Molly, a 6-year-old spayed bichon frise, was presented with a 2-month history of hematochezia and a 3-day history of inappetence and vomiting.

MAKE YOUR DIAGNOSIS

HEMATOCHEZIA IN A DOG

Samantha Parkinson, DVM
M. Katherine Tolbert, DVM, PhD, DACVIM
University of Tennessee

History

Hematochezia was initially mild but had progressed in severity. At presentation, Molly was defecating mostly frank blood with little discernible fecal material. Metronidazole (10 mg/kg PO twice a day), amoxicillin (10 mg/kg PO twice a day), and sulfasalazine (20 mg/kg PO 3 times a day) were previously prescribed for treatment of diarrhea but were discontinued 10 days before presentation after no apparent improvement. Heartworm and flea and tick preventives had also been discontinued.

Molly had a previous history of acute blindness, diagnosed as bilateral retinal detachment 5 weeks before presentation (***Figure 1***, next page). Blood pressure was mildly elevated at 160 mm Hg. Tests for infectious disease were negative. Additional testing was offered but declined. Immunosuppressive doses of prednisone (1 mg/kg PO twice a day) were prescribed for suspected steroid responsive retinal detachment. When retinal reattachment did not occur after 1 week of corticosteroid therapy, further evaluation was recommended but was declined by the owner.

Physical Examination

Molly had a lean BCS of 4/9 and was 5% dehydrated. Frank blood was found on rectal examination, and the ophthalmic examination remained unchanged. Temperature, pulse, and respiration were normal. No additional abnormalities were identified.

BCS = body condition score

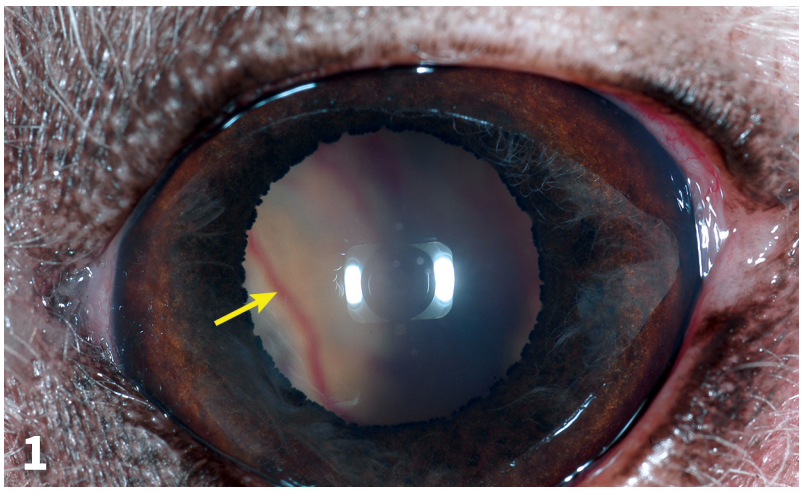
Diagnostic Results

Serum chemistry profile revealed hyperglobulinemia (globulin, 4.1 g/dL; reference interval, 2.0-3.2 g/dL) and hypoalbuminemia (albumin, 2.7 g/dL; reference interval, 3.2-4.1 g/dL). A CBC and rectal scrape were unremarkable. Urinalysis was initially considered to be normal, with a urine specific gravity of 1.030, absence of protein, and an inactive sediment. Abdominal ultrasonography revealed moderate thickening of the intestinal wall (up to 0.41 cm thick; normal thickness, <0.3 cm), which originated at the ileocecal junction and extended the length of the colon. Numerous lymph nodes surrounding the colon were also enlarged. Ultrasound-guided fine-needle aspiration of the thickened colonic mucosa and intraabdominal lymph nodes was performed; however, cytologic evaluation was nondiagnostic because of low cellularity.

ABCD = amphotericin B colloidal dispersion

Definitive Cytology Results

A subretinal tap was performed with the patient under general anesthesia. Cytology of the subretinal fluid (***Figure 2***) and reevaluation of urine sediment by the clinical pathologist revealed *Prototheca* spp-like organisms. Growth of *P zopfii* was evident on fungal culture of the urine.



▲ Molly's left eye 5 weeks before presentation. Complete bullous retinal detachment with a right subretinal exudate (**arrow**) can be observed.

Diagnosis

Prototheca

ASK YOURSELF

QUESTION 1
What is protothecosis?

QUESTION 2
What are the most common ways *Prototheca* spp infection manifests clinically?

QUESTION 3
How is protothecosis diagnosed, and what is the appropriate treatment?

QUESTION 4
How should I monitor a patient receiving amphotericin B and itraconazole?

Prognosis

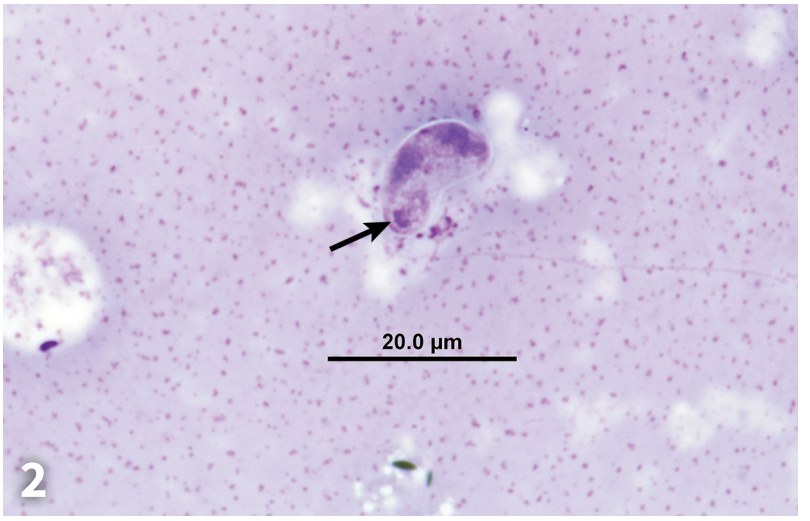
Poor-to-grave. There is a single reported case of a dog surviving ≥12 months.[1] This dog had both colonic and ophthalmologic involvement; it is likely that previous immunosuppression from prednisone caused an acute worsening of the condition. Prognosis can likely worsen with neurologic and/or ophthalmic system involvement.[1]

Treatment

Molly was initially treated with amphotericin B colloidal dispersion (ABCD; 0.5 mg/kg IV over 4-6 hours) every 48 hours for 4 treatments. On the fourth day of treatment, Molly also received itraconazole (5 mg/kg twice a day). *Prototheca* spp infection is generally considered a progressive, terminal disease; thus, daily itraconazole was continued long-term.

Outcome

Molly's hematochezia improved dramatically with ABCD and itraconazole treatment. Her stool remained soft for several weeks, but her appetite and feces returned to normal within the first month of treatment. Five months into treatment, Molly developed neurologic signs, including vocalization and ataxia; terbinafine at a low dose (10 mg/kg PO once a day; because of itraconazole continuation) was added to the treatment protocol because of suspicion of advanced disease. Neurologic signs resolved following treatment, and at the time of this publication (2 years after diagnosis), the patient is alive and being treated with itraconazole (5 mg/kg twice a day) and terbinafine (10 mg/kg PO once a day). The authors have recommended she continue this treatment for life.



▲ Single *Prototheca zopfii* organism observed in a cytologic preparation of subretinal fluid. *P zopfii* is a round-to-oval organism with a thin, clear cell wall and granular, blue-gray-to-purple interior structures. The organism can be observed above the magnification legend. The red-to-purple round structures (**arrow**) represent endospores, which can sometimes be observed. *(100× objective)*

DID YOU ANSWER?

QUESTION 1

What is protothecosis?

Prototheca spp are achlorophyllous, saprophytic algae that are ubiquitous in the environment; however, infection is rare. *Prototheca* spp organisms are round-to-oval with a thin, clear cell wall and granular basophilic cytoplasm.[2] They should be differentiated from *Chlorella* spp, green algae that have much larger starch granules present in the cytoplasm.[3] Only 2 species, *P zopfii* and *P wickerhamii*, are known to be pathogenic.[3]

In humans, immunosuppression has been shown to predispose patients to disseminated infection,[4] but risk factors leading to disease development in dogs have not been identified. Dogs with protothecosis do not pose a risk to humans or other animals in the household. However, infected animals may serve as sentinels to indicate a higher prevalence in the area. *Prototheca* spp are commonly identified in areas with raw and treated sewage, slime flux, and animal waste and can contaminate flowing and standing water.[4]

QUESTION 2

What are the most common ways *Prototheca* spp infection manifests clinically?

The most common clinical sign associated with protothecosis in dogs is diarrhea of large-bowel origin with associated hematochezia. From there, the organism can undergo hematogenous or lymphatic spread throughout the body.[5] Clinical signs unrelated to the GI tract are highly variable and are associated with organ system(s) affected by ocular (eg, granulomatous chorioretinitis, retinal degeneration, exudative retinal detachment, acute blindness), neurologic (eg, head tilt, circling, ataxia, paresis), and renal (eg, polyuria, polydipsia, azotemia) involvement.[6,7]

Alternatively, *P wickerhamii* infection can result in cutaneous disease after traumatic inoculation of organisms; this is common in humans and cats. A combination of surgical management and systemic therapy is recommended for these patients and is sometimes curative.[3]

QUESTION 3

How is protothecosis diagnosed, and what is the appropriate treatment?

Protothecosis can be tentatively diagnosed based on identification of the organism on cytology and/or histopathologic examination of affected tissues. However, to definitively diagnose protothecosis, culture is necessary.[1]

Widely accepted treatment recommendations have not been formulated, even in humans, as the disease occurs rarely.[3] However, a dog that reportedly survived for ≥1 year (before being lost to follow-up) was treated successfully with a combination of amphotericin B and itraconazole,[1] making this a potential therapeutic consideration.

QUESTION 4

How should I monitor a patient receiving amphotericin B and itraconazole?

Amphotericin B is available in many formulations. A lipid-based formulation, which is less nephrotoxic and has better tissue penetration, is recommended.[8] Before starting amphotericin B, a renal profile and urinalysis should be performed to evaluate for subclinical kidney disease, which can be exacerbated with treatment. During amphotericin B treatment, a urinalysis, including sediment examination, should be evaluated for casts before each treatment, as cylindruria may be the first sign of renal damage. By the time azotemia is observed, renal damage is often severe. This makes serum chemistry analysis an insensitive method of evaluating for potential toxicity.

Before starting treatment with itraconazole, liver values should be evaluated. Hepatotoxicity is a common side effect of itraconazole[9] and may require dose decreases or drug discontinuation. Liver values should be evaluated during the first 2 weeks of therapy and rechecked every 2 to 3 months thereafter.

References

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