“Sam’s Clever Cough”

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Introduction

The following case report will highlight severe bacterial bronchopneumonia in a foal as the result of primary agent, *Klebsiella pneumoniae*. The increasing development of antimicrobial resistance in *Klebsiella* spp is a concern in human medicine as it is a common cause of pneumonia following mechanical ventilation.[3,6] Mechanical ventilation while under general anesthesia is a predisposing factor for the development of *Klebsiella* spp pneumonia for the adult horse, but not as commonly for the foal.[3] In foals, bacterial pneumonia is a common sequalae to a primary viral respiratory infection.[2] Another common cause of development of bacterial pneumonia in the foal is a history of neonatal sepsis.[2] *Klebsiella* spp are one of the most common bacteria isolated from sepsis in neonates.[2,7] This case report will review the presentation and clinical signs, diagnostics, pathophysiology, and treatment of bacterial pneumonia caused by *Klebsiella* spp. in foals as well as the outcome of this patient, Sam.

History and Presentation

Sam was an approximately 2.5-month-old Quarter Horse colt. He presented on emergency to Mississippi State University College of Veterinary Medicine's Equine Medicine and Surgery Department on July 25, 2020, for coughing, increased respiratory effort, and depression of two weeks duration that worsened on the day of presentation. Sam's referring veterinarian reports that Sam and his mare were a part of a breeding herd where several foals were also experiencing milder respiratory clinical signs, with Sam the most severely affected foal. Sam had previously presented at birth following an assisted delivery when it was noted that the mare was agalactic. Sam was consequently treated for failure of passive transfer with plasma transfusions, ceftiofur, and supportive care. The owners gave Sam a weight-appropriate dose of flunixin meglumine orally prior to his July 25th admission into the hospital.

On presentation, Sam was depressed, but still alert and responsive. He had appropriate affinity to his mare although his appetite was poor. He weighed 130 kilograms with a body condition score of 5/9 (5 being ideal). His mucous membranes were pink and moist with an increased capillary refill time of three seconds. He had copious amounts of mucopurulent nasal discharge bilaterally and was observed coughing during the entirety of the exam. Vital parameters included a temperature of 101.1° F, a heart rate of 96 beats per minute, and a respiratory rate of 60 breaths per minute. His increased respiratory effort was exaggerated on exhalation and there was an evident heave line, indicating chronic increased abdominal effort during respiration. Cardiopulmonary auscultation revealed diffuse crackles and wheezes bilaterally, but no murmurs or arrhythmias were appreciated. A tracheal rattle was appreciated during auscultation of the distal trachea suggestive of fluid within the tracheal lumen at the level of the carina. His joints and umbilicus palpated within normal limits and there was no evidence of hypopyon on ophthalmic examination. No evidence of sepsis on physical exam was appreciated. The remainder of his physical exam was within normal limits.

Diagnostic Approach

Following initial physical examination, a sonographic exam of the lung fields was performed along with the collection of a sample from the nasal cavity for culture and sensitivity. Although a transtracheal wash sample would be the "gold-standard" for identifying the causative organisms of Sam's pneumonia, he was not stable enough for sedation at the time of presentation.[2,7] There was diffuse "comet-tails" and "hepatization" of the lung parenchyma on ultrasound consistent with pulmonary consolidation and abscessation. The abscesses were most prominent on the ventral right side at the level of the 12th intercostal space between the point of the shoulder and the point of the elbow.

Blood was collected for a complete blood count, large animal chemistry profile, and IgG concentration. His presenting blood work was consistent with active inflammation represented by an increased white blood cell count (18,000/ul) with toxic changes on morphology, mature neutrophilia (16,916/ul), increased fibrinogen (800 mg/dl), and increased globulins (4.5 g/dl). His foal IgG results were >800 mg/dl suggesting adequate IgG concentrations.

Based on the severity of his clinical signs and the appearance of his lungs on ultrasound, Sam was presumptively diagnosed with severe bilateral bacterial pneumonia from primary infection with *Rhodococcus equi*. The nasal swab obtained on presentation had growth of *Streptococcus equi* ssp *zooepidemicus*, *Staphylococcus intermedius*, and *Enterobacter cloacae*, which were all sensitive to the initial choice of antibiotic therapy.

Sam showed mild improvement of clinical signs on this therapy but continued to exhibit febrile episodes of increasing magnitude. After a few days of slight improvement, his cough and ease of respiration began to worsen again. He also developed diarrhea, likely secondary to his antibiotic therapy and the stress of hospitalization. Repeat complete blood count and a large animal chemistry profile were submitted on 7-28-2020. His large animal chemistry profile results are as follows: low sodium (125 mmol/L), low chloride (90 mmol/L), high alkaline phosphatase (431 U/L), increased globulins (4.9 g/dl), and high creatinine kinase (694 U/L). The low electrolytes are consistent with the diarrhea he was experiencing. The increase in alkaline phosphatase was likely due to bone metabolism, which is normal for a growing individual, and creatinine kinase was likely due to his increased abdominal effort during respiration as well as his increased time spent in lateral recumbency. Results of the complete blood count are as follows: increased white blood cell count (17,940/ul), increased fibrinogen (600mg/dl), and neutrophilia with bands present (14,172/ul segmented, 179/ul bands). These results are

suggestive of a worsening infection and a repeat thoracic ultrasound was performed. While the consolidation and abscessation had slightly improved since the time of presentation, he was not clinically improving, and his bloodwork suggested a need for reassessing his antimicrobial therapy. A sterile blood sample was obtained on 8-2-2020 for blood culture to ensure Sam was not bacteremic. There was no growth on the blood culture confirming Sam was not bacteremic.

On 8-3-2020, Sam was sedated with xylazine and butorphanol and a transtracheal wash aspirate obtained and submitted for culture and sensitivity, cytology, and gram-staining. Results of cytology and gram-staining did not reveal any organisms but were consistent with active inflammation by the presence of numerous degenerative neutrophils. The transtracheal aspirate had growth of *Enterobacter cloacae* (also present on nasal swab culture), *Klebsiella oxytoca*, and *Klebsiella pneumoniae*. The primary pathogenic organism, *Klebsiella pneumoniae*, was sensitive to imipenem, ceftazidime, and amikacin. Based on the sensitivity pattern, Klebsiella pneumonia became the primary pathogen of concern regarding Sam's failure to improve clinically. It is also important to note that other organisms could be contributing to Sam's lung pathology but not present on culture since Sam had been on antibiotics for several days prior to obtaining the transtracheal wash aspirate.

Pathophysiology

Klebsiella spp are gram-negative, rod-shaped, facultative anaerobic bacteria that are normally present in both the alimentary tract and urogenital tract of the healthy horse.[3] While the exact tissue pathology caused by *Klebsiella* spp is not well understood, it has been frequently isolated from acute interstitial pneumonia cases.[3,5] Acute interstitial pneumonia is a severe and sudden onset of respiratory distress and tends to be difficult to treat once identified.[5] Post-mortem examination of foals with acute interstitial pneumonia reveal firm lungs that fail to

collapse once the thorax is opened with rib impressions.[5] Histologically there is significant loss of alveolar architecture, edema with hyaline membrane formation, and macrophages as the predominating cell type within the infiltrate.[5] Hyperplasia of alveolar type II cells is also appreciated in majority of acute interstitial pneumonia cases.[5] Sam's clinical presentation is not consistent with acute interstitial pneumonia.

The majority of bacterial pneumonia cases in foals are a result of a mixed population of gram-negative and gram-positive agents.[2,7] As previously stated, primary viral infections are a common cause of the development of a bacterial pneumonia in foals, especially those kept on a breeding operation where they are in close contact with many other foals. A primary viral infection predisposes the foal for the development of a secondary bacterial pneumonia by damaging mucociliary clearance, epithelial cells of the upper respiratory tract, and alveolar type II cells of the lower respiratory tract which leads to a decrease in the production of surfactant and collapse of the airway.[2]

Treatment and Management

Sam's initial treatment included antibiotics with known efficacy to *Rhodococcus equi*, azithromycin (10 mg/kg PO q24h) and rifampin (10 mg/kg PO q24h).[8] Additionally, for supportive care while in hospital, he was placed on flunixin meglumine (1.1 mg/kg IV) as needed for control of his pyrexia, sucralfate (25 mg/kg PO q8h) to mitigate the development of gastric ulcers, and nebulization with levalbuterol (1.25mg in 1.5mL saline) followed by manual coupage to aid respiration through bronchodilation and clearance of purulent debris.

Sam developed diarrhea on day four of hospitalization, likely secondary to the azithromycin treatment. Although macrolide treatment is generally well tolerated by foals, mild, self-limiting antibiotic-induced diarrhea occurring within the first 5 days of treatment is well-

documented.[4] Oral administration of ProBios (1 scoop provided with product twice daily), and Platinum Balance (1 scoop provided with product twice daily), were added to Sam's treatments for gastrointestinal support.[8] He was given a one day's worth of 180mL (three doses) of BioSponge by mouth. His diarrhea resolved and no further administrations of BioSponge were required. The ProBios and Platinum Balance oral supplementation continued through the remainder of his hospitalization. An intravenous catheter was placed into the left jugular vein for the administration of fluid therapy boluses with Lactated Ringers Solution as needed for dehydration secondary to his diarrhea. Careful attention and care of his catheter included regular flushing with heparinized saline, monitoring the catheter site for signs of thrombophlebitis, administration of triple antibiotic ointment to the insertion site, and single-use injection ports.

Sam was carefully monitored for increases in respiratory rate and temperature. His hydration and appetite were assessed by evaluation of his urine specific gravity as well as marking when he was observed nursing. On 7-30-2020, Sam was administered of fenbendazole (2.5 mg/kg) orally to mitigate potential Ascarid pulmonary larval migrations, which could be a contributing factor to Sam's lung pathology.[2,7] Sam's antibiotics were changed from rifampin and azithromycin to more broad-spectrum coverage with amikacin (29 mg/kg IV q24h) and ampicillin (29 mg/kg IV q8h) on 8-3-2020 while results of his transtracheal wash culture were pending.[8] Once results were obtained, both amikacin and ampicillin were continued, as *Klebsiella pneumoniae* was sensitive to amikacin, and ampicillin provided broad-spectrum antibacterial coverage for organisms that may be contributing to his pathology but did not grow on culture.

Case Outcome

When treating bacterial pneumonia in foals, clinical improvement should be observed within 48-72 hours of starting appropriate antimicrobial therapy.[2] Once Sam began treatment with amikacin and ampicillin, there was drastic improvement of his clinical signs and respiratory effort. Due to his improvement, nebulization and coupage were discontinued on 8-4-2020. He was no longer experiencing intermittent febrile episodes and therefore no longer required flunixin meglumine administration. His mucopurulent nasal discharge transitioned to serous before resolving altogether. On 8-10-2020, oral doxycycline (10 mg/kg PO q12h) was started as the owners could not administer intravenous medications at home. Doxycycline is reported to be an appropriate choice of antimicrobial therapy for macrolide-resistant *R. equi* as well as *Klebsiella* spp.[1,2] In Sam's case, *Klebsiella pneumoniae* was resistant to doxycycline. However, the other bacteria isolated, *Klebsiella oxytoca* and *Enterobacter cloacae*, were sensitive to doxycycline and Sam was suspected to have a polymicrobial infection that could not be represented in entirety by his tracheal aspirate. Since doxycycline is a broad-spectrum antibiotic, it was determined to be the best oral option for Sam to continue after discharge from the hospital.[1] A repeat complete blood count on 8-13-2020 revealed a marked improvement in his inflammatory response with results as follows: white blood cell count within normal limits, mature neutrophilia (8,570/ul), and a normal fibrinogen. His intravenous catheter was removed on 8-13-2020. Sam was discharged from the hospital on 8-17-2020 after a 24-day hospital stay, 7-day ampicillin treatment, and 10-day amikacin treatment. His at-home therapy included continuing doxycycline, Platinum Balance, Probios, and a fenbendazole deworming protocol. Sam continued to improve at home without complication until his pneumonia was resolved.

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