Salmon poisoning disease in two Malayan sun bears

Jackie J. Gai, DVM, and Stanley L. Marks, BVSc, PhD, DACVIM, DACVN

Case Description—2 captive sun bears (*Helarctos malayanus*) were evaluated because of acute onset of vomiting, mucoid diarrhea, lethargy, and anorexia 1 week after eating live trout from a northern California reservoir.

Clinical Findings—In 1 of the bears, a CBC and serum biochemical analyses revealed mild anemia, mild eosinophilia, moderate lymphopenia, moderate hypoalbuminemia, and high serum γ-glutamyltransferase activity. Ultrasonographic examination of the same bear revealed ascites and mesenteric lymphadenopathy. Histologic examination of gastrointestinal tract biopsy specimens revealed moderate to severe lymphoplasmacytic and eosinophilic gastritis, enteritis, and colitis. Ova of *Nanophyetus salmincola*, the trematode vector of *Neorickettsia helminthoeca* (a rickettsial organism that causes salmon poisoning disease), were detected in fecal samples from both bears.

Treatment and Outcome—The bears were treated with oxytetracycline, doxycycline, praziquantel, and famotidine. Within 1 week after initiation of treatment, the appetite and fecal consistency of each bear were considered normal. Fecal ova shedding began 4 days after onset of clinical signs and ceased 9 days later.

Clinical Relevance—Salmon poisoning disease can be rapidly fatal in untreated animals, but if diagnosed early and treated appropriately, full recovery can be achieved. Domestic dogs and captive exotic bears are highly susceptible to clinical disease after ingestion of trematode-infected fish. Salmon poisoning disease may develop outside the geographic range in which the causative organism is endemic as a result of the transplantation of infected fish for sport fishing; veterinarians practicing in areas where infected fish may be transplanted should be aware of appropriate diagnostic and treatment protocols. (*J Am Vet Med Assoc* 2008;232:586–588)

ZOO ANIMALS

A 25-year-old 83-kg (182.6-lb) male sun bear (*Helarctos malayanus*; bear 1) developed a sudden onset (day 1) of vomiting, anorexia, lethargy, and mucoid diarrhea. There were multiple diarrheic stools in the bear's enclosure; 1 stool contained a small amount of frank blood. Twenty-four hours later (day 2), a 20-year-old 47-kg (103.4-lb) female sun bear (bear 2) that shared bear 1's enclosure also develop similar clinical signs and excreted soft, mucoid, malodorous feces. Both captive-born bears resided at the Oakland Zoo (located in the east San Francisco bay area). Questioning of the zookeepers revealed that both bears had been fed live trout from a local reservoir 1 week earlier.

Zinc sulfate fecal flotation was performed on loose feces collected from bear 1 on the first day that clinical signs were evident; results were negative for parasitic ova and oocysts. Initial differential diagnoses for bear 1 included bacterial or viral gastroenteritis, stress colitis, and parasitism. Keepers were instructed to withhold food and only offer water for 24 hours. When bear 2 developed the same clinical signs the next day, an infectious or toxic cause was suspected. Fecal specimens collected from bear 1 (day 2) and bear 2 (day 4) were submitted to a veterinary reference laboratory for assessment, which included bacterial culture for *Salmonella* spp, *Shigella* spp, *Campylobacter* spp, and *Yersinia* spp as well as detection of *Clostridium difficile* toxin A via an ELISA. Fecal specimens collected from both bears were also submitted for detection of parvovirus (by use of an ELISA) and occult blood. Bacterial, viral, and toxin tests yielded negative results, but occult blood was evident in fecal specimens from both bears.

Because of progressive anorexia, diarrhea, and severe lethargy, bear 1 was anesthetized and examined on day 3. Abdominal ultrasonography revealed mild ascites, mesenteric lymphadenopathy, and a distended stomach that was filled with fluid. Peripheral lymph nodes were not palpable because of the bear's thick skin, heavy musculature, and subcutaneous fat. Abdominal radiographic findings were unremarkable, although there was evidence of severe spondylosis. The bear was allowed to recover from anesthesia. Cytologic examination of an aspirate of the free abdominal fluid revealed a modified transudate; following centrifugation, it was determined that the fluid contained a mixture of eosinophils and neutrophils with fewer macrophages and mature lymphocytes. The presence of eosinophils suggested a possible parasitic cause, although an absolute cell count was not provided by the laboratory. Results of a CBC indicated that bear 1 had mild normocytic, normochromic nonregenerative anemia (Hct, 32.5%; reference range, 36% to 46%), mild eosinophilia (696 cells/μL; reference range, 275 to 545 cells/μL), and moderate lymphopenia (406 cells/μL; reference range, 1,178 to

From the Oakland Zoo, 9777 Golf Links Rd, Oakland, CA 94605 (Gai); and the Department of Veterinary Medicine and Epidemiology, School of Veterinary Medicine, University of California, Davis, CA 95616 (Marks). Dr. Gai's present address is 136 Brookdale Dr, Vacaville, CA 95687.

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Address correspondence to Dr. Gai.

1,706 cells/µL). Serum biochemical analyses revealed moderate hypoalbuminemia (2.3 g/dL; reference range, 2.9 to 3.7 g/dL) and high γ-glutamyltransferase activity (138 U/L; reference range, 12 to 84 U/L). Reference ranges for clinicopathologic variables in *H malayanus* were obtained from the International Species Information System, which is a database that is extensively used by zoo veterinarians.

Because of the persistence of clinical signs, bear 1 was anesthetized again on day 4 and underwent gastroduodenoscopy and colonoscopy with biopsy specimen collection. Gastroscopy revealed patchy erythema of the gastric mucosa and a large volume of green fluid in the stomach. Grossly, the duodenal mucosa appeared pale, rough, and thick; the colonic mucosa appeared slightly erythematous. Histologic examination of gastric biopsy specimens revealed multifocal moderate lymphoplasmacytic and eosinophilic gastritis; severe lymphoplasmacytic and eosinophilic erosive enteritis with villous epithelial attenuation were detected in duodenal biopsy specimens. Histologic examination of colonic biopsy specimens revealed mild to moderate erosive lymphoplasmacytic and eosinophilic colitis.

On day 4, a fecal flotation test was performed by a registered veterinary technician in the zoo hospital on a loose fecal specimen collected from bear 2. The test revealed multiple large, gold-colored, operculated trematode ova. Ova of similar appearance were identified in a loose fecal specimen that was collected from bear 1 on day 5. Fecal specimens from both bears were submitted to the parasitology laboratory at the Veterinary Medical Teaching Hospital at the University of California, Davis, and the ova were identified as those of *Nanophyetus salmincola,* the trematode vector of *Neorickettsia helminthoeca* (a rickettsial organism that causes salmon poisoning disease).

Both bears were treated with oxytetracycline (10 mg/kg [4.5 mg/lb], IM, q 24 h) for 12 days followed by doxycycline (10 mg/kg, PO, q 12 h) for 21 days. They also received praziquantel (4 mg/kg [1.8 mg/lb], IM, q 24 h) for 3 days, followed by a single dose (12 mg/kg [5.5 mg/lb], PO) 5 days later. Intramuscular injections were administered via pneumatic darts delivered through a carbon dioxide–powered dart gun. Both bears also received famotidine (0.5 mg/kg [0.23 mg/lb], PO, q 12 h) for 7 days. The bears' appetites progressively improved 2 days after treatment was initiated, and the consistency of the feces slowly returned to normal within 7 days. For 30 days after confirmation of *N salmincola* ova shedding, fecal flotation tests were performed daily on specimens collected from both bears; surveillance fecal flotation tests were performed weekly for an additional 90 days. Ova shedding began on day 4 after onset of clinical signs and ceased approximately 9 days later.

Discussion

Salmon poisoning disease is caused by a rickettsial organism, *N helminthoeca*, which preferentially infects a species of trematode, *Nanophyetus salmincola*. The trematode requires 2 intermediate hosts to complete its life cycle: a snail (*Juga silicula*, also referred to as *Oxytrema silicula*) and a fish (usually a salmonid). The Pacific giant salamander (*Dicampton ensatus*) is also a competent second intermediate host.[1] When infected fish are consumed by the parasite's definitive host, trematode metacercariae excyst from the fish and attach to the host's intestinal mucosa, thereby introducing *N helminthoeca* into the bloodstream. This inoculation of rickettsiae occurs during the prepatent period for the trematode (5 to 8 days), which may explain why clinical signs often appear before trematode ova are shed in the host's feces.[1] Natural definitive hosts include many species of fish-eating mammals and birds; accidental or aberrant hosts include domestic dogs, captive bears, and humans. Coyotes have been infected experimentally and appear to develop clinical disease that is similar to that which affects domestic dogs.[2] Humans have become infected after eating raw or incompletely cooked fish, but clinical disease is not as severe in humans as it is in dogs.[3]

Salmon poisoning disease syndrome is characterized by vomiting, diarrhea, lymphadenopathy, and lethargy and is often fatal if untreated.[4] Clinical signs of salmon poisoning disease usually develop within 5 to 7 days after ingestion of parasitized fish but may take longer to become evident.[1] If diagnosed early and treated appropriately, there is a good chance for full recovery.[4] In dogs, salmon poisoning disease may be suspected if the individual has a recent history of eating raw fish and clinical signs consistent with the disease and responds to specific treatment for salmon poisoning disease.[4] Hematologic and serum biochemical findings in affected domestic dogs are often nonspecific, although thrombocytopenia and lymphopenia were identified in 14 of 16 and 34 of 43 dogs, respectively, evaluated in 1 study.[4] Presumptive diagnosis is made on the basis of identification of *N salmincola* ova in feces via fecal flotation testing; confirmation of the diagnosis is provided by microscopic identification of *N helminthoeca* in macrophages within a lymph node aspirate specimen.[5] Despite the fact that the parasitic ova were detected via zinc sulfate flotation (specific gravity, 1.20) of fecal samples from the bears of this report, it should be noted that flotation solutions with higher specific gravities (1.27) are typically required to successfully detect the relatively dense ova of *N salmincola*.[6] Eggs recovered by use of standard sugar flotation solutions (specific gravity, 1.27) are somewhat deformed but easily recognizable.[6] A fecal sedimentation technique[7] is a viable alternative to fecal flotation testing for the detection of *N salmincola* ova.

Diagnosis and treatment of disease in captive wild animals are associated with unique challenges. For bears, diagnostic procedures are usually performed during anesthesia because these animals are not routinely trained for voluntary cooperation and can be highly dangerous. Both bears of this report developed similar clinical signs, but clinical signs became apparent in bear 1 first, and most of the diagnostic procedures (except for fecal tests) were therefore performed on that bear only. Fine-needle aspiration of the large mesenteric lymph nodes in bear 1 was considered but not performed because of the depth of the nodes in the bear's abdomen and the risk of intestinal perforation.

Oxytetracycline was selected as the most appropriate antimicrobial for administration because a concentrated form of the drug could be administered IM via the use of darting equipment. Because we were not aware of any published dosage guides for praziquantel administration in bears, the doses given IM were extrapolated from recommended doses for dogs and cats. The single dose of 12 mg of praziquantel/kg administered orally was based on recommendations from clinicians at the University of California, Davis who had experience in treating dogs with salmon poisoning disease.

To our knowledge, this is the first report of salmon poisoning disease in captive Malayan sun bears, a species that is native to Asia. Wild black bears (*Ursus americanus*), which are native to the area in which *N salmincola* is endemic (ie, coastal rivers and streams in the Pacific Northwest region of the United States), have been found to be infested with the fluke but appear to be resistant to development of clinical signs of salmon poisoning disease.[8] By contrast, zoo bears fed raw or improperly frozen fish have contracted the disease; however, the bear species most affected have been those that are not native to the Northwest coastal areas (ie, polar, sloth, Himalayan, and European brown bears).[8] It appears that salmon poisoning disease in sun bears has similar characteristics as the disease in domestic dogs: gastrointestinal illness is severe, and there is a positive response to appropriate treatment. It is plausible that bears that are native to the area in which *N salmincola* is endemic have coevolved with the parasite and are immune to its pathogenic effects, whereas exotic bear species may be naïve to the parasite and become sick after exposure. In their observations of the feeding behavior of wolves in coastal British Columbia, Darimont et al[9] reported that those animals prefer to eat the heads of salmon only. It was postulated that the wolves seek a beneficial omega-3 fatty acid that is present in high concentrations in the brains and eyes of salmon and speculated that this feeding behavior may be an evolutionary adaptation to avoid ingestion of *N salmincola*, which are most concentrated in kidneys and muscles of fish.

The geographic range of *N salmincola* (and hence cases of naturally occurring salmon poisoning disease) is thought to be limited by the natural range of *J silicula* (*O silicula*), the snail intermediate host. This snail inhabits freshwater streams in an area that extends from British Columbia south to northern California and as far east as Idaho. Several fish hatcheries in northern California are known to harbor trematode-infected fish. Because those hatcheries supply fish for transplantation into lakes and reservoirs for sport fishing, there is potential for salmon poisoning disease to develop in animals located well outside the suspected natural range of *N salmincola*.[8] Therefore, veterinarians working in areas where these fish may have been transplanted should include salmon poisoning disease in the list of differential diagnoses for dogs or bears with gastrointestinal signs of anorexia, diarrhea, vomiting, and weight loss and a history of exposure to raw fish. In affected animals, diarrhea can progressively worsen and become bloody, mimicking the clinical characteristics of parvoviral enteritis. Thorough freezing and cooking of infected fish reportedly inactivates the trematode,[5] although caution regarding the feeding of potentially infected fish to any susceptible animal is still warranted.

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