History

An 8-year-old sexually intact male white alpaca was submitted for necropsy after being referred to a private veterinary hospital because of a history of circling and ataxia for a few hours.

Clinical and Gross Findings

Physical examination performed by the referring veterinarian did not reveal any other abnormalities, but the clinical signs rapidly progressed and the alpaca died 24 hours later. No neurologic examination was performed. At necropsy, the carcass was in good body condition. A well-demarcated, sessile, white, and firm nodule measuring 3 cm in diameter was attached to the gingival surface of the gum at the level of the right superior molar teeth. Its cut surface was diffusely white and soft. Bilaterally expanding and effacing the adrenal medullae, there were white to red, soft nodules that bulged out from the parenchyma on the cut surface. Similar nodules ranging from 2 to 4 cm in diameter also expanded the renal cortex and medulla and the left ventricular myocardium. Gastric lymph nodes were enlarged, diffusely white, and soft and had lost nodal architecture. Cerebral gyri were flattened, with subtentorial herniation of the left occipital lobe and cerebellar herniation through the foramen magnum. Bilaterally, the ventral aspect of the brainstem corresponding to the site of insertion of the trigeminal and facial cranial nerves as well as the left pyriform lobe were expanded and effaced by well-demarcated, soft, pale to tan nodules approximately 1 cm in diameter that were contiguous with the underlying areas at the base of the skull (Figure 1). Small, brown, hard, and gritty nodules ranging from 2 to 5 mm in diameter were observed on the superficial leptomeninges (1 nodule at the right cerebellopontine angle and 3 nodules at the ventrolateral portion of the left temporal lobe). There was no compression of adjacent tissues. No evidence of otitis was observed.

Formulate differential diagnoses from the history, clinical findings, and Figure 1—then turn the page →
Histopathologic Findings

The white and soft nodules grossly observed in the oral cavity, adrenal medullae, kidneys, myocardium, gastric lymph nodes, cranial nerves, and brain were examined histologically. The nodules were expansive masses composed of neoplastic round cells morphologically consistent with lymphocytes (Figure 2). Regardless of the affected organ, these neoplastic cells were arranged into closely apposed sheets supported by scant preexisting remaining tissue or collagen bundles. Individual neoplastic cells had moderate pleomorphism and a scant to moderate amount of round, eosinophilic, homogeneous cytoplasm with distinct cell borders. Nuclei were round to oval and composed of coarsely stippled or dense chromatin with 1 to 2 nucleoli and moderate anisokaryosis. Mitotic rate ranged from 0 to 3 mitotic figures/hpf (400X). Neoplastic cells were additionally observed infiltrating the subependymal spaces in the lateral ventricles with mild extension to the underlying neuroparenchyma. Replicate sections were submitted for immunohistochemical analysis with anti-CD3 and anti-CD79a antibodies. Most of the neoplastic lymphocytes had cytoplasmic immunostaining for CD79a but no immunostaining for CD3. The small superficial leptomeningeal nodules consisted of well-demarcated granulomas composed of a central area of caseous necrosis and mineralization surrounded by layers of epithelioid macrophages, multinucleated giant cells, and fewer lymphocytes and plasma cells admixed with fibrous tissue. No organisms were observed in these areas in sections stained with acid-fast, periodic acid–Schiff, or Grocott methenamine silver special stains.

Morphologic Diagnosis and Case Summary

Morphologic diagnosis: multicentric B-cell lymphoma affecting the oral cavity, adrenal medullae, kidneys, myocardium, gastric lymph nodes, cranial nerves, and brain and multifocal cerebral leptomeningeal caseous granulomas.

Case summary: multicentric B-cell lymphoma with cerebral involvement in an alpaca.

Comments

The gross and histologic findings in the alpaca of the present report were consistent with multicentric lymphoma, and the diagnosis was confirmed by the immunostaining of neoplastic cells for CD79a.1,2 Immunohistochemical analysis has been used to confirm the diagnosis of lymphoma in New World camels and to differentiate lymphoma from other neoplasms (especially neuroendocrine and primitive malignant round cell tumors) that develop in these species.2,3 It seems that B-cell lymphomas develop with slightly greater frequency than T-cell lymphomas in alpacas and llamas.2,4 The leptomeningeal caseous granulomas in the case described in this report were very small and superficial. Based on location and lesion morphology, differential diagnoses would include infection with Mycobacterium spp or a fungal organism.4 However, application of special stains to sections of the granulomas did not reveal any causative agent. The etiology of the leptomeningeal granulomas could not be determined, and given the lack of compression and reaction in the adjacent tissues, these lesions were considered incidental findings in the alpaca of this report.

Lymphoma has been identified as the most common or the second most common neoplasm in New World camelids in the United States in several retrospective studies,2,7,8 but to our knowledge, lymphoma directly involving the CNS in llamas or alpacas has not been described. Affected camels range from < 1 to 23 years of age, and no sex predilection has been reported.2,8 Nevertheless, for an unknown reason, alpacas seem to be affected by lymphoma at an early age, compared with llamas4,7;9–11; a similar early-age effect is observed with non–retrovirus-associated spontaneous bovine lymphoma in calves.12 The potential role of retroviral infection in alpacas with lymphoma is unknown; no evidence of viral infection in association with these tumors has ever been described, nor has a serologic study been reported in which antibodies against bovine leukemia virus have been detected in New World camelids affected by lymphoma.7,13

Although the common clinical picture in New World camelids affected by lymphoma includes nonspecific signs such as anorexia, signs of depression, and emaciation,7 the alpaca of this report had progressive circling and ataxia. On physical examination, animals with lym-
phoma may have peripheral lymphadenopathy; however, for the alpaca of this report, peripheral lymphadenopathy was not reported by the referring veterinarian and was not detected during necropsy. Gross inspection of the alpaca’s brain and skull revealed neoplastic invasion into the site of insertion of the trigeminal and facial nerves and left piriiform lobe, with compression of the brainstem, secondary cerebral edema, flattening of gyri, and left occipital lobe and cerebellar herniation. In addition, microscopic examination of sections of nodules revealed that neoplastic cells had also expanded and infiltrated the subependymal spaces in the lateral ventricles and the underlying neuroparenchyma. Although some camels with lymphoma may develop clinical signs such as paresis and recumbency, which may therefore mimic a primary neurologic syndrome, it should be considered that these clinical signs may be attributable to severe debilitation caused by the widespread neoplasia.

On the basis of the gross and microscopic findings in the cranial nerves and brain, the clinical signs in the alpaca of this report were attributed directly to CNS involvement, with death most likely culminating from respiratory failure due to compression of the brainstem. Circling and ataxia may become apparent because of lesions in the cerebrum, brainstem, cerebellum, or cranial nerves. It is likely that the clinical signs in this alpaca were associated not only with the primary neoplastic infiltration of cranial nerves, brainstem, and piriiform lobe, but also with the secondary compression of adjacent structures (potentially compromising the vestibulocochlear nerve) and diffuse cerebral and cerebellar edema. Despite the lack of reports of lymphoma with direct involvement of the CNS parenchyma in camels, rare cases of lymphoma in alpacas with invasion of the spinal canal, outer surface of the spinal dura mater, and nerve roots have been reported. In those cases, neoplastic cells were detected only after microscopic examination, and no masses were grossly observed during necropsy. Similarly, it is well-known that lymphoma in cattle may cause neurologic signs as a result of invasion of the spinal canal and secondary spinal cord compression. However, similar to what seems to occur with camels, cases with direct nervous tissue compromise among cattle have been rarely reported.

The multicentric nature of lymphoma in the case described in the present report is consistent with previous descriptions of lymphoma in New World camels. Moreover, it appears that the liver and kidney are organs that are consistently affected in these cases, although we did not find any evidence of hepatic involvement in the alpaca of this report.

Clinical differential diagnoses for circling and ataxia in New World camels should include infection with Parelaphostrongylus tenuis, otitis media or interna, listeriosis, polioencephalomalacia, eastern equine encephalitis virus infection, West Nile virus infection, and rabies. No microscopic evidence of parasitic, bacterial, or viral encephalitis was observed in the alpaca of the present report. The small leptomeningeal granulomas could indicate a potential previous bacterial infection, but no causative agent was identified in these lesions.

References