Review article

Feline babesiosis : an endemic South African disease

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Abstract

Babesia felis, originally described from wild cats in the Sudan, was subsequently incriminated as causing clinical disease in domestic cats. Although babesiosis in domestic cats has been reported sporadically from various countries, as a significant disease it appears to be a disti-nctly South African phenomenon. Apart from an inland focus, feline babesiosis is reported regularly only from coastal regions. The infection is assumed to be tick-borne, but the vector has not been identified. Feline babesiosis tends to be an afebrile, chronic, low-grade disease. The most frequently reported complaints by owners are anorexia and lethargy. The main clinical findings are anaemia, depression and occa-sionally icterus. Concurrent infections (e.g. *Mycoplasma haemofelis*, FeLV, FIV) may contribute to the clinical picture. Laboratory findings commonly include regenerative anaemia, elevation of alanine transaminase (but not alkaline phosphatase) and total bilirubin concentrations and a variety of electrolyte disturbances. Secondary immune-mediated haemolytic anaemia can be seen occasionally. Drugs effective against other *Babesia* species give variable and questionable results. The drug of choice is primaquine phosphate, which effects clinical cure but does not eliminate the infection. Repeated or chronic therapy may be required.

Key words : Anaemia, *Babesia felis*, Cats, Feline babesiosis, Primaquine phosphate

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INTRODUCTION

Babesiosis of domestic cats has been reported sporadically from various countries, including France [4, 20], Germany [26], Thailand [18], India [27] and Zimbabwe [36], but does not seem to be a regularly occurring significant clinical disease in any country other than South Africa. Apart from an inland focus at Kaapschehoop (25° 35.40'S, 30° 46.18' E), a small village on the eastern escarpment of Mpumalanga Province [31], feline babesiosis is reported regularly only from South African coastal regions [17]. Incidence is highest along the southern Cape coast, with more sporadic occurrence in the eastern coastal areas and minimal disease reported from the west coast beyond Cape Town. Overall incidence is highest in summer, but seasonality is less pronounced in non-seasonal and winter-rainfall areas. Although feline babesiosis is assumed to be a tick-borne infectio n, the vector has not been identified.

THE CAUSATIVE ORGANISM

Apart from an earlier, dubious report [22], *Babesia felis*, described from an African wild cat (*Felis ocreata, syn. Felis sylvestris*) [39] in the Sudan in 1929 was the first piroplasm from cats to be reported and named [8]. This was followed by *Babesiella felis* in two captive pumas (*Felis concolor*) in a zoo in Egypt [6] ; *Nuttalia felis* var. *domestica* in a domestic cat in South Africa [16] ; *Babesia* cati in an Indian wild cat (*Felis catus*) [27] ; *Babesia herp-ailuri* in a South American jaguarundi (*Herpailurus yaguarundi*) [9] ; and *Babesia pantherae* in a leopard (*Panthera pardus*) in Kenya [10], all based on mor-phology and/or biology. The first species described based on molecular characterization was *Babesia leo* from lions (*Panthera leo*) in the Kruger National Park, South Africa [29]. Since then, *Babesia canis sergenti* has been described from domestic cats in Israel [1], also based on molecular characterization. The latter is a large piroplasm, and may be the same as the one reported previously from Zimbabwe [36]. Two further piroplasms have been described from cats : *Cytauxzoon* felis, which occurs in domestic and wild cats in the United States [19, 37, 38], and *Cytauxzoon manul*, described from Pallas's cats (*Oto-colobus manul*) [33].

Babesia felis, isolated from a wild-caught African wild cat in the Sudan, was found to be transmissible

to domestic cats, which developed a parasitaemia, but did not show any signs of clinical disease [8]. This difference was clearly noted by the first authors to report clinical feline babesiosis in South Africa, and they even proposed a different name for the causative organism : *Nuttalia* (=*Babesia*) *felis* var *domestica* [16]. It is unfortunate, therefore, that *Babesia felis* was subsequently applied to the causative organism of the potentially fatal disease of domestic cats in South Africa [12, 31]. Two isolates from a sick caracal (*Felis caracal*) have been sequenced and were found to be very similar to the disease-causing *B. felis* from domestic cats [29]. This raises the question whether *B. felis* reported from domestic and wild felids is, in fact, a single species. Confusion should be cleared up by applying molecular techniques. Unfortunately, Davis did not mention whether he had deposited any type specimens, so the chances are remote of locating for comparative purposes the original material on which the description was based.

Babesia felis was described by Davis [8] as a small, circular body with faint blue-staining cytoplasm and dark red-staining chromatin (with Giemsa's stain). The chromatin is usually peripheral, either as a small granule or dispersed around a varying proportion of the periphery of the parasite. The parasites may appear ring-shaped, and resemble young malaria parasites. Irregular forms also occur : amoeboid or irregularly circular. The diameter of the parasites usually ranges from 1 μm to 2.25 μm, with the majority measuring ca. 1.25 μm in diameter. Elongated forms and large piriform parasites occur infrequently [16]. Maltese crosses (4 piriform merozoites in a cruciform shape) are occasionally seen [17].

THE VECTOR

The vector of *B. felis* is assumed to be a tick, but is as yet unknown. The restricted geographical distribution of feline babesiosis in South Africa strongly suggests that the vector is a tick with very specific habitat requirements. The suggestion that *Haemaphysalis leachi* is the vector [25] is flawed. Firstly, it was assumed that transovarial transmission had taken place in the ticks. This is unlikely (although not impossible), as other small piroplasms seem to be transmitted stage-to-stage, for example the transmission of *C. felis* by *Dermacentor variabilis* [3]. Secondly, *H. leachi*, the only vector of *Babesia canis rossi*, is widespread in South Africa [21], which does not tally with the restricted distribution of *B. felis*.

CLINICAL SIGNS

In contrast to babesiosis in other domestic animals, feline babesiosis is not associated with pyrexia [16]. Most affected cats seem to be young adults of less than three years of age [13, 35]. No breed or sex predisposition is evident, but Siamese cats might be over-represented amongst purebred cats. The most frequently reported complaints by owners are depression/lethargy (92%) and anorexia (85%) [17]. The most common clinical signs are anorexia, listlessness and anaemia, followed by icterus [35]. Less common signs are weakness, constipation and pica [35]. The disease usually follows a chronic course [25], and affected animals may show little sign of illness until an advanced stage [13].

PARASITAEMIA

In a recent study, peripheral parasitaemias (n=55) ranged from 0.3% to 42.3%, with a median of 5.0%, while central parasitaemias (n=56) ranged from 0.2% tot 41.4%, with a median of 6.4% [35]. The strong correlation between central and peripheral parasitaemias indicates that sequestration of *B. felis*-infected red blood cells (RBC) in capillary beds is not a feature of the disease [13, 34].

HAEMATOLOGY

Macrocytic, hypochromic, regenerative anaemia is the most consistent haematological finding, although a large proportion of cats are not anaemic [35]. Anaemia, which can become severe in advanced cases [13, 35], is haemolytic, presumably resulting from both intravascular and extravascular erythrolysis. Artificially infected cats were most anaemic 21 days after infection [14]. In one study, moderate anaemia was found in 23% and severe anaemia in 34% of naturally infected cats [35]. Nucleated RBC were present in 70% of these cats, with counts ranging from 1 to 814 nRBC/100 white blood cells, with a median count of 10.5. Signs of bone marrow erythropoiesis were commonly evident on blood smear examinations and included the presence of reticulocytes, numerous nucleated RBC, marked anisocytosis, polychromasia, Howell-Jolly bodies in excess of 1% of RBC and basophilic stippling of some RBC [13, 35].

A statistically significant, but weak, negative correlation between central parasitaemia and haematocrit (Ht) appeared to be most pronounced with parasitaemia > 20%, with 90% of these cats having a Ht ≤ 15% [35]. Ht levels tended to be more randomly distributed with parasitaemia < 20%.

No characteristic changes are seen in total or differential leukocyte counts ; when abnormal values are present they are often accompanied by concurrent illness or infection. Thrombocyte counts are variable and thrombocytopenia is an inconsistent finding. The in-saline agglutination test can be positive in a number of cases, indicating that secondary immune-mediated haemolytic anaemia can also be a feature of this disease [35].

CLINICAL PATHOLOGY

The most remarkable clinico-pathological changes are elevation of hepatic cytosol enzyme activities and total bilirubin concentrations [15, 35].

Serum alanine transaminase (ALT) is significantly elevated in 89% of cats, whereas alkaline phosphatase and gamma glutamyltransferase are generally within normal limits [35]. This provides evidence of primary hepatocellular injury or inflammation in feline babesiosis. The hyperbilirubinaemia is most likely a result of haemolysis, but secondary hepatocellular injury is probably an additional contributing factor. ALT levels of cats with visible icterus were statistically significantly higher than those of non-icteric cats. There was also a significant correlation between ALT and total bilirubin concentrations [35].

In one study, total serum protein values were elevated in 32% of cats, while hyperalbuminaemia was recorded in 45% [35]. Hyperglobulinaemia was present in 23% of cats, in all cases due to polycloncal gammopathies. Abnormal globulin fractions were recorded in one third of the 77% of cats with normal total globulin concentrations. These included various combinations of abnormal α, β and γ globulin concentrations, but no consistent pattern of changes was seen. These changes can be ascribed to a combination of acute-and chronic-phase proteins produced in response to the *Babesia* antigens.

No characteristic changes in renal parameters are observed and serum urea and creatinine levels are mostly within normal limits, indicating that gross renal damage is not a consistent feature of the disease [15, 35]. No characteristic changes in serum electrolytes (sodium and potassium) are seen, although a variety of electrolyte disturbances can occur, and electrolyte concentrations should be monitored [35].

PATHOLOGY

Necropsy findings are characterised by extreme pallor of the viscera and thin, watery blood [15]. Pronounced icterus is rarely seen. The liver is often enlarged, frequently yellow or dark brown in colour, and in some cases the surface has a mottled appearance. The gall bladder may be distended. The intestinal tract usually contains thick yellow or brownish bile and the rectal contents are invariably yellow to orange. Urine, when present, is usually golden yellow. The carcase is usually not emaciated. Enlarged mesenteric lymph nodes are occasionally seen.

No specific uniform pattern is seen in the histopathology [15]. The most consistent findings in the liver are varying degrees of centrilobular necrosis, bile stasis and extramedullary haematopoiesis. Pigment, probably haemosiderin, may be found in the liver.

CONCURRENT INFECTIONS

Concurrent infections with *Haemobartonella felis* (= *Mycoplasma haemofelis*), feline leukemia virus (FeLV) and/or feline immunodeficiency virus (FIV) have been identified in a number of cats and this seems to have profound effects on response to treatment and outcome of the disease [35]. In one study, 14% of the affected cats tested positive for FIV infection and 32% tested clearly positive for FeLV infection [35]. Of these cats, 9 % had concurrent FIV and FeLV infections. In addition, 11% of the remaining cats showed equivocal test results for FeLV. Concurrent infection with *H. felis* was detected on both peripheral and central venous blood smears of 11% of the affected cats; one half of these cats also tested positive for concurrent FeLV infection. In this study, most of the affected cats > 3 years old had a concurrent illness or infection that could have influenced the cat's immune system.

TREATMENT

Davis [8] reported that trypan blue appeared to exercise no influence on the parasitaemia in two domestic cats artificially infected with *B. felis* isolated from a wild cat. In the first reported feline babesiosis

case in South Africa [16], the cat was treated intramuscularly with quinuronium sulphate ("Akiron") and was reported to be convalescing and to have regained its appetite 48 hours later. Within a week it had a slight relapse and the treatment was repeated. Uneventful recovery ensued. In a paper published during the same year, it was stated that recovery was in most cases effected by injection of trypan blue or quinuronium sulphate ("Acaprin"), at the same dosages as recommended for dogs [25].

Later tetracyclines, sometimes used in combination with trypan blue, and cephaloridine were recommended for treatment of feline babesiosis [5, 11, 34]. When efficacy of 10 drugs against *B. felis* infections was investigated experimentally, most drugs used against babesiosis in other domestic animals gave variable and questionable results [32]. Primaquine phosphate at 0.5mg/kg was highly effective, but frequently caused vomiting when administered orally and was lethal at dosages exceeding 1 mg/kg. In a recent investigation, rifampicin and a sulphadiazine-trimethoprim combination appeared to have an anti-parasitic effect but were inferior to primaquine, which had a dramatic effect on parasitaemia, but failed to eliminate *B. felis* infections [30]. In the same trial it was found that buparvaquone, enrofloxacin and danofloxacin had no significant anti-babesial effect. Despite its drawbacks, primaquine remains the drug of choice. Repeated or chronic therapy may be required. Doxycycline may add potential benefits in treatment of this disease. It may be added that a combined treatment with atovaquone and azithromycin, which has been shown to be effective against *Babesia gibsoni* [2], also a small piroplasm, has not been tested experimentally in feline babesiosis cases.

In a survey of South Africa veterinary practitioners, the vast majority of respondents (95%) used primaquine phosphate as the antibabesial of choice, with the remainder listing diminazene, doxycycline, imidocarb and oxytetracycline [17]. A generally-accepted dosage regimen for primaquine (1 mg per cat every 36 hours for 4 treatments, followed by 1 mg weekly for 4 weeks) was used by 36% of practitioners. The origin of this regimen is unclear. The correct dosage regimen for primaquine phosphate in feline babesiosis is 0.5mg/kg per os every 72 hours for 3 treatments, followed by 0.5mg/kg weekly for 3-4 weeks [32].

PROGNOSIS

Although response to therapy is usually good, and premunity is assumed to develop over time, the average mortality from feline babesiosis is estimated at 15% [17]. The chronicity of feline babesiosis, and its relatively low virulence, are probably related to the absence of sequestering in capillary beds, which leads to a higher visible parasitaemia. Cats are also relatively resistant to endotoxin [28]. Species that are refractory to endotoxin are also less to susceptible to babesiosis and show symptoms of disease at a higher parasitaemia than endotoxin-sensitive species [7].

REFERENCES

1. Baneth, G., Kenny, M. J., Tasker, S., Anug, Y., Shkap, V., Levy, A. and Shaw, S. E. 2004. Infection with a proposed new subspecies of *Babesia canis*, *Babesia canis subsp presentii*, in domestic cats. J. Clin. Microbiol. 42 : 99-105.
2. Birkenheuer, A. J, Levy, M. G. and Breitschwerdt, E. B. 2004. Efficacy of combined atovaquone and azithromycin for therapy of chronic *Babesia gibsoni* (Asian genotype) infections in dogs. J. Vet. Intern. Med. 18 : 494-498.
3. Blouin, E. F., Kocan, A. A., Glen, B. L., Kocan, K. M. and Hair, J. A. 1984. Transmission of *Cytauxzoon felis* Kier, 1979 from bobcats, *Felis rufus* (Schreber), to domestic cats by *Dermacentor variabilis* (Say). J. Wildl. Dis. 20 : 241-242.
4. Bourdeau, P. 1996. Feline babesiosis. Point Vet. 27 : 947-953.
5. Brownlie, J. F. 1954. Aureomycin in the treatment of piroplasmosis in the cat. J. S. Afr. Vet. Med. Assoc. 25 : 654.
6. Carpano, M. 1934. Sur les piroplasmoses des carnassiers et sur un nouveau piroplasme des felins (*Babesiella felis* chez le puma : *Felis concolor*). Bull. Techn. Sci. Serv., Min. Agric., Egypt 75 : 41-52.
7. Clark, I. A. 1982. Correlation between susceptibility to malaria and babesia parasites and to endotoxicity. Trans. Roy. Soc. Trop. Med. Hyg. 76 : 4-7.
8. Davis, L. J. 1929. On a piroplasm of the Sudanese wild cat (*Felis ocreata*). Trans. R. Soc. Trop. Med. 22 : 523-534.
9. Dennig, H. K. 1967. Eine unbekannte Babesienart beim Jaguarundi (*Herpailurus yaguarundi*). Klei-

ntierpraxis 12 : 146-152.
10. Dennig, H. K. and Brocklesby, D. W. 1972. *Babesia pantherae* sp. nov., a piroplasm of the leopard (*Panthera pardus*). Parasitology 64 : 525-532.
11. Dorrington, J. E. and du Buy, W. J. C. 1966. Ceporan : efficacy against *Babesia felis*. J. S. Afr. Vet. Med. Assoc. 37 : 93.
12. Futter, G. J. and Belonje, P. C. 1980. Studies on feline babesiosis. 1. Historical review. J. S. Afr. Vet. Assoc. 51 : 105-106.
13. Futter, G. J. and Belonje, P. C. 1980. Studies on feline babesiosis. 2. Clinical observations. J. S. Afr. Vet. Assoc. 51 : 143-146.
14. Futter, G. J., Belonje, P. C. and van den Berg, A. 1980. Studies on feline babesiosis. 3. Haematological findings. J. S. Afr. Vet. Assoc. 51 : 271-280.
15. Futter, G. J., Belonje, P. C., van den Berg, A. and van Rijswijk, A. W. 1981. Studies on feline babesiosis. 4. Chemical pathology, macroscopic and microscopic post mortem findings. J. S. Afr. Vet. Assoc. 52 : 5-14.
16. Jackson, C and Dunning, F. J. 1937. Biliary fever (nuttalliosis) of the cat : A case in the Stellenbosch District. J. S. Afr. Vet. Med. Assoc. 8 : 83-88.
17. Jacobson, L. J., Schoeman, T., and Lobetti, R. G. 2000. A survey of feline babesiosis in South Africa. J. S. Afr. Vet. Assoc. 71 : 222-228.
18. Jittapalapong, S. and Jansawan, W. 1993. Preliminary survey on blood parasites of cats in Bangkhen District Area. Kasetsart J. Nat. Sci. 27 : 330-335.
19. Kier, A. B. 1979. The etiology and pathogenesis of feline cytauxzoonosis. PhD Thesis, University of Missouri, Columbia. MO, USA.
20. Leger, N., Ferte, H., Berthelot, P., Nourry, D. and Brocvielle, P. 1992. Un cas de babesiose feline en Haute-Marne, France. Sci. Vet. Med. Comp. 94 : 249-252.
21. Lewis, B. D., Penzhorn, B. L., de Waal, D. T. and Lopez-Rebollar, L. M. 1996. Isolation of a South African vector-specific strain of *Babesia canis*. Vet. Parasitol. 63 : 9-16.
22. Lingard, A. and Jennings, E. 1904. A preliminary note on a piroplasmosis found in man and in some of the lower animals. Ind. Med. Gaz. 39 : 161 (original not seen ; quoted by Magrulkar, 1937).
23. Lopez-Rebollar, L. M., Penzhorn, B. L., de Waal, D. T. and Lewis B.D. 1999. A possible new piroplasm in lions from the Republic of South Africa. J. Wildl. Dis. 35 : 82-85.
24. Magrulkar, M. Y. 1937. On a piroplasm of the Indian cat (*Felis domesticus*). Ind. J. Vet. Sci. Anim. Husb. 8 : 243-246.
25. McNeil, J. 1937. Piroplasmosis of the domestic cat. J. S. Afr. Vet. Med. Assoc. 8 : 88-90.
26. Moik, K. and Gothe, R. 1997. *Babesia* infections of felids and a report on a case in a cat in Germany. Tieraerztl. Praxis 25 : 532-535.
27. Mudaliar, S. V., Achary, G. R. and Alwar, V. S. 1950. On a species of *Babesia* in an Indian wild cat (*Felis catus*). Ind. Vet. J. 26 : 391-395.
28. Otto, C. M. and Rawlings, C. A. 1995. Tumor necrosis factor production in cats in response to lipopoly-saccharide : an *in vivo* and *in vitro* study. Vet. Immunol. Immunopathol. 49 : 183-188.
29. Penzhorn, B. L., Kjemtrup, A. E., Lopez-Rebollar, L. M. and Conrad, P. A. 2001. *Babesia leo* n. sp. from lions in the Kruger National Park, South Africa, and its relation to other small piroplasms. J. Parasitol. 87 : 681-685.
30. Penzhorn, B. L., Lewis, B. D., Lopez-Rebollar, L. M. and Swan, G. E. 2000. Screening of five drugs for efficacy against *Babesia felis* in experimentally infected cats. J. S. Afr. Vet. Assoc. 71 : 53-57.
31. Penzhorn, B. L., Stylianides, E., Coetzee, M. A., Viljoen, J. M. and Lewis, B. D. 1999. A focus of feline babesiosis at Kaapschehoop on the Mpumalanga escarpment. J. S. Afr. Vet. Assoc. 70 : 60.
32. Potgieter, F. T. 1981. Chemotherapy of *Babesia felis* infection : efficacy of certain drugs. J. S. Afr. Vet. Assoc. 52 : 289-293.
33. Reichard, M. V., Van Den Bussche, R. A., Meinkoth J. H., Hoover, J. P. and Kocan, A. A. 2005. A new species of *Cytauxzoon* from Pallas' cats caught in Mongolia and comments on the systematics and taxonomy of piroplasmids. J. Parasitol. 91 : 420-426.
34. Robinson, E. M. 1963. Biliary fever (nuttalliosis) in the cat. J. S. Afr. Vet. Med. Assoc. 34 : 45-47.
35. Schoeman, T., Lobetti R. G., Jacobson, L. S. and Penz-horn, B. L. 2001. Feline babesiosis : signalment, clinical pathology and co-infections. J. S. Afr. Vet. Assoc. 72 : 4-11.
36. Stewart, C. G., Hackett, K. J. W. and Collett, M. G. 1980. An unidentified *Babesia* of the domestic cat (*Felis domesticus*). J. S. Afr. Vet. Assoc. 51 : 219-221.
37. Wagner, J. E. 1975. Cytauxzoonosis in domestic cats (*Felis domestica*) in Missouri. J. Am. Vet.

Med. Assoc. 167 : 874.
38. Wagner, J. E. 1976. A fatal cytauxzoonosis-like disease in cats. J. Am. Vet. Med. Assoc. 168 : 585.
39. Wilson, D. E. and Reeder, D. M. 1993. Mammal species of the world-a taxonomic and geographic refe-rence, 2 nd ed. Smithsonian Institution, Washington DC.

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