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Bacterial pneumonia in horses associated with *Escherichia coli* infection: report of five cases

[*Pneumonia bacteriana em equinos associada à infecção por* Escherichia coli*: relato de cinco casos*]

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ABSTRACT

Respiratory diseases have a major impact on sport horses and are often cited as the second most common reason for loss of training days and significant veterinary costs. Adult horses most commonly develop pneumonia when bacteria aspirated from the environment, nose, or oropharynx reach the lower airways and overwhelm the pulmonary defense mechanisms. This article report five cases of bacterial pneumonia in horses associated with infection by *Eschericia coli*. Five Quarter horses, three males and two females, with ages varying from 5 to 12 years, were examined for diagnosis of respiratory disease characterized by apathy, cough and lack of appetite. Auscultation of the thorax revealed increased harsh breath sounds dorsally, crackles, wheezes, and dullness of respiratory sounds ventrally. Manipulation of the trachea and larynx induced cough. Culture results were positive for *Escherichia coli.* The therapeutic protocol consisted of anti-inflammatory, antibiotic therapy, and supportive care. Flunixin meglumine was administered intravenously at 24-hour intervals over eight days. Ceftiofur sodium was prescribed intramuscularly, q.d., for 15 days. Horses were clinically monitored daily until complete remission of clinical signs. None of the animals relapsed, and all returned to routine athletic activities.

Keywords: antimicrobial therapy, ceftiofur, lung, respiratory disease

RESUMO

As doenças respiratórias têm um grande impacto nos cavalos de esporte e são frequentemente citadas como o segundo motivo mais comum para a perda de dias de treinamento e custos veterinários significativos. Os cavalos adultos desenvolvem mais comumente pneumonia quando bactérias aspiradas do ambiente, do nariz ou da orofaringe alcançarem as vias aéreas inferiores e sobrecarregam os mecanismos de defesa pulmonar. Este artigo tem como objetivo relatar cinco casos de pneumonia bacteriana em cavalos, associados à infecção por Eschericia coli. *Cinco cavalos da raça Quarto de Milha, três machos e duas fêmeas, com idades variando de cinco a 12 anos, foram examinados para diagnóstico de doença respiratória caracterizada por apatia, tosse e falta de apetite. A auscultação do tórax revelou aumento dos sons respiratórios ásperos dorsalmente, crepitação, sibilos e abafamento dos sons respiratórios ventralmente. Manipulação da traqueia induziu tosse. Os resultados da cultura foram positivos para* Escherichia coli. *O protocolo terapêutico consistiu em anti-inflamatório, antibioticoterapia e cuidados de suporte. Flunixina meglumina, na dose de 1mg/kg, foi administrada, por via intravenosa, em intervalos de 24 horas ao longo de oito dias, enquanto ceftiofur sódico, na dose de 2,2mg/kg, por via intramuscular, q.d., foi administrado durante 15 dias. Os cavalos foram monitorados clinicamente, todos os dias, até a remissão completa dos sinais clínicos. Nenhum dos animais apresentou recidiva, e todos retornaram às atividades atléticas de rotina.*

Palavras-chaves: pulmão, doença respiratória, ceftiofur, terapia antimicrobiana

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INTRODUCTION

Respiratory diseases have a major impact on sports horses in training and are often cited as the second most common reason of horses failing to perform (Melo *et al*., 2007). Lower respiratory infections are a common problem in adult horses, and can range from mild viral infections to severe, complicated bacterial infections (Melo *et al*., 2021).

Inhaled or aspirated bacteria from the upper respiratory tract are the primary cause of bacterial pneumonia in adult horses, unlike the situation in neonates in which bacterial pneumonia is often of hematogenous origin. As a result, most adult respiratory infections develop initially on the surface of the respiratory mucosa and then progress to involve the pulmonary parenchyma (McKenzie III, 2015).

Horses appear to be at a somewhat heightened risk for developing lower respiratory disease for several reasons. First, horses are typically managed in communal groups, allowing for the easy passage of viral and bacterial pathogens between individuals. Second, horses are often transported for long distances, which results in impaired lower respiratory immune function and development of inflammation in the lower respiratory tract. The frequent introduction of new horses to the farm or stable environment also increases the likelihood of introducing pathogens into the local population of animals (McKenzie III, 2015).

Although pathogenetic mechanisms associated with lower airway disease are complex and commonly multifactorial, risk factors that contribute to colonization of the lower airways with commensals from the upper respiratory tract and oral cavity include stress, long-distance transport, esophageal obstruction, and prolonged head elevation (Raidal *et al*., 1995; Davis, 2018).

It is ideal to identify horses that suffer from respiratory disease early in the course of events so that the clinician can provide specific and effective care that will enable a favorable prognosis to be given. This is facilitated by the fact that, from a diagnostic standpoint, many aspects of the equine respiratory tract are highly accessible and easily evaluated, and, when pathology is present, these conditions are often responsive to a variety of therapeutic modalities (McKenzie III, 2015).

Normally the lungs contain only small numbers of bacteria that are transient contaminants in the process of being removed by clearance mechanisms. When pulmonary defense mechanisms are overwhelmed, aspirated bacteria from the oropharynx may proliferate and cause pneumonia (Blunden and Mackintosh, 1991).

Bacterial lower respiratory infections have greater clinical impact because of the substantial risk for complications ranging from focal abscess formation to development of pleuropneumonia. The development of complicated pneumonia cannot always be prevented, but once present, it requires early and aggressive intervention to achieve acceptable outcomes.

Bacterial isolates commonly isolated from horses with pleuropneumonia include *Streptococcus equi* subsp *zooepidemicus*, *Streptococcus sp*., *Pasteurella sp*., *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter sp*., and *Actinobacillus sp*. Anaerobic isolates include *Bacteroides sp*., *Clostridium sp*., *Fusobacterium sp*., and *Peptostreptococcus* sp. (Sweeney *et al*., 1991; Reuss and Giguere, 2015).

This article reports five cases of bacterial pneumonia in horses associated with infection by *Eschericia coli*.

CASUISTRY

Five Quarter horses breed, housed in an equestrian training center in the Mossoró city, Rio Grande do Norte state, three males and two females, with ages varying from 5 to 12 years, were examined for diagnosis of respiratory disease characterized by apathy, cough and lack of appetite. Three animals had recently traveled to two sporting events and three days after landing began to manifest the clinical picture. The other two animals began to show clinical signs eight days later.

Upon inspection, apathy, tachypnea, and increased respiratory effort were observed. The data regarding the initial clinical examination are summarized in table 1. Auscultation of the thorax of five horses revealed increased harsh breath sounds dorsally, crackles, wheezes, and dullness of respiratory sounds ventrally. Manipulation of the trachea and larynx induced cough. The presence of nasal discharge was variable between the cases.

Table 1. Clinical examination findings of five horses with bacterial pneumonia associated with *Eschericia coli* infection

Parameter	*Case 1*	*Case 2*	*Case 3*	*Case 4*	*Case 5*
Heart rate	49	58	48	56	48
Breathing rate	25	30	24	31	26
Capillary perfusion time (seconds)	2	2	2	3	2
Rectal temperature (°C)	40,5	40	39,5	40,5	39,5
Mucous color	hyperemic	hyperemic	hyperemic	hyperemic	hyperemic
Abdominal respiratory effort	Present	Present	Present	Present	Present
Nasal discharge	Present	Absent	Present	Present	Present

Two animals were reluctant to walk on clinical examination. On percussion of the chest, painful response (pleurodynia) has been elicited. Thoracic ultrasound demonstrated consolidation of ventral lung lobes in one horse, and extension of the pneumonia to the pleural surfaces as evident by the presence of comet tails in four horses.

Blood samples were collected for blood count and determination of plasma fibrinogen. The results of the blood count and the determination of plasma fibrinogen are summarized in table 2. Tracheal aspirates were obtained to perform bacterial cultures. Bacterial culture was carried out onto blood agar plates and MacConkey agar followed by aerobic incubation at 37°C for 72 h. Any bacterial isolates were identified by Gram staining, microscopic and morphological appearance, cultural and biochemical characteristics according to the methodology described by Bianchi *et al*. (2020). Culture results were positive for *Escherichia coli.*

Regarding the pattern of antimicrobial sensitivity, the isolate showed resistance to amoxicillin, clavulanic acid, ampicillin, cephalexin, procaine penicillin, trimethoprim-sulfonamide, oxacillin, sulfamethoxazole and chloramphenicol. Regarding the sensitivity pattern, the isolated pathogen showed sensitivity to ceftiofur, cefovecin, ciprofloxacin, doxycycline, enrofloxacin, gentamicin, neomycin and polymyxin.

Table 2. Hematological findings in horses with bacterial pneumonia associated with *Escherichia Coli* infection

Variables	*Case 1*	*Case 2*	*Case 3*	*Case 4*	*Case 5*
Erythro ($x10^6$ μL^{-1})	7	6.27	6.5	6.5	7
Hemog (g dL^{-1})	11.1	8,7	8,9	12	11
PCV (%)	35	27	30	31	35
MCV (fL)	45	43	45	44	45
MCHC (g dL^{-1})	33	32	32	31	33
Leuco (cells/μL^{-1})	14.100	15.400	16.450	15.100	14.100
Seg (cells/μL^{-1})	9.870	12.088	13.770	10.830	9.870
Band (cells/μL^{-1})	0	0	0	0	0
Lympho (cells/μL^{-1})	3.243	1.932	2.580	3.243	3.243
Mono (cells/μL^{-1})	846	966	800	886	846
Eosi (cells/μL^{-1})	141	414	200	141	141
Baso (cells/μL^{-1})	0	0	0	0	0
Fib (mg dL^{-1})	850	940	920	800	850

Abbreviations: erythrocytes (Erythro), hemoglobin concentration (Hemog), hematocrit (PCV), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), total number of leukocytes (Leuco), segmented neutrophils (Seg), band cells (Band), lymphocytes (Lympho), monocytes (Mono), eosinophils (Eosi), basophils (Baso) and plasma fibrinogen (Fib).

A sixth animal was excluded from this report, as there was no possibility of carrying out laboratory tests because of referral to a reference surgical center for resolution of severe pleuropneumonia.

The therapeutic protocol consisted of anti-inflammatory and antibiotic therapy. Flunixin meglumine at a dose of 1mg/kg was administered intravenously at 24-hours intervals over eight days. Dipyrone at a dose of 15mg/kg was administered intravenously at 12-hour intervals over three days. Benzylpenicillin procaine (20.000IU/kg) was administered intramuscularly every 24 hours. However, after the result of the culture and microbial sensitivity test, ceftiofur sodium was prescribed at a dose of 2.2mg/kg, intramuscularly, q.d., for 15 days.

Horses were clinically monitored daily until complete remission of clinical signs. Four months after clinical resolution, the owners were contacted via telephone to provide information on the current clinical status of the horses. None of the animals relapsed and all returned to routine athletic activities.

DISCUSSION

Bacterial infections of the lower respiratory tract occur in horses of all ages but are of particular importance in sport horses. In mature race and sport horse, bacterial lower respiratory tract infection is not common and causes sporadic, potentially fatal, pneumonia and pleuropneumonia (Melo *et al*., 2021).

Infectious diseases of the lower or upper respiratory tract that develop with apathy, cough and nasal discharge are commonly referred by the generic term "catarrh" in several regions in the north and northeast of Brazil. This common name is shared by owners and equine practitioners, without establishing a definitive diagnosis or identifying the etiologic agent. Many equine practitioners, attribute these respiratory infections to *Streptococcus equi* infection, however, the collection of respiratory secretions for bacterial cultures to confirm the etiological agent is not yet routine.
The strangles is an infectious disease that affects horses from all ages and causes important economic losses in the equine-related business (Maciel *et al*., 2017).

In clinical cases of strangles, horses show the typical clinical signs of a generalized infectious process (depression, lack of appetite, fever), as well as nasal secretion, initially serous, which changes to mucopurulent and purulent in some days, productive cough, pain on palpation the mandibular region and an increase in the volume of lymph nodes, mainly submandibular, in addition to the extended neck position due to pain in the larynx and pharynx region (Moraes *et al*., 2009). The presumptive diagnosis is performed according to the clinical signs, with the gold standard being the bacterial culture with the identification of *S. equi* (Pansani *et al*., 2016; Ribas *et al*., 2018).

Although the strangles was included in the list of possible differential diagnoses during the clinical examination of the horses in this report, this hypothesis was excluded based on the clinical findings found. Although horses show the typical clinical signs of depression, lack of appetite, fever, as well as nasal secretion mucopurulent, pain on palpation the mandibular region and an increase in the volume of lymph nodes were not evident, nor was the extended neck position due to pain in the larynx and pharynx region.

The manifestation of clinical signs varied among the five horses, mainly in relation to the occurrence of nasal discharge and pleurodynia.

Slater (2007) stated that the severity of the clinical signs is proportional to the amount of lung affected, the degree of pulmonary necrosis, and the volume of pleural effusion. Affected horses show pyrexia, depression, some coughing, and variable mucopurulent nasal discharge that may be blood-tinged. Nasal discharge varies because of poor mucociliary clearance. Thus the scant nasal discharges often belie the large volumes of exudate that accumulate in the airway.

Another disease that was included in the list of differential diagnoses was glanders. It is a re-emerging disease in the country with outbreaks in several states in the Northeast and Southeast (Chaves *et al*., 2016). According to Ramos *et al.* (2021), between 2010 and 2019, 69 cases of glanders were diagnosed in the state of Rio Grande do Norte, making this disease one of the differential diagnoses of diseases of the respiratory system. Although all animals had

negative serology for glanders, blood samples were collected for new serology and all animals were negative.

The most common organisms associated with pneumonia in horses are opportunistic bacteria originating from the resident microflora of the upper respiratory tract. These bacteria are not capable of primary invasion and require diminished pulmonary defense mechanisms to establish infection. Notably, *S. equi* subsp. *zooepidemicus* remains the leading bacterial pathogen of the lower airways of adult horses suffering from pneumonia (Davis, 2018).

Septic pneumonia may occur secondary to others bacterial infection (Taylor, 2015). The most frequently isolated aerobic bacteria in cases of equine pneumonia/pleuropneumonia associated with SRIS are *β-streptococcus sp*., *Pasteurella sp*., *E. coli* and *Enterobacter sp*. (Sweeney *et al*., 1991; Taylor, 2015).

In the present report, *Escherichia coli* was the isolated etiologic agent. Although previous studies have shown that isolation of anaerobic bacteria and *E. coli* negatively impact survival in horses with bacterial pneumonia (Sweeney *et al*., 1991, Racklyeft and Love, 2000), all animals in the present report recover and perform again.

Escherichia coli is a largely commensal bacteria in the gastrointestinal tracts of mammals, but it has been reported to be a causal agent in some nosocomial infections (Sato *et al*., 2020), and as a cause of abortion in mares (Silva *et al*., 2020).

Escherichia coli may colonize and invade the respiratory tract through environmental exposure, aspiration, or spread from a non-respiratory site. Hematogenous dissemination can occur from a distant focus in the genitourinary or the gastrointestinal (GI) tract. However, in several cases, no hematogenous source could be identified. Increased oropharyngeal colonization with gram-negative bacilli occurs in patients with influenza and other infections of the upper part of the respiratory tract (Jonas and Cunha, 1982).

The *E. coli* strain isolated in the present report demonstrated resistance to Amoxicillin, Clavulanic acid, Ampicillin, Cephalexin, Procaine penicillin, Trimethoprim-sulfonamide, and Oxacillin. Many strains of *E. coli* have intrinsic or/and acquired antimicrobial resistance which should be addressed as a significant threat to public health. Resistant *E. coli* could be selected among gut microbiota due to indiscriminate use of antimicrobial agents (Sato *et al*., 2020).

Clinicopathologic findings are important in evaluating the horse with lower respiratory tract disease because leukocytosis, neutrophilia, and neutrophilic left shift with or without hyperfibrinogenemia often accompanies progression of lower respiratory bacterial infections (McKenzie III, 2015). All these findings reported in the literature were identified in this report. As a result of the satisfactory clinical evolution that the horses showed after the treatment was instituted, a second complete blood count was performed only at the end of antibiotic therapy. In this second blood count, the parameters evaluated had already returned to normal.

At the time of diagnosis of pneumonia, relevant history includes information that may support the primary etiology, such as recent viral respiratory infection, long-distance transport, strenuous exercise, immunosuppressive therapy, exercise-induced pulmonary hemorrhage, severe esophageal obstruction, or marked age (Davis, 2018). In adult horses, in contrast to foals, primary virus infections are an uncommon predisposition to pneumonia, and all horses in the report were immunized against viral pathogens commonly associated with respiratory conditions. Of the factors previously mentioned, only long-distance transport and strenuous exercise were identified in the history reported by the owner.

Horses in this report were elite athlete animals submitted to daily training and participation in weekly vaquejada competitions. Three horses had a history of traveling to competition in the 10-15 days prior to the manifestation of the clinical picture. The other two horses, had no travel history, however remained lodged in the same environment.

An exercise-associated increase in bacterial contaminants of the lower respiratory tract has been demonstrated experimentally. Strenuously exercised horses exhibit a tenfold and a 100-fold

increase, respectively, in the number of aerobic and anaerobic bacteria isolated from transtracheal aspirates relative to pre-exercise samples. The bacterial contamination, along with exercise-associated increases in bronchoalveolar cortisol concentrations, decreased pulmonary alveolar macrophage viability, and impaired phagocytic function, enables bacteria to proliferate and cause pneumonia (McKenzie III, 2015, Davis, 2018).

Transportation remains one of the most common causes of pneumonia and pleuropneumonia in the horse because physically restraining the head of the horse and preventing postural drainage enhances bacterial colonization of the lower respiratory tract.

Pneumonia and pleuropneumonia are usually sporadic diseases in individual horses with only a small risk of contagious transmission. However, the simultaneous occurrence of five cases in the same training center gives a contagious characteristic in this report.

Sepsis can defined as life-threatening organ dysfunction caused by a dysregulated host response to infection resulting in a systemic inflammatory response (Melo *et al*., 2010; Sheats, 2019). Although no consensus definition of sepsis in veterinary species is currently available, examples of published criteria used to diagnose SIRS include two or more of the following in adult horses: 1) Body temperature > 38.6◦C; 2) Heart rate > 60 beats/min; 3) Hyperventilation (respiratory rate > 30 breaths/min), and 4) White blood cell count > 12,500 cells/µl or < 4,500 cells/µl and 10% band neutrophils (Epstein *et al*., 2011; Sheats, 2019). Based on these diagnostic criteria, all animals in the present report have a clinical picture of SIRS.

Endoscopic evaluation is a useful tool in the medical clinic of horses in the diagnosis of diseases of the respiratory system and collection of samples (Barbosa *et al*., 2016). However, the absence of an endoscopic evaluation did not preclude the diagnosis from being made as the findings of the clinical examination, ultrasound, clinical pathology, and culture of the tracheal lavage made it possible to establish the diagnosis and establish an appropriate therapeutic protocol. Imaging studies may aid in the staging and localization of lower respiratory infections, with ultrasonography being particularly useful in assessing the superficial pulmonary tissues and the pleural cavity.

Medical therapy for bacterial pneumonia requires broad-spectrum antimicrobial therapy, anti-inflammatory drugs, supportive care, and in some cases surgical intervention for the removal of necrotic pulmonary foci (Davis, 2018). Antibiotic selection is simplified if bacteria are accurately identified because the susceptibility patterns for many organisms are predictable. A sensible initial regimen is penicillin together with gentamicin and metronidazole. This may need to be modified when the results of bacterial culture and sensitivity are known (Slater, 2007), and in the present report after results of the culture and sensitivity test, the use of ceftiofur was instituted.

Ceftiofur sodium has an appropriate antimicrobial spectrum for common opportunistic pathogens, and is often successful as the only therapy for uncomplicated pneumonia, proving to be an efficient antimicrobial in the present report.

In addition to antimicrobial therapy frequent patient monitoring is essential to determine patient status. In the present report, horses were reassessed initially every 12 hours and after satisfactory clinical evolution every 24 hours until the end of treatment.

Variety of acute and more chronic complications may develop. Acute complications include pneumothorax because of communication between necrotic lung and the pleural space. More chronic complications include pulmonary abscess, mediastinal abscess, pleural adhesions, pulmonary atelectasis, and fibrosis (Slater, 2007). All horses returned to athletic activities after 30 days, and no complications were observed.

CONCLUSIONS

Bacterial pneumonia is a potentially life-threatening condition. However, the early recognition and establishment of an adequate therapeutic protocol allows the horse to recover completely and return to its activities.

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