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NEVPC CASE #9

IDENTIFICATION NUMBER ON SOURCE MATERIAL: 164361-16 Cornell University

Disseminated Blastomycosis in a 3-year-old Doberman Pinscher

INSTITUTION

Cornell University Department of Biomedical Sciences; Section of Anatomic Pathology

SIGNALMENT

3-year-old, male castrated, Doberman Pincher

HISTORY

A 3-year-old, male castrated, Doberman Pinscher from the Adirondacks, NY was presented to Cornell University Hospital for Animals Emergency Service for respiratory distress. Nine months prior to presentation he had been evaluated for bilateral carpal swelling and radiographic evidence of an aggressive bone lesion. His carpi became progressively worse, and he began to show forelimb lameness together with coughing, sneezing and epistaxis. He was administered diphenhydramine as needed and amoxicillin for 30 days. Histological examination of a stained needle aspirate from an enlarged popliteal lymph node revealed histiocytic inflammation. He was administered 0.5 mg/kg (0.22 mg/lb) of prednisone PO, q 12 h for 7 days, and then 0.5 mg/kg (0.22 mg/lb), PO, q 24 h for 14 days and doxycycline, 5 mg/kg (0.22 mg/lb), PO, q 12 h for 30 days. Because the carpal swelling worsened at the end of this regiment, the dose of prednisone was increased to 1 mg/kg (0.45 mg/lb), PO, q 12 h, at which point his respiratory signs became more severe. Bronchoscopy showed inflamed, hemorrhagic bronchi and radiographs showed a progressive bilateral periosteal reaction and lytic lesions of the right and left distal radius and ulna, as well as a severe diffuse miliary nodular lung pattern. On presentation at Cornell, he was febrile (103.6º F), tachycardic (152 beats per minute), and panting. On thoracic auscultation, he had harsh lung sounds in all four quadrants, and his heart could not be auscultated over his lung sounds. He had cyanotic mucous membranes, but had a capillary refill time of less than two seconds and strong femoral pulses. Carpal joint effusion in both of his forelimbs and firm popliteal lymph nodes were noted bilaterally.

GROSS FINDINGS

Prior to post-mortem examination, educational computed tomography (CT) scans were recorded of the head, neck and thorax and confirmed that there was a bilateral and generalized miliary nodular pattern within the lungs. The CTs also revealed that there was periosteal new bone formation on the calvarium, further affirming the suspicion of a systemic disease process.

At necropsy, the dog was in good body condition (4 out of 9, Purina scale) with mild postmortem autolysis. Bilaterally, the carpal joints were severely enlarged, with the left being worse than the right. Both carpal joints were hard with focal, soft, depressed areas. On the medial aspect of the right carpus there was a 0.6 cm diameter full thickness defect containing 0.1 mL of creamy, soft material (draining tract). Bilaterally, the skeletal musculature of the brachium, predominantly the triceps brachii, was less prominent (atrophy). The left popliteal lymph node was firm.

The lungs were diffusely mottled dark red and light pink, failed to collapse and were mildly firm (interstitial pneumonia). Diffusely throughout the lungs were dozens of miliary, white-tan foci that extended into the parenchyma on cut section. The trachea contained approximately 2 mL of frothy, red fluid. On cut section, the large airways oozed a small amount of cloudy red to gray mucoid material (exudate).

Bilaterally, the distal one-third of the radius and ulna were expanded approximately 7 cm in diameter on the left and 5 cm in diameter on the right. On cut section, the right and left carpal joints exuded approximately 1 mL of viscous, brown, cloudy fluid (suppurative synovitis and periarthritis). The periarticular fascia on the medial aspect of the right and left carpi had cystic spaces filled with similar brown, cloudy fluid. On sagittal section, the periosteum of the distal one-third of the radius, ulna and carpal bones was gradually expanded towards the carpal joint up to 1.7 cm thick. The outer cortical surface was rough and uneven.

HISTOPATHOLOGIC FINDINGS

Lung: Affecting the entire parenchyma are numerous, multifocal to coalescing areas composed of central necrotic debris and degenerate inflammatory cells, surrounded by a layer of macrophages and occasional multinucleated giant cells admixed with lymphocytes, neutrophils, and rare plasma cells (pyogranuloma). Within these pyogranulomas and also scattered in all lobules are large numbers of intracellular and extracellular, 8-15 µm diameter, round yeast-like organisms with a 2-3 µm thick clear to basophilic, refractile capsule. The yeast-like organisms frequently exhibit broad-based budding. Occasionally some of the pyogranulomas are surrounded by concentric layers of fibrocytes and fibroblasts. Similar inflammatory cells and yeast-like organisms are also found free in the lumen of all airways.

Distal radius/ulna: Diffusely, the corical bone is expanded by numerous cavities filled with a large number of mostly macrophages together with fewer multinucleated giant cells, and rare lymphocytes (osteomyelitis). Randomly scattered in the inflammatory infiltrate are numerous yeast-like organisms occasionally exhibiting broad-base budding. The inflammatory infiltrate extends to the bone marrow spaces. The cortical bone is covered by an expanded layer of woven bone that is incompletely mineralized (periosteal reaction) and contains numerous osteocytes. The inflammatory infiltrate dissects through the periosteal reaction and adjacent fascia and skeletal muscles (fasciitis and myositis).

MICROBIOLOGICAL FINDINGS

Blastomyces dermatitidis was cultured from lung tissue collected at necropsy.

MORPHOLOGIC DIAGNOSES

Lungs: Severe, diffuse, chronic granulomatous bronchopneumonia with yeast-like organisms

Distal radius/ulna: Severe, locally extensive, chronic, pyogranulomatous osteomyelitis, fasciitis and myositis with yeast-like organisms

DISSCUSION

This is a classic case of disseminated blastomycosis caused by infection with *Blastomyces dermatitidis* with severe lung and skeletal involvement as well as secondary lesions in peripheral lymph

nodes and heart (not described). Although the classic presentation for fungal pneumonia on radiographs is a generalized, random, miliary nodular pattern, blastomycosis can have various presentations ranging from multiple pulmonary nodules, patchy or lobar lung consolidation (alveolar pattern), to a solitary pulmonary mass.[1] In this case, histopathology ruled out other potential causes of pulmonary nodules, such as neoplasia and infection with other mycoses including *Coccidioides immitis, Cryptococcus neoformans*, and *Histoplasma capsulatum*.

Blastomycosis is one of the most common systemic mycotic infection of dogs that live in endemic areas including the Ohio and Missouri river valleys, the southern Great Lakes, and southern mid-Atlantic states.[2] In the state of New York, the incidence of blastomycosis in dogs has increased over the past 20 years and is endemic in the Adirondacks where this dog lived.[3] Blastomycosis occurs in dogs and humans and is rare in other animals. Young, male, intact dogs living in endemic areas are at an increased risk of becoming infected.[3] Sporting dogs such as Labrador and Golden retrievers and Doberman Pinschers are more frequently affected.[4, 5]

Blastomyces dermatitidis is a saprophytic fungus found in moist acidic or sandy soil, with high organic content.[4] It is a thermally dimorphic fungus that forms septated mycelia in the environment, but becomes yeast in infected tissues. In its mycelial form, it produces conidia (spores) that are inhaled by the host and then phagocytized by alveolar macrophages.[5] In the presence of higher body temperature, spores become yeast with thick double-contoured outer walls and characteristic broad-based budding.[4, 5] The yeast causes local suppurative to pyogranulomatous inflammatory response, which may be self-limiting.[6] However, phagocytized yeasts can be transported into the pulmonary interstitium where they can disseminate hematogenously or through the lymphatic system to other organs.[6] Inoculation directly through a skin wound is also possible, but is rarely seen.[6] By contrast with other mycotic diseases including those caused by *Coccidioides immitis* and *Aspergillus* species where infectious spores can be easily aerosolized from infected tissues and transmit the disease, the yeasts of *B. dermatitidis* are not infective, and thus, do not require special biosafety precautions during necropsy.

Clinical signs with blastomycosis depend on the organ system most severely affected; however, respiratory signs is the most common clinical presentation.[5, 6] In dogs, *B. dermatitidis* often disseminates to the lungs, lymph nodes, skin, eyes, bones, reproductive system, and nervous system.[6] Lameness caused by osteomyelitis or paronychia is reported in 25% of dogs with blastomycosis, and fungal osteomyelitis is seen in 10-15% of cases.[6] In cases such as the one presented here, distinguishing between aggressive bone lesions (ABL) and non-aggressive bone lesions (nABL) is essential.[7] The radiographic pattern of ABL includes periosteal reaction, bone lysis, zones of transition, and progression over time.[7] Continuous new bone formation and reactive new bone formation can be associated with both ABL and nABL. Interrupted new bone formation and tumor new bone formation are associated with ABL. A long zone of transition between normal and abnormal bone is commonly associated with ABL, whereas a short zone of transition can be associated with both ABL and nABL. ABL can have similar appearance regardless of the cause, therefore distribution of lesions helps to prioritize the differential diagnosis (eg, focal monostotic, multifocal polyostotic, etc).

Itraconazole is the treatment of choice at a dosage of 5 mg/kg (2.27 mg/lb) every 24 hours for 60 days. Treatment should be continued for 30-60 days after resolution of clinical signs. Clinical signs often become more severe in the early phase of treatment, as the yeast organisms die off and elicit

severe inflammation.[6] Prolonged administration of prednisone might have contributed to the severe disseminated disease seen in this case.

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