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Case report

Babesia sp. infection in a zoo-housed polar bear (*Ursus maritimus*)

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ABSTRACT

A 28-year-old female polar bear (*Ursus maritimus*) housed in a zoo in Upstate New York presented with acute inappetence and lethargy. The bear's condition rapidly deteriorated, and because laboratory testing indicated severe hepatic and renal disease, the bear was humanely euthanized. Examination of a blood smear from a sample collected just prior to euthanasia revealed the presence of intra-erythrocytic inclusions, which were identified as *Babesia* sp. by PCR. Although it is unclear if babesiosis contributed to this bear's clinical signs, this is the first report of *Babesia* sp. infection in this species. Zoological institutions exhibiting polar bears and located in tick-endemic areas, as well as managers of wild populations, should be aware of this species' susceptibility to babesiosis.

1. Introduction

The incidence of tick-borne parasites has increased as a result of climate change and other factors (Alvardo-Rybak et al., 2016). *Babesia* is one four genera of hemprotozoan parasites referred to as piroplasmoses, and, along with *Theileria*, *Cytauxzoon*, and *Rangelia*, represent the second most commonly found hemoparasites in mammals after trypanosomes (Yabsley and Shock, 2013). *Babesia* parasites have a wide host range, including hundreds of mammal species, and clinical presentation can range from an incidental finding to severe disease and death. This combination of characteristics makes babesiosis a clinically relevant hemoparasite in veterinary practice.

The polar bear (*Ursus maritimus*), an IUCN-listed vulnerable species, is threatened throughout its natural range by loss of Artic sea ice. A sustainable population of zoo-housed polar bears could provide a hedge against extinction. With only 56 animals in the AZA-managed Species Survival Plan, each individual is important to this conservation goal. Polar bears are susceptible to a variety of infectious agents that have important effects on individual animals and population sustainability, and managers need to be aware of emerging diseases to provide appropriate veterinary care (Farge et al., 2015). Although tick-borne diseases have been described, to the best of our knowledge, this report describes the first identification of *Babesia* sp. infection in a zoo-housed polar bear to raise awareness of this disease of concern among zoo and wildlife veterinarians.

2. Case presentation

A 28 year old female polar bear (*Ursus maritimus*) housed at a zoo in Western New York presented with sudden onset anorexia, lethargy, and apparent discomfort. The bear rapidly deteriorated in spite of empiric, supportive treatments, and was humanely euthanized due to poor prognosis. A blood sample from the time of death revealed moderate thrombocytopenia (92×10^3/μL), severe azotemia, severe hyperbilirubinemia, and moderate elevation of liver enzymes including ALT, AST, and GGT. Basophilic signet ring intra-erythrocyte inclusions suggestive of *Babesia* merozoites were observed on a blood smear (Fig. 1). Subsequent PCR and DNA sequencing of partial 18S rRNA gene spanning the V4 hypervariable region identified an organism similar to *Babesia* spp. identified in black bears, raccoons (**Genbank: DQ028958.1**) [678/679 bp, 99% identity], and maned wolves (**Genbank: KR017880.1**) [677/679 bp, 99% identity] (Birkenheuer et al., 2006; Birkenheuer et al., 2007; Shaw et al., 2015). PCR targeting a 680 bp region of the 18S rRNA gene was used to amplify *Babesia* DNA extracted from EDTA whole blood using forward primer: piroplasma 18S-144 (5'-ACC GTG CTA ATT GTA GGG CTA ATA CA-3′) and reverse primer: Bcommon2R (5'-TGC TTT CGC AGT AGT TCG TC-3′) (Qurollo et al., 2017; Westmoreland et al., 2019; Birkenheuer et al., 2007). SNAP4Dx for *Borrelia*, *Ehrlichia, Anaplasma*, and heartworm and PCR for *Anaplasma, Bartonella, Ehrlichia, Mycoplasma*, and *Rickettsia* were negative.

Postmortem examination revealed an enlarged, distended gall bladder containing biliary sludge and two marble sized soft yellow

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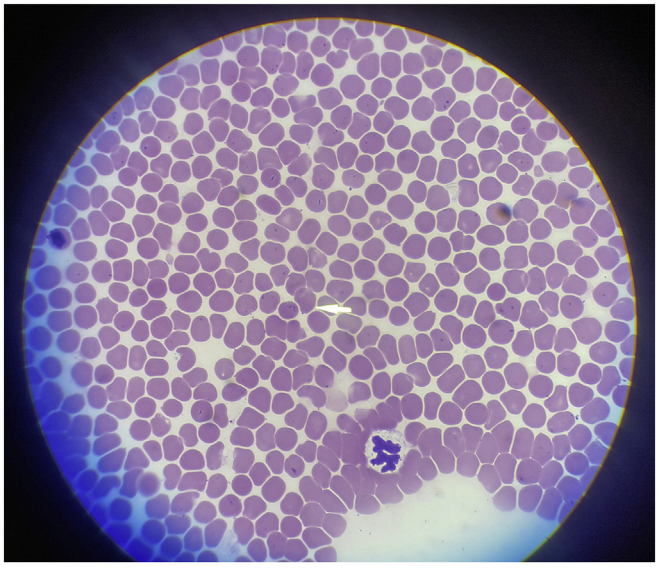

Fig. 1. Peripheral blood smear. Basophilic "signet ring" inclusions visible inside erythrocytes (arrow) on a blood smear prepared from peripheral blood sampled just prior to euthanasia. JorVet Dip Quick (Jorgensen Labs, Loveland, CO 80535, USA). 100×.

choleliths. The hepatic tissue surrounding the neck of the gall bladder was friable. Histologic examination revealed numerous small foci of lymphocytic/neutrophilic inflammation distributed throughout the hepatic parenchyma, mild centrilobular hepatocellular vacuolar change, and few small foci of random hepatocellular lytic necrosis. The gall bladder had mild to moderate lymphocytic inflammation in the lamina propria. The kidney had severe sclerotic change in the glomeruli and marked acute tubular necrosis. Some of the tubules contained luminal red pigment or fragmented erythrocytes. Marked lymphoplasmacytic/eosinophilic inflammation was distributed throughout the lamina propria of the small intestine and accompanied by some mild crypt and glandular hyperplasia. Adipose stores were abundant, and steatosis was prominent in the gall bladder and stomach.

Histologic findings suggest that multiple disease processes contributed to morbidity. The acute renal tubular pigment deposition and necrosis are suggestive of extravascular or intravascular hemolysis and hemoglobin nephrosis, and this lesion accounts for the bear's rapid deterioration. The hepatic lesions are suggestive of low grade sepsis, possibly originating from the gut, and in this regard, endotoxemia may also have contributed to the renal tubular necrosis. The enteric lesions are consistent with chronic inflammatory bowel disease. Advanced sclerotic changes in the kidney are typical of the aging changes in aged zoo-housed polar bears (LaDouceur et al., 2014), and this lesion may have impaired the bear's ability to compensate for the acute renal tubular necrosis.

3. Discussion

Babesiosis is an emerging zoonotic disease in companion animals, wildlife, and humans (Kogut et al., 2005; Penzhorn, 2006; Solano-Gallego and Baneth, 2011). To the authors' knowledge, this case represents the first occurrence of babesiosis in any zoo-housed bear species. Babesiosis did not engender a high degree of clinical suspicion due to the presumed low probability of infection with hemoparasites. This bear had been housed at the same zoo for the 26 years preceding clinical presentation. The animal was only fed commercially acquired food products from reputable vendors. Although the exhibit was open-air, caregivers had not observed signs of wildlife in the exhibit, and the region's harsh winters had traditionally limited the range of *Ixodes* ticks, the vector for babesiosis. However, babesiosis and other tick-borne illnesses such as lyme disease have increased in incidence throughout New York State (Kogut et al., 2005). Since *Babesia* and *Borrelia burgofei*, the causative agent of lyme disease, share the same reservoir (white-footed mouse, *Peromyscus leucopus*) and tick vector, both tick-borne diseases should be considered in wildlife species, even where risk of exposure is assumed to be low.

In veterinary species, the diagnosis of babesiosis is often made by visualizing the characteristic "signet-ring' intraerythrocytic organisms on blood smears. However, inclusions may be missed, especially in chronic cases when parasite numbers may be low. Since the species involved may affect the clinical disease course (Yabsley and Shock, 2013), PCR is the diagnostic method of choice. Historically, piroplasmids were characterized by their size, shape and host of origin as they were considered host-specific; however, PCR techniques have determined that many *Babesia* sp. once thought to be species specific can infect multiple hosts (Alvardo-Rybak et al., 2016). Canine babesiosis is typically characterized by hemolytic anemia, icterus, and hemoglobinuria. *Babesia* sp. have been identified in apparently healthy wild American black bears in New Jersey (Chern et al., 2016; Shaw et al., 2015) and African lions in South Africa as well as a variety of other carnivores around the world including hyena and mustelids (Penzhorn, 2006). In contrast, novel *Babesia* species have been identified as disease-causing agents in zoo-housed reindeer (Bartlett et al., 2009) and maned wolves (Phair et al., 2012). The affected animals in those cases developed severe anemia, more similar to the disease process in dogs and cats. Importantly, the species identified in this report is distinct from the disease-causing parasite in those reports.

With a median life expectancy of 24.3 years in AZA-accredited institutions, this geriatric polar bear had a number of co-morbidities. The acute renal lesion was suggestive of hemolysis and hemoglobin nephrosis, but it remains unclear if babesiosis was the sole cause, a contributing factor in conjunction with sepsis, or an incidental finding. The observations of asymptomatic infections in wild carnivores and the absence of fever and anemia in this case suggest that babesiosis in this animal may have been incidental. In Grevy's zebras, black rhinoceroses, and African lions, stress events, such as translocation, have been linked to clinical manifestation of previously latent babesiosis (Penzhorn, 2006), indicating that babesiosis may also be an important contributor to, if not primary cause of, morbidity or mortality. This aspect of the organism's pathogenicity is particularly important given that wild polar bears will face multiple stressors as climate change alters their habitat and behavior (Farge et al., 2015).

Treatment of babesiosis infection in zoo-housed maned wolves and reindeer followed recommendations for domestic animals (Ayoob et al., 2010; Bartlett et al., 2009; Phair et al., 2012). However, treatment was not always successful, and effective management of clinical cases often requires a combination of antiprotozoal drugs, intravenous fluid therapy, and blood transfusions. Large form *Babesia* sp. may be treated with intramuscular injections of imidocarb dipriopionate, while small form *Babesia* sp. require oral combination treatment with atovaquone and azithromycin (Baneth, 2018; Birkenheuer et al., 2008). While these antiprotozoal treatments may be feasible, their use is off-label with no available pharmacokinetics, and compliance may be a challenge in zoological species. Additionally, intensive supportive care may not be possible especially in polar bears where indwelling intravenous catheters cannot be maintained and blood is not readily available for transfusion. Thus, precluding tick attachment to the host is the most effective means of treatment. However, there are no anti-tick medications approved for use in wildlife, and topical products and collars used in companion animals are impractical for use in zoo species.

4. Conclusion

Although the clinical importance of *Babesia* sp. infection remains unknown, this case demonstrates that polar bears are at risk for babesiosis. Tick-borne diseases should be considered as possible differential

diagnoses even when risk of exposure is considered to be low. As climate change increases the range of tick vectors, wild polar bears may also be at risk. Veterinarians should include vector-borne infection screening as part of disease surveillance in this species. Additionally, zoological institutions in tick-endemic areas should re-evaluate risk and implement tick and rodent control and biosecurity measures to prevent tick-borne illnesses.

Ethical statement

This manuscript describes a clinical case. No animal experimentation occurred.

Declaration of Competing Interest

None.

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