Rhodococcus equi pleuropneumonia in an adult horse

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Abstract — A 10-year-old warmblood gelding was evaluated for intermittent pyrexia, dullness, weight loss, and progressive respiratory disease. Multifocal necrotic pneumonia and pleuritis due to *Rhodococcus equi* infection was diagnosed. Case management is discussed, as well as factors that may have led to this rare cause of pleuropneumonia in an adult horse.

Résumé — Pleuropneumonie à *Rhodococcus equi* chez un cheval adulte. Un cheval warmblood hongre de 10 ans a été évalué pour pyrexie intermittente, lenteur, perte de poids et maladie respiratoire progressive. Une pneumonie nécrotique multi-focale et une pleurésie causées par une infection à *Rhodococcus equi* ont été diagnostiquées. La conduite du traitement est discutée ainsi que les facteurs ayant pu conduire à cette rare cause de pleuropneumonie chez un cheval adulte.

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Rhodococcus equi is an important cause of a pyogranulomatous pneumonia in foals between 1 and 6 mo of age (1,2), with most cases occurring in foals younger than 4 mo. Less common manifestations of *R. equi* infection in foals are intestinal disease, immune-mediated polysynovitis, septic arthritis and osteomyelitis, and soft tissue infections (1,2). *Rhodococcus equi* is a soil organism, the growth of which is increased by herbivore manure (1–3); it can cause infection in wide variety of mammals, often following immunosuppression (2). It is an important opportunistic pathogen in immunosuppressed humans, such as with acquired immuno deficiency syndrome (AIDS) patients or organ transplantation patients who are receiving immunosuppressive therapy (2,4).

Disease due to *R. equi* is rare in adult horses (1). It manifests itself as an illness similar to that in foals, involving the lungs or the colon and related lymph nodes, or, rarely, as a uterine or wound infection (1,5–8). Acquired immunodeficiency of unknown cause in an adult horse that was complicated by *R. equi* septicemia with lung abscessation, reported by Freestone et al (5), and chronic pyogranulomatous lymphadenitis and enteritis caused by *R. equi* in a mare, reported by Genetzky et al (6), are the only cases described in detail.

A 10-year-old warmblood gelding (511 kg) was presented to the Ontario Veterinary College (OVC) with a 3-week history of recurrent fever, dullness, weight loss, and progressive respiratory disease following prolonged transportation. The horse had been transported to Ontario from New York State for a sale. Initial examination by the referring veterinarian 10 d prior to presentation at the OVC had revealed weight loss, increased lung sounds, and occasional cough. The horse was treated parenterally with trimethoprim-sulfadiazine, penicillin, and a thyroid supplement (dosages unknown). Response to treatment was poor, and 3 d prior to presentation at the OVC, the horse refused to eat and became more lethargic. Mild anemia, leukocytosis, hyperglobulinemia, and increased serum glucose were blood abnormalities reported prior to referral. The horse had no other major health problem in the 5 y prior to its present problem.

On admission, the horse was depressed and in poor body condition with a dry, dull hair coat. Rectal temperature (39.2°C), heart rate (60 beats/min), and respiratory rate (32 breaths/min) were all elevated. Mucous membranes were dark pink with normal capillary refill time. The animal was subjectively estimated to be 5% dehydrated. The lung sounds were absent bilaterally ventrally, indicative of lung consolidation, the presence of excess pleural fluid, or a space-occupying lesion. Percussion of the left lung field indicated a fluid line. It was not possible to characterize a definite fluid line on the right side. Thoracic radiographs revealed consolidation of the pulmonary parenchyma in the ventral pulmonary field and a heavy interstitial pattern of increased pulmonary radiopacity in the rest of the lungs. Thoracic ultrasonography showed the presence of pleural effusion with pleural roughening in the left hemithorax and minimal amount of pleural fluid and consolidation of lung tissue in the right hemithorax. A temporary chest drain was placed in the 7th intercostal space, 5 cm dorsal to the costochrondral junction, and samples of pleural fluid for bacteriologic culture and cytologic examination were obtained. Approximately 4 L of yellow cloudy fluid was drained from the left pleural space. Thoracocentesis of the right 6th intercostal space with a teat cannula, 2 cm dorsal to the costochondral junction, yielded no fluid. Cytologic examination of the fluid from the left pleural space revealed an increased cellularity (17.4×10^9/L cells; normal $< 10 \times 10^9$/L cells), consisting mostly of degenerating neutrophils. No bacteria were identified microscopically or in cultures. The pleural fluid had a high protein concentration (47 g/L, normal < 30 g/L), a low glucose concentration (2.8 mmol/L; normal > 3.7 mmol/L), and a normal

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concentration of lactate dehydrogenase (459 U/L; normal < 1000 U/L). Its pH was 7.0. Clinical pathological findings of pleural fluid were suggestive of a septic inflammatory reaction.

Blood analysis revealed a mild leukopenia (4.2×10^9 leukocytes/L; normal 4.9 to 14×10^9 leukocytes/L), likely due to inflammatory cells being recruited to the site of infection. The lymphocyte count was 0.13×10^9 cells/L (normal 1.3 to 4.7×10^9 cells/L) and the monocyte count was 0.08×10^9 cells/L (normal 0.1 to 0.8×10^9 cells/L). Total serum protein was within normal range (67 g/L), but the albumin:globulin ratio was low (0.60, normal 0.8 to1.3), due to low serum albumin concentration (25 g/L, normal 30 to 37 g/L) and mildly increased serum globulin concentration (42 g/L, normal 26 to 41 g/L). The hypoalbuminemia was attributed to the formation of a high-protein effusion into the pleural space and the mild hyperglobulinemia to the increased production of immunoglobulins. Plasma fibrinogen concentration was high at 6.7 g/L (normal 1.6 to 2.9 g/L). These findings were supportive of an ongoing, active inflammatory process. Arterial blood gas of the resting horse (breathing room air) was analyzed and yielded PaO_2 at 87.2 mmHg (normal 100 to 112 mmHg) and $PaCO_2$ at 34.4 mmHg (normal 42 to 47 mmHg).

Endoscopic examination of the airways showed moderate amounts of thick, brownish fluid in the ventral aspect of the trachea. At the level of the carina, a large amount of thick, brown purulent exudate, traceable from the 2nd bronchus of the right lung, was collected with a sterile indwelling catheter for laboratory evaluation. A small amount of exudate was also recovered with a sterile indwelling catheter from the left terminal bronchus. Cytologic examination of the tracheal and bronchial aspirates revealed high numbers of lytic neutrophils, consistent with marked suppurative infectious inflammation. Based on these initial tests, a diagnosis of severe septic pleuropneumonia with intrapulmonary abscesses was made. A ß-hemolytic *Streptococcus* spp. infection with gram-negative bacterial complication was suspected. Anaerobic infection was also considered. Initial therapy, therefore, consisted of IV fluid therapy with lactated Ringer's solution, (5 mL/kg body weight (BW)/h); penicillin G sodium (Penicillin G Sodium for Injection; Novopharm Limited, Toronto, Ontario), 22 000 IU/kg BW, IV, q6h; gentamicin (Gentamicin Sulphate Injection; The Veterinary Pharmacy, Guelph, Ontario), 6.6 mg/kg BW, IV, q24h; flunixin meglumine (Flunazine; Bimeda-MTC Animal Health, Cambridge, Ontario), 1.1 mg/kg BW, IV, q12h; and metronidazole (Apo-Metronidazole; Apotex Inc., Toronto, Ontario), 20 mg/kg BW, PO, q6h. The horse's condition worsened over the 48 h of hospitalization. Due to the poor response to the treatment and financial constraints, the horse was euthanized.

The bacterial cultures of tracheal and bronchial fluid samples obtained by lung endoscopy were reported only after the horse's death. They were positive for large numbers of *R. equi* in pure culture.

Postmortem examination revealed that the ventral region of the right caudal lung lobe was diffusely consolidated. Throughout the rest of the lung, there were small, firm, round, 3- to 5-cm tan nodules. On the cut surface, some of these were solid and tan-white, while others contained caseous material. Fibrin tags were on the pleural surface and clear red fluid was in the pleural space. Histologic examination of lung revealed marked, multifocal, obliterative inflammation comprised of large numbers of lymphocytes, plasmacytes, and neutrophils. There were marked amounts of mature, organized fibrous tissue interspersed in areas with increased numbers of fibroblasts, indicating chronic pneumonia. In some areas, the normal lung parenchyma was completely destroyed, with a few protein-filled alveolar spaces on the periphery. There were multiple foci of necrotic debris throughout the affected tissue. No abnormalities were identified in other organs.

Bacterial culture of the contents of the lung nodules revealed heavy infection with *R. equi*, with scanty numbers of *Escherichia coli*. The *R. equi* isolate was virulence associated protein A-positive (VapA) on Western blot analysis. Restriction enzyme digestion analysis of the virulence plasmid showed that this isolate possessed an 85 kb type I virulence plasmid, the commonest virulence plasmid type in foal isolates from Canada and the United States (9).

Clinical and laboratory findings were consistent with diagnosis of chronic, ongoing multifocal necrotic pneumonia and pleuritis due to *R. equi* infection. *Escherichia coli*, which commonly complicates pneumonia (10), was considered to be a less important factor in this case. No anaerobic bacteria were isolated.

Rhodococcus equi is a rare and uncommon etiologic agent of respiratory disease in the adult horse (11). Roberts et al (7) reported *R. equi* pleuropneumonia in an 18-year-old gelding, diagnosed after several weeks of debilitating disease. Other reports of *R. equi* infection in adult horses described infection that incorporated different organ systems (5,6). The case presented here is the first detailed report of *R. equi* respiratory infection in an adult horse. The distribution of lesions in the lungs was suggestive of aerosol infection (3). This is also the first report of the isolation of a virulence plasmid-positive *R. equi* expressing VapA from an adult horse with pleuropneumonia.

Foals are believed to be exposed to *R. equi* early in life and that immunologic memory from the exposure protects them throughout their adult life, an immunity probably reinforced by repeated exposure from the environment (12). In humans, infection with *R. equi* is almost invariably associated with immunosuppression, associated mainly with human immunodeficiency virus (HIV) infection or the use of immunosuppressive drugs. However, there are reports in human medicine of *R. equi* being a pathogen capable of producing primary disease in the immuno-competent patient (4,13).

Cell-mediated immunity is critical to protecting against *R. equi* infection (12). Because a diagnosis of *R. equi* infection was made only after the horse was dead, his immune status was not investigated. The hyperglobulinemia suggests that B cell function was intact, but the mild lymphopenia that was present only after admission to the OVC suggests that there was dysfunction in other lymphocyte populations. Lymphopenia is often recognized in the leukogram of sick animals. In this case, the lesion was limited to pulmonary tissue, which may

negate the presence of immunodeficiency. Although a majority of isolates of *R. equi* from patients with AIDS and from the intestinal tract and environment of horses do not possess the virulence plasmid, a proportion have virulence plasmids (9), as did the isolate from this horse. As happened in this case, *R. equi* infection in adult horses may be overlooked, clinically, and easily mistaken for other clinically similar pulmonary infections. Standard antimicrobial therapy that targets common aerobic and anaerobic bacteria most often associated with pleuropneumonia, as used in this case, is not effective in the treatment of severe infections with *R. equi* (14,15). If circumstances had allowed the horse to remain hospitalized, the antibiotic treatment of choice after the bacteriology report had been received, would have been a combination of erythromycin estolate or phosphate and rifampin. The treatment with trimethoprim sulfadiazine and penicillin prior to development of pleuropneumonia might have enabled a selection of bacteria that allowed proliferation and overgrowth of *R. equi*. However, this is not the usual behavior of *R. equi* and has never been described.

The prevalence of *R. equi* infection in immunocompromised humans increases (4). However, to evaluate the prevalence and clinical importance of primary or secondary *R. equi* infection in adult horses, more in-depth case reports, such as this, are needed. CVJ

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References

1. Giguere S, Prescott JF. Clinical manifestations, diagnosis, treatment, and prevention of *Rhodococcus equi* infections in foals. Vet Microbiol 1997;56:313–34.
2. Prescott JF. *Rhodococcus equi*: an animal and human pathogen. Clin Microbiol Rev 1991;4:20–34.
3. Hondalus MK. Pathogenesis and virulence of *Rhodococcus equi*. Vet Microbiol 1997;56:257–268.
4. Scott MA, Graham BS, Verrall R, Dixon R, Schaffner W, Tham KT. *Rhodococcus equi* — An increasingly recognized opportunistic pathogen. Am J Clin Pathol 1995;103:649–655.
5. Freestone JF, Hietala S, Moulton J, Vivrette S. Acquired immunodeficiency in a seven-year-old horse. J Am Vet Med Assoc 1987; 15;190:689–91.
6. Genetzky RM, Bettcher MP, Arp LH, White PL. *Corynebacterium equi* infection in a mare. Mod Vet Pract 1982;63:876–879.
7. Roberts MC, Hodgson DR, Kelly WR. *Corynebacterium equi* infection in an adult horse. Aust Vet J 1980;56:96.
8. Zink MC, Yager JA, Smart NL. *Corynebacterium equi* infections in horses, 1958–1984: a review of 131 cases. Can Vet J 1986;27:213–217.
9. Nicholson VM, Prescott JF. Restriction enzyme analysis of the virulence plasmids of VapA-positive *Rhodococcus equi* strains isolated from humans and horses. J Clin Microbiol 1997; 35:738–740.
10. Sweeney CR, Holcombe SJ, Barningham SC, Beech J. Aerobic and anaerobic bacterial isolates from horses with pneumonia or pleuropneumonia and antimicrobial susceptibility patterns of the aerobes. J Am Vet Med Assoc 1991;198:839–842.
11. Ellenberger MA, Genetzky RM. *Rhodococcus equi* infections: literature review. Compend Contin Educ Pract Vet 1986;8: S414–S424.
12. Hines MT, Paasch KM, Alperin DC, Palmer GH, Westhoff NC, Hines SA. Immunity to *Rhodococcus equi*: antigen-specific recall responses in the lungs of adult horses. Vet Immunol Immunopathol 2001;79:101–14.
13. Linares MJ, Lopez-Encuentra A, Perea S. Chronic pneumonia caused by *Rhodococcus equi* in a patient without impaired immunity. Eur Respir J 1997;10:248–250.
14. Sweeney CR, Sweeney RW, Divers TJ. *Rhodococcus equi* pneumonia in 48 foals: response to antimicrobial therapy. Vet Microbiol 1987;14:329–336.
15. Prescott JF, Nicholson VM. The effects of combinations of selected antibiotics on the growth of *Corynebacterium equi*. J Vet Pharmacol Ther 1984;7:61–4.