CANINE EHRLICHIOSIS : AN OVERWIEW

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Introduction

Canine ehrlichiosis also known as Canine rickettsiosis, Canine hemorrhagic fever, Canine typhus, Tracker dog disease and Tropical canin -ne pancytopenia. Canine ehrlichiosis is a tick-borne disease caused by an obligate intracellula -r parasite, *Ehrlichia canis,* which resides and replicates within mononuclear cells (Greene and Harvey, 1990). Although *E. canis* has a global distribution, including the United States, Northern and Southern African countries, Europe, SouthEast Asia, and India, high infection rates and disease in dogs are primarily observed in tropical and subtropical areas (Ewing, 1969; Neer *et al*, 2002). The association of *E. canis* with hemorrhagic disease in dogs was first described in 1969 (Huxsoll, 1968).

Etiology

Ehrlichiosis is caused by a group of small, gram-negative, pleomorphic, obligate intracellular cocci that infect different blood cells in various animal species and in humans. According to new classification of ehrlichiosis under family *Anaplasmataceae*, there are two leukotrophic diseases in dogs that are caused the genus *Ehrlichia* viz. Canine Monocytic Ehrlichiosis (caused mainly by *Ehrlichia canis*) and Canine Granulocytic Ehrlichiosis (caused by *Ehrlichia ewingii*). It should be noted that cross-reactivity and co-infection is common among the ehrlichiae.

Canine Monocytic Ehrlichiosis (*Ehrlichia canis*): Canine monocytic ehrlichiosis (CME) is caused by *E. canis*, an obligate intracellular bacterium with tropism for monocytes and macrophages. It is transmitted mainly by the ticks *Rhipicephalus sanguineus*, a brown ear tick (Skotarczak, 2003). It is seen mostly in the South Eastern and SouthWestern United States, although it is recognized in all states and worldwide. *Amblyomma* and *Dermacentor* ticks have also been included in transmission of this disease.CME has been reported throughout the world, with a higher frequency in tropical and sub-tropical regions. Disease occurs in both acute and chronic stages. The disease may be manifested by fever, depression, dyspnoea, anorexia, hemorrhages, edema and weight loss accompanied with laboratory findings of thrombocytopenia, leukopenia, anemia, and hypergammaglobulinaemia (de Castro *et al*., 2004; Unver *et al*. 2006).

Canine Granulocytic Ehrlichiosis (*Ehrlichia ewingii*): Canine Granulocytic Ehrlichiosis (CGE) caused by *Ehrlichia ewingii,* is a disease of neutrophils and rarely, eosinophils. CGE classically presents with mild signs including fever, lethargy, anorexia, weight loss, vomiting, diarrhea, severe but transient thrombocytopenia and transient mild nonregenerative anemia within effective erythropoiesis. The most common presenting clinical signs associated with *E. ewingii* include lameness and joint swelling due to polyarthritis. This form of ehrlichiosis is generally seen in the Southern and Mid-eastern United States.Ticks including *Ixodespacificus, Dermacent orvariabilis, Rhipicephalus sanguineus, Amblyomma americanum* and *Ixodes scapularis* have been implicated as vectors.

Transmission of Ehrlichia

Ehrlichia are transmitted by ticks mainly *Rhipicephalus sanguineus* and *Amblyomma americanum*, which passes an ehrlichia organis -m into the bloodstream when it bites. It is also possible for dogs to become infected through a blood transfusion from an infected dog (Ettinger and Feldman, 2000). The immature tick fed on the infected animal and passed the infection into another normal animal.

Pathogenesis of Ehrlichiosis

The pathogenesis of infection with *E. canis* is the most extensively studied. Infection occurs through salivary secretions of the tick at the attachment site during ingestion of a blood meal or through blood transfusions. If the adult *Rhipicephalus sanguineus* engorges on the dog during the acute stage, it can transmit the disease to other dogs for at least 155 days following detachment. Transmission by *Rhipicephalus sanguineus* is trans-stadial i.e. the tick acquires the bacteria by feeding on an infected dog in either the larvae or nymph form and the tick transmits the disease to another dog as either the nymph or adult form. The life

cycle of *Ehrlichia* is not yet completely understood but it is thought that it occurs in three intracellular forms. The initial bodies are small spherical structures (1-2 micrometers in diameter) which are believed to develop into larger multiple membrane-bound units known as morulae. The morulae are inclusions within the cytoplasm of the leukocyte. This morula is thought to then dissociate into small granules called elementary bodies.

After an incubation period of 8-20 days, the acute phase of infection occurs that lasts about 2-4 weeks. At this time, the organism multiplies within circulating mononuclear cells and the mononuclear phagocytes within the liver, spleen, and lymph nodes. The infected cells are then transported in circulation to the rest of the body, with a predilection for the lungs, kidneys and meninges. Cells infected with *Ehrlichia* adhere to the vascular endothelium and induce a vasculitis and subendothelial tissue infection. This subsequently leads to platelet consumption, sequestration, and destruction that result in the thrombocytopenia seen during this acute phase. Variable leukocyte counts and anemia may also develop progressively during this stage. After 6-9 weeks, dogs will either eliminate the parasite (if immunecompetent) or develop aparasitemia in which clinical signs absent to mild to severe. This stage is also characterized by variable persistence of thrombocytopenia, leukopenia, and anemia. Dogs that cannot mount an effective immune response will become chronically infected.

Symptoms of Ehrlichiosis

Symptoms of *Canine Ehrlichiosis* generally divide into three phases, each varying in severity. Clinical signs most frequently observed in dogs both naturally and experimentally (de Castro *et al*., 2004).Symptoms of *Canine Ehrlichiosis* generally divide into three phases, each varying in severity.

A. Acute phase: It occurs several weeks after infection and lasting for up to a month, can lead to fever and lowered peripheral blood cell counts due to bone marrow suppression.The *Ehrlichia* enter white blood cells and reproduce inside of them. In addition to the blood, these cells are found in the lymph nodes, spleen, liver and bone marrow. Platelets, the small cell fragments that help blood to clot, are often destroyed as well. As a result of the infection, the lymph nodes, liver, and spleen are often enlarged. Anemia, fever, depression, lethargy, loss of appetite, shortness of breath, joint pain and stiffness, and bruises are often seen. Many dogs will be able to fight off the infection. If not, they enter the subclinical phase. Clinical signs include a fever, petechiae, bleeding disorders, vasculitis, lymphadenopathy, discharge from the nose and eyes, and edema of the legs and scrotum. There are no outward signs of the subclinical phase. Dogs that are severely affected can die from this disease. Although people can get ehrlichiosis, dogs do not transmit the bacteria to humans; rather, ticks pass on the *Ehrlichia* organism. Clinical signs of human ehrlichiosis include fever, headache, eye pain, and gastrointestinal upset. It is quite similar to *Rocky Mountain spotted fever*, but *rash* is not seen in patients.

B. Sub-acute phase: The second phase, called the subclinical phase, has no outward signs and can last for the remainder of the dog's life, during which the dog remains infected with the organism. Some dogs are able to successfully eliminate the disease during this time. In some dogs the third and most serious stage of infection, the chronic phase, will commence. Very low blood cell counts (pancytopenia), bleeding, bacterial infection, lameness, neurological and ophthalmic disorders, and kidney disease, can result. Chronic ehrlichiosis can be fatal.In some cases dogs show only slight anemia. During this phase the *Ehrlichia* live inside the spleen. This phase can last for months or years. Ultimately, the dog either eliminates the Ehrlichia from the body or the infection may progress to the chronic phase.

C. Chronic phase: The chronic phase can be either mild or severe. Weight loss, pale gums due to anemia,lymphadenopathy, dyspnea, coughing, polyuria, polydipsia, lameness, neurological signs, bleeding due to thrombocytopenia, opthalmitis, edema (fluid accumulation) in the hind legs, and fever may be seen. Blood tests show that one or all of the different blood cell types are decreased. One cell type, the lymphocyte may increase and be abnormal in appearance. This can sometimes be confused with certain types of leukemia. If a dog becomes chronically infected, the disease can keep coming back, especially during periods of stress. In some cases, arthritis or a

kidney disease called 'glomerluonephritis' may develop.

A decrease in the number of platelets (platelets help the blood clot) in the blood is the most common laboratory finding in all phases of the disease. Changes in the protein levels in the blood are common. The most common protein, albumin, is decreased and other types of protein called 'globulins' are increased. Since one tick could be infected with and transmit more than one disease (e.g. Haemobartonellosis or Babesiosis), it is not all that uncommon to see a dog infected with more than one of these diseases at a time, which generally causes more severe symptoms.

Lesions

Gross pathological findings commonly observed are pale mucous membranes, lymphadenopathy, splenomegaly,ascites, and congestion, petechial and echymotichaemorrha -ges in the liver, lungs, spleen, heart,lymph nodes and kidneys. Hispathology of liver show centrilobular necrosis, mild degeneration in hepatocytes, plasmocytic– lymphocytic cellular infiltration, sinusoidal dilatation and hyperae-mia. Prominent mononuclear cellular infiltrate-on in the interalveolar septa and vasculitis are also observed in the lungs. Histopathological findings in the spleen show necrosis in the ger-minal centres and moderate increase in the plas -mocytic–lymphocytic cells with hyperaemia. Plasmocytic–lymphocytic cellular infiltration was observed in the kidney, especially in the periglomerularregion (de Castro *et al*., 2004; Unver*et al*., 2009).

Diagnosis

Diagnosis of Ehrlichiosis is mainly done by various methods which are described below

1. Diagnosis on the basis of appropriate history (travel, tick exposure etc.) and physical examination.
2. Serological Assay: Indirect fluorescent antibody test (IFA) test is themost commonly used serological assay for the diagnosis of *Canine Ehirlichiosis*(Wanner*et al*., 2001). In dogs experimentally infected with *E. canis,* IFA test has detected serum antibodies as early as 7 days after initial infection. There are a few potential drawbacks of using the IFA test for the diagnosis of *E. canis* infection. One major concern exists in endemic areas with dogs that are chronically infected and have a positive titer, but are otherwise healthy or show non-specific clinical signs. In these dogs, a positive antibody titer does indicate past exposure to *E. canis*, does not prove that ehrlichiosis is necessarily an active infection or the cause of the presenting clinical signs. In dogs with non-specific clinical signs, a repeat IFA test after 1 or 2 weeks may be beneficial to differentiate between primary *E. canis* infection and another secondary disease.
3. Cytological examination: Canine monocytic ehrlichiosis stain dark blue to purple with Romanowsky stain. Themorulae are well-defined, round to oval, eosinophilic to basophilic bodies found in host membrane-lined vacuoles within the cytoplasm of the mononuclear cells. The detection of morulae is uncommon except during the acute phase of the infection (Hibbler*et al*., 1986).
4. In endemic areas for *E. canis* many veterinarians routinely test healthy dogs for exposure using the Idexx Snap test for antibody The SNAP test for *E. canis* antibody is highly specific (100%) and sensitive (96.2%)**.**
5. PCR amplification is also a sensitive method for the detection of acute *E. canis*. Although there are currently several potential limitations e.g.if the PCR is negative on blood, it is still possible that the organism is present in other tissues such as the spleen or the number of organisms circulating in the blood could be below the assay's level of sensitivity (Harrus*et al*., 1998).It is recommended that this method be used in addition to serology for the initial diagnosis of ehrlichiosis, not instead of it.
6. The diagnosis of CGE differs from that of CME as E. ewingii has not yet been cultivated in an in vitro system; therefore antigens have not been available for comparative serological testing. Diagnosis of CGE requires visualization of morula within neutrophils in peripheral blood, joint effusions, and PCR or Westernimmunoblot. In a study using Western immunoblots, sera from dogs that were experimentally infected with E. ewingii were tested on E. canisantigens. Although there were no reactions with the dominant *E.canis* antigens, the sera produced binding patterns similar to those of anti-*E. canis* sera with high molecular proteins. This also may help with the diagnosis of CGE.

Diagnosis of canine in the early stage of infect-ion is important to ensure early treatment and a good prognosis. Dogs in the acute phase of the disease demonstrate dramatic improvement in hematologic and clinical responses 24-48 hours

after therapy. However, dogs in the chronic stage of the disease have a poor prognosis and may not improve following treatment. occurs and there are low levels of blood cells, the animal may not respond to treatment.

Treatment of Ehrlichiosis

Antibiotics, tetracycline or doxycycline are most commonly used. Treatment is usually for 3-4 weeks, even though the dog's symptoms generally improve after several days of therapy. Some dogs will need blood transfusions or intravenous fluids depending on the severity of the disease. Generally, the prognosis during the acute phase is good, if the animal is properly treated. Dogs that go on to the chronic phase have a poorer prognosis. German Shepherds and Doberman Pinschers tend to have a more severe chronic form of the disease.The drug, imidocarb, dipropionate, is sometimes used in conjunction with the antibiotics. It is given as an injection, but may not be available in all areas.Some of the damage caused by *Ehrlichia* may be due to the dog's own immune response to the organism. For this reason, if immune-mediated arthritis or decrease in platelets occurs, corticosteroids (e.g., prednisolone) may be given.

Prevention of Ehrlichiosis

1. Tick control is the main way to prevent ehrlichiosis. Products which repel and kill ticks such as those containing permethrins are excellent choices.
2. Tick collars containing the active ingredient likeamitraz (Preventic collars) are also used, sometimes in conjunction with permethrin products in those areas with high tick infestations. If a large number of cases of ehrlichiosis are diagnosed in an area, some veterinarians recommend placing dogs on low doses of tetracycline or doxycycline during the tick season.
3. There is no vaccine for ehrlichiosis.

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