Fungal diseases of the canine reproductive tract
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Abstract
Fungal diseases of the canine reproductive tract are uncommon. The most commonly described is blastomycosis, which is associated with disease in both male and female dogs. Secondary yeast infections of the reproductive tract, as are described in humans, are uncommon in dogs.

Keywords: Fungi, yeast, prostatitis, blastomycosis

Fungi are free-living organisms. They are heterotrophs, incapable of producing their own nutrients, which differentiates them from plants. Fungi release enzymes and absorb nutrients from their environment. Their cell wall is made of chitin, not of cellulose as is seen in plants, which makes them relatively resistant to microbial degradation and may make them more resistant to drug therapies that require uptake across the cell. Most are multicellular and filamentous. A group of fungal filaments are hyphae and groups of hyphae form a mycelium. Fungi may produce as much as one kilometer of hyphae in a single day in the right growing conditions.

Fungi may or may not exist as a single-celled yeast as part of their life cycle and may or may not form spores. There are two main phyla of fungi that are relevant to this discussion. These are the Ascomycota and the Basidiomycota. The Ascomycota include molds, yeasts, morels, truffles, and Dutch elm disease. This class of fungi is filamentous when growing and reproduces by producing spores called conidia at the end of modified hyphae called conidiophores. Yeasts are unicellular forms that reproduce by budding. Pathogenic fungi in this phylum include Aspergillus sp., Blastomyces dermatitidis, Candida sp., and Sporothrix schenckii. The basidiomycota include mushrooms and toadstools, rusts, smuts, stinkhorns, and shelf fungi. Most organisms in this phylum produce specialized club-shaped spores called basidia but the species that are pathogenic in small animal veterinary medicine do not. These species are Cryptococcus sp. and Rhodotorula sp., both of which exist primarily as yeasts.

There are relatively few reports in the literature of fungal diseases of the canine reproductive tract. Please note that this discussion will not include fungal diseases of dogs that have not been reported in the reproductive tract. These include histoplasmosis and coccidioidomycosis (Valley Fever). Diseases are presented in alphabetical order, not in order of prevalence or clinical significance.

Aspergillosis
Aspergillus sp. are widespread in a variety of climates worldwide, with hundreds of species in the genus. It was named by an Italian priest who thought the shape of the spore-forming structure in this genus resembled the container used to sprinkle holy water, called an aspergillum.

Nasal aspergillosis is the most common type of disease reported in dogs and it usually is due to Aspergillus fumigatus. Disseminated fungal disease due to Aspergillus sp. is most commonly reported in German Shepherd dogs. This breed predisposition may be due to abnormalities in amount or function of IgA with subsequent effects on mucosal immunity. Cases most commonly are reported in California and in Australia. Clinical presentation varies with organ system affected and may include gastrointestinal signs; pain, lameness and paraplegia; central nervous system signs; anorexia and muscle wasting; cutaneous edema, and ocular signs. Pyometra due to aspergillosis has been reported as has disseminated aspergillosis including uterine infection apparently brought on by the stress of breeding. There is a report of puppies either stillborn or that died shortly after birth due to diffuse aspergillosis. They were delivered by cesarean section to a bitch that developed neurologic signs due to diffuse aspergillosis and was euthanized shortly thereafter, leading the authors to deduce that transplacental transmission of the organism had occurred. There is one report of orchitis and epididymal atrophy secondary to aspergillosis in a dog.
Definitive diagnosis usually is made by identification of organisms on cytology or in urine sediment. Culture may be used to confirm the diagnosis. Serologic testing rarely is performed because of a high rate of false positive results in dogs with other systemic mycoses. Changes on routine bloodwork often are unremarkable but may include a mature neutrophilia on complete blood count (CBC) and increases in blood urea nitrogen, alkaline phosphatase, and alanine aminotransferase.

Amphotericin B is the treatment of choice, with itraconazole a secondary therapy if needed. Prognosis for cure in cases of disseminated disease is guarded. There is one report of treatment of disseminated aspergillosis with fluconazole in which the dog showed initial improvement but eventually demonstrated progression of disease and was euthanized. The male dog with orchitis was treated with itraconazole until culture of semen was negative but he failed to impregnate bitches after therapy and those bitches that he bred developed uterine disease of unreported etiology.

Blastomycosis

Systemic infection with blastomycosis was first reported in humans in the late 1800’s. Blastomycosis is the most commonly reported infection of the canine reproductive tract. Overall incidence of blastomycosis in dogs is 0.2 to 1.4% per year in endemic areas. Blastomyces dermatitidis is the causative organism. It exists in soil as a hyphal form and is most commonly found in the Mississippi, Missouri and Ohio river valleys and in the area of the Great Lakes. Other areas include the mid-Atlantic states and southeastern states, and southern Canadian waterways. In general, risk is increased in animals and humans with proximity to water. Some reports suggest greater prevalence in some seasons of the year while others refute those findings. There are reports of dogs infected with blastomycosis that had no history of having lived or traveled in endemic areas. The organism grows best in moist, acidic soil containing decaying vegetation and animal feces. Spores form directly on the hyphae, not on a distinct fruiting body, and usually are transmitted to the animal by inhalation. This is facilitated by disruption of the soil.

Once spores are inhaled, the higher body temperature of the infected animal promotes development of the yeast form of the organism, with infection most commonly localizing in the respiratory tract. Direct penetration of the organism, usually associated with trauma, may permit development of localized disease peripherally. With any route of exposure, there may be localized spread or systemic disease may be induced by spread through lymphatics or the bloodstream.

Clinical disease is most common in young dogs (2-4 years of age) and in large breeds, especially in hounds and sporting breeds. Reports differ regarding predisposition by gender, with some reporting no such predisposition and others reporting increased incidence in males. Signs may not appear for weeks to months after exposure and include anorexia, depression, weight loss, fever, lymphadenopathy, and respiratory signs including dyspnea, tachypnea, and cyanosis. Other systems that may be involved include the eye, skin, and bone. Central nervous system involvement is rare.

Blastomycosis has been reported as a cause of orchitis and prostatitis in dogs. Dogs presented for scrotal swelling, with or without palpable changes in the testes. Of four dogs in one study with prostatic infection, three were asymptomatic. Mammary gland infection also has been reported. Two of three dogs with mycotic mastitis in one case series also had lymphadenopathy and pulmonary disease.

Definitive diagnosis is by histopathologic demonstration of the yeast, which is thick-walled, 8-12 micrometers in diameter, lacks a capsule, and may bud with daughter cells having a broad-based attachment to the primary yeast cell. Direct tissue sampling (fine needle aspirate or biopsy) is superior to indirect samples (transtracheal wash, for example). The organism often is accompanied by granulomatous or pyogranulomatous inflammation. Changes on routine bloodwork often are unremarkable; hypoalbuminemia is reported in about 75% of cases, hyperglobulinemia in about 50% of cases, and hypercalcemia in about 10% of cases. Normocytic, normochromic anemia and moderate leukocytosis may be noted on CBC. Organisms may be visible in urine sediment from dogs with prostate infection. Characteristic radiographic findings in dogs with respiratory signs are a diffuse or nodular interstitial pattern or alveolar infiltration. Characteristic radiographic findings in dogs with bone...
involvement are osteolysis and periosteal proliferation. Culture of the organism is not routinely done because the organism is slow-growing and culture puts laboratory personnel at risk. Serologic testing has been described but is not definitive.

Treatment is curative in 70 to 75% of cases. Itraconazole is the treatment of choice for systemic disease when compared to ketoconazole and amphotericin B, although one author reported equal success with itraconazole alone or a combination of ketoconazole and amphotericin B and another study showed that while duration of therapy with itraconazole was shorter, longer term, equally successful therapy with fluconazole was less expensive. Affected dogs should be treated for at least two months and until clinical signs have been resolved for one month. Those cases with the poorest prognosis are those with involvement of three or more body systems and those with severe respiratory infection. Mortality usually occurs within the first seven days of treatment secondary to the inflammatory response that accompanies simultaneous death of numerous organisms.

A genetically engineered attenuated vaccine against Blastomyces dermatitidis has been described for use in dogs. This vaccine is not commercially available.

Candidiasis

Candida sp. exist as yeasts and are common in the environment and on alimentary, upper respiratory, and genital mucosal surfaces of animals and humans, where they mostly exist as harmless commensals whose overgrowth is inhibited by presence of normal bacterial flora. Candida sp. were identified in 6.4% of 100 vaginal samples and 2.2% of 93 preputial samples collected from healthy dogs. Candida albicans causes candidiasis, or thrush, in people, generally manifested as inflammation of a mucosal surface such as the oral cavity or vagina. Predisposing factors for candidiasis in humans include being immunocompromised from disease or drug therapy, disruption to the mucosal surface, and prolonged antibiotic use. Similar risk factors described in dog with urinary tract infection due to candidiasis include recent treatment with antibiotics or glucocorticoids, and concurrent disease, including diabetes mellitus.

There are reports of localized candidiasis in non-healing ulcers of the genital mucosa. The ulcer is covered by a white to grey plaque and has hyperemic margins. There also are reports of urinary tract infections due to candidiasis and systemic candidiasis; some of those dogs had concurrent prostate disease.

Candida sp. are visible as small, thin-walled, ovoid yeasts. Culture of the organism requires lysis centrifugation of the sample to cause release of the fungus from leukocytes. Because it is part of the normal flora, culture results must be interpreted carefully.

Lesions are treated topically with nystatin, gentian violet, or miconazole or amphotericin B antifungal creams or lotions. Treatment for prostatic infection is not described.

Cryptococcosis

Cryptococcus sp. also are yeast forms; technically, any growth as hyphae of this organism are classified in a different genus. The yeast cell of this species is covered by a gelatin-like capsule, which contains factors that appear to increase virulence of the organism.

The most common clinical manifestation of cryptococcosis is multisystemic disease with central nervous system signs. There are reports of urinary tract infections due to Cryptococcus neoformans, suggesting a possibility for infection of the reproductive tract in dogs. There is one report of a puppy dying of disseminated cryptococcosis at two weeks of age. The organism could be cultured from the vulvar secretions of that pup’s dam for a prolonged period but eventually cultures were negative and she went on to whelp a normal litter.

Rhodotorulosis

Rhodotorula sp. are pigmented yeasts that ordinarily live in soil but can be found in moist home environments, especially in bathrooms. These are commensal organisms on moist skin. In humans, infection occurs in immunosuppressed individuals. There is one report of urinary tract infection in a
dog and there is one report of epididymitis in a dog, both due to infection with *Rhodotorula mucilaginosa*.\(^{32,36}\) When grown on Sabouraud’s dextrose agar, the colonies have a distinct creamy orange to salmon color.

**Sporotrichosis**

*Sporothrix schenckii* is an important component of soil worldwide, acting as a decomposer of plant material. It is a hyphal form at environmental temperatures and a yeast form at body temperature. Because of its role in decomposition, it is readily found in landscaping materials including sphagnum moss, landscape timbers, and baled hay. It is most commonly transmitted as a pathogen through puncture wounds, with direct inoculation. Cutaneous and cutaneolymphatic disease are the most common manifestations with rare systemic disease in dogs.\(^{37}\) The organism has been isolated from the testes of systemically affected dogs.\(^{38}\) It is a polymorphic yeast, taking on round, oval, and cigar shapes, and is a difficult organism to identify on cytology as it requires special staining. Accuracy may be enhanced by concurrent immunohistochemistry and staining.\(^{39}\) Diagnosis often requires culture of a deep tissue biopsy. Disease is treated with appropriate antibiotics for secondary skin infection and with a long-term course of supersaturated potassium iodide. Some dogs may show signs of iodine toxicity with therapy, including ocular and nasal discharge, dry coat with excessive scaling, vomiting, depression, and collapse. If these signs occur, ketoconazole or itraconazole may be used for therapy.\(^{37}\)

**References**

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