Disseminated blastomycosis in a German shepherd dog

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Abstract — A 5-year-old German shepherd was evaluated after collapsing at home following a week of lethargy and anorexia. Systemic blastomycosis was diagnosed histologically at necropsy. Diagnosis and treatment were difficult due to unusual neurological symptoms, the absence of abnormalities on diagnostic tests, and the advanced stage of the disease at presentation.

Résumé — Blastomycose disséminée chez un chien Berger allemand. Le Berger allemand de 5 ans a été évalué après s'être effondré à la maison à la suite d’une semaine de léthargie et d’anorexie. Une blastomycose systémique a été diagnostiquée par histologie à la nécropsie. Le diagnostic et le traitement étaient difficiles étant donné les symptômes neurologiques inhabituels, l’absence d’anomalités aux tests diagnostiques et le stade avancé de la maladie au moment de la présentation.

A 5-year-old, intact, female German shepherd was presented to a veterinary clinic because of sudden collapse and difficulty in breathing (day 1). The dog had been ill for approximately 1 wk, exhibiting lethargy, poor appetite, and occasional sneezing and coughing. No vomiting or diarrhea was reported. Previous medical history was unremarkable, and there was no history of trauma or exposure to toxins. The dog had been vaccinated routinely, according to standard practice. Other dogs on the same property were clinically normal.

The dog was in thin body condition (weight 32.9 kg), unable to stand, and nonresponsive to external stimuli. Rectal body temperature was within the normal range (39.0°C), breathing was labored (40 breaths/min), and there was marked bradycardia (60 bpm). No cardiac arrhythmia was detected. The dog was approximately 8% dehydrated, with tacky mucous membranes and a moderate skin tent. Exophthalmos of the right eye was associated with marked swelling of the conjunctiva and a mild purulent ocular discharge. No abnormalities were noted on abdominal palpation or auscultation of the lung fields. Differential diagnoses included Addisonian crisis, trauma, abuse, exposure to a toxicant, acute viral disease, or septicemia. The exophthalmos was assumed to be due to a retrobulbar abscess, hematomata, or tumor.

A complete blood cell (CBC) count (QBC; IDEXX, Westbrook, Maine, USA) and biochemical profile (VetTest; IDEXX), including serum electrolyte levels (VetLyte; IDEXX) were done. There was mild anemia (hematocrit 0.33L/L; reference range, 0.37 to 0.55 L/L), and serum biochemical analyses and electrolyte levels were within normal ranges. Urinalysis was also unremarkable. No abnormalities were noted in survey radiographs of the abdomen (lateral and ventrodorsal) and thorax (right lateral, left lateral, and ventrodorsal). A full neurological examination was attempted. Spinal reflexes and cranial nerve function were intact, including direct and consensual pupilary light reflexes in both eyes. Differential diagnoses included rabies, lead poisoning, polymyositis, toxoplasmosis or neosporosis, meningitis, and brain tumor.

The dog was treated initially with IV electrolytes (Lactated Ringer’s Injection USP; Baxter Corporation, Toronto, Ontario); dexamethasone (Dexamethasone sodium phosphate; Vétoquinol, Joliette, Quebec), 1 mg/kg BW, IV; enrofloxacin (Baytril; Bayer, Etobicoke, Ontario), 5 mg/kg BW, IM, q12h; and penicillin (Procaine Penicillin G; Rhône-Merieux Canada, Victoriaville, Quebec), 20 000 U/kg BW, IM, q12h. On day 2, the dog was bright and responsive, eating well, and able to stand without assistance. Electrolyte therapy (50 mL/h) and treatment with glucocorticoid and antibiotics were continued. Because the dog had developed keratoconjunctivitis sicca, 3 to 4 drops of eye lubricant (Isopto tears 1%; Alcon Canada, Mississauga, Ontario) were instilled in both eyes, q6h. The dog continued to improve through day 3, and fluid therapy was discontinued. However, early on day 4, she became recumbent and minimally responsive, with labored respiration (60 breaths/min). Thoracic radiographs were repeated and revealed signs of bronchial infiltration. The dog’s condition continued to deteriorate and she died despite treatment with oxygen via mask; lactated Ringer’s solution, 1L, IV; amikacin (Amiglyde-V; Ayerst, Guelph, Ontario), 300 mg, IV; and doxapram hydrochloride (Dopram V; Ayerst), 140 mg, IV.

An immediate necropsy was performed and samples were submitted for histopathologic examination. The
dog was in poor body condition. Exophthalmos was caused by a retrobulbar abscess. The lungs were mottled red/brown and had a gritty texture on cut section. On gross examination, all other organs, including the brain, appeared normal. A test for rabies virus was negative. On microscopic examination, necrotizing granulomatous inflammation containing numerous *Blastomyces* spp. yeast forms was observed in the tissues of many organs, including the meninges, lung, and gastrointestinal tract. Disseminated blastomycosis was the diagnosis.

*Blastomyces dermatitidis*, a thermal dimorphic fungus, is the etiologic agent of blastomycosis in dogs and cats. The organism is ubiquitous; in North America, it is more common in the eastern seaboard of the United States; the Mississippi, Ohio, and St. Lawrence River valleys; the Great Lakes region; and southern Ontario than elsewhere (1,2). It exists as a mold in the soil or when cultured at room temperature, and as a broad-based, budding yeast form in tissues or when cultured at body temperature. The mold, which is the infectious form, is generally restricted to moist, acidic soil habitats that are rich in decaying vegetation. Such environments are found near river valleys or other waterways (3); in the habitats of wild animals, particularly beavers, pigeons, and waterfowl; and in areas of soil disruption, such as construction sites (4). There is no convenient or reliable means of detecting *B. dermatitidis* in the soil and it cannot be readily eliminated.

Although blastomycosis has been reported in a wide range of animal species, including horses, primates, dolphins, and cats, it is most commonly diagnosed in the dog. Dogs are probably infected with *B. dermatitidis* by inhalation of windborne or soilborne spores, which results in a primary focus of infection within the lung (1,3). In the alveoli, the spores transform into the yeast form and multiply within macrophages. Most often, this causes self-limiting pulmonary infection. As in this case, a generalized or disseminated form of blastomycosis may occur when the organism spreads via the blood or lymphatic system, causing pyogranulomatous inflammation (1) in the eyes; brain; bone; lymph nodes; urogenital system; and skin, subcutaneous tissues, or both. Direct inoculation into the subcutaneous tissue via puncture wounds has also been reported in dogs and humans, causing local cutaneous infection. While any dog may contract blastomycosis under the right circumstances, there is increased risk for 2- to 4-year-old, sexually intact, male dogs of sporting and hound breeds, which may be housed outside, and which are likely to be working in areas suitable for the growth of *B. dermatitidis* (2,5). Proximity to a body of water is also a significant risk factor (5).

The middle-aged female dog in this case was not involved in field work and was not considered at high risk. She was, however, housed outside and roamed a property that included small bodies of water. The client owned other dogs that were all housed outdoors; therefore, risk to them and to humans handling them was an issue.

Blastomycosis is not a zoonotic disease; however, owners of affected animals may be at risk through common environmental exposure (1,4). There was a possibility that this dog had been infected before being purchased in the southern United States at 2 y of age. Clinical signs of canine blastomycosis vary with the organ involved and are nonspecific (1,3,5). Cutaneous lesions may occur and are usually small and slightly raised, ulcerated areas with serosanguineous to purulent exudate. No skin lesions were found on this dog. Dogs with localized pulmonary disease usually exhibit anorexia; depression; exercise intolerance; weight loss; cough, dyspnea, or both; and fever that is nonresponsive to antibiotics. The dog in this case had been losing weight and experiencing exercise intolerance and occasional coughing during training sessions over the previous several months, but the owner had attributed these signs to warm summer weather. Generalized lymphadenopathy is common in disseminated disease, but it was not observed in this case. Ocular disease may include uveitis, glaucoma, subretinal granuloma formation, or retinal detachment. At necropsy, the exophthalmos in this dog appeared to be caused by granulomatous inflammation of intraorbital tissues. The lesions in the central nervous system (CNS) observed in this case are uncommon, but they may arise by direct extension from nasal or sinus cavities, or via hematogenous spread.

Systemic fungal disease was not recognized clinically in this case. Severe CNS disease masked clinical signs of the extensive fungal infection of the lungs and gastrointestinal tract. Poor response to glucocorticoid or antibiotic therapy might have suggested systemic fungal disease; however, there was an initial positive response to treatment, and more extensive tests would have been required to establish a definitive diagnosis.

Results of hematologic evaluation and serum biochemical tests are not diagnostic in dogs with blastomycosis (1,5). Nonregenerative anemia may occur, as in this case, in association with chronic inflammatory disease. There may be leukocytosis with a left shift, monocytosis, and lymphopenia. Even when albumin levels are low, total protein levels may be elevated because of increased inflammatory proteins and immunoglobulins. Hypercalcemia has been associated with blastomycosis (1). The most common radiographic change is a diffuse miliary or nodular interstitial pattern in the lungs (6). In this case, 2 sets of radiographs did not suggest severe lung disease, although granulomatous foci were palpable in the lungs at postmortem.

Definitive diagnosis of systemic mycotic infection is based on identification of fungal organisms in body tissues or fluids (1,3,7). Cytological analysis of tracheal wash specimens or bronchoalveolar lavage fluid is useful in suspected mycotic disease (7). Other appropriately stained specimens, such as impression smears of draining skin lesions or aspirates of lungs, lymph nodes, or both, may also be diagnostic. As in this case, *B. dermatitidis* may be diagnosed histologically, and its culture from tissue or exudates is possible. However, culture is very time consuming and poses a health risk to laboratory personnel. The most common diagnostic serologic test is agar gel immunodiffusion, which has a sensitivity and specificity of approximately 90% (8). More reliable serologic tests are being developed, including radioimmunoassay for *B. dermatitidis* antigen (8). Serologic testing of this client’s other dogs was declined due to the cost.

Animals with clinical signs of blastomycosis should be treated medically. Rarely, primary cutaneous or ocular
blastomycosis may be treated by surgical excision (1,3). The traditional therapy for acute, life-threatening systemic fungal infections is IV amphotericin B, which was effective in 2 of 3 dogs in 1 report (9). However, this drug may cause renal damage, and equally effective oral antifungal agents are now available. Ketoconazole, an imidazole, is effective, but the response to treatment occurs more slowly than with amphotericin B (10). Initial treatment with amphotericin B may be combined with long-term ketoconazole treatment to limit the adverse effects associated with amphotericin B. Itraconazole, a triazole antifungal, has been used in the treatment of human blastomycosis since the early 1990s, and it is effective in dogs when given with food at a dose of 5 mg/kg BW, q24h, for at least 60 d (10).

The prognosis for dogs with blastomycosis is best in cases of mild lung disease, more guarded for dogs with moderate to severe lung disease, and poorest for dogs with CNS involvement (1,9,10). In this case, successful treatment might not have been possible, even if the correct diagnosis had been made at initial presentation.

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**References**