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Review Article

Canine Distemper, Clinical Update, Based on our Medical Experience and Scientific Evidence

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Abstract

The objective of this research is to provide the clinical update of the canine Distemper, based on our experience with medical practice and scientific evidence, to provide updated support to multidisciplinary medical teams, to describe, address, and identify the most useful methods For diagnosis, apply urgent therapies to try to reduce the high morbidity and mortality caused by this health phenomenon, and be able to predict, considering that it is the most aggressive among many of the pathologies that canines present today and other non-domestic species. It was investigated, between the months of September to December 2021, analyzing the data collected to have a current vision of the behavior of this lethal noxa.

Keywords: Canine Distemper; Diagnosis; Treatments; Prognoses

Abbreviations

PCR: Polymerase Chain Reaction; CDV: Canine Distemper Virus; RNP: Ribonucleoprotein Complex; RNA: Ribonucleic Acid; mRNA: Messenger RNA; RNP: Ribonucleoprotein Complex; CNS: Central Nervous System; CD: Canine Distemper; EOG: General Objective Examination; Ag: Antigen; Ac: Antibody; IIF: Indirect Immunofluorescence; ELISA: Enzyme-Linked Immunosorbent Assay; IgM: Immunoglobulin M; IgG: Immunoglobulin G; CSF: Serological Analysis of Cerebrospinal Fluid; IFA: Fluorescent Antibodies; AgNP: Silver Nanoparticles

Introduction

The canine distemper virus (CDV) causes a multisystemic, highly contagious, cosmopolitan disease, named canine Moquillo, being the most widespread and lethal that occurs in canids [12]; being fatal in immunosuppressed puppies and dogs, it presents multiple cellular tropism (epithelial, lymphoid and neurological) mainly affecting the digestive tract, respiratory and nervous systems in many species [16]; it constitutes one of the most complex noxas when it comes to issuing a confirmatory diagnosis; is the first cause of death in canines due to infectious disease, it is believed that it originated in Spain in the eighteenth century, however, according to historical, molecular and epidemiological evidence, CDV would have originated in South America from the infection and adaptation of measles virus in dogs [20]. The disease has a very variable course and has several ways of presenting itself; Not all clinical signs are present, or at least not in a strictly ordered manner, depending on several factors such as the viral strain and the patient's immunological status [13]. As it is a viral disease that involves different organs and systems, conventional treatment is non-specific and supportive, due to the lack of specific treatments with antiretroviral drugs, so they must be adapted to each particular case.

After rabies, this noxa is recognized as the infectious disease that produces the second highest mortality rate in domestic dogs [23].

The objective of this research is to provide a clinical update, based on our experience with medical practice and scientific evidence.

Taxonomy and viral structure

This biological agent belongs to the order Mononegavirales, family Paramyxoviridae, genus Morbillivirus, pleomorphic, spherical, highly contagious, with a wide range of hosts, the majority belonging to the families of the order Carnivora, within it we have the family Canidae, Procyonidae, Mustelidae, Hienidae, Ursidae and Viverridae; It has also been described that it can affect big cats (lions, tigers and leopards), non-human primates and marine mammals [13]; It is considered a large virus, with an approximate diameter between 150-300 nm, negative-sense single-stranded RNA, helical, with a lipoprotein envelope, its genomic RNA is packaged by the nucleocapsid protein (N) and is replicated by the complex of the viral polymerase formed by the protein Large (L) and its cofactor, the phosphoprotein (P). The N, P and L proteins, together with the viral RNA, form the ribonucleoprotein complex (RNP), in charge of the sequential synthesis of messenger RNA (mRNA) from viral genes, or the replication of antigenomes (viral RNAs of polarity positive), with two integral membrane proteins in its lipid envelope containing the fusion protein (F) and the hemagglutinin protein (H), and a protein associated with the membrane that interacts with the RNP complex, named matrix protein (M) [16]. Each of these proteins has a specific function within the viral cycle and its replication. The N, P and L proteins together with the viral RNA form the ribonucleoprotein (RNP) complex, the H protein facilitates the attachment of the virus to the host cell membrane and the F protein carries out the fusion of the 2 membranes allowing the entry of viral RNP into the cytoplasm and starting the infectious cycle [26].

Predisposing factors for the presentation of noxa, without order of importance

- The carelessness and ignorance of the owners, in the due control of vaccinations.
- Delay of the owners in going to the doctor and low level of economic income.
- Failure to maintain the cold chain for vaccines.
- Do not revaccinate annually.
- Lack of control of stray canines that act as disseminators of the biological etiological agent.
- Inadequate aseptic and antiseptic procedures of medical and support personnel.

Transmissibility

It occurs when a healthy individual comes into contact with viral particles found in the environment, in the form of an aerosol. A patient can infect an area, even its exterior, for hours, thus producing contagion between individuals. In this way, an individual who has already overcome the disease can also transmit it up to four months after having recovered. The virus replicates in the lymphatic tissue of the respiratory tract, infecting the respiratory, gastrointestinal, and urogenital epithelia. It also affects the central nervous system (CNS) and the optic nerves. The host's immunity is what will determine the degree of viremia, that is, the level of severity.

Factors that threaten the proper diagnosis

Hemolysis: Occurs when materials are used without adequate asepsis, wet and of poor quality, inadequate selection and use of needle caliber, poor handling of samples, high and low temperatures.

Lipemia: Occurs when blood samples are taken in patients who have not fasted (8-12 hours), in patients with pancreatitis, hypothyroidism, hypoadenocortisism and/or kidney disorders.

Susceptibility

It is the condition of the organism that increases the probability that the individual will develop a certain disease. Then, the puppies, form part of the age group of greater susceptibility, especially those under 4 months. Although breast milk offers them some immunity, we must take all possible precautions, as the virus can also be transmitted through the fluids of infected animals, including remains in the water and in the food they have consumed. VDC is susceptible to heat and drying, it is destroyed at temperatures above 50 - 60 °C for 30 minutes. In secretions and tissues, the virus can survive up to 3 hours at room temperature, it can survive and be stored longer at cooler temperatures, at 0-4°C it can survive for a few weeks while at -65°C, the virus becomes stable and can last for at least 7 years. Therefore, freeze-drying is a good means of preservation for commercial vaccines and laboratory use [8].

Susceptible species

As the human population grows and expands, so do dog populations, because they are linked. There are reports that the global population of domestic dogs exceeds 700 million. This makes it the most abundant and widely distributed carnivore in the world and its population growth is strongly associated with human communities [24].

Canine distemper virus (CDV) has been reported in all families of terrestrial carnivores; There are cases such as: the Bengal fox in India; the red fox and the wolf in Italy; the African lion; the bobcat and the Canadian lynx; In this sense, domestic dogs represent a significant risk as reservoirs of infectious diseases, such as canine distemper (CD), especially for wild carnivores [24].

Symptomatology

Canine Distemper virus infection presents as a potentially fatal multisystem disease that can involve the CNS; Only in South America have 4 lineages different from those already known circulating on the continent been described [6]; It has four clinical forms: Respiratory, digestive, cutaneous, nervous, which can appear together or separately, and their combinations.

Clinical infection manifests itself in three forms: acute, subacute, and chronic.

- **Acute:** It is the most common form. The incubation period (from infection to appearance of clinical signs) is usually 7 to 14 days. From 3 to 7 days, fever and leukopenia occur, which usually go unnoticed. The fever subsides (hence the name Distemper) for a few days until a second febrile stage develops, accompanied by conjunctivitis, rhinitis, and anorexia. Gastrointestinal and respiratory signs such as cough, diarrhea, vomiting, anorexia, dehydration, and weight loss may follow. Secondary bacterial infections often complicate the clinical picture.
- **Subacute:** CNS signs may develop from systemic disease such as acute encephalomyelitis. The neurological presentation includes: sudden localized involuntary contractions of a muscle or group of them; paresis or paralysis often beginning in the hind limbs (ataxia); convulsions, hypersalivation, chewing movements, pedaling of the limbs, involuntary urination and/or defecation; hyperesthesia, vocalization, fear reactions, blindness. Depending on the severity of the infection, all or none of the neurological signs may be evident. After recovery from acute Distemper or an inapparent presentation, neurological disorders may take a few weeks or even months to present. Typical of this pathological process is hyperkeratosis on the foot pads and nose.
- **Chronicle:** Two chronic forms have been recognized in adult dogs. The first occurs as a result of an immune-mediated process that produces multifocal encephalitis (Multi Distemper Encephalomyeltis) that progresses slowly. This form normally occurs in dogs aged 4 to 8 years. It presents with hindlimb weakness, unresponsiveness to threat, paralysis, and head tremors. Recovery from this type of infection is possible. The second is chronic old dog encephalitis (Old Dog Encephalitis) is a progressive disorder that usually affects dogs older than 6 years. It presents with ataxia, circling movements, pressure of the head against objects and changes in behavior (no response to external stimuli or does not recognize the owners). The persistence of the virus in the CNS produces an inflammatory reaction, setting up a chronic encephalitis. These patients are not infectious.

Diagnosis: Fundamental elements

Medical history

- **Review:** compilation of patient identification and categorization data. Done properly and completely, the information obtained from it can guide the clinician towards the correct diagnosis. The data in a review are Species. Race. Sex. Age. Body size and weight. Cloak and signs.
- **Anamnesis of the patient and the environment**: set of questions or interrogation that the clinician asks the owner of the patient, caregiver, or person in charge, before and during the clinical examination, whose answers will guide a probable diagnosis and establish the appropriate treatment. To collect the necessary information, the method that the clinician has is important, as well as his or her ability to relate to the patient and their owners or managers. You must know what to ask and how to ask. In veterinary medicine, signs are collected (objective manifestation of the disease) but not symptoms, since these are subjective manifestations, for which they are perceptible only by the patient.
- **Physical examination:** General Objective Examination (EOG) begins with a distance examination of the subject (1 meter) and another close to the patient.

Remote EOG: includes the general inspection of the subject, which includes: constitution (conformation or biotype); nutritional status; skin condition; attitudes.

The EOG near the patient includes body temperature; examination of apparent mucosa; superficial lymph node examination; Breathing frequency; arterial pulse rate; hydration state.

Laboratory studies

Laboratory tests

It is a procedure in which a doctor or health professional takes samples (blood, urine or other fluid or tissue from the patient's body) to obtain information about their health.

The definitive diagnosis requires the demonstration of eosinophilic intranuclear and intracytoplasmic inclusion bodies (Lentz bodies): "Typical" [24].

The clinical manifestations of respiratory or gastrointestinal infection are nonspecific, and the diagnosis should not be based solely on the presentation of these signs.

The canine distemper virus diagnostic kit is designed to detect viral antigens in canine ocular and nasal discharge. Two monoclonal antibodies in the kit specifically bind to different epitopes on the antigens. After being absorbed into the cellulose sponge, the canine distemper antigens are displaced and bind to the monoclonal canine distemper virus antibody gold-colloid complex of the composite sponge, forming an Antigen-Antibody (Ag-Ab) complex. This complex is distributed in 3 layers Ab-Ag-Ab, with the antibody of another canine distemper virus antibody on the nitrocellulose membrane, making direct contact. Test results appear on the control and test lines, which use immunochromatography principles.

Indirect diagnostic studies

- **Serology:** Of all the virological diagnostic methods to confirm Distemper, serodiagnosis is the most used, although the tests are reliable, the problem occurs when interpreting the results.
- **Indirect immunofluorescence (IIF):** Based on infected cells and ELISA test based on purified virus. Although these two tests are commonly used, in the first there is the intervention of an operator for the interpretation of the results, which means that the same sample can give different values, in two different laboratories.

Seroconversion

The measurement of serum IgM and IgG antibodies can help in the diagnosis of Distemper, but the test does not differentiate passive maternal antibodies, vaccine antibodies and antibodies due to subclinical infections, from antibodies that are the product of the disease in puppies. in previously immunized patients and in those who have previously had contact with the virus. Canine distemper virus-specific IgM ELISA is a useful test, as IgM in infected dogs persists for 5 weeks to 3 months depending on the strain and host response. In vaccinated dogs IgM persists for approximately 3 weeks. False negatives can be observed in dogs that die acutely, without the presence of an immune response, and can also occur in subacute or chronic presentations.

Serological analysis of cerebrospinal fluid (CSF) (Encephalitis)

Neurological signs usually appear between 1 and 3 weeks, after the canine patient has recovered from the gastrointestinal and/or respiratory signs. Distemper can be diagnosed presumptively if there is increased protein concentration in CSF, called lymphocytic pleocytosis. Pleocytosis in the CSF is a sign that appears in meningitis and other infectious processes of the CNS and specific antibodies are detected in a sample not contaminated with peripheral blood.

Pathogenesis

We should bear in mind that when the patient presents with the clinical symptoms of the acute phase, at least 1 to 2 weeks have already passed since the patient was first exposed to the virus, therefore, it is imperative according to the predominant symptoms, try to locate the place where the virus can be found inside the organism, in order to be able to identify it, if possible, with direct diagnostic studies. Viral particles can be detected by fluorescent antibodies (IFA) in tonsil cells, lymph nodes, respiratory tree, conjunctival swabs, urinary sediment and CSF from 5 to 21 days post infection. The test is specific, if it is positive, the patient suffers from the noxa. The viral particle can be found in CSF cells, in animals with neurological signs, in 80% of cases. On rare occasions, recent vaccination can give false positives. More than one sample may be necessary to find and identify the virus, in subacute or chronic cases these tests may be negative, although the presence of the virus is not ruled out. It gives many false negatives.

Polymerase chain reaction (PCR)

The technique consists of taking a key portion of the viral RNA and multiplying it exponentially by enzymatic means; If there is a single RNA molecule in a sample (undetectable by any other method), with this reaction, after 20 steps (in cycles of 3 to 5 minutes each), we can obtain 1 million identical molecules. Compared to this technology, traditional antibody identification and detection tests are almost obsolete; A positive PCR result tells us, with almost no margin of error, that the RNA of the biological aetiological agent is present in the patient and if the RNA is present, the infection is certain.

Skin biopsy

A recent study found that canine distemper virus can be found in 1 cm superficial biopsies of normal dorsal neck skin, it is a reli-

able (sensitive and specific) ante-mortem test. The effect of vaccination on this test is uncertain and is probably less reliable during the neurologically advanced phase of the disease. Send the biopsy sample in formalin.

Necropsy and histopathology

We must analyze samples of the spleen, tonsils, lymph nodes, stomach, duodenum, bladder and brain, by histopathology and immunohistochemistry, since Distemper can be located in different tissues. It can be safely diagnosed with a histopathological study by a qualified pathologist. If Distemper is a population problem and a definitive diagnosis cannot be made by other methods, a necropsy is a worthwhile investment in a suspected dead dog to establish whether or not Distemper is present in that community.

Differential diagnosis

It is done with canine hepatitis, parvovirus, leptospirosis, toxoplasmosis, rabies. It is also based on virus isolation in cell cultures during the acute phase of the disease [23].

Immunity

Maternal antibodies are transferred exclusively with the colostrum and usually prevent infection in puppies 8 to 12 weeks of age. Dogs recovered from a natural infection will be immune for life. Immunity from vaccination in adult animals can last for several years and occasionally old dogs that were vaccinated when young are susceptible and become ill.

Treatments

It is not a curable disease, but it is treatable to alleviate the symptoms and control them. Secondary bacterial infections can be treated, and supportive treatment is also necessary: Antimicrobial treatment to control bacterial infections; medication to control symptoms, such as diarrhoea, vomiting and cough, in addition to neurological ones; care to remove dirt, secretions from the eyes and nose, and prevent pressure ulcers that appear when you remain immobile for a long time; try to get the patient to eat and drink (and if not, resort to appropriate fluid therapy); anti-inflammatories (provide special care with steroids). Infected individuals and those who have been in contact with them must stay away from other sensitive dogs, and it is urgent to adopt hygiene measures to prevent the spread of the disease (change of clothing for people in contact with the infected animal, use of disinfectants).

An investigation on the use of silver nanoparticles (AgNP) concluded that more than 90% of patients without neurological signs who received treatment for 7 to 15 days had a very high recovery rate without sequelae; According to the results of this research, it is believed that AgNP, act by interfering with viral infection because it blocks adhesion and consequently the entry of the virus into host cells, and also presented low toxicity [4].

Forecasts

Favorable or benign, when the patient's cure is expected; Doubtful or reserved, when there is uncertainty about the patient's evolution; Lethal, unfavorable or unfortunate, when the possible end of the condition is death, or when the zootechnical conditions of the patient are severely compromised. The prognosis for patients with severe neurological signs is lethal and euthanasia is recommended in individuals with progressive signs not compatible with a good quality of life. The life expectancy of a patient infected with CDV is very low, approximately more than 85% end up dying [4].

Prevention

Prevention is based on proper compliance with the vaccination schedule. This noxa is part of the first vaccination given to puppies, and often of all annual booster doses. Depending on the particular situation of the patient, the veterinarian will choose the most appropriate protocol for their needs.

Conclusion

- Canine Distemper is one of the most well-known canine infectious diseases by veterinarians, but more complex when it comes to issuing a confirmatory diagnosis.
- Canine distemper is the leading cause of death in dogs from infectious disease.
- A necessary factor for the dissemination of the biological etiological agent is direct contact.
- Host immunity is what will determine the degree of viremia.
- It has four clinical forms: Respiratory, digestive, cutaneous, nervous, which can appear together or separately, and their combinations.
- Secondary bacterial infections often complicate the clinical picture.
- Definitive diagnosis requires the demonstration of eosinophilic intranuclear and intracytoplasmic inclusion bodies (Lentz bodies).
- Of all the virological diagnostic methods to detect Distemper, serodiagnosis is the most widely used.

Conflict of Interest

There are no conflicts of interest or economics.

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