Student Clinical Report

Editor's Note: The AABP Board of Directors meeting in Washington, D.C., on July 21, 1980 approved a recommendation from the Forward Planning Committee to present prizes to encourage veterinary medicine students to write case reports for the Bovine Practitioner.

First Prize ($200):

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Neonatal Meningoencephalitis Associated with Infectious Bovine Rhinotracheitis Virus

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Introduction

The infectious bovine rhinotracheitis [IBR] virus (bovine herpesvirus 1) has a diverse pathogenicity associated with numerous clinical syndromes. These include a respiratory infection with severe inflammation of the upper respiratory mucosa, genital infections (infectious pustular vulvovaginitis [IPV] and infectious pustular balanoposthitis), conjunctivitis which can occur alone or together with infection of other systems,[1] fetal infection with abortion,[1 15] meningoencephalitis[2 3 4 6 9 10 13 19] and a septicemia in young calves.[17 18] Although IBR virus infection is widespread throughout the cattle industry, the encephalitic form is apparently rare.

Johnston *et al*, in Australia reported both natural and experimental meningoencephalitis in two to six month old calves caused by a suspected new virus. [13] After initial viral characterization, French named the new virus the N569 virus, only later to document that the N569 virus was actually the IBR-IPV virus.[7,8] This was the first reported case of meningoencephalitis caused by the infectious bovine rhinotracheitis virus. Barenfus *et al* were the first to report IBR virus induced meningoencephalitis in the United States[2] and since that time only a few natural cases have been reported.[3 4 9 10 19] This case of meningoencephalitis in a two-week-old calf is presented because of the infrequency of the encephalitic form of IBR in the United States and the calf involved is younger than any previously reported cases.

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Case Report

On July 5, 1983, a two-week-old female Holstein calf was brought to New Bolton Center, University of Pennsylvania, School of Veterinary Medicine, with the chief complaints of pyrexia and convulsions. The calf was born following a dystocia that was corrected uneventfully and the calf had promptly received colostrum. Since birth, the calf had intermittent fever spikes (up to 107°F) and an elevated respiratory rate that were unresponsive to antibiotic therapy. Despite the tachypnea and pyrexia, the calf continued to nurse and remained fairly bright until the day of presentation when the calf refused to nurse, spiked a fever of 107°F, and began convulsing. The calf was given 60 ml of 50% dextrose solution and 300 mg thiamine intravenously, cooled with ice, sedated with phenobarbital and transported to New Bolton Center.

The physical examination at presentation revealed tachypnea (70 breaths/minute), tachycardia (140 beats/minute), temperature 102.4°F, moderate abdominal distension, hemorrhages around the teeth, and severe weakness and depression. Respirations were labored with harsh lung sounds auscultated over the entire thorax. The calf would not move and seemed unaware of its surroundings, assumed a basewide stance only when lifted, and responded minimally to any type of stimuli.

Laboratory data revealed a leukocytosis due to a neutrophilia with 10% immature neutrophils and an elevated fibrinogen (846 mg/dl). The calf was also hypocalcemic (7.9 mg/dl), azotemic (creatinine 1.9 mg/dl) and hypoglycemic (41 mg/dl). The hematocrit was 30% and

the total protein was 6.1 g/dl.

Based on the initial problem list (severe depression and weakness, abdominal distension, harsh lung sounds, and a history of fever and convulsions) together with the laboratory data, the calf was believed to have pneumonia, meningitis and peritonitis. An intravenous catheter was placed in the jugular vein and 1 litre of 5% dextrose and 0.45% saline with 20 ml of calcium gluconate were administered.* Vitamin E and selenium were given subcutaneously and chloramphenicol succinate was started intravenously at 20 mg/lb body weight three times daily, in hopes of reaching high levels of this antibiotic within the cerebrospinal fluid (CSF). A hyperalimentation solution was continued intravenously at a slow drip throughout the night.[12]

The following morning the calf's clinical condition appeared unchanged and sodium sulfamethazine was added to the antibiotic regimen at 1.5 grain/lb body weight. Lumbosacral spinal fluid collected on the morning after hospital admission had a large increase in white blood cells (540/ul; normal = <5/ul), of which 91% were lymphocytes, 8% were monocytes and 1% were neutrophils, confirming the suspected meningitis. The sample was submitted for culture and sensitivity.

A second complete blood count showed a continued leukocytosis with a severe lymphopenia and marked increase in immature and vacuolated neutrophils (38%). The creatinine increased to 3.2 mg/dl. All laboratory values indicated that the calf's condition was deteriorating. One liter of fresh plasma was given intravenously to increase fibronectins, complement activity, macrophage function and other nonspecific immune mechanisms.

An arterial blood sample taken from the ear artery revealed a PO_2 of 60 mmHg and a PCO_2 of 54 mmHg, suggesting impaired gas exchange. The calf was placed on intranasal oxygen but subsequent arterial blood gases revealed continued deterioration of pulmonary function. Nebulization was initiated that evening in hopes of improving ventilation. The calf failed to respond to therapy and died at 3:00 a.m., July 7th, approximately 30 hours after hospital admission.

Pathology

Gross postmortem examination revealed an apparent pneumonia (the lungs were deep purple, firm noncrepitant and would not float in formalin), and pleuritis with numerous fibrous tags on both the visceral and parietal pleura. The right ventral lung was adhered to the thoracic wall and the pericardial sac. There was a serosanguineous pericardial effusion (30 ml) with flecks of fibrin and the abdomen was greatly distended with fluid and gas within the lumen of the bowel. The abomasum contained an opaque, whitish, pale yellow fluid and was also distended with gas. The liver appeared larger than expected for a 120 lb calf, was pale yellow with a prominent lobular pattern and the gallbladder was moderately distended. The mesenteric and mediastinal lymph nodes were markedly enlarged but retained their normal color, consistency and architecture. All other organ systems, including the brain, were considered normal on gross examination.

Microscopic examination revealed severe pulmonary interstitial congestion, multifocal necrotizing bronchiolitis, multifocal hepatic necrosis with perivascular cuffing and diffuse lymphoid depletion of follicles within the spleen. Eosinophilic intranuclear inclusion bodies were present in the frontal cortex, temporal cortex, basal ganglia and cerebellum. Mononuclear perivascular cuffing was seen in both the gray and white matter of the temporal and parietal cortexes and also in the basal ganglia. A mild myelitis was noted in the anterior medulla.

The numerous diffuse eosinophilic intranuclear inclusion bodies found within the neural tissue were compatible with infection by either IBR virus or pseudo-rabies virus (Porcine herpesvirus I). Brain tissue was submitted for viral isolation and IBR virus was identified by its cytopathic effect and the fluorescent antibody technique. No other body tissues were submitted for viral isolation.

Discussion

Meningitis in cattle is most ofter purulent, diffuse and secondary to an initial systemic bacterial infection.[1] Suppurative meningitis/encephalitis is characterized by a large increase in neutrophils, total protein and turbidity within the cerebrospinal fluid with bacteria being easily cultured.[5] Nonsuppurative meningitis/encephalitis in cattle is usually associated with a viral or *Listeria monocytogenes* infection.[1] It is characterized by a mild elevation of mononuclear cells and total protein within the CSF[5] and the inability to isolate a bacterial species with routine culturing techniques. A definitive diagnosis of nonsuppurative meningitis/encephalitis is made by viral isolation or the use of special culturing techniques for the identification of *L. monocytogenes*, along with compatible microscopic findings. Certain metabolic conditions (lead poisoning and thiamine deficiency) can look very similar clinically but have distinctly different pathological findings.[1]

In this particular calf, the very high fever spikes, elevated lymphocytes in the CSF, and the poor response to antibiotic therapy suggested a viral nonsuppurative meningoencephalitis. This was confirmed by the isolation of IBR virus from the brain and supported by the presence of eosinophilic intranuclear neural inclusion bodies and the inability to isolate bacteria from the brain and CSF. Whether the remaining lesions, particularly the pleuritis and lung changes, were due solely to the IBR virus or a secondary bacterial infection can only be speculated. A fatal systemic form of IBR virus infection has been reported in young calves.[17,18] Lesions included ulceration of the gastrointestinal tract particularly the rumen,[18] fibrinopurulent bron-

cho-pneumonia, moderate fibrinous peritonitis, and a nonsuppurative encephalitis was seen in one calf.[17] Gardiner also reported lesions involving the lungs and mesenteric lymph nodes in calves affected with IBR meningoencephalitis.[9] Therefore it seems that the lesions observed and the death of this calf could be attributed to the IBR virus alone.

With the history of prompt colostrum intake and apparent adequate immunoglobulin absorption (total protein = 6.1 g/dl), one must consider when and why the viral infection occurred. A late intra-uterine infection could be speculated on but Kendrick reported that the near term fetus when infected with IBR virus has only a slight viremia and lesions occur only at the point of inoculation with minimal systemic involvement.[15] In humans, the majority of neonatal Herpes Simples infections are often secondary to an unrecognized maternal involvement.[11] This is also true for canine species, but has not been documented in cattle. A newborn bovine fetus that is not colostrum-deprived but from a dam not having antibodies to IBR virus is susceptible to intranasal inoculation.[15] The dam of the calf in this report was a first calf heifer that had received two modified-live IBR vaccinations prior to breeding. This is typical vaccination protocol and should have resulted in adequate antibodies to the IBR virus.

A few possibilities for the cause of the viral infection include: 1) The calf was infected with the IBR virus prior to colostrum absorption. 2) The dam's colostrum was deficient or void of IBR virus neutralizing antibodies. 3) Inability of the calf's immunoglobulins to resist infection due to the presence of the virus within protective cells (leukocytes). 4) Inadequate or delayed absorption of antibodies. 5) A neurotropic strain of IBR virus which may not be neutralized by antibodies to the vaccine strain. Several authors have suggested that a specific neurotropic strain of IBR virus does exist.[4,9,10] Wiseman states that neurotropic strains of IBR virus do not produce severe respiratory signs and that experimental infections with respiratory tract isolates do not give rise to nervous signs.[20] It is known that the IBR herpesviruses can travel from a peripheral inoculated site to the CNS by way of nerves and produce a persistent infection.[16] However, clinical signs of meningitis/encephalitis do not usually develop in those cases. In Argentina, the pathogenicity of a specific strain of neurotropic IBR virus (L-114) isolated from calves with encephalitis has been experimentally demonstrated.[4] More work needs to be done before it can be stated that a specific neurotropic strain of IBR virus exists.

Whatever the predisposing factors were to the infection of this calf, the meningoencephalitis produced was histopathologically similar to previously reported cases.[2 4 9 10 13] Only in one previous case has the spinal cord been involved.[3] Inclusion bodies seen in this calf have not always been present in previous reports,[2 3 9 10 13 19] but IBR virus was isolated from the affected animals. It is possible to isolate IBR virus from neural tissues of animals not actually suffering from IBR meningoencephalitis.[20] This may have been the case in at least one report.[19]

Infectious bovine rhinotracheitis viral meningoencephalitis is rare and the exact pathophysiology for its development is yet to be discovered. It has a very widespread clinical picture being reported in cattle as old as three years[3] and, as the calf in this report, as young as two weeks. The neurological signs can vary from convulsions, ataxia, amaurosis and depression[2 4 9 10 13] to only hind limb paralysis, weakness and incoordination when the spinal cord is involved.[3] Other signs include ptyalism, odontoprisis, head presssing, bellowing and aggressive behavior. Affected calves are typically under ten months of age with anorexia being the first clinical sign.[1] Pyrexia is usually present but Barenfus stated that all of the calves in his report remained afebrile from the onset of clinical signs of death.[2] Central nervous system signs usually prevail followed by depression and death within 3-5 days after the onset of neurologic signs.[1] Usually there are no gross postmortem lesions at necropsy.[2 3 9 10 13]

In contrast, the calf in this report was two weeks of age, did not develop anorexia and neurologic signs until two days before death, and had gross systemic lesions not usually present in IBR meningoencephalitis. Also, this report describes a single isolated case of IBR meningoencephalitis with no other animals in the herd affected. This is not characteristic of viral infections in general and specifically IBR encephalitis. Few isolated cases of only one or two animals have been reported.[3 10 18] The majority of reports are epizootics with multiple animals of approximately the same age being affected.[2 4 9 13 19]

The prognosis for cattle with IBR meningoencephalitis is extremely poor and once neurologic signs develop, death is nearly inevitable. Very few animals have recovered after showing clinical neurologic signs.[4 9 13 19] Treatment is usually futile and primarily supportive but recent advances have been made in treatment of human neonatal encephalitis with adenine arabinoside (Vidarabine).[11 14] Vidarabine reduced mortality from 70% in control patients to 28% in treated patients.[14] Acycloguanosine (Acyclovir) is another new antiviral compound with a high level of activity against herpesvirus infections in laboratory animals.[14] These antiviral agents may become important future treatment regimens for animals affected with herpesvirus (IBR) meningoencephalitis.

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