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Overview of Canine Monocytic Ehrlichiosis

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Abstract

Canine monocytic ehrlichiosis is a serious tick-transmitted, globally distributed disease of dogs that is caused by *Ehrlichia canis*. It primarily affects platelets, monocytes, and granulocytes. Acute infections in dogs respond favourably to therapy, however chronic disease results in bone marrow failure and death. The disease can be diagnosed based on clinical manifestations, haematology, microscopy, indirect immunofluorescence test (IFAT), enzyme-linked immunosorbent assay (ELISA) and polymerase chain reaction (PCR). For canine ehrlichiosis, Tetracycline or Doxycycline are usually recommended for a period of 3-4 weeks. Tick prophylaxis is key in preventing canine ehrlichiosis and is best achieved using ectoparasitic drugs that repel and kill ticks before they attach.

Keywords: Canine monocytic ehrlichiosis, Thrombocytopenia, Doxycycline.

INTRODUCTION

Canine monocytic ehrlichiosis also known as Canine haemorrhagic fever, Canine rickettsiosis, Canine typhus, Tracker dog disease and Tropical canine pancytopenia is a tick-transmitted fatal rickettsial disease of domestic dogs and wild canids, caused by an obligate intracellular bacterium, *Ehrlichia canis.* It has tropism for monocytes and macrophages (Azmi *et al.*, 2013). The organisms are transmitted by *Rhipicephalus sanguineus* (brown dog tick) rapidly within 3 hours of tick attachment to dog and can also be transmitted through transfusion of infected blood (Ettinger and Feldman, 2000). These pleomorphic organisms may occur as intracytoplasmic inclusions in circulating monocytes, either singly or in compact colonies called 'morula'. Canine monocytic ehrlichiosis is worldwide in distribution, with a higher frequency in tropical and subtropical regions. The disease affects multiple organs and systems and occurs in acute, sub-acute and chronic phases. Ehrlichiosis is characterized by signs of fever, anorexia, weight loss, lethargy, epistaxis, haemorrhages, edema of hind limbs and scrotum, anaemia and lymphadenopathy. Haematological alterations include thrombocytopenia, leukopenia and hyper-gammaglobulinemia. In canine

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ehrlichiosis, there is no predilection of age or sex; however, Siberian Huskies and German Shepherds are more likely to develop severe clinical manifestations. Environmental factors like high temperature and low humidity favour the growth of vectors, so dogs living in such circumstances are at greater risk of disease. Definitive diagnosis involves the demonstration of morulae on cytology and blood smears, detection of antibodies through an indirect immunofluorescence test (IFAT), and DNA amplification by polymerase chain reaction (PCR).

PATHOGENESIS

Infection occurs through salivary secretions of the tick at the site of attachment during ingestion of a blood meal or through blood transfusions. Transmission by *Rhipicephalus sanguineus* is trans-stadial. *Ehrlichia* is thought to occur in three intracellular forms. The initial bodies are small spherical structures that are believed to develop into larger multiple membrane-bound units known as morulae. The morulae are inclusions within the cytoplasm of the leukocyte, they dissociate into small granules called elementary in about 2-4 weeks. The incubation period ranges from 8–20 days. In acute infections, the organism invades and 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, particularly to the lungs, kidneys, eyes and meninges. Cells infected with *Ehrlichia* adhere to the vascular endothelium and induce vasculitis which leads to Disseminated intravascular coagulopathy (Bhatia *et al.*, 2010). At this stage, severe clinical manifestations like high fever, anaemia and thrombocytopenia, can be observed. Dogs suffering from persistent infection develop a more lethal form of chronic disease, where the pathogen attacks the bone marrow and destroys the immune system. As a result, other opportunistic infectious agents further aggravate the situation. Severe thrombocytopenia leads to massive hemorrhages and death.

CLINICAL FINDINGS

Canine monocytic ehrlichiosis is characterized by three stages, acute, subclinical and chronic each varying in symptoms depending on the immune system of the dog and existence of co-infections with other tick-borne diseases.

Acute phase

This phase lasts for 3-5 weeks and is characterized by clinical signs of fever, anorexia, lethargy, depression, splenomegaly, lymphadenopathy, severe anaemia and thrombocytopenia. Conjunctivitis, pale mucous membranes, epistaxis, haematemesis, melena, petechial and ecchymotic haemorrhages on oral gums and ventral abdomen due to thrombocytopenia, edema of hind limbs and scrotum, ascites due to hypoproteinemia, lameness, and some neurological symptoms may be noticed. Dogs that are severely affected may die. Many dogs will be able to recover from the infection. If not, they enter the subclinical phase.

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Subclinical phase

The dogs successfully eliminate the *Ehrlichia* organisms from the body. However, some dogs develop persistent subclinical infections, act as asymptomatic carriers and become an important source of infection for months and years. In this phase, the animal apparently looks normal and healthy and does not present any clinically visible signs but upon haematological testing, mild thrombocytopenia can be detected. The infection may progress to the serious stage of infection, the chronic phase.

Chronic phase

The chronic phase can be either mild or severe. Weight loss, pale mucus membranes and gums due to anaemia, depression, lymphadenopathy, lameness, neurological signs, petechiae, bleeding due to thrombocytopenia, edema in the hind legs, and fever may be seen. In some cases, arthritis or 'glomerulonephritis' may develop. Recurrent clinical and haematological signs include thrombocytopenia, anemia, and pancytopaenia. In severe cases, the response to antibiotic therapy is poor and dogs often die from massive haemorrhage, severe debilitation or secondary infections.

PATHOLOGICAL FINDINGS

Haematological abnormalities are variable and overlapping, that include thrombocytopenia, hypergammaglobulinemia, hypoalbuminemia, and hyperglobulinemia. In chronic form, aplastic pancytopenia, granular lymphocytosis, mild elevation in liver enzymes and renal azotemia were found (Rungsipipat *et al.*, 2009). Gross pathological findings commonly include pale mucous membranes, lymphadenopathy, splenomegaly, ascites and congestion, petechial and ecchymotic haemorrhages in the liver, lungs, spleen, heart, lymph nodes and kidneys. Histopathology reveals plasmocytic–lymphocytic cellular infiltration in the liver, lungs, spleen and kidney (De Castro *et al.*, 2004).

DIAGNOSIS

Based on the history of tick exposure and physical examination of dog. Detection of *Ehrlichia canis* morulae within monocytes or lymphocytes in blood smear prepared from blood collected from the ear tip of the dog. Examination of buffy coat smear or lymph node cytology. The limitation of microscopy is that, it is extremely insensitive in the chronic and subclinical phases and unable to differentiate *Ehrlichia* species. Serological assays like indirect immunofluorescence test (IFAT) and enzyme-linked immunosorbent assay (ELISA) are used for the detection of antibodies. Molecular diagnosis like PCR amplifies the DNA of the pathogen and provides strong and clear evidence about the active ongoing disease.

TREATMENT

Tetracyclines or Doxycyclines are most used antibiotics usually for a period of 3-4 weeks. Tetracycline @ 22 mg/kg bw, three times a day for 21 days, or Doxycycline @ 10 mg/kg bw, per orally, once daily for four weeks is more efficacious and considered as the drug of choice. Supportive therapy with blood transfusion, polyionic isotonic fluids and Vitamin B-complex may hasten the

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recovery.

Dogs in the acute phase of the disease show dramatic improvement in haematological and clinical responses after 24-48 hours of therapy. Whereas, dogs in the chronic stage may not respond to treatment and have a poor prognosis. Hence, diagnosis of canine in the early stage of infection is important to ensure early treatment and a good prognosis.

PREVENTIVE STRATEGIES FOR CANINE MONOCYTIC EHRLICHIOSIS

In dogs, even after the complete recovery from natural infection after treatment, they do not develop long lasting immunity to *E. canis* infection and there are still chances of re-infection. Hence, prevention is possible by proper control of tick population and treating the infected dogs in early phase. Control of vectors by spraying suitable acaricides at regular intervals, by careful removal of ticks manually or by monitoring of environmental factors related to tick growth, are fundamental control procedures in handling ehrlichiosis. Topically acting synthetic pyrethroids (e.g. flumethrin) act as repellents (and kill) thus preventing tick attachment are proven to protect dogs against transmission of *E. canis.* In areas with heavy tick infestation, collars containing actives like amitraz can be used. In regions where the disease is endemic, prophylactic use of Doxycycline especially during summer and spring (tick season) can lower the risk of infection (Davoust *et al.,* 2005). Dogs traveling from endemic areas must be screened for canine monocytic ehrlichiosis before entering.

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