CASE REPORT

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Treatment of disseminated *Strongyloides* spp. infection in an infant Sumatran orangutan (*Pongo abelii*)

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Abstract

Strongyloides nematodes have been reported in all species of great apes with orangutans ≤5 years old most susceptible to severe clinical disease. This brief communication describes the first published case of antemortem diagnosis and treatment of disseminated strongyloidiasis in a clinically affected 5-month-old Sumatran orangutan (*Pongo abelii*).

KEYWORDS
great ape, ivermectin, parasite, pneumonia

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Strongyloides nematodes affect millions of people worldwide and have been reported in all great ape species and some Old World primates.[1-6] The most common species affecting great apes are *Strongyloides stercoralis* and *Strongyloides fuelleborni*.[1,4] Most infected animals and humans are asymptomatic shedders; however, immunocompromised or immunologically-naïve individuals are most likely to be affected with clinical disease that can develop into a fulminant fatal illness.[2,3,7,8] This parasite can survive for months in the environment, and increased skin contact with infected soil substrates is a risk factor for infection.[2,3,6] Transmammary transmission of *Strongyloides* spp. has been documented in dogs, sheep, rats, pigs, and in a single human case.[9-13]

While the complex life cycle of this parasite has been published in detail elsewhere, it is the migration of the *Strongyloides* larvae through the respiratory system and then gastrointestinal tract that causes clinical symptoms.[2,3] Many fatal human cases involve hyperinfection, a state of accelerated autoinfection, characterized by increased larval migration and larval loads in the gastrointestinal and pulmonary systems.[3,8] Symptoms vary greatly depending on the parasite load and host health and can include non-specific signs such as lethargy or more specific signs like cough, dyspnea, diarrhea, constipation, inappetence, and abdominal pain.[2,3,14]

Of the great apes, orangutans ≤5 years old appear to be the most susceptible to severe clinical disease, likely due to their immunologically-naïve status.[4,6,14-16] Several fatalities have been reported in the literature in this species,[6,15,16] as well as in young

chimpanzees and gorillas.[5] While other reports have described effective eradication strategies in asymptomatic adults utilizing preventative deworming schedules,[17] this is the first published report to describe antemortem diagnosis and treatment of disseminated strongyloidiasis in a clinically affected great ape infant.

On May 29, 2015, a 5-month-old female Sumatran orangutan, *Pongo abelii*, presented with acute lethargy and a periodic dry, non-productive cough. This animal was housed in a zoological institution with its family group consisting of 2.2 adults, where the animal health department must provide best-practice veterinary care for all animals. This orangutan family group was provided both indoor and outdoor housing. The outdoor yards consisted of natural substrates, while the indoor housing was composed of artificial trees, concrete rockwork, fire-hoses, hammocks, and platforms for climbing and various enrichments for mental stimulation in compliance with USDA requirements. The orangutans were also provided wood wool, hay, blankets, and browse. The orangutans were fed a balanced diet overseen by a PhD-certified nutritionist which was provided in variable ways day-to-day including during training sessions, in enrichment devices, via scatter-feeding, etc. Oral amoxicillin (10 mg/kg mg BID, 50 mg/mL suspension; Virbac AH, Inc., Fort Worth, TX, USA) and acetaminophen (10 mg/kg BID, 32 mg/mL suspension; McNeil Consumer Healthcare, Fort Washington, PA, USA) were given on the day of presentation. Initial improvement was documented, but on the second day, the infant was less active and slow to nurse. Coughing was no longer noted but the depth of respirations was increased in sternal recumbency.

TABLE 1 Blood work parameters obtained during anesthetized examination of an infant orangutan diagnosed with *Stongyloides* spp. infection

Parameter	iStat CG4	iStat CG8	Abaxis	Serum chemistry	CBC
CK (U/L)	–	–	–	36	–
Glucose (mg/dL)	–	107	112	112	–
T. Protein (g/dL)	–	–	5.7	5.3	–
Albumin (g/dL)	–	–	4.2	3.64	–
Globulin (g/dL)	–	–	1.5	1.7	–
BUN (mg/dL)	–	–	16	17.2	–
Creat (mg/dL)	–	–	0.4	0.58	–
Ca (mg/dL)	–	–	9	9.6	–
iCa++ (mg/dL)	–	1.24	–	–	–
Phos (mg/dL)	–	–	5.9	6.1	–
Na (mEq/L)	–	121	126	120	–
Cl (mEq/L)	–	–	–	89	–
K (mEq/L)	–	5.5	5.8	5.5	–
ALP (U/L)	–	–	268	384.3	–
ALT (U/L)	–	–	18	15.1	–
AST (U/L)	–	–	–	9.4	–
GGT (U/L)	–	–	–	69.9	–
T. Bili (mg/dL)	–	–	6	6.81	–
Amylase (U/L)	–	–	45	–	–
WBC ($*10^3$ cells/μL)	–	–	–	–	39.4
RBC ($*10^6$ cells/μL)	–	–	–	–	2.59
HGB (g/dL)	–	8.2	–	–	7.9
HCT (%)	–	24	–	–	25.5
Neutrophil (%)	–	–	–	–	42
Neut ($*10^3$ cells/μL)	–	–	–	–	16.55
Band (%)	–	–	–	–	1
Band ($*10^3$ cells/μL)	–	–	–	–	0.39
Lymph %	–	–	–	–	43
Lym ($*10^3$ cells/μL)	–	–	–	–	16.94
Monocyte %	–	–	–	–	11
Mono($*10^3$ cells/μL)	–	–	–	–	4.33
Eosinophil (%)	–	–	–	–	3
Eos ($*10^3$ cells/μL)	–	–	–	–	1.18
PLT ($*10^3$ cells/μL)	–	–	–	–	346
Arterial pH	7.33	7.337	–	–	–
pCO2 (mm Hg)	33.6	29.7	–	–	–
Total CO2 (mEq/L)	17.7-19	15.9-17	–	–	–
Lactate (mmol/L)	6.07	–	–	–	–

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; Ca, calcium; CBC, complete blood cell count; CK, creatine kinase; Cl, chloride; CO2, carbon dioxide; Creat, creatinine; Eos, eosinophil; GGT, gamma-glutamyl transferase; HCT, hematocrit; HGB, hemoglobin; iCa++, ionized calcium; K, potassium; Lymph/Lym, lymphocyte; Mono, monocyte; Na, sodium; Neut, neutrophil; pCO2, partial pressure of carbon dioxide; Phos, phosphorous; PLT, platelets; RBC, red blood cell count; T. Bili, total bilirubin; T. Protein, total protein; WBC, white blood cell count.

On days 3-4, the orangutan showed poor medication compliance, was not seen nursing regularly, and had increased respiratory effort when sleeping (respiratory rate ~60 breaths/min). As the animal was refusing oral medications, antimicrobials were switched from oral amoxicillin to intramuscular azithromycin (20 mg/kg SID, 100 mg/mL injection; Apotox Corp., Weston, FL, USA). Opportunistic free-catch urinalysis was unremarkable (USG 1.018, pH 6.0, yellow/clear with moderate debris and rare red blood cells).

On day 5, the infant was induced with 5% isoflurane via facemask (Isothesia; Henry Schein Animal Health, Dublin, OH, USA), intubated (3.0 mm endotracheal tube [ETT]), and maintained on 0.5%-1% isoflurane to facilitate complete evaluation, obtain diagnostic testing, and administer treatment. Intravenous azithromycin (10 mg/kg), ceftazidime (50 mg/kg, 100 mL/mL injectable; Hospira Worldwide, Inc., Lake Forest, IL, USA) and subcutaneous meloxicam (0.1 mg/kg, 5 mg/mL injectable; Norbrook Laboratories Limited, County Down, Northern Ireland) were administered during the procedure. Thoracic auscultation revealed elevated respiratory rate (60 breaths/min) and harsh lung sounds with intermittent crackles on the left side of the chest, heard both prior to intubation and after instituting intermittent positive pressure ventilation. The orangutan hyperventilated throughout anesthesia (end tidal carbon dioxide 26-29 mm Hg) but oxygen saturation was within clinically acceptable limits on pulse oximeter.

Bilateral dried nasal discharge was present and the abdomen was bloated. Feces collected via rectal swab were yellow and unformed. The gingiva was discolored light yellow predominantly near tooth eruption sites. Whole body radiographs showed the mild hepatomegaly, gas-distended intestinal loops suggestive of ileus, and patchy interstitial infiltrates with air bronchograms in the left lung fields. Abdominal ultrasound revealed hyperechoic periportal areas in the liver. Slight gall bladder wall thickening was present. Nasal swab cytology showed squamous epithelial cells, bacilli, megabacteria, and white blood cells. Right tonsil swab culture revealed no growth of pathogens. Nasopharyngeal swab submitted for respiratory pathogen multiplex PCR did not detect the following pathogens: *Bordetta pertussis*, *Chlamydophila pneumoniae*, *Mycoplasma pneumoniae*, Adenovirus, Coronavirus (HKU1, NL63, 229E, OC43), Influenza (A subtype H1, H3, 2009 H1, B), Metapneumovirus, and Parainfluenza 1, 2, 3, and 4 (Barnes Jewish Hospital, St. Louis, MO, USA).

Blood was collected for complete blood cell count and serum chemistry (Advanced Veterinary Laboratory, St. Louis, MO, USA), blood glucose (Accu-Chek Aviva Plus; Roche, Indianapolis, IN 46256), plasma chemistry (Abaxis, Inc., Union City, CA, USA), and blood gas analysis (iStat CG4+, iStat CG8+; Abbott Point of Care Inc., Abbott Park, IL, USA). Patient-side testing showed normoglycemia (glucose 129 mg/dL), hyponatremia, hypochloremia, hyperkalemia, and elevated total bilirubin, consistent with icteric oral mucous membranes (Table 1). These findings were confirmed on laboratory tested samples; in addition, mild elevation in gamma glutamyl transferase (GGT) and increased direct fraction compared to indirect fraction of bilirubin were noted (Table 1). Complete blood cell count showed leukocytosis with equal neutrophil to lymphocyte distribution and mild anemia (Table 1). Cytology from mucous and hemorrhage from the ETT showed white blood cells, transitional cells, and squamous epithelial cells and culture grew *Staphylococcus aureus* sensitive to all tested antibiotics (including azithromycin) except ampicillin and clindamycin.

No pathogens were isolated on fecal culture. Fecal direct examination was negative for parasites. Modified Wright-Giemsa stain showed gram-positive bacilli and megabacteria were present. Fecal gram stain and modified Wright-Giemsa stain revealed 7 larval parasites morphologically consistent with *Strongyloides* species (Figure 1).[4] The animal was diagnosed with pneumonia and icterus due to disseminated *Strongyloides* infection and was prescribed oral ivermectin (0.5 mg/kg, 10 mg/mL suspension; Norbrook Laboratories Limited). Oral azithromycin (20 mg/kg PO SID for 5 days, 250 mg/mL suspension; Greenstone LLC, Peapack, NJ, USA) and meloxicam (0.12 mg/kg PO SID for 3 days, 1.5 mg/mL suspension; Norbrook Laboratories Limited) were instituted post-anesthesia.

The day after anesthesia, the orangutan was nursing well and taking all medications. By the next day, the infant was less bloated, appeared brighter, and was more active. Ten days post-presentation, the behavior was normal and gingival icterus had resolved. Recheck fecal was positive for nematode larva (1+) via Baermann concentration technique. Ivermectin (0.25 mg/kg PO) and meloxicam (0.12 mg/kg PO) were prescribed once weekly for 3 treatments. All adult orangutans (2.2) were negative on routine and Baermann fecal screening. All orangutans were started on monthly ivermectin (0.2 mg/kg PO) as a preventative. Orangutan bedding protocols were changed to eliminate hay and reuse of cleaned wood wool. This individual has not had any recurrence of clinical symptoms nor parasites in fecal examinations in over 2 years since diagnosis, treatment, and initiation of monthly ivermectin prophylaxis.

While bronchial lavage was not performed, diagnosis in this case was based on compatible clinical symptoms, thoracic radiographs, hepatic ultrasound, exclusion of other causes of pneumonia, response
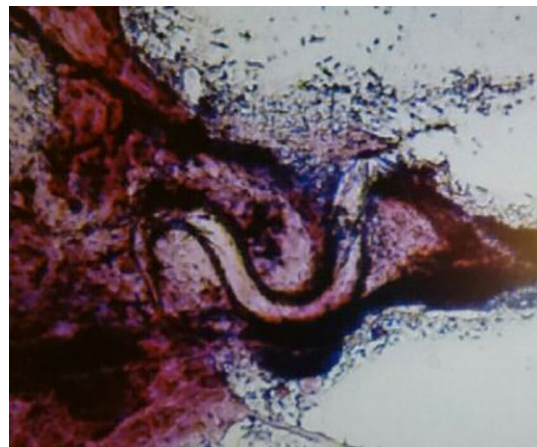

FIGURE 1 Fecal gram stain showing larval parasite morphologically consistent with *Strongyloides* species in a 5-mo-old Sumatran orangutan (*Pongo abelii*) diagnosed with disseminated *Strongyloides* spp. infection

to treatment, and finding *Strongyloides* in the feces.[2,7,14,18] It is suspected that this animal contracted the parasite from contaminated substrates, although transmammary transmission cannot be ruled out. While single fecal samples are only 50% sensitive for diagnosis, using Baermann or formalin-ethyl acetate concentration techniques can improve sensitivity.[2,3] Alternatively, serial fecal examinations for several weeks may be necessary to detect this parasite.[6] *Strongyloides* speciation was not pursued in this case and diagnosis was based on previously described distinguishable morphologic characteristics.[4]

Treatment options for *Strongyloides* infection include azole drugs and ivermectin.[2,3,18] Oral ivermectin has become the treatment of choice, as it has shown better rates of larval clearance with fewer negative side effects.[3,6,8,14] The mortality rate of disseminated strongyloidiasis in humans remains high, and prognosis is especially poor if patients require oxygen support or mechanical ventilation.[3,8] Treatment in this case was likely successful due to intervention prior to severe respiratory compromise.

This is the first published report to describe antemortem diagnosis and treatment of disseminated strongyloidiasis using oral ivermectin in an infant orangutan. This report emphasizes the value of prophylactic anthelmintic use and eradication of *Strongyloides* in this species, especially in groups with pregnant, lactating, or infant orangutans.[6,17] Interestingly, all adult animals in this breeding group had been negative on routine fecal screenings in the years leading up to this case; however, Baermann or formalin-concentrating techniques were not routinely used during that time. Recommended control measures include maintaining exemplary exhibit hygiene and utilization of Baermann or formalin-concentrating fecal screening techniques to identify and treat subclinical infections in all orangutans.

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