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Case report



Canine trypanosomosis cases: monitor lizard as an unusual vector

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Abstract

Trypanosomosis is a well-known sub-Saharan disease. The human form was discovered in The Gambia over 100 years ago. Canine trypanosomosis in The Gambia has never been mentioned in the scientific literature, let alone the involvement of veranus species in its transmission to dogs. The disease's most important vector is the tsetse fly. This fly is abundant in The Gambia, and its infamy for transmitting the disease has been well established. A lot of research efforts have been put into understanding the critical role of this pest in the transmission of the protozoan and the disease in livestock. This report confirms the presence of the disease in domestic dogs in The Gambia, and three canine cases with varied clinical signs, different hematological pictures accompanying the disease, and different effective treatment approaches are reported. Early detection can prevent severe illness and help patients to recover better. This report enhances our understanding on canine trypanosomosis, transmission of the pathogen, and strategies for managing the disease. This report is significant, as it is the first mention of monitor lizards in the transmission of trypanosome parasites to dogs during the fighting between them.

Keywords

Canine African trypanosomosis, trypanosome, trypanocide, hemoparasite screening, monitor lizard, oral transmission

Introduction

Trypanosomosis was first described in dogs in 1908 (Verones and Focaccia, 2002). Different species of the protozoan have been implicated in canine trypanosomosis. Among the species implicated, *Trypanosoma brucei* and *Trypanosoma evansi* are considered prevalent (Jones et al., 2003). The major vector is the tsetse fly (genus *Glossina*), endemic in areas with forested water bodies (Uilenberg, 1998). Transmission occurs during hematophagy, when the tsetse fly injects saliva before sucking the blood of its host. Other biting insects can also serve as mechanical vectors (Desquesnes, 2004). Oral route transmissions have also been reported (Raina et al., 1985; Sangeetha et al., 2002). The clinical presentation of the disease includes acute, subacute, and chronic forms. Common symptoms include hyperthermia, corneal opacity, emaciation, anorexia, vomiting, hypersalivation, hyperventilation, and seizures. Clinical signs can progress to death rapidly (Eloy and Lucheis, 2009). The primary chemotherapeutic agent used in the treatment of canine trypanosomosis is diminazine aceturate. The drug is used with caution because of its cytotoxic effect (Aquinos, 2000). Relapses, despite treatment, have been reported.

One hundred and twenty years ago, the trypanosoma was first isolated in humans, from an European ship captain in The Gambia (Ford, 1902). Although in The Gambia trypanosomosis has been demonstrated in livestock, there has been no report in dogs, though the disease has been reported in neighboring Senegal (Sophie et al., 2015). The three cases reported here show the presence of the disease with varied clinical signs. The authors are not aware of any case reports of canine trypanosomosis in the Gambia.

Oral transmission of canine trypanosomosis is not very common. Evidence has shown that the monitor lizard (*Varanus* spp.) can serve as a host for trypanosoma (Njagu et al., 1999), but there is no report of its involvement in the transmission of the disease to the dogs.

This case report aims to contribute to the scientific knowledge of practicing clinicians, especially in areas where the

disease is endemic. Clinicians will have to include screening for trypanosome parasites in their routine screening protocol when a dog with a history of rough encounters with monitor lizards or a hyperthermic patient is presented in endemic areas.

Case report

Case 1

A 4-year-old female German shepherd was presented during emergency hours of the clinic with pale ocular mucous membrane, tachypnea, tachycardia, anorexia, a rectal temperature of 41.4 degrees Celsius, and a body weight of 26 kg. There were no other significant findings during the clinical examination. Although an immediate diagnostic test could not be done at that time, a blood sample was collected and stored for hemoparasite screening. Differential diagnoses were bacterial septicemia and hemoparasite infection. 260 mg of enrofloxacin (Interflox-100, Interchemie, Netherlands) SC, 3 ml of multivitamin (Oligovit, Kela, N.V., Belgium) SC, and 5.2 mg of meloxicam (Metacam, Boehringer Ingelheim, USA) IM were administered.

Blood was screened about 10 hours after collection. The result was positive for trypanosomes (protozoans appear to be long, slender organisms with an undulating membrane, a free flagellum at the anterior end, a pointed posterior end, and a small subterminal kinetoplast). 91mg of Diminazene diaceturate (Diminakel plus, Kela NV, Belgium) solution was administered intramuscularly. The dog recovered after 24 hours. The dog was reassessed on days 23, 25, 27, and 51 after the initial presentation. Blood screened for trypanosoma was negative. A relapse was not reported. Tests and results are shown in Tables I–II.

Case 1		
German Shepherd		
Age: 4 years		
Clinical Laboratory Test		
BIOELISACRUZI@ (biolab-Merleux S. A)	Results	Normal Values
<i>Trypanosoma brucei</i>	Positive	Negative
Woo Test	Positive (<i>Trypanosoma Sp</i>)	

Table I. Trypanosoma test result for case 1.

Case 1	
German Shepherd	
Age: 4 years	
Clinical Laboratory Test	
Heamatology	
WBC	3.09x 10 ⁹ /L
RBC(Erythrocytes)	4.56X10 ⁹ /µL
HGB (Hemoglobin)	9.3g/dL
HCT (Hematocrit)	20.6%
MCV (mean corpuscular volume)	60.5fl
MCH	21.3pg
MCHC	33.1g/dL
PLT (platelets)	355X10 ³ /µL
LYM (lymphocytes)	59.1%
MO (monocytes)	11.3%
GR(granulocytes)	74.8%
RDWCV	16.4fl
PCT	0.47%
MPV	10.1fl
Biochemistry	
Ikaline Phosphatase(serum)	111U/L
Bilirubin Total (serum)	1.04mg/dL
Creatinine(serum)	2.67 mg/dL
Transaminase GGT(serum)	23U/L
Transaminase AST(serum)	77U/L
Transaminase ALT(serum)	54U/L
Urea (plasma or serum)	52mg/dL
BIOELISACRUZI@ (biolab-Merleux S. A)	
<i>Trypanosoma brucei</i>	Negative
Woo Test	Negative

Table II. Post treatment results for case 1: Hematology, clinical biochemistry and Trypanosoma test.

Case 2

An adult Cane Corso weighing 33.8 kg was presented with a recent history of fighting with an adult monitor lizard and killing it about 3 days prior to presentation. Clinical examination reveals inappetence, adipsia, lethargy, a swollen or puffy face, purulent bilateral ocular discharge, a pale ocular mucous membrane and a rectal temperature of 39.6 degrees Celsius.

Based on a presumptive diagnosis of bacterial septicemia, which is common in similar cases previously treated by the author, 340,000 IU procaine penicillin G/340,000 IU benzathine penicillin G/680 mg Dihydrostreptomycin sulfate was administered subcutaneously (Penstrep-400 LA, Interchemie, Netherlands). 4mg dexamethasone (Glucortin-20, Interchemie, Netherlands) IM and 40mg thiamine disulfide nitrate/10mg riboflavin/120 mg nicotinamide/40 mg pyridoxine hydrochloride/40mg pantothenate/400 ug hydroxocobalamin were administered subcutaneously. 10 tablets of 40mg thiamine disulfide nitrate/10mg riboflavin/120 mg nicotinamide/40 mg pyridoxine hydrochloride/40mg pantothenate/400 mg hydroxocobalamin were dispensed to be administered twice daily. Three days later, the dog's appetite improved, his swollen face subsided, although his body weight dropped to 32.4 kg, his rectal temperature was 39.5 degrees Celsius, and his ocular mucous membrane was pale. 40 mg thiamine disulfide nitrate/10mg riboflavin/120 mg nicotinamide/40 mg pyridoxine hydrochloride/40mg pantothenate/400 ug Hydroxocobalamin was administered subcutaneously: 340,000 IU procaine penicillin G/340,000 IU benzathine penicillin G/680 mg Dihydrostreptomycin sulfate (Penstrep-400 LA, Interchemie, Netherlands) was administered subcutaneously, and 4 mg of dexamethasone (Glucortin-20, Interchemie, Netherlands) was administered intramuscularly. The dog was re-examined the following day. The caregiver reported that its appetite had improved but not fully recovered. Rectal temperature: 39.4 degrees Celsius. 40mg thiamine disulfide nitrate/10mg riboflavin/120 mg nicotinamide/40 mg pyridoxine hydrochloride/40mg pantothenate/400 ug Hydroxocobalamin was administered subcutaneously. The caregiver was advised to report back to the clinic if the condition does not improve in 2 days.

Seven days after the last treatment, the dog was re-presented to the clinic exhibiting the following symptoms: lethargy, unsteady gait, jaundice, severe anemia, pale ocular and oral mucous membranes, moderate loss of skin turgor, enophthalmos, dry mucous membranes, dehydration, and a rectal temperature of 39.4 degrees Celsius. It should be noted that the dog was bathed prior to presentation. The owner said the dog had not improved significantly since the last treatment.

A blood sample was collected for a Woo test. The test was positive for trypanosomes with a heavy infestation. 32 mg of Isometamidium chloride hydrochloride (Intromidium, Interchemie, Netherlands), and 40 mg of thiamine disulfide nitrate/10mg of riboflavin/120 mg of nicotinamide/40 mg of pyridoxine hydrochloride/40mg of pantothenate/400 ug Hydroxocobalamin was administered subcutaneously.

The dog was hospitalized and placed on 500 mL of 0.9% normal saline infusion, 500 mL of 5% dextrose infusion IV, and 1000 mg of Metamizole sodium (Restiva, Troikaa Pharmaceuticals Ltd., India) administered IV. The dog did not respond to treatment, and it was progressively declining. The prognosis was grave. The owner elected for euthanasia.

Case 3

An approximately 6-month-old male Mastiff Mixed breed was presented in a vegetative state. Prior to presentation, the dog came from a veterinary clinic earlier that day, where he received a penicillin-streptomycin injection, was dewormed, and 20mg of famotidine tablets had been dispensed to the owner for home administration. However, the dog's condition did not improve. When presented to our clinic, the rectal temperature was 39.10 °C, the body weight was 17.9 kg, it appeared to be mildly underweight, with pale ocular mucous membrane, pale oral mucous membrane, mild tachycardia, and weak limbs. The dog's condition progressed to sudden seizures, howling, and profuse salivation. Prior to the illness, the dog habitually visited the beach regularly for exercise. It was noted that the dog had been vaccinated twice for parvovirus and once for canine distemper, parainfluenza, canine hepatitis, and canine leptospirosis. A blood sample was collected for a complete blood count (CBC) and a Woo test (see Table III). The results indicated a high level of trypanosome infestation. The dog was hospitalized and was placed on 5% Dextrose saline IV, Diminazene diacetate (Diminakel Plus, Kela NV, Belgium) IM, and 2ml multivitamin (Oligovit, KELA S.A., Belgium) subcutaneously.

Case 3	
Mastiff	
Age: 6 month	
Clinical Laboratory Test	
Heamatology	
WBC	5.8 x 10 ³ /uL
Lymphocyte	71.2%
Monocyte	14.2%
Granulocyte	14.6%
Lymphocyte#	4.1x10 ³ /uL
Monocyte	0.8x10 ³ /uL
Granulocyte	0.9x10 ³ /uL
RBC	2.6 x10 ⁶ /uL
Hemoglobin	6.9g/dL
PCV	22.5%
MCV	76.0 fL
MCH	22.3 pg
MCHC	30.9 g/dL
RDWSD	42.9 fL
RDWCU	13.6 %
PLT	233x 10 ³
MPV	7.9 fL
PDW	12.7%
PCT	0.20%
P-LCR	30.2%
Woo Test	positive for <i>Trypanosoma sp</i>

Table III. Hematology and Trypanosoma test result for case 3.

On the second day, 40 mg thiamine disulfide nitrate/10 mg riboflavin/120 mg nicotinamide/40 mg pyridoxine hydrochloride/40 mg pantothenate/400 ug Hydroxocobalamin was administered subcutaneously, while maintained on 5% dextrose saline IV. A total of 2500 mL was administered at a flow rate of 180 mL/hour. A blood sample was collected and screened again for trypanosomes using the Woo test; the result was negative. The dog was discharged, and 14 tablets of 40 mg thiamine disulfide nitrate/10 mg riboflavin/120 mg nicotinamide/40 mg pyridoxine hydrochloride/40 mg pantothenate/400 mg hydroxocobalamin were dispensed to be administered twice daily. The dog was monitored for 30 days post-treatment; no relapse was reported.

Discussion

Although other sanguinivorous flies have been implicated in the transmission of trypanosomosis, *Glossina* species remains the most important vector of animal trypanosomosis in sub-Saharan Africa (Desquesnes, 2004). Experimental transmission in rats via the oral route and natural oral transmission in dogs have been reported. The prepatent periods reported vary from 4 days to 38 days (Anene et al., 1989; CVBD, 2010; Maraghi et al., 1995; Moloo et al., 1973; Raina et al., 1985; Sangeetha, 2022). Oral injury might aid entry of the parasite into the bloodstream; in case 2, although there was no visible injury in the oral cavity or the body at the time of presentation, microtrauma could not be ruled out. Penetration of the parasite via intact buccal and gastrointestinal mucosa into systemic circulation has been reported. (Maraghi et al., 1995; Moloo et al., 1973; Raina et al., 1985; Sangeetha, 2022).

Several wildlife species have been implicated as carriers of trypanosomes, including *Varanus* species. A study conducted in Kenya showed that the monitor lizard could serve as a carrier of *Trypanosoma brucei* (Njagu et al., 1999). Nevertheless, there were no reports of the transmission of animal trypanosomosis from a monitor lizard to a dog. Generally, monitor lizards do not attack dogs unprovoked. They would bite in defense. Their oral cavity is laden with bacteria, which can cause infection of the wound created by their bite (Tehrani et al., 2008; Abrahamian, 2011; Boyd et al., 2021). Some reports have claimed their bites are venomous (Koludarov et al., 2017; Vikrant and Verma, 2014). In their article *Enter the Dragon: The Dynamics and Evolution of Anguimorpha Lizard Venoms*, the *Varanus* species was indicted as venomous (Koludarov et al., 2017), while Sweet, in his article *Chasing the Flamingoes: Toxifera and the Misinterpretation of Venom in Varanid Lizards*, refutes any claim that these creatures possess any venom (Sweet, 2016). For a small animal clinician, venomous or not, ignoring the potential severity of an adult monitor lizard's bite could be 'a game of death'. Injury from an adult monitor lizard needs to be taken seriously. It is safer to assume that such injury is a contaminated wound and consider a possible toxic influence from proteins in

the oral glands that some authors claimed might at the very least act like a venom (Abrahamian and Goldstein, 2011; Koludarov et al., 2017; Vikrant and Verma, 2014; Mebs et al., 2020). The author has found the use of broad-spectrum parenteral antibiotics and anti-inflammatory agents to be helpful in the management of Varanus species-induced injury and its complications. These cases were successfully treated as infected wounds with no elaborate laboratory analysis prior to treatment; there has never been a case of canine trypanosomosis with a veranus species as the vector reported in a scientific journal. In case 2, a continuum of major symptoms that can be associated with trypanosomosis and a buildup of parasites in the blood that cascaded into an irredeemable pathophysiology are evident. There was weight loss, fever, and anemia as seen in pale mucous membranes, which is associated with trypanosomosis (Nwoha and Anene, 2011b). These symptoms persisted despite treatment, and although there was a moment of insignificant drop in the body temperature, it cannot be used as a yardstick for true recovery as intermittent fever is common in trypanosome infections (OIE, 2018). In retrospect, the case showed a gradual decline, which could be associated with an increase in parasitemia (OIE, 2008; Nwoha and Anene, 2011a), and early episodes of improvements in appetite were actually due to the vitamins administered, which have been shown to exhibit inhibitory activities on trypanosomes (Edoga et al., 2020; Anukwuorji et al., 2022). Prior to its encounter with the monitor lizard, the dog was healthy and had not displayed any of the clinical signs seen during the initial presentation. The infection route could be orodigestive by ingesting infected blood from the monitor lizard or possibly cutaneous via micro-injury inflicted by the lizard.

As shown in this report, trypanosome screening of the victim's blood will be appropriate in areas where trypanosomosis is endemic. Whereas the other two dogs in cases 1 and 3 were not infected via oral route, their recent history of a visit to a forested beach indicated that the likely vector is the tsetse fly, which is abundant in The Gambia (Rawlings et al., 1993). Whatever the route of transmission, the pathophysiology of canine African trypanosomosis is predictably similar. It impacts the circulatory system, as seen in all three cases. Anemia is a preponderant telltale sign associated with the extracellular parasite. The mechanism of anemia in trypanosomosis is multifaceted; it involves the interplay of several factors that result in hemolytic anemia. This is clearly seen in the hematology of the cases in tables II and III: markedly low packed cell volume (PCV), indicating red blood cell destruction (Igbokwe and Anosa, 1989; Anosa, 1988). Most common among these factors are erythrocyte injury caused by the lashing action of trypanosome flagella, undulating pyrexia, platelet aggregation, toxins and metabolites from trypanosomes, lipid peroxidation, and malnutrition (Mbaya et al., 2012).

This protozoan enters the hemolymphatic system and invades the host organs and tissues, resulting in several clinical manifestations, such as anemia, mainly via the mechanism of extravascular hemolysis in the mononuclear phagocytic system of the host. The pathogenesis of anemia in animal trypanosomosis is likely multifactorial and cannot be restricted to one mechanism, as shown by Naessens et al. (2005). Other clinical signs include oedematous swellings of the eyelids, lips, and skin beneath the lower jaw. The disease is also capable of affecting the central nervous system (Nwoha and Anene, 2011a; Anene et al., 1989a). The trypanosome antigen challenge induces lymphocytosis, as seen in Table III, and can persist for some days post-recovery, as seen in Table II. This could be followed by lymphopenia as the challenge progresses (Emeribe and Anosa, 1991). In cases 1 (post-recovery) and 3, there were significant leucocytosis or granulocytosis. Although leucopenia occurs in experimental and natural infections of *T. brucei*, leucocytosis occurs more frequently. Leucopenia is recorded in the chronic phase (Abenga, 2011).

In table II, a mild monocytosis persists for 23 days post-treatment, whereas significant monocytosis could be seen in the acute phase of case 3, as shown in table III. Monocytes have been reported to be matched by the proliferation of macrophages in tissues during trypanosomosis. This is consistent with responsive anemia (Emeribe & Anosa, 1989). Although most of the hematological values in case 1 were within the normal range 23 days post-treatment, most of the blood biochemical values were significantly high. The usual accompanying biochemical profiles in trypanosomosis are those of increased blood urea nitrogen (BUN), alanine transferase (ALT), aspartate aminotransferase (AST), gamma glutamyl transferase (GGT), and serum creatinine, as seen in case 1 (Shugaba et al., 1994).

Lesions associated with canine African trypanosomosis include congestive, inflammatory, coagulopathies, and sometimes hemorrhages in the heart and central nervous system. Organ damage has been reported in *T. evansi*. Oedema is also observed in the head, thorax, and forelimbs. The liver and spleen are congested and enlarged, while cut surfaces of the kidney reveal hemorrhages at the corticomedullary junction (Green, 2006; Eloy and Lucheis, 2009; Nwoha and Anene, 2011). Splenomegaly is usually a feature of the acute or parasitemic phase of the infection, and it is mainly due to erythrocyte and lymphocyte sequestration and an increase in macrophage population.

Another major symptom in acute cases, although not pathognomonic, is pyrexia. It may not always be present at the time of presentation, as seen in case 3. It is commonly recorded during the acute phase of the disease when there is a high level of circulating parasites (Greene, 2006; Anosa, 1988), which can easily be detected in the blood during microscopic examination. The Woo test was used in all the cases described. Although the BIOCRUZI ELISA was used in case 1 and *T. brucei* was diagnosed, its specificity and sensitivity cannot be determined by the authors since the

test was done in a private lab, although this was complimented by the Woo test done in-house. The morphology of the parasite corresponded to *T. brucei*. Pyrexia is absent during the chronic phase (Green, 2006) or in cases where the patient had been medicated with antipyretics prior to presentation. It is essential to control the fever, as prolonged hyperthermia puts strain on the organs and the circulatory system; hence, the use of antipyretics is important. (Naessens et al., 2005)

In case 1, meloxicam was the drug of choice. It controls fever without resulting in significant immunosuppression. Meloxicam works by blocking the effects of the enzymes cyclooxygenase COX-1 and COX-2, which prevent prostaglandin synthesis. Prostaglandins elevate body temperature and make nerve endings more sensitive to pain transmission. (Pawlukianiec et al., 2020)

Diminazene aceturate (DA) is commonly used in the treatment of trypanosomiasis in both livestock and dogs. Although effective, relapses after a single intramuscular dose have been reported. The toxicity of this drug is not uncommon in dogs. It is administered parenterally at a dose rate of 3.5-7 mg/kg in dogs. DA has a poor prophylactic effect. It may be necessary to repeat the administration after 48 hours (Anika, 1990; Akpa et al., 2008). DA has a low safety margin and cannot be combined simultaneously with other trypanocides. Relapse could be due to the drug's inability to cross the blood-brain barrier or the parasite developing resistance (Murray and Jennings, 1983). Other drugs, such as cymelarsan and magnesium chloride, have been used (Rashid et al., 2014). Drug-resistant isolates have been identified (Obi et al., 2021).

Multivitamins are useful as an adjunct treatment for canine trypanosomiasis. It has been shown that vitamin B12 has an antiparasitic effect on trypanosome parasites (Cicarelli et al., 2012). This might have been responsible for the initial improvement of the dog in case 2 when treated with antibiotics, multivitamins and dexamethasone.

Since relapse is common in canine trypanosomiasis, dogs that have a previous history of infection or that live in endemic areas should be routinely tested to monitor the possibility of infection. The safety margin as well as the therapeutic index of common trypanocides should be improved. Dogs with recurrent infections, treated with potentially organotoxic trypanocide, should have their vital organs screened to detect pathologic sequelae early. More effort should be geared towards the development of an effective vaccine against the disease as resistance to drugs is increasing, the control of insect vectors, and the development of multispecies rapid test kits for African trypanosomiasis. While an effective vaccine holds the promise of eradicating the disease, the laxity and misuse of common trypanocide by unqualified personnel will increase the drug-resistant variants. There is an urgent need for veterinary regulatory bodies in endemic areas to put in place strict drug control measures to prevent unauthorized personnel from purchasing and using trypanocides.

This report also shows the possibility of oral transmission from Nile monitor lizards to domestic canines, so consideration should be given to trypanosome screening in a case involving a dog fighting or consuming a monitor lizard. The report clearly establishes the presence of canine trypanosomiasis in The Gambia. It is the hope of the authors that this case report will arm clinicians with the information they need to deal with similar cases. It will serve as bedrock to spur further research into this deadly disease.

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