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Aetiopathogenesis
Canine distemper virus (CDV) belongs to the Morbillivirus genus and the Paramyxoviridae family. It is relatively large (120-250 nm) and has a nucleocapsid with helical symmetry whose genetic code is in the form of a simple RNA. The nucleocapsid is enclosed in a lipoprotein envelope which contains membrane glycoproteins with different biological functions. CDV produces proteins which enter the membranes of infected cells making them susceptible to attack by the immune system as well as being able to induce cell fusion by direct dissemination.

The virus is weak under adverse conditions and easily destroyed by UV light and high temperatures. Routine disinfection of dog pounds and hospitals with quaternary ammonium, or phenols, is capable of destroying it. In addition to the domestic dog, other species may also be affected including the bear, lion, tiger, civet, ferret, wolf, etc.

The virus is transmitted by inhalation, direct contact with bodily fluids including urine, or transplacental, up to 60-90 days after infection. Immunity after the disease lasts throughout entire life of the animal, which does not occur with the vaccination. The development of the disease depends on the immune response of the individual. It is estimated that 25-75% of dogs are susceptible to developing the sub-clinical disease, but eliminate the virus without clinical manifestations. Although the majority of these individuals completely eliminate the virus, some may retain it in the CNS. There is a lower disease prevalence and mortality in brachycephalic breeds compared with dolichocephalic breeds.

Following natural exposure to the virus, viral replication occurs in the lymphatic tissue of the upper respiratory system during the first 24h. After 4-6 days, there is extensive distribution of the virus to other lymphoreticular tissues as a result of viraemia; it presents clinically with fever and analytically with lymphopenia. After 8-9 days, the virus reaches epithelial tissues, which translates to its distribution in bodily secretions and in the CNS. At this point, two things may occur: if the animal is capable of maintaining adequate immune response, the virus may be eliminated prior to presenting any clinically evident signs. Otherwise, if the immune system is incapable of eliminating the virus at this stage, the animal will present clinical signs that may resolve if there is adequate immune response a posteriori. If the animal is immunocompromised, the infection develops into the clinical disease leading to death. Irrespective of the immune response, CNS distribution of the virus may occur. This occurs through haematogenous dissemination and from the choroid plexus via the CSF, which explains the periventricular and subpial distribution of the lesions. The type of CNS lesions will depend on multiple factors such as age, immunocompromised state and the neurotrophic and immunosuppressor nature of the virus.

Clinical manifestations
Young unvaccinated or immunocompromised animals often develop systemic disease with the presence of ocular, nasal, respiratory and/or gastrointestinal signs. These may progress to neurological disease in 1-3 weeks. The presence of pustular or vesicular dermatitis is often associated with the CNS disease; however, the presence of hyperkeratosis is associated with various neurological signs. The analytical results are characterised by the presence of absolute lymphopenia. Blood extension observations
demonstrate the presence of intracytoplasmatic inclusions in circulating lymphocytes, erythrocytes and monocytes. An interstitial lung pattern may be detected in the chest x-rays during the early or alveolar phase if there is a bacterial complication. If the animal develops neurological signs, these are characterised by seizures, mental state disturbances, circling, blindness and myoclonus. The CNS lesions observed are typical of widespread acute encephalitis (polioencephalomalacia).2

In vaccinated animals, the development of neurological complications would depend on the immune status at the time of exposure and the virulence of the virus. These animals may develop sub-clinical systemic disease or may present minimal clinical signs (loss of appetite, fever, etc.). The virus may penetrate the CNS and cause subacute or chronic encephalitis characterised clinically by multifocal neurological signs (vestibular, cerebellar, postural deficits, paralysis, etc.). Lymphopenia may not occur in these cases. Analysis of the CSF may demonstrate slight lymphocytic pleocytosis.3 Histopathologically, CNS lesions may present lymphocytic infiltration in the perivascular cuffs, vacuolization of the white matter (demyelination), astrocytosis and malacia affecting mainly, but not exclusively, the cerebellum and the telencephalon. Viral inclusions are found mainly, but not exclusively, in astrocytes.

In immunocompetent animals, capable of developing adequate immune response, the virus may persist in the CNS after sub-clinical infection leading to the appearance of chronic and progressive inflammatory disease of the grey matter of the cerebral hemispheres and the encephalic trunk. This is called “Old Dog Encephalitis” and is characterised by the presence of perivascular cuffing and, occasionally, viral inclusions. Since being first described, few cases of this clinical manifestation have been reported.

Cases of post-vaccinal distemper have been described in association with the administration of the live virus in animals not previously vaccinated.4 Clinical signs are characterised by pyrexia, anorexia, aggressive episodes, haemorrhagic diarrhoea and ataxia. In these cases, pathologic lesions are restricted to the encephalic trunk and the posterior horn of the spinal cord. It is common to find intranuclear inclusions while intracytoplasmic inclusions are less common in the neurons of these locations, associated with perivascular cuffing but with no inclusions in other organs of the body.

**Diagnostic protocol**

In the case of unvaccinated or immunocompromised animals, serum values are unreliable due to possible false negatives (immunosuppression caused by virus). If there are systemic clinical signs, the virus may be detected in bodily fluids (urine, CSF, serum, blood, saliva and faeces) using RT-PCR, identification of intracytoplasmatic inclusions in CSF or blood, or using immunodiagnostic techniques for biopsies or cytology.

The greatest diagnostic challenge is with vaccinated animals that only present neurological signs. Serum values are not useful in these cases due to possible false negatives. However, the comparison of serum values and CSF in distemper and parvovirus may help diagnosis due to the local immunoglobulin production in the CNS. RT-PCR can identify the virus in blood, serum or CSF in some cases. Recently vaccinated animals (<14 days) may be positive for the vaccine strain with this test and the positive has been detected several months after vaccination (personal observation). Unfortunately, in the majority of cases, a definitive diagnosis can only be reached with CNS immunohistochemical autopsy findings.

In cases of post-vaccine encephalitis, diagnosis is possible by demonstrating the virus in the CNS in the autopsy due to the eminent neurotropic nature of the vaccine strains.

**Treatment**

Despite the advances in our understanding of the pathophysiology of the disease in recent years, treatment continues to be supportive. The aim is prevention of the disease itself or of secondary...
infections and treatment of the clinical signs associated with the disease (seizures, gastroenteritis, pneumonia...). The majority of animals overcome the systemic disease with the exception of neurological signs. Onset of seizures leads to poorer prognosis, irrespective of the clinical form of the disease. The development of vesicular disease leads to good prognosis as this indicates adequate antibody production.

**Prevention**

In spite of the possibility of post-vaccinal distemper, the best method to prevent the disease is vaccination with a live attenuated virus. Increased serum levels ($\geq 1/100$) after vaccination protects against the disease. The magnitude of this increase in serum levels depends to a large extent on the type and brand of the vaccine used. Current guidelines recommend revaccination every 2-3 years. The administration of chemotherapy or immunosuppressive doses of glucocorticoids for three weeks does not appear to affect the humoral immune response in regularly vaccinated animals.

**References**