

Systemic Blastomycosis in a Labrador Retriever in Upstate New York

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Summary

This report describes a case of systemic blastomycosis in a 1 ½ year-old male castrated Labrador Retriever from upstate New York that was diagnosed at Cornell University's Hospital for Animals in May 2006. "Bailey" originally presented for evaluation of a draining tract at the level of his left popliteal lymph node, gagging, coughing, lethargy and inappetance. He resides in Indian Lake, NY, a small town in Adirondack Park that is endemic for *Blastomyces dermatitidis* and has had no history of travel outside of the area. He was diagnosed with systemic blastomycosis with severe pulmonary involvement based on thoracic radiographs and ancillary tests, including impression smear, swab and culture and agarose gel immunodiffusion. Bailey responded well to long-term oral itraconazole therapy. At eleven months post-diagnosis, there was resolution of the draining tract, continued improvement of the fungal pneumonia as viewed on thoracic radiographs and no signs of itraconazole-induced hepatotoxicity.

Introduction

Blastomycosis is a fungal infection that primarily affects the lungs and may disseminate to other organ systems via blood and lymphatics. It is caused by the dimorphic fungus *Blastomyces dermatitidis*. Blastomycosis is primarily a disease of dogs and humans with dogs having a greater susceptibility to infection and shorter prepatent period.¹ Young, male, large breed dogs are most commonly affected with sporting dogs, hounds, Labrador Retrievers and Doberman Pinschers over-represented.^{1,2,3} Common clinical signs include fever, mild to severe exercise intolerance, dyspnea, dry hacking cough, anorexia, depression, weight loss, cutaneous ulcerative or proliferative nodules or

plaques and ocular disease (uveitis, chorioretinitis, glaucoma, panophthalmitis).^{1,3,4} Less commonly encountered signs include hypoxemia, lameness, reproductive signs (orchitis, prostatitis, mastitis) and CNS signs (depression, seizures, neurologic deficits).

Growth and survival of *B. dermatitidis* is favored by sandy, acidic soil and moisture.^{1,2,3} Geographic distribution in North America is generally confined to the Mississippi, Missouri and Ohio River valleys, as well as, mid-Atlantic states, Quebec, Manitoba and Ontario.¹ Small endemic foci outside of the typical distribution area are now believed to exist with clusters of cases reported in New York, South Dakota and Colorado.^{1,4,5,6} This report details a case of systemic blastomycosis in a 1 ½ year-old male castrated Labrador Retriever from upstate New York that was diagnosed at Cornell University's Hospital for Animals in May 2006.

Signalment

Bailey is a 1 ½ year-old male castrated Labrador Retriever. He lives in Indian Lake, NY which is a small town in Adirondack Park in upstate New York. It is situated on a lake and surrounded by numerous other bodies of water, forests and mountains.

Case History

On May 10, 2006, the owner first noticed an area of focal inflammation and mass lesion on Bailey's left hindlimb in the area of the left popliteal lymph node. He was treated by a local veterinarian with oral diphenhydramine and clavamox. The inflammation persisted, and Bailey was treated with subcutaneous cortisone at a second veterinarian the following day. At that time, the owner also began cold packing the

lesion twice daily. One week later (5/17), a draining tract erupted in the area of the mass lesion with serosanguinous discharge. The referring veterinarian lanced the mass and placed a drain. On 5/21, Bailey began to experience respiratory signs that included gagging, a dry non-productive cough and serous nasal discharge. On the evening of 5/23, Bailey became lethargic and inappetent. He presented to Cornell University's Hospital for Animals the following day (5/24) for further evaluation and diagnostic testing. During this two week period, Bailey did not experience any episodes of vomiting, diarrhea, sneezing or wheezing. In addition, he had no history of travel outside of Indian Lake, NY. At the time of presentation, Bailey was up-to-date on vaccinations and was on oral clavamox and monthly heartworm preventative. One other dog lived in the household and was reportedly healthy with the exception of osteoarthritis.

Chief Complaint

Bailey had three primary complaints upon presentation at Cornell. First, Bailey had focal inflammation and a draining tract at level of the left popliteal lymph node that had persisted for two weeks despite medical treatment. He also had episodes of gagging and dry, non-productive coughing during the previous 72 hours. Finally, Bailey was inappetent and lethargic.

Clinical Findings

On presentation, Bailey was quiet and alert. He had a body condition score of 5 out of 9 with a weight of 30.5 kg. He was febrile (rectal temperature = 104.5°F) and tachypneic with harsh lung sounds in all fields. No pulmonary crackles or wheezes were

auscultated, and no nasal discharge was noted. The cardiovascular exam was within normal limits. In the region of the left popliteal lymph node, there was focal inflammation and a roughly elliptical area of alopecia measuring 6 cm x 4 cm. Within this area, there existed a draining tract with a moderate amount of purulent discharge. The left popliteal lymph node was moderately enlarged, and both inguinal lymph nodes were questionably enlarged. In addition, there was mild edema in the left hock. No neurologic signs or gait abnormalities were detected. An ophthalmology consultation was performed and was within normal limits. The remainder of Bailey's physical examination was unremarkable.

Diagnostic Tests

Complete blood count (CBC) and blood chemistry on 5/24 revealed a high normal neutrophil count (9600 neutrophils/uL) with a left shift (300 band neutrophils), mild hypoalbuminemia (2.9 g/dl) and mildly increased alkaline phosphatase (182 U/L). The coagulation panel and urinalysis were unremarkable. On 5/25, thoracic radiographs were performed and revealed a severe multi-focal nodular soft-tissue pattern in all lung fields. Radiographs of the left hindlimb were negative for bony involvement but showed soft tissue swelling and subcutaneous emphysema consistent with popliteal lymphadenopathy and a draining tract. Abdominal ultrasound was also performed revealing enlargement of the left medial iliac lymph node. An impression smear performed 5/25 revealed pyogranulomatous inflammation with a small number of *Blastomyces sp.* This was confirmed by a swab and culture of the draining tract and agarose gel immunodiffusion (AGID), which tests for anti-*Blastomyces dermatitidis* antibodies. There was no growth

on urine culture.

Problem List

- Inflammation and purulent draining tract in the region of the left popliteal lymph node
- Respiratory signs – tachypnea, harsh lung sounds, gagging, dry non-productive cough
- Lymphadenopathy - left popliteal, bilateral inguinal, left medial iliac
- Edema left hock
- Fever
- Lethargy
- Inappetance
- High normal neutrophil count with left shift
- Mild hypoalbuminemia
- Mildly elevated alkaline phosphatase
- Multi-focal pulmonary nodules in all lung fields
- Systemic *Blastomyces dermatitidis* infection

Diagnosis

Bailey was diagnosed with systemic blastomycosis. All of the clinical and laboratory abnormalities could be explained by the presence of this mycotic infection with the exception of increased alkaline phosphatase. Since there was no apparent bony involvement, alkaline phosphatase elevation was attributed to the cortisone injection

received at the referring veterinarian two weeks prior to presentation.

Treatment

The current treatment of choice for systemic blastomycosis in dogs, and that used for Bailey, is oral itraconazole.^{1,3,4,7} Itraconazole is a fungistatic triazole compound.⁷ It should be given orally at a dose of 5 mg/kg twice daily for the first five days, then 5 mg/kg once daily.^{1,3} Treatment should last a minimum of 60 days and at least one month after resolution of all signs. Severe lung disease should be treated for a minimum of 90 days. Itraconazole is effective for ocular, but not CNS, involvement. The most important side effect is anorexia due to hepatotoxicity.

Amphotericin B, ketoconazole and fluconazole are less commonly used in the treatment of blastomycosis in dogs. Amphotericin B has similar efficacy to itraconazole, but severe side-effects, including nephrotoxicity, are more common.⁷ It may be used in combination with ketoconazole or itraconazole in severely hypoxemic patients.^{1,3} Ketoconazole and fluconazole are considerably less effective in treating systemic blastomycosis although fluconazole has better CNS penetration.

As in Bailey's case, a cutaneous lesion may exist. Antibiotics are commonly used to prevent or treat secondary bacterial infection. Bailey was treated with intravenous Unasyn (15 mg/kg twice daily) while in the hospital and oral clavamox (15 mg/kg twice daily) at home.

Prognosis

Prognosis for systemic blastomycosis in dogs is typically good, and clinical cure

occurs in approximately 70-75% of cases treated with itraconazole.^{1,3} Prognostic factors for survival include brain involvement, severity of pulmonary disease and number of organ systems affected. Brain involvement is often fatal. Among dogs experiencing severe pulmonary disease, the fatality rate may reach 50% in the first week post-diagnosis.¹ In addition, respiratory signs may worsen in the first two to three days of treatment with antifungal agents due to rapid die-off of fungal organisms and the subsequent inflammatory response. The inflammation can often be lessened with intravenous steroids. According to one source, treatment failure is also more likely in dogs with three or more organ systems infected with *B. dermatitidis*.³ Eye involvement is common in blastomycosis, and patients with endophthalmitis and / or glaucoma have poor prognoses for vision improvement.¹

Twenty to twenty-five percent of patients may relapse after apparently successful treatment with antifungal agents.¹ It is associated with severity of initial lung disease and usually occurs in the first six months post-therapy. Relapse can be treated successfully with another course of itraconazole. Recovered patients are immune to future re-infection.

Outcome

Bailey was discharged from Cornell on 5/30/06, six days after admission. At that time he remained febrile, but his lung sounds were improved, and he had decreased inflammation and discharge associated with the draining tract in his left hindlimb. Thoracic radiographs were unchanged from admission. He was discharged on oral itraconazole (5 mg/kg once daily) and clavamox (15 mg/kg twice daily for 10 days), as

well as, meloxicam (0.1 mg/kg once daily for 5 days), a non-steroidal drug used for its anti-inflammatory and anti-pyretic properties.

Bailey's progress was monitored with serial thoracic radiographs and blood chemistry panel every two to three months. Thoracic radiographs improved steadily over the course of eleven months with resolution of the pulmonary nodules. Radiographs in December 2006 revealed a mild, mixed asymmetric interstitial and bronchial pattern worse in the right cranial and middle lung lobes which could be attributed to resolving fungal pneumonia or residual scarring. The most recent thoracic radiographs, taken in March 2007, revealed stable disease.

Liver enzymes were used to monitor for hepatotoxicity secondary to long-term itraconazole therapy. No clinical or laboratory evidence of hepatic disease was observed in the eleven months post-diagnosis. In addition, the inflammation and discharge in the left popliteal region subsided, and the draining tract healed during this time period leaving a small, alopecic area. At eleven months post-diagnosis, Bailey remained on oral itraconazole (5 mg/kg once daily). Length of anti-fungal treatment was to be determined at his next visit based on thoracic radiographs.

Discussion

While Bailey fits the typical signalment for a dog with systemic blastomycosis (young, male, large breed), he does not live within the geographic area often described (Mississippi, Missouri or Ohio River valleys, mid-Atlantic states, Quebec, Manitoba or Ontario).^{1,2,3} Small endemic foci outside of the typical distribution area are being reported with increasing frequency. A paper by Cote et al. describes six cases of

blastomycosis diagnosed in dogs from New York State between 1991-1992, three of which had no history of travel outside of NY.⁵ In addition, seven cases of dogs with blastomycosis were treated at Colorado State University between 1980-1990.¹ It is interesting to note that, even within endemic areas, *Blastomyces dermatitidis* organisms are not widespread. Instead, a point source is much more likely. Most people and animals within endemic areas do not show evidence of exposure (serologic or dermal), and the majority of those that are exposed become ill.¹ Subclinical infection is rare. This is in sharp contrast to most other fungal infections, in which a large proportion of those within an endemic area have serologic evidence of exposure, and very few of those exposed show clinical signs.

These observations suggest a specific ecologic niche for *Blastomyces dermatitidis*. Outbreaks are typically associated with sandy, acidic soil. This is supported by a study published by the Centers for Disease Control and Prevention describing the diagnosis of two people with occupationally acquired blastomycosis in a prairie dog relocation program in Colorado in 1998 presumably due to increased exposure to *B. dermatitidis* organisms deep in the soil.⁶ Moisture is also an important growth factor for *B. dermatitidis*. In a study in Wisconsin, 95% of dogs with blastomycosis lived within 400m of a body of water.¹ Additionally, in a Louisiana study, dogs with blastomycosis were ten times more likely than controls to live within 400 m of a body of water.¹ Moisture, including rain or dew, may facilitate the release of infectious spores, and strictly indoor cats and dogs have also reportedly been infected.

Bailey lives in Indian Lake, NY, a small community located in Adirondack Park in upstate New York that is believed to be an endemic “hot-spot” of *B. dermatitidis*. The

town is surrounded by many small bodies of water. Since 1997, 50% of blastomycosis cases treated at the Cornell University Hospital for Animals (n=8) have resided in Indian Lake (unpublished data). Eighty-eight percent of these cases live within a 75 mile radius of Indian Lake, and all but one case lives in close proximity to water. This data, taken together with Bailey's lack of travel outside of the region, strongly supports the notion of an endemic focus of *B. dermatitidis* in upstate New York.

Conclusion and Clinical Relevance

When making a list of differential diagnoses, veterinarians often prioritize based on geographic distribution of infectious organisms. Some diagnoses may be left off of the list entirely because they are not thought to occur in a given geographic area. As demonstrated by Bailey, blastomycosis is being diagnosed with increasing frequency in people and animals outside of what is regarded as the typical endemic area. Although geographic distribution should help veterinarians prioritize their list of differential diagnoses, it is dangerous to exclude diagnoses based on this criterion alone.

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