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Case Report

Metastatic Leiomyosarcoma Causing Ataxia in a Horse

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ABSTRACT

A 24-year-old Thoroughbred mare had a history of weight loss, progressive bilateral hind limb weakness, and ataxia. An infectious neurologic disease was suspected, and the mare was euthanized due to poor prognosis. At necropsy, a yellow firm mass replaced most of the skeletal muscles of the left thigh. Numerous similar nodules were in several other muscles and in multiple organs, including brain and spinal cord. Microscopic examination revealed a leiomyosarcoma with disseminated metastases. Although of rare occurrence, this case is a reminder of noninfectious causes of ataxia in horses.

1. Introduction

Ataxia is a common sign of neurologic disease in horses. The most common causes are cervical stenotic myelopathy, equine degenerative myeloencephalopathy, and equine protozoal myeloencephalitis (EPM) [1]. Neoplasms, both primary and metastatic, are rare additional causes of neurologic signs of horses [2]. Leiomyosarcoma (LMS) is a rare malignant neoplasm derived from smooth muscle. In veterinary medicine, LMS is most commonly seen in the intestine of dogs [3] and is considered locally invasive but slow to metastasize. Equine LMS is rare. We report a case of LMS arising from the left hind limb with disseminated metastases including in the central nervous system (CNS) leading to neurologic manifestation clinically suspected to be infectious in origin.

2. Materials and Methods

2.1. Case

A 24-year-old Thoroughbred mare with a 1-month history of weight loss and lameness of the right hind limb nonresponsive to treatment with nonsteroidal anti-inflammatory drugs was presented to the School of Veterinary Medicine at Louisiana State University. The clinical signs progressed over the next 2 weeks to bilateral hind limb paresis and ataxia. Based on the clinical signs, infectious diseases of CNS were considered as differential diagnoses including EPM, verminous encephalomyelitis, and equine herpes virus-1 infection. Due to poor prognosis, the horse was humanely euthanized and was submitted for postmortem examination.

At necropsy, a 45 × 15 × 15–cm, firm neoplastic mass replaced approximately 70% of the gracilis, adductor, and semimembranosus muscles of the left hind limb (Fig. 1). On cut surface, the mass was poorly demarcated, firm, and yellow. Numerous smaller, smooth, white to yellow, and firm neoplastic nodules were observed in several other skeletal muscles and in the lungs, the heart (Fig. 2), both adrenal glands (Fig. 3), spleen, capsule of the left kidney,

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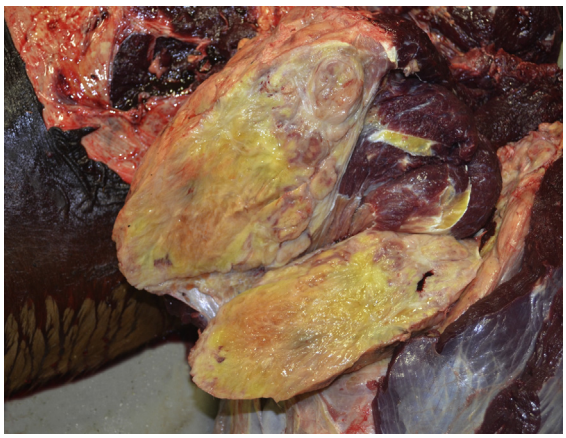

Fig. 1. Leiomyosarcoma, left hind limb. A 45 × 15 × 15–cm, firm mass virtually completely replaces the gracilis, adductor, and semimembranosus muscles.

the brain (right lateral ventricle, frontal lobe, and cerebellum) (Fig. 4), and the spinal cord (T2 segment).

2.2. Histology and Immunohistochemistry

Sections of all tissues were fixed in 10% neutral buffered formalin and then subsequently paraffin-embedded following routine procedures, sectioned at 5 μm, and stained with hematoxylin and eosin. Selected sections from the main mass were stained with phosphotungstic acid–hematoxylin (PTAH). Immunohistochemistry was performed on selected sections of the intramuscular hind limb mass. The primary antibodies, summarized in Table 1, targeted smooth muscle actin (SMA), myogenin, MyoD1, desmin, and myoglobin. For SMA, myogenin, desmin, and myoglobin, dewaxing, antigen retrieval, and staining were performed on the Leica BOND MAX IHC and ISH Staining System (Buffalo Grove, IL). For MyoD1, the Autostainer Link 48 (Dako North America, Carpinteria, CA) automated stainer was used. The chromogen was 3,3′-diaminobenzidine, and the sections were counterstained with Meyer's hematoxylin. Positive immunohistochemical controls were normal small intestine (SMA) as well as fetal (myogenin and MyoD1) and adult (desmin and myoglobin) skeletal muscle to which the appropriate antisera were added. For negative controls, the primary antibodies were replaced with homologous nonimmune sera.

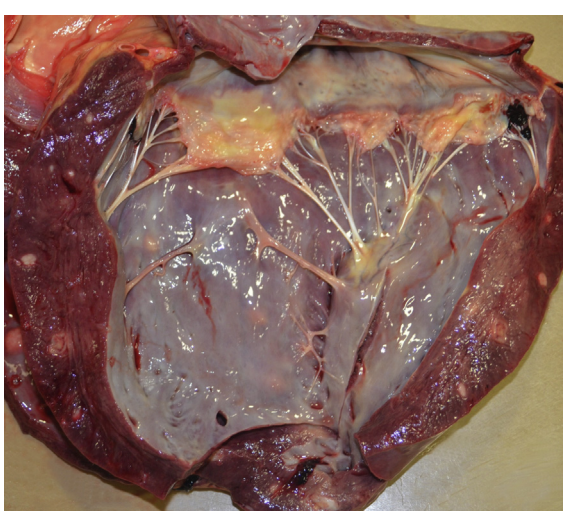

Fig. 2. Metastatic leiomyosarcoma, heart. Well-delineated, smooth, white to yellow, firm nodules, ranging between 1 and 4 cm in diameter, are present throughout the myocardium of both cardiac ventricles.

3. Results

Histologically, the mass replacing most of the proximal left hind limb musculature was composed of markedly pleomorphic polygonal to spindle cells with a mitotic index of 12 per 10 high power fields (400×) arranged in streams and bundles multifocally set in a densely hyalinized eosinophilic stroma (Fig. 5). In the PTAH-stained sections, most of the cells in the neoplastic mass lacked cross-striations except for some spindle cells at the periphery interpreted as entrapped skeletal myofibers. Large numbers of eosinophils were throughout the neoplasm (Fig. 5 inset). Nerve bundles in the surrounding skeletal muscle had multifocal axonal degeneration, an alteration that was also present in the sciatic nerve. The nodules at the various other sites were histologically similar to the main neoplastic mass in the left hind limb.

In the immunohistochemically labeled sections, approximately 95% of the neoplastic cells had strong and diffuse cytoplasmic expression of SMA (Fig. 6). The neoplastic cells lacked expression of myogenin, MyoD1, desmin, and myoglobin, consistent with the diagnosis of LMS.

4. Discussion

Leiomyosarcoma in horses has been documented in the testicle, urogenital tract, the lung, and the bone [4–7]. Equine LMS has also been reported in the stomach [8] and duodenum [9], but, these may actually have been gastrointestinal stromal tumors because immunohistochemistry for CD117 (receptor tyrosine kinase KIT) was not performed. In the horse of this case, the primary neoplasm replaced approximately two-thirds of the skeletal musculature of the proximal left hind limb. The neoplastic mass was deeply embedded in the thigh musculature, which likely delayed clinical manifestation and allowed for the development of metastases in multiple organs including the brain and the spinal cord with resultant neurologic signs.

Leiomyosarcoma in humans is classified into several types based on the location of the neoplasm [10]. The intra-abdominal type, which occurs in the retroperitoneum, mesentery, or omentum, is the most common variant, accounting for almost 50% of all LMS. Most of these neoplasms have poor prognosis. The cutaneous type is thought to originate from the arrector pili muscle and typically presents as a small nodule in the dermis with optimistic prognosis by complete resection. The vascular type, derived from the tunica media of blood vessels, is rare. Its most