



CANINE MONOCYTIC EHRLICHIOSIS – THE NEWER PERSPECTIVES OF ITS DIAGNOSIS AND TREATMENT

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ABSTRACT

Canine monocytic ehrlichiosis is a highly fatal disease of dogs usually diagnosed by clinical signs, although non-significant signs are present and can be effectively managed with oral and parenteral tetracyclines. In the present study, generalised weakness, pale to icteric mucosa, lymphadenitis, petechial haemorrhages on the ventral abdomen, pedal edema, epistaxis and orchitis were the common significant signs. However, incoordinated gait, edematous face and seizures were also infrequent. Significantly reduced ($P<0.05$) mean total erythrocyte count, Hb, PCV, total leukocytes with thrombocytopenia along with a significantly elevated ($P<0.05$) mean ALT with low levels of serum proteins were hematobiochemical alterations noticed in the affected dogs. Blood smear made from buffy coat revealed morula of *E. canis* in the monocytes of 8 dogs. Whereas, SNAP 4DX plus test showed positive towards the antibodies of *Ehrlichia canis* and / or *Ehrlichia ewingii* of 13 samples, thus confirming ehrlichiosis in 13 dogs. Therapy with rifampicin, 10 mg/kg, bid, orally, for 21 days helped in complete recovery of all the cases.

KEY WORDS: Canine monocytic Ehrlichiosis, SNAP 4DX plus test, rifampicin.

INTRODUCTION

Canine monocytic ehrlichiosis (CME) is a cosmopolitan disease of dogs that is caused by the tick-borne rickettsia, *Ehrlichia canis*. *Ehrlichia* spp., like the closely related genus *Anaplasma*, are biologically transmitted among vertebrates by ticks of the family Ixodidae and *Rhipicephalus sanguineus*, the “brown dog tick,” is considered the primary vector of *E. canis*. In addition to its global importance to canine health, this vector-pathogen-vertebrate interaction provides useful transmission and disease models for zoonotic tick-borne bacteria, the majority of which naturally infect dogs (Dumler *et al.*, 2001). Ehrlichiosis is a serious febrile and potentially fatal disease of dogs usually diagnosed by clinical signs, although non-significant and pathognomic signs are present (Woody and Hoskins, 1991). The tetracyclines both oral and parenteral are the drugs of choice and are effective treatment of *E. canis* (Davidson *et al.*, 1998). However, oral doxycycline was reportedly associated with the lowest incidence of disease recrudescence following treatment, but with questions regarding the efficacy of this antibiotic for elimination of *E. canis*. Keeping the significance of diagnosis and management of ehrlichiosis in dogs the present study was designed and reported.

MATERIALS & METHODS

Dogs of various breed, age and sex that were presented with the signs of recurrent fever, off food, edema of dependent parts and epistaxis with or without the history of tick infestation to Teaching Veterinary Clinical Complex of CVSc Hyderabad were considered for the study. Whole blood was collected for hematology and serum chemistry. Further, the suspected dogs were

subjected for SNAP 4DX plus test (IDEXX Laboratories, United States) for confirmation of canine ehrlichiosis. Later the dogs that were confirmed for *E. canis* were subjected for treatment with rifampicin, 10 mg/kg, orally, for 3 weeks. However, other supportive drugs such as, hematonics, acaricides and antihistamines were also given for respective periods.

RESULTS

Almost all the affected dogs revealed similar signs such as, generalised weakness, emaciation, and pale to icteric mucosa, lymphadenitis, petechial haemorrhages on the ventral abdomen, pedal edema, epistaxis and orchitis (fig. 1 to 7). Two of the affected dogs also revealed incoordinated gait, edematous face and seizures. Presence of ticks on their body in general and interdigits and inside the base of the ear (fig. 8) was also noticed in few cases. Significantly low ($P<0.05$) levels of mean total erythrocyte count ($4.8 \pm 1.20 \times 10^6/\text{ml}$), haemoglobin ($6.2 \pm 1.10 \text{ g/dl}$) and packed cell volume ($37.2 \pm 0.98 \%$) with leukopenia ($4.98 \pm 1.22 \times 10^3/\text{ml}$) and thrombocytopenia ($82.4 \pm 1.32 \times 10^3/\mu\text{l}$) were the hematological findings. Whereas, biochemically there was a significantly increased ($P<0.05$) activity of mean alanine amino transferase ($286 \pm 1.46 \mu\text{l}$) with low levels of serum proteins ($4.1 \pm 1.32 \text{ mg/dl}$) and serum albumins ($1.2 \pm 0.22 \text{ mg/dl}$) but increased globulins ($3.0 \pm 1.20 \text{ mg/dl}$) were noticed in the affected dogs. Blood smear examination made from buffy coat revealed morula of *E. canis* in the monocytes of 8 dogs. Further, SNAP 4DX plus test showed positive towards the antibodies of *Ehrlichia canis* and / or *Ehrlichia ewingii* of 13 samples, thus confirming ehrlichiosis in 13 dogs. As the SNAP 4DX plus test didn't differentiate the antibodies against

Ehrlichia canis and *Ehrlichia ewingii*, a positive test result of either of these species was thus confirmed as canine ehrlichiosis. In the present study, history also revealed that 8/13 dogs that were confirmed for ehrlichiosis of the present study, were said to be subjected for treatment with doxycycline @10 mg/kg, BID, orally for three weeks also showed a recurrent episode of canine monocytic ehrlichiosis. Whereas, following therapy with rifampicin,

10 mg/kg, bid, orally, and other supportive drugs, marked improvement was noticed in 8 dogs from day 3 and in the rest from day 5 but with complete clinical recovery along with a negative result for SNAP 4DX plus test on day 21 of therapy. Thus confirming the complete elimination of *E. canis* organisms from the circulation of the affected but recovered dogs by the end of the therapeutic period.



FIGURE 1: *E. canis* affected dog – pale conjunctiva



FIGURE 2: bleached gingival mucosa – *E. canis* dog



FIGURE 3: Icteric gingival mucosa – *E. canis* dog



FIGURE 4: Icteric abdomen – *E. canis* dog



FIGURE 5: Canine ehrlichiosis – bilateral nasal bleeding



FIGURE 6: Canine ehrlichiosis – bilateral petechial hemorrhages on abdomen



FIGURE 7: Canine monocytic ehrlichiosis – note emaciated, weak physical condition



FIGURE 8: Numerous ticks studded in the ear lobe

DISCUSSION

Ehrlichia canis causes a potentially fatal disease in dogs that requires rapid and accurate diagnosis in order to initiate specific therapy leading to a favourable outcome. Anemia, anorexia, ataxia, conjunctivitis, depression, fever, ocular discharge, and vomiting were the significant signs noticed in acute canine monocytic ehrlichiosis (Neer and Harrus, 2006). The authors also documented pancytopenia in these cases. Long-term mild or severe chronic phases of canine ehrlichiosis can also occur, with recurrent clinical and hematologic signs that include pancytopenia, hemorrhage, monocytosis, lymphocytosis and weight loss. Whereas, Little and Sussane, (2010) opined that a low packed cell volume in the blood is a common indicator of the presence of *E. canis* and a blood smear can be done to determine if morulae is present in leukocytes to definitively diagnose the infection. Because this process is

often long and tedious, the presence of antibodies that appear within seven days post-infection to *E. canis* in blood can be used to effectively diagnose a patient. Gary *et al.* (2015) reported that ehrlichiosis is relatively common vector borne infections in dogs and in their study it was found that 95% dogs were seropositive for *Ehrlichia* species. Stillman and Monn (2014) documented that the SNAP 4Dx Plus Test, detects antibodies produced by five pathogens, which include *A. phagocytophilum*, *A. platys*, *B. burgdorferi*, *E. canis* and *E. ewingii*, in addition to detection of heartworm antigen. Further, Thatcher *et al.*, (2015) and O'Connor *et al.* (2006) also opined that the IDEXX SNAP 4Dx Plus Test was substantially more sensitive than other rapid in-clinic serologic assays for detection of antibodies to canine monocytic ehrlichiosis. Because the vector of *E. canis* uses canine species as a primary host, this bacteria is most commonly associated

with dogs but multiple human cases have been reported (Perez *et al.*, 2006). Tetracyclines are considered to be first-line drugs in the treatment of canine monocytic ehrlichiosis caused by *Ehrlichia canis* (Harrus *et al.*, 2012). However, only doxycycline has been critically evaluated in experimental or natural disease and there are conflicting reports on the clearance of the infection following different doxycycline treatment protocols (Gaunt *et al.*, 2010). Although doxycycline alleviates clinical ehrlichiosis in dogs, there are questions regarding the efficacy of this antibiotic for elimination of *E. canis*. Some reports suggested persistence of infection following doxycycline regimens of naturally and experimentally infected dogs during postacute CME (Bartsch and Greene 1996). Other reports suggested *E. canis* clearance after doxycycline treatments of dogs during acute ehrlichiosis (Harrus *et al.*, 2004). However, the utility of antibiotic treatments to minimize the possibility of *E. canis* transmission should be confirmed. In the present study 8/13 dogs that were under study were reported to have relapsing episodes of ehrlichiosis, in spite of therapy with doxycycline for considerable period. The findings in the present study are in opinion with McClure *et al.* (2010) and Schaefer *et al.* (2007) who documented that, treatment with various doxycycline regimens failed to eradicate the infection in 25%–100% of the acutely, sub clinically or chronically infected dogs, despite their clinical and haematological recovery. Collectively, current evidence implies that doxycycline effectively ameliorates the *E. canis*-induced clinical and haematological abnormalities, but is not consistently effective in clearing the infection. In addition, some dogs may be intolerant to doxycycline, thus justifying the evaluation of medications that could be used as alternatives to doxycycline. Rifampicin, also known as rifampin, is an antibiotic used to treat a number of bacterial infections, such as, tuberculosis, leprosy and legionella, among others. Rifampicin is also recommended as an alternative treatment for infections with the tick-borne disease pathogens, *Borrelia burgdorferi* and *Anaplasma phagocytophilum* when treatment with doxycycline is contraindicated, such as in pregnant women or in patients with a history of allergy to tetracycline antibiotics. Rifampicin is easily absorbed from the gastrointestinal tract; its ester functional group is quickly hydrolyzed in the bile and it is catalyzed by a high pH and substrate-specific esterase. After about six hours, almost the entire drug is deacetylated. Even in this deacetylated form, rifampin is still a potent antibiotic; however, it can no longer be reabsorbed by the intestines and it is subsequently eliminated from the body. The findings of the present study are in accordance with Schaefer *et al.* (2008) who opined that the rifampicin may be an alternative chemotherapeutic agent to doxycycline for the treatment of CME. The authors further documented that the rifampicin was effective (15 mg/kg/12 h orally for 7 days) in alleviating subclinical ehrlichiosis associated hemtological changes in dogs. However, rifampicin objectively hastened resolution of thrombocytopenia, but was inconsistent in eliminating the acute *E. canis* infection (Schaefer *et al.*, 2008). As the drug was not completely effective in eliminating the *E. canis* when given at the dose rate of 10mg/kg for 1 week and the common side effects associated with increased dosage, the drug was administered at the safe dosage but with prolonged

duration as suggested by (McClure *et al.*, 2010 and Greene and Calpin 2012). Further the clinical improvement and improvement in platelets, leukopenia and anemia of the ehrlichia affected dogs of the present study is in accordance with Harrus *et al.* (2012).

CONCLUSION

Based on the present findings, it may be concluded that, SNAP 4DX plus test is the most sensitive means of diagnosing *ehrlichiosis* associated with either *Ehrlichia canis* or *Ehrlichia ewingii*. Though doxycycline was found to be the drug of choice, rifampicin may be considered as an alternative antibacterial agent for canine monocytic ehrlichiosis, particularly for relapsing cases and in those which are intolerant to doxycycline.

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