Student Clinical Paper

Hepatic Abscessation in a Holstein Cow

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Introduction

Hepatic abscessation can occur in ruminants of any age or sex, but is primarily associated with feedlot cattle consuming diets with a high content of rapidly fermentable carbohydrates.[1,2] Such diets can produce a ruminal lactic acidosis and rumenitis, with a secondary devitalization and erosion of the ruminal epithelium providing a point of entry for bacteria to enter into the portal circulation and colonize the liver. Most hepatic abscesses in cattle are subclinical, with clinical cases presenting as a vague syndrome including non-localizing signs such as weight loss, decreased milk production, periods of anorexia and pyrexia, and diarrhea or constipation. The following case report illustrates the history and clinical signs of a cow suffering from hepatic abscessation, the diagnostic work-up pursued and post-mortem findings.

Initial Data

An on-farm physical examination was conducted on a 3 ½ year-old Holstein cow that had freshened nine days previously. The presenting complaint was intermittent anorexia immediately post-partum, or picking at roughage while refusing grain, and low milk production (1.4 kg/d; first lactation total milk production was 73 kg). The animal had been treated with procaine penicillin G (Ethicillin, rogar/STB, London, Ontario) as she had a retained placenta. Three days post-calving she was pyrexic (40.0°C) and the producer elected to place her on intramuscular oxytetracycline hydrochloride (Liquamycin LP, rogar/STB, London, Ontario) as well. The cows appetite improved over the next four days, but the day prior to veterinary attention being sought she had became anorectic.

Upon examination the cow was quiet but alert, with a rectal temperature of 39°C, pulse rate of 70 beats/min and respiratory rate of 32 breaths/min. Auscultation of the thorax and abdomen were unremarkable except for a moderate muffling of heart sounds on both the left and right sides of the animal. On per rectal examination no abnormalities were detected. A sample of faeces was collected and was judged to be normal. A California Mastitis Test on the milk and evaluation of the urine for the presence of ketones were negative.

Initial Assessment and Plans

Given the non-specific signs observed, and the observation that a full sister to this cow had been diagnosed with dilated cardiomyopathy (DCM), this was considered to be a diagnostic rule-out. Abdominocentesis was performed at a site on the ventral midline 10 cm cranial to the udder. A slightly viscous, non-turbid, pale, straw-colored fluid was obtained and samples were submitted for cytology. Venous blood samples were collected for hematological and serum biochemical examination. Initial hematology revealed that the erythron and leukon were in the normal range. Serum concentrations of total bilirubin were moderately elevated (27 μmol/L; reference range:1.7-10.3 μmol/L). The peritoneal fluid had a specific gravity of 1.027 and a total protein content of 49 g/L.

The elevated total serum bilirubin observed in this cow indicated the possibility of hepatic disease,[3] biliary obstruction or intravascular haemolysis, however, it may also have been due to the anorexia. The specific gravity and total protein level in the peritoneal fluid was suggestive of moderate inflammation[4]. A more thorough evaluation of this fluid, including total erythrocyte and leukocyte counts and a differential would have aided in the further classification of the peritoneal fluid. The nature of the peritoneal fluid suggested that a localized peritonitis due to hepatic abscessation or traumatic reticuloperitonitis were possible diagnostic rule-outs. Lymphosarcoma was another rule-out considered. The cow did not exhibit distension and pulsation of the jugular veins or edema of the submandibular area, brisket and ventral abdomen typically seen in DCM.[5,6]

Secondary Data

Upon admission to the Veterinary Teaching Hospital, Ontario Veterinary College, four days later, the cow was quiet, alert and responsive, in moderately good body

condition (630 kg), pyrexic (40.3°C), with elevated pulse (96 beats/min) and respiratory (40 breaths/min) rates. The pulse rate dropped over the course of the physical exam to 72 beats/min. The mucous membranes were pink and the capillary refill time was approximately 2 seconds. On auscultation, moderately increased lung sounds were heard over the right ventral lung field. No jugular pulse was visible and no precordial impulse was palpable on the left side. Heart sounds were muffled when auscultated over the left thorax. No abnormalities were detected upon percussion of the thorax. The rumen was hypomotile (1-2 weak contractions/min) and little rumen fill was evident. The cow had a mild diarrhea and there were no abnormal findings per rectal examination. The uterus was judged to be well involuted and a follicle was present on the right ovary. The cow did ventroflex in response to a withers pinch and did not respond positively to sternal compression.

Secondary Assessment

Given the clinicopathological findings on the ascitic fluid, the pyrexia observed in this cow during the second examination was considered to be most likely due to a peritonitis. The initially elevated respiratory and heart rates may have been due to the pyrexia, peritonitis, and/or excitement. The elevated lung sounds may have indicated primary lung pathology that would also explain the elevated heart and respiratory rates and the pyrexia. These could also have been attributed to a thromboembolic showering of the lungs with bacteria and pyogenic debris from a hepatic abscess that communicated via the caudal vena cava. The normal heart rate and absence of jugular distension tended to rule-out a congestive heart failure. The muffled heart sounds may have been attributable to pleural or pericardial effusions, however, percussion results and cow-side tests for traumatic reticuloperitonitis were normal. The rumen hypomotility and lack of rumen fill were consistent with anorexia and pyrexia. Except for the ascites discovered on the initial examination of this cow, no localizing signs were present. The main diagnostic rule-outs remained traumatic reticuloperitonitis, hepatic abscessation, other chronic infections such as forestomach abscesses, Johne's disease, parasitism and lymphosarcoma.

Secondary Plans

Diagnostic plans included additional blood collection for a complete blood count and serum biochemical profile, including albumin and globulins, plasma fibrinogen and whole blood glutathione peroxidase (GSH-Px) levels. An additional abdominocentesis including evaluation of cellular elements was performed. Collection of urine and rumen fluid was also performed. Electrocardiographic and echocardiographic evaluation of the cow was planned.

Erythrogram parameters were normal except for a moderate degree of anisocytosis. A mild leukocytosis was present ($13.7x10^9$/L; normal 3.8-11.0x10^9/L), attributable to an increase in segmented neutrophils ($9.04x10^9$/L; normal 0.7-4.9x10^9/L). There was no left shift or presence of toxic neutrophils. The hematocrit was 0.24 L/L (normal 0.24-0.36 L/L) and total serum protein was 82 g/L (normal 14-80 g/L).

The mature neutrophilia was indicative of chronic inflammation. Chronic inflammation, in turn, can result in a decrease in erythropoeisis and thus explain the low-normal hematocrit observed.[1,2] The mild hyperproteinemia was attributable to a moderate hyperglobulinemia (61 g/L; normal 26-48 g/L). A concomitant hypoalbuminemia (20 g/L; normal 30-38 g/L) was present, and resulted in an albumin:globulin ratio of 0.3 (normal 0.6-1.2). An increase in gamma-globulin fraction (26 g/L; normal 5-18 g/L) was responsible for the elevated total globulin level in the blood. Most hypergammaglobulinemias are attributable to chronic immune stimulation due to antigenic persistence, such as in chronic parasitic, bacterial or viral infections. The hypoalbuminemia might be explained by an increased rate of removal of albumin from the blood, such as sequestration in the peritoneal cavity, rather than a reduced rate of synthesis by the liver, since the liver has a large reserve of synthetic capacity for albumin.[1,2] A normal urine specific gravity and absence of protein in the urine indicated that a protein-losing nephropathy was not present. Terminally, serum albumin concentrations may decrease. Blood levels of the acute phase protein fibrinogen and GSH-Px were normal. Evaluation of rumen fluid yielded no abnormal findings.

The serum biochemistry profile indicated liver involvement. Serum gamma-glutamyl transferase (GGT) was elevated (107 μ/L; normal 0-35 μ/L) indicating cholestasis, such as canalicular damage. Total (9 μmol/L; normal 0-2 μmol/L), conjugated (4 μmol/L; normal 0-1 μmol/L) and free (5 μmol/L; normal 0-2 μmol/L) bilirubin were also elevated indicating a degree of both hepatocellular damage and cholestasis. The elevated levels of conjugated bilirubin may partly be explained by the anorectic state of this animal. The conjugated:total bilirubin ratio was 0.44, close to the figure of 0.5 indicative of bile blockage or intrahepatic cholestasis in cattle[1].

Abdominocentesis on this cow yielded a fluid grossly similar to that previously described with the specific gravity being 1.033, total protein 53 g/L, and the number of leukocytes $4.40x10^9$/L. Upon microscopic examination there was a proteinaceous background with crescent formation, and a cell differential of 85% well-preserved neutrophils and 15% macrophages with a few mesothelial cells. A moderate number of erythrocytes were

present and the occasional platelet was observed. Erythrophagia was frequent and occasionally cytophagia was observed. No cytologic abnormalities were observed in the identified cells, and no bacteria were visible. The classification of the fluid would be one of a proteinaceous non-septic inflammatory effusion. Such effusions are typically seen in conditions like traumatic reticuloperitonitis and chronic peritonitis.[4]

No abnormalities were observed on an electrocardiographic and echocardiographic examination. The fractional shortening (FS) of the left ventricular internal diameter (LVID) was 0.33 ([LVID, diastole - LVID, systole]/LVID, diastole). The FS value provided is a means of three observations, however, removal of the lowest value (0.20) resulted in a mean FS of 0.40. The latter value is similar (0.41, sd 0.035) to that reported by Yamaga and Too[7] for 15 adult Holstein cows weighing an average of 589 kg. Given the results of the physical examination, the clinicopathological data, and the echocardiographic examination, the primary diagnostic rule-outs were: traumatic reticuloperitonitis, forestomach abscess, or hepatic abscessation.

Two days after presentation, a left paralumbar fossa exploratory laparotomy was performed under proximal paravertebral anaesthesia. Findings included large volumes of peritoneal fluid, numerous large fibrin clots, a left and slightly dorsal displacement of the abomasum, and the presence of approximately 3 small (2-3 cm diameter) abscesses in that portion of the omentum that could be externalized. Given the poor prognosis for return to production due to the severe diffuse peritonitis, it was elected to euthanize this cow.

Upon gross pathological examination, the hydration status, fat store, and muscle mass were judged to be normal. There was a large (30x15 cm), heavily encapsulated abscess in the dorsal aspect of the liver, the contents of which were viscus and white in character (Figure 1). A small suppurative tract (0.5 cm diameter) was found to have partially penetrated through the caudal vena cava at this point. The hepatic capsule was thickened and fibrotic, and the liver was tough. The hepatic vasculature appeared dilated in areas and there was a distinct lobular pattern. The abdominal cavity contained approximately 20 L of a muddy brown fluid, containing numerous large fibrin clots. The peritoneum was mildly hyperaemic and there were scattered 2-4 cm diameter white, raised friable plaques on the omentum. The caudal mediastinal lymph node was markedly hyperplastic and edematous, measuring approximately 15x5x7 cm. There were a few scattered fibrous adhesions of the visceral and parietal pleura. The morphologic diagnosis was one of chronic-active focal hepatic abscessation, with a moderate degree of hepatic fibrosis, vena caval phlebitis and an associated severe, subacute, fibrinous diffuse peritonitis. Additional histopathological findings included: Liver; marked congestion of sinusoids in the periacinar zones and vacuolation of hepatocytes in the periportal zones. Kidney; moderate proliferative glomerulopathy. Lung; mild pulmonary congestion and erythrocytes and proteinaceous material in scattered alveoli. Heart; mild chronic-active epicarditis. Gastrointestinal tract; moderate infiltrative eosinophilic and lymphocytic enteritis. *Fusobacterium necrophorum*-type rods were seen on a smear of the abscess contents. Given the presence of the suppurative connecting tract between the hepatic abscess and the caudal vena cava, it is likely that a periodic bacteremia/septicemia was responsible for the lesions observed in the different tissues.

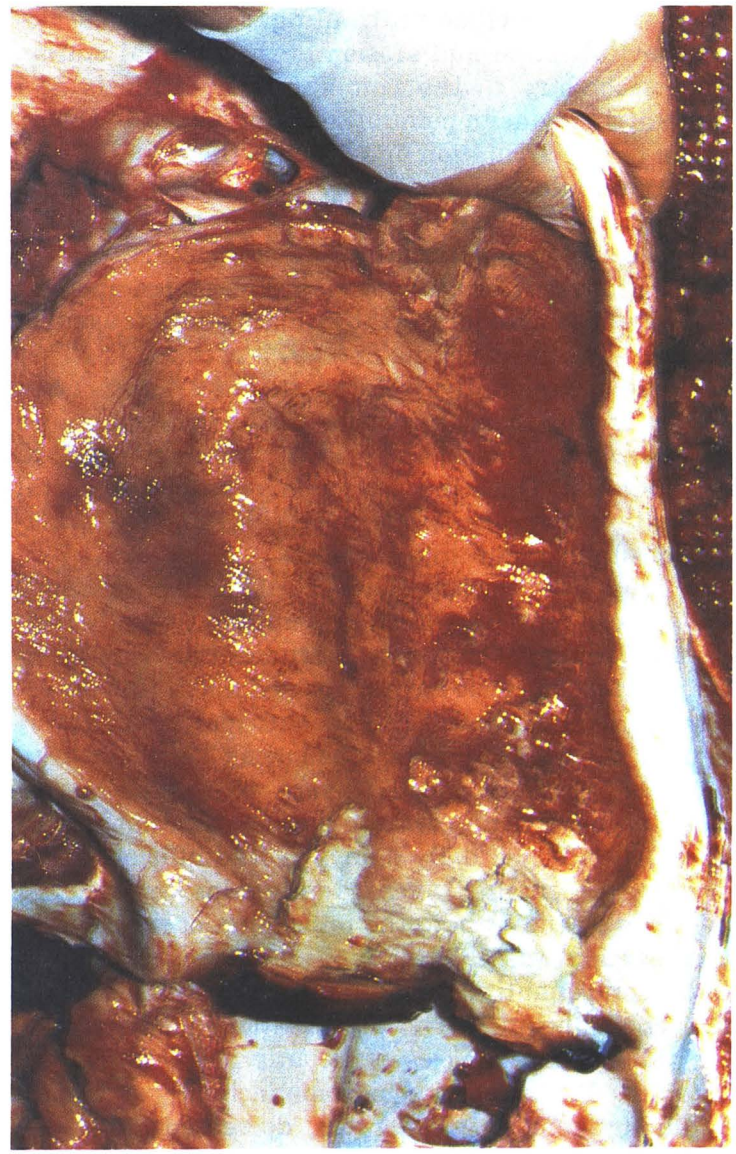

Figure 1. Heavily encapsulated abscess (30x15 cm) located in the dorsal aspect of the liver of a Holstein cow.

Evaluation

Ruminants of any age or sex can develop hepatic abscessation, however, this problem is primarily associated with feedlot cattle consuming rations high in rapidly fermentable carbohydrate.[1,2] This carbohydrate is rapidly fermented to volatile fatty acids causing a concomitant rapid reduction in rumen pH. Under these conditions the rumen microflora produce more lactic acid, further contributing to the acidic environment, thus permitting the growth of *Streptococcus bovis, Lactobacilli* and other gram-positive cocci, while inhibiting the growth of fiber degrading gram-negative bacteria.[4] The protozoal population of the rumen is also drastically reduced. The lack of effective fiber in these diets does not provide for adequate rumination, and the reduction in saliva production reduces the amount of buffers reaching the rumen, further contributing to the rumen acidosis. Devitalization and erosion of the ruminal epithelium secondary to the ruminal lactic acidosis and rumenitis provides a point of entry for bacteria to enter in the portal circulation and colonize the liver[1,2]. Traumatic reticuloperitonitis may also lead to hepatic abscessation through liver penetration by the foreign body, extension of peritonitis, or bacteremia.[2]

Fusobacterium necrophorum, a normal component of the rumen microflora, is the primary etiologic agent of hepatic abscesses in cattle in 80-97% of cases.[1,2,8] Other bacteria occasionally isolated include *Actinomyces pyogenes* and *Streptococcus, Staphylococcus,* and *Bacteroides* organisms alone or in combination with *F. necrophorum*. Once these organisms enter the portal circulation they colonize the liver, resulting in a formation of single or multiple abscesses.

Most hepatic abscesses in cattle are subclinical if the abscess remains walled off, and are typically incidental findings at necropsy.[1,2] Studies involving thousands of feedlot cattle have suggested that a 16% prevalence of liver abscesses can be anticipated,[9] however, figures as high as 78%[10] and as low as 3%[11] have been reported. Severely affected livers, containing one or more large active abscesses, have been associated with adversely affected daily gains,[10,12] feed efficiency and dressing percentage.[10] Average daily gains were reduced by 8% in a study where the prevalence of severe liver abscessation was 13% (48% of all abscessed livers).[10] Little or no quantitative information is available on the impact of subclinical liver abscessation in dairy cattle.

Most clinical cases of hepatic abscessation are manifested as a vague syndrome including such non-localizing signs as weight loss, decreased gains, decreased milk production, and periods of anorexia and pyrexia, and diarrhea or constipation[1,2]. Cows may be reluctant to move or exhibit pain upon palpation of the caudal margin of the thorax. Differential diagnoses include other causes of weight loss discussed previously. A number of sequelae can occur following liver abscessation and erosion of the abscess into the caudal vena cava: (a) sudden death due to a syndrome resembling anaphylactic shock associated with rupture of the abscess into the vena cava; (b) epistaxis and hemoptysis due to ruptured pulmonary aneurysms, hematomas or abscesses subsequent to embolism of septic material from a vena caval thrombus; (c) severe dyspnea, coughing and abnormal lungs sound following rupture of an abscess that is not immediately fatal.[1,2]

Clinicopathological findings include those described for the present case. During the acute phase of liver damage, plasma fibrinogen may be elevated (>6 g/L), along with elevated serum GGT, aspartate aminotransferase (AST) or sorbitol dehydrogenase (SDH)[2]. These may subside to normal levels upon abscess encapsulation. If obstruction of bile flow occurs, a rare occurrence, serum bilirubin parameters are increased. Ultrasound examination or exploratory celiotomy can identify hepatic abscesses in some cases, however, most cases are diagnosed at necropsy.

Once the presence of a hepatic abscess has been ascertained or suggested, the animal is more economically salvaged by slaughter. If antibiotic treatment is attempted, long-term parenteral therapy with penicillin or oxytetracycline has been suggested.[2] Control of liver abscesses is most readily accomplished by preventive measures. In feedlot cattle provision of starter rations containing 50-60% roughage are recommended, as well as a gradual change to higher concentrate rations. Antibiotics such as chlortetracycline, oxytetracycline and tylosin added to feedlot rations have been shown to reduce the prevalence of liver abscesses, presumably by reducing the population of pathogenic bacteria which escape from the rumen and embed in the liver.[11] The addition of such antibiotics to lactating dairy rations is prohibited, therefore, careful dietary management is required in the prevention of hepatic abscesses. Gradually adapting the peripartum cow to the lactation ration is an important consideration. The requirement of adequate fiber levels (19-21% acid detergent fiber on diet dry matter basis[13]) to maintain the fat test will maintain a rumen environment that should not predispose the animal to liver abscessation. Provision of the concentrate portion of the ration after dry roughage, or in small frequent meals will also attenuate the swings in rumen pH seen when high concentrate rations are fed. The feeding of rumen buffers, such as sodium bicarbonate, has also been used to prevent or ameliorate the low rumen pHs observed when diets high in rapidly fermentable carbohydrate are fed.[2]

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Student Clinical Reports

The AABP Board of Directors has approved a recommendation from the Forward Planning Committee to encourage students to write case reports for this journal and to award prizes.

The first prize ($200.00) is awarded to Lawrence W. Cahill, University of Geulph.

The second prize ($100.00) is awarded to Michael Coe, Kansas State University.

The third prize ($75.00) is awarded to Erin Troy, University of Wisconsin.

Gram-Negative Endotoxemia In Cattle: Coliform Mastitis And More.

Craig Bendickson, DVM, Technical Service Veterinarian, Sanofi Animal Health, Inc.

Information for producers and their veterinarians.

Gram-negative bacteria are the main cause of several performance-robbing diseases, including pneumonia, mastitis, and enteritis. Mastitis (inflammation of the cow's udder, usually caused by bacteria) is a costly problem faced by dairy producers across the United States. According to the National Mastitis Council, mastitis costs dairy producers more than $2 billion each year, an average of $181 for every milk cow in the U.S. Reduced milk production, discarded milk, cost of antibiotics, veterinary services, cost of replacement cows, decreased cull value of infected cows and additional labor all contribute to the economic loss.

Endotoxemia is a part of coliform mastitis. But coliform mastitis is far from the only disease complex associated with endotoxemia.

Coliform Mastitis, Endotoxemia

Coliform mastitis is a particularly devastating form of mastitis. Coliforms are gram-negative bacteria (*E. coli, Klebsiella, Enterobacter*) which may produce an acute, sometimes fatal form of mastitis. This sudden, severe coliform mastitis may have effects on the entire body due to poisons called endotoxins, which are released by the gram-negative bacteria as they reproduce and die during the course of the disease.

When these poisons or endotoxins reach the blood stream in significant levels, the result is endotoxemia. Endotoxemia is characterized initially by a high fever, which may subsequently drop to below normal body temperature. Drowsiness, loss of appetite, dehydration, poor circulation, shock and many times death are also signs of endotoxemia.

Other Causes of Endotoxemia.

Endotoxemia, which may affect cattle at any age, is a part of coliform mastitis. But coliform mastitis is far from the only disease complex associated with endotoxemia.

Other important gram-negative bacterial infections, including *Pasteurella* pneumonia, *E. coli* enteritis/scours, *Salmonella* enteritis and pneumonia, may all result in this severe endotoxemic syndrome.

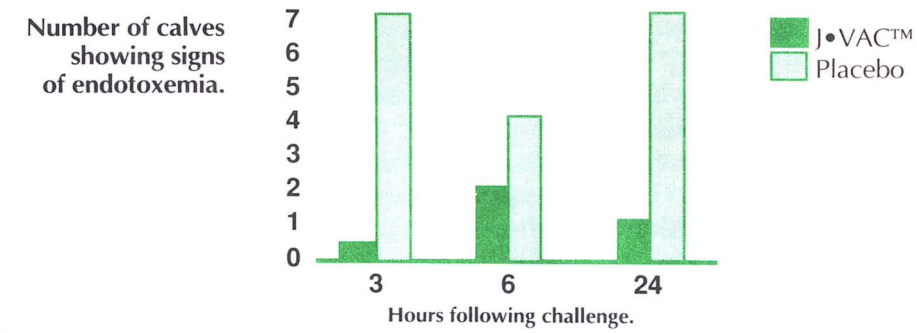
Although there are distinct differences among these gram-negative bacteria, they contain similar endotoxins that produce much the same result when they enter the animal's blood stream.

Fortunately, this similarity also allows for a common point of defense. Scientists at Sanofi Animal Health, Inc. and at various universities have worked to develop a technology which produces a broad defense against gram-negative bacteria and their resultant endotoxins. The benefit can be significant by reduction in losses due to gram-negative endotoxemia associated with coliform mastitis, pneumonia, and enteric diseases such as salmonellosis and *E. coli* scours.

Sanofi Animal Health's J•VAC™ is a result of this technology. J•VAC is an anti-endotoxin vaccine which utilizes the J5 mutant *E. coli* core antigen technology. Through the exposure of common core antigens, the J5 mutant *E. coli* allows the animal's immune system to develop resistance to the effects of the endotoxins. This resistance is seen in 1) the reduction of replication of gram-negative bacteria and 2) the blocking of the action of free and/or bound endotoxins in the body. J5 vaccine studies have shown a significant reduction in losses – and corresponding income benefits of $32 per cow – in dairy herds with a history of coliform mastitis and endotoxemia.*

Consult your veterinarian for more information about J•VAC *E. coli* vaccine.

J•VAC™ Endotoxin Challenge Study



Study involved: 400-600 lb. calves were immunized with two injections of J•VAC™ or two injections of a placebo. Each group contained 12 calves. The calves were challenged by subcutaneous injection of 8 µg/kg *Salmonella typhimurium* LPS (endotoxin) per kg of body weight. Clinical signs of endotoxemia included labored breathing and/or depression.

* Gonzalez, R. N., Mohammed, H.O., Cullor, J.S., Jasper, D.E., "Efficacy and Financial Benefits of Preventing Clinical Coliform Mastitis in Dairy Cows by a Mutant (J5) Escherichia Coli Vaccine," New York State College of Veterinary Medicine, Cornell University, and School of Veterinary Medicine, University of California Davis.

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