

An afebrile heartwater-like syndrome in goats

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Heartwater is a serious limiting factor for sheep and goat production in the major endemic area of sub-Saharan Africa and therefore most knowledge, research and control methods originate from this region. Whilst the usual or common clinical presentations can be used to make a presumptive diagnosis of heartwater with a good measure of confidence, this is not always the case, and animals suffering from heartwater may be misdiagnosed because their cases do not conform to the expected syndrome, signs and lesions. One aberrant form found occasionally in the Channel Island breeds of cattle and some goats is an afebrile heartwater-like syndrome. The most constant and characteristic features of this heartwater-like syndrome comprise normal temperature, clinical signs associated with generalised oedema, and nervous signs, especially hypersensitivity. The presumption that the disease under investigation is the afebrile heartwater-like syndrome entails a tentative diagnosis based on history and clinical signs and the response to presumed appropriate treatment (metadiagnosis). The afebrile heartwater-like syndrome presents similarly to peracute heartwater but without the febrile reaction. Peracute cases of heartwater have a high mortality rate, enabling confirmation of the disease on post-mortem examination. Recognition of the afebrile heartwater-like syndrome is important to prevent deaths and identify the need for appropriate control measures.

Introduction

Heartwater has been well documented in the past and the causative organism is currently classified as an α -proteobacterium, *Ehrlichia ruminantium* (Allsopp 2009). Cattle are less susceptible to heartwater than sheep and goats and a considerable variation in susceptibility between breeds has been reported (Donkin *et al.* 1992; Uilenberg 1983). Matheron *et al.* (1987) demonstrated genetic resistance in Creole goats in Guadeloupe due to a recessive sex-linked gene, whereas Angora goats are highly susceptible to heartwater (Du Plessis, Jansen & Prozesky 1983). Whether an animal will develop heartwater or not also depends on factors such as species, breed, age, degree of natural resistance and immune status (Bath, Van Wyk & Pettey 2005).

Oberem and Bezuidenhout (1987) discussed the role of wild ruminants, guinea fowl, tortoises and scrub hares as reservoir hosts and their importance where stringent tick control in domestic animals is practised. The presence of these wild reservoirs, immunological strain differences of *E. ruminantium* and cross protection between strains are important factors in the epidemiology of heartwater (Du Plessis *et al.* 1989; Jongejan, Uilenberg & Franssen 1988). Infection rate in ticks, fluctuations in tick abundance and tick control also play a role (Uilenberg 1983).

The course of heartwater can be peracute, acute, subacute or chronic (Kusiluka & Kambarage 1996). The most common clinical signs include listlessness, poor appetite, decreased milk yield and nervous symptoms ranging from mild incoordination to pronounced convulsions (Bath, van Wyk & Pettey 2005). Fever of 40 °C or higher usually persists for 3–6 days and is followed by a drop to subnormal levels shortly before death (Bath, Van Wyk & Pettey 2005). However, not all clinical cases appear to develop a fever reaction and may exhibit other neurological signs such as hind limb paralysis and unusual behaviour patterns. Experience of the authors and other investigators (Dr A.F. Fisher & Dr S.R. van Amstel, pers. comm. 2012) indicates that there may be another form of heartwater, usually peracute in onset but lacking the typical fever reaction. Van Amstel first referred to cases that he had observed as having 'cold heartwater' and postulated that the presence or absence of fever reactions may be due to the amounts of interleukin (IL) 6 and tumour necrosis factor present at the time (S.R. van Amstel, pers. comm. 2012), but these cases were never recorded. Certain goat breeds and Channel Island cattle breeds may be more prone to develop this afebrile heartwater-like syndrome.

Three cases of afebrile heartwater-like syndrome in goats are described.

Clinical cases

The following cases were either seen by the authors or reported to the authors by private practitioners. Other cases have been discussed with the authors previously but were not recorded and so have not been included.

Case 1

A male, eight-tooth Saanen goat developed neurological signs including hyperaesthesia, nystagmus and paddling. The rectal temperature of the goat was 39 °C, which is normal for the goats in the Onderstepoort region. The temperature of the goat was monitored on the morning and evening of admission and again the following morning. The temperature did not rise or fall during that time. A tentative diagnosis of pituitary abscessation as the main cause of the clinical signs was made owing to the absence of a febrile reaction. The temperature was taken again the following morning with no changes recorded and the goat died later that day despite being treated with broad spectrum antibiotics (drug and dosage unknown) and was sent for necropsy where a diagnosis of heartwater was confirmed on brain smear examination. Hydrothorax and hydropericardium were also present at necropsy.

Case 2

A young (no permanent teeth) Boergoat presented as 'behaving strangely', according to the owner. The goat was attempting to climb out of the stall and also showed occasional head pressing although the rectal temperature was normal. This goat was immediately treated with tetracycline at a dose of 10 mg/kg and recovered uneventfully. A presumptive diagnosis of heartwater was made on response to treatment. The goat was kept under observation in the clinic for three days and then discharged. Rectal temperature was recorded daily and at no time was a fever reaction recorded.

Case 3

Twenty-two Boergoats in the Cathcart region (A.F. Fisher, pers. comm. 2012), all male, with does that were running in an adjoining camp, had died during the week. Approximately 30–40 had been reported dead in the neighbouring Gwatyu region. Some had been treated by the owner with tetracyclines (dosages and trade names unknown). Of those treated, some showed signs of improvement and some died. Two goats were seen by Dr Fisher and normal temperatures were recorded at the time of clinical evaluation. The goats died and brain smears were examined but no *Ehrlichia* organisms were seen and the smears were sent to a pathologist for evaluation. The presence of *Ehrlichia* organisms was confirmed by the pathologist. Another two goats were presented to Dr Fisher for further examination. Clinical signs included hind limb paralysis (as seen in the goats on the farm) that appeared to develop overnight, as no clinical signs were observed previously by the farmer. The goats were described as eating and alert, with one being slightly aggressive (possibly due to its inability to escape owing to the paralysis). The temperatures of the goats

were 39.1 °C and 39.0 °C respectively. Over the next 24 h – 48 h the clinical signs progressed to opisthotonus, nystagmus, galloping and hyperaesthesia. Over the two days the rectal temperature of the goats did not increase or decrease. The worst affected goat died and a necropsy was performed by Dr Fisher. Lesions observed included hydropericardium, slight splenomegaly, 3+ *Haemonchus contortus* (on a scale of 1+ being very few and 4+ being very many) infestation and the presence of approximately 12 *Amblyomma* (male) ticks. No lung oedema was observed macroscopically. Heartwater was confirmed on brain smear examination. The remaining goat was treated using tetracycline at 10 mg/kg and recovered.

Discussion

The goats in all three cases showed some signs of neurological involvement but no febrile reaction. The goat breeds affected included Boergoats and Saanens. The afebrile heartwater-like syndrome has not been diagnosed in any indigenous breeds other than Boergoats.

Diagnosis of heartwater in live animals is almost invariably based on clinical signs. It is conceded that a clinical diagnosis based only on signs and response to treatment is not as certain as a diagnosis based on specific, reliable and rapid tests. However, tests for heartwater in any manifestation are not always reliable.

Currently the only definitive way of confirming a diagnosis of *E. ruminantium* is by demonstration of the organisms in Giemsa or CAM's Quick-stained brain smears (Bezuidenhout *et al.* 1994). However, demonstrating the organism on brain smears does not necessarily confirm heartwater as some strains of *E. ruminantium* do not cause clinical heartwater and some do not cause any clinical signs (Allsopp *et al.* 2007).

As serum tests such as IFA are not specific for *E. ruminantium*, a polymerase chain reaction (PCR) test has been developed to provide a more specific test (Steyn *et al.* 2008). PCR will detect heartwater, but with the extraordinary genetic variability of the organism (Allsopp 2009) a positive result does not always indicate that observed clinical signs were due to heartwater, as some genetic variants are more pathogenic than others. For example, 70 clinically healthy Boergoats tested positive using PCR in a heartwater-free area (Allsopp *et al.* 1997). According to an authority on heartwater (B.A. Allsopp, pers. comm. 2013), although PCR can demonstrate the presence of *E. ruminantium* it must be noted that the definition of what comprises *E. ruminantium* is not entirely certain (Loftis, Levin & Spurlock 2008). Furthermore, the current cost of the test is approximately R320 per sample (Dr H.C. Steyn, Onderstepoort Veterinary Institute, pers. comm. 2013) and only if the concentration of genetic material is high enough can the laboratory sequence the sample and compare it with the database. Farmers and private practitioners do not routinely use these tests to confirm suspected cases where animals have been treated and recovered, as it is too costly and impractical. As Allsopp (2009) noted, definitive diagnoses are not often performed in endemic areas. Thus diagnosis has to rely

on signs, circumstances and reactions to treatment for the foreseeable future. Heartwater is by no means unique in this respect, since there are many other diseases like pneumonia that have to be dealt with in the same way. In order to save lives, it is extremely important to reach the presumptive diagnosis timeously and initiate appropriate treatment, while bearing in mind other possible differential diagnoses.

Since heartwater is usually closely associated with a fever, often > 40 °C, it is understandable and usual to attribute clinical signs not featuring fever to some other disease. Peripituitary abscessation in goats is an important differential diagnosis since it also does not involve fever (Bath, Van Wyk & Pettey 2005). However, the clinical signs are less pronounced, the animal is more depressed, there is usually a relative or absolute neutrophilia in blood samples, and animals seldom respond to a single treatment with tetracyclines. At post-mortem examination, there is no sign of oedema, brain smears are negative for heartwater and signs of bacterial infection around the hypothalamus can be seen, with a range of bacteria visible in smears of these lesions (Bath & De Wet, 2000). Other important differential diagnoses include plants causing neurological signs, and ionophores. There are 21 plants known to cause neurological or locomotor signs that could be confused with heartwater (Kellerman, Coetzer & Naudé 1990). Since they are all toxic, no fever would be expected but there would be no response to treatment with tetracyclines or related drugs. Only plants that occur in heartwater-prone areas would need to be considered, which reduces the list to less than ten. Clinical signs of ionophore toxicity include feed refusal, listlessness, stiffness, abnormal gait and diarrhoea, but again there would be no response to treatment with tetracyclines.

During the early febrile stages of heartwater, administration of tetracyclines at a dose rate of at least 10 mg/kg usually results in recovery (Bath, Van Wyk & Pettey 2005). More pathogenic strains of *E. ruminantium* may require daily treatment with tetracyclines (10 mg/kg) for up to five days. An initial dose of 20 mg/kg administered slowly intravenously may be necessary in these cases. The patient should then be monitored for signs of hypocalcaemia and treated for this where necessary. This applies to afebrile heartwater-like cases as well. In the advanced stages of the disease, additional supportive therapy must be considered (Bath, Van Wyk & Pettey 2005), although this is not always successful. Supportive treatments include stabilisation of membranes and blocking the effect of vasoactive compounds released with cellular death (Van Amstel & Oberem 1987) and drugs active in reducing oedema (Shakespeare *et al.* 1998). Partial exsanguination may help alleviate the symptoms, presumably by reducing oedema by drawing extra-vascular fluid back into the circulatory system (Bath, Van Wyk & Pettey 2005).

When there is no fever present, a presumptive diagnosis must nevertheless be made on the presence of other characteristic clinical signs, history and often the response to presumed appropriate treatment. A fairly consistent clinical sign of heartwater also seen in afebrile heartwater-like cases is

hyperaesthesia. Tapping the affected animal on the head and eliciting a hyperaesthetic reaction that includes rapid blinking of both eyes can assist with the early diagnosis of heartwater-like syndromes in afebrile cases.

Although preventative measures should always be preferred over treatment for all livestock diseases, in the case of heartwater, prevention is limited as an option due to a number of factors. Firstly, the 'vaccine' is not a true vaccine but an infection, and it can lead to severe clinical signs and death if reaction to the vaccine is not followed up with sufficient treatment. Secondly, another follow-up treatment is often required. Thirdly, the vaccine has to be kept at very low temperatures (on dry ice) to remain infective. Fourthly, the vaccine on thawing must be rapidly injected intravenously. Fifthly, the time lapse before a fever reaction triggers treatment can vary considerably and thus animals have to be monitored for extended periods. Sixthly, not all animals respond with a fever reaction. In these cases, where there are valuable animals involved, enzyme-linked immunosorbent assay (ELISA) has been used in the past to demonstrate whether or not vaccination has resulted in the production of antibodies. This is not always reliable. Seventhly, a few animals may die without showing clinical signs. Eighthly, vaccinated animals must be continuously exposed to field challenges (natural boosters) by maintaining sufficient infected ticks. This is very difficult to gauge since the degree of infection in a tick population cannot be measured. Ninthly, the common practice of regular blocking of the entire herd or flock with tetracyclines is not only time-consuming and expensive, it also leads to a heartwater-prone group of animals and will probably lead to the emergence of tetracycline-resistant organisms. Lastly, the practice of 'dipping clean' is also problematic. Any breakdown in dipping can lead to disease outbreaks; the animals are completely susceptible and regular dipping of all livestock will lead to the build-up of ticks resistant to ectoparasiticides.

Thus, until better preventive measures are developed (especially a true vaccine), the control of heartwater must include early recognition of the disease and prompt treatment. The ability to recognise all the different forms of heartwater that may be encountered is a key requirement for treating animals early and effectively.

Conclusion

Although in some of the reported cases *Ehrlichia* was demonstrated on brain smears, as discussed above it cannot be confirmed beyond all doubt that these cases were heartwater. Also, in those that recovered after treatment for presumed heartwater, other *Ehrlichia* species may have been the cause of this afebrile heartwater-like syndrome. The importance of this case report is thus to inform veterinarians that heartwater-like clinical signs without a fever reaction may respond to treatment usually given for heartwater and that heartwater should not be ruled out as a differential diagnosis in such instances. It is clear that more research is required in the fascinating field of heartwater.

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Competing interests

The authors declare that they have no financial or personal relationship(s) that may have inappropriately influenced them in writing this article.

Author's contributions

R.L. (University of Pretoria) wrote the manuscript and collected the data on the clinical cases; K.P.P. (University of Pretoria) contributed towards the information in the introduction and discussion; G.F.B. (University of Pretoria) contributed towards the abstract wording, information in the introduction and discussion as well as final editing.

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