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Extramedullary plasmacytoma in a horse with ptyalism and dysphagia

Sandra McConkey, Alfonso López, John Pringle

Abstract. A Clydesdale mare was examined for weight loss, inappetence, ptyalism, and dysphagia. The main abnormality revealed by serum biochemistry was a marked hyperglobulinemia, and protein electrophoresis revealed a monoclonal gammopathy in the gamma region. The urine was positive for Bence Jones proteins. These findings suggested a plasma cell tumor. The neoplasm could not be located with extensive antemortem examination. At postmortem, neoplastic cells morphologically compatible with plasma cells and positive for equine IgG with immunoperoxidase staining infiltrated the pericardium, mediastinal stromal tissues, adrenal glands, meninges, atrioventricular valves, aorta, abdominal and thoracic fat, and nerves, including the trigeminal nerve. The neoplastic cells invading the cranial nerves were responsible for many of the presenting signs.

A 10-year-old 604-kg Clydesdale mare was referred to the Veterinary Teaching Hospital at the Atlantic Veterinary College (AVC) for weight loss, inappetence, ptyalism, and apparent dysphagia of several weeks duration. A complete blood count and a serum biochemistry profile evaluated by the referring veterinarian 2 weeks earlier showed no significant abnormalities. The mare had not responded to a short course of intramuscular procaine penicillin.

On physical examination at the AVC, the mare had a poor hair coat, normal pulse and rectal temperature, and an increased respiratory rate of 40 breaths/minute. Frequent chewing motions were observed, with saliva dripping from the muzzle. Further examination included a detailed inspection of the oral cavity and endoscopic evaluation of the pharynx, guttural pouches, upper esophagus, and trachea. During endoscopic examination, the only abnormalities were a weak swallow reflex when the endoscope made contact with the laryngeal structures and a large pool of clear tenacious fluid in the distal trachea. The tracheal fluid was aspirated for examination. Cytologic evaluation revealed low numbers of large squamous epithelial cells and numerous bacteria, which was characteristic of saliva. The roots of the teeth were radiographed, but no abnormalities were observed. A clinical diagnosis of dysphagia of unknown neurologic origin was made. No other cranial nerve deficits or gait abnormalities were observed on neurologic examination.

Blood was submitted for a complete blood count (CBC) and a serum biochemical profile. The CBC revealed a mild leukocytosis ($16.8 \times 10^9/\text{liter}$; reference range, $5.5\text{--}12.5 \times 10^9/\text{liter}$) characterized by a mild mature neutrophilia ($8.568 \times 10^9/\text{liter}$; reference range, $2.7\text{--}6.7 \times 10^9/\text{liter}$) and a mild lymphocytosis ($8.2 \times 10^9/\text{liter}$; reference range, $1.5\text{--}5.5 \times 10^9/\text{liter}$). The only significant change on the biochemical profile was a marked hyperproteinemia (102 g/liter; reference range, 60–77 g/liter) caused by a hyperglobulinemia (72 g/liter; reference range, <40 g/liter). Protein electrophoresis showed a narrow spike in the gamma globulin area supportive of a monoclonal gammopathy (Fig. 1). Urine was

tested for Bence Jones proteins.^{1,8} The results were ambiguous with heat precipitation but were positive using a toluene sulfonic acid test,² which supported the diagnosis of a plasma cell tumor. Differential diagnosis for dysphagia of neurogenic origin also included lead toxicity and equine protozoal myelitis (EPM). Lead concentration in heparinized blood was 30 ppb (normal, <250 ppb), and a Western blot procedure using serum to check for EPM was negative.

Bone marrow was aspirated from the sternum, and radiographs of the cervical and spinous process were taken in an attempt to make a definitive diagnosis of plasma cell myeloma. The results from these tests were normal. Although neoplasia could not be confirmed with these examinations, a tentative diagnosis of plasma cell myeloma was made based on the monoclonal gammopathy and presence of Bence Jones proteins.^{1,7,9–11,13} The mare returned home because the owner wished to try alternative therapy. The mare died 2 weeks later and was returned to the AVC for a postmortem examination.

At necropsy, the horse was in good body condition. The thoracic cavity contained 2 liters of transparent yellow fluid, and the mediastinal tissues, particularly around the aorta and esophagus, appeared notably thickened. There were small amounts of clear fluid in the pericardial sac, and the wall of the pericardium was diffusely thickened because of infiltration of a pale, slightly gelatinous material. The semilunar valve, pulmonary artery, and tricuspid valve had a nodular appearance. Mesenteric lymph nodes and spleen were essentially normal, and the liver showed a discrete zonal pattern. Excessive perirenal stromal tissue covered both adrenal glands. Edema was noted in muscles of the hind legs, and the popliteal lymph nodes were enlarged and diffusely pale on cut surfaces. The cervical spinal pachymeninges had two locally extensive areas ($2.0 \times 2.0 \times 0.03$ cm) of red discoloration.

Microscopically, there was a neoplastic mononuclear cell infiltrate within the pericardium, mediastinal stromal tissues, adrenal glands, meninges, atrioventricular valves, aorta, abdominal and thoracic fat, and nerves (Fig. 2), including the cranial nerves. Bone marrow examined from multiple sites was negative for tumor cells. Neoplastic cells were characterized by slight pleomorphism, scant cytoplasm, and a prominent Golgi zone. There was 2-fold anisokaryosis, 1 or more conspicuous nucleoli, and 1 or 2 mitotic figures per $400\times$ field. The cytoplasm and cell membrane of many neo-

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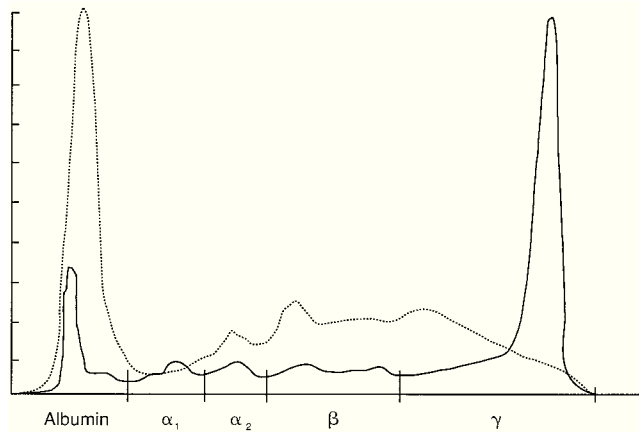


Figure 1. Electrophoretograms. Serum of affected mare (solid line) showing the monoclonal gammopathy, and serum of a normal horse (dotted line).

plastic cells were positive for equine IgG using immunoperoxidase staining with a primary antibody of rabbit anti-horse IgG and a secondary antibody of goat anti-rabbit conjugated with horseradish peroxidase.^a These morphologic and immunostaining characteristics were indicative of a plasma cell tumor. Congo red stains for amyloid were negative.

Plasma cell tumors are uncommon neoplasms that have been reported in several species, including humans, cats, dogs, and horses.^{1,11,12,14} In humans, these tumors are classified as secretory if they produce significant quantities of a monoclonal antibody or as nonsecretory if no antibody is produced. Monoclonal gammopathies can be associated with plasma cell myelomas, macroglobulinemias, some malignant lymphomas, chronic lymphocytic leukemia, canine ehrlichiosis, and benign idiopathic monoclonal gammopathies.⁹

Plasma cell myelomas,¹¹ malignant lymphomas,¹⁵ and idiopathic monoclonal gammopathies¹³ have all been reported in the horse.

Plasma cell tumors are also commonly classified by their location.¹ Myelomas are single neoplasms of malignant plasma cells within the bone marrow; they may or may not progress to multiple sites. Extramedullary plasmacytomas do not involve the bone marrow. Plasma cell leukemias have $>2 \times 10^9$ circulating plasma cells per liter, and these cells comprise at least 20% of the total differential cell count.¹ Extramedullary myelomas in the horse have been reported in the lymph nodes, spleen, liver, lung, brain, and orbit.¹⁰ This horse had a secretory extramedullary plasmacytoma involving several nerves and connective tissue. Protein electrophoresis of this horse's serum revealed a monoclonal gammopathy. Unfortunately, no serum was available for immunoelectrophoresis to specifically define the paraprotein. However, the positive staining of IgG with immunoperoxidase within malignant cells suggests that the paraprotein was IgG. IgG is the most common paraprotein in both horses and humans.⁵ It can be associated with a hyperviscosity syndrome. Although the viscosity was not determined here, there were no clinical signs such as bleeding or a retinopathy to indicate its presence.

Plasma cell tumors occur following neoplastic transformation of an early B cell that retains the ability to mature to a plasma cell. Clinical signs vary with the location of the neoplasm and the quantity of paraproteins produced by the neoplastic cells. In the horse, clinical signs are generally nonspecific and include weight loss, anorexia, fever, increased susceptibility to infections, and limb edema.¹⁰ Neurologic signs such as hind end ataxia progressing to paralysis have been previously reported in horses with plasma cell tumors within the spinal canal compressing the spinal cord.⁷

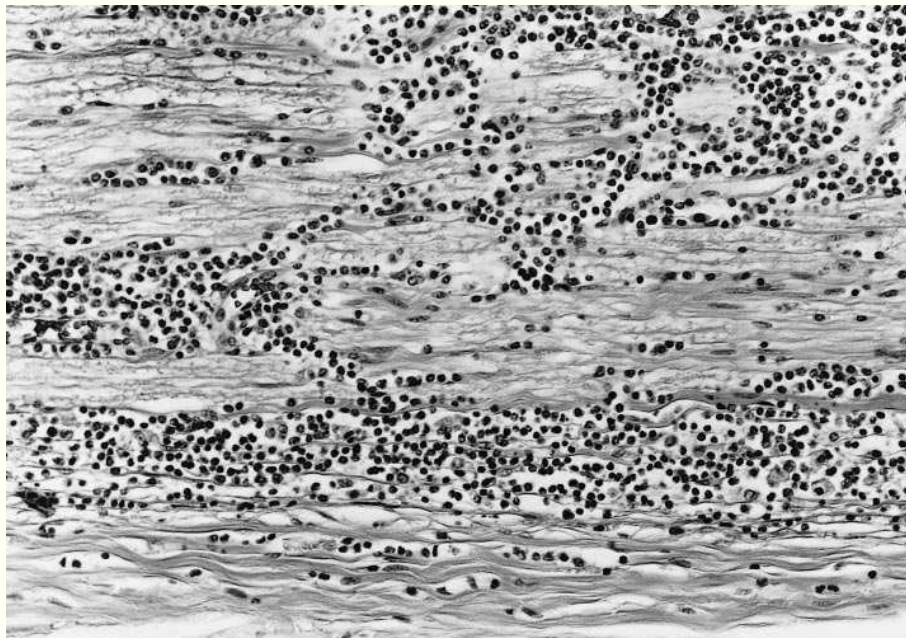


Figure 2. Peripheral nerve showing extensive infiltration and separation of fibers by large numbers of neoplastic round cells.

In dogs, pathologic fractures of the vertebrae,⁴ extradural masses,³ and hyperviscosity due to the presence of high concentrations of paraproteins within the blood have all been associated with neurologic signs.⁵ The presenting signs of dysphagia and ptyalism in this horse were attributed to neoplastic involvement of the trigeminal nerve. To our knowledge, these clinical signs have not been previously reported in plasma cell myeloma in the horse.

In humans, Waldenstrom's macroglobulinemia can cause a peripheral neuropathy that is characterized by a marked monoclonal gammopathy of IgM. In some patients, the IgM acts as an antibody to various glycolipids or glycoproteins in the myelin, such as myelin-associated glycoprotein, and can cause complement-mediated demyelination.^{1,6} This condition has not been reported in horses but could explain the distribution of neoplastic cells and subsequent dysphagia. Marek's disease in chickens can produce a similar neoplastic infiltration by lymphoproliferative cells into peripheral nerves.⁵

The distribution of the neoplastic cells in this horse was very unusual because the plasma cell infiltrate did not involve the bone marrow or the usual tissues involved in equine extramedullary plasmacytomas (typically liver, spleen, or lymph nodes). Rather, the neoplastic cells were most prevalent in nervous and connective tissue.

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Primary hepatic hemangiosarcoma with pulmonary metastasis in a New Zealand White rabbit

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Hemangiosarcoma is a malignant tumor of endothelial cells that occurs more frequently in dogs than in any other species of domestic animals.⁷ Incidences of canine hemangiosarcoma range from 0.3% to 2%, with a mean age at occurrence of 8–10 years.^{2,13} The spleen and heart are the most common sites of occurrence, and the pattern of metastasis varies with the location of the primary tumor. Splenic

hemangiosarcomas more commonly metastasize to other abdominal organs, and cardiac hemangiosarcomas typically metastasize to the lungs. Tumors of vascular origin in lagomorphs have rarely been reported in the literature. One case designated at the time as a malignant peritoneal endothelioma was described in 1927,¹² and a benign ovarian hemangioma was reported in 1949.⁶ In a more recent report in 1984, hemangiosarcoma was described in both a wild rabbit and a laboratory New Zealand White rabbit.¹¹ The site of origin in the wild rabbit was judged to be the soft tissues of the subcutis, and many visceral organs were involved, in-

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