Tyzzer's disease in an 11-day-old foal

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Abstract — An 11-day-old pony became depressed, anorectic, and pyrexic 2 days after the topsoil of its paddock had been turned over. Rapid progression to colic and head pressing occurred, despite intensive therapy for Tyzzer's disease, and the foal died within 7 h of the appearance of central nervous system signs.

Résumé — Un poney de 11 jours devient abattu, anorexique et fébrile deux jours après que la terre végétale de son enclos ait été retournée. Les symptômes évoluent rapidement vers les coliques et le «pousse-au-mur», malgré un traitement intensif contre la maladie de Tyzzer. Le poney meurt sept heures après l'apparition des premiers signes d'affection du système nerveux central.

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An 11-day-old Pony of America filly was presented with depression and diarrhea. She had shown less interest in following the mare into the barn the previous evening and, in the morning, was not nursing and seemed lethargic. When examined, the foal was depressed and showed little awareness of her surroundings. The filly's mucous membranes were pale and the sclerae were visibly icteric. The foal had a rectal temperature of 40.8°C, a strong heart rate of 180 beats/min, and a respiratory rate of 60 breaths/min, with abdominal respiration and mild abdominal distension. Differential diagnoses included acute hepatitis due to *C. piliforme,* neonatal isoerythrolysis, bacterial septicemia, and toxic hepatitis.

Blood samples were taken and the foal was treated with lactated Ringer's solution (MTC Pharmaceuticals, Cambridge, Ontario), 1.0 L, IV. Other therapies included flunixin meglumine (Cronyxin, Vetrepharm, London, Ontario), 6 mg/kg bodyweight (BW), IV; dexamethasone (Dexamethasone 5, Vetoquinol Canada, Joliette, Quebec), 0.4 mg/kg BW, IV; trimethoprim (5 mg/kg BW) and sulfadoxine (14 mg/kg BW) (Trivetrin, Mallinckrodt Veterinary, Ajax, Ontario), IV; and benzathine penicillin G (17 000 U/kg BW) and procaine penicillin G (17 000 U/kg BW) (Penlong XL, rogar/STB, London, Ontario).

The biochemical profile showed increases in alanine transferase (ALT) (40 U/L; reference range, 0 to 14 U/L), γ-glutamyl transferase (GGT) (115 U/L; reference range, 0 to 71 U/L), and total bilirubin (116 μmol/L; reference range, 0 to 69 μmol/L). Serum globulin was 38 g/L (reference range, 18 to 36 g/L). The foal was mildly leukopenic, with a white blood cell count of 5.6×10^9 cells/L (reference range, 6 to 12.5×10^9 cells/L). Blood glucose was low (4.84 mmol/L; reference range, 6.05 to 14.88 mmol/L), and there was hyponatremia and hypochloremia. A tentative diagnosis of Tyzzer's disease was made on the basis of age, history, and clinical presentation.

Tyzzer's disease is an acute hepatitis caused by *Clostridium piliforme* (formerly *Bacillus piliformis*) (1), an organism found in the soil and endemic in certain areas or on certain farms. Foals are affected at 1 to 5 wk of age and are commonly found dead on pasture with no prior clinical signs. Often, infected foals first show pyrexia, tachypnea, and tachycardia, but illness may not be noticed until 48 h later, when they become lethargic. The condition rapidly progresses to high fever, shock, convulsions, and death within 24 to 48 h. Some foals develop jaundice and severe diarrhea late in the disease.

Clostridium piliforme is a spore-forming, soil- and manure-borne bacterium, which may be endemic on some farms. Adult horses are rarely affected, but may be carriers and sources of infection to susceptible foals (2). Coprophagia and soil investigation by foals place them at greatest risk of exposure. Further probing of this foal's history revealed that soil in the paddock had been turned over 2 d previously and that the foal had been observed actively smelling and rooting in the soil. It is possible that the movement of the soil disturbed clostridial spores.

After ingestion, spores pass to the liver via the hepatic portal system. *Clostridium piliforme* causes acute necrotizing hepatitis, which progresses rapidly in foals. Bacteremia and septicemia cause myocarditis, colitis, and pulmonary hemorrhage. Hepatic encephalopathy ensues and death occurs soon after the commencement of seizure activity. There is one report of successful treatment of a foal with putative Tyzzer's disease (3), but there are no reports of confirmed cases that were successfully treated.

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Kelly St. Denis will receive a copy of Saunders Comprehensive Veterinary Dictionary courtesy of Harcourt-Brace Canada Inc.

In this case, despite the grave prognosis, the owners elected to treat the foal intensively for 24 h. Fluids containing 0.9% sodium chloride (Baxter, Mississauga, Ontario) and 10% sodium bicarbonate (MTC Pharmaceuticals, McGaw, Cambridge, Ontario) were administered at a shock rate of 60 mL/kg BW/h, to a total volume of 200 mL, then at maintenance plus replacement rate to a total volume of 3.0 L of 0.9% sodium chloride and 300 mL of 10% sodium bicarbonate. Treatment with trimethoprim-sulfadoxine and flunixin meglumine were repeated. Ranitidine (Kenral, Don Mills, Ontario), 50 mg, IV, was administered to reduce the risk of gastric ulceration. The foal responded to therapy, becoming more alert and responsive, showing interest in its surroundings, and starting to drink water. However, within 12 h, the foal exhibited mild signs of colic and early signs of hepatic encephalopathy (head pressing), with a rectal temperature of 37.1°C. The foal was dead within 7 h of the onset of these signs.

Postmortem findings included multifocal hepatic necrosis; diffuse yellow and blue mottling of the spleen; icterus affecting the gastrointestinal tract, body fat, and skin; multifocal petechiae and ecchymoses in the small intestine; pulmonary hemorrhage; renal medullary necrosis; and hemorrhagic cystitis.

As *C. piliforme* cannot be cultured by using either routine or special bacteriological methods, it must be grown in egg or cell culture (4). Definitive diagnosis of Tyzzer's disease usually depends on microscopic observation of bacilli in Warthin-Starry-stained sections of liver.

Microscopic examination revealed severe, random, diffuse, subacute hepatic necrosis, with a moderate neutrophil reaction. No inclusion bodies or intracellular bacteria were visible after staining with hematoxylin and eosin (H&E), but staining with the Warthin-Starry stain revealed moderate to small numbers of long, slender bacilli, consistent with *C. piliforme*. The surface of the colon was autolysed with foci of fibrinous reaction in the lamina propria, and there was serosal hemorrhage in the small intestine. No specific lesions were found in the kidney or myocardium.

Confirmation of Tyzzer's disease usually requires that *C. piliforme* be present in the liver in numbers large enough to be visible in H&E-stained sections. The aggressive antimicrobial therapy used in this case may have been responsible for the unexpectedly small numbers of bacilli observed. Difficulty in visualizing the bacteria without the use of Warthin-Starry stain has been reported (5).

Careful foal and paddock management are essential on farms with a history of Tyzzer's disease. Young foals should remain in well-grassed paddocks, away from potentially contaminated soil. Manure should be removed regularly, and barn and stall areas should be cleansed with 0.3% sodium hypochlorite to eliminate spores (6). Sudden changes in foal behavior and activity should always be regarded with suspicion, and medical care sought immediately.

Although there are no reports of Tyzzer's disease being treated successfully, early and aggressive therapy for septic shock may prove helpful (7). The foal should receive polyionic fluid therapy with 5% to 10% dextrose, as needed, to correct hypoglycemia, and 5% sodium bicarbonate, as required, to combat metabolic acidosis, which is often severe in foals with Tyzzer's disease. It is also recommended that affected foals be treated with 1.0 to 2.0 L of hyperimmune plasma containing antibodies raised against bacterial lipopolysaccharide, and with pentoxifylline (8.4 mg/kg BW, PO, q12h) (7). High-dose antibiotic therapy with potassium penicillin, amikacin, chloramphenicol, or trimethoprim-sulfadoxine is recommended.

Strain-specific antibody is passively transferred from immune mares to their foals (8), but the possibility of vaccination on farms where *C. piliforme* is endemic has not been addressed. The existence of other effective clostridial vaccines (against *C. chauvei, C. botulinum, C. tetani,* etc.) suggests that development of a vaccine is feasible. Ribosomal RNA sequencing was required to identify *C. piliforme* as a clostridial species (1), and cross immunity with clostridial vaccine species is unlikely. However, a comparison of the susceptibility to *C. piliforme* of foals nursing mares, unvaccinated or fully vaccinated for *C. tetani,* might provide valuable information about cross immunity.

Current studies have revealed that isolates of *C. piliforme* from different sources share some common antigens but have diverse protein and antigen profiles (8–10). Some strains are host-specific, while others are cross-infective (9). Serologic analysis has shown that horses are susceptible to at least 2 distinct strains (8). These data may predict difficulty in developing a *C. piliforme* vaccine for immunization of prepartum mares. Until such a vaccine is available, environmental hygiene should be considered to be of the utmost importance in preventing Tyzzer's disease in foals.

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