History

A 4-year-old Holstein cow had a history of chronic emaciation and profuse brownish green diarrhea, which was entirely liquid and described as being like water from a hose. The cow was euthanized by an IV overdose sodium pentobarbital injection 5 to 6 weeks after calving because of extreme weakness.

Clinical and Gross Findings

At necropsy, the cow had a body condition score of 2 of 5 and was dehydrated. There was marked loss of muscle mass, serous atrophy of epicardial and perirenal fat depots, and fluid effusion in the abdominal cavity (1.7 L), thoracic cavity (700 mL), and pericardial cavity (40 mL). The wall of the left atrium of the heart was rigid and had a hard and irregular endocardial surface because of the presence of irregular prominent whitish opaque plaques. Extending 25 cm from the heart base, the intimal lining of the thoracic aorta (predominantly the supravalvular portion of the aorta) was similarly affected (Figure 1).

The mesenteric lymph nodes, particularly the ileocecal nodes, were enlarged, pale, and edematous. Prominent lymph vessels extended from the intestinal serosa through the mesentery to the mesenteric nodes. The ileal mucosa was diffusely thickened and corrugated. Formulate differential diagnoses from the history, clinical findings, and Figure 1—then turn the page →
**Histopathologic Findings**

Tissue samples from the heart (including left atrium), affected areas of the aorta, ileum, and ileocecal lymph nodes were processed for histologic examination. The endocardium of the left atrium was irregularly expanded by connective tissue, edema, and multifocal areas of basophilic granular deposits (mineralization; Figure 2). Extensive areas of mineralization were also observed in the tunica media of the aorta. The lamina propria of the ileum was diffusely thickened because of the presence of dense sheets of large epithelioid macrophages, mixed with fewer lymphocytes, plasma cells, and rare neutrophils. The inflammatory infiltrate separated and displaced the crypts. Villi were diffusely blunted or absent (Figure 3). The submucosa was diffusely expanded by marked edema and a linear band of lymphocytes and plasma cells. Similar inflammatory cells also cuffed the submucosal and serosal lymphatic vessels. In the ileocecal lymph nodes, multiple aggregates of epithelioid macrophages and multinucleate Langhans-type giant cells effaced as much as 30% of both the nodal cortex and medulla. Within the remaining cortical lymphoid tissue, there were large reactive germinal centers. Large numbers of acid-fast bacilli were detected via Ziehl-Neelsen staining within the cytoplasm of epithelioid macrophages in the ileal lamina propria and ileocecal lymph node.

**Additional Laboratory Findings**

Prior to euthanasia, microbial culture of a fecal sample, testing of a serum sample via an ELISA, and testing of a blood sample with in vitro interferon gamma assay that used Johnin purified protein derivative as the cell stimulant in place of *Mycobacterium bovis* purified protein derivative all yielded positive results for *Mycobacterium avium* subsp *paratuberculosis*. Serum samples were also tested for antibodies against bovine leukemia virus (BLV) by ELISA, and results were positive.

**Morphologic Diagnosis and Case Summary**

Morphologic diagnosis: severe, multifocal to coalescing, left atrial endocardial and thoracic aortic medial mineralization; severe, chronic, diffuse, granulomatous ileitis with villous atrophy and ileocecal lymphadenitis with intralesional acid-fast bacilli.

Case summary: cardiac and aortic mineralization in a cow with granulomatous ileitis.

**Comments**

The gross and microscopic lesions in the ileum and ileocecal lymph nodes of the cow of this report were typical of paratuberculosis (Johne's disease); however, the atrial and aortic lesions identified in this cow are not always observed in animals with Johne's disease. Calcification of the ascending aorta and the endocardium of the left atrium is present in up to 25% of animals with clinical signs of Johne's disease and can also develop.
in cattle that have other prolonged debilitating diseases, such as tuberculosis or hairy vetch poisoning. The endocardium and large elastic arteries are prone to mineralization because of their abundant elastic fibers. Activated macrophages are thought to have a role in the synthesis of vitamin D₃ metabolites that are deposited in those locations of the cardiovascular system. Differential diagnoses for this lesion are poisoning by calcinogenic plants and hypervitaminosis D. Plants associated with mineralization of the cardiovascular system in cattle include *Cestrum diurnum* and *Trisetum flavescens* (both present in certain regions of the United States) as well as *Solanum malacoxylon.*

Johnes disease is an insidious chronic infectious disease primarily of domestic and wild ruminants and rarely also of pigs, equids, captive primates, and other species. The disease is caused by *M. avium* subspecies *paratuberculosis*, a facultative intracellular acid-fast bacillus. Among cattle, the disease is characterized by intractable diarrhea, emaciation, and hypoproteinemia in animals >19 months old. Clinically, the cow of the present report had typical signs of Johnes disease, which is characterized by progressive weight loss and continuous chronic diarrhea that does not respond to treatment while the animal’s appetite generally remains good. Differential diagnoses for the clinical signs of emaciation, profuse diarrhea, and weakness in classic cases of Johnes disease include gastrointestinal endoparasitism, bovine viral diarrhea–mucosal disease, enzootic bovine leukosis, salmonellosis, and renal amyloidosis.

The cow of the present report was positive for *M. avium* subspecies *paratuberculosis* and BLV. However, there was no histologic evidence of lesions caused by BLV in the tissues examined. Reportedly, only <3% of animals infected with this virus develop lymphomatous multisystemic infiltrate. Although it is generally accepted that BLV infection causes immunosuppression, the mechanism of such an effect on the immune system and resultant disease susceptibility are poorly understood. Deleterious effects of immunosuppression in cattle as a result of BLV infection have been suggested by early culling, decreased milk production, and prolonged nonpregnant periods among seropositive cows.

In cattle with Johnes disease, the infection is systemic and the microorganism may be present in milk, semen, and urine. It may also cross the placenta. However, exposure is mainly by ingestion of microorganisms shed in feces.

Given that, in the field, orofecal contact is generally more frequent among dairy cattle than among beef cattle, this explains the higher prevalence of Johnes disease in dairy cows, compared with findings in beef cattle. Susceptibility to infection is greatest during the first 30 days after birth, although clinical disease does not usually develop in cattle until 2 to 5 years of age. This long incubation period has been termed the iceberg effect because, in an infected herd, a few animals may have clinical signs of Johnes disease and yet a much greater number are subclinically infected. Stress, such as parturition (as in the case described in this report), transport, and low plane of nutrition may convert a subclinical case into an overt clinical case. The mycobacteria are ingested and pass through the upper portion of the gastrointestinal tract to the ileum, where they are engulfed by the M cells in the dome epithelium over the intestinal lymphoid follicles and transported to macrophages in the underlying lamina propria and submucosa. The microorganisms inhibit the conversion of phagosomes to phagolysosomes in macrophages, proliferate in the cytoplasm, and infect adjacent macrophages, thereby expanding the population of infected cells and recruiting elements of the humoral and cell-mediated arms of the immune system to the site.

The major lesions of Johnes disease are usually confined to the ileum, cecum, and proximal portion of the colon and the draining lymph nodes. Disseminated loci of granulomatous inflammation in the intestinal tract reflect a distinct profile of local cytokine expression and, combined with the villous atrophy, result in malabsorption, progressive emaciation, and ultimately death. Because of a lack of responsiveness to treatment, control of this insidious disease depends on testing, culling of infected animals, and strict attention to hygiene and other husbandry measures to prevent spread of infection. Achievement and maintenance of Johnes disease-free status within every cattle herd should be the ultimate goal.

References