Septic pleuritis and abdominal abscess formation caused by *Rhodococcus equi* in a foal

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EQUINE

- *Rhodococcus equi* is a gram-positive coccoid to rod-shaped intracellular bacterium that can induce disease involving multiple body systems in foals.
- In foals, infection with *R equi* commonly causes pyogranulomatous pneumonia.
- Administration of azithromycin and rifampin is an effective antimicrobial combination for treatment of *R equi* infection.

A 3-month-old 105-kg (231-lb) female Arabian horse was evaluated at the Louisiana State University Veterinary Teaching Hospital because of a history of fever, respiratory distress, lethargy, and decreased appetite of 5 days' duration. The foal had been examined previously by the referring veterinarian and had received treatment with antimicrobials for pneumonia. Collection of a transtracheal aspirate specimen was attempted by the referring veterinarian without success; as a result, subcutaneous emphysema had developed along the left jugular furrow and cranial aspect of the right thoracic wall.

On initial evaluation at the hospital (day 0), the foal was quiet, alert, and responsive. Its coat condition was poor. Breathing was labored with an abdominal component, and decreased breath sounds were ausculted in both ventral hemithoraces. Rectal temperature (39.2°C [102.5°F]), heart rate (84 beats/min), and respiratory rate (52 breaths/min) were high. The mucous membranes were slightly injected, and the capillary refill time was < 2 seconds. No coughing or nasal discharge was evident. Mild effusions of the carpal and tarsal joints were also palpated bilaterally, but there was no evidence of lameness.

A CBC revealed normocytic, normochromic anemia (Hct, 26.7%; reference range, 32% to 52%); moderate leukocytosis (20,700 WBCs/µL; reference range, 5,000 to 11,000 WBCs/µL); neutrophilia (17,800 neutrophils/µL; reference range, 2,700 to 6,700 neutrophils/µL) with a left shift (200 bands/µL; reference range, 0 to 100 bands/µL); monocytosis (1,100 monocytes/µL; reference range, 0 to 800 monocytes/µL); severe hyperfibrinogenemia (1,200 mg/dL; reference range, 100 to 500 mg/dL); and mild thrombocytosis (298,000 platelets/µL; reference range, 90,000 to 240,000 platelets/µL). Results of serum biochemical analyses included mildly high creatine kinase activity (855 U/L; reference range, 0 to 350 U/L) and hypoalbuminemia (2.3 g/dL; reference range, 3.0 to 4.1 g/dL). Quantitative analyses of serum IgG, IgA, and IgM concentrations were within reference limits.

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Collection of a transtracheal aspirate specimen was attempted but was unsuccessful because of the severe subcutaneous emphysema and tissue edema. Transendoscopic aspiration was not attempted because of the size and level of respiratory distress of the foal. A thoracic ultrasonographic examination revealed a large amount of pleural effusion associated with the left hemithorax; the effusion was detected from the fifth to the ninth intercostal spaces and extended dorsally to a level aligned with the midpoint of the scapula. The fluid on the right side of the thorax was not easy to visualize ultrasonographically because of the subcutaneous emphysema but was apparent in some intercostal spaces. Atelectatic and consolidated lung tissue was present bilaterally, and the ventral margins of the lungs could be identified surrounded by pleural fluid (**Figure 1**).

Thoracic radiography revealed increased soft tissue opacity bilaterally causing decreased visualization of the cranio- and caudoventral areas of the lungs; this finding was consistent with pleural effusion. Thoracocentesis was performed on each side of the thorax by use of 14-gauge 3-inch IV catheters.[a] A 5-mL sample of fluid was collected from each side. Pleural fluid analysis revealed total protein concentration of 4.4 g/dL, nucleated cell count of 121,600 cells/µL (70% neutrophils with moderate degree of nuclear degeneration and 30% macrophages), phagocytosed bacteria (rods), and a large number of RBCs (260,000 RBCs/µL), all of which were consistent with severe septic inflammation. An unmeasured volume of free-flowing fluid was removed from each side of the thorax prior to removal of the catheters.

Ultrasonographic examination of the abdominal cavity revealed a large mass (13 to 14 cm in diameter) with a discrete wall located adjacent to the ventral aspect of the left body wall at the level of the 10th intercostal space, extending to the right side of the midline and just caudal to the umbilical scar. The content of the cranial aspect of the mass was heterogeneous with multiple hyperechoic areas; the appearance of the content in the caudal part of the mass was more homogenous with an obvious interface between anechoic and echogenic fluid suggestive of abdominal abscess formation (**Figure 2**). No excessive free abdominal fluid or other abnormalities were detected ultrasonographically. Aspiration of the abdominal mass by use of an 18-gauge 3-inch IV catheter[a] recovered a purulent exudate that contained many poorly preserved nucleated cells (most likely necrotic neutrophils) and large numbers of rod-shaped bacteria that confirmed abdominal abscess formation. Septic pleuritis and abdominal abscess formation caused by *Streptococcus zooepidemicus*, *Rhodococcus equi*, or a gram-negative rod bacterium were the primary differential diagnoses.

While results of bacterial cultures of pleural fluid and the aspirate specimen of the abdominal mass were

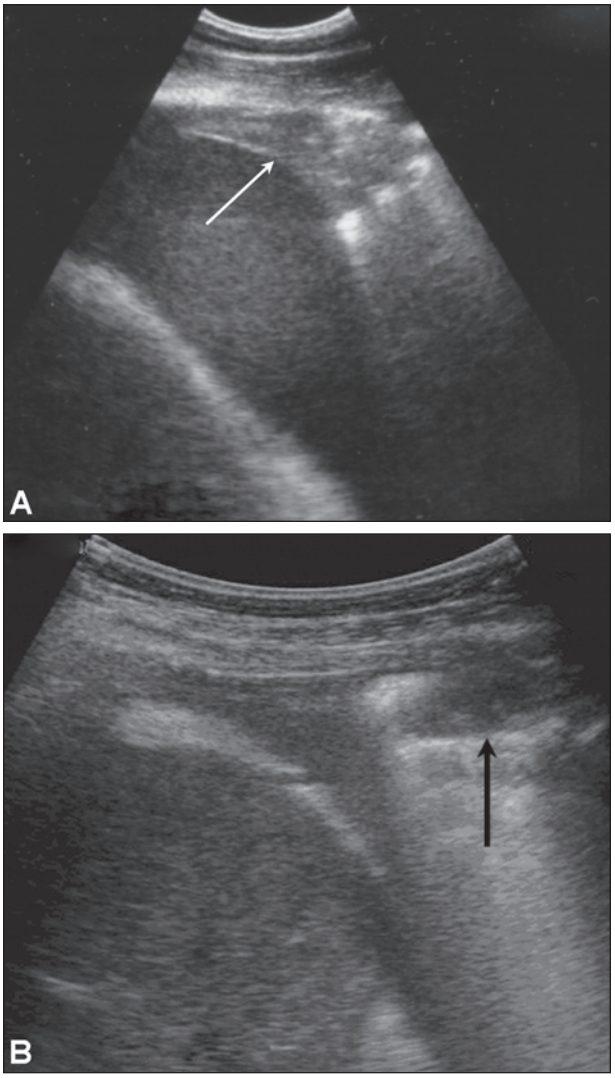

Figure 1—Ultrasonographic images of the thorax of a 3-month-old foal infected with *Rhodococcus equi*. A—Presence of pleural effusion with an area of atelectasis (arrow) in the right lung. B—Area of consolidation within the right lung (arrow). Dorsal is to the right side of each sonogram. These images were obtained from the right hemithorax at the level of the seventh and ninth intercostal spaces by use of a 3.5-MHz convex array transducer at a displayed depth of 8 cm.

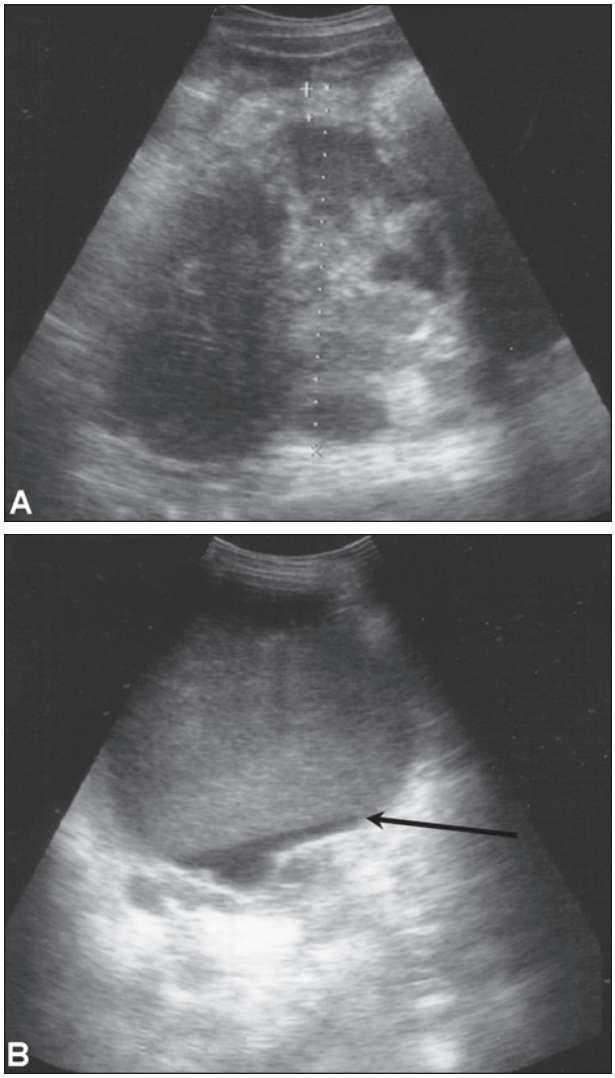

Figure 2—Ultrasonographic images of the abdomen of the foal in Figure 1. A—The cranial part of a large abdominal abscess is visible as a heterogeneous structure (13.6 cm in diameter). B—The caudal part of the abscess was a homogenous fluid-filled structure located against the ventral abdominal wall with an obvious interface between echogenic and anechoic fluid (arrow). These images were obtained from the left ventral abdominal wall by use of a 3.5-MHz convex array transducer at a displayed depth of 20 cm.

pending, the foal received broad-spectrum antimicrobials including penicillin G potassium (22,000 U/kg [10,000 U/lb], IV, q 6 h), gentamicin (6.6 mg/kg [3.3 mg/lb], IV, q 24 h), and metronidazole (15 mg/kg [6.8 mg/lb], PO, q 8 h). The foal's high rectal temperature, heart rate, and respiratory rate and noticeable respiratory effort persisted for 48 hours. The foal was intermittently anorexic but remained well hydrated (PCV, 30% [reference range, 32% to 52%]; plasma total protein concentration, 6.9 g/dL [reference range, 5.2 to 7.8 g/dL]). Arterial blood gas analyses revealed hypoxia (P_{O_2}, 49 mm Hg [reference limit, > 80 mm Hg]; P_{CO_2}, 38 mm Hg [reference range, 40 to 50 mm Hg]; and oxygen saturation, 85.9% [reference limit, > 95%]). Nasal oxygen insufflation at a rate of 5 L/min was initiated. Daily ultrasonographic examinations of the thorax during the next 3 days revealed no change in the amount of pleural effusion. Bacterial cultures of the pleural fluid and the aspirate specimen of the abdominal mass yielded growth of *R equi*. The foal was afebrile, but heart and respiratory rates remained high, mucous membranes were slightly cyanotic, and capillary refill time was prolonged despite oxygen therapy. Administrations of penicillin G potassium and gentamicin were discontinued, and azithromycin (10 mg/kg [4.5 mg/lb], PO, q 24 h for 5 days then q 48 h) and rifampin (5 mg/kg [2.3 mg/lb], PO, q 12 h) were added to the treatment regimen.

On day 6, the foal was bright, alert, and responsive; it had moderate to good appetite and no signs of cyanosis. The oxygen insufflation was discontinued on day 10. A CBC revealed normocytic, normochromic anemia (Hct, 25.8%); leukocytosis (26,900 WBCs/μL); neutrophilia (24,200 neutrophils/μL) with the pres-

ence of band neutrophils (100 cells/µL); hyperfibrinogenemia (1,000 mg/dL); and thrombocytosis (623,000 platelets/µL).

On day 13, an ultrasonographic evaluation of the thoracic and abdominal cavities revealed a substantial decrease in the quantity of the pleural effusion. A small amount of fluid was detected at the level of the seventh to eighth intercostal spaces on the right side of the thorax and the sixth intercostal space on the left. Normal breath sounds could be ausculted over the entire lung bilaterally, with the presence of harsh sounds ventrally in the region of the sixth to eighth intercostal spaces. There were no changes in the size and appearance of the abdominal abscess at this time. The foal was discharged from the hospital on day 13; the owner was given instructions to continue the antimicrobial treatment (azithromycin, rifampin, and metronidazole) and provide stall confinement for 3 weeks.

At reevaluation 3 weeks later, the foal was bright, alert, and responsive. Heart and respiratory rates and temperature were within reference limits; the coat condition had improved, and the foal had gained 22 kg (48.4 lb) in weight. A CBC revealed normocytic, normochromic anemia (Hct, 25.3%) and thrombocytosis (411,000 platelets/µL), but WBC and plasma fibrinogen concentrations were within reference limits. Radiographically, there was no evidence of pleural effusion, lung consolidation, or thoracic abscesses. Ultrasonographic examination of the thorax revealed only diffuse areas of pleural roughening (so-called comet tail artifacts). The abdominal abscess was decreased in size (9 to 10 cm diameter). The foal was discharged the same day, and the owner was instructed to continue antimicrobial treatment with the exception of metronidazole.

The foal was examined again 8 weeks after the initial evaluation. The foal was in good body condition (weight, 148 kg [325.6 lb]), and temperature, heart rate, and respiratory rate were within reference limits. No abnormal lung sounds were detected during thoracic auscultation. A CBC revealed normocytic, normochromic anemia (Hct, 24.7%) and thrombocytosis (354,000 platelets/µL), but WBC and plasma fibrinogen concentrations were within reference limits. The owner reported that the foal had been bright, alert, and responsive; since the last evaluation, the foal's temperature had been within reference range, and appetite was excellent. Ultrasonographic examination of the thorax revealed very small areas of pleural roughening (comet tail artifacts). The abdominal abscess was not detected ultrasonographically. The foal was discharged, and the owner was instructed to continue administration of azithromycin and rifampin; exercise restriction was no longer required. The antimicrobial treatment was then discontinued, and the foal and mare were reintroduced to the herd. Ten months after the initial evaluation, the owner reported no complications with the foal's progress and development.

Rhodococcus equi is a common and devastating type of pneumonia that affects foals from 1 to 6 months of age.[1] Typically, infection results in suppurative bronchopneumonia, which may be associated with extensive abscess formation and suppurative lymphadenitis.[2] The disease can also develop as an intestinal form that includes enterocolitis and typhlitis with multifocal granulomatous or suppurative inflammation of the mesenteric lymph nodes; other clinical signs may include nonseptic polysynovitis, septic arthritis, osteomyelitis, uveitis, cellulitis, and subcutaneous abscesses.[1,3] In foals, the presence of extrapulmonary disorders caused by *R equi* can be associated with a worse prognosis despite successful treatment of pneumonia.[1]

Pleural effusion is an uncommon clinical finding in foals with pneumonia. Chaffin and Martens[1] reported 2 cases of pleural effusion in foals infected with *R equi*. A possible cause of septic pleuritis in foals with *R equi* pneumonia could be the extension of a pulmonary abscess into the pleural space, resulting in inflammation and subsequent effusion, or it could develop secondary to interference with lymphatic drainage in the lungs as a result of lung disease. Pleural effusion caused by *R equi* in adult horses has been reported[4] only in immunocompromised individuals. Pleuropneumonia frequently develops in foals with severe combined immunodeficiency; in those foals, *Pneumocystis carinii* and adenovirus are the most commonly identified respiratory pathogens.[5] Severe combined immunodeficiency was excluded in the foal of this report on the basis of the lymphocyte count and quantitative analyses of serum IgG, IgA, and IgM.

In the foal of this report, diagnoses of unusual *R equi*–associated pulmonary lesions (consolidated and atelectatic lung and pleural effusion) with extrapulmonary lesions, such as joint effusion and an extensive intra-abdominal abscess, were made. The large intra-abdominal abscess differs from the classic mesenteric suppurative lymphadenitis caused by *R equi* in which multiple small lymph nodes are involved. Nay[6] described a large intra-abdominal abscess caused by *R equi* in a Thoroughbred foal, which was detected during postmortem examination. To the authors' knowledge, there are no reports of successful treatment of foals with an extensive intra-abdominal abscess or pleural effusion caused by *R equi*. Despite the improvement of the pulmonary disorders in the foal of this report, a poor prognosis was initially given to the owner; the size and location of the intra-abdominal abscess were believed to predispose the foal to colic because of the close relation and possible adhesions of the abscess to abdominal organs, especially portions of the small intestine. A better prognosis was given after the last abdominal ultrasonographic evaluation because the abscess had decreased in size and was no longer ultrasonographically visible. The joint effusion was thought to be the result of nonseptic polysynovitis because lameness was never evident and the effusion resolved a few days after treatment was established. Indicators of infection or inflammation included in the CBC (plasma fibrinogen concentration and WBC and platelet counts) were useful measures of response to treatment in the foal of this report in that changes in these values correlated with clinical improvement.

Treatment of *R equi* infection should include administration of lipid-soluble antimicrobials capable of intracellular penetration, a factor that is considered a critical aspect for the successful outcome of treatment if abscess formation is involved.[7] For many years, the in vitro synergism of erythromycin and rifampin has been leveraged in treatment of pneumonia caused by *R equi*

in foals; however, notable adverse effects of this drug combination have also been described. Administration of erythromycin and rifampin to foals has resulted in diarrhea, hyperthermia, and respiratory distress.[8] Bacterial resistances to rifampin[9,10] and erythromycin[11] have been reported. Mares have developed acute, sometimes fatal, colitis associated with *Clostridium difficile* infection when their foals were treated for *R equi* pneumonia with an erythromycin-rifampin combination.[12]

Azithromycin, a macrolide antimicrobial, has been used alone or in combination with rifampin for the treatment of *R equi* infections in foals. Azithromycin has some advantages over erythromycin including higher bioavailability (which decreases the frequency of administration), a larger apparent volume of distribution, and a higher degree of lipid solubility (thereby achieving concentrations of the antimicrobial in peritoneal and synovial fluids that are equivalent to that in serum and improving the tissue and phagocytic cell uptake).[13] Furthermore, the authors are not aware of any published reports of secondary effects such as hyperthermia or bacterial resistance associated with the use of azithromycin, although this does not preclude the possibility of their occurrence.

The combination of azithromycin and rifampin has had favorable effects, compared with other antimicrobials, in the treatment of pneumonias in mice.[14] In vitro, the azithromycin-rifampin combination is more effective than each antimicrobial alone and has been associated with a decreased probability of development of bacterial resistance to rifampin.[15] Recently, clarithromycin was reported[16] to be more efficacious than erythromycin or azithromycin in the treatment of *R equi* pneumonia in foals and could be considered as another treatment option. Metronidazole was included in the treatment of the foal of this report because of the potential for anaerobic bacteria to cause intra-abdominal abscesses and pleural effusion, even though in this foal, anaerobic bacterial infection was not detected via bacterial culture. Administration of metronidazole was discontinued after the first month of treatment.

a. Angiocath, BD Angiocath Infusion Therapy Systems Inc, Sandy, Utah.

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