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Therapeutic management of Ehrlichiosis in dogs

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Abstract
The present study was carried out to investigate the haemato-biochemical changes and therapeutic management of canine ehrlichiosis. Seven male and 3 female dogs between 3-4 years old were presented to Enrich pet clinic, Hyderabad with non-specific clinical signs like dullness, in-appetence with pyrexia, hematochezia and petechial haemorrhages on the abdomen and ears observed in few. Blood samples were used for screening of blood samples for any pathogen, haemo-biochemical parameters and molecular detection of suspected blood pathogen. Haematological evaluations revealed a decline in total leucocytes and total platelet count. Serum biochemical examinations revealed altered liver and kidney function tests. The blood smear evaluation revealed the morula stage of *Ehrlichia canis* in the monocytes. The molecular tests revealed the *Ehrlichia canis* in the blood samples. All the dogs effectively recovered after treatment with doxycycline 10mg/kg B.wt for 32 days along with supportive medication.

Keywords: Canine, doxycycline, ehrlichiosis

Introduction
Canine monocytic Ehrlichiosis (CME), one of the most prevalent tick-borne illnesses, is caused by the rickettsial pathogen *Ehrlichia canis*, which lives as morulae in canine monocytes and macrophages (Simpson, 1972) [18]. Of the five Ehrlichia species, E. canis is the most significant species that affects dogs. Other species are *E. chaffeensis*, *E. ewingii*, *E. murise*, and *E. Ruminantium* (Dummler *et al.*, 2001) [2]. Species that act as natural carriers of infection are dogs, coyotes, red foxes, and golden jackals (Neer 1998) [11]. The most common means of transmission is through the biting of a *Rhipicephalus sanguineus* brown dog tick. It is commonly known as Canine rickettsiosis, tropical canine pancytopenia, canine haemorrhagic fever, Nairobi bleeding condition, tracker dog sickness, haemorrhagic fever, and canine tick typhus. *Ehrlichia canis*, a gram-negative, obligate intracellular bacteria (order Rickettsiales, family Anaplasmataceae), causes a frequent tick-borne sickness that affects dogs. Rickettsial infections are more prevalent in tropical and sub-tropical areas like India owing to the predominant tick population (Dummler *et al*., 2001) [2]. The infection is usually transmitted transtadially by the tick among the canine population.
The incubation period is 8-20 days and the illness progresses through three stages: acute, subclinical, and chronic. According to Silva *et al*. (2016) [17], Affected Dogs have lymphadenopathy, splenomegaly, hepatomegaly, thrombocytopenia, bleeding tendency, cardiac/renal issues, Hypergammaglobulinemia and myelosuppression due to its multisystemic nature and typical clinical signs that can be observed are anorexia, fever, depression, lethargy, weight loss, muscle soreness, bleeding from the nose, oedema in the hind limbs, Oculo-nasal discharges, ulcerative stomatitis at the time of presentation and most cases are asymptomatic (Oliveira *et al*., 2019) [13].
According to chronic and subclinical phases that endure for a long time and contain recurrent clinical symptoms such as pancytopenia, follow acute illness. White blood cells and platelets significantly decrease in affected dogs, which is attributed to myeloid depression (Harrus *et al*., 1996; Selim *et al*., 2020) [4, 15]. Thrombocytopenia is related to autoimmune mechanisms, with decreased survival and aggregation capacity. Increased levels of liver-specific enzymes and other renal-related biochemical markers were indicative of canine liver diseases (Niwetpathomwat *et al*., 2006) [12]. Hepatomegaly, lymphadenopathy, and haemorrhages in numerous visceral organs were discovered during the post-mortem investigation (Lakkawar *et al*., 2003) [9]. It requires an immediate and accurate diagnosis to begin appropriate therapy that will result in a favourable prognosis (McBride *et al*. 2001) [7].

It is done by clinical examination followed by a blood picture and observing Giemsa-stained blood smears for the presence of morulae in monocytes (Nakaghi *et al*., 2008) [10] and molecular confirmation.

Martials and Methods

Out of 35, 10 dogs of 3-4 years of different breeds and both sexes (7 Males and 3 Females), were suspected of Ehrlichiosis at Enrich pet care clinic, Hyderabad, with a history of anorexia (8 in no.), high fever, severe panting, and vomiting (5 in no.) and haematochezia (1 in no.). Clinical examination showed pale conjunctiva and an enlarged popliteal lymph node in few, heavy tick infestation (4 in no.), cutaneous and mucosal petechiae (2 in no.), unilateral epistaxis (3 in no.) and melena and prolonged bleeding from venipuncture sites was observed in one dog. The haematological findings showed marked anaemia and thrombocytopenia and a blood smear examination revealed the presence of morulae in leucocytes in four cases and further confirmation with PCR at Diagno Pet, Hyderabad was done.

Two thin blood films of each blood sample were prepared, dried, and then fixed in absolute methyl alcohol for 1–2 min. Each smear was immersed into diluted Giemsa stain for 30–45 min, and then washed with distilled water to remove excess stain. Glass slides were left to dry and further examined under oil immersion lens at 100 X. Ehrlichiosis. CBP, LFT and KFT were performed at the hospital using Byovet Smart 3Dx. PCR diagnosis was done at Diagno Pet, Hyderabad

Results and Discussion

The Giemsa stained smear on examination revealed the morulae stage of *E. canis* in the leucocytes which recorded overall prevalence of 28.5% (n=35) (Fig.1). The complete blood pictured revealed marked drop in platelets in all the ten cases with marked thrombocytopenia in four dogs and six dogs were severe exhibiting severe pancytopenia of which four dogs showed elevated levels of ALP, ALT, AST and Urea levels.

Seven dogs out of the ten had a smooth recovery without any sequelae, one required a blood transfusion and two dogs with aggravated clinical signs had grave prognoses. Doxycycline therapy (10mg/kg b.wt PO) for 32 days along with supportive fluid therapy, oral liver supports and platelet growth-promoting supplements are provided.

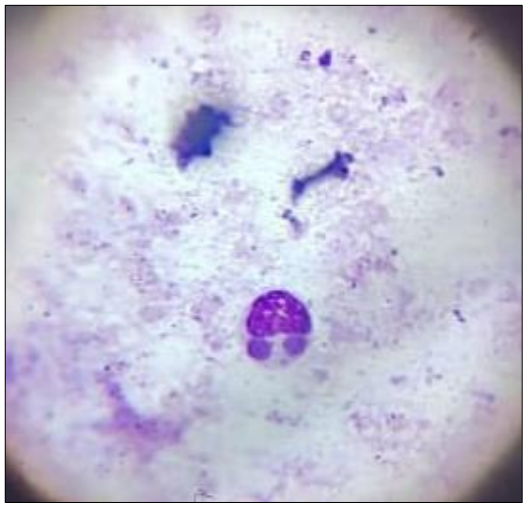

Fig 1: The morulae stage present in the monocyte stained by Geimsa stain in dogs suspected of *E. canis*

Based on *in vitro* investigations, doxycycline has replaced tetracyclines as the first-line antibiotics used to treat CME. Regardless of the disease phase, the American College of Veterinary Internal Medicine recommended 10 mg/kg, per so (PO), once a day for four weeks (Mylonakis *et al*., 2004) [8]. Doxycycline administration may not be tolerated by all dogs due to anorexia, vomiting, diarrhoea, or due abrupt post-treatment increases of alanine aminotransferase and alkaline phosphatase activity. When Doxycyclin is ineffective, glucocorticoids are utilized as an additional treatment (Waner and Harrus, 2013) [21]. Due to its low MIC of 0.03 mg/ml against E. canis, rifampicin is an alternative to doxycycline (Schaefer *et al*., 2008) [14]. However, current evidence suggests that the total daily rifampicin dose for dogs should not exceed 10 mg/kg (Mylonakis *et al*., 2004) [8]. Testing for persistent infections 1-2 months post-treatment is recommended to avoid false positives. Both suppression of ehrlichia mia and tissue sequestration could adversely influence successful PCR amplification because organism load may be below the analytical sensitivity of current molecular assays (Neer *et al*., 1998) [11].

Rational or balanced crystalloid solutions and/or whole blood transfusions are considered to stabilise dogs with severe anaemia (Shipov *et al*., 2008) [16]. In case of Thrombocytopenia, Desmopressin (1-deamino-8-D-arginine vasopressin, DDAVP), an enhancer of platelet function by increasing serum levels of von Willebrand factor, resolved bleeding in three dogs with thrombocytopenia, presumptively-associated with CME (Giudice *et al*., 2010) [3] or platelet components (platelet-rich plasma or platelet concentrate are advised, if possible or a unit of fresh whole blood (standard 450 mL collection bag) increases the platelet count of a 20 kg dog by approximately 20,000–30,000/mL, which can provide temporary, life-saving hemostasis (Mylonakis *et al*., 2004) [8]. In the absence of septicemia, iron sulfate supplements (100–300 mg, PO, once daily, for 3–5 months were advised at least 2 h before, or after oral doxycycline, as iron depletion was recorded in dogs with myelosuppressive CME (Mylonakis *et al*., 2004) [8]. Recurrence of thrombocytopenia 2–4 weeks after the cessation of doxycycline indicates treatment failure, re-infection, or concurrent infection with organisms that are partially doxycycline-responsive but not curable (e.g. *Babesia* spp. and *Bartonella* spp.) (Neer *et al*., 1998) [11]. Hyperglobulinemia tends to progressively resolve 3-6 months after the initiation of treatment.

Conclusion

Canine ehrlichiosis can be successfully treated if detected early, before the onset of multiorgan failure. In a few instances, it can reoccur due to persistence or due to irregular medication followed by the owner.

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