SERUM CONCENTRATIONS OF TUMOUR NECROSIS FACTOR IN DOGS NATURALLY INFECTED WITH BABESIA CANIS AND ITS RELATION TO SEVERITY OF DISEASE

by

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Résumé

Canine babesiosis, caused by the tick-borne protozoan *Babesia canis rossi*, is an economically important and potentially fatal disease of dogs in South Africa. The host’s response to many infectious diseases is mediated (at least in part) by intercellular messengers called cytokines. One of the most important cytokines released is tumour necrosis factor (TNF).

A study was designed to measure serum concentrations of TNF in dogs naturally infected with canine babesiosis and to relate TNF concentrations to clinical severity, mortality, rectal temperature and parasitaemia.

There was a statistically significant difference in TNF concentrations between groups of differing disease severity, with a general trend of increasing mean log(TNF) with increasing severity of disease. A noteworthy finding was that dogs with hypoglycaemia had very high TNF (mean 15.03 ng/ml compared to a mean of 2.32 ng/ml for other sick dogs without hypoglycaemia). When TNF values were compared between survival and non-survival groups, there was no significant difference. The rectal temperature of the dogs in this study did not show any statistically significant association with TNF concentrations. When parasitaemia and TNF were examined within groups of infected dogs, there was no significant relationship. However, when the sample size was increased by pooling all infected dogs and treating them as a single group, there was a highly significant positive correlation \( p = 0.003 \) between parasitaemia and serum TNF concentrations.

The results of this study were encouraging and indicate that canine babesiosis may share a similar pathophysiology with human malaria in terms of TNF being associated with disease severity. One of the most significant findings in this study was the presence of very high TNF values in two of three dogs with hypoglycaemia. Hypoglycaemia has not been previously recorded in dogs with babesiosis and is a potentially important finding particularly in view of the hypoglycaemia associated with malaria in humans. Malarial hypoglycaemia is correlated with a higher mortality in humans, especially in pregnant women and children. If the findings of this study can be
confirmed and expanded, they may lend further support to the use of canine babesiosis as a model for some of the problems encountered in human malaria research.
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List of Abbreviations

ALP = alkaline phosphatase
ALT = alanine transaminase
ANOVA = analysis of variance
CNS = central nervous system
EDTA = ethylenediaminetetraacetic acid
ELISA = enzyme-linked immunosorbent assay
IFN-γ = interferon-gamma
IL-1 = interleukin-1
IL-6 = interleukin-6
MODS = multiple organ dysfunction syndrome
mRNA = messenger ribose nucleic acid
mTNF = membrane expressed tumor necrosis factor
MTS = 3-[4,5-dimethylthiazole-2-yl]-2,5-diphenyltetrazolium bromide
NCPO = non-cardiogenic pulmonary oedema
NF-κβ = nuclear factor kappa beta
OVAH = Onderstepoort Veterinary Academic Hospital
PaO₂ = partial pressure of oxygen within the pulmonary artery
PAO₂ = partial pressure of oxygen within the alveoli
PO = pulmonary oedema
rcTNF = recombinant canine TNF
SIRS = systemic inflammatory response syndrome
sTNF = soluble tumor necrosis factor
sTNFR = soluble tumor necrosis factor receptors
TNF = tumor necrosis factor
TNFR₁ = TNF receptor I
TNFR₁I = TNF receptor II