Clinical Snapshot

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CASE PRESENTATION

A 1-year-old spayed pug presented with progressive diarrhea of approximately 6 weeks’ duration that was nonresponsive to antibiotic therapy. The dog maintained a good appetite with no vomiting but had recently developed ascites and pleural effusion. Abnormalities noted on physical examination included tachycardia (180 bpm), inspiratory dyspnea, decreased heart and lung sounds, severe abdominal distention with a palpable fluid wave, severe muscle wasting, and a poor haircoat. Laboratory abnormalities included mild regenerative anemia, moderate hypoalbuminemia, mild hyperglobulinemia, and increased levels of alkaline phosphatase. The peritoneal fluid had a specific gravity of 1.011 and a total protein level of <2.5 g/dL. The total nucleated cell count was 425 cells/µL, with 53% mononuclear cells, 40% nondegenerate neutrophils, and 7% small lymphocytes. Cytology of a cytospin sample of abdominal fluid revealed the cells in Figure A.

1. What is the cytologic diagnosis?
2. What are the treatment options and considerations?
3. What is the prognosis for this dog?

(See page 577 for answers and explanations.)
Severe disseminated histoplasmosis. The central macrophages contain many 3- to 5-µm organisms with a thin, nonstaining cell wall (Figure B) that are consistent with *Histoplasma capsulatum*. Although development of a pure transudate can be seen with hypoalbuminemia, it is inconsistent with the presence of *Histoplasma* organisms in the fluid. This suggests an inability to mount a strong inflammatory response to the *Histoplasma* organisms.

The standard treatment for histoplasmosis is oral itraconazole at 10 mg/kg once or twice daily. There is no accurate way to monitor response to therapy, so treatment should continue for 4 to 6 months or until at least 2 months after resolution of clinical signs. Itraconazole is a selective fungal cytochrome p450 inhibitor; therefore, its side effects are limited to mild liver enzyme elevation and cutaneous reactions. However, the gastrointestinal absorption of itraconazole is not reliable in animals in which the intestines are severely affected.

Ampoterin B is a polycene macrolide that binds ergosterol preferentially to cholesterol, thus creating aqueous pores that permit ion fluxes sufficient to cause fungal cell lysis. It has poor oral absorption, so it is administered parenterally. It is used in severe or refractory cases or when oral absorption of itraconazole is questionable. Because muscle wasting and poor haircoat were noted in this case, the oral absorption of itraconazole was questioned and not relied on as the sole therapy. The deoxycholate formulation of amphotericin B can cause severe nephrotoxicity, but the various lipid formulations (colloidal dispersion [Amphotec; Sequus, Menlo Park, CA], liposome encapsulated [AmBisome; Astellas Pharma, Deerfield, IL], and lipid complexed [Abelec; The Liposome Co., Princeton, NJ]) are less toxic, allowing administration of higher doses. The lipid forms are selectively absorbed by the reticuloendothelial system, which allows for higher concentrations at the site of infection with minimal renal damage.

The prognosis for this dog is extremely guarded. In general, disseminated histoplasmosis has a fair to guarded prognosis that depends on the degree of dissemination and severity of clinical signs. Alone, the pulmonary form has a good prognosis and has even been shown to resolve spontaneously, depending on the severity of the disease. However, treatment for the pulmonary form is still recommended because dissemination can follow before the immune system has a chance to clear the infection.

**REFERENCES**