Diagnostic peritoneal lavage for identification of blastomycosis in a dog with peritoneal involvement

Cheri Nielsen, MS, DVM; Christine S. Olver, DVM, PhD, DACVP; Melissa M. Schutten, DVM; David C. Twedt, DVM, DACVIM

- In dogs, systemic blastomycosis can cause peritonitis.
- Diagnostic peritoneal lavage may be useful in identifying the cause of infectious peritonitis.
- Blastomycosis can develop sporadically in dogs without any history of travel to areas in which the disease is endemic and in otherwise healthy dogs without any evidence of immune system compromise.

A 6-year-old castrated male Dalmatian was referred to the veterinary teaching hospital at Colorado State University for further evaluation of hematemesis. The dog had had polyuria, polydipsia, and a poor appetite for the past 2 weeks and had become increasingly lethargic over the past several days. Two days prior to examination at the veterinary teaching hospital, the dog had been unwilling to rise and was examined by the referring veterinarian, who reported a fever (rectal temperature, 41.2°C [106.2°F]), generalized muscle wasting, signs of mild discomfort during abdominal palpation, and signs of marked discomfort during palpation of the lumbar portion of the spine.

The dog had been obtained from an animal shelter in Sioux Falls, SD, as a puppy and had not traveled outside of southeastern South Dakota until 18 months prior to examination when the owner moved to Cheyenne, Wyo. The dog had been taken back to eastern South Dakota on a few occasions, with the most recent trip being 4 months prior to examination.

Diagnostic testing by the referring veterinarian revealed mild anemia (Hct, 32.1%; reference range, 40% to 55%) and mild, mature neutrophilia (11,100/µL; reference range, 2,800 to 10,500/µL) with a normal total WBC count. Serum biochemical analysis revealed low urea nitrogen concentration (5.8 mg/dL; reference range, 7 to 27 mg/dL), hypoalbuminemia (1.9 g/dL; reference range, 2.7 to 3.8 g/dL), and high alkaline phosphatase activity (667 U/L; reference range, 23 to 212 U/L). Creatinine concentration was within reference limits (1.0 mg/dL; reference range, 0.5 to 1.8 mg/dL).

The dog was hospitalized by the referring veterinarian and given fluids IV along with enrofloxacin (2.5 mg/kg [1.1 mg/lb], IM, q 12 h), ampicillin (22 mg/kg [10 mg/lb], SC, q 12 h), and ketoprofen (3.5 mg/kg [1.6 mg/lb], SC, once). The dog reportedly was vomiting while hospitalized, and metoclopramide (0.3 mg/kg [0.14 mg/lb], route and frequency not reported) and sucralfate (30 mg/kg [13.6 mg/lb], PO, frequency not reported) were added to the treatment regimen. Positive-contrast radiography with barium did not reveal any evidence of gastrointestinal tract obstruction. The dog improved clinically and was discharged the following day; the owner was instructed to administer prednisone (1.3 mg/kg [0.6 mg/lb], PO, q 24 h). Approximately 12 hours after discharge, however, the dog began vomiting large quantities of blood and was referred to the veterinary teaching hospital.

Physical examination abnormalities identified at the veterinary teaching hospital on day 1 included listlessness, pale mucous membranes with a capillary refill time of 2 seconds, generalized muscle wasting, signs of pain during palpation of the cranial aspect of the abdomen and lumbar portion of the spine, hind limb paraparesis, and a low rectal temperature (36.5°C [97.8°F]). Melena was evident on rectal examination. Results of funduscopic examination and thoracic auscultation were unremarkable, and no peripheral lymphadenopathy was evident. A CBC, serum biochemical profile, and urinalysis were performed. Results of the urinalysis were within reference limits. Hematologic abnormalities included nonregenerative anemia (Hct 28% [reference range, 40% to 55%], reticulocyte count, 37,360/µL [reference range, 0 to 60,000/µL]) and absolute leukocytosis (22,700/µL; reference range, 4,500 to 15,000/µL) with a left-shift (band neutrophil count, 500/µL; reference range, 0 to 200/µL), neutrophilia (20,900/µL; reference range, 2,600 to 11,000/µL), and mild lymphopenia (900/µL; reference range, 1,000 to 4,800/µL). Serum biochemical abnormalities included azotemia (SUN, 74 mg/dL [reference range, 7 to 32 mg/dL], creatinine, 3.3 mg/dL [reference range, 0.7 to 1.8 mg/dL]), hyperphosphatemia (8.9 mg/dL; reference range, 2.1 to 6.0 mg/dL), hypoalbuminemia (2.0 mg/dL; reference range, 2.5 to 4.0 mg/dL), hyperbilirubinemia (total bilirubin, 0.6 mg/dL; reference range, 0 to 0.3 mg/dL), high alkaline phosphatase activity (556 U/L; reference range, 18 to 160 U/L), high aspartate transaminase activity (65 U/L; reference range, 16 to 50 U/L), high creatine kinase activity (522 U/L; reference range, 50 to 275 U/L), and low bicarbonate concentration (13.2 mEq/L; reference range, 16 to 25 mEq/L). The urine was inadequately concentrated given the degree of azotemia, with a specific gravity of 1.020.

From the Departments of Clinical Sciences (Nielsen, Twedt) and Microbiology, Immunology, and Pathology (Olver, Schutten), College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO 80523. Dr. Nielsen's present address is the Department of Small Animal Clinical Sciences, College of Veterinary Medicine, University of Minnesota, St Paul, MN 55108.

Address correspondence to Dr. Nielsen.

Tentative diagnoses were iatrogenic acute renal failure and gastrointestinal tract ulceration secondary to nonsteroidal anti-inflammatory drug and corticosteroid administration. Differential diagnoses for the clinical signs and laboratory abnormalities that existed prior to treatment included multisystemic infectious or inflammatory disease and neoplasia. The dog was admitted to the critical care unit for fluid diuresis and supportive treatment pending further diagnostic testing the following day. Sucralfate (30 mg/kg, PO, q 8 h), famotidine (0.6 mg/kg [0.27 mg/lb], IV, q 24 h), omeprazole (0.6 mg/kg, PO, q 24 h), and metoclopramide (1 mg/kg/d [0.45 mg/lb/d], IV as a continuous-rate infusion) were administered. Approximately 5 hours after the onset of treatment, the dog appeared more alert and seemed less sensitive to lumbar palpation but later had an episode of collapse while walking. The mucous membranes were pale with a prolonged capillary refill time of 3 seconds, femoral pulse strength was fair, a lead-II ECG was unremarkable, and PCV was 25% with a total solids concentration of 6.2 g/dL. Four-quadrant abdominocentesis[1] did not yield any fluid. Because intra-abdominal disease was still suspected, diagnostic peritoneal lavage was performed, as it is a more sensitive diagnostic test.[1] Fluid that was obtained was markedly cellular, with a differential WBC count of 90% neutrophils, 8% large mononuclear cells (macrophages), and 2% lymphocytes. Most of the neutrophils were slightly degenerate. There were numerous extracellular structures with a round to oval shape; a 1-µm-thick, clear-staining capsule; a basophilic interior; and broad-based budding (**Fig 1**). Organisms were consistent with *Blastomyces* spp, and fungal culture was recommended for confirmation. The hematemesis and melena continued overnight, and the PCV decreased to 18%. The dog was transfused with 1 unit of type-matched stored whole blood.

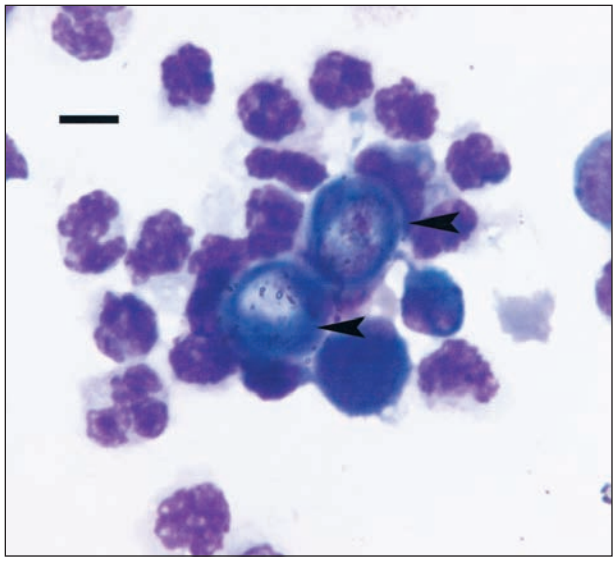

Figure 1—Photomicrograph of a direct smear of fluid obtained by means of diagnostic peritoneal lavage in a dog with blastomycosis. Several extracellular, round to oval structures that are 10- to 15-µm in width and have a 1-µm-thick, clear-staining capsule, basophilic interior, and broad-based budding can be seen (arrowheads). The organisms are surrounded by slightly degenerate neutrophils. Wright-Giemsa stain; bar = 10 µm.

On day 2, abdominal ultrasonography was performed. The left kidney had decreased corticomedullary definition with resistive indices of 0.86 and 0.87 (reference range, < 0.70).[2,3] The right kidney was poorly visualized. The liver and spleen appeared unremarkable. A small amount of peritoneal effusion was evident. There were areas of mixed echogenicity in the lateral body wall that were thought to be associated with a neoplastic, reactive, or infectious process in the mesentery. Ultrasound-guided aspirates of this tissue were obtained and found to have a mixed population of nondegenerate neutrophils, macrophages, and very reactive mesothelial cells. There were also numerous fungal organisms that appeared typical of *Blastomyces* spp. Aspirates were submitted for fungal culture, and serologic testing for fungal infection was performed. Results of serologic testing for aspergillosis, coccidioidomycosis, and histoplasmosis were negative, but results of testing for blastomycosis were positive. Thoracic radiography revealed a nodular, interstitial to peribronchial pattern in the lungs with mild enlargement of the sternal lymph node; no abnormalities of the cardiovascular system were seen.

Follow-up laboratory testing revealed that the SUN concentration had increased (106 mg/dL), the creatinine concentration had decreased (2.8 mg/dL), and the hypoalbuminemia had worsened (1.7 mg/dL). Electrolyte abnormalities included hypernatremia (159 mEq/L; reference range, 142 to 152 mEq/L), hyperkalemia (5.5 mEq/L; reference range, 3.5 to 5.2 mEq/L), and hyperchloremia (130 mEq/L; reference range, 108 to 120 mEq/L). A CBC revealed a normal total WBC count (14,500/µL) with improvement in the left shift (band neutrophils, 400/µL) and neutrophilia (12,900/µL), but progression of the lymphopenia (300/µL). The PCV after the transfusion was administered was 21%, with a total solids concentration of 5.5 g/dL; results of the CBC did not provide any evidence of regeneration.

Intravenous fluid therapy was adjusted to address the dog's electrolyte abnormalities. Treatment with misoprostol (0.3 mg/kg, PO, q 8 h) and cefoxitin (22 mg/kg, IV, q 8 h) was initiated. Treatment with liposomal amphotericin B and itraconazole was recommended, but could not be initiated because of the client's financial constraints. Administration of the traditional dosage form of amphotericin B, although less expensive, was considered contraindicated because of the dog's acute renal failure. The dog's hematemesis resolved despite continued melena, the PCV stabilized between 22% and 25%, and the urine output was > 3.0 mL/kg/h (1.4 mL/lb/h) with fluid therapy. The dog's appetite improved, and its condition appeared clinically stable.

On day 3, the dog's azotemia had continued to improve (SUN, 74 mg/dL; creatinine, 2.0 mg/dL), the hyperphosphatemia had decreased (8.4 mg/dL), and the electrolyte abnormalities had resolved. However, over the course of that day, the dog's clinical status rapidly worsened. The dog became anorectic and started vomiting bilious fluid. Urine output decreased to between 1 and 2 mL/kg/h (0.45 and 0.9 mL/lb/h) with no change in fluid therapy. Because of financial con-

straints limiting treatment, the client elected to take the dog home where it died 2 days later.

A complete necropsy was performed. The dog had a body condition score of 3 on a scale from 1 to 5 with no clinically important external lesions and minimal autolysis. Approximately 250 to 300 mL of yellow, turbid fluid was present in the abdominal and thoracic cavities. There were multiple fibrinous adhesions between the omentum, body wall, small intestines, and a 10-cm, irregular, friable peripancreatic nodule. Disseminated throughout the mucosal surfaces of the stomach, small intestines, and urinary bladder and within the omentum, mesentery of the small intestine, and abdominal wall musculature were many 1- to 5-mm-diameter, raised, friable, pale yellow-brown irregular nodules. All lung lobes contained multiple 2- to 7-mm-diameter, well-demarcated, yellow-white, irregular, firm nodules that extended into the parenchyma on cut surface. No gross abnormalities of the vertebral column, spinal cord, brain, kidneys, liver, spleen, heart, skin, or eyes were seen.

Tissue specimens were fixed in neutral-buffered 10% formalin, routinely processed, and cut at a thickness of 5 µm; sections were stained with H&E and examined by means of light microscopy. Histologic examination revealed multifocal to coalescing aggregates of intact and degenerate neutrophils, large vacuolated macrophages, and occasional multinucleated giant cells, lymphocytes, and plasma cells with variable amounts of fibrosis surrounding many 8- to 10-µm-diameter, thick-walled, intra- and extracellular, spherical, broad-based budding, yeast-like cells. These lesions were found within the mucosa and submucosa of the small intestines, mesentery of the small intestines, kidneys, skeletal muscle of the abdominal wall, lung, liver, urinary bladder, and spleen. A single 50- to 60-µm-diameter focus of yeast-like cells cuffed by small amounts of mononuclear cells was seen in the hippocampus; the remaining cerebrum and cerebellum were unremarkable. No lesions were seen in the spinal cord or skin. A tentative diagnosis of severe disseminated granulomatous disease with intralesional *Blastomyces dermatitidis* was made. The diagnosis was later confirmed on the basis of results of fungal culture of ultrasound-guided abdominal aspirates.

Blastomycosis is a pyogranulomatous fungal disease caused by the dimorphic fungus *B dermatitidis* and is transmitted via inhalation of aerosolized conidiophores. *Blastomyces* spp is thought to be a soil saprophyte, although the organism is difficult to culture from the environment. The disease is typically geographically restricted to areas around the Mississippi, Ohio, Missouri, Tennessee, and St. Lawrence Rivers and the southern Great Lakes,[4] and most affected animals reportedly live within a short distance of a body of water.[5-7] Infection usually originates in the lungs and may disseminate to other organs. Body systems other than the pulmonary system that are most commonly affected include the lymphatic system, eyes, skin, and bones, with CNS involvement seen in < 5% of cases.[4]

Blastomycosis has been identified in humans and dogs in nonendemic areas, albeit rarely. An early study[8] of prevalence that included 1,476 human cases and 384 canine cases in the United States, confirmed on the basis of results of fungal culture or pathologic examination, reported no canine cases in Wyoming, South Dakota, or Colorado and 1, 4, and 4 human cases, respectively, in these states. In the same year, a case report[9] of 3 human cases from southeastern South Dakota was published. A literature search revealed no reports of human or canine cases of blastomycosis from Wyoming or South Dakota since that time. Recently, 2 human cases were reported in the front range region of Colorado[10] following occupational exposure to soil contaminated by prairie dogs; no canine cases have been reported recently in that state.

Involvement of the alimentary tract is apparently rare with systemic blastomycosis. Extension to the spleen and liver is common in humans,[11] but apparently uncommon in dogs. An early study[12] of experimentally infected dogs reported splenic and renal involvement in 4 of 5 untreated dogs and liver involvement in 2 of 5 untreated dogs. However, a recent retrospective study[7] of 115 dogs with naturally acquired blastomycosis and an earlier series[13] of 47 dogs reported no cases with gastrointestinal, hepatic, or splenic involvement. On the other hand, in the more recent of these studies,[7] 16% of the dogs were reported to have vomiting or diarrhea, and although the authors attributed these clinical signs to concurrent antimicrobial treatment or parasitism, it is not possible to rule out gastrointestinal tract blastomycosis on the basis of information provided in the report. Splenic involvement has been reported in a ferret[14] and cat[15] with systemic blastomycosis, and concurrent hepatic and renal involvement were also reported in the cat. Involvement of the gastrointestinal tract in humans with blastomycosis is rare, with the esophagus being the most common site.[11,16] Peritoneal blastomycosis has been described in just 3 human patients, 2 of whom had disseminated disease[17,18] and 1 of whom had isolated peritoneal blastomycosis.[19] Gastrointestinal tract involvement was recently reported in a dog with disseminated blastomycosis,[20] but has not been confirmed in several case series[7,12,13,21] of affected dogs. To our knowledge, involvement of the peritoneum in dogs with blastomycosis has not been reported previously.

Blastomycosis is usually easily diagnosed because of the large number of organisms in lesions in affected animals.[4] Samples with the highest diagnostic yield (> 65%) are typically vitreous aspirates, cutaneous impression smears, and aspirates from affected eyes, skin, and lymph nodes.[7] Although most affected dogs have pulmonary involvement,[4] the diagnostic yield of tracheal wash specimens and bronchoalveolar lavage fluid is typically lower, with 1 study[7] reporting yields of 30% and 25% and another[22] reporting yields of 42% and 71%, respectively. The dog described in the present report did not have involvement of the eyes, skin, or peripheral lymph nodes and had no evidence, on the basis of history and results of physical examination, of pulmonary involvement at the time of admission.

Abdominocentesis and diagnostic peritoneal lavage are simple, minimally invasive procedures that yield samples for cytologic analysis. They are indicated

in dogs suspected to have peritonitis or postoperative gastrointestinal tract dehiscence and those with a history of blunt abdominal trauma, penetrating abdominal trauma, or acute abdomen.[1] The frequency of complications associated with these techniques in dogs has not been reported. However, a study[23] of horses reported serious complications in < 0.5% of awake patients that underwent abdominocentesis. Although abdominocentesis requires less time and equipment to perform, dogs must typically have at least 5 mL of abdominal fluid/kg (2.3 mL/lb) for fluid to be detected with this technique.[24] Diagnostic peritoneal lavage has been shown to be a much more sensitive technique for recovering abdominal fluid and evaluating abdominal injuries in dogs.[24,25] Ultrasonography can be used to detect small amounts of effusion and guide abdominocentesis efforts. However, ultrasonography is not always readily available, and diagnostic peritoneal lavage should be considered a viable alternative in such cases.

Use of abdominocentesis to diagnose histoplasmosis in dogs has been reported,[26,27] and abdominocentesis has been advocated as a rapid and accurate diagnostic technique for this fungal disease.[28,29] To our knowledge, diagnostic peritoneal lavage has not been previously described for the diagnosis of infectious peritonitis that is not secondary to gastrointestinal tract rupture or penetrating abdominal wounds. In the dog described in the present report, this technique was used to rule out hemoabdomen secondary to a ruptured splenic or hepatic tumor or perforated gastrointestinal tract ulcer. Although abdominocentesis was performed initially, there was not enough fluid in the abdomen to yield a sample without ultrasound guidance. Because abdominal disease was still suspected, diagnostic peritoneal lavage was performed, and a diagnosis of systemic blastomycosis was made on the basis of results of cytologic examination of lavage fluid. Diagnostic peritoneal lavage appears to be a useful technique in diagnosing infectious peritonitis when the amount of abdominal fluid is below the limit of detection for abdominocentesis.

Itraconazole is considered the treatment of choice for most dogs with blastomycosis, although amphotericin B may be added to the treatment regimen in severely affected dogs. Success rates of 70% to 75% have been reported with treatment, with treatment failure being most common in dogs that have multisystemic disease or hypoxemia secondary to severe pulmonary involvement.[4] Fluconazole has been effective in the treatment of humans with blastomycosis when administered at high dosages[30] and crosses the blood-brain barrier, which may be an advantage in patients with CNS involvement. However, its efficacy in dogs has not been evaluated. Ketoconazole alone was effective in the treatment of 3 of 4 dogs in 1 study[31] and 3 of 9 dogs in another.[32] In the dog described in the present report, the prognosis for recovery was poor given the extent of disease. However, ketoconazole could have been offered as a treatment since it is generally inexpensive, not nephrotoxic, and not excreted by the kidneys so that it does not require adjustment of dosage in dogs with renal failure. Ketoconazole is water-soluble, and in healthy dogs, CSF concentrations are only 10% of serum concentrations,[33] but with inflammation of the meninges, penetration may be improved. This dog had no clinical evidence of CNS or ocular involvement at the time of treatment.

This case is unique on a number of counts. The dog came from a geographic region in which *B dermatitidis* is not considered to be endemic and did not have any history of travel to endemic areas. Sporadic clusters of blastomycosis in dogs have recently been reported in nonendemic areas,[21] and such reports may have public health importance, as dogs are considered to be sentinels for human disease.[34] This dog had no evidence of underlying disease that would result in an impaired immune system and had not received any immunosuppressive drugs prior to developing blastomycosis. Additionally, peritoneal involvement has not previously been reported in dogs with blastomycosis, and gastrointestinal tract involvement has only rarely been reported.

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