Pathology in Practice

History

An 11-year-old 482-kg (1,060-lb) Quarter Horse gelding was referred for evaluation of azotemia. The gelding had a 4-month history of weight loss, with a decrease in appetite during the preceding 3 weeks. The horse had sudden onset of forelimb ataxia 1 week before the referral evaluation, which resolved following administration of dexamethasone (0.04 mg/kg [0.018 mg/lb], PO, q 24 h for 3 days) and dimethyl sulfoxide (0.06 g/kg [0.027 g/lb] in 10% solution, IV, administered once). At that time, serum biochemical analyses revealed that the horse’s BUN concentration was 59.2 mg/dL and creatinine concentration was 6.2 mg/dL; these values were provided without reference ranges. The horse had been dewormed with ivermectin biannually (spring and fall). Additionally, ivermectin was given 8 and 4 weeks before the referral evaluation.

Clinical and Gross Findings

On initial examination, the horse had a body condition score of 3 (on a 1 to 9 scale). Rectal temperature (38.2°C [100.8°F]) was within reference limits, but heart rate (54 beats/min) and respiratory rate (30 breaths/min) were considered high. All other examination findings, including results of a neurologic evaluation, were considered normal. Clinico-pathologic abnormalities included hyperfibrinogenemia (500 mg/dL; reference range, 100 to 400 mg/dL), hyperproteinemia (10.5 g/dL; reference range, 6.0 to 8.0 g/dL), hypoalbuminemia (2.8 g/dL; reference range, 3.3 to 4.6 g/dL), azotemia (BUN concentration, 65.9 mg/dL; reference range, 14 to 21 mg/dL); creatinine concentration, 5.3 mg/dL [reference range, 1.0 to 2.1 mg/dL]); hypochloremia (93 mEq/L; reference range, 102 to 114 mEq/L), and high serum concentrations of calcium (15.1 mEq/L; reference range, 10.6 to 12.8 mg/dL), phosphorus (6.9 mg/dL; reference range, 2.6 to 5 mg/dL), and magnesium (1.43 mg/dL; reference range, 1.43 to 2.08 mg/dL). Urinalysis of a voided midstream sample revealed isosthenuria (specific gravity, 1.010), microscopic hematuria (3+; reference range, negative to trace), proteinuria (1+; reference range, negative to trace), pyuria (30 to 40 WBCs/hpf; reference range, ≤ 5 WBCs/hpf), and the presence of bacteria (4+; reference range, negative to few), epithelial cells (> 100 cells; reference range, ≤ 10 cells/hpf), and a few parasitic larvae.

Transabdominal ultrasonographic evaluation of both kidneys revealed bilateral renomegaly with loss of corticomedullary differentiation and normal architecture. Widespread, small, circular areas of hypeerechogenicity and irregularly round, large, hypoechoic to anechoic structures were present bilaterally.

Collectively, the diagnostic test results suggested a grave prognosis, and the owner elected euthanasia. Necropsy was performed. On gross examination, there was bilateral severe renomegaly; both kidneys were 20 cm in length and 30 cm in width (reference range for the right kidney, 13 to 15 cm in length and 15 to 18 cm in width; reference range for the left kidney, 15 to 18 cm in length and 11 to 15 cm in width). The capsular surface of each kidney was markedly irregular. Multiple pale nodules were evident on the capsular surface; on section, these areas corresponded to irregular and poorly demarcated regions of pallor that effaced the renal parenchyma and often obscured distinction between the cortex and medulla. Multifocal nodular lesions had central cystic cavitated areas (1 to 10 cm in diameter) that contained small amounts of clear to serosanguineous fluid (Figure 1). There was moderate diffuse distension of the left ureter. Perirenal lymph nodes were markedly enlarged (approx 4 or 5 times as large as the size of those nodes expected in a healthy horse). The lymph nodes were firm and pale white to tan in color and lacked a distinct nodal architecture on the cut surface. Additional gross lesions were not observed, although the CNS was not evaluated. Sections of the kidneys, lymph nodes, lungs, liver, gastrointestinal tract, pancreas, heart, adrenal glands, thyroid glands, and skeletal muscle were collected for histologic examination.

Formulate differential diagnoses from the history, clinical findings, and Figure 1—then turn the page →

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Histopathologic Findings

In sections of the kidneys, the renal interstitium was diffusely expanded because of dense aggregates of macrophages with fewer neutrophils, eosinophils, lymphocytes, plasma cells, and Langhans-type multinucleated giant cells intermixed with necrotic debris and fibrin. Inflammatory cells replaced up to 90% of the renal parenchyma, surrounded remnant tubules and glomeruli, and formed poorly demarcated nodules that were centered on numerous rhabditiform nematode parasitic larva, adults, and ova. There was diffuse atrophy and loss of glomeruli and tubules, and the remaining glomerular tufts were often shrunken, fibrotic (glomerulosclerosis), and surrounded by bands of dense fibrous connective tissue (Figure 2). Thickening of the glomerular basement membrane and terminal capillary loops of less-affected glomeruli was observed. Remnant renal tubules were multifocally moderately dilated and contained finely granular eosinophilic casts with rare embryonated ova or larval nematodes. Morphological features of female adult nematodes included a thin eosinophilic cuticle; a cylindrical body (15 to 20 µm in diameter); tapered ends; rhabditiform esophagus with a characteristic corpus, isthmus, and bulb; and a reflected ovary (Figure 3). Nematode larvae were smaller in size (approx 8 to 12 µm in diameter) and also had characteristic rhabditiform esophagi. Ova measured approximately 10×30 µm to 10×35 µm and occasionally contained larval nematodes.

Histologic lesions were also observed in the perirenal lymph nodes and lungs. Multiple coalescing nodular aggregates of inflammatory cells surrounded large numbers of parasitic larvae and adults in all regions of the lymph nodes. Multifocal nodular aggregates of macrophages intermixed with neutrophils and eosinophils surrounded low numbers of larval nematodes within the pulmonary parenchyma. Mineral deposition was observed in the gastric mucosa and alveolar septal walls as well as in the basement membranes of numerous bronchioles, bronchi, and pulmonary blood vessels. There was diffuse mild eosinophilic colitis, but parasites were not observed. Sections of pancreas, liver, adrenal glands, thyroid glands, heart, and skeletal muscle were histologically normal.

Figure 2—Photomicrograph of a section of the left kidney of the horse in Figure 1. Sheets of inflammatory cells expand the interstitium and surround scattered remnant tubules (arrow) or glomeruli (asterisk). Numerous nematode larval and adult forms are observed in the section (arrowheads). Remnant glomeruli are sclerotic and obsolete. H&E stain; bar = 100 µm.

Figure 3—Photomicrographs of adult nematodes within sections of the renal parenchyma of the horse in Figure 1. Characteristic features of the adults include a tapered anterior end, classic rhabditiform esophagus (arrow in panel A), and reflection of the ovary (arrow in panel B). H&E stain; bar = 25 µm.
Morphologic Diagnosis

Severe, chronic, diffuse, granulomatous interstitial nephritis and renal lymphadenitis with numerous intralesional nematodes consistent with Halicephalobus gingivalis; and multifocal chronic granulomatous pneumonia with larval nematodes and alveolar mineralization.

Comments

In the horse of this report, the gross and microscopic lesions were consistent with verminous nephritis caused by H gingivalis with dissemination of the parasites to the lungs. Halicephalobus gingivalis is a ubiquitous, saprophytic, free-living, rhabditiform nematode of soil and decaying organic matter that has sporadically been associated with opportunistic, granulomatous infections in equids and humans. Little is known about the life cycle, mode of infection, and pathogenesis of this parasite. Postulated routes of infection include penetration of compromised skin or mucous membranes, inhalation, transmammary infection of suckling foals, and ascending urogenital infection. Infection with H gingivalis may be restricted to local granuloma formation but dissemination to multiple organ systems more commonly occurs, likely via hematogenous and lymphatic routes. Preferred sites of infection in horses include the CNS, kidneys, maxilla, mandible, regional lymph nodes, eyes, and lungs.

Clinical signs of infection with H gingivalis vary depending on the tissues involved; neurologic signs and renal disease typically predominate. Diagnosis is based on histopathologic evidence of a granulomatous inflammatory process with intralesional ova, rhabditiform nematode larvae, and pathogenic female adults that have characteristic morphological features, in particular a pointed tail and a reproductive tract with characteristic dorsoflexion of the ovary and ventroflexion of the uterus. Antemortem diagnosis may be difficult in equids with internal infection. Infection with H gingivalis has a high fatality rate; to our knowledge, there are only 3 reports of treatment success in affected equids. The first reported case involved prepubital granulomas that resolved following systemic treatment with ivermectin and diethylcarbamazine. The second case involved a horse with a granuloma over an eye that resolved following surgical debulking, topical ivermectin application, and repeated systemic administration of high doses of ivermectin. Additionally, in a donkey with lesions restricted to 1 kidney, unilateral nephrectomy was curative.

In the horse of this report, signs of chronic renal failure were predominant. In previous reports of equine halicephalobiasis, renal lesions were commonly accompanied by CNS lesions, and with a few exceptions, clinical signs of CNS involvement were evident and led to death rapidly. Interestingly, the horse of this report had a brief episode of unexplained forelimb ataxia that resolved quickly with medical treatment 1 week prior to the referral evaluation. Thorough examination at the referral evaluation revealed no signs of CNS disease. However, in light of the physical examination findings and clinicopathologic abnormalities, differential diagnoses that were considered included bilateral verminous nephritis, renal neoplasia, pyelonephritis, immune-mediated glomerulonephritis, and polycystic kidney disease. Collectively, the results of the urinalysis and the abnormal ultrasonographic findings were suggestive of verminous nephritis. Histologic evaluation of renal tissue yielded a definitive diagnosis of H gingivalis infection. The presence of similar lesions in the lungs was suggestive of hematogenous spread of the infection, which has previously been reported in the veterinary medical literature.

References