traumatic processes. In granulation tissue, myofibroblasts are probably derived from local fibroblasts in response to mechanical stress (Fisher, 2004). In the case reported there was no history of a traumatic or inflammatory process, but since the horse was already older and used for several activities, the possibility of previous trauma was not ruled out.

These myofibroblastic sarcomas in domestic animals occur mainly in subcutaneous tissues of the head, neck, and extremities (Bell *et al.*, 2011; Tsuchiya *et al*., 2012; Hojo *et al*., 2012; Silva *et al.*, 2012; Kannegieter *et al.*, 2010) and are rarely observed in the bone and viscera (Newman *et al.*, 1999). The location is important for diagnosis since the tumor does not present clinical signs in early stages. For this reason, myofibrosarcoma in the subcutaneous tissue are easily visualized and can be diagnosed by biopsy, unlike the case reported when the neoplasm triggered severe systemic clinical signs and was only identified in the post-mortem evaluation as Newman *et al*. (1999) also related.

Based on necropsy and histopathological examination, neoplastic involvement in other organs was ruled out, with its origin in the omentum being characterized. Neoplasms, particularly myofibrosarcoma, of omental origin are uncommon in horses. To our knowledge, cases of unifocal myofibrosarcoma of the omentum have never been described in horses so far.

Newman *et al*. (1999) reports a solitary abdominal sarcoma of myofibroblastic origin, but does not determine the primary origin, hypothesizing that the origin was the muscular wall of a mesenteric vessel. The omentum may undergo metaplasia and has faster revascularization since the organ is composed of endothelial cells and it also presents pro-angiogenic factors, such as fibroblast growth factor and endothelial vascular growth factor, as well as promoting in vivo angiogenesis (Agner *et al.*, 2001), thus being a possible origin of the tumoral mass demonstrated in our report.

Myofibroblastic sarcoma can be classified as low grade or high grade. Low-grade myofibrosarcomas are infiltrative tumors, usually in deep soft tissue, which can recur but rarely metastasizes. It displays a range of microscopic appearances from fasciitis-like to fibrosarcoma-like and all cases present at least focally display nuclear pleomorphism, and neoplastic cells had mild atypia and a low mitotic rate (1-6 per 10 high power fields). High-grade myofibroblastic sarcoma is characterized by pleomorphic sarcomas which are composed of atypical

spindle, polygonal, and giant cells showing myofibroblastic differentiation that show numerous mitoses and abundant collagen production and is usually only detected by electron microscopy lesions. In addition, numerous mitotic figures (more than 10 per 10 high power fields) and tumor necrosis usually accompany these tumors (Fisher, 2004). Considering the histological characteristics, localization, and lack of metastasis the myofibroblastic sarcoma of the present report was classified as low grade.

The immunohistochemistry evaluation was performed to confirm the diagnosis since is not possible to differentiate from other soft tissue sarcomas by histological examination with light microscopy. Silva *et al.* (2012) refers that the positive expression in immunohistochemistry for vimentin and alpha muscle actin (HHF35) and a lack of desmin and S100 protein expression as a diagnostic pattern for myofibrosarcoma, which corroborates with the result in the case described except for the positive expression of S100 protein. The positive expression of the case can be observed in some cases of myofibroblastic sarcoma as reported by Eyden *et al.* (1991), Bell *et al*. (2011) and Fisher (2004).

The differential diagnosis includes nodular fasciitis and fibromatosis, and other types of low-grade spindle-cell sarcoma, such as fibrosarcoma and leiomyosarcoma (Silva *et al.*, 2012). Nodular fasciitis does not display necrosis or nuclear atypia and displays variable cellularity and myxoid microcysts containing lymphocytes and erythrocytes. Fibromatosis is negative for alpha-smooth muscle actin and does not present malignant features. Based on immunohistochemistry was eliminated fibrosarcoma, which is negative for alpha-smooth muscle actin and leiomyosarcoma, which is positive for desmin. (Fisher, 2004).

CONCLUSIONS

This report adds to the neoplastic studies in horses, demonstrating details about necropsy, histopathological, and immunohistochemistry analysis of the tumor, as in this case the origin and type of neoplasm are rare, characterized as a non-metastatic unifocal omental myofibrosarcoma.

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