

In dogs, pathologic fractures of the vertebrae,<sup>4</sup> extradural masses,<sup>3</sup> and hyperviscosity due to the presence of high concentrations of paraproteins within the blood have all been associated with neurologic signs.<sup>5</sup> 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.<sup>1,6</sup> 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.<sup>5</sup>

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

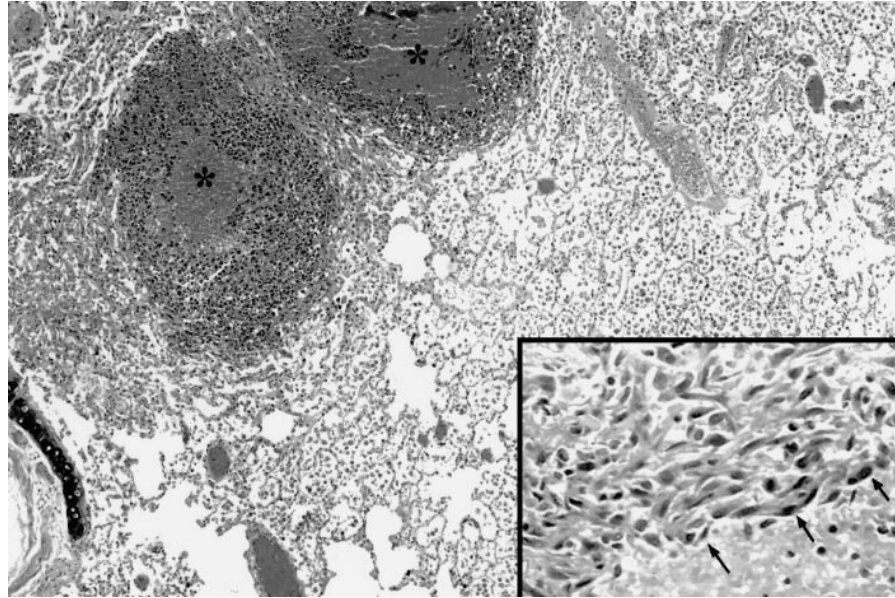
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Hemangiosarcoma is a malignant tumor of endothelial cells that occurs more frequently in dogs than in any other species of domestic animals.<sup>7</sup> Incidences of canine hemangiosarcoma range from 0.3% to 2%, with a mean age at occurrence of 8–10 years.<sup>2,13</sup> 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,<sup>12</sup> and a benign ovarian hemangioma was reported in 1949.<sup>6</sup> In a more recent report in 1984, hemangiosarcoma was described in both a wild rabbit and a laboratory New Zealand White rabbit.<sup>11</sup> 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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**Figure 1.** Lung; New Zealand White rabbit. Neoplastic pulmonary nodules with blood-filled cavernous spaces (stars). *Insert:* higher magnification of spindle cells lining a blood-filled cavernous space (arrows). HE.

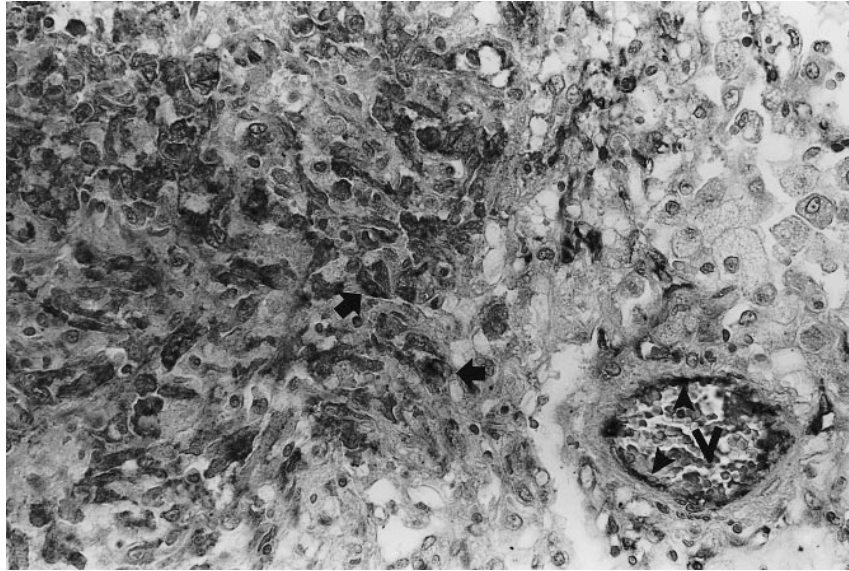
cluding the intestines, liver, and heart. The New Zealand White rabbit was euthanized for serum collection, and multiple liver and pulmonary nodules were found that were diagnosed histologically as hemangiosarcoma; however, neither the primary site nor the age of this animal were specified. Here, we describe the unexpected death of an aging laboratory New Zealand White rabbit from acute hemoperitoneum due to primary hepatic hemangiosarcoma. The endothelial phenotype of this tumor was demonstrated by immunohistochemical detection of the endothelial cell marker CD31.

A 5-year-old 4.5-kg male New Zealand White rabbit from a conventional colony was maintained for the production of immunoglobulins. The animal was found dead in its cage without premonitory signs and was submitted to the diagnostic laboratory for a complete pathologic examination. The rabbit was in good body condition and had a slightly distended, fluctuant abdomen. Markedly pale mucous membranes, subcutis, and musculature were also noted. Approximately 150 ml of partially clotted blood was present in the peritoneal cavity. Multiple dark red to black round, fluctuant nodules ranging from pinpoint to 2.5 cm in diameter were on the capsular surface of the liver. The larger nodules were confluent along the ventral border of the liver, and there was a focal area with adherent clotted blood and fibrin. Additional nodules were embedded in the parenchyma and consisted of irregular blood-filled cavities of various sizes. The lungs had multiple, uniformly disseminated pinpoint to 4-mm slightly raised, pale gray, and dark red nodular foci over the pleural surface and throughout the parenchyma. The dark red foci were rimmed by a narrow zone of pale gray discoloration. Tissues taken at necropsy were fixed by immersion in 10% neutral buffered formalin, routinely processed, embedded in paraffin, sectioned at 5  $\mu$ m, and stained with hematoxylin and eosin (HE).

Microscopically, the liver was characterized by multifocal,

poorly circumscribed blood-filled cavernous spaces of various sizes. These spaces were separated from the hepatic parenchyma by streams of plump, tightly packed spindle cells that in many cases extended to the central aspects of the cavity to form irregular blood-filled vascular channels. Cells had poorly defined cytoplasmic boundaries with scant eosinophilic cytoplasm and a large, oval, often cleaved nucleus with finely stippled chromatin and inconspicuous nucleoli. Mitotic figures were rare. Venous thrombi were occasionally seen within the larger hepatic veins. The lungs contained numerous well-circumscribed nodular masses of various sizes composed of disorganized, tightly packed spindle cells with morphology similar to that of the masses seen in the liver (Fig. 1). Within the larger masses, the cells typically formed blood-filled cavernous spaces. In many areas, alveolar spaces contained large masses of fibrin. Numerous thrombi were also seen within the medium-size pulmonary veins. The presence of CD31 antigen was identified in the neoplastic cells by immunochemistry (Fig. 2). Staining was patchy to diffuse in the cytoplasm of most neoplastic cells, and diffuse cytoplasmic staining was present in the normal endothelial cells of the pulmonary vasculature.

The immunohistochemical detection of von Willebrand's factor (factor VIII-related antigen) is the primary method utilized in most veterinary diagnostic laboratories to aid in the diagnosis of suspected vascular tumors. Results of von Willebrand's factor (vWF) immunostain in this case were inconclusive because of intense background staining resulting from the use of rabbit polyclonal anti-vWF antibody in rabbit tissues. Platelet endothelial cell adhesion molecule (PECAM), also known as CD31, is a 100-kD glycoprotein that mediates the adhesion between platelets and endothelial cells.<sup>8</sup> CD31 is regarded as a useful marker for endothelial cells in human tissues and is recognized by the monoclonal mouse antibody JC70.<sup>9</sup> In a recent study, the same antibody also recognized CD31 antigen on canine endothelial cells



**Figure 2.** Lung; New Zealand White rabbit. CD31 immunostain of a normal pulmonary vessel (V) adjacent to a nodule of neoplastic cells. Note the cytoplasmic staining of neoplastic cells (arrows) and normal endothelial cells (arrowhead).

and was more sensitive in detecting canine vascular tumors than was anti-vWF antibody.<sup>4</sup> In this rabbit, positive staining was localized to endothelial cells from the normal pulmonary vasculature, suggesting that the antibody demonstrates specificity for rabbit CD31 in formalin-fixed, paraffin-embedded tissues. In addition, positive staining was observed in neoplastic cells, supporting an endothelial phenotype. This is the first demonstration of the utility of this antibody in rabbit tissues.

In general, spontaneous hemangiosarcomas among other commonly used laboratory animals are rare, but they have been reported in mice,<sup>5</sup> gerbils,<sup>1</sup> and rats.<sup>3</sup> The most common spontaneous neoplasm in lagomorphs is uterine adenocarcinoma, with an incidence as high as 80% in does 5–6 years of age.<sup>14</sup> Lymphoid tumors are the most common neoplasm of juvenile and young domestic rabbits.<sup>10</sup> Incidences of other less common tumors may be difficult to establish in aging populations because the rabbit is not commonly used in long-term studies. This and previous reports indicate that although sporadic in nature, hemangiosarcomas should be included in the differential list of neoplasms that may afflict aging rabbits.

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