Title: Pulmonary and cutaneous blastomycosis in a dog

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Clinical History: Four-year-old female mongrel dog from Barstow (high desert area, California) with history of multiple skin lesions and severe dehydration. Supportive care was attempted but the animal died a few hours after admission. The veterinarian requested necropsy due to presumptive animal neglect and bestiality due to ulcerated lesions around the vagina and all over the skin.

Gross and Histologic Findings:

Figure 1. A. Skin of the elbow. B. Lung, caudodorsal aspect. C. Lung, H&E, 400X. D. Lung, PAS, 400X.
**Morphologic diagnoses:**
- Skin: Ulcerative dermatitis, multifocal.
- Lung: Pyogranulomatous pneumonia, multifocal to coalescing, with numerous intralesional yeasts morphologically compatible with *Blastomyces dermatitidis*.

2. **Etiologic diagnoses:** Pulmonary Blastomycosis / Cutaneous Blastomycosis
3. **Histologic features that support the diagnosis:** Presence of 15-25 µm diameter yeasts with a thick capsule and broad-based budding.

**Gross Findings:** The body condition was thin with reduced deposits of adipose tissue in the abdominal cavity. Multiple ulcerative lesions were identified in the skin. In internal organs, the lungs were diffusely firm and pale red, with multiple 0.2 to 0.6 cm diameter nodules dispersed throughout the pulmonary parenchyma. Surrounding the right ureter, inguinal lymph nodes, and abdominal aorta, iliac arteries and associated structures, dissecting between the dorsal abdominal musculature, and reaching the musculature of the right pelvis, there was abundant yellow exudate, which was concentrated in a nodule (abscess) in the retroperitoneal area, from where the exudate dissected into the other adjacent structures.

**Histologic Findings:** The most significant findings were necrosuppurative to granulomatous pneumonia, dermatitis (all analyzed sections) and panniculitis, mastitis, myositis, lymphadenitis, glossitis, adrenalitis, peritonitis, and retroperitonitis, with innumerable intralesional fungal yeasts, which measured 15-25 µm diameter, had a thick capsule, and displayed frequent broad-based budding.

**Ancillary Testing:** DNA sequencing of a 529 base pair region of the 28S rRNA gene identified the intralesional fungus as most closely related to *Blastomyces dermatitidis*.

**Discussion:** Blastomycosis is non-contagious infectious disease produced by *Blastomyces dermatitidis* (BD). BD is a dimorphic fungus that grows as a mycelium (*Ajellomyces dermatitidis*) that reproduces sexually with the final production of infectious spores (Aleuriconidia). It is frequently found in wet soils enriched with organic matter. The areas considered endemic for BD infections are Mississippi, Ohio, the St. Lawrence River valley, and the Atlantic states of the USA. In animals, hyphae or conidia reach the respiratory system though the nasal cavity. In the alveolar spaces, they are phagocytized by macrophages, where they transform into pathogenic yeasts and express different virulence factors, interfering with the host immune response and triggering dissemination to other organs though lymphatic and hematogenous routes. The most common tissues affected are the skin and bones. The cutaneous form occurs in 20-50% of all patients with systemic Blastomycosis, with a predilection for the nasal plane, face and plantar cushions.
Primary cutaneous presentation is infrequent and is associated with laceration of the skin; a systemic dissemination to the skin must be ruled out.

Among the virulence factors expressed by BD, BAD1 (Blastomyces adhesin-1) and DpplIVA (dipeptidyl-peptidase IVA) are fundamental for the pathogenesis within the host. During the transition between conidia to yeast, BD increases the transcription of BAD-1, which promotes tissue adhesion and immune evasion. BD also secretes the serine protease DpplIVA that contributes to the degradation of the granulocyte-macrophage colony-stimulating factor and inhibits the recruitment of immune cells. Other virulence factors are Cysteine synthase (important in the transition to yeast), Cysteine dioxygenase (growth promoter of BD in keratinized structures) and RYP1-4 (required for the yeast phase 1-4).

Historically, the diagnosis of Blastomycosis has been based on direct detection of BD in tissues and fungal culture (gold standard). These methods are described as complementary to each other, but several discrepancies have been reported. Histopathology allow the observation of the yeast, but it does not allow its identification, which depends on many factors, such as training of the diagnostician, quality of the sample, and processing. On the other hand, fungal culture is a robust and irrefutable technique, but the fungal growth is slow, which delays the diagnosis and treatment. It is important to consider that Blastomycosis is a zoonotic disease, which can carry risk for the laboratory personnel. Nowadays the diagnosis can be reached with molecular tests, which have high sensitivity and specificity. For the identification with PCR, fungal ribosomal RNA is currently used with success. The most commonly used biomarkers are ribosomal RNA operons (5.8S, 18S, 28S, ITS1 and ITS2). The BAD1 gene has also been proposed for the demonstration of the fungus, with similar results as reported for 18S.

In summary, a case of systemic Blastomycosis in a dog from southern California is described herein. Blastomycosis is common in states of the Atlantic region of USA, which have proper weather conditions for the fungus; this case is highly unusual, however, because of the area from which it comes from (high desert area of Barstow, California). Systemic Blastomycosis should be considered in cases with multiple ulcerative lesions in the skin and should not be ruled out based only on geographic location.

References:


*The Diagnostic Exercises are an initiative of the Latin Comparative Pathology Group (LCPG), the Latin American subdivision of The Davis-Thompson Foundation. These exercises are contributed by members and non-members from any country of residence. Consider submitting an exercise! A final document containing this material with answers and a brief discussion will be posted on the CL Davis website ([http://www.cldavis.org/diagnostic_exercises.html](http://www.cldavis.org/diagnostic_exercises.html)).

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