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Pathology in Practice

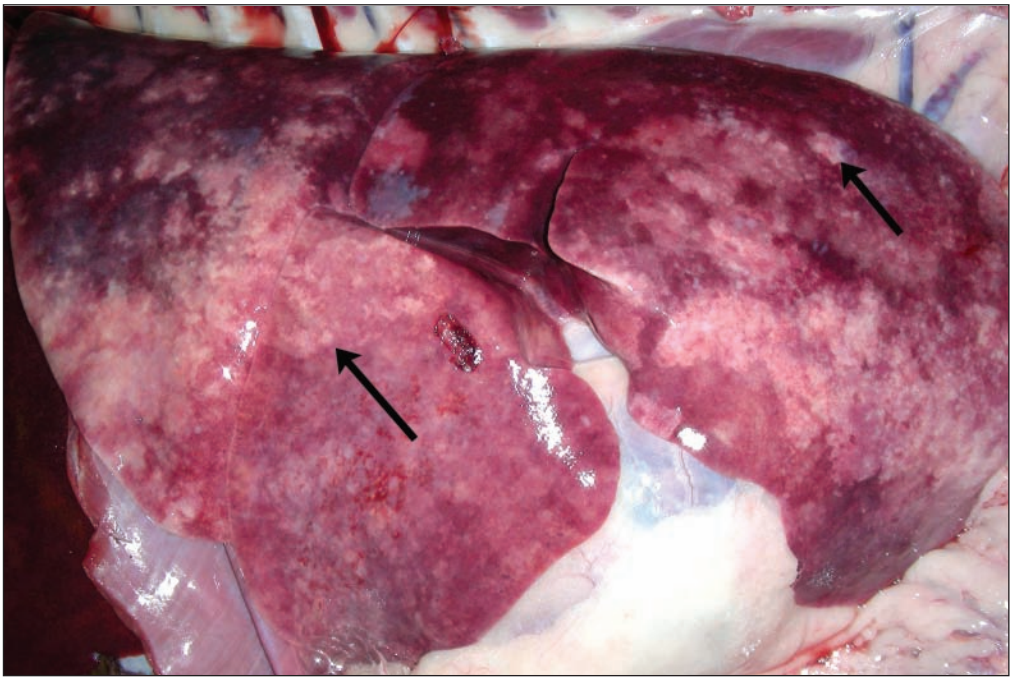

Figure 1—Photograph of the thoracic cavity of a 2-year-old male dog that had a 1-month history of lethargy and anorexia and 5-day history of coughing, ataxia, and weakness. Notice that the lungs are poorly collapsed, heavy, meaty, and mottled dark red to pale pink and that the pleural surface contains numerous, multifocal to coalescing, discrete white consolidated areas (arrows).

History

A 2-year-old sexually intact male German Shepherd Dog was evaluated at the Veterinary Teaching Hospital at the University of Illinois College of Veterinary Medicine because of a 1-month history of lethargy and anorexia and a 5-day history of coughing, ataxia, and weakness. The dog's vaccination history was unknown.

Clinical and Gross Findings

Upon initial examination, the dog was ataxic yet able to walk, had delayed proprioception in the hind limbs, and had signs of severe pain, especially throughout the caudal aspect of the lumbar region and hind limbs. Bilateral corneal ulcers and absent corneal reflexes were also observed. Test results indicated that the dog was negative for heartworm and canine parvovirus infection. Titers of serum antibodies against *Blastomyces* spp and *Histoplasma* spp were not suggestive of infection.

The dog was euthanized and underwent necropsy. Gross examination revealed that the dog was in good body condition. Upon opening the thoracic cavity, the lungs were poorly collapsed, heavy, and mottled dark red to pale pink; the pleural surface contained numerous, pinpoint, multifocal to coalescing, discrete white consolidated areas (**Figure 1**). The parenchyma was diffusely dark red and wet and exuded red semiopaque fluid on the cut surfaces.

Bilaterally, the corneas contained central ventrally located acute ulcers that were approximately 2 X 2 mm. No remarkable gross lesions were observed in other organs, including the brain and spinal cord.

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

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Histopathologic Findings

Multifocally, the bronchi and bronchioles were denuded or lined by epithelial cells that were shrunken, hypereosinophilic, and pyknotic (necrosis); swollen with pale vacuolated cytoplasm (degeneration); hypertrophied with vesiculate nuclei and basophilic cytoplasm (regeneration); or attenuated (**Figure 2**). Often, the terminal bronchiolar lumina were obliterated by granulation tissue admixed with desquamated epithelial cells, neutrophils, macrophages, lymphocytes, plasma cells, and pyknotic and karyorrhectic cellular debris. The alveolar spaces were flooded by numerous alveolar macrophages with large foamy cytoplasm, abundant fibrin, necrotic debris, and eosinophilic proteinaceous fluid. The alveolar septa were regionally lined by type 2 pneumocytes and were thickened by edema and moderate numbers of macrophages, lymphocytes, plasma cells, and neutrophils. The pleura, interlobular septa, and adventitia of the larger vessels were expanded by edema. Small to moderately sized perivascular and peribronchial aggregates of lymphocytes, plasma cells, and epithelioid macrophages were also present.

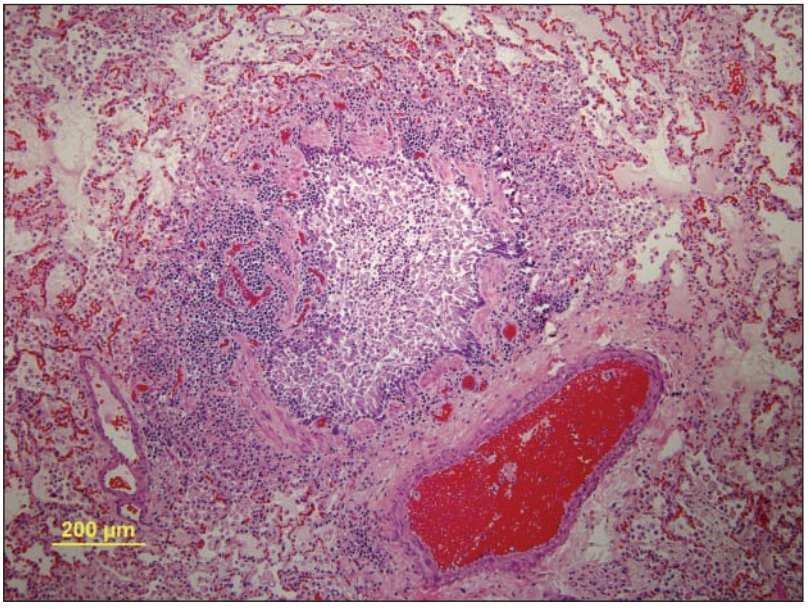

Figure 2—Photomicrograph of a section of lung tissue obtained from the dog in Figure 1. Notice that the bronchiole is surrounded by large numbers of inflammatory cells and is lined by attenuated epithelium. The bronchiole lumen contains desquamated cells admixed with inflammatory cells. The surrounding smooth muscles are hyperplastic, and the alveolar spaces are flooded by moderate numbers of vacuolated macrophages and edema. H&E stain; bar = 200 µm.

Microscopic examination of sections of the brain and spinal cord revealed expansion of the Virchow-Robin spaces throughout the white and gray matter by many lymphocytes and plasma cells and fewer macrophages. Similar inflammatory cells were also observed within the leptomeninges. Multifocally, the gray and white matter were rarified and infiltrated by large numbers of macrophages, lymphocytes, and plasma cells, and random aggregates of microglial cells (glial nodules; **Figure 3**). Several neurons were hypereosinophilic, shrunken, and angular and contained eccentrically located nuclei and centrally dispersed Nissl substance (necrosis). Within the brain, the glial cells and neurons occasionally contained a single intranuclear eosinophilic viral inclusion with peripheral aggregation of chromatin (**Figure 4**). Multiple spheroids with swollen and hypereosinophilic axons were also scattered throughout the white matter of the spinal cord. The spinal cord changes were observed throughout its entire length, with the most severe lesions present within the lumbar region.

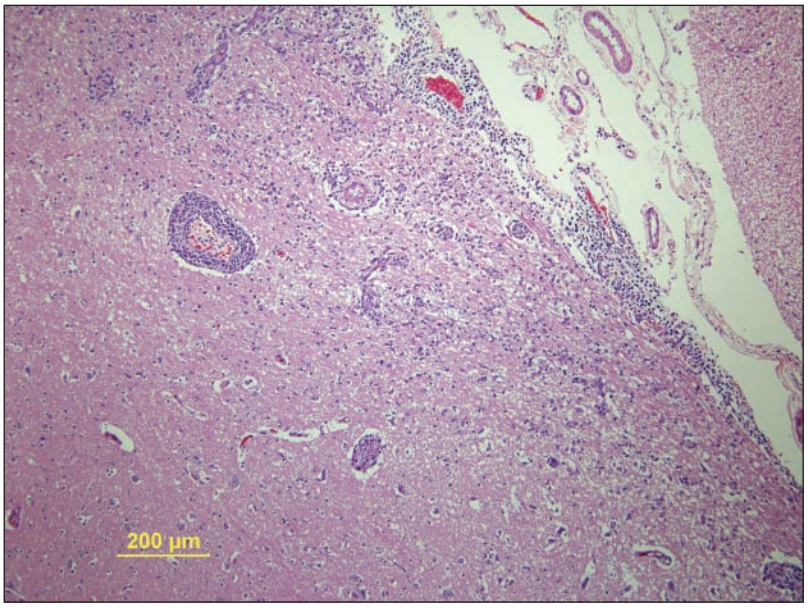

Figure 3—Photomicrograph of a section of brain tissue obtained from the dog in Figure 1. Notice that moderate numbers of inflammatory cells are present in Virchow-Robin spaces and perivascular regions in leptomeninges. The superficial cortex is rarified and contains scattered inflammatory cells. H&E stain; bar = 200 µm.

Morphologic Diagnosis

Severe, chronic, multifocal to diffuse, necrotizing bronchointerstitial pneumonia with bronchiolitis obliterans; marked, chronic, multifocal, lymphoplasmacytic, and histiocytic meningomyelitis with intranuclear eosinophilic inclusions; and marked, chronic, multifocal, lymphoplasmacytic and histiocytic meningoencephalitis with glial nodules and intranuclear eosinophilic inclusions.

Comments

For the dog of this report, the gross and histopathologic lesions in the lungs and CNS along with viral inclusions were consistent with a diagnosis of dis-

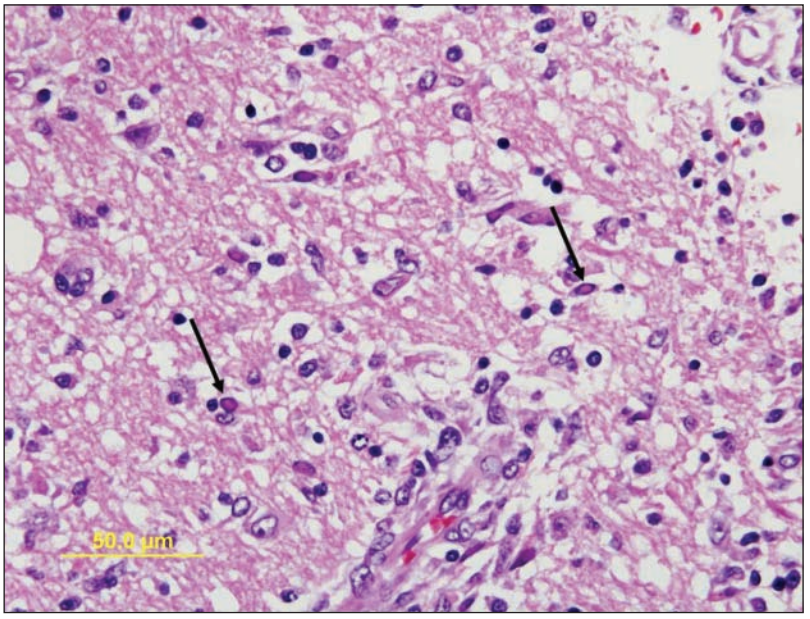

Figure 4—Photomicrograph of a section of brain tissue obtained from the dog in Figure 1. Notice that small numbers of glial cells, lymphocytes, plasma cells, and macrophages are present in the rarified neuropil. Often, glial cells and neurons contain a single, eosinophilic, intranuclear inclusion (arrows) with peripherally aggregated chromatin. H&E stain; bar = 50 µm.

temper. This diagnosis was corroborated by results of immunohistochemical analysis of sections of the lungs and CNS, which indicated that those tissues were positive for canine distemper virus (CDV). Although intranuclear inclusion bodies were present in cells throughout the brain and spinal cord, no inclusion bodies were observed within cells in the lungs, despite the positive results of immunohistochemical analysis.

Distemper in dogs is caused by CDV, which is a member of the genus Morbillivirus in the family Paramyxoviridae.[1] Canine distemper virus infects all families of terrestrial carnivores, including Canidae, Felidae, Hyaenidae, Mustelidae, Procyonidae, Ursidae, and Viverridae.[1]

Clinical signs of systemic infection with CDV primarily involve the CNS and respiratory and gastrointestinal systems and are most common in young dogs that are exposed to the virus when passive immunity is declining (ie, at 3 to 4 months of age).[2] Infection with CDV can also result in ocular disease, cutaneous lesions, dental defects, and abortions.[3,4] Canine distemper virus is pantropic and can cause immunosuppression via viral-mediated necrosis of lymphocytes; therefore, clinical signs are often exacerbated by secondary infections, including *Bordetella* infection, adenovirus infection, pneumocystis infection, toxoplasmosis, Tyzzer's disease, sarcocystosis, encephalitozoonosis, cryptosporidiosis, and *Escherichia coli* infection.[2,5]

In dogs infected with CDV, the disease process has an acute systemic phase that may be followed by a chronic phase characterized by demyelization throughout the CNS.[5] At the acute stage, the virus, which is usually acquired via inhalation, infects local macrophages within the nasal mucosa.[6] The virus then spreads to regional lymph nodes, where viral replication ensues, leading to a primary viremia.[6] Two to 6 days after exposure, the virus is present in all lymphoid tissues throughout the body.[2,5–7] During this acute phase of lymphoid system infection, profound immunosuppression develops and clinical signs include serous nasal and ocular discharge, conjunctivitis, anorexia, fever, signs of depression, vomiting, and diarrhea.[2,5]

A second phase of viremia develops 5 to 9 days after exposure, during which the virus is present within leukocytes and free in the plasma; these leukocytes spread the virus to infect the CNS and epithelial cells of the respiratory, urinary, and gastrointestinal tracts.[2,5,7,8] However, further disease progression toward the chronic stage of distemper is dependent on the immune status of the infected dog. Dogs with high titers of neutralizing antibodies and adequate cellular immunity can clear the virus with complete recovery by 2 weeks after initial exposure.[2] In dogs with less efficient immune responses, the disease could progress, resulting in CNS signs, including convulsions, myoclonus, nystagmus, ataxia, postural reaction deficits, hyperesthesia, paralysis, and blindness.[2,5] In addition to neurologic abnormalities, dogs with inadequate immune responses often develop a systemic infection of the epithelial tissues, resulting in clinical signs of respiratory tract and enteric diseases, with shedding of the virus in respiratory secretions, feces, and urine.[2]

Canine distemper virus can reach the CNS via leukocytes or hematogenously via infected platelets.[9] Once in the CNS, CDV can invade astrocytes, microglia, oligodendrocytes, neurons, ependymal cells, and choroid plexus cells.[5] Infected oligodendrocytes are directly affected by the virus, ultimately leading to the characteristic lesions of demyelination; however, astrocytes are the main cell population that is typically infected.[5,6]

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