Equine Pleuropneumonia

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Introduction

Pleuropneumonia is a potentially deadly, time consuming and costly lower respiratory infection for the equine industry. It is associated with a high mortality rate of 43.3-87.6% as well as a 61% statistic of returning to full racing potential.[1,9] Pleuropneumonia has been called many different terms since the beginning of the twentieth century such as contagious pneumonia, shipping pneumonia, equine infectious pneumonia and influenza pectoralis.[5] Pleuropneumonia is linked to a predisposing condition that compromises the pulmonary defense mechanisms allowing for a secondary bacterial infection to occur. [3,5,6,7,9] Mortality rates increase with chronicity due to the production of pleural effusion, fibrin loculations, and lung consolidation.[9] Diagnosis, and treatment of pleuropneumonia is known to be extensive, labor intensive and often frustrating to resolve. Early identification of infection and treatment is key to improving survival rates. Aggressive antimicrobial management is extremely important, however surgical intervention is often needed to resolve secondary abscesses and lung atelectasis.

History and Presentation

Thoroughbreds that are currently in training are most likely to develop pleuropneumonia.[9-12] Standardbreds are also a common breed to develop pleuropneumonia. Currently sex predilection and specific age predilection have not been thoroughly studied. Some studies report adult horses typically around 5 years of age.[3] Horses presenting with pleuropneumonia will often have a history of physiologic stress, aspiration or previous infection. Potentially 25% of horses shipped a long distance will develop pleuropneumonia.[9] Chances of developing pleuropneumonia increases 10 fold when a horse is put under repetitive strenuous exercise.[9] Other historical events such as recent anesthetic procedure, near-drowning, recent viral infection are common in pleuropneumonia cases.

Clinical signs and presentation will vary depending on the severity and chronicity of the infection. Horses can present in three stages peracute, acute and chronic. In the peracute stage, the horse will often show nonspecific respiratory signs such as inappetance, pyrexia, lethargy and exercise intolerance.[10] The horse may show signs of pleurodynia or pain caused by pleural inflammation. Pleurodynia signs include pawing at the ground, shorter strides, standing with elbows abducted or flinching upon percussion of their chest.[3,9,10] In the peracute stage lung sounds may be normal upon auscultation. Many will have dyspnea, tachycardia, tachypnea (these vary in peracute patient). Severe acute stages may also present with jugular pulses and flared nostrils.[12] A cough is often absent or extremely soft due to pain. Acute and chronic stages involve the development of pleural effusion, fibrin and lung consolidation that will intensify clinical signs.[12] Along with the clinical signs described previously, these horses will now have absent or dull ventral lung sounds.[3,10,12] There will be harsh lung sounds in the dorsal lung field.[10] While auscultating, cardiac sounds will radiate due to the pleural effusion. A dark possibly fetid nasal discharge may be present if there is an anaerobic infection.[13] Chronic cases will present with weight loss and an overall wasted appearance.[12]

Pathophysiology

Majority of pleuropneumonia cases are polymicrobial infections with aerobic bacteria infections more common than anaerobic. The most common isolates are *Streptococcus spp.*, *Streptococcus equi sbsp. zooepidemicus* (β-Hemolytic spp).[1-7, 9-12,15] Other aerobic bacteria include *Escherichia coli, Actinobacillus equuli, Enterococcus spp* and *Klebsiella*.[1-7, 9-12,15] Anaerobic isolates that equate to one third of the cases are *Bacteroides* spp. *Fusobacterium* spp. and *Clostridial spp*.[1-7, 9-12,15]

Aspiration of opportunistic aerobic and anaerobic bacteria is the main route of infection. As previously stated a predisposing incident weakens pulmonary defense mechanisms allowing bacterial colonization. Incidents include near-drowning aspiration, post anesthetic aspiration, post viral infection and most commonly noted long distance shipping and strenuous exercise.[9] Viral infections (influenza and equine herpes virus 4), near-drowning or post anesthesia aspiration causes damage of the lung parenchyma epithelium and hinders the mucociliary apparatus.[6,7,9] Viral infections have been shown to decrease tracheal clearance rates aiding in viral and bacterial colonization.[16] Long distance shipping and strenuous exercise have similar mechanisms of aspiration of bacteria with the negative effect of prolonged head elevation.[7,9]

Focusing on shipping stress and strenuous exercise as mechanisms, lack of clearance is the main concern in the body's response to infection. Pulmonary alveolar macrophage impaired function is not consistently supported in current research but is the main focus of non-cleareance.[6,7] An increase in cortisol concentration results in decreased amount, life span and phagocytosis abilities of pulmonary alveolar macrophages (PAM).[6,7] This has been shown evident from oxidative burst activity of pulmonary alveolar macrophages as well as peripheral blood neutrophils.[5-7] Prolonged elevation of the horse's head for 6-12 hours (in transportation or post exercise), has also been linked to increased burden on the mucociliary apparatus and decreases alveolar cellular clearance mechanisms.[6,7,9]

Regardless of mechanism of aspiration or reason of non-clearance the infection spreads from peripheral lung parenchyma to the visceral and parietal pleura.[9] Pleuropneumonia can be broken down into three stages: Exudative stage, Fibrinopurulent stage and Organization stage.[2] The inflammatory response begins in the lung parenchyma and pleura. Neutrophils damage vasculature by margination causing increased permeability.[2] Vasculature's oncotic pressure will

decrease, and hydrostatic pressure will increase; producing sterile pleural effusion.[2] Fibrinopurulent stage begins as bacteria begin to invade the pleural effusion.[2] Neutrophils and macrophages follow bacteria into the effusion, causing more cellular debis.[2] At this point it is no longer a sterile effusion it is now a septic effusion. Loculation of the fluid begins as fibroblasts begin to deposit fibrin. Organization stage commences as fibrin deposition continues. The fibrin is deposited on the visceral and parietal pleura resulting in extreme loculations and pleural peel which is inelastic eventually rendering the lung lobe ineffective.[2,9,10,12] As the lung lobe continues to be void of oxygen it begins to necrose, which exacerbates severe respiratory distress, ventilation: perfusion mismatch and can lead to endotoxemia and possible death.[1,9,14]

Differential Diagnoses

Although, ~70% of horses (in the USA) with pleural effusion have pleuropneumonia non-specific clinical signs can be attributed to other diagnoses.[11] Non-specific respiratory signs, pleurodynia signs, lethargy, reluctance to move and inappetance can be mistaken for colic, acute laminitis and possible exertional rhabdomyolysis.[3,5] Pleural effusion is most likely caused by bacterial colonization but can be attributed to: trauma, esophageal perforation, neoplasia, pericarditis, congestive heart failure, diaphragmatic hernia, hypoproteinemia, and chylothorax.[9] Further diagnostics including a rectal exam should be performed.

Diagnostic Approach/Considerations

As in many diseases a thorough physical exam plays a large role in diagnosing pleuropneumonia. Presumptive diagnosis of pleuropneumonia can be diagnosed by respiratory auscultation. However the uses of other diagnostic procedures will give a definitive diagnosis as well as a better understanding for treatment. A rebreathing test should be performed first to evaluate lung sounds.[3] In mild cases a rebreathing test will reveal harsh lung sounds in dorsal lung fields.[9] A CBC will reveal a leukopenia in acute and a leukocytosis in chronic infections

attributed to an absolute neutrophilia with evidence of anemia.[2,5,9,11] Leukopenia can also be seen in severe cases where consumption out weighs production.[9] The length of infection will dictate serum chemistry abnormalities. In the acute stage there will be hyperfibrinogenemia, while hypoalbuminemia and hyperglobulinemia develop with chronicity. [2,3,5,9,11] Hyponatremia and hypochloremia are attributed to sequestration into the pleural effusion.[3] Other chemistry abnormalities include azotemia, metabolic or respiratory acidosis.[2,3,5,9,11]

Radiographs should be taken after pleural effusion drainage. Radiographs can either show a bronchial lung pattern with acute pleuropneumonia but can progress to an alveolar lung pattern with chronic cases.[12] Alveolar pattern will show air bronchograms with border effacement. Cranial thorax abscessation can also be identified via thoracic radiographs.

Ultrasonography is one of the most valuable diagnostic tools in pleuropneumonia. Lung consolidation, volume of pleural effusion, amount fibrin accumulation, pulmonary abscesses and state of the diaphragm can all be evaluated using ultrasound. Proper technique of scanning using a 3.5-5 MHz transducer, dorsoventrally, investigating all intercostal spaces is imperative.[12] Effusion will vary from anechoic to hypoechoic with consolidated lungs and fibrin appearing soft tissue hyperechoic. The intensity of echogenicity in the lung lobes reveals if the lobe is properly aerated.[12] Bright white echoic areas can either be aerate lung lobes or may be indicative of an anaerobic infection that is producing gas. Ultrasound is also used as a guide for thoracocentesis and chest tube placement.

Transtracheal wash (TTW) with cytology, aerobic and anaerobic cultures are used to identify microorganisms contributing to the pleuropneumonia. TTW should be obtained before any anti-microbial intervention is started or at least 24 hours since last dose.[14] Septic inflammation will have degenerative neutrophils with intra-/extra-cellular bacteria.[14] If culture

results contrast clinical signs, contamination should be considered as source of growth. Finally thoracocentesis with cytology, aerobic and anaerobic culture is extremely valuable. It will differentiate between sterile vs septic effusion.[5] A 7.5cm teat cannula with an extension set and three-way stopcock should be placed with ultrasound guidance or blindly in the 7th or 8th intercostal space.[3] Normal pleural fluid is a light color and odorless and when analyzed protein is less than 2.5 g/dL and nucleated cells are less than 8000 g/dl.[9] With septic effusion, neutrophil count will be elevated with increase opacity and a foul smell. The lactate will be increased, while pH is decreased, and intra-/extra-cellular bacteria will be visible upon cytology.[9,14]

Treatment and Management Options

Treatment and management must stop the ongoing infection, remove effusion, aid in fibrin resolution and support the patient symptomatically. Draining effusion improves ventilation, reduces bacteria/toxins and inflammatory mediators.[3,5] It can be done intermittently if there is smaller amounts of fluid using a teat cannula (as previously described). However, it is common for patients to produce 10 liters of exudate justifying the need for indwelling tubes.[14] One study reported 64% of horses studied needed indwelling drains for an average of 4 days.[14] A 24 or 32 French thoracic cannula with trochar is used with a Heimlich one way valve to seal the tube, and prevent pneumothorax.[4] Tube placement, drainage and valve should be evaluated multiple times a day, as it may crack, detach or obstruct making it inoperable.[4,14] Complications include pneumothorax, local cellulitis and abscessation around the tube.

Empiric antibiotic therapy is imperative to control pleuropneumonia infections. Antibiotic protocol can be modified once cultures are returned. While *Streptococcus equi sbsp. zooepidemicus* is likely involved, polymicrobial infections including anaerobes may be present, thus a four-quadrant spectrum antibiotic with good lung distribution is justified. [1-7, 9-12,15]

Penicillins are used to cover gram-positive aerobic bacterial infections, but must be combined with other antibiotics. The addition of gentamicin or enrofloxacin will cover gram negative bacteria.[9] Enrofloxacin has better efficacy in purulent debris, penetrates macrophages and neutrophils and better efficacy against *Enterobacteriaceae*.[9] However metronidazole is the antibiotic of choice for anaerobic coverage with increase efficacy against *Bacteroides fragilis.*[13] Chloramphenicol is extremely effective against both aerobes and anaerobes, its use is reserved for severe cases due to its use in human medicine. [1-7, 9-12,15] It should be noted that fibrin loculations decrease penetration of antimicrobials.[15]

Non-steroidal anti-inflammatories are often used to combat pleurodynia. Flunixin meglumine or phenylbutazone can be used.[2,3,5,9] Severe pleurodynia may warrant the use of opioid pain relief but with the risk of gastrointestinal stasis. Depending on the status of the patient, intravenous fluid administration and oxygen supplementation may be necessary. Pleuropneumonia horses have high metabolic rates, and since they tend to go off feed, a wide variety of feed options and fresh water should be made available.[10] These horses are inclined to develop gastric ulcers because they are off feed, requiring the need for gastrointestinal protectants such as ranitidine, omeprazole, and sucralfate.[3,9] With the large amount of antibiotics killing off gastrointestinal flora, probiotics can be helpful to reduce the risk of colitis. Probiotics need to be administered at staggered times to the antibiotics, because the antibiotics will inactivate the probiotics. Thoracic ultrasonography every 24-48 hours is used to evaluate level of effusion, lung aeration and abscessation.[9]

The efficacy of intrapleural fibrinolytics to dissolve fibrin is currently debated. Recombinant tissue plasminogen activators (rTPA) (most commonly used) have been used in human medicine is shown to decrease amount of fibrin loculations but has not been thoroughly

proven in horses.[8] One retrospective studied showed 85% of patients improved with decreased amounts of fibrin via ultrasonography.[15] Two studies from Tomlinson et al. found survival rates with TPA to be 72% while survival rates without TPA were 68%. This is a small difference and at this time there is not enough evidence to support these outcomes.[14,15]

If medical management fails to resolve pleuropneumonia, a thoracotomy will be indicated. The exact time to decide to go to surgery has not been studied, but it is currently up to the preference of the clinician.[4,9,13] Thoracotomies can be performed under standing sedation or general anesthesia.[4,9] Thoracotomies are used for effusion drainage, removal of abscesses and possible lung lobectomies. Rib resection is often recommended to aid in drainage.[4] Possible complications include uni- or bi-lateral pneumothorax, incisional cellulitis and abscessation.[4,12] Incisional complications were more common in patients with anaerobic infections.[13] One study suggests 88% surgery survival rate with 46% return to racing potential.[4]

Expected Outcome and Prognosis

A diagnosis of pleuropneumonia carries a good to poor prognosis depending on severity of the infection and start of treatment. Survival rates vary in different studies but range from 43-77%.[3,14] Overall survival rates have improved over recent years, if the infection is addressed early. Survival rates of anaerobic infections have improved from 21% to 50%.[13,14] Developing abscesses, and anaerobic infections continue to be poor prognostic indicators. Many horses are euthanized to due poor prognosis, financial constraints or low probability of returning to function.

Conclusion

Pleuropneumonia is a severe lower respiratory infection caused by aspiration of upper airway bacteria. Progression is linked to decrease functionality of pulmonary defense

mechanisms.[6,7] Pleural effusion and fibrin loculations cause lung consolidation, abscesses and respiratory distress. Clinical signs vary from non-specific respiratory signs to absent ventral lung sounds with radiating cardiac sounds. Intensive antimicrobial medical management and potentially surgical intervention is required. Even with extensive care many patients are euthanized.

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