VET 433A Deep Mycoses

Mycoses Overview

- When to suspect fungal disease
  - Hx of travel to endemic areas or soil disturbance
  - Immunosuppressed animals with any new illness
  - Young, purebred dogs
  - Hx and PE findings
    - Pulmonary signs
    - Extrapulmonary signs
      - Osteomyelitis/discospondylitis
      - Draining nodular skin lesions, claw bed lesions
      - Parenchymal organ involvement
      - Ocular lesions
      - Meningoencephalitis
  - Lesions on thoracic rads
    - Hilar lymphadenomegaly
    - Miliary or nodular interstitial patterns
    - Lobar consolidation
    - Pleural effusion
    - Cavitary lung lesions
  - Chem and CBC can be unremarkable
    - Maybe hypercalcemia +/- azotemia
  - Failure to respond to antibacterial drugs
  - Clinical signs worsen after initial improvement with glucocorticoids
- Treatment
  - Azole antifungals with/without amphotericin B
    - Itraconazole or fluconazole
      - Inhibit fungal sterol synthesis
      - Itraconazole penetrates the CNS, eyes and urine poorly

        - Fluconazole is **NOT** active against molds
    - Amphotericin B
        - Binds fungal sterols with increased membrane permeability
            - Ergosterol over mammalian cholesterol
        - NEPHROTOXIC
        - Given parenterally MWF basis in D5W for a month or until azotemia develops
        - Monitor kidney values prior to each infusion
        - Two formulations
            - Deoxycholate (most nephrotoxic)
                - Given over 4-6h with diuresis
            - Lipid-complex
                - Given over 2h without diuresis
    - Months to years of treatment
    - May be $$$
    - Signs can worsen for 2-3 days before they get better due to a die-off period
        - CNS involvement usually has a poor prognosis
- <u>Adverse effects of treatment</u>
    - Elevated liver enzymes
    - If ALT > 400 U/L or inappetence/vomiting develops, discontinue
    - Ulcerative dermatopathy (itraconazole)
    - Diarrhea (high doses of fluconazole)

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Organism	Description	Epidemiology	Pathogenesis	Clinical Signs	Diagnosis and Treatment
Coccidioidomycosis *Coccidioides spp.*	Soil-borne dimorphic fungus Arthrospores disperesed in air and inhaled Young, adult, often purebred dogs Rare to see feline disease	Sandy, alkaline soil High temperatures Low elevation *rain, dust storms, earthquakes, digging behavior in dogs Southwestern USA, Mexico, Central and South America Arizona, SW Texas, California	1-3 week incubation period Arthrospores inhaled > form spherule (pomegranate dz) Arthrospores enter bronchioles, alveoli, peribronchiolar and subpleural tissue Dissemination to hilar LN and other organs over 3-4 months with immunosuppression Course of disease = months to years Reactivation of subclinical infection w/ immunosuppression	Humans: Respiratory signs Canine Cough Systemic signs Lameness, lymphadenomegaly, skin lesions, ocular lesions, right-sided CHF Skin lesions begin as SQ masses or nodules and may ulcerate	Labs and rads may be normal May have signs of hyperglobulinemia, hypoalbuminemia and proteinuria Cytology and histopathology to see spherules Antibody detection very sensitive (rare false negatives) <u>Treatment</u> Antifungal drugs >1y or lifelong in dogs w/ disseminated cases Itraconazole is the most effective Amphotericin B for disseminated dz then azoles Monitor titers every 1-3 months during tx
Blastomycosis *Blastomyces spp.*	Dimorphic fungus Thick, refractile, double cel wall	Water sources and acid, sandy soil	Spores are inhaled and converted to yeast in lungs	Non-specific	Cytology and histopathology

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	Broad-based budding	Upper Midwest Mississippi, Missouri and Ohio river valleys, mid-Atlantic states (Quebec, Manitoba and Ontario) Rain and construction work facilities – spore release Dogs and Humans, rarely cats Dogs can be sentinels for human infection	Dissemination to skin and SQ tissues, bone, CNS, eye, prostate, testes	Nodular or draining skin lesions Lymphadenopathy Signs of pulmonary involvement Ocular involvement Lameness CNS signs	Culture only if necessary Antigen testing Urine antigen tests > 90% sensitive Cross-reactivity with *Histoplasma* antigen <u>Treatment</u> Azoles, amphotericin B Minimum of 6 mo
Histoplasmosis *Histoplasma spp.*	Soil-borne dimorphic fungus Prefers moist, humid conditions an N-rich organic matter Disseminated in bat guano	Temperate and subtropical regions worldwide OH, MI, MO river valleys Some parts of northern and southern California Cats are just as susceptible as dogs	Incubation period of 12-16 days Mycelia produce microconidia and macroconidia > inhaled Microconidia become yeast in tissues Bud intracellulary within MACROPHAGES as well as extracellularly Disseminate via blood and lymph	<u>Cats</u> Disseminated dz Pulmonary involvement Organomegaly and lymphadenomegaly Conjunctivitis, chorioretinitis, retinal detachment, optic neuritis, bone involvement <u>Dogs</u> Pulmonary involvement with hilar lymphadenomegaly GI involvement in North America	Cytology and histopathology Sensitive Rectal scrapings Aspirates, biopsies Culture if needed Antigen test (urine) Cross-reactivity with *Blastomyces* antigen

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				Liver and spleen Bone marrow Rare ocular and skin involvement	
Cryptococcosis ***Cryptococcus neoformans*** ***Cryptococcus gattii***	*Cryptococcus neoformans* (dogs) *Cryptococcus gattii* (dogs and cats) Dimorphic fungus Narrow-based budding, thick polysaccharide capsule Grows as yeast in culture Important cause of meningitis in AIDS patients	*Cryptococcus neoformans* likes pigeon guano *Cryptococcus gattii* Australia (*Eucalyptus spp*) Western USA Likes Douglas fir in Pacific NW Subclinical carriage in nasal passages of around 1/10 dogs and cats Cats are more susceptible than dogs American Cocker Spaniels and Siamese seem to be predisposed	Deposited in nasal cavities Local extension or hematogenous spread MENINGES EYE Lymph nodes Skin +/- bone and kidneys	Cats Usually upper respiratory, CNS, ocular or skin Pulmonary involvement is uncommon Dogs *C. neoformans* infection CNS and ocular involvement are common Widespread dissemination to all sites (GIT, LN, pancreas, myocardium, kidneys, liver) *C. gattii* infection Localized nasal cavity cryptococcomas Localized cutaneous masses	Cytology and histopathology Sensitive and usually the diagnosis is cytological Can culture Latex *Cryptococcus* agglutination test Antigen test -serum or CSF (risk of herniation) Treatment Deoxycholate amphotericin B Fluconazole Prednisolone E tube feeding
Sporotrichosis ***Sporothrix spp***	Dimorphic fungus, worldwide, especially subtropical regions Round, oval or cigar-shaped yeast in tissues	Soil rich in decaying organic matter Rose growers, hay bale handlers, sphagnum moss, Christmas tree farmers, hunting dogs, cat claws		Three forms Cutaneous Single or multiple nodules, localized Most common	Cytology and histopathologyc Many organisms in cats, rare in dogs

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		Cats can transmit infection to humans! Transmission is possible without a break in the skin		Can resemble cryptococcosis Cutaneolymphatic Follows lymphatics on distal limbs Disseminated Rare	Pleomorphic yeasts intra- and exra-cellularly Can culture if needed Treatment Itraconazole Good prognosis