Case Number: 17

Presenter & Institution: Jaimie L. Miller, DVM; University of Wisconsin

Case History

Signalment: 2 month old female Thoroughbred foal

Clinical History:

This foal presented with 4 day history of respiratory disease/increased respiratory effort. Attempted treatment on farm with amoxicillin and then Exceed with no improvement. On presentation, foal was lethargic/dull with increased respiratory effort (rate ~ 40 breaths per minute) with an abdominal component especially on expiration. Mucous membranes were dark pink and injected; the sclera were also severely injected. Mucus was ausculted within the trachea and a palpable rattling was felt over the trachea. All lung fields had harsh, loud, rubbing sounds cranioventrally and crackles and wheezes heard through all lung fields. Remainder of exam within normal limits. Thoracic radiographs and ultrasound revealed widespread pulmonary abscesses. The foal was started on clarithromycin/rifampin but continued to decline over the next few days with increased respiratory effort and heart rate. Three days after presentation, the foal began to display severe dyspnea and signs of mild colic that became more severe as day went on. The foal was found in severe distress in lateral recumbency and died that evening.

Gross Findings:

The oral mucous membranes are red with a hyperemic red line at the junction of the teeth and lower gums.

The thoracic cavity contains 100 ml of a serosanguinous non-clotting fluid. The trachea is filled with yellow frothy mucoid material extending 1/3 of the way up the trachea. The lungs do not collapse upon opening the thoracic cavity. Throughout the lung lobes, there are hundreds of multifocal to coalescing, firm to soft, pale tan to light yellow, round, raised nodules ranging from 3 mm in diameter up to 40 mm in diameter and contain yellow suppurative to caseous material on cut section. The lungs variably float when placed in formalin. The tracheobronchial lymph nodes are markedly enlarged and on cut section contain multiple well demarked light yellow soft nodules with central areas of necrosis.

The mesenteric lymph nodes are moderately enlarged and on cut section contain multiple well demarcated yellow soft nodules. The gastrointestinal tract is unremarkable. Bilaterally, the stifles and tarsal joints contain a moderately increased amount of bright yellow synovial fluid with decreased viscosity and the synovium is mottled yellow to red.

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Case Results

Histopathologic description:

Over 85% of the alveolar spaces and bronchiolar lumina are infiltrated by numerous neutrophils and macrophages with lesser numbers of multinucleated giant cells, lymphocytes and plasma cells. The cells are mixed with abundant fibrin, brightly eosinophilic homogenous material (edema), and bright eosinophilic hyalinized membranes. There are multifocal areas in which the inflammation disrupts and effaces alveolar septa and areas with liquefactive necrosis composed of cellular debris intermixed with degenerate neutrophils and macrophages. Rare macrophages contain intracellular coccobacilli.

Morphologic diagnosis:

Lungs: Severe, chronic, multifocal to regionally extensive, necrotizing pyogranulomatous bronchopneumonia with intrahistiocytic coccobacilli, abscessation and edema

Laboratory testing:

Ante mortem tracheal wash culture: Heavy growth of *Rhodococcus equi*

Comments:

In addition to the pulmonary lesions, there is also marked multifocal necrotizing pyogranulomatous lymphadenitis with abscessation in tracheobronchial and mesenteric lymph nodes. Both the pulmonary and lymph node lesions are consistent with infection with *Rhodococcus equi*. Histologically, there is also moderate diffuse proliferative lymphoplasmacytic synovitis that is more consistent with an immune-mediated polysynovitis rather than a septic arthritis.

Rhodococcus equi is a facultative, intracellular, Gram-positive bacterium that is present in soil and feces and is often enzootic on farms[2]. It is an important cause of pneumonia and occasionally enteric disease in 2-4 month old foals, and may affect foals up to 6 months of age[1]. There are two classic forms of the disease: suppurative to pyogranulomatous bronchopneumonia and ulcerative enterocolitis. Approximately half of the foals affected with the respiratory form also have concurrent intestinal lesions, though intestinal lesions alone are not common[2]. Occasionally, lymph nodes, joints, bones,

genital tract, and other organs may also be affected[2]. There are sporadic reports of *R. equi* in other species, including cattle, goats, pigs, dogs, cats, and immunocompromised humans[2].

Pulmonary infection results from inhalation bacteria, often facilitated by a dusty, contaminated environment. Enteric infections may result from ingestion of soil-contaminated feed, or swallowing expectorated material from the lungs[1]. The bacteria are quickly phagocytosed by alveolar macrophages, but are able to survive and multiply intracellularly. Some studies suggest *R. equi* can block phagosome-lysosome fusion by some unknown mechanism, while other studies suggest *R. equi* is instead able to produce molecules that suppress acidification of phagolysosomes resulting in their intracellular survival and replication[3]. Eventual destruction of the macrophage leads to release of the organism into surrounding tissue, further phagocytosis by macrophages, and repeated intracellular survival and replication. Unlike macrophages, neutrophils are able to easily kill *R. equi*; however, extensive tissue destruction usually results from the release of lysosomal enzymes and reactive oxygen species[3]. This damage of pulmonary parenchyma permits entry of *R. equi* into alveoli and bronchioles and access to the mucociliary apparatus, allowing transportation to the nasopharynx where it can be swallowed and lead to infection of the alimentary system[3].

Most foals present with chronic infections, seen as depression, cough, weight loss, and respiratory distress, although some may present with acute infection with rapid death due to severe bronchopneumonia[2]. Diarrhea, arthritis, or subcutaneous abscess formation can occur in either form[2]. Affected foals usually develop disease in the summer, and present with pyrexia, tachypnea, dyspnea, cough, and mucopurulent nasal discharge[1]. Cytology and bacterial culture can be used to identify *R. equi* from tracheal washes, as was done in this case. As an alternative, PCR has been successful in the diagnosis of *R. equi* in tracheal aspirate in live foals[2]. Grossly, pyogranulomatous bronchopneumonia is generally cranioventral, although most of the lung can be affected in severe cases[1]. Pleuritis is uncommon and tracheobronchial lymph nodes are enlarged and may contain caseous necrosis[1]. Histologically, *R. equi* begins as suppurative bronchopneumonia and progresses to pyogranulomatous pneumonia by day 4 post infection, with intracytoplasmic Gram-positive bacteria visible in plump uni- or multi-nucleate, particularly degenerative, macrophages[1]. Tracheobronchial lymph nodes can have necrotizing pyogranulomatous lymphadenitis[3].

If the alimentary system is involved, similar lesions are most commonly seen in the colon, cecum, and associated lymph nodes, and occasionally the small intestine[1]. Colonic ulceration begins centered on lymphoid follicles and may extend through the wall of the intestine[1]. Approximately one-third of affected foals have polyarthritis that may cause severe lameness, suppurative synovitis, and positive joint cultures. In contrast, other foals have milder, probably immune-mediated polyarthritis, characterized by sterile joints, lymphoplasmacytic synovitis, mononuclear cells in joint fluid, and immunoglobulin deposits in synovium[1]. This form if synovitis was present in this case. Widespread dissemination of infection in foals can occasionally cause abscesses in the skin, liver or spleen, vertebral or long bone metaphyseal osteomyelitis, and hypopyon[1]. *Rhodococcus equi* may also cause ulcerative lymphangitis, and has been associated with metritis and abortion in mares, metritis in cows, pneumonia in calves, and tubercle-like lesions in lymph nodes of pigs and cattle[1].

The virulence of *R. equi* varies depending on virulence factors encoded by plasmids (virulence-associated protein A [vapA] gene)[2]. VapA protein is detectable in 88-89% of isolates from pneumonic lungs[1]. However, additional plasmid-encoded proteins, such as recently described vapB and vapC, and other virulence factors of *R. equi*, including glycolipids containing long-chain mycolic acids, capsular polysaccharide, and the "equi factors" cholesterol oxidase and choline phosphohydrolase, also likely contribute to the development of disease[1].

References:

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